Surgical site infections: prevention and treatment

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Clinisupplies Ltd.	Draft Guidance Appendix I	195	Box 7 (Sprowson 2018)	The inclusion criteria (p8, line 11, table Appendix A) states that RCTs with a sample size of more than 200 are a relevant study design. The paper authored by Sprowson et al (2018) has been excluded because it was considered "not a relevant study design" despite the fact that the paper clearly describes an RCT of over 2000 people so it is unclear why this has been excluded. The line above, Sprowson (2014), references the publication of the protocol of the RCT. The 2018 publication by Sprowson appears to be of a high quality and is not covered by any of the exclusion criteria detailed in the Draft Guidance. The paper appears to be of high quality and would make a valuable addition to the evidence base as it covers a large (UK) patient population and included the relevant intervention and outcomes. In light of comment 1, we considered that perhaps the Sprowson paper (2018) could have been excluded because it states that "The layer closed with Vicryl was dependent on the preference of the surgeon ranging from deep fascia to subcutaneous layer" and the precise layer closed was not detailed and could therefore have included the subcutaneous layer. However, Thimour-Bergstrom (2013) which has been included, specifically stated that *"Subcutaneous layer closed with 3.0 multifilament polyglactin suture coated with triclosan (Vicryl Plus®)"* (this is on p19 in the Intervention column). Other papers which are included in the evidence review don't necessarily include detail on which layers were stitched or include wording such as "separate subcutaneous sutures were optional, depending on the surgeon's preference". We believe the Sprowson paper (2018) should be included as it contributes a significant piece of good quality evidence and meets all the inclusion criteria.	Thank you for your comment. As specified in the review protocol (Evidence Review D, Appendix A) RCTs with a sample size of ≥ 200 subjects were included. The Sprowson 2014 paper was excluded from the review because it is a quasi-randomised trial. In the study, it is stated that treatment allocation was based on date of surgery. This means that allocation was not truly random and a study with such design carries a greater risk of selection bias. Furthermore, our protocol states that quasi-randomised trials would only be utilised if less than 5 RCTs were identified. As we were able to meet our defined threshold, this study was excluded. We also ran additional sensitivity analyses and identified that inclusion of this study did not greatly impact our overall results and thus did not change the conclusions made by the committee. The exclusion list has been updated to reflect our reasoning for exclusion.
Association of Breast Surgery	Evidence Review B	General	General	In breast surgery when re-prepping a patient once the operation has been performed and prior to breast implant insertion, the wound is open but Chlorhexidine is not licensed for internal use, so Betadine is often used for the re-prepping process.	Thank you for your comment. Recommendations 1.3.7 to 1.3.10 focus on the use of skin antiseptics prior to skin incision. Use of antiseptics and antibiotics prior to wound closure is covered by recommendations 1.3.18 and 1.3.19. No evidence was found in evidence review C on the use of Betadine (Povidone iodine) in breast implant surgery.
Infection Prevention Society	Evidence Review B	19	7 and 29	The whole economic analysis is flawed and seems to have been biased towards the use of CHG. The most effective treatment (regardless of whether a second agent present) is alcohol. Why was this not modelled? But the estimates for risk reduction associated with CHG used in the economic model are not borne out in the evidence included in the review. This is because the Lee paper compares CHG in alcohol with aqueous PI, includes vaginal procedures (no incision), includes studies that measure skin colonisation not SSI etc. This study therefore does not provide robust data on which to answer the question – is CHG more cost effective than PI. It can only do this is the included studies are of reasonable quality, measures SSI as an outcome and includes only PI or CHG in the same formulation (either with or without alcohol).	Thank you for your comment. The section to which your comment pertains refers to a published economic analysis (Lee et al., 2010) that we assessed as subject to potentially serious limitations. We believe that we were able to avoid some of the shortcomings of this publication in our own original economic analysis. However, we did not identify any evidence on the use of alcohol alone, and we are uncertain on what evidence you assert that it is effective without a second agent. Our network meta-analysis suggested that both alcohol and chlorhexidine have independent effects on reducing the incidence of SSIs, although the only effect that was observed at a 95% confidence level is that people who receive chlorhexidine have a lower incidence of SSIs than people who receive povidone iodine. The independent effect of alcohol compared with water as an excipient favoured alcohol, though the results were consistent with no difference, at a 95% confidence level. These results also imply the effect of chlorhexidine versus povidone iodine is at least as large as the effect of alcohol vs aqueous.
Infection Prevention Society	Evidence Review B	21	19	Hibiscrub is not a surgical skin preparation	Thank you for your comment. The UK marketing authorisation for HibiScrub has now been added to the footnote.
Becton Dickinson	Evidence Review B	21	9	Table 3 includes three products containing chlorhexidine 2% / isopropyl alcohol 70% that have been compared in a cost-utility analysis. ChloraPrep and ChloraPrep with Tint are both approved medicinal products, whereas the Ecolab 2% chlorhexidine-product is not licensed as a medicinal product. We believe that this should be clarified as it is an important distinction between the products.	Thank you for your comment. It is not accurate to state that these 3 products are compared in a cost–utility analysis; rather, separate analyses are provided using the estimated costs of each. The current licensing status of available preparations is clearly stated in a footnote associated with the relevant recommendation (1.3.9).
Infection Prevention Society	Evidence Review B	34	16	These studies did not measure SSI as an outcome and should not have been included	Thank you for your comment. Five out of the six studies highlighted in this section were included in evidence review B but downgraded for indirectness as these did not specify how an SSI was identified. These studies were not excluded as they meet our inclusion criteria

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					and investigated surgical site infection as a secondary outcome. One study [Xu 2017] did state that postoperative infection was defined as the need for antibiotics or surgical intervention. Furthermore, as highlighted on page 196 in Evidence review B, the 5 studies which were downgraded for indirectness were not included in the network meta-analysis or meta-regression which were used to inform recommendations.
Infection Prevention Society	Evidence Review B	34	43	but compared to an aqueous agent therefore not clear if CHG or alcohol that generated the effect	Thank you for your comment. As highlighted, the Dariouche 2010 compared 2% chlorhexidine with 70% alcohol with povidone iodine scrub and paint. This study contributed to the meta- regression which was conducted to explore the additive effect of the agent and excipient. This model assumed that the 4 treatment groups (Aqueous povidone iodine, chlorhexidine in alcohol, povidone iodine in alcohol and aqueous chlorhexidine) can be broken down to 1) alcohol compared to aqueous 2) povidone iodine compared to chlorhexidine. The findings of the meta-regression showed that chlorhexidine in alcohol was associated with the lowest incidence of surgical site infections. The effect of chlorhexidine versus povidone iodine is at least as large as the effect of alcohol vs aqueous. .For further information on this model please refer to Appendix H.
Infection Prevention Society	Evidence Review B	34	8	This includes the time to infection (30 days for superficial and deep up to 1 year for organ space). This should have been clearly considered in retrieving and appraising the evidence	Thank you for your comment. The definition of surgical site infection was detailed on page 8, line 2-8. The definition from the Centres for Disease Control and Prevention was used. Furthermore, studies which did not specify definition of a surgical site infection and follow up period were downgraded for indirectness.
Infection Prevention Society	Evidence Review B	36	4	this should be mentioned in the recommendation as it is important	Thank you for your comment. The committee took contraindications related to the use of chlorhexidine into consideration when drafting recommendations. Therefore different recommendations were made based on different clinical scenarios including when chlorhexidine is a contraindication.
Becton Dickinson	Evidence Review B	37	39	This paragraph states that 'While, these applicators are available in different sizes, thorough application of the antiseptic may not occur'. We are concerned about this wording. The instructions for use of the applicators containing the antiseptic solution are clearly stated in the approved product information. Therefore if the healthcare professional use the product as indicated, a thorough application of the antiseptic will occur and will allow the expected disinfection of the skin. Also, education and training about ChloraPrep is provided to healthcare professionals to allow for standardisation and compliance. We believe that this sentence should be deleted from the document. If the committee disagrees, the wording needs to be amended to acknowledge that <u>all</u> antiseptics could be misapplied, and state that it is imperative that solutions are applied as indicated in the product SmPC, and training sought where-ever possible.	Thank you for your comment. Amendments have been made to the rationale and impact section for this recommendation to provide further clarification. We have also removed the sentence 'While, these applicators are available in different sizes, thorough application of the antiseptic may not occur' in which you had concerns.
Infection Prevention Society	Evidence Review B	37	7	Given the inadequacies of the economic analysis indicated above, this statement seems highly unlikely to be true. The economic analysis supporting chlorhexidine in alcohol suggests that ChloraPrep (2% CHG in alcohol) would be cost effective for all surgery due to reduction in SSI. However, this is based on a flawed analysis of the reduction in SSI associated with CHG in alcohol and the use of inappropriate and very weak evidence to model costs. Any form of alcohol based solution is likely to be cost effective yet if Chloraprep were used for all surgeries, at a minimum of 16 times the cost of other alcohol-based formulations (and more than one applicator per procedure commonly required) it would have a major economic impact on the NHS and divert scarce resources.	Thank you for your comment. Although the other alcohol based solutions are cheaper, they are associated with considerable costs for associated paraphernalia and the sterilisation of equipment, which make the cost of use approach that of a single applicator of Chloraprep. We examine the impact of the need for additional applicators in sensitivity analysis. We do not directly compare Chloraprep with administration of chlorhexidine in alcohol from a bottle; however, the results of our separate analyses are available for readers to compare. The committee's recommendations do not specify that Chloraprep must be used (though they note the licensing status of the options that are currently available). The committee also made research recommendations that aim to resolve uncertainty about the true requirements for each case (e.g. 'double-prepping', which could have a meaningful impact on the costs of different approaches).
Becton Dickinson	Evidence Review B	38	4-5	We acknowledge that products in bulk solution require the use of forceps that can be sterilised and reused. However, there are ancillary items that need to be taken into account when these products are used: multiple gauzes, galley pots for each patient etc. that will need to be disposed of as clinical waste, or re-sterilised.	Thank you for your comment. In our economic analysis, we have taken all costs into consideration that the committee agreed were material to the decision. In the cases of gauzes, galley-pots, disposal, etc., the committee agreed that resource-use would not materially vary between the preparations being compared, except in the case of pre-packaged chlorhexidine + alcohol applicators (ChloraPrep). Sensitivity analysis showed that

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				Also, appropriate disposal (in accordance with COSHH/SmPC) of the remaining bulk solution needs to be taken into account from a cost and environment point of view. We believe there's an opportunity to amend this section to more fairly reflect the process steps, costs and environmental considerations required when comparing different solutions and their administration.	a different conclusion would be reached only if these costs exceeded around £30 per operation extra for chlorhexidine applicators (see figure HE27). Therefore, the committee agreed that it was unnecessary to account for the very small cost differences in consumables that might be ascribed to one approach or another.
ENT UK	Evidence review C	General	General	The evidence examined in this piece of work covers a very heterogeneous group of conditions, operations, and microbial / antimicrobial profiles, from which it is difficult to perceive an accurate conclusion.	Thank you for your comment. Meta-analyses conducted as part of this review took this into consideration. Firstly, with a number of studies reporting different surgery types, the evidence was stratified with subgroup analyses based on surgery type and wound category The committee also took heterogeneity into consideration when making recommendations and their discussions have been captured in the Rationale and Impact section in Evidence review C.
Medtronic	Evidence Review C	General	General	We believe it is important and timely to review and consider the inclusion of antibacterial envelopes within this evidence review, as stated in comment #1. The TYRX™ Absorbable Antibacterial Envelope is a sterile, single-use surgical mesh envelope for a cardiac implantable electronic device (CIED) when implanted into the pocket. TYRX is made of a knitted lycopene II mesh coated with a mixture of an absorbable tyrosine-based polyarylate polymer containing the antimicrobial agents rifampicin and minocycline, each at a concentration of 102 µg/cm2. TYRX anchors the CIED and provides a substrate for tissue in-growth. After implantation, and as the TYRX envelope anchors the implanted device, the absorbable polyarylate polymer elutes the antibiotics while the polymer is being absorbed by the patient's body. The antibiotic agents (rifampicin and minocycline) reach the MIC90 level within two hours after implantation and maintain that level of tissue concentration for a minimum of 7 days. The mesh substrate is absorbed by the body in approximately nine weeks. After absorption of the mesh substrate, there is no residual foreign body remaining in the tissue pocket to serve as a potential nidus of infection. There is a growing evidence base on the efficacy of TYRX[1-4], and the results of World-wide Randomized Antibiotic Envelope Infection Prevention Trial (WRAP-IT), a randomised, prospective, multi-centre, single blinded study, will be reported in early 2019. This study, which includes UK centres, will evaluate the ability of the TYRX envelope to reduce major CIED infections through 12-months post-procedure following CIED implants or replacements: https://clinicaltrials.gov/ct2/show/NCT02277990 **References** 1. Koleck et al.. PACE 2013; 36:354–361. 2. Mittal et al. Heart Rhythm. 2014; 11(4):595-601. 3. Kolek MJ et al J Cardiovasc Electrophysiol 2015; 26 4. Shariff 2015 J Cardiovasc Electrophysiol. 2015 Jul;26(7):783-9. doi: 10.1111/jce.12684.	Thank you for your comment. The use of antibacterial envelopes is outside the scope of this current update of the guideline. The use of TYRX absorbable antibacterial envelope is currently being considered by the NICE Technology Appraisals team. Further detail can be found at https://www.nice.org.uk/guidance/proposed/gid-ta10370
Infection Prevention Society	Evidence Review C	28	25	This statement would only be true if the SSI were superficial or deep only. This may be the relevant in the case of triclosan sutures (as per the Renko study which excluded deep/organ space SSI) but then the search question should have been only related these SSI rather than all SSI.	Thank you for your comment. As stated in the review protocol (please refer to Appendix A in Evidence Review D), studies examining surgical site infection, including SSIs up to 30 days and 1 year were included.
Infection Prevention Society	Evidence Review C	28	36	How can it be acceptable to take low quality evidence and pool it to get an unbiased recommendation?	Thank you for your comment. As detailed in the methods section (Appendix B in Evidence Review C), in any meta-analysis where some (but not all) of the data came from studies at high risk of bias, a sensitivity analysis was conducted and results from both the full and restricted meta-analyses were presented. The sensitivity analyses are presented within GRADE tables located in Appendix G. Furthermore, the committee did note the quality of the evidence (discussions captured in the Rationale and Impact section in Evidence Review C) and also applied their clinical judgement when forming recommendations.

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Infection Prevention Society	Evidence Review C	28	7	This statement is not true. Deep/organ space infections, especially in orthopaedics and cardiac surgery where a non-human implant is left in the wound can take several months to become apparent.	Thank you for your comment. The committee took your comment into consideration and made amendments to the 'Outcomes that matter most' section in Evidence Review D. This section acknowledges that the committee took different time points into consideration, from up to 30 days to up to 1 year.
North Bristol NHS Trust	Evidence review D	General comment	General comment	This was communicated to me by one of our Consultant Colorectal Surgeons for inclusion in consultation feedback: 'We measure 30 day SSI for all elective colorectal surgery. We implemented a bundle of care in 2013 which included the following: 1. 2% Chlorhexidine 2. Wound Protectors (now taken out due to new evidence showing no efficacy) 3. Antibiotic Impregnated sutures. 4. A second dose antibiotics after 4 hours This reduced SSI from at least 16%-8% which has been sustained for almost 5 years. Therefore is in support of the antibiotic impregnated sutures'.	Thank you for your comment. We welcome your support of the guideline.
ENT UK	Evidence review D	8	16-17	It is not clear why studies were excluded which involved closure of the subcutaneous layer and the use of drains. These might be considered essential factors to take into account when examining evidence to minimise surgical site infections.	Thank you for your comment. The closure of the subcutaneous layer was considered to be out of scope by the guideline committee as this involved the use of drains. The closure of the subcutaneous layer was considered in studies which examined the closure of multiple layers of the skin however the subcutaneous layer was not looked at in isolation.
Johnson & Johnson Medical Ltd	Evidence Review D	27	40	We welcome the statements by the GDG in the evidence review that it is likely that the increased cost of triclosan-coated sutures will be outweighed by savings from a reduction in the number of SSIs, which are costly to treat. This is aligned to the published health economic literature, and from real-world experience and feedback from users of these sutures. However, we would like to flag that in previous NICE Guidelines (2009) NICE recognised the cost of treating an SSI to be £4,300 which was highlighted by NICE as a likely underestimation of the true cost. We were interested to read that NICE now considered the average cost of managing a single patient with an SSI at £3,122.86 which is lower than in previous years. How has this new lower cost been calculated?	Thank you for your comment. In the most recent update (2019 Guideline) – the cost of an SSI is calculated by multiplying the average number of bed days for each of the 18 surgeries considered, from two data sources that underpin this model. The data sources were Jenks, and PHE data. The cost of an additional bed day was £312.29 and the average additional number of bed days in the base case was 10.0, resulting in an SSI cost of £3122.86. In the 2009 Guideline, the cost of an SSI is purported to be £3,500 (The last paragraph in section D2.2). This was derived with similar methodology to the most recent cost of an SSI. The average number of bed days came from the NNINS survey, which was 11.4 days and the cost of each additional day was £307, resulting in an SSI cost of £3,500. The difference in cost between this guideline and the previous guideline is driven primarily by the number of additional bed days, which is similar, but not the same, due to different data sources.
British Orthopaedic Association	Evidence review D	195		The guideline committee have stated that a key trial of this suture undertaken in NHS patients was not a relevant study design. This trial needs to be considered as it is the one most applicable to orthopaedic patients in England. (Sprowson 2018). The guideline lacks credibility without inclusion of this large study. Please reconsider.	Thank you for your comment. As specified in the review protocol (Evidence Review D, Appendix A) RCTs with a sample size of ≥ 200 subjects were included. The Sprowson 2014 paper was excluded from the review because it is a quasi-randomised trial. In the study, it is stated that treatment allocation was based on date of surgery. This means that allocation was not truly random and a study with such design carries a greater risk of selection bias. Furthermore, our protocol states that quasi-randomised trials would only be utilised if less than 5 RCTs were identified. As we were able to meet our defined threshold, this study was excluded. We also ran additional sensitivity analyses and identified that inclusion of this study did not greatly impact our overall results and thus did not change the conclusions made by the committee. The exclusion list has been updated to reflect our reasoning for exclusion.
Johnson & Johnson Medical Ltd	Evidence review D – Benefits and Harm	29	30-37	Johnson & Johnson would like to take this opportunity to respond to the Committee statements in the "Benefits and Harm" section of the Guideline. It is correct that there have been no reports of adverse reactions as a result of using triclosan-coated sutures. Furthermore, there is no evidence of harm arising from an increase in antimicrobial resistance from use of triclosan-coated sutures, and we request that this be removed from the Guideline.	Thank you for your comment. The committee took your comment into consideration and the benefits and harms section has been amended. The benefits and harms section now includes the following paragraph: One potential harm of an increased use of triclosan-coated sutures is the emergence of antimicrobial resistance. While resistance has not been reported, these effects may need to be considered if future evidence shows further benefits of using triclosan-coated sutures over standard sutures in different types of surgery.

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				Triclosan is an antiseptic agent that has been in widespread use for more than 40 years worldwide in a variety of consumer products. There are to date no clinical reports of antimicrobial resistance after 50+ years of use in a broad array of consumer products which are used in multiple and often on a daily (e.g. chronic) basis as compared to the acute and targeted use of triclosan in sutures which has shown a demonstrable clinical benefit. There have been voiced concerns that triclosan poses an environmental risk. The concern is typically with "free" or "raw" triclosan making it into the water system, into surface water, into lakes and streams, and further into the environment. Possible sources are topical triclosan containing products including soaps, shampoos, cleaners, cleansers, toothpastes, washes, etc. Antibacterial sutures would not contribute to this environmental risk as any suture or packaging not utilized in the operative procedure is discarded by healthcare facilities as medical waste and is incinerated. If triclosan were to reach the environment, it is readily broken down by exposure to light (photodegraded). The photodegradation products of triclosan have been further shown to be biodegraded by bacteria. Triclosan sutures in the body also do not create an environmental concern as the small amount of triclosan on the suture is broken down and metabolized in the body and excreted in a neutralized, inactive form via the kidneys. It is important that uses of triclosan with demonstrable health benefits, such as some medical applications, are distinguished from those where there is no proven benefit such as use in certain consumer products. For example, triclosan is listed nationally in Sweden as subject for risk reduction measures and is one of the most frequently banned substances in public procurement documents in Sweden. Recently however an exception was made for antibacterial sutures, recognizing their advantages for patients (Stockholm County Council RFP, 2016). With regard to bacterial resistance, triclosan, like any other biocide, can be shown to contribute to the selection of less susceptible bacteria in in vitro laboratory evaluations; however this effect has not been seen in vivo (clinically). The few in situ studies investigating long-term triclosan exposure (i.e. at least 6 months) did not indicate changes in resistance susceptibility in the predominant bacteria selected for monitoring but the changes in the entire flora were not evaluated. There is so far no epidemiological data	Furthermore, the committee were aware of the WHO and EUnetHTA Guidelines however NICE and their guideline committees take an independent view and analysis of the evidence in forming its recommendations.

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				linking outbreaks of antimicrobial resistant human and zoonotic pathogens following exposure to triclosan from cosmetics and other products. Given the short-term nature of suture use, it is highly unlikely that such use would do anything other than reduce the risks of postoperative infection. WHO and EUnetHTA Guidelines both include a position on this subject, and we recommend that the GDG also review these alongside our request to amend the potential harm section of the SSI Guideline documents.	
Johnson & Johnson Medical Ltd	Evidence review D - Methods	General	General	Whilst appreciating that the GDG considered that the evidence overall favoured use of triclosan-coated sutures over standard sutures for reducing SSI, we would like to provide some further perspective on the evidence base. Triclosan-coated sutures are currently adopted in the UK across at least 19 surgical specialities, and as the NICE review states, a significant number of RCTs have been published on their use. We were surprised that NICE excluded all systematic review and meta-analyses from the evidence review and would like to request that this decision is reviewed so the 'best available published evidence' is used to inform the GDG considerations. Most significantly, we would like to raise the recent WHO Global Guideline for the Prevention of SSI where meta-analysis and meta regressions concluded that antimicrobial-coated sutures were effective to prevent SSI and suggested the use of triclosan-coated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery.	Thank you for your comment. The protocol for evidence review D outlines that only primary level data RCTs were included. However systematic reviews and meta-analyses were examined as a source of RCTs. This allowed us to make our own analysis of the RCT data. The committee were aware of the WHO Guideline however NICE and their guideline committees take an independent view of the evidence in forming its recommendations.
Johnson & Johnson Medical Ltd	Evidence review D - methods	General	General	Again, whilst appreciating that the GDG considered that the evidence overall favoured use of triclosan-coated sutures over standard sutures for reducing SSI, we were interested to see the difference in outcome for the GRADE assessment of the evidence by NICE. Since 2016, The World Health Organization (WHO), The Center for Disease Control and Prevention (CDC) and The European network for Health Technology Assessment (EUnetHTA) have also issued specific guidelines or health technology assessments on the use of triclosan-coated sutures. Both WHO and CDC organisations also employed GRADE assessment and concluded that the evidence was moderate-quality after performing a meta-analysis that included at least 9 of the same RCTs included in the NICE review (13 studies). EUnetHTA also concluded that the evidence was moderate-quality although this was based on another meta-analysis of 7 studies from the NICE review. As no published meta-analysis is included in this review by NICE (only RCTs), we request that the rationale for this difference in grading could be further detailed as moderate is consistently noted across these international guidelines after applying the GRADE framework. Furthermore, there is no biological explanation to expect effect modification across the subgroups i.e. why does use of triclosan-coated sutures result in high quality evidence for its effectiveness in paediatrics and be debatable in adults? Conclusions are included in our response here for completeness: <u>WHO</u> In a recently published WHO Guideline from November 2016, based on a SR/MA published by Wu et al., 2016 [104], the WHO panel suggests "*the use of triclosan-coated sutures for the purpose of reducing the risk of SSI, independent of the type of surgery"*. Their recommendation is conditional, with **moderate quality of evidence noted.** <u>CDC</u>	Thank you for your comment. This evidence review was developed using the methods and processes described in Developing NICE guidelines: the manual (2014). Please refer to the document for further information. It is difficult to compare and justify the GRADE assessment findings between evidence review D to those by the WHO, CDC and EUnetHTA as evidence review D stratified the data by follow up period and surgery type. Furthermore, the committee were aware of the WHO and EUnetHTA Guidelines however NICE and their guideline committees take an independent view and analysis of the evidence in forming its recommendations.

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				Moderate-quality evidence suggested tradeoffs in the use of triclosan-coated sutures to reduce overall SSI rates. A meta-analysis (N=5388) of 14 RCTs160-173 in colorectal, abdominal, lower limb revascularization, cardiac, breast, cerebrospinal fluid shunt, and mixed surgeries provided high-quality evidence for the reduction in the incidence of "overall SSI" with the use of triclosan-coated sutures. EUnetHTA "*All the clinical data assessed in this report are related to triclosan-coated sutures. No published clinical studies on chlorhexidine-coated sutures have been identified. A statistically significant benefit of triclosan-coated sutures in reducing the risk of total incisional SSIs was demonstrated in our SR/MA, based on moderate quality RCTs data.*" "*According to the GRADE assessment, the quality of these RCTs was* ***moderate.***"	
Northumbria Healthcare NHS Foundation Trust	General	General	General	Excellent focus on key questions	Thank you for your comment. We welcome your support of the guideline.
Northumbria Healthcare NHS Foundation Trust	General	General	General	Triclosan coated sutures. We performed a large investigator initiated RCT into the use of triclosan coated sutures in the NHS in a highly relevant area of surgery – hip and knee replacement. This included over 2500 patients. Despite being funded by Ethicon (the manufacturers) the study found that the sutures were ineffective. Although I doubt this study inclusion will change the final guidance there is no justification to exclude this trial in the analysis. The panel have chosen to exclude this paper as "not a relevant study design" when it is designed as a pragmatic randomised trial in NHS patients. I am keen to know why the design isn't relevant explicitly and who on the panel specifically gave that advice.	Thank you for your comment. As specified in the review protocol (Evidence Review D, Appendix A) RCTs with a sample size of ≥ 200 subjects were included. The Sprowson 2014 paper was excluded from the review because it is a quasi-randomised trial. In the study, it is stated that treatment allocation was based on date of surgery. This means that allocation was not truly random and a study with such design carries a greater risk of selection bias. Furthermore, our protocol states that quasi-randomised trials would only be utilised if less than 5 RCTs were identified. As we were able to meet our defined threshold, this study was excluded. We also ran additional sensitivity analyses and identified that inclusion of this study did not greatly impact our overall results and thus did not change the conclusions made by the committee. The exclusion list has been updated to reflect our reasoning for exclusion.
British Orthopaedic Association	General	General	General	Thank you for the efforts of the committee to review the evidence on this important topic. The British Orthopaedic Association would like some clarification on why some key evidence was excluded, and seek reassurance that it will be included in the final guideline.	Thank you for your comment. A thorough search of the evidence base for the four update topic areas was conducted with all key RCT evidence identified. Reasons for exclusion are provided in the appendices of the evidence reviews in the excluded studies tables. As specified in the review protocol (Evidence Review D, Appendix A) RCTs with a sample size of ≥ 200 subjects were included. The Sprowson 2014 paper was excluded from the review because it is a quasi-randomised trial. In the study, it is stated that treatment allocation was based on date of surgery. This means that allocation was not truly random and a study with such design carries a greater risk of selection bias. Furthermore, our protocol states that quasi-randomised trials would only be utilised if less than 5 RCTs were identified. As we were able to meet our defined threshold, this study was excluded. We also ran additional sensitivity analyses and identified that inclusion of this study did not greatly impact our overall results and thus did not change the conclusions made by the committee. The exclusion list has been updated to reflect our reasoning for exclusion.
Department of Health and Social Care	General	General	General	Thank you for the opportunity to comment on the draft for the above guideline. I wish to confirm that the Department of Health and Social Care has no substantive comments to make, regarding this consultation.	Thank you for your comment.
NHS England	General	General	General	While this guideline is generic, there is a specific current issue in colorectal surgery. A significant proportion of colorectal surgeons in England have started to use oral antibiotics pre-op to alter the patient's gut microbiome in the belief that this reduces SSI risk. This follows extensive use of this practice in America with some published results implying reduced infection risk. It would be very helpful if this NICE guidance either opines on this practice or signals it as an area to be addressed in research. (CIC)	Thank you for your comment. The NICE Surveillance team has looked again at this topic and have concluded that antibiotic prophylaxis combined with mechanical bowel preparation should be updated and will be undertaken as part of a surveillance exceptional review.

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NHS England	General	General	General	On a general point, the guidance supports the use of triclosan-coated sutures for closure. It's not clear whether this implies that triclosan-coated sutures should be preferred over all other closure methods, or whether they are just being proposed as better than uncoated sutures. Where surgeons currently close wounds with skin staples, the guidance should be clearer on whether they should switch to triclosan-coated sutures (this would have quite a big impact on the duration of some operations) (CIC)	Thank you for your comment. The recommendation has been amended in light of your comment to provide further clarification - When using sutures, consider using triclosan-coated sutures.
Royal College of Nursing	General	General	General	The Royal College of Nursing (RCN) welcomes the update of the NICE guideline: surgical site infections: prevention and treatment. The RCN invited members who care for patients with wound and infections to review the draft guideline consultation document on its behalf. The comments below reflect the views of our reviewers.	Thank you for your comments.
Healthcare Improvement Scotland	General	General	General	I have discussed with our members and we have no comments on the consultation documents.	Thank you for your comments.
Willingsford Ltd	General	General	General	Singh & Blakley 2018 report that animal studies have consistently found ototoxic effects of chlorhexidine and alternative products for use in facial regions should be considered. Toxicity studies in man have not confirmed these results, but these are unlikely to be performed.	Thank you for your comment. The reviews conducted as part of this update focused on RCT evidence, therefore animal studies were not included. Additionally, it should be noted that patients undergoing a surgical procedure that did not involve a visible incision, and therefore did not result in the presence of a conventional surgical wound were excluded from the review. Furthermore, while reviewing the evidence on nasal decolonisation, the guideline committee did note that caution must be taken when using a chlorhexidine body wash in people presenting with contraindications. The committee also highlighted alternative products that may be utilised and also formulated a research recommendation to identify the effectiveness of these interventions. As part of this research recommendation, adverse events was identified as an important outcome.
Royal College of Anaesthetists	Guideline	General	General	The timing of the administration of antibiotics - the guide says at the start of anaesthesia but reference should be made to NAP6 and ask for earlier administration to be consistent. Ideally antibiotics should be administered earlier and not wait for the anaesthetist, but practicalities often dictate that it is administered at induction.	Thank you for your comment. The timing of perioperative anaphylaxis was outside the scope of this guideline update. Antibiotic prophylaxis is currently covered by recommendation 1.2.11 to 1.2.17 in CG74 guideline.
Royal College of Anaesthetists	Guideline	General	General	Current guidance from the AAGBI and RCoA is to prefer 0.5% chlorhexidine in alcohol when performing neuraxial blocks over 2% in the absence of evidence of any difference in infection prevention but in the presence of evidence that chlorhexidine is neurotoxic - this should be mentioned in the NICE document.	Thank you for your comment. Neuroaxial blocks are outside the remit of this guidance. With regards to surgical site infection, only one study was identified which compared the effectiveness of 0.5% chlorhexidine in alcohol and 2% chlorhexidine in alcohol. When it came to the decision making process, the meta-regression was utilised. This model assumed that the 4 treatment groups (Aqueous povidone iodine, chlorhexidine in alcohol, povidone iodine in alcohol and aqueous chlorhexidine) can be broken down to 1) alcohol compared to aqueous 2) povidone iodine compared to chlorhexidine. As this model focused on the agents and excipients recommendations do not specify the concentrations that should be utilised.
Clinisupplies Ltd.	Guideline	General	General	Noting your inclusion/exclusion criteria, the following studies were not considered within the draft: 1. Karip (2016) – not listed but would be excluded anyway as less than 200 patients 2. Rasic (2011) – not listed but would be excluded anyway as less than 200 patients 3. Soomro (2017) - Does antibiotic coated polyglactin helps in reducing surgical site infection in clean surgery? 378 patients in benign breast surgery. Meets inclusion criteria (RCT, >200).	Thank you for your comment. All three studies were identified in our searches, however these were excluded after assessment at title and abstract stage. Karip 2016 and Rasic 2011 were excluded due to number of participants and Soomro 2017 was excluded as this included the closure of the subcutaneous layer, which is excluded in this review.
UK Clinical Pharmacy Association (UKCPA) Pharmacy Infection Network	Guideline	General	General	Many Trusts have now moved to using Octenisan (octenidine) washes and nasal ointment for MRSA decolonisation rather than chlorhexidine washes and Bactroban (mupirocin) nasal ointment since these are not classed as medications and therefore do not require a prescription. Octenisan washes can also be used for babies including preterm babies.	Thank you for your comment. The guideline committee noted that caution must be taken when considering the use of chlorhexidine in people presenting with contraindications. They noted that interventions such as octenisan and polyhexanide could be used as part of the decolonisation bundle. However, due to a lack of evidence on these interventions, no recommendations could be made. In order to explore the effectiveness of these interventions, the committee made a research recommendation.

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UK Clinical Pharmacy Association (UKCPA) Pharmacy Infection Network	Guideline	General	General	As there are periodic shortages with mupirocin, what is NICE position on available alternatives? E.g Naseptin, octenisan nasal ointments.	Thank you for your comment. During the development of the review protocol, the committee did take other interventions into consideration (highlighted in Table 1 in Evidence Review A). However, no studies of relevant study design were identified which examined the effectiveness of chlorhexidine and neomycin gel (naseptin) or octenisan gel. Due to this the committee were unable to make recommendations on the use of available alternatives However, the committee incorporated these alternative interventions into the four research recommendations developed as part of evidence review A (please see Appendix K). For further information, please refer to 'The committee's discussion of the evidence' in evidence review A. .
Infection Prevention Society	Guideline	General	General	The outcome measure of SSI is critical to the valid interpretation and assimilation of data for this guideline however the description on page 13 is vague and it is obvious from a number of included RCTs that studies based on outcome measures of 'skin colonisation' which is absolutely not a SSI. To reliably measure an SSI outcome then the study methods must include a defined surveillance method and case definitions - if absent then the study is not relevant to the RQ. The skin colonisation studies are therefore not appropriate to consider as evidence for preventing SSI and should be excluded. This problem is clearly apparent in the skin colonisation data but also raises concerns that a similar lack of robust application of consistent outcome measures for SSI applies to the other sections which we are unable to check in such detail.	Thank you for your comment. Five out of the six studies highlighted in this section were included in evidence review B but downgraded for indirectness as these did not specify how an SSI was identified. These studies were not excluded as they meet our inclusion criteria and investigated surgical site infection as a secondary outcome. . Furthermore, as highlighted on page 196 in Evidence review B, the studies which were downgraded for indirectness due to lack of definition were not included in the network meta-analysis or meta-regression which were used to inform recommendations.
Infection Prevention Society	Guideline	General	General	The document appears to have been aimed at both professionals and the public but is presented in a highly simplistic way that is not helpful for informing practice, the absence of discussion of any of the evidence or tis quality makes it misleading, and does not provide support for statements with an indication of the relevant evidence or its weight.	Thank you for your comment. The guideline document outlines the recommendations in their entirety as well as why those recommendations were made and their impact on practice. The guideline also makes links to the evidence review. Recommendations are informed by the evidence of effectiveness and cost effectiveness with committee discussion and interpretation. Information on the evidence included and its quality is also detailed in evidence review documents.
British Infection Association	Guideline	General	General	Please could NICE give a recommendation or a view on "smoking cessation prior to elective surgery"	Thank you for your comment. Smoking cessation is out of scope for the four questions explored as part of this update. Information for patients and carers is currently covered by recommendations 1.1.1 to 1.1.4 in the CG74 guideline. Guidance on smoking cessation is also covered as part of NG92 guideline (Stop smoking interventions and services). Your comment will also be passed on the NICE surveillance team, for consideration when future updates of the guideline are planned.
British Infection Association	Guideline	General	General	The guideline appears to be a sensible update and as an organisation we strongly support this guideline.	Thank you for your comment. We welcome your support of the guideline.
NHS England	Guideline	General	General	The emphasis of the guidelines is quite rightly on prevention of the infection but there is very little information or recommendation regarding role of primary care clinicians in the identification and care for such cases in the community.(MJ)	Thank you for your comment. The four questions reviewed as part of this update focused on the preoperative and postoperative phase of surgery. Therefore, the role of primary care clinicians in the identification and care of patients was out of scope for these questions.
DHSC - Advisory Committee on Antimicrobial Prescribing, resistance and Healthcare Associated Infection	Guideline	General	General	The Committee expresses disappointment to see that no recommendations have been made in this updated guideline for SSI surveillance with feedback to clinicians as a means of reducing the risk of SSI.	Thank you for your comment. SSI surveillance was out of scope for this update. However recommendations on SSI surveillance have been made in the Public Health guideline (PH36) Healthcare-associated infections: prevention and control. A quality statement on surveillance has been made in QS49: Surgical site infection (Quality Statement 7). There is also a pathway on the prevention and control of healthcare-associated infections.
Becton Dickinson	Guideline	General	General	We welcome this robust and comprehensive review of the available evidence and the updated recommendations on antiseptic skin preparation.	Thank you for your comment. We welcome your support of the guideline.
Becton Dickinson	Guideline	General	General	We are concerned that this recommendation does not emphasize the need for single patient use of the antiseptic skin preparation.	Thank you for your comment. In this review, the effectiveness of a number of different products was examined. The recommendations that were made do not specify particular products for use but the committee were aware that some of the interventions have marketing authorisation. These have been listed in the footnote in the guideline. As stated

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				Multi-patient use solutions pose a risk to patients from extrinsically contaminated solutions. See: FDA Drug Safety Communication Chang CY, Furlong L-A. Microbial stowaways in topical antiseptic products. N Engl J Med 2012;367:2170-3 Weber DJ, Rutala WA, Sickbert-Bennett EE. Outbreaks associated with contaminated antiseptics and disinfectants. Antimicrob Agents Chemother 2007;51:4217-24, Contamination of alcohol prep pads with Bacillus cereus group and Bacillus species — Colorado, 2010. MMWR Morb Wkly Rep 2011;60:347 Allergy injection-associated Mycobacterium abscesses outbreak — Texas, 2009 In the UK, since the turn of the century products granted marketing authorisation have needed to demonstrate a terminally sterilised solution and require single use. As disinfection of the skin surface is a vital first step in any invasive medical procedure, it would seem prudent to ensure the risk on introducing contaminants is minimised. The Epic3 guidelines for preventing healthcare-associated infections in NHS hospitals include the recommendation for single-use application of antiseptic preparation for cutaneous antisepsis prior to the insertion of central venous access devices and peripheral vascular access devices, and for catheter and catheter site care (H. P. Loveday et al. / Journal of Hospital Infection 86S1 (2014) S1–S70). The NICE Quality Standard QS61 for Infection prevention and control also include the recommendation for single-use application of antiseptic preparation for vascular access device site care and management (www.nice.org.uk/guidance/qs61). As the result of their ongoing evaluation of infrequent but continuing reports of infections resulting from antiseptic products labelled for preoperative or pre-injection skin preparation, the FDA requested that manufacturers package antiseptics indicated for preoperative or pre-injection skin preparation in single-use containers (FDA Drug Safety Communication). Therefore, we believe it would be most beneficial to the patients if the NICE guideline was aligned on other published guidelines and recommendations.	by the stakeholder single use of products is considered by the MHRA as part of their marketing authorisation in which we cross refer to.
Royal College of Nursing	Guideline	General	General	The revised recommendations within the guidelines seem appropriate in relation to the research presented.	Thank you for your comment. We welcome your support of the guideline.
Royal College of Nursing	Guideline	General	General	The rationale and impact sections for each change provides clear logical explanation and consideration of the impact on practice.	Thank you for your comment. We welcome your support of the guideline.
Royal College of Nursing	Guideline	General	General	The recommendations for future research are consistent with the gaps identified in current research and clinically relevant.	Thank you for your comment.
Royal College of Nursing	Guideline	General	General	Although changes to practice may be associated with a change in the resources required, it is anticipated that effective implementation of this guideline has potential for cost savings associated with reduced surgical site infections incidence and severity.	Thank you for your comment.
Cochrane Wounds	Guideline	General	General	Negative pressure wound therapy (NWPT) is widely used and disposable devices for use on closed surgical wounds for SSI prevention have been developed and are in use. There are also a number of on-going NIHR HTA funded trials of NPWT for different types of surgical wounds this area. We suggest that this is an important intervention to consider the evidence for in a SSI prevention Guideline. There is a current Cochrane Review in this area which is being updated and is out for peer review. In confidence (and pre-peer review so with caveats) the abstract has been included	Thank you for your comment. Negative pressure wound therapy was examined during the surveillance process and a decision was made that this would not be reviewed as part of this update. The following guidance has also been produced by NICE on negative pressure therapy: IPG467 - Negative Pressure wound therapy for the open abdomen. Additionally, guidance on PICO negative pressure wound dressings for closed surgical incisions is currently in development. This updated guideline NG74 will cross refer to these guidelines where appropriate.

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				here for reference. If you require any further information about planned or in-process reviews please don't hesitate to contact us. **Background** Indications for the use of negative pressure wound therapy (NPWT) are broad and include prophylaxis for surgical site infections (SSIs). While existing evidence for the effectiveness of NPWT remains uncertain, new trials necessitate an updated review of the evidence for the effects of NPWT on postoperative wounds healing by primary closure. **Objectives** To assess the effects of negative pressure wound therapy for preventing surgical site infection in wounds healing through primary closure. **Search methods** In February 2018 we searched: the Cochrane Wounds Specialised Register; CENTRAL, Ovid MEDLINE (including In-Process & Other Non-Indexed Citations); Ovid Embase and EBSCO CINAHL Plus. We also searched clinical trials registries for ongoing and unpublished studies, and checked reference lists of relevant included studies as well as reviews, meta-analyses and health technology reports to identify additional studies. There were no restrictions with respect to language, date of publication or study setting. **Selection criteria** We included trials if they allocated patients to treatment randomly and compared NPWT with any other type of wound dressing, or compared one type of NPWT with a different type of NPWT. **Data collection and analysis** Four review authors working independently assessed trials using pre-determined inclusion criteria. We carried out data extraction, risk of bias assessment using the Cochrane risk of bias tool and quality assessment according to GRADE methodology. **Main results** This second update includes 25 additional intervention trials, taking the total number to 30 (2957 participants) and two economic studies nested in trials. Surgeries included abdominal and colorectal (n = 5); caesarean section (n = 5); knee or hip arthroplasties (n = 5); groin surgery (n = 5); fractures (n = 5); laparotomy (n = 1); vascular surgery (n = 1); sternotomy (n = 1); breast reduction mammoplasty (n = 1) and mixed (n = 1). Four studies met our criteria for being at low risk of bias; six studies were at high risk of bias. The remaining 20 studies were unclear. The evidence was judged to be low or very low certainty for all outcomes, with serious risk of bias and very serious imprecision. **Primary outcomes** Mortality was reported in three studies (416 participants; follow-up 30 to 90 days or unspecified). There is no clear to suggest NPWT reduces the risk of death compared with standard dressings (RR 0.62, 95% CI 0.25 to 1.55; low certainty evidence; downgraded one level for serious risk of bias and one level for serious imprecision). Twenty-five studies reported on the outcome of SSI. The evidence from 23 studies (2533 participants; 2547 wounds; follow-up 30 days to 12 months or unspecified) showed that NPWT may reduce the rate of SSI (RR 0.64, 95% CI 0.52 to 0.79; low certainty evidence, downgraded two levels for serious risk of bias.	

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				Dehiscence was reported in 14 studies. We combined results from 12 studies (1507 wounds, 1475 participants; follow-up 30 days to an average of 113 days or unspecified) that compared NPWT with standard dressings. It is uncertain whether NPWT reduces risk of wound dehiscence compared with standard dressings (RR 0.79, 95% CI 0.55 to 1.14; very low certainty evidence, downgraded two levels for very serious risk of bias and one level for serious imprecision). **Secondary outcomes** Very low-certainty evidence from six trials (1021 participants) reported on the incidence of reoperation. We are uncertain whether NPWT increases or decreases reoperation rates when compared with a standard dressing (RR 1.04, 95% CI 0.70 to 1.54), downgraded for very serious risk of bias and serious imprecision) or if there is any clinical benefit associated with NPWT for reducing wound-related readmission to hospital within 30 days (RR 0.93, 95% CI 0.56 to 1.53; 7 studies, 1271 participants; very low certainty evidence, downgraded for very serious risk of bias and serious imprecision). It was also uncertain whether NPWT reduces the incidence of seroma compared with standard dressings (RR 0.67, 95% CI 0.45 to 1.00; 6 studies, 568 participants; very low certainty evidence, downgraded twice for very serious risk of bias in several domains and once for serious imprecision). It was uncertain if NPWT reduced or increased the risk of haematoma when NPWT was compared with a standard dressing (6 trials, 831 participants; RR 1.00; 95% CI 0.37 to 2.71; very low certainty evidence, downgraded for two levels for very serious risk of bias and two levels for very serious imprecision. It is uncertain if there is a higher risk of developing blisters when NPWT is compared with a standard dressing (6 studies, 597 participants; RR 7.00; 95% CI 3.33 to 14.70; very low certainty, downgraded two levels for very serious risk of bias and twice for very serious imprecision). Quality of life was not reported separately by group but was used in two economic evaluations to calculate a quality-adjusted life year (QALY). There was no clear difference in incremental QALYs for NPWT relative to standard dressing when results from the two trials were combined; (RR 0.00; 95% CI -0.00 to 0.00). The evidence was rated as moderate-certainty. One trial concluded that NPWT may be more cost-effective than standard care, estimating an Incremental cost-effectiveness ratio (ICER) value of £20.65 per QALY gained. A second cost-effectiveness study estimated that NPWT was cost-saving and improved QALYs compared with standard dressings. The overall quality of the reports was rated as very good; we did not grade the evidence beyond this as it was based on modelling assumptions. **Authors' conclusions** Despite the addition of 25 trials, results are consistent with our earlier review with the evidence judged to be low or very low certainty for all outcomes. Consequently, uncertainty remains about whether NPWT compared with a standard dressing reduces or increases the incidence of important outcomes such as dehiscence, seroma or cost. Given the cost and widespread use of NPWT for SSI prophylaxis, there is an urgent need for larger, well-designed and conducted trials to evaluate the effects of newer NPWT products designed for use on clean, closed surgical incisions. Such trials should focus initially on wounds that may be difficult to heal, such as sternal wounds or incisions on obese patients.	
Public Health England	Guideline	General	General	Peri-operative oxygen therapy – Should consider revisiting evidence to recommend as WHO guidelines recommend 80% fraction of inspired oxygen therapy based on moderate evidence. http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=1	Thank you for your comment. Maintenance of patient homeostasis was reviewed during the surveillance process and a decision was made that new evidence on perioperative oxygenation was unlikely to change guideline recommendations. Therefore, this topic was not reviewed as part of this update. Perioperative oxygenation is currently covered by recommendation 1.3.11 in the CG74 guideline. Your comment will be passed to the NICE surveillance team, for consideration when future updates of the guideline are planned.

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Public Health England	Guideline	General	General	Given that WHO guidelines now recommend the following and many UK hospital sites considering or delivering this it would be important that NICE reviews the evidence in this area. WHO SSI guidelines state "The panel suggests that preoperative oral antibiotics combined with mechanical bowel preparation (MBP) should be used to reduce the risk of SSI in adult patients undergoing elective colorectal surgery. http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=1	Thank you for your comment. The NICE Surveillance team has looked again at this topic and have concluded that antibiotic prophylaxis combined with mechanical bowel preparation should be updated and will be undertaken as part of a surveillance exceptional review.
Healthcare Infection Society	Guideline	General	General	We congratulate NICE for a high-quality review of preoperative skin preparations, which is long overdue. The recognition of the lack of evidence to distinguish between different concentrations of chlorhexidine in alcohol is very welcome. We support the recommendation for randomised trials to look at the outcomes following 0.5% and 2.0% chlorhexidine in alcohol.	Thank you for your comment. We welcome your support of the guideline.
University Hospital Birmingham NHS Foundation Trust	Guideline	General	General	We advocate routine re-drape and change of gloves prior to abdominal wall closure; would NICE have a view about this?	Thank you for your comment. Re-drape and change of gloves prior to abdominal wall closure was out of scope for four questions explored as part of this update. Incise drapes and gloves are currently covered by recommendations 1.3.3-1.3.4 and 1.3.6 in the CG74 guideline.
University Hospital Birmingham NHS Foundation Trust	Guideline	General	General	At Heartlands Hospital, Birmingham, we have introduced a 'bundle of interventions' based on existing NICE recommendations and have achieved a reduction in SSI rate from 29-22% in our emergency laparotomy and elective major colorectal patients. We have submitted a manuscript for peer-review but cannot (yet) provide you with published evidence. We have divided our bundle into pre / intra and post-op components and believe that this has facilitated engagement of clinicians with activity to reduce SSI. As well as addressing individual interventions that can reduce SSI; perhaps NICE would like to give their opinion on 'bundling' interventions and how this can help motivate clinicians to focus on reducing SSI.	Thank you for your comment. Bundled interventions were outside the scope of the four questions that were explored as part of this update. However, the committee were aware that interventions can be bundled and incorporated this approach to review question 1 which focused on nasal decolonisation (for more information, refer to Evidence Review A). Furthermore, please do share the successful implementation of the NICE guidance through the NICE Shared Learning Awards.
University Hospital Birmingham NHS Foundation Trust	Guideline	General	General	We have created a business case for routine surveillance of SSI in our major surgical patients. Would NICE have a view on whether surveillance in its own right is an intervention that can reduce SSI?	Thank you for your comment. SSI surveillance was out of scope for this update. However recommendations on SSI surveillance have been made in the Public Health guideline (PH36) Healthcare-associated infections: prevention and control. Furthermore a quality statement on surveillance has been made in QS49: Surgical site infection (Quality Statement 7).
Royal College of Paediatrics and Child Health	Guideline	General	General	This guideline is well written and addresses all relevant points.	Thank you for your comment. We welcome your support of the guideline.
Willingsford Ltd	Guideline	General	General	The guideline in many sections recommend the use of antiseptics, e.g. chlorhexidine for the disinfection of skin prior to surgery. However, new findings by Public Health England has demonstrated that antiseptics, contrary to common opinion, do give rise to antimicrobial resistance and the type of resistance may be associated with higher risks than that seen for antibiotics. Shepard et al. (2018) reported that exposure to sublethal doses of the antiseptic octenidine allowed several different strains of *Pseudomonas aeruginosa* to develop cross-tolerance to other antiseptics, and in one strain - which was isolated from a wound - this cross-tolerance extended to several different antibiotics. The level of tolerance was quite substantial, i.e. in several cases a 32-fold increase in concentrations of antiseptics was required to reach the same Minimum Inhibitory Concentration as seen in previously unexposed strains - causing de facto clinical resistance. Furthermore, this change was permanent. A study by the same group (Wand et al. 2016) found that *Klebsiella pneumoniae* was able to develop tolerance to chlorhexidine and that 5 out of 6 strains showed cross-resistance to the last-resort antibiotic, colistin. The ability of antiseptics to induce cross-resistance to other antiseptics and antibiotics in many bacterial strains therefore seem to be a common phenomenon and this is highly	Thank you for your comment. The committee identified antimicrobial resistance as an important outcome of interest and was explored as part of this review (highlighted in Table 1 in Evidence Review B). While no evidence was identified, the committee were aware that there is a potential risk of multidrug resistance. The committee took this into consideration when drafting research recommendations and included antimicrobial resistance as an important outcome of interest. Recommendation 1.2.3 also cross refers to the NICE guideline on antimicrobial stewardship: systems and processes for effective antimicrobial medicine use (NG15). For further information on the committee's discussion, please refer to Evidence Review B.

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				worrying because the resistance extends to several groups of compounds and will consequently have widespread impact. This needs to be considered in relation to antimicrobial stewardship.	
Becton Dickinson	Guideline	8-9	19-20 1	We believe that it should be clarified that the recommended 'antiseptic skin preparations' should be medicinal products. Note 1 in Table 1 mentions the two approved medicinal products at the time of the consultation. In addition, it states that other formulations of chlorhexidine in alcohol did not have UK marketing authorisation for these uses, and that the prescriber should follow relevant professional guidance, taking full responsibility for the decision. We welcome the addition of the footnote, and would suggest readers are pointed to the MHRA's guidance Note 8 as a useful guide (MHRA A guide to what is a medicinal product). Chlorhexidine is a common active ingredient used in both medicinal and biocidal products. As disinfection of the skin prior to invasive medical procedures is a medicinal indication, we believe that wherever possible only medicinal products should be used for this purpose in order to prevent surgical site infections, and therefore should be recommended. The MHRA, in Guidance Note 8 published in March 2016, stated that chlorhexidine is classified differently for different presentations and uses. These are: • Medical Use: Topical disinfectants for clinical use (e.g. pre-operatively) • Medical Device: Disinfectant for medical equipment • Biocide: General use as disinfectant (e.g. washing hands). The MHRA has confirmed that chlorhexidine containing products for disinfection of the skin prior to invasive medical procedures are classified as medicinal products; noting health risks associated with using chlorhexidine and highlighting the need to use an appropriately authorised product for its specific intended use, in accordance with manufacturer's instructions for use, as the best way of minimising harm. Companies or manufacturers selling chlorhexidine products, or allowing them to be supplied for a medicinal use, where there is no marketing authorisation for that product, are in breach of the Human Medicines Regulations 2012. Similarly in 2016, the RCS and MHRA issued a joint statement on the use of topical chlorhexidine for skin preparation prior to surgery, stating that operating theatres should be using the medicinally licensed product over those which are classed as a general disinfectant. Using the appropriately authorised product for its specific intended use, in accordance with the manufacturer's instructions for use, is the best way of minimising harm (Joint RCS/MHRA Statement on use of Topical Chlorhexidine for Skin Preparation Prior to Surgery). Therefore, it would be most beneficial to patients, and support effective risk/benefit surveillance in antiseptic usage, if this guideline were to emphasise that only an appropriately assessed medicinal product be used for antiseptic skin preparation prior to invasive surgical procedures.	Thank you for your comment. The footnote in recommendation 1.3.9 has been amended to highlight medicinal products to provide further clarification. The committee also acknowledges the importance of following MHRA advice regarding the application of skin antiseptics.
Action on Smoking and Health	Guideline	4	2-17	Whilst the guidance is regarding the 'prevention and treatment' of surgical site infections, there is little reference to the prevention of surgical site infections. In particular, there is no reference to smoking, a significant risk factor for surgical site infection. There is strong evidence of higher risks and worse surgical outcomes when a patient continues to smoke. The risks associated with smoking mean that it is not always safe for surgery to take place and, as a result, some surgeons will not carry out procedures until a	Thank you for your comment. Smoking cessation is out of scope for the four questions explored as part of this update. Information for patients and carers is currently covered by recommendations 1.1.1 to 1.1.4 in the CG74 guideline. Guidance on smoking cessation is also covered as part of NG92 guideline (Stop smoking interventions and services). Your comment will also be passed onto the NICE surveillance team, for consideration when future updates of the guideline are planned

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				patient is able to abstain from smoking.[i] Smokers are 38% more likely to die after surgery than non-smokers.[ii] Following surgery smokers: • **have higher risks of post-operative surgical site infection**[iii,iv,v,vi,vii,viii] • have impaired wound healing[ix,x,xi] • have higher risks of lung and heart complications[xii,xiii,xiv] • require longer hospital stays and higher drug doses[xv] • are more likely to be admitted to an intensive care unit[xvi] • have increased risk of emergency re-admission[xv] To emphasise the first point, smoking is significantly associated with wound infection after surgery, regardless of frequency and level of smoking behaviour.[iv] A randomized controlled trial following smoking and non-smoking participants found that, after reviewing a total of 228 wounds made in the participants, in smokers the wound infection rate was 12% compared with 2% in never smokers.[xvii] A review of 140 cohort studies found risk of surgical site infection for patients who smoke to be over 2 times that of a non-smoker.[xi] Furthermore, the risk of surgical site infection almost doubles if a patient smokes on the day of surgery.[xviii] Quitting smoking before surgery reduces the risk of postoperative complications.[v,xix] It reduces lung, heart and wound-related complications, it decreases wound healing time and reduces the average length of stay in hospital. All health professionals have a key role to play in encouraging smokers to quit and given current health concerns, future health concerns, and healthcare professional advice are ranked as the first, second and fourth most prominent reasons to trigger a quit attempt, respectively,[xx] surgery provides a prime opportunity to deliver smoking cessation support to patients. To make surgical care more effective and efficient, an integrated approach to patient care which includes joined up working between and across primary and secondary care, should be taken. This should take "fitness for surgery" into account and encourage smoking cessation prior to surgical intervention as good practice. GPs are normally the first point of contact for patients. As a matter of routine, they should identify smokers and offer smoking cessation interventions as recommended in NICE guidance NG92 (stop smoking interventions and services).[xxi] It is important that primary care physicians ensure their patients understand the consequences of smoking in the perioperative period and how quitting or temporarily abstaining can mitigate these risks. Surgery can and should be used as a "teachable moment" to promote smoking cessation. In addition to providing general anaesthesia before an operation, anaesthetists also assess patient wellbeing and fitness before surgery through what is now known as perioperative medicine. This involves discussing the risks and benefits of the proposed operation, ensuring that the appropriate care required for a full recovery is in position and providing timely perioperative interventions to reduce the risk of postoperative complications. Promoting smoking cessation through such assessments is, therefore, highly appropriate. Helping patients to stop or reduce the amount they smoke before any form of anaesthetic needs to become an important goal for anaesthetists. They can help by:	

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				• Discussing the merits of stopping smoking before surgery with patients. • Involving trained staff to assist in smoking cessation interventions. • Referring patients to a specialist smoking cessation service. • Involving hospital and community pharmacies in assisting in the process of smoking cessation. • Ensuring that smoking cessation is reinforced postoperatively for a long-term healthier lifestyle. The point at which the patient and surgeon agree that surgery should take place should also be seen as a 'teachable moment' where patients are often more receptive to intervention and more motivated to quit. When discussing the risks of any potential procedure, the surgeon should outline the reduction in risk associated with smoking cessation and work with perioperative medicine teams to increase a patient's fitness for surgery by encouraging those who smoke to stop. As outlined above, advice from healthcare professionals is a key motivator for quit attempts, therefore, advice from surgeons to quit smoking is appropriate and effective. Furthermore, NICE guidance (PH48)[xv] recommends that smokers using secondary care services are identified and offered intensive support to quit. Support should include; • the provision of stop smoking pharmacotherapies • the referral of patients who smoke to specialist stop smoking services • the adjustment of drug doses for people who have stopped smoking; drugs that are affected include clozapine, olanzapine, theophylline and warfarin. Whilst smoking cessation is the preferred option, where an individual is unable or unwilling to stop smoking, a program of harm reduction (NICE Guidance PH45) [xxii] should be followed to support temporary abstinence or smoking reduction. This should include the provision of behavioural support and nicotine replacement therapy and/or electronic cigarettes. Finally, the benefits of cessation are not just to the patient. Health problems associated with smoking have a severe financial impact on the NHS. Current smoking is estimated to cause over 430,000 admitted secondary care episodes in England annually, costing the NHS over £620 million.[viii] The smoking-attributable cost of wound infection following surgery costs the NHS in England at least £2.5 million annually, arising from 11,662 episodes of care.[viii] This figure is believed to almost certainly be an underestimate.[viii] Therefore, including the delivery of smoking cessation support in guidance on the prevention and treatment of surgical site infection is vital both for patient health and the NHS's financial sustainability.	
ENT UK	Guideline	4	2-8	Patient susceptibility to SSI is influenced by many factors including their health, nutritional status, diabetes, cancer, immunosuppression, concomitant treatments etc. It might therefore be useful to specify that the information and advice given will be tailored to the patient, as well as including standard information and advice.	Thank you for your comment. Patient susceptibility is out of scope for the four questions explored as part of this update. Information for patients and carers is currently covered by recommendations 1.1.1 to 1.1.4 in the CG74 guideline. NICE guideline NG45 on pre-operative tests makes recommendations on which tests to offer people before minor, intermediate and major or complex surgery, taking into account specific comorbidities (cardiovascular, renal and respiratory conditions and diabetes and obesity).
Stryker	Guideline	4	3	Leading science states that using an antiseptic pre-operatively will allow for a broad spectrum kill and persistence to reduce bacteria on patient and the risk of SSI. When it comes to using an antiseptic, an impregnated CHG cloth, that will not be rinsed off by the	Thank you for your comment. Preoperative showering is currently covered by recommendation 1.2.1 in CG74, which states that patients should be advised to shower or have a bath (or help patients to shower, bath or bed bath) using soap, either the day before,

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				patient, has demonstrated to leave considerably more CHG on the skin than a CHG soap/solution-based product, up to 27x the CHG with no gaps in coverage (Edmiston CE, et al., Preoperative Shower Revisited: Can High Topical Antiseptic Levels Be Achieved on the Skin Surface Before Surgical Admission?, J Am Coll Surg 2008;207:233-39.). This provides a cumulative, broad spectrum, and persistent application prior to surgery to reduce the risk of surgical site infections. Advising a patient to use an antiseptic the night before and morning of surgery will allow for sustained microbial kill of bacteria on the patient's skin and has demonstrated to have an impact on multiple service lines in hospitals. Evidence supports this in the use of multiple service lines, some examples are on total knee arthroplasty patients that saw a 73% reduction (Johnson AJ, et al., Chlorhexidine Reduces Infections in Knee Arthroplasty, J Arthroplasty. 2013 Jun;26(3):213-8) and total hip arthroplasty, which had a 71% reduction (Kapadia BH, et al., Pre-admission cutaneous chlorhexidine preparation reduces surgical site infections in total hip arthroplasty, J Arthroplasty.2013 Mar;28(3):490-3.). A consideration could be the use of an antiseptic bath prior to surgery to reduce the risk of surgical site infections would reduce risk of harm and rehabilitation from an infection for patients.	or on the day of surgery. This recommendation was outside of scope for this update. During the update of the recommendation on nasal decolonisation, the committee noted that a bundled approach may be taken which involves nasal decolonisation including a chlorhexidine wash. Therefore, evidence identified did demonstrate this bundled approach to be effective and therefore recommendations were made to reflect practice and the evidence of effectiveness. The guideline committee did note chlorhexidine wipes are available and these were discussed in the evidence review
University Hospital Birmingham NHS Foundation Trust	Guideline	5	2	I agree that patients should be encouraged to shower or have a bath (or patients should be helped to shower, bath 3 or bed bath) using soap, either the day before, or on the day of, surgery. However, this fails to recognise the reality of the modern NHS with patients admitted on the day of surgery for elective surgery, or admitted as emergencies. We advocate a 'pre-prep' wash of the surgical site, groins and perineum on table (under anaesthetic) with chlorhexidine soap. This is a pragmatic way to ensure all patient are physically clean prior to skin prep.	Thank you for your comment. Preoperative showering was out of scope for the four questions explored as part of this update. Preoperative showering is currently covered by recommendation 1.2.1 in the CG74 guideline.
DHSC - Advisory Committee on Antimicrobial Prescribing, resistance and Healthcare Associated Infection	Guideline	5	21-24	**1.2.6 Patient theatre wear** This remains unchanged since 2008 and does not take into account that many day case ophthalomology units do not require patients undergoing eye surgery under local anaesthetic to remove their own clothes and therefore they are not given 'specific theatre wear' although they do ensure that what they are wearing provides easy access to the operative site and for placing IV cannulae. It definitely takes into account the patients comfort and dignity. We would suggest that the wording should be changed to remove the term 'specific theatre wear' to allow for ophthalmology and similar types of surgery which would not require the removal of own clothes.	Thank you for your comment. The clinical effectiveness of patient theatre wear was reviewed during the surveillance process with no new evidence identified. Therefore, this topic was not reviewed as part of this update.
Infection Prevention Society	Guideline	5	6 to 9	Is this recommendation specifically related to patients who have tested positive for S. aureus in pre-assessment screening? Targeted screening is carried out for high risk surgery only, such as orthopaedics surgery. S. aureus is a likely cause of SSI for all surgical patients if no screening is carried out. Recommendation is not clear.	Thank you for your comment. The committee took your comment into consideration and has elaborated on its draft recommendation. The recommendation states that nasal decolonisation should be considered before procedures in which S. *aureus is* a likely cause of a surgical site infection. However, the recommendation continues to allow flexibility, the committee recommended that such procedures should be locally determined taking into account patient risk factors such as nasal carriage status and impact of infection. For further information, please refer to rationale and impact section in the guideline.
British Orthopaedic Association	Guideline	5	7	This is an excellent recommendation but we fear it is non-specific and will fail to be implemented. Would the panel consider specific examples, like cardiothoracic surgery or implant surgery, where the impact of infection is very high. It is suggested the text on guideline page 17, line 23, is also used here. Staphylococcus is a likely cause of any SSI.	Thank you for your comment. The committee took your comment into consideration and redrafted the recommendation. The new recommendation states that nasal decolonisation should be considered before procedures in which *S. aureus* is a likely cause of a surgical site infection. To allow flexibility between centres, the committee recommended that such procedures should be locally determined taking into account patient risk factors such as nasal carriage status and impact of infection. To facilitate this, references to specific surgeries were also removed. For further information, please refer to rationale and impact section in the guideline.
UK Clinical Pharmacy Association (UKCPA)	Guideline	5	7	Is the recommendation of eradication for all S.aureus patients now rather than MRSA colonised patients. Is this a correct reading of the guidance? How is our supply chain for Bactroban set up for such a major change in practice? We struggle to main MRSA coloniser supplies at present; a MSSA colonised cohort would see 15-20 fold increase in numbers based on current projection.	Thank you for your comment. The committee took your comment into consideration and has elaborated on its draft recommendation. The recommendation states that nasal decolonisation should be considered before procedures in which *S. aureus* is a likely cause of a surgical site infection. However, the recommendation continues to be locally determined

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Pharmacy Infection Network					taking into account the surgical procedure, patient risk factors and impact of surgery. For further information, please refer to rationale and impact section in the guideline.
Infection Prevention Society	Guideline	5	7	Why no statement on PI which appears to out perform mupirocin? Why has CHG wash not merited a statement as best evidence is for treatment that involves CHG wash regardless of nasal decolonisation?	Thank you for your comment. 1) During the review of the evidence, only one study was identified which compared mupirocin with 5% povidone iodine. This study did not identify a significant difference between the two interventions. Therefore, no recommendations were made about the use of povidone iodine. 2) The main focus of this review question was on nasal decolonisation. However during protocol development the guideline committee noted that a bundled approach (nasal decolonisation and chlorhexidine body wash) may be used. Therefore evidence which focused on bundled intervention was included.
Royal College of Nursing	Guideline	5	7	Although the recommendation is appropriate, as Staphylococcus aureus is a likely pathogen for many surgical incisions, the generic phrasing of the recommendation will make it challenging for clinicians to consistently define which procedures will be targeted. There is risk that this recommendation could potentially be implemented inconsistently between organisations. Examples of good practice may help illustrate and guide key high risk areas.	Thank you for your comment. The committee took your comment into consideration and has elaborated on its draft recommendation. The recommendation states that nasal decolonisation should be considered before procedures in which *S. aureus* is a likely cause of a surgical site infection. However, the recommendation continues to be locally determined taking into account the surgical procedure, patient risk factors and impact of surgery. For further information, please refer to rationale and impact section in the guideline.
Public Health England	Guideline	5	7	Nasal mupirocin - Suggest revisiting evidence given other guidelines (WHO) strongly recommend use of mupirocin for cardiothoracic and orthopaedic surgeries and indicate moderate levels of evidence for other types of surgery.	Thank you for your comment. The committee redraft the recommendation to state that that nasal decolonisation should be considered before procedures in which S. aureus is a likely cause of a surgical site infection as locally determined taking into account surgical procedure, patient risk factors and impact of infection. In order to allow centres some flexibility in terms of what is considered a high risk surgery for them, the committee did not define specific surgical procedures in the recommendation, but specified that this should be locally determined. For further information, please refer to rationale and impact section in the guideline. Furthermore, the committee were aware of the WHO Guideline however NICE and their guideline committees take an independent view and analysis of the evidence in forming its recommendations.
Healthcare Infection Society	Guideline	5	7	Mupirocin reduces S aureus infection in the short term but widespread use at this hospital in the past was associated with rise in resistance. If used in selected groups of patients e.g. MRSA resistance has not emerged. Use of mupirocin in up to 50% of operations i.e. S aureus a risk would increase resistance to mupirocin which is required for MRSA decolonisation. Screening would identify around 30% of patients as being carriers but another 20% will be intermittent carriers. Body wash is less of an issue regarding resistance. Mupirocin resistance is highly likely and surveillance is not going to prevent that rise.	Thank you for your comment. Antimicrobial resistance was an outcome of interest in this evidence review however comparative evidence was not identified. The committee did consider the risk of resistance and recommended that surveillance should be maintained to ensure good practice. As there was a lack of evidence on antimicrobial resistance, the committee consideerd this was worthy of further investigation and was therefore included as an outcome of interest in the 4 research recommendations made for this topic. Recommendation 1.2.3 also cross refers to the NICE guideline on antimicrobial stewardship: systems and processes for effective antimicrobial medicine use (NG15). For further information, please refer to the rationale and impact section, the committee's discussion of the evidence section and Appendix K, all of which are located in Evidence Review A.
Stryker	Guideline	5	7	The NICE draft states: "Consider nasal mupirocin in combination with a chlorhexidine body wash before procedures in which Staphylococcus aureus is a likely cause of a surgical site infection." Evidence supports the use of an impregnated CHG cloth that will not be rinsed off to increase the amount of CHG on a patient's skin. The persistence and broad spectrum kill of CHG, specifically to Staphylococcus aureus (Time Kill and MIC Testing conducted by an independent laboratory; data on file.), maintains and accumulates after multiple applications, up to 27x more CHG on the skin with no gaps in coverage using a cloth versus a solution/soap based CHG product (Edmiston CE, et al., Preoperative Shower Revisited: Can High Topical Antiseptic Levels Be Achieved on the Skin Surface Before Surgical Admission?, J Am Coll Surg 2008;207:233-39.). A consideration could be to consider nasal mupirocin in combination with a chlorhexidine impregnated cloth before procedures in which Staphylococcus aureus is a likely cause of a surgical site infection.	Thank you for your comment. During the committee discussion the committee did note that chlorhexidine wipes are also available for use. Discussions around the use of chlorhexidine wipes were captured within the other factors which the committee took into account section of the evidence review.
University Hospital	Guideline	5	General	I note that there is no comment in the draft guideline about the advisability of smoking cessation and weight loss prior to surgery for elective patients.	Thank you for your comment. Smoking cessation is out of scope for the four questions explored as part of this update. Information for patients and carers is currently covered by recommendations 1.1.1 to 1.1.4 in the CG74 guideline. Guidance on smoking cessation is

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Birmingham NHS Foundation Trust					also covered as part of NG92 guideline (Stop smoking interventions and services). Furthermore recommendations on weight loss prior to surgery were made in CG 189 Obesity: identification, assessment and management - recommendation 1.7.8. Your comment will also be passed onto the NICE surveillance team, for consideration when future updates of the guideline are planned.
ENT UK	Guideline	6	17	The use of prophylactic antibiotic therapy in the presence of implanted devices has little evidence and does not prevent colonisation by biofilms. Biofilms should be a priority for future research, as they are impervious to antibiotics, are probably the main reason for explantation of implanted devices in the head and neck. This would be a suitable research priority in terms of cost effectiveness, due to the high cost of implantable devices.	Thank you for your comment. Antibiotic prophylaxis was reviewed during the surveillance process and a decision was made that this would not be reviewed as part of this update. The topic of antibiotic prophylaxis is currently covered by recommendations 1.2.11 to 1.2.17 in the CG74 guideline. Your comment will be passed onto the NICE surveillance team, for consideration when future updates of the guideline are planned.
University Hospital Birmingham NHS Foundation Trust	Guideline	6	5	I agree that staff wearing non-sterile theatre wear should keep their movements in and out of the operating area to a minimum. We have achieved this by placing Internal locks on theatre doors that are locked once the surgery has started. We have also provided cordless telephones. These 2 practical initiaives have reduced footfall in theatre.	Thank you for your comment and for providing this information.
University Hospital Birmingham NHS Foundation Trust	Guideline	6	8	I am concerned that you have failed to mention routine use of oral antibiotics with mechanical bowel prep for patients undergoing elective colorectal surgery. The evidence appears strongly supportive of this measure: McSorley ST et al. Meta-analysis of oral antibiotics, in combination with preoperative intravenous antibiotics and mechanical bowel preparation the day before surgery, compared with intravenous antibiotics and mechanical bowel preparation alone to reduce surgical-site infections in elective colorectal surgery. BJS Open. 2018 May 10;2(4):185-194. doi: 10.1002/bjs5.68. eCollection 2018 Aug. Comparative Effectiveness and Risks of Bowel Preparation Before Elective Colorectal Surgery. Koller SE, Bauer KW, Egleston BL, Smith R, Philp MM, Ross HM, Esnaola NF. Ann Surg. 2018 Apr;267(4):734-742.	Thank you for your comment. The NICE Surveillance team has looked again at this topic and have concluded that antibiotic prophylaxis combined with mechanical bowel preparation should be updated and will be undertaken as part of a surveillance exceptional review.
Public Health England	Guideline	7	18	Hand decontamination – These guidelines contrast with those by World Health Organization (WHO), which advise antimicrobial soap and water followed by alcohol hand rub or antiseptic surgical solution. This may make it more challenging to change in practice if there are conflicting guidelines unless there is a rationale for changing evidence. http://apps.who.int/iris/bitstream/handle/10665/250680/9789241549882-eng.pdf?sequence=1	Thank you for your comment. Hand decontamination was reviewed as part of the surveillance process and a decision was made that this would not be reviewed as part of this update. Hand decontamination is currently covered by recommendations1.3.1 and 1.3.2 in CG74. Your comment will also be passed onto the NICE surveillance team, for consideration when future updates of the guideline are planned.
University Hospital Birmingham NHS Foundation Trust	Guideline	7	7	We would wish to see NICE explicitly recommending that antimicrobial prophylaxis should not be extended beyond the duration of the surgery. We still have surgeons advocating for "24 hours" of prophylaxis.	Thank you for your comment. Antibiotic prophylaxis was reviewed during the surveillance process and a decision was made that this would not be reviewed as part of this update. The topic of antibiotic prophylaxis is currently covered by recommendations 1.2.11 to 1.2.17 in the CG74 guideline. Your comment will be passed to the NICE surveillance team, for consideration when future updates of the guideline are planned.
Oxford University Hospitals NHS Foundation Trust	Guideline	8	14	Chlorhexidine 500mls is not licenced for this recommended use. Has the committee considered this issue?	Thank you for your committee. The committee did discuss marketing authorisation of different skin antiseptic products. The footnote in recommendation 1.3.9 has been amended to highlight the marketing authorisation to provide further clarification.
Clinisupplies Ltd.	Guideline	8	16	This states that "studies were also excluded if they: Examined closure of subcutaneous layer" but this is NOT included in the Table in Appendix A - Review Protocols. The other exclusion criteria are approximately the same but not identical. Having searched the Draft Guidance document this is the only time "subcutaneous layer" is mentioned apart from details of one of the included papers – see comment 2. Having discussed with many leading Healthcare Professionals on this, we are unclear as to why clinical papers including the subcutaneous layer would be excluded from consideration, as many Surgical Site Infections (SSIs) are to be found in the subcutaneous layer and should therefore be an important consideration. We would ask for the reasoning behind this	Thank you for your comment. The closure of the subcutaneous layer was considered to be out of scope by the guideline committee as this involved the use of drains. The closure of the subcutaneous layer was considered in studies which examined the closure of multiple layers of the skin however the subcutaneous layer was not looked at in isolation.

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				exclusion, as superficial incision SSIs have been included in other clinical papers which are included within the analysis (see comment 2).	
British Orthopaedic Association	Guideline	8	19	Given that NICE has previously examined the evidence and found alcoholic chlorhexadine has a similar effectiveness to alcoholic povidone-iodine we are surprised there is sufficient new evidence to change that guidance. Is the panel aware that there is approximately one theatre fire within NHS England each month due to the skin prep catching fire. Crucially alcoholic povidone iodine is not flammable and hence safer with respect to theatre fires.	Thank you for your comment. The rationale and impact section for this recommendation has been amended in light of your comment by removing the use of 'rare' and adding precautions in relation to flammable products and the risk of burns. Furthermore, reference to alcohol antiseptic solutions being flammable in evidence review B has been amended to some alcohol antiseptic solutions to reflect that alcoholic povidone iodine is not flammable. For further information, please refer to Evidence Review B.
Becton Dickinson	Guideline	8	19-20	We are concerned that the use of the wording 'options may include' weakens the recommendation and leaves ambiguity about the solutions that might be selected. Therefore we believe that the recommendation should be strengthened by amending the wording to 'options include those in table 1'.	Thank you for your comment. As well as making recommendations based on their knowledge and experience, the committee also took the quality of studies into consideration. The committee considered the evidence was not sufficient to make a stronger recommendation hence the use of 'options may include' in rec 1.3.9. For further information on the decision making process please refer to the 'rationale and impact' section.
Infection Prevention Society	Guideline	9	1	The first statement in the table statement is not supported by the evidence. Skin prep agents that include alcohol and either Pi or CHG have 2 active agents not one. It is therefore inappropriate to compare different agents unless both are aqueous or alcohol-based solutions. The majority of evidence in review B compares various mixtures of aqueous and alcohol based solutions and valid conclusions cannot be drawn about the difference efficacy of PI or CHD from combining these studies. The meta-analyses (review B, page 152) that compare alcohol with aqueous based solutions indicates that there is consistent evidence that alcohol based solutions are more effective that aqueous ones regardless of the second agent (albeit that some of the studies do not have an SSI outcome and should therefore be excluded). Therefore this a reasonable recommendation for the guideline to make based on the evidence. The meta-analysis of CHG in alc vs PI in alc (review B page 150) includes Savage and Xu which had an outcome measure of skin cultures not SSI and Broach which found no significant difference between CHG and PI. Berry (page 146) was excluded as poor quality in the 2008 guidelines and it did not have a robust method of defining and detecting SSI. The statement suggesting that CHG should be preferred is therefore based on 1 study – Tuilli. And the summary statistic is not significant. The Park study comparing aqueous PI and CHG (page 155) shows no difference in these agents. Taken together, the evidence therefore supports using alcohol based solutions where possible but is insufficient to make a strong recommendation about using CHG or PI.	Thank you for comment. While meta-analyses utilising all evidence were conducted, two separate network meta analyses and a meta regression model were also conducted, with the meta-regression being used in the decision making. This model assumed that the 4 treatment groups (Aqueous povidone iodine, chlorhexidine in alcohol, povidone iodine in alcohol and aqueous chlorhexidine) can be broken down to 1) alcohol compared to aqueous 2) povidone iodine compared to chlorhexidine. For further information on this model refer to Appendix H. Furthermore, studies such as Savage 2009 and Berry 1982 were not included in this analysis.
Infection Prevention Society	Guideline	9	1	This statement is not supported by the evidence (there is only one study that measures this and it favoured PI but was a non significant difference)	Thank you for your comment. The meta- regression model was used in the decision making process, which utilised direct and indirect evidence. The findings of the meta-regression showed that chlorhexidine in alcohol was associated with the lowest incidence of surgical site infections. Recommendation 1.3.9 provides an option for povidone-iodine only when chlorhexidine is contraindicated.
Infection Prevention Society	Guideline	9	1	The risk of CHG allergy although small needs to be mentioned	Thank you for your comment. Recommendations drafted by the guideline committee offer different options based the clinical scenario, which includes when chlorhexidine is contraindicated. Furthermore, hypersensitivity associated with chlorhexidine was further discussed in Evidence review B, Page 36, line 3.
Infection Prevention Society	Guideline	9	1	Table 1. Aqueous solution of chlorhexidine. The concentrations of these antiseptics are detailed in the evidence review; Page 192: Chlorhexidine in aqueous solution = Aqueous CH scrub (4%) and paint (2%), 0.5% CH in aqueous solution. Clinical practice in England for preparation of sites next to mucous membranes would not use these concentrations, as they are not available in the market. Aqueous CHG scrub 4% is available (as a single application and without paint), but is used only for surgical scrubbing of hands and bodywashing. Aqueous CHG solutions that are available and are routinely used for this application contain 0.012% CHG (Unisept/Tisept). Therefore, the recommendation to use aqueous CHG solutions is not supported by evidence relating to products available on the market and does not reflect practice.	Thank you for your comment. The footnote in recommendation 1.3.9 has been amended to highlight products and their associated marketing authorisations.

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Healthcare Infection Society	Guideline	9	1	Some patients cannot tolerate chlorhexidine or povidone iodine so alternative is needed. There is good evidence that 2% chlorhexidine in alcohol should be preferred to 0.5% chlorhexidine – see WHO recommendations.	Thank you for your comment. Only one study was identified which compared the effectiveness of 0.5% chlorhexidine in alcohol and 2% chlorhexidine in alcohol. When it came to the decision making process, the meta-regression was utilised. This model assumed that the 4 treatment groups (Aqueous povidone iodine, chlorhexidine in alcohol, povidone iodine in alcohol and aqueous chlorhexidine) can be broken down to 1) alcohol compared to aqueous 2) povidone iodine compared to chlorhexidine. As this model focused on the agents and excipients recommendations do not specify the concentrations that should be utilised. Furthermore, the committee were aware of the WHO Guidelines however NICE and their guideline committees take an independent view and analysis of the evidence in forming its recommendations.
Becton Dickinson	Guideline	9	5	We acknowledge and welcome that the updated recommendation include precautions to protect patient safety (risk of burns with diathermy). However, we believe this should be strengthened with the addition of the following recommendations, in line with the ChloraPrep SmPC and applicable to any other alcoholic based solutions: - Remove soaked materials, drapes or gowns before proceeding with the intervention - Do not use excessive quantities of product and do not allow the solution to pool in skin folds or under the patient or drip on sheets or other material in direct contact with the patient - Ensure no excess product is present prior to application of an occlusive dressing after the use of antiseptic skin preparation Indeed, NRLS/NHSLA data shows increasing rates of fire incidents: NHS England Surgical Safety Patient Safety Expert Group meeting notes (see also: Compensation for burns during surgery Surgical fires: perioperative communication is essential to prevent this rare but devastating complication FDA Preventing Surgical Fires) As alcohol-based preparations are flammable, these recommendations are essential for the patients' safety when this type of antiseptic skin preparation is used before surgery.	Thank you for your comment. The committee were in agreement and the rationale and impact section for this recommendation (rather than the recommendation itself) has been amended in light of your comment by adding precautions in relation to flammable products and the risk of burns. For further information, please refer to Evidence Review B.
Infection Prevention Society	Guideline	9	Note	Pre-operative skin antiseptics are applied to intact skin and sold as medicinal products as General Sales List (GSL) not Prescription Only (PO). Therefore, these products are not prescribed. The availability of antiseptics for use for pre-operative skin preparation in the market is currently restricted due to an outstanding (since 2016), yet to be published, public consultation on the specific requirements for antiseptics from the MHRA.	Thank you for your comment. The footnote in recommendation 1.3.9 has been amended to highlight medicinal products to provide further clarification.
Infection Prevention Society	Guideline	9	Note	this implies that other products are not deemed safe to use whereas in reality MRHA is refusing to evaluate and licence any other products and therefore they cannot obtain 'authorisation'.	Thank you for your comment. This is outside the remit of NICE. The footnote in recommendation 1.3.9 has been amended to highlight medicinal products to provide further clarification.
Deltex Medical Limited	Guideline	10	1	We are concerned that there is not enough clarity around the recommendation to 'maintain adequate perfusion during surgery'. It has been clinically proven multiple times that Surgical Site Infections (SSI's) are increased if the patient's haemodynamics are not correctly managed during surgery. There are now multiple Randomised Controlled Trials (RCT's) showing significant reductions in post-operative SSI's when a haemodynamic protocol following the Oesophageal Doppler Monitor (ODM) is utilised. The most recent multi-centre RCT published in the BJA in March 2018 (FEDORA) showed an 80% reduction in superficial SSI's and a 76% reduction in deep SSI's between the intervention and control groups. These SSI's are caused primarily due to sub-optimal management of the patients haemodynamics (blood flow and blood pressure) during surgery and should be a NEVER event as they are completely avoidable. The ODM has NICE guidance (MTG3) and continues to demonstrate reductions across all post-operative complications when used in conjunction with a haemodynamic protocol. Therefore it show be made very clear in these	Thank you for your comment. There is currently NICE guidance available on oesophageal doppler unit: MTG3 CardioQ- ODM oesophageal doppler monitor. Furthermore, during the surveillance process new evidence was identified with regards to perioperative perfusion and hydration. This will be covered by a new NICE guideline on perioperative care in adults which is currently in development.

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				Guidelines that during surgery the patient should be normovolaemic with an adequate blood pressure for perfusion of the vital organs	
Medtronic	Guideline	10	10	**Antiseptics and antibiotics before wound closure section.** We recommend that the Committee consider the use of antibacterial envelopes in cardiac implantable electronic devices (CIEDs) to prevent surgical site infection within the recommendations. TYRX™ Absorbable Antibacterial Envelope (Medtronic plc, Mounds View, MN) is used during surgical implantation of CIEDs to anchor the device and prevent infection. CIEDs include Pacemakers (PM), Implantable Cardioverter-Defibrillators (ICDs), and Cardiac Resynchronisation Therapy (CRT) devices. By placing CIEDs within a TYRX antibacterial envelope at implant, infection rate is significantly reduced in patients at risk of device-related infections by 69% to 100% compared to patients who did not receive TYRX.[1-4] TYRX is already accepted and in use in the NHS, with approximately 70 centres across the UK currently using this technology, either with selected high-risk patients or in all CIED patients. TYRX has been routed to the NICE Technology Appraisal Programme and is currently in the scoping phase. Hence it is important that the Committee are made aware of this technology and consider it for potential inclusion in the Clinical Guideline in line with the TA process.	Thank you for your comment. The use of antibacterial envelopes is outside the scope of this current update of the guideline. The use of absorbable antibacterial envelope is currently being considered by the NICE Technology Appraisals team.
British Orthopaedic Association	Guideline	10	11	Was the guideline panel aware of this study? This are numerous case series also. https://www.ncbi.nlm.nih.gov/pubmed/16094267	Thank you for your comment. The Cheng 2005 study (*Efficacy of dilute betadine solution irrigation in the prevention of postoperative infection of spinal surgery*) which has been highlighted examines the use of betadine irrigation of spinal surgical wounds. This study does not match the review protocol for this evidence review. Additionally, in this review evidence from RCTs were prioritised, therefore case series studies were excluded.
DHSC - Advisory Committee on Antimicrobial Prescribing, resistance and Healthcare Associated Infection	Guideline	10	14-19	**1.3.20 and 21 Closure methods** There seems to be no evidence reviewed or recommendations made about other skin closure methods such as tissue adhesives which is widely used for some types of surgery.	Thank you for your comment. Tissue adhesives were listed as interventions of interest in the review protocol, however no studies were identified which t meet the inclusion criteria. The committee agreed that tissue adhesives play an important role in clinical practice. So, they have added a research recommendation. Evidence review D has been amended accordingly For further information, please see Appendix I in evidence review D.
Royal College of Nursing	Guideline	10	15	We welcome the proposed change.	Thank you for your comment.
Public Health England	Guideline	10	15	Closure methods – Other than wound dehiscence, scarring can also be a consideration with staples/clips. Is there a reason why the recommendation shouldn't extend to all procedures (rather than just C-section)?	Thank you for your comment. Seven studies were identified which compared staples with sutures. Among these studies 3 studies focused on caesarean sections. The committee noted that there was not enough evidence to recommend sutures over staples in all studies. For further information, please see rationale and impact in Evidence Review D.
British Orthopaedic Association	Guideline	10	18	Key evidence has been excluded. See comment 10.	Thank you for your comment. As specified in the review protocol (Evidence Review D, Appendix A) RCTs with a sample size of ≥ 200 subjects were included. The Sprowson 2014 paper was excluded from the review because it is a quasi-randomised trial. In the study, it is stated that treatment allocation was based on date of surgery. This means that allocation was not truly random and a study with such design carries a greater risk of selection bias. Furthermore, our protocol states that quasi-randomised trials would only be utilised if less than 5 RCTs were identified. As we were able to meet our defined threshold, this study was excluded. We also ran additional sensitivity analyses, and identified that inclusion of this study did not greatly impact our overall results and thus did not change the conclusions made by the committee. The exclusion list has been updated to reflect our reasoning for exclusion.

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Johnson & Johnson Medical Ltd	Guideline	10	18	Johnson & Johnson Medical Ltd. welcomes the recommendation by NICE for the NHS to consider using triclosan-coated sutures to reduce the risk of SSI. This recommendation to the NHS further builds on recent endorsements from the following organisations: World Health Organisation, Center for Disease Control and Prevention and EUnetHTA, which all include evidence based recommendations for the use of triclosan-coated sutures to reduce the risk of SSI.	Thank you for your comment. We welcome your support of the guideline.
Johnson & Johnson Medical Ltd	Guideline	10	18	Whilst acknowledging that recommendation 1.3.12 by NICE is for the NHS to consider triclosan-coated sutures to reduce the risk of SSI, and in the 'Rationale and Impact' section of Guideline the Committee agreed that the evidence overall favoured triclosan-coated sutures over standard sutures for reducing SSI, we would like to flag a concern at this stage that the "especially for paediatric surgery" reference in the recommendation itself could be incorrectly interpreted as "only in paediatric surgery". For clarity, we request that the GDG reflect on this comment and consider revising the recommendation 1.3.12 to simply remove the explicit emphasis to paediatrics, as per the WHO, CDC and EUnetHTA approach.	Thank you for your comment. Studies which compared triclosan sutures to non-triclosan sutures explored a number of different surgery types. Among the studies, the committee found the evidence for the use of triclosan sutures in paediatric surgery to be more compelling. For further information on the committee's discussion of the evidence, please refer to Evidence Review D. Furthermore, the committee were aware of the WHO, CDC and EUnetHTA Guidelines however NICE and their guideline committees take an independent view and analysis of the evidence in forming its recommendations.
Oxford University Hospitals NHS Foundation Trust	Guideline	10	18	Given that the pooled evidence suggests the use of Triclosan sutures reduces the number of SSIs and the cost of the sutures is likely to be outweighed by the reduction of Surgical Site Infection, should the recommendation be stronger?	Thank you for your comment. As well as using their clinical knowledge, the committee also took the quality of evidence into consideration when drafting recommendations. The committee noted that there was limited evidence of varying quality which did not capture all populations. Due to this a strong recommendation could not be made. For further information on committee's discussion of the evidence please refer to Evidence Review D.
University Hospital Birmingham NHS Foundation Trust	Guideline	10	18	We are concerned that the recommendation to "consider using triclosan-coated sutures, especially for paediatric surgery" does not appropriately reflect the weight of evidence for Plus sutures. The available Level 1 evidence appears robust; example: Meta-analysis and trial sequential analysis of triclosan-coated sutures for the prevention of surgical-site infection. de Jonge SW, Atema JJ, Solomkin JS, Boermeester MA. Br J Surg. 2017 Jan;104(2):e118-e133. doi: 10.1002/bjs.10445.	Thank you for your comment. Studies which compared triclosan sutures to non-triclosan sutures explored a number of different surgery types. Among the studies, the committee found the evidence for the use of triclosan sutures in paediatric surgery to be compelling. For further information on the committee's discussion of the evidence, please refer to Evidence Review D.
Cochrane Wounds	Guideline	10	6 to 9	Regarding the following recommendations in the draft Guideline which are unchanged from 2008 • Do not use wound irrigation to reduce the risk of surgical site infection. [2008] • Do not use intracavity lavage to reduce the risk of surgical site infection. [2008] We would like to bring to your attention the findings of a recent Cochrane review and flag an on-going network meta-analysis in this area which is being conducted by researchers at the University of Bristol and which we (Cochrane Wounds members) are collaborating on. The network meta-analysis is using data from the Cochrane review below: we have included a copy of the abstract from the published review for reference and suggest this may be an area of future focus. Norman G, Atkinson RA, Smith TA, Rowlands C, Rithalia AD, Crosbie EJ, Dumville JC. Intracavity lavage and wound irrigation for prevention of surgical site infection. Cochrane Database of Systematic Reviews 2017, Issue 10. Art. No.: CD012234. DOI: 10.1002/14651858.CD012234.pub2. **Background** Surgical site infections (SSIs) are wound infections that occur after an operative procedure. A preventable complication, they are costly and associated with poorer patient outcomes, increased mortality, morbidity and reoperation rates. Surgical wound irrigation is an intraoperative technique, which may reduce the rate of SSIs through removal of dead or	Thank you for your comment. During the surveillance process the evidence for intercavity lavage and wound irrigation was examined, and a decision was made that new evidence was unlikely to change current recommendations. Therefore this was not reviewed as part of this update. Your comment will also be passed on the NICE surveillance team, for consideration for when future updates of the guideline are planned.

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				damaged tissue, metabolic waste, and wound exudate. Irrigation can be undertaken prior to wound closure or postoperatively. Intracavity lavage is a similar technique used in operations that expose a bodily cavity; such as procedures on the abdominal cavity and during joint replacement surgery. **Objectives** To assess the effects of wound irrigation and intracavity lavage on the prevention of surgical site infection (SSI). **Search methods** In February 2017 we searched the Cochrane Wounds Specialised Register; the Cochrane Central Register of Controlled Trials (CENTRAL); Ovid MEDLINE; Ovid Embase and EBSCO CINAHL Plus. We also searched three clinical trials registries and references of included studies and relevant systematic reviews. There were no restrictions on language, date of publication or study setting. **Selection criteria** We included all randomised controlled trials (RCTs) of participants undergoing surgical procedures in which the use of a particular type of intraoperative washout (irrigation or lavage) was the only systematic difference between groups, and in which wounds underwent primary closure. The primary outcomes were SSI and wound dehiscence. Secondary outcomes were mortality, use of systemic antibiotics, antibiotic resistance, adverse events, re-intervention, length of hospital stay, and readmissions. **Data collection and analysis** Two review authors independently assessed studies for inclusion at each stage. Two review authors also undertook data extraction, assessment of risk of bias and GRADE assessment. We calculated risk ratios or differences in means with 95% confidence intervals where possible. **Main results** We included 59 RCTs with 14,738 participants. Studies assessed comparisons between irrigation and no irrigation, between antibacterial and non-antibacterial irrigation, between different antibiotics, different antiseptics or different non-antibacterial agents, or between different methods of irrigation delivery. No studies compared antiseptic with antibiotic irrigation. *Surgical site infection* Irrigation compared with no irrigation (20 studies; 7192 participants): there is no clear difference in risk of SSI between irrigation and no irrigation (RR 0.87, 95% CI 0.68 to 1.11; I2 = 28%; 14 studies, 6106 participants). This would represent an absolute difference of 13 fewer SSIs per 1000 people treated with irrigation compared with no irrigation; the 95% CI spanned from 31 fewer to 10 more SSIs. This was low-certainty evidence downgraded for risk of bias and imprecision. Antibacterial irrigation compared with non-antibacterial irrigation (36 studies, 6163 participants): there may be a lower incidence of SSI in participants treated with antibacterial irrigation compared with non-antibacterial irrigation (RR 0.57, 95% CI 0.44 to 0.75; I2 = 53%; 30 studies, 5141 participants). This would represent an absolute difference of 60 fewer SSIs per 1000 people treated with antibacterial irrigation than with non-antibacterial (95% CI 35 fewer to 78 fewer). This was low-certainty evidence downgraded for risk of bias and suspected publication bias.	

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				Comparison of irrigation of two agents of the same class (10 studies; 2118 participants): there may be a higher incidence of SSI in participants treated with povidone iodine compared with superoxidised water (Dermacyn) (RR 2.80, 95% CI 1.05 to 7.47; low-certainty evidence from one study, 190 participants). This would represent an absolute difference of 95 more SSIs per 1000 people treated with povidone iodine than with superoxidised water (95% CI 3 more to 341 more). All other comparisons found low- or very low-certainty evidence of no clear difference between groups. Comparison of two irrigation techniques: two studies compared standard (non-pulsed) methods with pulsatile methods. There may, on average, be fewer SSIs in participants treated with pulsatile methods compared with standard methods (RR 0.34, 95% CI 0.19 to 0.62; I2 = 0%; two studies, 484 participants). This would represent an absolute difference of 109 fewer SSIs occurring per 1000 with pulsatile irrigation compared with standard (95% CI 62 fewer to 134 fewer). This was low-certainty evidence downgraded twice for risks of bias across multiple domains. *Wound dehiscence* Few studies reported wound dehiscence. No comparison had evidence for a difference between intervention groups. This included comparisons between irrigation and no irrigation (one study, low-certainty evidence); antibacterial and non-antibacterial irrigation (three studies, very low-certainty evidence) and pulsatile and standard irrigation (one study, low-certainty evidence). **Secondary outcomes** Few studies reported outcomes such as use of systemic antibiotics and antibiotic resistance and they were poorly and incompletely reported. There was limited reporting of mortality; this may have been partially due to failure to specify zero events in participants at low risk of death. Adverse event reporting was variable and often limited to individual event types. The evidence for the impact of interventions on length of hospital stay was low or moderate certainty; where differences were seen they were too small to be clinically important. **Authors' conclusions** The evidence base for intracavity lavage and wound irrigation is generally of low certainty. Therefore where we identified a possible difference in the incidence of SSI (in comparisons of antibacterial and non-antibacterial interventions, and pulsatile versus standard methods) these should be considered in the context of uncertainty, particularly given the possibility of publication bias for the comparison of antibacterial and non-antibacterial interventions. Clinicians should also consider whether the evidence is relevant to the surgical populations under consideration, the varying reporting of other prophylactic antibiotics, and concerns about antibiotic resistance. We did not identify any trials that compared an antibiotic with an antiseptic. This gap in the direct evidence base may merit further investigation, potentially using network meta-analysis; to inform the direction of new primary research. Any new trial should be adequately powered to detect a difference in SSIs in eligible participants, should use robust research methodology to reduce the risks of bias and internationally recognised criteria for diagnosis of SSI, and should have adequate duration and follow-up.	
DHSC - Advisory Committee on Antimicrobial Prescribing, resistance and Healthcare	Guideline	11	1-2	**1.3.22 Wound dressings** Negative pressure wound therapy is sometimes used on surgical wounds healing by primary intention particularly when exudate is expected to be high or dehiscence higher risk due to patient risk factors such a high BMI. This growing intervention has not been considered.	Thank you for your comment. Negative pressure wound therapy was examined during the surveillance process and a decision was made that this would not be reviewed as part of this update. The following guidance has also been produced by NICE on negative pressure therapy: IPG467 - Negative Pressure wound therapy for the open abdomen. Additionally, guidance on PICO negative pressure wound dressings for closed surgical incisions is currently in development. This updated guideline NG74 will

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Associated Infection					cross refer to these guidelines where appropriate. Your comment will also be passed onto the NICE surveillance team, for consideration for when future updates of the guideline are planned.
Smith & Nephew	Guideline	11	1-3	We would like to suggest that a risk stratification recommendation is included to identify the appropriate type of dressing for patients with different risk factors for developing SSI. We are aware that a guidance is currently in process for PICO NPWT dressings for closed surgical incisions, and if this is published then it may be useful to create a link to this guideline under the wound dressings section. The draft guidelines for PICO NPWT currently state that patients who are at high risk of developing an SSI as per risk factors described in 'preventing and treating SSI' guidance, should be considered for PICO. All other patients e.g. low risk of developing SSI, should get an interactive dressing.	Thank you for your comment. Negative pressure wound therapy was examined during the surveillance process and a decision was made that this would not be reviewed as part of this update. The following guidance has also been produced by NICE on negative pressure therapy: IPG467 - Negative Pressure wound therapy for the open abdomen. Additionally, guidance on PICO negative pressure wound dressings for closed surgical incisions is currently in development. This updated guideline NG74 will cross refer to these guidelines where appropriate.
Willingsford Ltd	Guideline	11 12	18-23 1-8	In relation to the dressing of wound to heal by primary and secondary intention: 1) Dumville et al. 2016 reviewed evidence regarding the ability of dressings vs. no dressing to reduce surgical site infections and concluded: "It is uncertain whether covering surgical wounds healing by primary intention with wound dressings reduces the risk of SSI, or whether any particular wound dressing is more effective than others in reducing the risk of SSI, improving scarring, reducing pain, improving acceptability to patients, or is easier to remove." 2) The FDA in 2016 in an executive review concluded that dressings containing antibiotics or antiseptics do not have any effect against wound infections or in supporting wound healing. 3) A large number of studies have shown that antiseptics are cytotoxic and this effect will necessary interfere with the healing process as the compounds will kill the newly formed cells. 4) As outlined above under note 1, it has very recently been shown that both antibiotics and antiseptics will contribute to the development of antimicrobial resistance and these new data indicate that this risk is greater with antiseptics due to their ability to cause cross-tolerance. Current status is consequently that there are no studies that clearly support a specific wound dressing that can reduce the risk of infection and/or be used for the treatment of an infected wound, even if the risk of creating AMR is ignored. Newer studies have found that NPWT, e.g. VAC or PICO, can be used preventively to reduce, but not eliminate the risk of SSI and once treatment failure has occurred, NPWT can only be used on wounds covered by less than 40% slough, it is not directly effective in removing infection and many wounds do not respond to NPWT. Micropore particle technology (MPPT) is a novel technology that reliably removes wound infections and support healing for a wide range of acute and chronic wounds and ulcers. This approach does not kill the bacteria but instead creates conditions that enable the body's immune system to establish the correct balance of microbes in the wound, and achieving this balance means removing the infection. The technology does not rely on any antimicrobial effects and will consequently not contribute to AMR. - In a clinical study of necrotic, infected wounds, MPPT removed wound infections and promoted start of healing 60% quicker than a topical antibiotic (gentamicin) and a topical antiseptic (iodine) and reduced hospitalisation days for acute wounds, e.g. dehisced surgical wounds (41%), diabetic foot (31%) and venous leg ulcers (19%). - In a clinical audit at Bristol University Hospital for dehisced surgical wounds, MPPT was compared to standard-of-care, which consists of 1 week with UrgoClean to remove slough from the wound followed by 2-more weeks with NPWT to promote healing. MPPT was able for all wounds in the evaluation to reach this healing stage, i.e. free of infection and start of healing, following once daily application for 4-5 days; this included wounds that had not responded to NPWT. Cost estimates indicated savings of 67%. While it was an open evaluation against historic data, the size of the difference in time	Thank you for your comment. Wound dressings was reviewed as part of the surveillance process and a decision was made that this would not be reviewed as part of this update as new evidence was unlikely to change the current recommendations. Your comment will also be passed onto the NICE surveillance team, for consideration when future updates of the guideline are planned. The following guidance has also been produced by NICE on negative pressure therapy: IPG467 - Negative Pressure wound therapy for the open abdomen. Additionally, guidance on PICO negative pressure wound dressings for closed surgical incisions is currently in development. This updated guideline NG74 will cross refer to these guidelines where appropriate.

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				to healing between NPWT and MPPT, means that the difference was real. All wounds closed following MPPT. - In community care, MPPT has been used on a range of acute and chronic wounds and ulcers that had not responded to other approaches, including NPWT, and in all cases MPPT was able to promote healing. - MPPT is not antimicrobial and it has not given rise to any adverse events such as wound irritation, allergy, bleeding or any signs of cytotoxicity. It has been used on exposed bone and tendon as well as on sutures. MPPT acts as a passive immunotherapy that through the microbiome supports the immune system such that the immune cells can remove wound infections and regain control of the healing process. MPPT does not contribute to AMR. Clinical findings show that it can be used on wounds to close by secondary intention in connection with surgery as well as later in case of wound dehiscence. The only limitation is that it should not be applied to an actively bleeding wound as the blood will clog the pores inside the particles and they will lose their effect. MPPT does not have to be covered by a secondary dressing, which makes it easy to use in difficult-to-dress locations. Clinical data show that it removes wound infections and facilitates healing 60% quicker than antibiotics and antiseptics, and for dehisced surgical wounds, in 4-5 days it reached the same stage of wound healing that required 3 weeks using standard-of-care based on NPWT. MPPT should consequently be considered for use after surgery as an option to prevent infection and support healing for wounds to close by secondary intention as well as in case of treatment failure leading to wound dehiscence for the removal of wound infection and support of healing.	
University Hospital Birmingham NHS Foundation Trust	Guideline	11	2	We would like the committee's view on the use of topical negative pressure dressings on the closed incision for high risk wounds. We recognise the recent publication of the NEPTUNE study that is not supportive of the use of TNP dressings (Negative Pressure Wound Therapy Use to Decrease Surgical Nosocomial Events in Colorectal Resections (NEPTUNE): A Randomized Controlled Trial. Murphy PB, Knowles S, Chadi SA, Vogt K, Brackstone M, Van Koughnett JA, Ott MC. Ann Surg. 2018 Nov 29. doi: 10.1097/SLA.0000000000003111.) However, the other available evidence appears supportive and this should be addressed by the committee (Negative Pressure Wound Therapy for Closed Laparotomy Incisions in General and Colorectal Surgery: A Systematic Review and Meta-analysis. Sahebally SM, McKevitt K, Stephens I, Fitzpatrick F, Deasy J, Burke JP, McNamara D. JAMA Surg. 2018 Nov 1;153(11):e183467. doi: 10.1001/jamasurg.2018.3467.)	Thank you for your comment. Negative pressure wound therapy was examined during the surveillance process and a decision was made that this would not be reviewed as part of this update. The following guidance has also been produced by NICE on negative pressure therapy: IPG467 - Negative Pressure wound therapy for the open abdomen. Additionally, guidance on PICO negative pressure wound dressings for closed surgical incisions is currently in development. This updated guideline NG74 will cross refer to these guidelines where appropriate. Your comment will also be passed on the NICE surveillance team, for discussion for when future updates of the guideline are planned.
British Orthopaedic Association	Guideline	14	10	Why have the committee fixed on mupirocin when other products are available, purporting to do the same. Other products have wide use for this indication across the NHS. Surely we should widen the research recommendation to include them.	Thank you for your comment. During the development of the review protocol, the committee did take other interventions into consideration (highlighted in Table 1 in Evidence Review A). However, no studies of relevant study design were identified which examined the effectiveness of mupirocin alternatives. Therefore the committee were unable to make recommendations on the use of available alternatives . However, the committee incorporated these alternative interventions into the four research recommendations developed as part of evidence review A (please see Appendix K). For further information, please refer to 'The committee's discussion of the evidence' in evidence review A.
British Infection Association	Guideline	14	10	The testing of mupiricin is required but in addition we would include testing naseptin or octenidine in nasal decolonisation, not only mupirocin, particularly given concerns about the induction of resistance.	Thank you for your comment. During the development of the review protocol, the committee did take other interventions into consideration (highlighted in Table 1 in Evidence Review A). However, no studies of relevant study design were identified which examined the effectiveness of mupirocin alternatives. Therefore the committee were unable to make recommendations on the use of available alternatives. However, the committee incorporated these alternative interventions into the four research recommendations developed as part of evidence review A (please see Appendix K). For further information, please refer to 'The committee's discussion of the evidence' in evidence review A.
Royal College of Anaesthetists	Guideline	14	13	**Universal nasal decolonisation and chlorhexidine wash in patients undergoing surgery** - Concerned by the recommendation for universal nasal decolonisation and	Thank you for your comment. The committee took your comment into consideration and redrafted the recommendation. The new recommendation states that nasal decolonisation

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				chlorhexidine wash in patients undergoing surgery where there is a high risk of staph aureus infection. The evidence seems weak with the 9 RCTs that were finally included mostly being rated as of low or very low quality. This was mainly because of randomisation bias. It is thought that the evidence only really supports such measures in patients shown to be nasal carriers of staph aureus but because of the economics the review team have chosen to recommend it for all patients undergoing certain types of surgery. These surgeries are not defined but say that clinical teams will know what these are. It is also not specified when to start and finish the treatment. It all seems a bit haphazard and whilst it is stated that this is to make practice more consistent, it is unclear whether it will achieve this aim at all. The question of antibiotic resistance is dismissed as being unlikely. It is preferred for the team to specify a regimen and types of surgery to be included in this recommendation and ideally, that treatment be limited to those found to be carriers, although it is acknowledged that testing is not 100% effective.	should be considered before procedures in which S*. aureus* is a likely cause of a surgical site infection. To allow flexibility, the committee recommended that such procedures should be locally determined taking into account patient risk factors such as nasal carriage status and impact of infection. To facilitate this, references to specific surgeries were also removed. With regards to timing of nasal decolonisation, the committee noted that mupirocin and chlorhexidine bundle can be given 3 days prior to surgery and up to 3 days after. However, with no evidence exploring the effectiveness of the timing of nasal decolonisation, the committee were unable to comment on when the bundle should be administered. Additionally the committee did identify timing of nasal decolonisation as an important area of research and drafted a research recommendation. For further information on committee's discussion of the evidence please refer to Evidence Review A.
Royal College of Nursing	Guideline	16	17- 19	Nasal decolonisation treatment We are concerned that these recommendations could potentially cause confusion and lack of consistency in care. The guideline states that the development committee were unable to define specialities, patient group, or timings of decolonisation due to lack of evidence. It would seem unwise therefore to make any recommendation regarding treatment. It was stated that the guideline better reflects current practice and allows centres more flexibility, however this appears to reiterate the fact that there is no consistency of treatment. If there is insufficient evidence the guideline should just state that it is unable to make a recommendation. There is no benefit to say '*you can if you want'.* This does not deal with the current variation in practice.	Thank you for your comment. The committee took your comment into consideration and redrafted the recommendation. The new recommendation states that nasal decolonisation should be considered before procedures in which S. aureus is a likely cause of a surgical site infection. To allow flexibility, the committee recommended that such procedures should be locally determined taking into account patient risk factors such as nasal carriage status and impact of infection. To facilitate this, references to specific surgeries were also removed. With regards to timing of nasal decolonisation, the committee noted that mupirocin and chlorhexidine bundle can be given 3 days prior to surgery and up to 3 days after. However, with no evidence exploring the effectiveness of the timing of nasal decolonisation, the committee were unable to comment on when the bundle should be administered. Additionally the committee did identify timing of nasal decolonisation as an important area of research and drafted a research recommendation. For further information on committee's discussion of the evidence please refer to Evidence Review A
Royal College of Nursing	Guideline	16	18	Nasal decolonisation treatment We are concerned that this recommendation will cause a significant cost implication to many trusts. As the guideline development committee has identified that there is limited evidence of the benefit of nasal decolonisation, the cost of swabbing and treating will add an undue burden on NHS Trusts.	Thank you for your comment. The committee's interpretation of the systematically identified and appraised evidence and original economic evaluation was that nasal decontamination is likely to reduce the rate of SSIs in a way that leads to a net reduction in costs, saving trusts money overall. However, as detailed in the relevant 'rationale and impact' section, the committee recognised that the evidence was not clear enough to make a strong ('offer') recommendation. Therefore, the committee agreed that it was appropriate to make a 'consider' recommendation targeted at the people who are most likely to benefit. The strength of this recommendation indicates that the balance of current evidence supports the use of decontamination, but that important uncertainties remain. Therefore, it is appropriate for clinicians and commissioners to use their judgement in considering whether this intervention is appropriate in any individual case or class of cases.
Infection Prevention Society	Guideline	16	21	This should say S.aureus SSI not 'infection' as it is a guideline about preventing SSI not infection in general.	Thank you for your comment. The section highlighted in your comment refers to the committee discussions that took place when making recommendations. This discussion took into account the evidence identified. One study (Bode 2010) reported lower incidence of S. aureus nosocomial infections. Line 21 on Page 16 refers to this information. As our guidelines are developed using plain English the term 'Staphylococcus aureus infections caught in hospital' was used. For further information on the language used in NICE guidance, please refer to the NICE Manual.
British Orthopaedic Association	Guideline	16	22	The guideline implies that these infections are "caught in hospital". This isn't known to be correct and the evidence suggests the bacteria are most likely from the patient's own bacterial flora (Bode, NEJM). This is of course why the treatment works. If these words are used then lawyers may use it to blame hospitals and staff when infections occur.	Thank you for your comment. The nasal decolonisation review identified evidence on the use of mupirocin alone and mupirocin in combination with chlorhexidine body wash. One study was identified that showed that mupirocin alone resulted in a reduction in S. aureus nosocomial infections (Perl 2002). The statement on page 16, line 22 of evidence review A

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					reflects this finding. Evidence review A has also been amended with references to 'caught in hospital' changed to 'developed in hospital'.
Infection Prevention Society	Guideline	16	24	it would be helpful to point out that only one third of people carry this organism on their skin or in their nose (and reference this statement)	Thank you for your comment. Information presented in the section highlighted in your comment relates to the evidence that was identified in the review and why the committee made the recommendations. As nasal *S. aureus* carriage was not discussed explicitly when drafting recommendations, the statement highlight in the comment cannot be added in.
Infection Prevention Society	Guideline	17	1	infections are acquired in hospital	Thank you for your comment. As our guidelines are developed using plain English the term 'infections caught in hospital' was used. For further information on the language used in NICE guidance, please refer to the NICE Manual.
Infection Prevention Society	Guideline	17	19	Why should new recommendations reflect current practice rather than the evidence?	Thank you for your comment. The committee took both the evidence and their clinical knowledge into account when forming recommendations. The committee also agreed that new recommendations may also be reflective of current practice. For further information, please refer to the rationale and impact section in the guideline.
Royal College of Nursing	Guideline	17 / 18	27 /17	This recommendation will be a challenging change in practice because children do not tolerate nasal treatment well. The development committee have stated that there are potential side effects that are a concern (page 17, line 27) including a burning sensation and local reactions. We would anticipate that this is more likely to occur in children. As there is limited evidence to demonstrate the efficacy of this, and taking into account the emotional trauma and distress caused to children and young people, we do not feel that the benefits outweigh the negatives. Therefore we do not currently follow this process.	Thank you for your comment. The committee acknowledges the difficulties of implementing this intervention to children but feel the benefits do outweigh the negatives. The following addition has also been made to the ' Other factors the committee took into account' section in evidence review A. 'it was also noted that children may find it difficult to tolerate nasal decolonisation'.
Infection Prevention Society	Guideline	17	28	'caution against'	Thank you for your comment. The wording of this sentence has been amended.
Infection Prevention Society	Guideline	17	6	these statements are conflicting and unhelpful without more detailed explanation. What are specialist surgeries? The data suggests that it's the CXG that may be the important preventative treatment rather than the mupirocin.	Thank you for your comment. The committee took your comment into consideration and redrafted the recommendation. The new recommendation states that nasal decolonisation should be considered before procedures in which S*. aureus is* a likely cause of a surgical site infection. To allow flexibility, the committee recommended that such procedures should be locally determined taking into account patient risk factors such as nasal carriage status and impact of infection. For further information, please refer to rationale and impact section in the guideline.
Infection Prevention Society	Guideline	18	17	The meta-analysis includes a number of studies that show the efficacy of PI although comparing aqueous with alcohol based solutions is incorrect given that this the latter includes 2 active agents. The Park study of aqueous agents showed no difference between CHG and PI.	Thank you for your comment. Studies which compared alcohol based products with aqueous based products were included in the meta- regression. The meta- regression which was conducted to explore the additive effect of the agent and excipient. This model assumed that the 4 treatment groups (Aqueous povidone iodine, chlorhexidine in alcohol, povidone iodine in alcohol and aqueous chlorhexidine) can be broken down to 1) alcohol compared to aqueous 2) povidone iodine compared to chlorhexidine. This meta-regression was used when drafting the recommendations. For further information on this model please refer to Appendix H
Infection Prevention Society	Guideline	18	7	The evidence shows that alcohol based solutions are associated with a lower incidence of SSI. There is only a small (one study) amount of evidence that CHG in alcohol better than PI. Given that no firm advice has been given about mupirocin/CHG (where there is more evidence) it seems inconsistent to offer firm advice on using CHG.	Thank you for your comment. Recommendation 1.3.9 provides a series of options for antiseptic skin preparation based on evidence of effectiveness plus current best practice regarding contraindications. Please refer to the rationale and impact section in evidence review A for further detail on why the committee made this recommendation.
Infection Prevention Society	Guideline	18	9	This seems to conflict with the previous statement	Thank you for your comment. For further detail on how the committee developed research recommendations please refer to the 'Committee's discussion of the evidence' section in Evidence Review A. Thank you for your comment. Recommendation 1.3.9 provides a series of options for antiseptic skin preparation based on evidence of effectiveness plus current best practice regarding contraindications. Please refer to the rationale and impact section in evidence review A for further detail on why the committee made this recommendation.
Infection Prevention Society	Guideline	19	12 to 20	Povidone iodine should not be an option only for patients with hypersensitivity to chlorhexidine, as the evidence supporting aqueous CHG solutions is not reflecting what is currently available in the market	Thank you for your comment. The committee drafted recommendations based on the evidence identified, the strength of this evidence and their clinical knowledge. The committee noted that different clinical scenarios may occur where one product may not be applicable. Therefore the committee recommended different options that may be utilised

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					based on these scenarios. The committee were aware of marketing authorisations of different products and the footnote for 1.3.9 has been amended to capture this information.
British Orthopaedic Association	Guideline	19	29	One theatre fire related to the use of alcoholic skin prep per month within NHS England was reported to the NLRS in 2013 when national reports were last collated. These events aren't rare.	Thank you for your comment. The rationale and impact section for this recommendation has been amended in light of your comment by removing the use of 'rare' and adding precautions in relation to flammable products and the risk of burns. For further information, please refer to Evidence Review B.
British Orthopaedic Association	Guideline	21	11	Did the guideline group consider https://www.ncbi.nlm.nih.gov/pubmed/27803231 for patients with a hip fracture? For information this trial is being repeated to confirm effect. https://doi.org/10.1186/ISRCTN15606075	The Sprowson paper was excluded from the review because it is a quasi-randomised trial. In the study, it is stated that treatment allocation was based on date of surgery. This means that allocation was not truly random and a study with such design carries a greater risk of selection bias. Furthermore, our protocol states that quasi-randomised trials would only be utilised if less than 5 RCTs were identified. As we were able to meet our defined threshold, this study was excluded. We also ran additional sensitivity analyses,and identified that inclusion of this study did not greatly impact our overall results and thus did not change the conclusions made by the committee. The exclusion list has been updated to reflect our reasoning for exclusion.
British Orthopaedic Association	Guideline	21	11	"In addition, the clinical evidence suggested that antibiotic-loaded bone cement did not reduce the number of surgical site infections." This statement is not compatible with "The evidence is too limited to make a recommendation". HIPQIP national audit (National Joint Registry) Data suggests effectiveness of antibiotic bone cement – see below. The area is in fact controversial but the suggestion by NICE that it has no effect is misguided given the large amount of international registry data available. For this reason and for comment No. 6 we suggest removal of the statement "In addition, the clinical evidence suggested that antibiotic-loaded bone cement did not reduce the number of surgical site infections." Aims Antibiotic-loaded bone cements (ALBCs) may offer early protection against the formation of bacterial biofilm after joint replacement. Use in hip replacement is widely accepted, but there is a lack of evidence in total knee replacement (TKR). ALBCs are more costly than plain cement, and there are concerns regarding mechanically stability and increased antibiotic resistance. The objective of this study is to evaluate the use of ALBC in a large population of TKR patients in order to give a recommendation about its use based on a risk-benefit profile. Patients and Methods: Data from the National Joint Registry (NJR) of England and Wales was obtained for all primary cemented TKRs between March 2003 and July 2016. Patient, implant and surgical variables were analysed. Cox proportional hazards models were used to assess the influence of ALBC on risk of revision. Body mass index (BMI) data was available in a subset of patients. Results: Of 731,214 TKRs, 15,295 (2.1%) were implanted with plain and 715,919 (97.9%) with ALBC. There were 13,391 revisions; 2391 were performed for infection. After adjusting for other variables, ALBC had a significantly lower risk of revision for any cause (Hazard Ratio [HR] 0.85, 95% Confidence Intervals [CIs] 0.77-0.93, p<0.01). For both aseptic causes of revision (HR 0.85, 0.77-0.95, p<0.01) and revisions for infection (HR 0.84, 0.67-1.01, p=0.06) the risk associated with ALBC was lower. When BMI was added into the model (432,003 TKRs), the results were similar (all cause revision – HR 0.76, 0.65-0.89, p<0.01, aseptic revisions – HR 0.81, 0.67-0.98, p=0.03, revision for infection – HR 0.65, 0.49-0.87, p<0.01).	Thank you for your comment. The clinical evidence of effectiveness on antibiotic-loaded bone cement was based on evidence from 1 RCT. The why the committee made the recommendations section of evidence review C has been amended stating there was not enough RCT evidence to make a recommendation for this intervention. The protocol for this evidence review outlined the inclusion of RCT data and did not look at national audit data which the committee considered was not appropriate for this review question.

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				Prosthesis survival at 10 years for TKRs implanted with ALBC was 96.3% [95% CIs 96.3-96.4] compared with 95.5% [95.0-95.9] in those implanted with plain cement. On a population level, where 100,000 TKRs are performed annually, this is equivalent to 800 fewer revisions at 10 years if ALBC was used. Conclusions: After adjusting for a range of variables, ALBC was associated with a significantly lower risk of revision. Using ALBC does not increase mid-term implant failure rates. Surgeons using plain cement for primary TKRs should consider changing to ALBC in order to reduce overall revision risk.	
Healthcare Infection Society	Guideline	22	19	There are several meta-analyses that suggest Triclosan sutures are superior to other sutures. The evidence is good and should be recommended and likely to save costs. (I have been an author on one review)	Thank you for your comment. As highlighted in the review protocol, RCTs and systematic reviews of RCTs were considered. Systematic reviews which were reviewed at full text stage and were subsequently excluded have been listed in Appendix I in Evidence Review D.
Infection Prevention Society	Guideline	22	20	It would be more helpful to focus on the types of surgery for which there is evidence of efficacy. This is primarily colorectal surgery Review D page 148 (Justinger & Nakamura). Galal involved different types of surgery but there randomization process is obscure and there are major differences in types of procedure between control and intervention groups which were likely to bias the results in favour of intervention.	Thank you for your comment. Studies which compared triclosan sutures to non-triclosan sutures explored a number of different surgery types. Among the studies, the committee found the evidence for use of triclosan sutures in paediatric surgery to be compelling, which the committee wished to highlight in the recommendation. All studies were assessed for risk of bias using the Cochrane Risk of Bias tool. These are included in Appendix E.
British Orthopaedic Association	Guideline	23	2	We disagree. This may have a major effect on clinical practice if NICE recommends the use of triclosan sutures without examining key evidence. There is a single supplier of these sutures and prices may increase if trusts feel obliged to use them. It may have a significant effect on suture costs.	Thank you for your comment. The committee's interpretation of the systematically identified and appraised evidence was that triclosan sutures are likely to reduce the rate of SSIs, and any additional expenditure is likely to be more than recouped by savings associated with reduced SSIs. Therefore, the committee agreed that use of triclosan sutures is likely to save trusts money overall. However, as detailed in the relevant 'rationale and impact' section, the committee recognised that the evidence was of varying quality and covered heterogeneous types of surgery. Therefore, the committee agreed that it was appropriate to make a 'consider' recommendation (allied to an additional research recommendation that seeks to clarify the circumstances under which triclosan sutures provide most benefit). The strength of this recommendation indicates that the balance of current evidence supports the use of triclosan sutures, but that important uncertainties remain. Therefore, it is appropriate for clinicians and commissioners to use their judgement in considering whether this intervention is appropriate in any individual case or class of cases. The guideline committee was most convinced by evidence in the paediatric setting, and drew attention to this in its recommendation.
Clinisupplies Ltd.	Guideline	23	General	How the recommendations might affect practice: The Guideline states that the recommendations are unlikely to have a major impact on current practice. We believe that this statement underestimates the impact that NICE support of triclosan-coated sutures will have on the cost burden to the NHS. In a cost-pressured environment where the cost of the coated sutures could increase their spend by up to 25% on absorbable sutures that is a significant burden on trusts. It is worthy of noting that only one manufacturer markets the coated suture (which is patented until 2022), and their suture range dominates the marketplace at the highest price within the market. Other, equally good quality sutures are now available, but at a lower price to the NHS. An endorsement of the coated suture would inhibit other players from entering the market as a trust will usually buy from one supplier. When the evidence is not clear cut this inhibition of market dynamics could be detrimental to hospitals trying to procure better value products.	It is unclear on what basis you assert that 'equally good quality sutures' are available. The committee's interpretation of the systematically identified and appraised evidence was that triclosan sutures are likely to reduce the rate of SSIs compared with standard sutures. No evidence was available on other types of suture with similar benefits. However, as detailed in the relevant 'rationale and impact' section, the committee recognised that the evidence was of varying quality and covered heterogeneous types of surgery. Therefore, the committee agreed that it was appropriate to make a 'consider' recommendation (allied to an additional research recommendation that seeks to clarify the circumstances under which triclosan sutures provide most benefit). The strength of this recommendation indicates that the balance of current evidence supports the use of triclosan sutures, but that important uncertainties remain. Therefore, it is appropriate for clinicians and commissioners to use their judgement in considering whether this intervention is appropriate in any individual case or class of cases. The guideline committee was most convinced by evidence in the paediatric setting, and drew attention to this in its recommendation.

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				The health economic offset of SSIs has not been clearly documented in our opinion. The length of stay due to an SSI and readmittance to hospital will be the largest cost impacts, as opposed to the cost of antibiotic treatment. Readmittance has not been documented in any of the studies, and length of stay has been unclearly defined and not included in many. We note the Forest plots (Guideline Evidence Reviews, Appendix F, page 152), which in abdominal and lower limb arterial favour standard sutures over Colorectal, and a minimal impact in colorectal. With the inclusion of the 2,437 patients within the Sprowson paper (Comment 2 above), where length of stay was not significant we believe that this may demonstrate a significantly different picture.	Thank you for your comment. The health economic appendix details the sources used for data that described length of inpatient stay as a result of acquiring an SSI due to different types of surgeries. Furthermore, the appendix details how the length of stay and associated were calculated for the economic model using these data. The Sprowson paper did not meet our inclusion criteria so would not be a consideration as part of this issue. As specified in the review protocol (Evidence Review D, Appendix A) RCTs with a sample size of ≥ 200 subjects were included. The Sprowson 2014 paper was excluded from the review because it is a quasi-randomised trial. In the study, it is stated that treatment allocation was based on date of surgery. This means that allocation was not truly random and a study with such design carries a greater risk of selection bias. Furthermore, our protocol states that quasi-randomised trials would only be utilised if less than 5 RCTs were identified. As we were able to meet our defined threshold, this study was excluded. We also ran additional sensitivity analyses, and identified that inclusion of this study did not greatly impact our overall results and thus did not change the conclusions made by the committee. The exclusion list has been updated to reflect our reasoning for exclusion.
Healthcare Infection Society	Guideline	24	7	The size and quality of the trials in caesarean section is more persuasive than the smaller trials which have been carried out in orthopaedic surgery. Caesarean section, which should be a clean procedure, has more in common with total hip replacement than with heavily contaminated abdominal surgery. A meta-analysis published in the BMJ in 2010 by UK authors came down in favour of sutures in total hip replacement and little further evidence has been produced since then. It is extremely difficult to do a worthwhile trial in this area because the incidence of superficial wound infection is quite low and the incidence of deep infection, which is the more serious complication is very low. It would be reasonable to recommend that sutures should be considered for total hip replacement, whilst recognising the low quality of the evidence. The BMJ review is at: BMJ 2010; 340 doi: https://doi.org/10.1136/bmj.c1199 (Published 17 March 2010)	Thank you for your comment. The systematic review included in the reference (Smith 2010) included randomised controlled trials and non-randomised controlled trials. Based on our review protocol, only RCTs containing a population of greater than 200 people were included. Based on this criteria only 1 study (Buttaro 2015) was identified which included people undergoing hip arthroplasty. The committee therefore considered there wasn't enough evidence to make a recommendation for total hip replacement. For more information on how the committee's discussion of the evidence, please refer to Evidence Review D.
Healthcare Infection Society	Guideline	27	11	We support the general recommendation against using antibiotics in the wound and on the skin at the end of surgery or during surgery on the basis of the lack of evidence and the risk of promoting antibiotic resistance. There are however sound theoretical and microbiological reasons why the application of an anti-septic to the skin prior to skin closure may be a good idea in joint replacement surgery. In orthopaedic surgery it is common practice to use clear or iodine impregnated incise drapes for joint replacement surgery. The purpose of the drape is, at least in part, to seal off the rest of the surgical drapes and prevent the pumping of contaminated air into the operative field during surgery. Whilst the drape acts as a barrier covering the skin during surgery at the end of surgery there are certainly residual organisms underneath the drape. It makes sense to kill these organisms prior to wound closure. It would be extremely difficult to carry out a randomised trial of the use of an anti-septic in this situation because of the multiple other variables and the low incidence of wound problems. We would suggest that the recommendation should be to use an anti-septic (definitely not an antibiotic!) on the skin before wound closure provided that the patient is entered into an SSI surveillance scheme, possibly either the Public Health England SSI registry or the National Joint Registry.	Thank you for your comment. Incise drapes were outside the scope of this question. Incise drapes are currently covered by recommendations 1.3.3 and 1.3.4 which state that non-iodophor-impregnated incise drapes should not be used routinely as they may increase the risk of surgical site infection. Furthermore, if an incise drape is required, use an iodophor-impregnated drape unless the patient has an allergy. Evidence review C did not find any evidence on the application of an anti-septic to the skin prior to skin closure in joint replacement surgery so the committee did not consider this intervention.
3M UK PLC	Guideline	27	7	The proposed wording recommends the specific active ingredient **mupirocin,** the concern is that this restricts and discourages innovation for other entrants, that may produce or develop an alternative that can demonstrate **nasal decolonisation** to an equivalent level	Thank you for your comment. During the development of the review protocol, the committee did take other interventions into consideration (highlighted in Table 1 in Evidence Review A). However, no studies of relevant study design were identified which examined the

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				and overcome current challenges of mupirocin (for example, several applications required, reliance on patient application, cost, resistance implications). Wording could be inclusive of new products that are confirmed as effective through rigorous registration processes, that already exist.	effectiveness of mupirocin alternatives. Therefore the committee were unable to make recommendations on the use of available alternatives. However, the committee incorporated these alternative interventions into the four research recommendations developed as part of evidence review A (please see Appendix K). For further information, please refer to 'The committee's discussion of the evidence' in evidence review A.
Medicines and Healthcare Products Regulatory Agency	Guideline	9 and 19	5 and 27	As noted in the guideline you need to avoid pooling under drapes and fumes under drapes. However, the risk (a potential for fire with electrosurgical devices and/or light cables) is not explained. Although this risk is highlighted on page 19, I am not sure if the risk is highlighted enough in the main section. The rationale and impact section for this does not seem to think it is a very high risk. For example, when using electrosurgical devices there have been instances of burns with light cables left on drapes during laparoscopic surgery which could lead to fire.	Thank you for your comment. The rationale and impact section for this recommendation has been amended in light of your comment by adding precautions in relation to flammable products and the risk of burns. For further information, please refer to Evidence Review B.
Homerton University Hospital	Guideline	202	2	1.Which patient groups, contamination groups and which layers gain the most benefit from the use of triclosan-coated or triclosan-impregnated sutures? Comments: My unpublished work looked at SSI bundle for colorectal surgery. Triclosan-impregnant suture was used as part of SSI bundle. Although this is not an RCT, the SSI bundle reduced the SSI rate by half the pre SSI bundle baseline and maintained the SSI rate below the national average.	Thank you for your comment and for providing this information.
British Infection Association	Questions	General	General	Answers to questions above: 1. The big impact change include introduction of mupirocin for all orthopaedic and cardiac surgery, and the change from staples to sutures in C-section. Both will be training challenges and the C-section recommendation may be contested. 2. Cost implications for mupiricin. And for the training of change in practice in point 1. 3. SSI best practice group could assist with roll out of changes 4. We are happy with the proposed C-section changes and support them.	Thank you for your comment and for highlighting these important implementation issues. In response: 1) Amendments have been made to the guideline (how the recommendations might affect practice section) acknowledging that nasal decolonisation and sutures for caesarean section may have training implications. 2) The cost implications for mupirocin has been considered as part of the economic analysis 3) Thank you for this suggestion 4) Thank you for your comment
British Association of Paediatric Surgeons	Guideline			1. We would recommend use of antibiotic prophylaxis in the immunocompromised/immunosuppressed patient. There is evidence in particular with solid organ transplantation that SSIs are significant in such patients with severe associated morbidity and mortality. (Transpl Infect Dis. 2003 Jun;5(2):72-8.Surgical site infections following pediatric liver transplantation: risks and costs.) 2. Of note, neonates are not immunologically mature and extreme low birth weight neonates may be particularly vulnerable. 3. Such neonates are also vulnerable to the application of iodine containing products. Iodophor impregnated drapes are not commonly used. Though the evidence base for absorption is not available for drapes, there is a significant body of evidence supporting transcutaneous absorption of iodine skin prep causing significant hypothyroidism in neonates. https://www.pediatr-neonatol.com/article/S1875-9572(12)00166-0/fulltext 4. The application of dressings is not always practicable or desirable in children who are skilled in removing them in such a way that causes more damage and infection risk. The application has therefore always been selective in our patients.	1. Thank you for your comment. The use of antibiotic prophylaxis was outside the scope of this guideline update. 2. Thank you for your comment. This topic was outside the scope of this guideline update. 3. Thank you for your comment. The use of drapes is outside the scope of this guideline update. The committee also made the following recommendation for pre-term babies - Be aware of using skin antiseptics in babies, in particular the risk of severe chemical injuries with the use of chlorhexidine (both alcohol-based and aqueous solutions) in preterm babies. The committee acknowledged that there was no evidence on the use of skin antiseptics in babies. However, the committee were aware of risks, such as burns, associated with their use in this population, and wished to highlight this. Furthermore, the committee noted that the Medicines and Healthcare products Regulatory Agency (MHRA) has published advice on the use of chlorhexidine for skin disinfection in premature babies (see MHRA chlorhexidine solutions: reminder of the risk of chemical burns in premature infants 4. Thank you for your comment. This topic was outside the scope of this guideline update.
Public Health England	Economic Report	2	1	Table HE02 - It is stated that the interventions are evaluated with or without a chlorhexidine bodywash. This could confound the results, especially given the findings of HE2 RQ2.	Thank you for your comment. It is true of the evidence underpinning the assessment that the independent effects of mupirocin and chlorhexidine bodywash are difficult to disentangle – see Evidence review A. There is some evidence showing that mupirocin on its own is effective in reducing S. aureus infection ns in carriers, though the evidence was more compelling in RCTs comparing the combination of mupirocin and chlorhexidine bodywash to

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					placebo/no treatment. What the review does not provide is evidence on the effect of chlorhexidine bodywash alone. Therefore, in order to avoid the possibility of misattributing efficacy, we cost the intervention as comprising both elements, and the committee's recommendations reflect this by stating that both should be provided. We can be relatively confident that people receiving mupirocin and chlorhexidine bodywash will receive benefits of a similar magnitude to those observed in the trials; any attempt to model either as monotherapy would be much more speculative.
Public Health England	Economic Report	2	1	Table HE02 - One of the listed outcomes is antimicrobial resistance, yet this does not seem to be considered as an outcome in the results. Given that the findings claim universal mupirocin is the dominant intervention strategy, consideration needs to be given to the development of resistance.	Thank you for your comment. No data were available to consider this outcome in quantitative terms; however, the committee gave careful consideration to the issue (see 'Benefits and harms' in Evidence review A) and made a research recommendation that aims to fill the current gap in the evidence-base.
Public Health England	Economic Report	3	32	Consideration could be given to study setting (e.g. other interventions, hospital type) such that the appropriateness of meta-analyses can be assessed.	Thank you for your comment. These considerations are encompassed in the preceding bullets (i.e. that the selected studies should report outcomes that correspond as closely as possible to the health states and events simulated in the model and that the selected studies should report a population that closely matches the target population; though we have revised this second point to be clearer that we are interested in all characteristics of the population, not just the country from which data were drawn).
Public Health England	Economic Report	3	35	The model structure is static, and does not consider onward transmission. This makes sense if only endogenous progression to infection of colonised patients is being considered. However, given that surgical site infection (SSI) risk for 30 days is being considered (this is also ambiguous, see point 16 below) then the interventions may well have impact on transmission potential, and thus on transmission-related infection events. The carriage or non-carriage status of patients is an important component of this model structure, and will be impacted by transmission (which itself will be impacted by the intervention).	Thank you for your comment. Although – as a matter of theory – it would be possible to develop a dynamic model accounting for onward transmission, this approach would substantially increase the complexity of the analysis and its data requirements in a way that is almost certain to prove intractable. Moreover, we can be confident, in this instance, that it would add little value for decision-making purposes. Accounting for onward transmission can only increase the cost effectiveness of preventative measures and, since universal decontamination was already found to be cost effective in this analysis, it is clear that the qualitative result of the model would not change.
Public Health England	Economic Report	3	42	The model allows for only two outcomes – death or recovery. Other outcomes connected to SSI (e.g. long-term disability) should be considered.	Thank you for your comment. This would complicate the analysis to no material benefit. We would need credible data on long-term sequelae (which are unlikely to be available), and may need to model the whole lifetimes of affected people. The only benefit of such an approach would be to make an intervention that already appears cost effective look slightly more cost effective.
Public Health England	Economic Report	5	2	There is no apparent adjustment for the SSI risk estimates including both elective and emergency admissions/operations, the latter being generally associated with a higher SSI risk.	Thank you for your comment. Risk stratification was not within the scope of this guideline update. We do provide sensitivity analysis showing the relationship between baseline SSI risk and net benefit of intervention (see figure HE07), which may be used to estimate the likely impact in any population for which the reader has reliable information.
Public Health England	Economic Report	5	11	We assume 'PHE registry' refers to our national surveillance programme. If so, please note that this is undertaken on open incisional procedures. As such, some of these parameters may be at variance with the wider population of surgical patients.	Thanks for this clarification; we have incorporated it in our revised report.
Public Health England	Economic Report	5	14	For the PHE data in Table HE03, please note that results for cholecystectomy, CABG and cardiac (non-CABG) based on those reported in our annual publication are incorrect. The reported cardiac (non-CABG) results are actually for CABG, CABG results are for cholecystectomy and cholecystectomy results are for cardiac (non-CABG).	Thank you. We have corrected.
Public Health England	Economic Report	5	16 - 24 (continued on p6)	Whilst we respect the decision of the committee to use whichever data sources they see fit, there is an erroneous comparison between the PHE data and that reported in the study by Jenks et. The comparisons made in HE04 include community-onset SSIs captured through post-discharge surveillance for the Jenks data; by contrast, reporting of data on this category of SSIs was not included in the PHE data. As such, the commentary is misleading as the two datasets are not comparable. We request that this table be reformulated to include comparable data and that the accompanying text includes an informed reassessment of the PHE data.	Thank you for your comment. We do not believe that it is erroneous to compare the Jenks et al. (2014) and PHE data – it is the whole point of the exercise to emphasise differences in weighing up the pros and cons of each. We do not conclude that one source is fundamentally better than the other; rather we see them as complementary sources of evidence reflecting more and less conservative estimates of the true incidence of SSIs. That said, we see how aspects of the textual description in the consultation draft make it look like more of a value judgement, and we have revised this section accordingly.
Public Health England	Economic Report	5	17	'a PHE registry' is presumably the PHE Surgical Site Infection Surveillance Service (it is not a registry as such). Please note the data cited are from NHS participants in the programme only.	Thank you; we have corrected to PHE SSI surveillance service throughout. We have also noted that the data in the report reflect NHS episodes only.

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Infection Prevention Society	Economic Report	5	23	It is not possible to determine how representative the data from one hospital is of other hospitals in the UK and this estimate may equally be biased	Thank you for your comment, in the light of which; we have revised this sentence.
Infection Prevention Society	Economic Report	6	4	Since there are virtually no hospitals in England which routinely capture robust SSI surveillance data on all types of surgery the members of the committee would not possess data that would enable them to say the Jenks study estimates were 'more representative of their own area of practice'	Thank you for your comment. It should be understood that the committee comprised experts with a lifelong professional focus in SSI; therefore, we value their opinion as to the face validity of different estimates.
Public Health England	Economic Report	6	6 - 10	The overall % of SSIs due to S. aureus from either Jenks et al or PHE will reflect the relative volume of different type of surgery as the risk of S. aureus infection varies between procedures. If overall figures are required (all types of surgery), these should be derived by applying the category-specific S. aureus SSI rates to national Hospital Episode Statistics (HES) data.	Thank you for your comment. We acknowledge that it is a limitation of our analysis that we have been unable to derive granular data to estimate the underlying risk of S. aureus infection in each subpopulation. However, we think this is relatively unlikely to have a substantial impact on findings, given that there is a clear finding in the overall population, and sensitivity analysis shows that universal decontamination would be preferred at all but the very lowest levels of risk (below 0.3%; see figure HE07)
Public Health England	Economic Report	6	12 - 14	We note the assumption that NHS hospitals are not currently screening patients preadmission and suggest that the validity is assessed.	Thank you for your comment. The justification we provide is that screening is 'not currently recommended', which is true.
Public Health England	Economic Report	6	15	For the PHE data in Table HE04, the reported 11.0% for the proportion of SSIs caused by *S. aureus* refers to inpatient-detected SSIs only. For inpatient and readmission-detected SSIs, the proportion reported in our SSI annual report is 20.2%	Thanks for this information; we have amended to note.
Public Health England	Economic Report	7	14	We suspect this reduction in baseline SSI incidence may be biased if the reduction is proportional across carriers and non-carriers.	Thank you for your comment. The alternative method of estimating baseline rates does not have this feature; the reader is free to prefer the results from that analysis if they wish. (Although, ultimately, we show that results are not materially affected by this choice.)
Public Health England	Economic Report	8	8	With regards to treatment effects, the discrepancy between screening site and impact of nasal decolonisation should be acknowledged.	Thank you for your comment. Our analysis does not lead us to believe that screening status has any impact on the **relative** effectiveness of the intervention (though, of course, it will be a key determinant of absolute incidence and cost effectiveness).
Public Health England	Economic Report	9	15	Table HE06. - The table should include the outcome measure for all studies. Some may have been at an individual level and other at cohort-level. Whether a meta-analysis is appropriate is hard to ascertain (also, as mentioned previously, it is debatable whether studies with and without chlorhexidine use can be combined within a meta-analysis).	Thank you for your comment. These are the data from section F.6 in Evidence review A (although, for our computational purposes, on an odds ratio scale rather than the relative risks that are presented there). We have inserted a cross-reference to clarify. We do not understand your distinction between individual- and cohort-level results: cohorts do not get SSIs; individuals do.
Northumbria Healthcare	Economic Report	10	10	We believe the current economic model significantly underestimates the mortality risk associated with surgical site infection following hip or knee arthroplasty. There have been several recent studies examining the effects of prosthetic joint infection (PJI) following hip or knee arthroplasty. One study from the Danish Hip Arthroplasty Register (1), which includes data on over 68,500 primary THRs, found that 1 year mortality for patients undergoing revision for PJI was 8% (95% CI, 6%-11%). Whilst a meta-analysis (2) on mortality associated with PJI of a total knee replacement found a mortality rate of 4.33% (95% CI, 3.14% - 5.51%) per year. Both of these figures are significantly higher than the 0.29% and 0.14% for mortality with SSI for hip and knee prosthesis in the current economic model. It is well known and accepted that mortality rates are higher than common cancers such and breast and prostate cancer (3). 1. Gundtoft PH, Pedersen AB, Varnum C, Overgaard S. Increased Mortality After Prosthetic Joint Infection in Primary THA. *Clin Orthop Relat Res*. 2017;475(11):2623-2631 2. Lum, Zachary C. et al. Mortality During Total Knee Periprosthetic Joint Infection. The Journal of Arthroplasty , Volume 33 , Issue 12 , 3783 – 3788 3. J Arthroplasty. 2018 Oct;33(10):3238-3245. Are We Winning or Losing the Battle With Periprosthetic JointInfection: Trends in Periprosthetic Joint Infection and MortalityRisk for the Medicare Population. Kurtz SM, Lau EC, Son MS, Chang ET, Zimmerli W, Parvizi J	Thank you for your comment. We discuss our consideration of the available evidence in HE1.2.4.1, including the observation that recent evidence is not unambiguous about the effect of SSI on mortality. The data from PHE only relate to inpatient deaths; we would expect these to be substantially lower than 1-year rates in the publications you cite. We also note that the Danish study is restricted to a subgroup of patients who had SSI-related revision; again, one would expect far higher event-rates in that high-risk population, and it would be inappropriate to use such data in an analysis of all SSIs. We would also emphasise that the model is not very sensitive to this parameter, as shown in figure HE08: even if SSIs were associated with no increase in mortality, the model would still find universal mupirocin to be a dominant strategy.

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Stakeholder	Document	Page No	Line No	Comments Please insert each new comment in a new row	Developer's response Please respond to each comment
British Orthopaedic Association	Economic Report	10	10	We believe the current economic model significantly underestimates the mortality risk associated with surgical site infection following hip or knee arthroplasty. There have been several recent studies examining the effects of prosthetic joint infection (PJI) following hip or knee arthroplasty. One study from the Danish Hip Arthroplasty Register (1), which includes data on over 68,500 primary THRs, found that 1 year mortality for patients undergoing revision for PJI was 8% (95% CI, 6%-11%). Whilst a meta-analysis (2) on mortality associated with PJI of a total knee replacement found a mortality rate of 4.33% (95% CI, 3.14% - 5.51%) per year. Both of these figures are significantly higher than the 0.29% and 0.14% for mortality with SSI for hip and knee prosthesis in the current economic model. It is well known and accepted that mortality rates are higher than common cancers such and breast and prostate cancer (3). 4. Gundtoft PH, Pedersen AB, Varnum C, Overgaard S. Increased Mortality After Prosthetic Joint Infection in Primary THA. *Clin Orthop Relat Res*. 2017;475(11):2623-2631 5. Lum, Zachary C. et al. Mortality During Total Knee Periprosthetic Joint Infection. The Journal of Arthroplasty , Volume 33 , Issue 12 , 3783 – 3788 6. J Arthroplasty. 2018 Oct;33(10):3238-3245. Are We Winning or Losing the Battle With Periprosthetic JointInfection: Trends in Periprosthetic Joint Infection and MortalityRisk for the Medicare Population. Kurtz SM, Lau EC, Son MS, Chang ET, Zimmerli W, Parvizi J	Thank you for your comment. We discuss our consideration of the available evidence in HE1.2.4.1, including the observation that recent evidence is not unambiguous about the effect of SSI on mortality. The data from PHE only relate to inpatient deaths; we would expect these to be substantially lower than 1-year rates in the publications you cite. We also note that the Danish study is restricted to a subgroup of patients who had SSI-related revision; again, one would expect far higher event-rates in that high-risk population, and it would be inappropriate to use such data in an analysis of all SSIs. We would also emphasise that the model is not very sensitive to this parameter, as shown in figure HE08: even if SSIs were associated with no increase in mortality, the model would still find universal mupirocin to be a dominant strategy.
Public Health England	Economic Report	10	16	Given that the model is probabilistic, the range of uncertainty in this parameter, captured in this recent review, could be captured by using a full distribution.	Thank you for your comment. We do subject the relevant parameters to variation in our PSA. We also provide a deterministic sensitivity analysis varying the impact of SSI on mortality across a broad range of values (see figure HE08).
Infection Prevention Society	Economic Report	10	32	These estimates do not appear to have taken any account of the difference in risk of mortality associated with the type of SSI- the coello paper demonstrated that the odds of death were primarily associated with deep/organ space SSI and varied by category of surgery. There are important variations in risk of developing deep/organ space SSI associated with different procedures, especially when 'all surgical procedures' are included as suggested in the Jenks dataset. This is likely to include a far greater proportion of minor procedures associated with a lower risk of SSI than the PHE dataset which is intentionally focused on major procedures with a higher risk of SSI and more severe SSI.	Thank you for your comment. We believe it is incorrect to suggest that the Coello paper demonstrated differential relative effects of SSI on mortality across different types of surgery. The published adjusted odds ratios are completely consistent with a null hypothesis of no difference between different surgery types (p=0.38; I2=7%). We have added this information to the report, to support our assumption of equivalent relationship between SSI and mortality across different surgery types.
Public Health England	Economic Report	10	39 - 45	We would be happy to share data on mortality in patients with and without SSI from the PHE surveillance data to circumvent the need to make this extrapolation.	Thank you for your comment. This is a calculation rather than an extrapolation. However, it does rely on the assumption that the relative effect of SSI on mortality is constant across different types of surgery. Data from the Coello study show this is likely to be approximately true (the published adjusted odds ratios are completely consistent with a null hypothesis of no difference between different surgery types [p=0.38; I2=7%]) Coupled with the model's relative insensitivity to this parameter, we feel confident that the data you are generously offering would only add marginal value to our analysis.
Public Health England	Economic Report	12	9	A non-negligible proportion of SSI will result in long-term detriment to quality of life. This could have a considerable impact on the model. Could the proportion of SSI leading to long term effects be estimated from the literature and included within the model.	Thank you for your comment. While you are undoubtedly correct that there are long-term sequelae to SSIs, we take the view that modifying the analysis in this way would complicate it to no material benefit. We would need credible data on long-term effects (which are unlikely to be available), and may need to model the whole lifetimes of affected people. The only benefit of such an approach would be to make an intervention that already appears cost effective look slightly more cost effective.
Infection Prevention Society	Economic Report	12	29	SSI related utility will be affected by the proportion of the SSI that are deep/organ space	Thank you for your comment. This is a plausible assertion, though we are unaware of any data to support it.

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Infection Prevention Society	Economic Report	28	18	Aqueous chlorhexidine is not available as a general surgical skin preparation and therefore is not relevant in a cost model	Thank you for your comment. The licensing status of each preparation is now noted in the relevant recommendations.
Infection Prevention Society	Economic Report	29	1	5th bullet point - it is far more common that institutions use a prep bottle per list or day and therefore avoid wastage. The requirement to use several applicators for major incisions or procedures with more than one incision has not been accounted for in the costings.	Thank you for your comment. As noted in the bullet-point you cite, our base-case assumption is that units will use a single bottle and avoid wastage. We explore the impact of multiple applicators in sensitivity analyses (see figure HE26 and HE27)
Infection Prevention Society	Economic Report	29	7	Any model is only as good as the data used to populate it. The overwhelming majority of studies used to inform this model have been assessed as low quality and many have at least moderate levels of bias. This does not provide suitable data on which to make such definitive estimates of costs.	Thank you for your comment. It is not true to state that the 'overwhelming majority of studies used to inform this model have been assessed as low quality' – as detailed in evidence review B, the overall quality of the NMA was graded as moderate, and relatively few of the included studies were judged to be at serious risk of bias.
Infection Prevention Society	Economic Report	31	4	It is not at all clear how this additional data was used in creating the models	Thank you for your comment. This is explained on p. 29
Infection Prevention Society	Economic Report	31	4	These estimates do not have face validity. Aqueous CHG is not a general surgical skin prep (only plastics + urology) and contain very low concentrations of CHG - it would therefore not be realistic to suggest it is associated with a lower risk of SSI than aqueous iodine - probably reflecting the poor quality of data used to inform the model. Similarly the suggestion that povidone iodine in alcohol is associated with a 25% greater risk of SSi than CHG in alcohol does not seem realistic or supported by the data.	Thank you for your comment. It cannot be said that the data are not supported by the data, and nor does the fact that the results of a synthesis of systematically identified best-available evidence are not in line with some peoples expectations mean that the evidence lacks face-validity. On the contrary, the committee agreed that the network meta-analysis undertaken for this question represented a more rigorous synthesis of the available data than has previously been available and, accordingly, they agreed that the results provided a robustly evidence-based foundation for their guidance.
Infection Prevention Society	Economic Report	31	6	This table is unclear. As mentioned previously aqueous CHG is not a general skin preparation so it is not clear what the surgeons in this survey were using and why. The type of surgery has an effect of the skin preparation selected and therefore these data are influenced by the mix of surgery/surgeons included in the survey. The % total uses adds up to 150% and it is therefore not clear what this means or how it has been derived.	Thank you for your comment. As described on p. 29, these data are used to weight the estimates of SSI probability from the unit in question in order to arrive at an estimate of baseline risk (with povidone iodine). Thank you for pointing out the error with percentages; this has been corrected.
Infection Prevention Society	Economic Report	33	3	Many larger incisions will require the use of more than one applicator. If using the assumptions for liquid preparation then this should assume 150ml per incision which equates to 6!	Thank you for your comment. We explore the impact of multiple applicators in sensitivity analyses (see figure HE26 and HE27)

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