

Anti-staphylococcal bundle to reduce surgical site infections in orthopaedic and cardiac surgery

Feedback summary of discussion paper and next steps

March 2017

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Purpose

This paper provides the health sector with a summary of stakeholder feedback on the
use of an anti-staphylococcal bundle for orthopaedic and cardiac surgery, Health Quality
& Safety Commission (the Commission) responses to feedback, and provides an
overview of next steps.

Executive summary

- 2. The most commonly isolated pathogen and cause of surgical site infections (SSIs) in New Zealand and globally is *Staphylococcus aureus* (*S. aureus*).1'2 *S. aureus* accounts for about 30 percent of orthopaedic SSIs identified in DHB patients.3
- 3. At a Strategic Infection Prevention & Control Advisory Group (SIPCAG) meeting on 25 October 2016, the group considered the systematic review and meta-analysis undertaken by the Royal Australasian College of Surgeons (RACS) and the draft discussion paper on a proposed bundle and agreed there was enough evidence to support discussion with the sector.
- 4. Anti-staphylococcal bundles for elective surgical patients have been implemented internationally over the past two decades; however, preoperative screening methods and decolonisation agents vary greatly. Recent feedback from district health boards (DHBs) reveals that the current approaches to reducing the risk of staphylococcal SSIs range from no protocol to both preoperative screening and decolonisation protocols in cardiac and orthopaedic surgery.
- 5. Decolonisation is a strategy to reduce the patient's microbial load of *S. aureus* before their surgical procedure so their risk of infection is decreased. A recent study concluded that screened and subsequently treated patients were approximately 50 percent less likely to require revision due to prosthetic joint infection compared to those not screened and treated.4

¹ Saadatian-Elahi M, Teyssou R, Vanhems P. 2008. *Staphylococcus aureus*, the major pathogen in orthopaedic and cardiac surgical site infections: a literature review. *International Journal of Surgery* 6(3): 238–45.

² Cantlon CA, Stemper ME, Schwan WR, et al. 2006. Significant pathogens isolated from surgical site infections at a community hospital in the Midwest. *Am J Infect Control* 34(8): 526–9.

³ Discussion paper: Anti-staphylococcal bundle to reduce surgical site infections in orthopaedic and cardiac surgery. November 2016. URL: http://www.hqsc.govt.nz/assets/Infection-Prevention/Surgical-Site-Infection-Surveillance/SSIIP-discussion-paper-anti-staph-bundle-to-reduce-SSIs-Nov-2016.pdf (accessed 24 March 2017).

⁴ Malcolm TI, Robinson LD, Klika AK, et al. 2016. Predictors of *Staphylococcus aureus* Colonization and Results after Decolonization. *Interdisp Perspec on Infect Dis.* 8 pages.

- 6. The RACS systematic review and meta-analysis summarises the potential benefits of implementing a standardised bundle of anti-staphylococcal interventions to reduce orthopaedic and cardiac SSIs caused by staphylococci.5
- A discussion paper, including information about the proposed bundle and its estimated costs, was distributed to numerous stakeholders across New Zealand to seek their views.
- 8. This paper provides a summary of the feedback received, the Commission responses, and the recommended next steps which include:
 - results of discussion paper questions
 - general themes of the concerns raised with the Commission responses
 - anti-staphylococcal bundle protocol for consideration of implementation
 - timeline for scope and approach of bundle implementation.

Background

- 9. In June 2016 the Commission's SSII Programme contracted RACS to conduct a systematic review and meta-analysis. The systematic literature review and meta-analysis expanded on a previously published report (base reference),6 which covered literature between 1995 and 2011. RACS incorporated more recent studies with a main emphasis on skin and nasal decolonisation interventions that drive SSI reduction. A final report was created and attached as a supplemental document to the discussion paper distributed to health sector stakeholders. This information was also summarised in an article recently published in Australian & New Zealand Journal of Surgery, provided in Appendix 1.
- 10. The potential components of an anti-staphylococcal bundle include:
 - S. aureus preoperative screening
 - nasal decolonisation
 - skin decolonisation.

⁵ Systematic Review of the Surgical Site Infections in Cardiac and Orthopaedic Surgery. August 2016. URL: http://www.hqsc.govt.nz/assets/Infection-
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http://www.hqsc.govt.nz/assets/Infection-
http://www.hqsc.govt.nz/assets/Aureus_Aureus_Aug_2016_FINAL.pdf
<a href="Prevention-PR/S_aureus_Aureus_

⁶ Schweizer M, Perencevich E, McDanel J, et al. 2013. Effectiveness of a bundled intervention of decolonization and prophylaxis to decrease Gram positive surgical site infections after cardiac or orthopaedic surgery: systematic review and meta-analysis. *BMJ* 346: f2743 doi: 10.1136/bmj.f2743.

- 11. The Commission sought feedback on the following six aspects:7
 - potential benefit of introducing an anti-staphylococcal bundle in New Zealand
 - universal decolonisation vs. preoperative screening and decolonisation of patients colonised with S. aureus
 - povidone-iodine as first-choice nasal agent
 - nasal treatment administered twice the day before and once the morning of surgery
 - skin application administered twice the day before and once the morning of surgery
 - both skin and nasal components should be part of the bundle.
- 12. The review and feedback period occurred between 8 November and 16 December 2016. There were a total of 54 responses with 54 percent of them representing individuals only and 46 percent representing organisations including medical colleges. The responses represented feedback from both the public and private sector.
- 13. The proportion of SSIs caused by staphylococci among orthopaedic and cardiac patients from April 2014 to June 2016 varied between DHBs (the burden of staphylococcal SSI per DHB during this period is highlighted in Appendices 2 and 3). Staphylococci were recovered from 57 percent of SSIs; 12 percent in mixed growth and 45 percent as pure cultures. *S. aureus* and CNS were isolated in pure growth in 31 and 13 percent of SSIs respectively. The implementation of a standardised bundle across New Zealand is appropriate because 19 of the 20 DHBs have had *S. aureus* SSIs during the past two years.
- 14. Currently some DHBs have screening and/or decolonisation protocols. A survey was taken of all 20 DHBs in September 2016 that provided us with information of their current preoperative screening and decolonisation practices for cardiac and orthopaedic surgical patients. Six DHBs screen for MRSA and or MSSA preoperatively. Six DHBs have a nasal decolonisation protocol while nine DHBs have a skin decolonisation protocol. Six DHBs indicated they document compliance related to their decolonisation process. However, reliable compliance data is not collected currently. Specific DHB practice is represented in Appendix 4, page 28.

Feedback on discussion paper

- 15. A majority of the stakeholders who provided feedback to the discussion paper supported implementing an anti-staphylococcal bundle and agreed with the specific recommendations provided in the discussion paper.
- 16. The responses to the discussion paper questions are listed in Table 1.

⁷ Discussion paper: Anti-staphylococcal bundle to reduce surgical site infections in orthopaedic and cardiac surgery. November 2016. URL: http://www.hqsc.govt.nz/assets/Infection-Prevention/Surgical-Site-Infection-Surveillance/SSIIP-discussion-paper-anti-staph-bundle-to-reduce-SSIs-Nov-2016.pdf (accessed 24 March 2017).

Table 1: Results of discussion paper questions

Question	Yes	No	Support
Do you think there would be benefit in adding an anti- staphylococcal bundle to the existing interventions associated with the Surgical Site Infection Improvement (SSII) programme?	43	8	84%
Based on logistics and simplicity, we recommend universal decolonisation (decolonise all orthopaedic and cardiac surgical patients with topical nasal and skin agents). Do you agree?	37	14	73%
Based on potential resistance with mupirocin use, we recommend povidone-iodine for nasal decolonisation as our first choice. Mupirocin is considered an alternative agent. Do you agree?	43	7	86%
Based on logistics and simplicity, we recommend the chosen nasal preparation is administered twice the day before and once the morning of surgery. Do you agree?	41	4	91%
Based on logistics and simplicity, our first choice for skin decolonisation is chlorhexidine (wash or wipes) administered twice the day before and once the morning of surgery. Triclosan would be recommended as a second choice for chlorhexidine allergy. Do you agree?	40	8	83%
Based on the meta-analysis, we recommend that any bundle should consist of <i>both</i> nasal and skin components. Do you agree?	41	6	87%

17. Concerns from sector feedback were compiled by the Programme team into general themes with responses added to address the concerns, Table 2.

Table 2: Comments on 'anti-staph bundle' feedback

* Comments recorded reflect those made in reply to more than one question. Only included once to reduce repetition.

Comment/ concern	Point(s) made	Reply
Quality of ev	vidence	
Comment*	Expert opinion only. Data from observational studies not RCTs.	Agree. The RCTs showed a trend but was not statistically significant. Meta-analysis is however an accepted method of summarising data from several studies.
		Based on the GRADE framework,8 the use of an anti-staphylococcal bundle to reduce SSIs would be 'strong recommendation; moderate quality evidence'.
Question 1:	Benefit in adding bundle	
Comment	Doing some of this already.	Noted. Implementing a standardised bundle ensures every orthopaedic and cardiac surgical patient receives the same standard of care regardless of which DHB performs their procedure.
Comment	'Should we wait for more evidence or undertake within a trial format?' Also mentioned by others, eg. the Commission could consider a pilot program to test that the assumed benefits are realisable in the New Zealand setting.	The Programme is not set up to undertake formal research trials. Approximately 20 percent of DHBs have a bundle in place already. Historical data is already collected, so monitoring SSI rates for those who adopt a bundle on at least an 'intention to treat' basis. It is possible there will be a group of early adopter DHBs and their results could be summarised to record the outcome of bundle adoption.
Comment/ concern*	concerns about operationalising difficulty with ensuring logistics of access to treatment a limiting factor that could become	Noted. Considerable work would need to be undertaken to map the process for supplying information and treatment agents to patients before surgery. Logistics related to determining and documenting compliance of administrating treatment will also need to be developed. Funding implications also need to be addressed. These and other factors associated with

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⁸ Guyatt GH, Oxman AD, Vist GE, et al. 2008. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 336(7650): 924-6.

Comment/	Point(s) made	Reply
	problematic is the logistics of getting the product, povidone-iodine, to the patient	implementing the bundle will be worked through as part of the multi-disciplinary collaborative approach described later in this paper.
	may require reminders to patients	
	issues with compliance and adequacy of administration with outpatients	
	using scripts would not work as a lot of our patients would not be in the position to get the script filled due to cost, transport etc.	
Comment*	Patient education/information (multiple comments)	Noted. Co-design is needed to assist in developing patient materials. These may be verbal, written, visual, eg YouTube, etc. These need to include information /choice for skin preparation (wipe vs. soap). Allergy/potential reactions also needs to be addressed.
Concern*	Effects on skin flora, replacement with other pathogens	Short term bundle use (1–2 days) is not thought to cause long term changes in the skin flora. The concept is to reduce the likelihood of wound contamination with staphylococci at the time of surgery. Cessation after only a few doses, along with cessation of IV surgical prophylaxis, should not cause prolonged or adverse changes to patient flora. Use of chlorhexidine body washes, in conjunction with high rates of hand hygiene compliance, in the ICU setting has not been associated with a switch in colonisation with drug resistant pathogens. For this reason we would not expect the bundle to lead to 'replacement' bacterial pathogens.
Concern	Has been tried in the past. Doesn't work. Our biggest problem in any case is not	References to failed attempts of anti-staph bundle implementation in the past not provided by the responder but maybe

Comment/	Point(s) made	Reply
	with <i>S. aureus</i> but with coagulase negative staph. infecting prostheses. These bugs are everywhere on staff and patient also	individual trials included in the meta- analyses. Combining studies in meta- analysis is an accepted method for analysing the literature. More infections in the Programme are
	floating in convection currents in the air carried on shed human skin scales.	caused by pure growth cultures of <i>S. aureus</i> than coagulase-negative staphylococci (CNS) (31 percent vs. 13 percent respectively). The SSII programme team has summarised data for each DHB to see if there are any significant differences in species and the type of SSI (superficial/deep). Please refer to Appendices 2 and 3.
		CNS also reside in the nose, and while the data is not there as it is for <i>S. aureus</i> , most CNS SSIs are likely to be due to the patient's own flora. A bundle may also have a positive effect on CNS SSI as well but this has not been addressed in the literature. Because of the historical data in the New Zealand programme it would be possible to follow any change in SSI, due to <i>S. aureus</i> or CNS, in NZ with respect to bundle application.
		Strict adherence to infection prevention activities keeps the proportion of SSI caused by CNS at a low level. CNS SSI may be due to wound contamination from other sources, eg. skin squames in theatre, and so theatre clothing, air flow and traffic control are also important.
Question 2:	Universal decolonisation	
Comment	Again could it be in a trial format? Patient may want the choice of the screening option; could this be available on user pays basis?	A formal trial protocol is not logistically achievable at a national level. Laboratory provider contracts vary and would make patient choice/charging difficult logistically.
Concern	We have the concern with this blanket approach that we will not know new MRSA	Noted. If MRSA screening is applied based on patient risk history then that should continue so that MRSA can be detected

Comment/	Point(s) made	Reply	
	patients and they will not get the prophylaxis antibiotic treatment.	and surgical prophylaxis adapted accordingly, ie. the addition of vancomycin to cefazolin. The universal bundle protocol should not override current MRSA screening policies but it may provide additional cover in situations where MRSA screening is missed or the result is not actioned.	
Question 3: Povidone-iodine as first choice nasal agent			
Concern	 There is not enough evidence to consider Betadine as a nasal agent. Povidone-iodine needs to be checked that it is effective and works given the limited evidence. It is not well studied. 	Noted. While the data are limited, povidone- iodine was chosen as first choice because of concerns over current mupirocin resistance rates as well as the possibility of contributing to increased mupirocin resistance. For those who prefer mupirocin it is an alternative agent.	
Concern	Clear strategies need to be available for patients with reactions to povidone-iodine	Noted. Although true allergic reactions are rare (0.4-0.7 percent) and infrequently occur following application of povidone-iodine on intact skin, patient education materials will include the typical signs and symptoms of an allergic reaction and follow-up actions recommended. Studies suggest that there are fewer symptoms due to nasal povidone-iodine than nasal mupirocin use.	
Question 4:	Nasal application day before	and morning of surgery	
Question	What is the rationale behind three doses vs. two doses (to match the pre-op showering/cleansing) vs. five days to match decolonisation protocols? The evidence is all based on no less than five days' use so why the suggestion	Some studies have used < 5 days. The optimal number of days has not been identified. The 'day before/morning of' surgery (three doses) was chosen to maximise compliance (longer dosing regimens are thought to be less likely to have full compliance) and benefit (three doses of CHX produces a residual reduction in skin flora).	
	of three days only? Will this still be effective? Some concern regarding	In the end for those DHBs that feel a longer duration is justifiable, they can choose that.	

Comment/	Point(s) made	Reply
	adherence – possibility of getting at least some treatment used if suggested being for the week before?	
Question 5:	Chlorhexidine (CHX) as first	choice for skin agent
Question/ concerns	 Is use of Triclosan still an acceptable alternative? Are there any other alternatives? I believe Triclosan should not be used as a decoloniser due to questionable efficacy. We feel that Triclosan should NOT be used and if allergic to chlorhexidine, soap and water would be second line therapy. Some concern about the suggested use of Triclosan as a second choice due to the information out there about Triclosan being harmful. 	Noted. Respondents did not provide references on Triclosan issues. However United States FDA issued a final rule in September 2016 that states 'companies will no longer be able to market over-the-counter antibacterial washes containing Triclosan (among other specific active ingredients) because manufacturers did not demonstrate that the ingredients are both safe for long-term daily use and more effective than plain soap and water in preventing illness and the spread of certain infections.' Note that this rule is related to long-term use of Triclosan to prevent infections (our protocol is short-term usage of three applications). The programme team is currently undertaking a literature review to obtain data on triclosan's impact on skin flora numbers. If there is insufficient information, simple soap and water would be the alternative option if there is a chlorhexidine allergy.
Question 6:	Bundle to have both compor	nents
Concern	I don't believe the meta- analysis answers this question, or for that matter, the original question of whether any of this is beneficial.	View noted. Meta-analysis reported on the bundle components and both components were used in almost all studies to reduce SSIs.
	As mentioned earlier, I am not convinced that the de-colonising of skin flora is the safest option. It should consist of neither. Any bundle should have the skin	

Comment/	Point(s) made	Reply
	component but not every patient should receive a nasal agent.	
Cost		
Comment	Unless paid for by the Ministry of Health – I would not support doing; this is expensive	Cost would be a matter for adopting DHBs to cover. Cost-benefit analysis predicts that if a bundle has only a modest benefit, it would generate savings.

Recommended bundle

18. Taking into account that some DHBs already have an anti-staphylococcal bundle in place along with the strong sector support for use of an anti-staphylococcal bundle, two options for the bundle were considered and endorsed by SIPCAG, Table 3.

Table 3: Bundle recommendations for both cardiac and orthopaedic elective procedures

Recommended bundle (two options)			
Option	Nasal decolonisation	Skin decolonisation	Compliance documentation
1. Universal Decolonisation: no MRSA/MSSA pre-surgical screening	All elective orthopaedic and cardiac surgical patients Recommended agent: Povidone-iodine Alternative agent: Mupirocin Regimen: twice day before	All elective orthopaedic and cardiac surgical patients Recommended agent: Chlorhexidine Alternative agents: Triclosan or soap and water	Audit and document application of both nasal and skin decolonisation agents by patient
	and morning of surgery	Regimen: twice day before and morning of surgery	
2. Targeted Decolonisation: MRSA and MSSA pre-surgical screening of elective orthopaedic and cardiac surgical patients	MRSA and/or MSSA carriers only Recommended agent: Povidone-iodine Alternative agent: Mupirocin Regimen: twice day before and morning of surgery	MRSA and/or MSSA carriers only Recommended agent: Chlorhexidine Alternative agents: Triclosan or soap and water Regimen: twice day before and morning of surgery	Audit and document application of both nasal and skin decolonisation agents by patient

19. The majority of DHBs that currently decolonise their orthopaedic and cardiac patients do pre-surgical screening for MRSA colonisation and then treat colonised patients only. The targeted decolonisation approach would need to include pre-surgical screening for both MRSA and MSSA due to the high number of MSSA SSI cases. A change in the screening approach would be required for DHBs that currently have an anti-MRSA bundle only. For those DHBs that prefer not to screen their patients for MRSA and MSSA, a universal decolonisation option is available which is logistically simpler and more cost-effective.

Bundle implementation

20. There are different models for implementing a standardised intervention in DHBs utilising quality improvement methodologies. These range from an intensive and formal collaborative approach, to a less intensive phased approach over a longer timeframe.

There are advantages and disadvantages with different approaches, and different cost and resourcing implications.

- 21. In developing a standardised national bundle and process, it would be beneficial to draw on the experience and lessons learned from those DHBs who already have elements of an anti-staphylococcal bundle in place.
- 22. The Commission intends to support a small number of DHBs to take part in a formal collaborative process to activate this bundle or adapt their current bundle. A collaborative approach is when a group of organisations or individuals come together in a structured approach to learn and work together towards a common aim. This consists of action periods where teams work in their own DHBs to test and refine small changes, and then come together at scheduled whole group meetings where ideas and learning is shared. The collaborative uses structured quality improvement methodologies to test small changes.
- 23. For the anti-staph collaborative this will involve participants from the DHBs identifying existing and new components of an anti-staph bundle which will be tested, adapted and adopted in their own DHB. These findings will ultimately inform a national standard of core components for an anti-staph bundle, with the ability for some localisation.
- 24. Since orthopaedic and cardiac clinical pathways vary, it will be important to develop the processes separately but utilise similar protocols where possible for consistency and ease of rollout. Work to adopt the bundle may be able to be integrated with learnings from the Ministry of Health's Enhanced Recovery After Surgery (ERAS) programme, which focuses on improving the patient journey for joint arthroplasty procedures.
- 25. Patient education will be a key step for success of the proposed bundle. Incorporating co-design methodology will therefore be part of the implementation process.
- 26. Some form of compliance checking will be necessary to verify that the protocol and patient pathway are working, both during the collaborative and once the bundle is implemented. Through the collection of data, DHBs will be able to identify areas for improvement that are supported by structured quality improvement activities. Once the practice is embedded then the process of collecting compliance data will be assessed and may no longer be required.

Next steps

Milestone	Approximate deadline
Design of collaborative approach, informed by visits to DHBs who already have a form of anti-staphylococcal bundle	28 April 2017
Request for participation of DHBs in anti-staph collaborative, starting early in the new financial year	12 May 2017
Confirmation of DHBs participating in anti-staph collaborative	30 June 2017

Appendix 1: Systematic review of a patient care bundle in reducing staphylococcal infections in cardiac and orthopaedic surgery

REVIEW ARTICLE



Systematic review of a patient care bundle in reducing staphylococcal infections in cardiac and orthopaedic surgery

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Key words

meta-analysis, patient care bundle, Staphylococcus aureus, surgical site infection, systematic review.

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Accepted for publication 17 November 2016.

doi: 10.1111/ans.13879

Abstract

Surgical site infections (SSIs) are serious adverse events hindering surgical patients' recovery. In Australia and New Zealand, SSIs are a huge burden to patients and healthcare systems. A bundled approach, including pre-theatre nasal and/or skin decolonization has been used to reduce the risk of staphylococcal infection. The aim of this review is to assess the effectiveness of the bundle in preventing SSIs for cardiac and orthopaedic surgeries. The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. Published literature was searched in PubMed, Embase and Cochrane Library of Svstematic reviews. Identified articles were selected and extracted based on a priori defined Population-Intervention-Comparator-Outcome and eligibility criteria. Data of randomized controlled trials (RCTs) and comparative observational studies were synthesized by meta-analyses. Quality appraisal tools were used to assess the evidence quality. The review included six RCTs and 19 observational studies. The bundled treatment regimens varied substantially across all studies. RCTs showed a trend of Staphylococcus aureus SSIs reduction due to the bundle (relative risk = 0.59, 95% confidence interval (CI) = 0.33, 1.06) with moderate heterogeneity. Observational studies showed statistically significant reduction in all-cause and S. aureus SSIs. with 51% (95% CI = 0.41, 0.59) and 47% (95% CI = 0.35, 0.65), respectively. No publication biases were detected. SSIs in major cardiac and orthopaedic surgeries can be effectively reduced by approximately 50% with a pre-theatre patient care bundle approach.

Introduction

Surgical site infections (SSIs) are the second most common cause of nosocomial infection.1 SSIs are associated with a prolonged hospital stay and increased re-hospitalization and mortality rates, as well as additional healthcare costs. In the Australian and New Zealand healthcare systems, between 2 and 13% of hospitalized patients develop a healthcare-associated infection, of which 20% are SSIs.^{2,3} In Australia, healthcare-associated infection counts for 180 000 patients and 2 million bed days each year. The costs associated with these incidents are significant. In 2003, the cost of healthcare-associated infections to the New Zealand healthcare system was estimated at NZ\$85.26 million,4 and the costs associated with only 126 SSIs in one Australian state were recently reported to be in excess of AU\$5 million.⁵ Infections in surgical sites occur in 1-4% of cardiac surgery patients and are associated with poor outcomes and increased mortality.6 SSIs following total joint replacement procedures are also uncommon (1-3%) but can also have devastating consequences. As infection preventions are relatively

inexpensive, costing approximately \$20 for each patient, with the avoidance of only a small number of SSIs the intervention will likely be cost-effective.

The most commonly isolated pathogen in SSIs is *Staphylococcus aureus*, usually arising from the patients' own bacterial flora (from skin, mucous membranes and the gastrointestinal tract). Reducing *S. aureus* SSIs is a target of current clinical practice. Standard practice includes antibiotic prophylaxis with β-lactam or alternative agent (e.g. cefazolin, clindamycin or vancomycin), provided as a single dose administered at the correct time before preceding the operation. Some hospitals also use an anti-staphylococcal pre-theatre bundle. The bundle consists of nasal and/or skin decolonization where topical applications of ointment such as mupirocin are used with or without antibacterial body washes or wipes, usually chlorhexidine, before admission to theatre. ^{1,8} Although the effectiveness of this bundled approach has been tested in a number of trials and a systematic review, ¹ published results have been inconsistent and the overall impact of these measures is still unclear.

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In this review, we define 'the patient care bundle' to be pretheatre nasal and/or skin decolonization, in addition to standard care. The aim of this systematic review is to expand the evidence base of an earlier systematic review,¹ to assess the effectiveness of bundled prophylaxis in preventing SSI with Gram-positive bacteria among patients undergoing cardiac or total joint replacement procedures. The results will inform whether the bundled intervention should be adopted as part of a standard SSI prevention protocol.

Methods

The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.9 Three bibliographic databases including PubMed, Embase and the Cochrane Library of Systematic Reviews were searched from inception to June 2016. Based on a priori defined Population-Intervention-Comparator-Outcome, a comprehensive search strategy (provided in Table S1) was applied to these databases. Studies that reported patients of all ages (including paediatric patients) receiving elective cardiac (with sternotomy) or orthopaedic surgeries (arthroplasty) were included. The intervention was a patient care bundle, defined as the pre-theatre use of nasal and/or skin decolonization. The comparator was placebo or standard care, however defined. The primary outcome was SSI whether reported as SSI (all-cause), infections caused by S. aureus, methicillin-resistant S. aureus (MRSA) or methicillin-sensitive S. aureus (MSSA). Subgroups were reported separately where possible.

Study inclusion and exclusion criteria were applied during study selection. Comparative studies including randomized controlled trials (RCTs) and cohort studies were included. Animal studies or articles published in languages other than English were excluded. All identified reference citations were reviewed by title and abstract by one researcher (NM) and checked by another (DF). Excluded studies were noted with reasons. Included studies underwent full-text review. Final inclusions were confirmed through discussion with all authors.

Using a standardized extraction template designed *a priori*; one reviewer (NM) undertook data extraction. A second reviewer (AC or DT) checked data extractions. Discrepancies were resolved through discussion. Extracted information included baseline characteristics, pre-surgical bacteria screening, timing, duration, dosage and administration routes of any intervention. Descriptive statistics were extracted or calculated for all safety and effectiveness outcomes in individual studies.

Included RCTs were assessed using the Cochrane Risk of Bias tool. ¹⁰ The Downs and Black scoring system was used to assess the quality of comparative cohort studies. ¹¹ Quality appraisal was undertaken by one reviewer (NM) and checked by a second (DT or AC or DF), with disagreements were resolved through discussion. Results of quality assessments were narratively summarized.

The outcome of all-cause SSI and infections caused by $S.\ aureus$, MRSA and MSSA bacteria were meta-analysed. A random effect model on relative risks (RRs) were engaged due to the diversity in treatment regimens. To describe heterogeneity prediction intervals and f^2 values were calculated. Forest plots were generated to illustrate the meta-analyses results. R 3.3.1 and the package 'metafor' were utilized to conduct all meta-analyses. ¹²

Results

The literature search identified 7178 published articles across all databases. The PRISMA flow chart illustrates study selection (provided in Fig. S1).

Randomized controlled trials

Six RCTs, comprising 4213 patients, assessed the bundled intervention for SSI prevention.^{13–18} Five of the RCTs contributed data to meta-analyses. The remaining RCT was a comparison of different bundles hence was reported separately.¹⁸ Detail of treatment bundles are provided in Table 1. Treatments varied across studies, by choice of antibiotic and dose. All patients were adults. Two of the RCTs.^{15,16} included cardiac surgery patients, and three included orthopaedic surgery patients. ^{14,15,17} All surgeries were assumed to be elective procedures, although two RCTs.^{13,16} did not report this information. Three RCTs.^{13,14,16} used screening results to determine patient eligibility and only included *S. aureus* positive patients. The length of followup ranged from 4 weeks to 12 months. The overall quality of the RCTs was from medium to high as assessed by the Cochrane Risk of Bias Tool.¹⁰ Three studies were not blinded for patients and did not have all the data reported. ^{14,15,18} Quality assessment of individual RCTs are provided in the Supporting Information.

Infections (Figs S2,S3) were as defined by the National Healthcare Safety Network Centre for Disease Control and Prevention in four RCTs. $^{13-15.18}$ Results of meta-analyses on *S. aureus* SSIs were based on data from five RCTs, with data for cardiac and orthopaedic surgeries available from Bode *et al.* 13 (Fig. 1). The overall result showed a trend of 41% improvement (RR = 0.59, 95% CI = (0.33, 1.06)) in avoiding *S. aureus* SSIs when using an anti-staphylococcal pretheatre bundle compared to placebo. However, the bundle was not statistically better than placebo, and these analyses showed statistical heterogeneity (prediction interval = (0.22, 1.59), $I^2 = 32.72\%$).

Observational studies

Nineteen observational studies, comprising 128 632 patients, were included. All studies contributed to the meta-analysis. 19-36 Nine of the eligible studies 19,22,24,25,27-30,35 included cardiac patients and nine^{20,21,23,26,31–33,36,37} included orthopaedic patients; the remaining studies included both types of patients. Two cardiac studies were on paediatric populations 19,25 and the remaining were all adults. Decolonization protocols for observational studies were more varied than those in RCTs (Table 1). Mupirocin (2% ointment) was used under different regimens by 18 studies, 19,20,22-37 and povidone-iodine was used in two studies as the nasal decolonization agent. 21,33 Chlorhexidine was used for skin decolonization in patients in the form of soaps for showering 19,20,26-29,34,35,37 or wipes for skin cleansing.21 Mouthwash using chlorhexidine was applied to patients in one study. 21 All observational studies reported the use of surgical antibiotic prophylaxis, with various regimens. The quality of the included observational studies was assessed by The Downs and Black scoring system. 11 The overall level of bias was from medium to high. The quality of reporting was medium, given 15 out of 19 studies involved historical controls with no clear specifications of what controlled measures were undertaken. All studies were excellent regarding external validity but internal

Table 1 Protocols of treatment bundles for all studies

Study		Nasal decolonization	Skin decolonization		
Study types	Agent	Application protocol	Agent	Application protocol	Additional antiseptic measures
RCTs Bode <i>et al.</i> ¹³ RCT	(Intervention) Mupirocin (2%)	(Intervention) Before surgery: twice a	(Intervention) Chlorhexidine soap (40 mg/mL)	(Intervention) Before surgery: once a day for	
	(Comparator) Placebo	day tor 5 days (Comparator) Placebo	snower (Comparator) Placebo	5 days (Comparator) Placebo	
Kalmeijer <i>et al.</i> ¹⁷ RCT	(Intervention) Mupirocin (2.15%)	(Intervention) Before surgery: twice	(Intervention) No skin decolonization	(Intervention) No skin decolonization	
	(Comparator) Placebo	a day for 1 day (Comparator) Placebo			
Konvalinka <i>et al.</i> ¹⁶ RCT	(Intervention) Mupirocin (2%)	(Intervention) Before surgery: twice a	(All patients) Chlorhexidine soap (2%) and	(All patients) Before surgery: 12 h on the day	
	(Comparator) Placebo	(Comparator)	isopropyl alcohol (4%) before knife-to-skin	A looking to	
Phillips <i>et al.</i> ¹⁸ RCT	(Intervention) Mupirocin (2%)	(Intervention) Before surgery: 5 days prior	(All patients) Chlorhexidine (2%) whole	(All patients) On the day of surgery	
	(Comparator) Povidone-iodine (5%)	to surgeny (Comparator) (Comparator) (Comparator) (Comparator)	body wipe		
Segers <i>et al</i> , ¹⁵ RCT	(Intervention) Chlorhexidine (0.12%) 10 mL (Comparator)	white 2 for surgery (Intervention) Before surgery: four times a day up to the day of surgery (Comparator)	(All patients) Chlorhexidine soap (40 mg/mL) shower	(All patients) Before surgery: 1 day	(All patients) Oral rinse with CHG (0.12%) 30 s four times a day Hair removal with clippers
Sousa <i>et al.</i> ¹⁴ RCT	Placebo (Intervention) Mupirocin (2%)	Placebo (Intervention) Before surgery: twice a day, 5 days before surgery	(Intervention) Chlorhexidine soap	(Intervention) Before surgery: 5 days	
Observational studies	(Comparator) No decolonization	(Comparator) No decolonization			
Adler <i>et al.</i> ¹⁹ Observational study	(Intervention) Mupirocin	(Intervention) Before surgery: twice a day for 5 days	(Intervention) Chlorhexidine gluconate (CHG) shower; 2% CHG/70% isopropyl alcohol skin prenafration	(Intervention) Before surgery: once a day for 2 days, skin preparation before knife-to-skin	
Baratz et al. ²⁰ Observational study	(Intervention) Mupirocin (2%)	(Intervention) Before surgery: twice a day	(Intervention) Chlorhexidine (4%) soap	(Intervention) Before surgery: daily for 5 days	
Bebko <i>et al.</i> ²¹ Observational study	(Intervention) Povidone-iodine (5%)	(Intervention) On the day of surgery in the morning	(Intervention) Chlorhexidine (2%) soap	(Intervention) Before surgery: once the night before the day of surgery	(Intervention) Oral rinse with chlorhexidine (0.12%) once the night before
Cimochowski <i>et al.</i> ²² Observational study	(Intervention) Mupirocin	(Intervention) Before surgery: twice on the night before and the morning	(Intervention) No skin decolonization	(Intervention) No skin decolonization	Á lagaine
Gernaat-van der Sluis et al. ²³ Observational study	(Intervention) Mupirocin	After surgery: continued for 5 days (Intervention) Before surgery: twice on the day before	(Intervention) No skin decolonization	(Intervention) No skin decolonization	

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Study Study types	Agent	Nasal decolonization Application protocol	Skin der Agent	Skin decolonization Application protocol	Additional antiseptic measures
Hadley et al. ³⁷ Observational study Jog et al. ²⁴ Observational study	(Intervention) Mupirocin (2%) (Intervention) Mupirocin (2%)	On the day of surgery: once in the morning intervention? Before surgery: for 5 days (frequency unknown) (Intervention) (Intervention) Before surgery: three times daily Continued after surgery until culture returns negative for MRSA.	(Intervention) Chlorhexidine (2%) soap (Intervention) Triclosan (2%)	(Intervention) Before surgery: for 5 day (frequency unknown) (intervention) Before surgery: three times daily Continued after surgery until culture returns negative for MRSA	
Katayanagi ²⁸ Observational study Kim <i>et al.</i> ²⁶ Observational study Kluytmans <i>et al.</i> ²⁷ Observational study Kohler <i>et al.</i> ²⁸	(Intervention) Mupirocin (Intervention) Mupirocin (2%) (Intervention) Mupirocin (Intervention) Mupirocin	(Intervention) On the day of surgery: immediately before and last for 2 days after surgery (Intervention) Before surgery: twice a day for 5 days (Intervention) One day before surgery and last for 5 days until discharge (Intervention) Before surgery: twice a day for minimum 5 days	(Intervention) No skin decolonization (Intervention) Chlorhexidine (2%) soap (All patients) Chlorhexidine or povidone- iodine soap (Intervention) Chlorhexidine (4%) soap	(Intervention) No skin decolonization (Intervention) Before surgery: once daily for 5 day (All patients) Detail not provided (Intervention) Before surgery: once a day for minimum 4 days	(Intervention) Octenidine hydrochloride impregnated washing gloves were used instead for bedridden patients
Marcrell et al. " Observational study Nicholson and Huesman" and Pulesman" and Price et al. " Observational study Rao et al. " Observational study Rao et al. " Observational study Sankar et al. " Observational study Schweizer et al." Observational study Schweizer et al."	(Intervention) Mupirocin (Intervention) Mupirocin (Intervention) Mupirocin (2%) (Intervention) Mupirocin (Intervention) Mupirocin (Intervention) Mupirocin or povidone-iodine (Intervention) Mupirocin	Intervention) Before surgery; 3 days (Intervention) Before surgery; twice a day until Before surgery; twice a day until the culture result is available (Intervention) Before surgery; no less than 6 doses (Intervention) Before surgery; twice a day for 5 days (Intervention) Before surgery; twice a day for futurs negative for MRSA (Intervention) Before surgery; twice a day for minimum 5 days	(Intervention) Chlorhexidine showering (Intervention) No skin decolonization (Intervention) No skin decolonization (Intervention) Chlorhexidine soap (Intervention) Agent unknown (Intervention)	(Intervention) Before surgery: 3 days (Intervention) No skin decolonization (Intervention) No skin decolonization (Intervention) Before surgery: daily for 5 days including day of surgery (Intervention) One week prior to hospital admission (Intervention) Before surgery: one daily for 5 days of including day of surgery (Intervention) Before surgery: one daily for 5 day of surgery 5 day of surgery	
Walsh et al. ³⁵ Observational study Wilcox et al. ³⁶ Observational study	(Intervention) Mupirocin (Intervention) Mupirocin	Walsh et al. ³⁵ (Intervention) (Intervention) Observational study Mupirocin (or 5 days until discharge for 5 days until discharge for 5 days until discharge (exclude emergency cases) Wilcox et al. ³⁸ (Intervention) (Intervention) Observational study Mupirocin Before surgery: once on the day before surgery: continue for 4 days	(Intervention) No skin decolonization (Intervention) Triclosan (2%)	(Intervention) No skin decolonization (Intervention) Before surgery: the day or night before	

Fig. 1. Meta-analysis of randomized controlled trials for *Staphylococcus aureus* surgical site infections.

	Bu	ndle	Comp	parator						
Author(s) and Year (N = 5)	SSI	Total	SSI	Total	Population					Relative Risk [95% CI]
Cardiac Surgery (n = 3)										
Bode et al. 2010	3	218	15	171	s.aureus	•	-	→		0.16 [0.05 , 0.53]
Segar et al. 2006	23	485	29	469	nos			-		0.77 [0.45 , 1.31]
Konvalinka et al. 2006	5	130	4	127	s.aureus		-	•		1.22 [0.34 , 4.44]
RE Model for Subgroup							-	\rightarrow	-	0.55 [0.18 , 1.66]
Orthopaedic Surgery (n = 3)										
Bode et al. 2010	1	83	3	79	s.aureus	-				0.32 [0.03 , 2.99]
Kalmeijer et al. 2002	5	315	8	299	nos		-	•	→	0.59 [0.20 , 1.79]
Sousa et al. 2016	2	89	3	139	s.aureus		-	-	200	- 1.04 [0.18 , 6.11]
RE Model for Subgroup								+		0.62 [0.26 , 1.47]
Random effect model								-	-0	0.59 [0.33 , 1.06]
I squred = 32.72%; Prediction Interv	al = (0.22	, 1.59)				-	Favours Bundle	_	Favours	comparators ->
						0.05	0.25	1.00	2.72	7.03
							Relat	ive Ris		

validity was poor. Expectedly, all of the included observational studies rated low regarding confounding biases, due to the absence of randomization or blinding, or the lack of confounding adjustment. Sample size of the observational studies were much larger than RCTs, with over half the studies reporting a power calculation (see Table S2 for the detailed quality assessment results).

SSIs were reported in all the included studies. The National Healthcare Safety Network definition of SSIs was adopted by 14 studies, $^{20-23,25-28,30,31,34-37}$ All-cause SSIs, *S. aureus* SSIs, SSIs due to MRSA and MSSA were reported by the included observational studies. The meta-analysis of all 19 observational studies found a significant decrease in risk of all-cause SSIs for the bundled treatment compared with its comparator (RR = 0.49, 95% CI = (0.41, 0.59), $\vec{l}^2 = 46.86\%$) (Fig. 2). Results of cardiac and orthopaedic surgical subgroups were similar to the overall results (RR = 0.50 and 0.49, respectively). Ten studies contributed to the meta-analysis of *S. aureus* SSIs (Fig. 3). Compared to all-cause SSIs, the benefit of a bundle was similar to *S. aureus* SSIs with less heterogeneity (RR = 0.47, 95% CI = (0.35, 0.65), $\vec{l}^2 = 11.52\%$). The bundled treatment was more effective to prevent *S. aureus* SSIs in cardiac surgery with a risk reduction of 62% (RR = 0.38, 95% CI (0.22, 0.67)).

Sensitivity analyses and publication bias

Sensitivity analyses showed that there were no influential studies across all analyses. Accumulative meta-analyses performed across study by years of publication showed no trends or patterns. Funnel plots to detect publication biases were visibly symmetrical (data not shown) indicating that there was no substantial publication bias.

Discussion

Surgical site infection can be a serious complication after surgery that affects patient well-being, prolongs hospital stay, increases surgical mortality and morbidity, and imposes huge financial burden on health systems. 38-40 While SSIs remain difficult to eradicate, studies continue to tackle the issue. The components of the bundles are diverse, with each study having a slightly different protocol. Among the systematic reviews identified by this study, three studies had inconclusive results with regard to the effectiveness of antibiotics or nasal decolonization in reducing SSIs. 38.41.42 Using published data; we found that the patient care bundle was significantly more effective than standard care

for cardiac or orthopaedic surgeries in observational studies, especially for *S. aureus*-related infections. In contrast, the patient care bundle in RCTs showed a protective trend for *S. aureus* SSIs without achieving statistical significance. The varied outcome between RCTs and observational studies likely reflects a complex yet important insight of the application of the bundled intervention in clinical practice, which is reflected in the observational data but less so in the bounds of a formally implemented clinical trial.

For the purpose of this review, we defined 'a bundled treatment' to be the addition of pre-theatre nasal and/or skin decolonization, to standard care (including, e.g. the use of surgical antibiotic prophylaxis). However, this definition of 'bundle' is not universally adopted. One of six systematic reviews¹ used the term 'bundle' to compare with standard care; however, neither 'bundle' nor 'standard care' was clearly specified. As a generic term, 'Bundled intervention', has been utilized by studies external to this review, although generally with different meanings across different clinical settings. 43.44

In contrast to observational studies, the results from RCTs did not achieve statistical significance for the patient care bundle. Three of the included RCTs that assessed nasal decolonization had no reduction in SSI rate. ^{14,16,17} This variation between RCTs and observational studies was also observed in previous systematic reviews. ^{1,8,41} The rigour in conducting RCTs would require consistent administration of both nasal decolonization and surgical antibiotic prophylaxis.

Antibiotic prophylaxis helps prevent SSIs when the correct agent is given at the right dose and at the correct time. Since all included studies used surgical antibiotic prophylaxis in both arms, the effect of SSI reduction may be attributable to both the bundle and the use of antibiotics. In contrast, we observed that the majority of the observational studies reported a treatment standardization process, which included optimized antibiotic regimens 19,22,23,35 and improved compliance in nasal decolonization. 18,43,45 While the observational studies demonstrated greater effectiveness, they are more vulnerable to bias, or confounding factors, although they are more likely to reflect real-life clinical practice.

Nasal carriage of *S. aureus* is a well-established risk factor for SSIs after major surgery. ⁴¹ Many studies in this review conducted presurgical *S. aureus* screening to determine the carrier status of the patients. Treatment plans were then customized according to the screening results. Although the impact of *S. aureus* screening was not

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Author(s) and Year (N = 20) Orthopaedic Surger Hadley et al. 2010 elative Risk [95% CI] Total 414 0.88 [0.36 , 2.17 0.73 [0.44 , 1.22 21 1644 6 33 Baratz et al. 2015 3434 3080 Gernaat-van der Sluis 1260 0.50 [0.27 . 0.92 34 66 20 24 13 1 2 7 Schweizer et al. 2015 Rao et al. 2011 Kim et al. 2010 0.48 [0.28 , 0.82] 0.44 [0.23 , 0.83] 0.41 [0.21 , 0.80] 0.29 [0.10 , 0.88] 11059 20642 13 7019 5293 365 231 43 Bebko et al. 2015 344 Sankar et al. 2005 Price et al. 2008 0.24 [0.01 , 5.78] 0.20 [0.01 , 4.05] 0.11 [0.02 , 0.51] 164 43 Wilcox et al. 2003 1135 420 RE Model for Subgroup 0.50 [0.39 , 0.64] Cardiac Surgery (n = 10) Schweizer et al. 2015 Jog et al. 2008 0.86 [0.46 , 1.63] 0.67 [0.36 , 1.25] 0.67 [0.46 , 0.97] 13 17 37 12 12 7 3257 7576 765 646 469 1077 101 697 23 81 19 18 12 Kohler et al. 2015 945 Martorell et al. 2004 Nicholson et al. 2006 466 954 73 0.63 [0.31 , 1.28] 0.59 [0.29 , 1.22] 0.42 [0.17 , 1.02] Katayanagi 2015 Walsh et al. 2011 0.38 [0.23 , 0.62 20 2496 59 2766 854 752 971 0.34 [0.16 , 0.75] 0.28 [0.11 , 0.75] 0.22 [0.12 , 0.41] 27 6 23 Cimochowski et al. 2001 992 Kluytmans et al. 1996 Adler et al. 2012 RE Model for Subgroup 0.49 [0.37 , 0.64] Random effect model 0.49 [0.41 . 0.59] 0.25 1.00 2.72 7.03

Fig. 2. Meta-analysis of observational studies all cause surgical site infection by surgical groups.

a research question of this review, this introduced a level of uncertainty. Nevertheless, previous systematic reviews have already established the effectiveness of the intervention based on pre-surgery *S. aureus* screening in preventing SSIs.^{38,46} The choice between combining screening with a personalized treatment regimen versus universal application of a decolonization intervention to reduce the occurrence of SSIs will depend on local factors, for example, how the patient's clinical pathway is organized and their regional antibiotic susceptibility profile.

This review was undertaken in the context of the New Zealand SSI Improvement (SSII) Programme. Two recent local clinical

guidelines on SSIs for cardiac and orthopaedic surgery are published by the Health Quality and Safety Commission, Ministry of Health, New Zealand. The guidelines recommend cefazolin as the first-line antibiotic, with clindamycin or vancomycin reserved for patients with β-lactam allergy. Vancomycin is added to cefazolin for known MRSA carriers. The use of alcohol-based antiseptic solutions including chlorhexidine gluconate or povidone-iodine is recommended for skin antisepsis before the surgical incision. These recommendations are consistent with most of the standard care regimens described in the included studies. In terms of decolonization, *S. aureus* screening, nasal decolonization with mupirocin and body wash using

Author(s) and Year (N = 10) Bundle Orthopaedic surgery (n = 3) Total ative Risk [95% CI] Total SSI SSI Gernaat-van der Sluis et al. 1998 1044 1260 0.60 [0.24 , 1.49] Baratz et al. 2015 13 3434 21 3080 0.56 [0.28 , 1.11] Schweizer et al. 2015 0.48 [0.28 , 0.82] 17 11059 66 20642 RE Model for Subgroup 0.52 [0.36 , 0.77] Cardiac Surgery (n = 7) Schweizer et al. 2015 0.86 [0.46 , 1.63] 13 3257 35 7576 752 0.54 [0.11 , 2.57] 116 Cimochowski et al. 2001 854 11 992 0.42 [0.13 , 1.32] Martorell et al. 2004 469 11 466 0.27 [0.08 . 0.97] Nicholson et al. 2006 16 0.22 [0.07 , 0.66] 954 1077 Kohler et al. 2015 0.21 [0.03 , 1.69] Adler et al. 2012 971 310 0.18 [0.05 , 0.62] RE Model for Subgroup 0.38 [0.22 . 0.67] Random effect model 0.47 [0.35 , 0.65] I squared = 11.52%; Prediction Interval = (0.30, 0.75) Relative Risk

Fig. 3. Meta-analysis of observational studies by *Staphylococcus aureus* surgical site infections for observational studies.

chlorhexidine were recognized by the Australian Guideline for the Preventing and Control of Infection in Healthcare⁴⁹ as an effective measure for cardiac and orthopaedic surgery although no direction is provided regarding the implementation of these interventions in hospitals.

Limitations

Studies on minor orthopaedic surgery and studies dedicated to shoulder surgery were excluded from this review. Certain groups of specialized surgeries were also excluded such as spinal surgery, maxillofacial surgery or cardiac device implantation procedures with small incisions. Further research is encouraged to investigate how SSIs can be effectively reduced for those procedures. Regarding meta-analysis of all-cause SSIs, we have assumed that SSIs in cardiac and orthopaedic surgery were predominately caused by Gram-positive bacteria. This assumption may have overestimated the pooled effectiveness of the treatment effect. Moreover, due to the nature of observational studies it was not possible in this review to adjust for possible confounding factors because of lack of detail in the reporting of historical controls. Study designs varied greatly in respect to treatments in both study arms. Adherence to the other interventions known to reduce the risk of a SSI, surgical antibiotics prophylaxis and use of an alcohol-containing skin antisepsis, was not reported in most of the studies; experience from the SSII Programme has shown that without measurement and feedback, adherence may be less than optimal. However, based on the very low heterogeneity and narrow prediction intervals of the meta-analyses, it is unlikely that any other studies either existing, or published in the future, would substantially affect the results. The risk of resistance to the decolonization agents were not investigated in this study due to low level of reporting, and should be an area of future research.

Conclusion

The evidence base for a patient care bundle to reduce SSI is complex and diverse. With the use of an appropriate patient care bundle, SSIs in orthopaedic and cardiac surgery can be effectively reduced by approximately 50%, especially for *S. aureus*-related SSIs.

Acknowledgement

This study was funded by the New Zealand Health Quality and Safety Commission.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Figure S1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses chart for study selection.

Figure S2. Risk of bias for all randomized controlled trials.

Figure S3. Risk of bias summary for randomized controlled trials.

Table S1. Population-Intervention-Comparator-Outcome criteria. **Table S2.** Quality assessment of observational studies (study post-2013).

Appendix 2: Current burden of staphylococcal SSI in orthopaedic patients per DHB

Table 4: Mixed growth cultures (aggregate of April 2014 to June 2016 data)

				Mixed gro	wth cultures	*
DHB	# Procedures	# Total SSI	# S. aureus SSI	S. aureus proportion of mixed staph	# coagulase negative staph (CNS)	CNS proportion of mixed staph
Auckland	1459	12	0	0	0	0
Bay of Plenty	1738	23	3	75%	1	25%
Canterbury	2912	20	2	40%	3	60%
Capital & Coast	1048	16	0	0	0	0
Counties Manukau Health	1777	34	0	0	0	0
Hauora Tairāwhiti	295	3	0	0	1	100%
Hawke's Bay	845	8	0	0	0	0
Hutt Valley	664	11	2	67%	1	33%
Lakes	856	14	3	75%	1	25%
MidCentral	1080	6	0	0	0	0
Nelson Marlborough	1282	10	0	0	1	100%
Northland	1170	15	2	67%	1	33%
South Canterbury	366	1	0	0	0	0
Southern	1529	15	0	0	1	
Taranaki	645	4	0	0	0	0
Waikato	2158	30	4	50%	4	50%
Wairarapa	328	0	0	0	0	0
Waitemata	2651	25	0	0	0	0
West Coast	201	5	2	100%	0	0
Whanganui	648	9	0	0	0	0
Grand total	23,652	261	18	56%	14	44%

^{*} Duplicates removed (*S. aureus* only was recorded for any coag-negative staph and *S. aureus* mixed culture).

Table 5: Pure growth cultures (aggregate of April 2014 to June 2016 data)

				Pure gro	wth cultures	
DHB	# Procedures	# Total SSI	# S. aureus SSI	S. aureus proportion of pure growth staph	# coagulase negative staph (CNS)	CNS proportion of pure growth staph
Auckland	1459	12	4	80%	1	20%
Bay of Plenty	1738	23	8	53%	7	47%
Canterbury	2912	20	5	63%	3	37%
Capital & Coast	1048	16	5	63%	3	37%
Counties Manukau Health	1777	34	7	64%	4	36%
Hauora Tairāwhiti	295	3	1	100%	0	0
Hawke's Bay	845	8	2	67%	1	33%
Hutt Valley	664	11	1	33%	2	67%
Lakes	856	14	7	88%	1	12%
MidCentral	1080	6	1	100%	0	0
Nelson Marlborough	1282	10	2	33%	4	67%
Northland	1170	15	6	86%	1	14%
South Canterbury	366	1	1	100%	0	0
Southern	1529	15	10	100%	0	0
Taranaki	645	4	2	100%	0	0
Waikato	2158	30	7	58%	5	42%
Wairarapa	328	0	0	0	0	0
Waitemata	2651	25	8	73%	3	27%
West Coast	201	5	1	100%	0	0
Whanganui	648	9	4	100%	0	0
Grand total	23652	261	82	70%	35	30%

Table 6: Proportion of staphylococcus (aggregate of April 2014 to June 2016 data)

DHB	# Procedures	# Total SSI	Proportion due to pure S. aureus	Proportion due to pure CNS	Proportion due to total pure staph
Auckland	1459	12	33%	8%	42%
Bay of Plenty	1738	23	35%	30%	65%
Canterbury	2912	20	25%	15%	40%
Capital & Coast	1048	16	31%	19%	50%
Counties Manukau Health	1777	34	21%	12%	32%
Hauora Tairāwhiti	295	3	33%	0%	33%
Hawke's Bay	845	8	25%	13%	38%
Hutt Valley	664	11	9%	18%	27%
Lakes	856	14	50%	7%	57%
MidCentral	1080	6	17%	0%	17%
Nelson Marlborough	1282	10	20%	40%	60%
Northland	1170	15	40%	7%	47%
South Canterbury	366	1	100%	0%	100%
Southern	1529	15	67%	0%	67%
Taranaki	645	4	50%	0%	50%
Waikato	2158	30	23%	17%	40%
Wairarapa	328	0	0%	0%	0%
Waitemata	2651	25	32%	12%	44%
West Coast	201	5	20%	0%	20%
Whanganui	648	9	44%	0%	44%
Grand total	23652	261	31%	13%	45%

Appendix 3: Current burden of staphylococcal SSI in cardiac patients per DHB

Table 7: Mixed growth cultures (aggregate of October 2014 to June 2016 data)

				Mixed growth	cultures*	
DHB	# Procedures	# Total SSI	# S. aureus SSI	S. aureus proportion of mixed staph	# coagulase negative staph (CNS)	CNS proportion of mixed staph
Auckland	1960	72	6	55%	5	45%
Canterbury	437	20	2	67%	1	33%
Southern	249	17	0	0%	0	0%
Total	2646	109	8	57%	6	43%

^{*} Duplicates removed (*S. aureus* only was recorded for any coag-negative staph and *S. aureus* mixed culture).

Table 8: Pure growth cultures (aggregate of October 2014 to June 2016 data)

				Pure growth	cultures	
DHB	# Procedures	# Total SSI	# S. aureus SSI	S. aureus proportion of pure growth staph	# coagulase negative staph (CNS)	CNS proportion of pure growth staph
Auckland	1960	72	17	65%	9	35%
Canterbury	437	20	6	100%	0	0%
Southern	249	17	4	100%	0	0%
Total	2646	109	27	75%	9	25%

Table 9: Proportion of staphylococcus (aggregate of October 2014 to June 2016 data)

DHB	# Procedures	# Total SSI	Proportion due to pure S. aureus	Proportion due to pure CNS	Proportion due to total pure staph
Auckland	1960	72	24%	13%	36%
Canterbury	437	20	30%	0%	30%
Southern	249	17	24%	0%	24%
Total	2646	109	25%	8%	33%

Appendix 4: Current DHB practice for screening and decolonisation

Responses from DHBs may reflect an anti-staphylococcus protocol specific to patients meeting high risk criteria on admission rather than a standard bundle for all elective cardiac or orthopaedic surgical patients.

DHBs with current M	RSA preoperative screenii	ng protocol				
Cardiac procedures	Orthopaedic	procedures				
Southern	Taranaki	Hauora Tairāwhiti				
	Hawke's Bay	Wairarapa				
	Lakes	Southern				
DHBs with current M	SSA preoperative screening	ng protocol				
Cardiac procedures	Orthopaedic	procedures				
Capital & Coast	Hawke's Bay	Bay of Plenty				
	Capital & Coast					
DHBs with curre	DHBs with current nasal decolonisation protocol					
Cardiac procedures	Orthopaedic procedures					
Canterbury	Hawke's Bay	Hauora Tairāwhiti				
Capital & Coast	Lakes	Taranaki				
DHBs with curre	ent skin decolonisation pro	otocol				
Cardiac procedures	Orthopaedic	procedures				
Canterbury	Hawke's Bay	Taranaki				
Capital & Coast	Lakes	Wairarapa				
Southern	Southern	West Coast				
	ent compliance documentation of					
nasal and/or skin decolonisation						
Cardiac procedures	Orthopaedic	procedures				
Capital & Coast	Hawke's Bay	West Coast				
Southern	Southern	Whanganui				
	Taranaki					