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TITL


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ABSTRACT

Introduction:
Surgical site infection (SSI) after minor skin excisions has a significant impact on patient morbidity and healthcare resources. Skin antisepsis prior to surgical incision is used to prevent surgical site infection, and is performed routinely worldwide. However, in spite of the routine use of skin antisepsis, there is no consensus regarding which antiseptic agents are most effective.

Methods and analysis:
The study design is a prospective randomised controlled trial (RCT) with the aim of investigating the impact of two different antiseptic preparations upon the incidence of superficial surgical site infection in patients undergoing minor skin excisions. The intervention of 0.5% chlorhexidine gluconate (CHG) in 70% alcohol will be compared with 0.5% chlorhexidine gluconate in aqueous solution. The trial will be conducted in four Australian General Practices over a 9-month period, with 920 participants to be recruited. Consecutive patients presenting for minor skin excisions will be eligible to participate. Randomisation will be on the level of the patient. The primary outcome is superficial surgical site infection in the first 30 days following the excision. Secondary outcomes will be adverse effects including anaphylaxis, skin irritation, contact dermatitis and rash and patterns of antibiotic resistance.

Ethics and Dissemination: The study has been approved by the James Cook University Human Research Ethics Committee (HREC). Findings will be disseminated in conference presentations and journals and through online electronic media.

Registration Details: The trial is registered with the Australian New Zealand Clinical Trials Registry, registration number: ACTRN12615001045505.

Discussion: RCTs conducted in General Practice differ from hospital based projects in terms of feasibility, pragmatism and funding. The success of this trial will be cemented in the fact that the research question was established by a group of GPs who identified an interesting question which is relevant to their clinical practice and not answered by current evidence.

Study Strengths

- Practical clinical question relevant to clinical practice
- Recruitment of clinicians and participants will be very feasible
- Independent outcome assessor will assess photographs of all infections
- Conduct of trial in General Practice will provide clinically relevant results to end user

Study Limitations

- Diagnosis of infection has element of subjectivity
- Practice based outcome assessors will not be blinded
BACKGROUND

It is routine practice prior to surgery to carry out preoperative cleansing of the skin with antiseptic preparations at the site of surgical incisions (preoperative skin antisepsis). [1-3] The purpose of preoperative skin antisepsis is to reduce the incidence of surgical site infection (SSI) by removing microorganisms on the skin through a combination of mechanical removal and chemical killing. [1, 3, 4] The incidence of SSI arising from surgery in general practice is usually 1-3%, but has been recorded at rates as high as 10%. [5-8] The consequences of SSI include pain and discomfort for patients, increased healthcare-associated costs and temporarily reduced occupational and recreational productivity and functionality. [1, 3, 4, 9] As a result, reducing the incidence of SSIs is in the interest of all stakeholders in healthcare.

The most commonly used preoperative skin antiseptic preparations are povidone iodine (PVI) and chlorhexidine gluconate (CHG). Both are available in aqueous and alcoholic preparations and in multiple different concentrations. [1, 3, 4] Both PVI and CHG are effective against a wide range of gram positive and negative bacteria, viruses and fungi, though CHG has a more appreciable residual antiseptic activity on the skin after application. [1, 2, 4]

Surprisingly, despite the routine use of preoperative skin antisepsis, there is no definitive scientific consensus regarding which antiseptic preparation is most effective at preventing SSI. [1, 4, 9] There is even less definitive data available for antisepsis prior to clean surgery, which the Centre for Disease Control (CDC) defines as “an uninfected operation in which no inflammation is encountered and the respiratory, alimentary, genital or uninfected urinary tract is not entered” (CDC, 2011). [10] Prior studies of wound infection after minor surgery in General Practice in the Mackay region have shown a SSI rate of approximately 9.5% - an incidence which is much higher than expected based on published results of similar cohorts in other regions of Australia and the world. [11-14] The reason for this high infection rate is unclear, but may be related to the hot, humid environment or to patient behaviour in our rural setting. On one hand, this infection rate is suboptimal, as the CDC suggests that an acceptable rate of SSI after clean minor surgery is less than 5% [15]. However, in settings where there is a low risk of infection after clean surgery, studies of over 5,000 procedures may be required to detect a clinically relevant difference in infection from an intervention with statistical confidence, making such trials unfeasible [16]. Conversely, because of the high rate of infection in our patient cohort and the high minor surgery workload in rural general practice [17], a study of skin antisepsis for the prevention of SSI in our setting is highly feasible.

In general, the evidence base guiding appropriate selection of antiseptic agents is poor. A landmark study found 2% CHG in 70% isopropyl alcohol to be superior to an aqueous solution of 10% PVI, however, as alcohol is known to have significant antimicrobial properties this was likely to be an active treatment component in this study [18]. Most recent meta-analyses, including a Cochrane review, concur that it is difficult to make conclusive statements about whether there are differences in the efficacy of CHG and PVI [1, 2, 9] and the latest guideline on surgical skin antisepsis released by the Queensland Department of Health agrees with this position. [4] The Queensland Department of Health does however endorse the use of alcoholic solutions in preference to aqueous preparations, [4] and two recent meta-analyses have asserted that there is some evidence to suggest that alcoholic solutions may be more effective than aqueous solutions. [1, 2] Nonetheless, both meta-analyses agree that the marked heterogeneity in type and application of antiseptic preparations between available studies hinder direct comparisons between them. [1, 2] This, combined with the overall low statistical power of almost all available studies makes it difficult to draw firm conclusions about the proposed superiority of alcoholic solutions. [1, 9]
Previous research in the Mackay region [6, 7, 19, 20] and recent interviews (pers. comm.)
have revealed that the majority of Mackay general practitioners (GPs) use CHG in
preference to PVI, one of the reasons behind this being perceptions of 'messiness' and skin
staining. Therefore for practical reasons, our team has chosen to examine the difference
between alcoholic and aqueous CHG, rather than comparing the relative efficacy of CHG
and PVI.

The aim of our study is to determine whether there is a difference in the incidence of SSI
after minor skin excisions in general practice (clean surgery) when alcoholic chlorhexidine
 gluconate is used for preoperative skin antisepsis in comparison to aqueous chlorhexidine
 gluconate.

We hope this research will provide more authoritative direction about skin antisepsis to
clinicians carrying out clean surgery. If our research demonstrates a difference in efficacy
between alcoholic and aqueous CHG, its dissemination may lead a change in behaviour
which may serve to reduce overall incidence of SSI after minor skin excisions in general
practice in Australia.

METHODS AND ANALYSIS

Study centre

This study will be conducted in four private general practices in Mackay, Queensland
(latitude 21E8S). Mackay is a rural centre with around 100 local GPs servicing a population
of 112,798. [21] The study team have previously carried out a number of successful
randomised controlled trials (RCTs) on minor skin excisions within the Mackay region. [6, 8,
19, 20]

Study design

This is a prospective randomised controlled trial (RCT) comparing the intervention of 0.5%
CHG in 70% alcohol with 0.5% aqueous CHG surgical skin preparation for the prevention
of SSI following minor skin excisions conducted in general practice. Data will be collected
over a 9 month period. The study will be conducted in accordance with the CONSORT
statement.

Intervention

The intervention of surgical skin antisepsis with 0.5% CHG in 70% alcohol will be compared
with the control group of 0.5% CHG aqueous solution. The 0.5% concentration of CHG
aligns with guidelines released by the Queensland Centre for Healthcare Related Infection
Surveillance and Prevention. [22] The 70% alcoholic concentration of CHG is standard for
alcoholic preoperative skin preparations. [2]

Recruitment of study participants

Consecutive patients over the age of 18 with capacity to give informed consent, who present
to participating GP practices for minor skin excisions, will be invited to participate. The
practice nurses will be responsible for recruitment. A number of provisions have been
developed to assure informed consent. Firstly, all eligible participants will be provided with a
participant information sheet before giving written informed consent. In addition, practice
nurses, rather than practice GPs, will recruit patients. This is intended to minimise risk of
perceived coercion, as nurses are somewhat less responsible for direct decisions regarding
patient care than the patient’s GP. Further, all nurses involved in the trial will receive formal
training regarding appropriate consenting procedures.
Randomisation

In this prospective RCT, randomisation will be performed at the level of the patient. The random sequence will be generated from a computer-generated random number table. Allocation concealment will be attained by using sealed, numbered, tamperproof opaque envelopes such that neither the patient, nor the clinicians involved in their care, will be aware of their allocation until after they have consented to be a part of the trial, thereby minimizing selection and confounding bias. The research team involved in the assessment or treatment of patients will have no role in the assignment process. The patients will be blinded to treatment allocation, although there are differences in the alcoholic skin preparation which are identifiable to the patient. Blinding of the operating doctors to the assigned skin antiseptic is not feasible given the differing smell of the two solutions.

Inclusion criteria

- All patients over the age of 18 undergoing minor skin procedures at the participating practices during the study period who:
  - have capacity to give informed consent and;
  - are able to return for removal of sutures
- Patients who are not presenting for:
  - excision of sebaceous cyst
  - suturing of lacerations
  - excisions not requiring sutures, such as shave biopsies
  - punch biopsies
  - excisions on body sites where adrenaline is contraindicated

Exclusion Criteria

- Allergy to alcohol or chlorhexidine
- Evidence of infection at or adjacent to the operative site
- Current use of antibiotics
- Clinical indication for antibiotic treatment following excision (besides SSI)
- Peri-ocular excisions
- Patients with a primary language other than English for which certified translation services for that language are not available

Surgical and Wound Protocol

A surgical and wound management protocol will standardise the management across both study arms. The protocol is modelled on previous protocols used in similar trials, as well as international guidelines, [6, 8, 10, 19, 20] and was developed in consultation with participating doctors and nurses. As per this protocol, skin antisepsis will be applied in a consistent manner for both study arms - drapes, gloves, sutures, local anaesthetic and dressings will be the same across all sites and post-operative wound care processes will be identical, with all patients receiving a standard set of verbal and written post-operative wound care instructions.

Outcome Measures

Primary outcome measure
The primary outcome measure is the incidence of post-operative surgical site infection occurring within 30 days of the procedure (defined below). Patients’ wounds will be assessed for evidence of SSI when they present for removal of sutures; at any other time if they present for wound review due to signs and/or symptoms of SSI, or opportunistically if they re-present for any other reason. Wound assessment will be carried out by doctors or nurses at each general practice and the presence or absence of SSI recorded... There will be standardised in-house training regarding the definition of infection. All infections will be photographed and assessed for infection by a second blinded independent outcome assessor to improve validity and reliability.

If patients are deemed to have an SSI, they will be treated with antibiotics as clinically indicated, and as per standard practice, all wounds with a purulent discharge will be swabbed.

Secondary outcome measure

Secondary outcome measures will be

1. Adverse reactions to the preoperative skin antiseptic agent, manifesting as any one of
   a. anaphylaxis
   b. skin irritation or contact dermatitis
   c. rash

2. Microbiology of infected wounds with a purulent discharge, and any patterns of antibiotic resistance

Definitions

Surgical site infection

Surgical site infection will be determined in accordance with a modified version of the CDC definition for superficial surgical site infection:

- Infection occurs within 30 days after the excision, AND
- Infection involves ONLY skin or subcutaneous tissue of the incision, AND
- At least ONE of the following:
  o Purulent drainage with or without laboratory confirmation from the superficial incision
  o At least one of the following signs or symptoms: pain or tenderness, localised swelling, redness or heat
  o Diagnosis of superficial SSI by the GP
- Stitch abscesses, characterised by minimal inflammation and discharge confined to the points of suture penetration, will not be included as SSIs [6, 8, 10]

Data Collection

Data will be primarily collected through use of a written spreadsheet which will be completed by practice nurses. A member of the research team will visit practices on a fortnightly basis to audit the data collection.

Baseline data will be collected regarding patient demographics, including age, sex, occupation and smoking status, as well as co-morbidities such as diabetes mellitus or peripheral vascular disease and current relevant medications, such as anticoagulants and immunosuppressants. Data will also be recorded regarding the excision itself, such as the incision length, the suture size and the type of excision performed (i.e. simple, flap, 2-layer procedure). A body site map will be used to record excision site and the histology of the
lesion will also be recorded. Each item of data has been chosen based on data extracted from other trials on risk factors for SSI. [5-8]

Sample Size Calculation

Our sample size was calculated on the basis of previous studies of surgical site infection in the Mackay region - pooled analyses showed a weighted mean SSI rate of 9.35%, which has been rounded up to 10% as our predicted baseline infection rate. [6, 19, 20] We decided that an absolute reduction in the SSI rate of 5% (to 5%) would be clinically significant. To reach this conclusion with statistical confidence, a power in excess of 80% and a significance level of 0.05, a total of 435 patients would be required in the intervention group and 435 patients in the control group, thus 870 in total.

Our previous similar trials have had a drop-out rate of less than 5%, so we will enrol an additional 50 patients to counter potential attrition, providing a final sample size of 920. [6, 8, 19, 20]

Data Analysis

The primary analysis is an intention to treat analysis including all participants who undergo randomisation. The analysis will be performed taking the individual person as the unit of analysis. All reported p values will be two tailed and for each analysis p<0.05 will be considered statistically significant. The main analysis will follow the intention-to-treat principle. Baseline data across control and intervention groups will first be assessed for marked differences. The incidence of SSI (the primary dependent variable) in each of the two groups of the trial will then be compared using Pearson’s chi-square test. Multivariable logistic regression analysis will be applied in case differences exist between intervention and control groups at baseline and the analysis requires adjustment for confounders. We will also carry out sensitivity testing for lost to follow-up patients and per protocol analysis for non-compliers to assess for the possible effects of systematic biases on results.

Potential problems

Based on our previous studies, we feel that recruitment of adequate patient numbers is feasible, however if we fail to recruit patients, we will invite additional General Practices to participate.

In our previous studies we have found that assessing for infection at time of removal of sutures facilitates a high rate of follow-up. Any patients not followed-up will be analysed on an intention to treat basis.

We have not planned to perform an interim analysis as we feel that variation of antisepsis is a minor intervention, and the outcome of SSI is usually a minor medical issue which is treated with a course of antibiotics. An interim analysis would further increase the required sample size reducing the feasibility of our trial.

DISSEMINATION

This project is due for completion one year after commencement of data collection. The translation of important findings to clinical practice will be facilitated through dissemination in conference presentations and journals as well as electronic media. The researchers will also aim to publish their findings on a range of Australian FOAM (Free Open Access Meducation) websites to reach the next generation of technology-savvy health professionals. A written lay
summary of the results will also be displayed at the participating general practices for the
information of study participants.

ETHICAL CONSIDERATIONS

This project has been reviewed and approved by the James Cook University Human
Research Ethic Committee; HREC approval ID H6065. We do not expect the interventions of
this study to place participants at any significant risk of harm, as we hypothesise a lower
incidence of SSI in the intervention group due to the use of alcoholic CHG. In any case, SSI
is a minor condition which can be easily treated without significant long term sequelae. To
assure privacy and confidentiality, all data spreadsheets and consent forms will be kept in a
locked cupboard throughout the trial, then transferred to a locked safe at the conclusion of
the trial, where they will be kept for 15 years. Patients will be de-identified in all data
collection.

DISCUSSION

Very few large RCTs are conducted in a primary care setting [23, 24]. Difficulties have been
reported in recruiting both patients and clinicians [25], and RCTs have been reported as
being methodologically and practically difficult to conduct in general practice. [11] However,
it is important that clinical practice be informed by adequate primary care evidence.
Otherwise GPs, the end-user of the research process, who attempt to practise evidence-
based medicine may have flawed tools and the guidelines they use may not be applicable to
the patients they see. [26, 27]

Funding for primary care research in Australia is very limited, particularly compared with UK
and Netherlands with only 2% of NHMRC grants awarded to primary care research between
based research in issues of funding, feasibility and pragmatism, and we have used our
experience from conducting previous successful trials in general practice to inform the
design and methods of the present study[6, 8, 19, 20]. Our study will be conducted for a total
cost of $20,000 which is similar to our previous trials.

Skin excisions form a large proportion of the workload of Australian GPs [17] and this is even
greater in Queensland, the state with the highest incidence of skin cancer in the world. [29]
This effect is magnified in regional towns such as Mackay, where there are no permanent
dermatologists or plastic surgeons. Using a research question which is relevant to our
clinical situation increases the feasibility of recruitment of patients because of our high case
load of patients presenting for skin excisions.

Our research question is practical and clinically relevant. Local clinicians do not use betadine
antisepsis because of perceptions of ‘messiness’ and skin staining. Therefore, in order to be
pragmatic our team has chosen to examine the difference between alcoholic and aqueous
CHG, rather than comparing the relative efficacy of CHG and PVI. We have also found that
using a clinically relevant research question engages general practitioners and practice
nurses and facilitates practitioner recruitment, as well as increasing the potential for
translation into clinical practice[30].

Our surgical and wound management protocol was developed in consultation with
participating doctors and practice nurses, which again increases the ownership and
practicality of the project. Occasionally, scientific rigor may be compromised at the expense
of pragmatism. For instance in contrast with hospital based research, it is simply not
practically or financially feasible to have an independent outcome assessor assessing each wound at each of the three geographically dispersed practices. To compensate for this, infections will be photographed and assessed for infection by a second independent and blinded outcome assessor, who will re-assess every wound.

It is also not feasible to have an independent researcher to recruit patients. In our trial practice nurses will be responsible for recruitment. A number of provisions have been developed to assure informed consent. This is intended to minimise risk of perceived coercion, as nurses are somewhat less responsible for direct decisions regarding patient care than the patient’s GP. The practice nurses are also responsible for data collection and are paid on a fee per service basis that compensates them for their time. The study involves very little extra work for the participating GPs – they are not responsible for any data collection, and were only required to have knowledge of the process involved in order to answer any possible queries.

The trial will provide guidance to GPs regarding skin antisepsis, and will inform current clinical guidelines and healthcare worker education. If we detect a measurable decrease in incidence of SSI with alcoholic CHG, this may result in a change in clinical practice which could reduce SSI rates following clean surgery. As this is a pragmatic trial, the findings can potentially be immediately translated into clinical practice.

ACKNOWLEDGEMENTS
The authors thank Ms Debbie Kimber, Ms Julie O’Sullivan, Dr Sheldon Browning, Dr Luke Notely, Dr Andrew O’Neil, Dr Andrea Cosgrove.

Authors Contributions
CH conceived the study idea and oversaw the development of the study design and protocol. DC led the development of the study protocol. AH, MD, and JB assisted with the development of the study design and protocol. PB assisted with the sample size calculation and statistics. All authors contributed to the drafting of the manuscript.

COMPETING INTERESTS
None declared

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Royal Australian College of General Practitioners Family Medical Care Education and Research Grant: $13 500

REFERENCES


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Protocol for randomized controlled trial comparing aqueous with alcoholic chlorhexidine antisepsis for the prevention of superficial surgical site infection after minor surgery in general practice – the AVALANCHE trial.

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ABSTRACT

Introduction:
Surgical site infection (SSI) after minor skin excisions has a significant impact on patient morbidity and healthcare resources. Skin antisepsis prior to surgical incision is used to prevent surgical site infection, and is performed routinely worldwide. However, in spite of the routine use of skin antisepsis, there is no consensus regarding which antiseptic agents are most effective. The AVALANCHE trial will compare Aqueous Versus Alcoholic Antisepsis with Chlorhexidine for Skin Excisions.

Methods and analysis:
The study design is a prospective randomised controlled trial (RCT) with the aim of investigating the impact of two different antiseptic preparations upon the incidence of superficial surgical site infection in patients undergoing minor skin excisions. The intervention of 0.5% chlorhexidine gluconate (CHG) in 70% alcohol will be compared with 0.5% chlorhexidine gluconate in aqueous solution. The trial will be conducted in four Australian General Practices over a 9-month period, with 920 participants to be recruited. Consecutive patients presenting for minor skin excisions will be eligible to participate. Randomisation will be on the level of the patient. The primary outcome is superficial surgical site infection in the first 30 days following the excision. Secondary outcomes will be adverse effects including anaphylaxis, skin irritation, contact dermatitis and rash and patterns of antibiotic resistance.

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Study Strengths
• Practical clinical question relevant to clinical practice
• Recruitment of clinicians and participants will be very feasible
• Independent outcome assessor will assess photographs of all infections
• Conduct of trial in General Practice will provide clinically relevant results to end user

Study Limitations
• Diagnosis of infection has element of subjectivity
• Practice based outcome assessors will not be blinded
BACKGROUND

It is routine practice prior to surgery to carry out preoperative cleansing of the skin with antiseptic preparations at the site of surgical incisions (preoperative skin antisepsis). [1-3] The purpose of preoperative skin antisepsis is to reduce the incidence of surgical site infection (SSI) by removing microorganisms on the skin through a combination of mechanical removal and chemical killing. [1, 3, 4] The incidence of SSI arising from surgery in general practice is usually 1-3%, but has been recorded at rates as high as 10%. [5-8] The consequences of SSI include pain and discomfort for patients, increased healthcare-associated costs and temporarily reduced occupational and recreational productivity and functionality. [1, 3, 4, 9] As a result, reducing the incidence of SSIs is in the interest of all stakeholders in healthcare.

The most commonly used preoperative skin antiseptic preparations are povidone iodine (PVI) and chlorhexidine gluconate (CHG). Both are available in aqueous and alcoholic preparations and in multiple different concentrations. [1, 3, 4] Both PVI and CHG are effective against a wide range of gram positive and negative bacteria, viruses and fungi, though CHG has a more appreciable residual antiseptic activity on the skin after application. [1, 2, 4]

Surprisingly, despite the routine use of preoperative skin antisepsis, there is no definitive scientific consensus regarding which antiseptic preparation is most effective at preventing SSI. [1, 4, 9] There is even less definitive data available for antisepsis prior to clean surgery, which the Centre for Disease Control (CDC) defines as “an uninfected operation in which no inflammation is encountered and the respiratory, alimentary, genital or uninfected urinary tract is not entered” (CDC, 2011). [10] Prior studies of wound infection after minor surgery in General Practice in the Mackay region have shown a SSI rate of approximately 9.5% - an incidence which is much higher than expected based on published results of similar cohorts in other regions of Australia and the world. [11-14] The reason for this high infection rate is unclear, but may be related to the hot, humid environment or to patient behaviour in our rural setting. On one hand, this infection rate is suboptimal, as the CDC suggests that an acceptable rate of SSI after clean minor surgery is less than 5% [15]. However, in settings where there is a low risk of infection after clean surgery, studies of over 5,000 procedures may be required to detect a clinically relevant difference in infection from an intervention with statistical confidence, making such trials unfeasible [16]. Conversely, because of the high rate of infection in our patient cohort and the high minor surgery workload in rural general practice [17], a study of skin antisepsis for the prevention of SSI in our setting is highly feasible.

In general, the evidence base guiding appropriate selection of antiseptic agents is poor. A landmark study found 2% CHG in 70% isopropyl alcohol to be superior to an aqueous solution of 10% PVI, however, as alcohol is known to have significant antimicrobial properties this was likely to be an active treatment component in this study [18]. Most recent meta-analyses, including a Cochrane review, concur that it is difficult to make conclusive statements about whether there are differences in the efficacy of CHG and PVI [1, 2, 9] and the latest guideline on surgical skin antisepsis released by the Queensland Department of Health agrees with this position. [4] The Queensland Department of Health does however endorse the use of alcoholic solutions in preference to aqueous preparations, [4] and two recent meta-analyses have asserted that there is some evidence to suggest that alcoholic solutions may be more effective than aqueous solutions. [1, 2] Nonetheless, both meta-analyses agree that the marked heterogeneity in type and application of antiseptic preparations between available studies hinder direct comparisons between them. [1, 2] This, combined with the overall low statistical power of almost all available studies makes it difficult to draw firm conclusions about the proposed superiority of alcoholic solutions. [1, 9]
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We hope this research will provide more authoritative direction about skin antisepsis to clinicians carrying out clean surgery. If our research demonstrates a difference in efficacy between alcoholic and aqueous CHG, its dissemination may lead a change in behaviour which may serve to reduce overall incidence of SSI after minor skin excisions in general practice in Australia.

**METHODS AND ANALYSIS**

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This study will be conducted in four private general practices in Mackay, Queensland (latitude 21E8S). Mackay is a rural centre with around 100 local GPs servicing a population of 112,798. [21] The study team have previously carried out a number of successful randomised controlled trials (RCTs) on minor skin excisions within the Mackay region. [6, 8, 19, 20]

**Study design**

This is a prospective randomised controlled trial (RCT) comparing the intervention of 0.5% CHG in 70% alcohol with 0.5% aqueous CHG surgical skin preparation for the prevention of SSI following ‘minor skin excisions’ – benign or malignant skin lesions excised under local anaesthetic - conducted in general practice. Data will be collected over a 9 month period. The study will be conducted in accordance with the CONSORT statement.

**Intervention**

The intervention of surgical skin antisepsis with 0.5% CHG in 70% alcohol will be compared with the control group of 0.5% CHG aqueous solution. The 0.5% concentration of CHG aligns with guidelines released by the Queensland Centre for Healthcare Related Infection Surveillance and Prevention. [22] The 70% alcoholic concentration of CHG is standard for alcoholic preoperative skin preparations. [2] The antiseptic solutions will be purchased from an independent supplier with research funding.

**Recruitment of study participants**

Consecutive patients over the age of 18 with capacity to give informed consent, who present to participating GP practices for minor skin excisions, will be invited to participate. The practice nurses will be responsible for recruitment. A number of provisions have been developed to assure informed consent. Firstly, all eligible participants will be provided with a participant information sheet before giving written informed consent. In addition, practice nurses, rather than practice GPs, will recruit patients. This is intended to minimise risk of perceived coercion, as nurses are somewhat less responsible for direct decisions regarding
patient care than the patient’s GP. Further, all nurses involved in the trial will receive formal training regarding appropriate consenting procedures.

Randomisation

In this prospective RCT, randomisation will be performed at the level of the patient with an allocation ratio of 1:1. The random sequence will be generated from a computer-generated random number table. Allocation concealment will be attained by using sealed, numbered, tamperproof opaque envelopes such that neither the patient, nor the clinicians involved in their care, will be aware of their allocation until after they have consented to be a part of the trial, thereby minimizing selection and confounding bias. The research team involved in the assessment or treatment of patients will have no role in the assignment process. The patients will be blinded to treatment allocation, although there are differences in the alcoholic skin preparation which are identifiable to the patient. Blinding of the operating doctors to the assigned skin antiseptic is not feasible given the differing smell of the two solutions. The practice nurse or doctor assessing outcomes will be blinded to the treatment allocation, as will the practice nurse collecting data and the investigator team.

Inclusion criteria

- All patients over the age of 18 undergoing minor skin procedures at the participating practices during the study period who:
  - have capacity to give informed consent and;
  - are able to return for removal of sutures
- Patients who are not presenting for:
  - excision of sebaceous cyst
  - suturing of lacerations
  - excisions not requiring sutures, such as shave biopsies
  - punch biopsies
  - excisions on body sites where adrenaline is contraindicated

Exclusion Criteria

- Allergy to alcohol or chlorhexidine
- Evidence of infection at or adjacent to the operative site
- Current use of antibiotics
- Clinical indication for antibiotic treatment following excision (besides SSI)
- Peri-ocular excisions
- Patients with a primary language other than English for which certified translation services for that language are not available

Surgical and Wound Protocol

A surgical and wound management protocol will standardise the management across both study arms. The protocol is modelled on previous protocols used in similar trials, as well as international guidelines, [6, 8, 10, 19, 20] and was developed in consultation with participating doctors and nurses. As per this protocol, skin antisepsis will be applied in a consistent manner for both study arms - drapes, gloves, sutures, local anaesthetic and dressings will be the same across all sites and post-operative wound care processes will be identical, with all patients receiving a standard set of verbal and written post-operative wound care instructions.

Outcome Measures
Primary outcome measure

The primary outcome measure is the incidence of post-operative surgical site infection occurring within 30 days of the procedure (defined below). Patients’ wounds will be assessed for evidence of SSI when they present for removal of sutures; at any other time if they present for wound review due to signs and/or symptoms of SSI, or opportunistically if they re-present for any other reason. Wound assessment will be carried out by doctors or nurses at each general practice and the presence or absence of SSI recorded. There will be standardised in-house training regarding the definition of infection. All infections will be photographed and assessed for infection by a second blinded independent outcome assessor to improve validity and reliability. If patients are deemed to have an SSI, they will be treated with antibiotics as clinically indicated, and as per standard practice, all wounds with a purulent discharge will be swabbed.

Secondary outcome measure

Secondary outcome measures will be
1. Adverse reactions to the preoperative skin antiseptic agent, manifesting as any one of
   a. anaphylaxis
   b. skin irritation or contact dermatitis
   c. rash
2. Microbiology of infected wounds with a purulent discharge, and any patterns of antibiotic resistance

Definitions

Surgical site infection

Surgical site infection will be determined in accordance with a modified version of the CDC definition for superficial surgical site infection:
- Infection occurs within 30 days after the excision, AND
- Infection involves ONLY skin or subcutaneous tissue of the incision, AND
- At least ONE of the following:
  o Purulent drainage with or without laboratory confirmation from the superficial incision
  o At least one of the following signs or symptoms: pain or tenderness, localised swelling, redness or heat
  o Diagnosis of superficial SSI by the GP
- Stitch abscesses, characterised by minimal inflammation and discharge confined to the points of suture penetration, will not be included as SSIs [6, 8, 10]

Data Collection

Data will be primarily collected through use of a written spreadsheet which will be completed by practice nurses. A member of the research team will visit practices on a fortnightly basis to audit the data collection.

Baseline data will be collected regarding patient demographics, including age, sex, occupation and smoking status, as well as co-morbidities such as diabetes mellitus or peripheral vascular disease and current relevant medications, such as anticoagulants and immunosuppressants. Data will also be recorded regarding the excision itself, such as the...
incision length, the suture size and the type of excision performed (i.e. simple, flap, 2-layer procedure). A body site map will be used to record excision site and the histology of the lesion will also be recorded. Each item of data has been chosen based on data extracted from other trials on risk factors for SSI. [5-8]

Sample Size Calculation

Our sample size was calculated on the basis of three previous studies of surgical site infection in the Mackay region [6, 19, 20]. These studies used mostly aqueous chlorhexidine as surgical antisepsis. Pooled analyses showed a weighted mean SSI rate of 9.35%, which has been rounded up to 10% as our predicted baseline infection rate. [6, 19, 20] We decided that an absolute reduction in the SSI rate of 5% (to 5%) would be clinically significant. To reach this conclusion with statistical confidence, a power in excess of 80% and a significance level of 0.05, a total of 435 patients would be required in the intervention group and 435 patients in the control group, thus 870 in total.

Our previous similar trials [6,8,19,20] have had a drop-out rate of less than 5%, so we will enrol an additional 50 patients to counter potential attrition, providing a final sample size of 920. [6, 8, 19, 20]

Data Analysis

The primary analysis is an intention to treat analysis including all participants who undergo randomisation. The analysis will be performed taking the individual person as the unit of analysis. All reported p values will be two tailed and for each analysis p<0.05 will be considered statistically significant. The main analysis will follow the intention-to-treat principle. Baseline data across control and intervention groups will first be assessed for marked differences. The incidence of SSI (the primary dependent variable) in each of the two groups of the trial will then be compared using Pearson’s chi-square test. Multivariable logistic regression analysis will be applied in case differences exist between intervention and control groups at baseline and the analysis requires adjustment for confounders. We will also carry out sensitivity testing for lost to follow-up patients and per protocol analysis for non-compliers to assess for the possible effects of systematic biases on results.

Potential problems

Based on our previous studies, we feel that recruitment of adequate patient numbers is feasible, however if we fail to recruit patients, we will invite additional General Practices to participate. In our previous studies we have found that assessing for infection at time of removal of sutures facilitates a high rate of follow-up. Any patients not followed-up will be analysed on an intention to treat basis. We have not planned to perform an interim analysis as we feel that variation of antisepsis is a minor intervention, and the outcome of SSI is usually a minor medical issue which is treated with a course of antibiotics. An interim analysis would further increase the required sample size reducing the feasibility of our trial.

DISSEMINATION

This project is due for completion one year after commencement of data collection. The translation of important findings to clinical practice will be facilitated through dissemination in
conference presentations and journals as well as electronic media. The researchers will also aim to publish their findings on a range of Australian FOAM (Free Open Access Meducation) websites to reach the next generation of technology-savvy health professionals. A written lay summary of the results will also be displayed at the participating general practices for the information of study participants.

ETHICAL CONSIDERATIONS

This project has been reviewed and approved by the James Cook University Human Research Ethic Committee; HREC approval ID H6065. We do not expect the interventions of this study to place participants at any significant risk of harm, as we hypothesise a lower incidence of SSI in the intervention group due to the use of alcoholic CHG. In any case, SSI is a minor condition which can be easily treated without significant long term sequelae. To assure privacy and confidentiality, all data spreadsheets and consent forms will be kept in a locked cupboard throughout the trial, then transferred to a locked safe at the conclusion of the trial, where they will be kept for 15 years. Patients will be de-identified in all data collection.

DISCUSSION

Very few large RCTs are conducted in a primary care setting [23, 24]. Difficulties have been reported in recruiting both patients and clinicians [25], and RCTs have been reported as being methodologically and practically difficult to conduct in general practice. [11] However, it is important that clinical practice be informed by adequate primary care evidence. Otherwise GPs, the end-user of the research process, who attempt to practise evidence-based medicine may have flawed tools and the guidelines they use may not be applicable to the patients they see. [26, 27]

Funding for primary care research in Australia is very limited, particularly compared with UK and Netherlands with only 2% of NHMRC grants awarded to primary care research between 2000 and 2008. [28] General practice based research differs in many ways from hospital based research in issues of funding, feasibility and pragmatism, and we have used our experience from conducting previous successful trials in general practice to inform the design and methods of the present study[6, 8, 19, 20]. Our study will be conducted for a total cost of $20,000 which is similar to our previous trials.

Skin excisions form a large proportion of the workload of Australian GPs [17] and this is even greater in Queensland, the state with the highest incidence of skin cancer in the world. [29] This effect is magnified in regional towns such as Mackay, where there are no permanent dermatologists or plastic surgeons. Using a research question which is relevant to our clinical situation increases the feasibility of recruitment of patients because of our high case load of patients presenting for skin excisions.

Our research question is practical and clinically relevant. Local clinicians do not use betadine antisepsis because of perceptions of ‘messiness’ and skin staining. Therefore, in order to be pragmatic our team has chosen to examine the difference between alcoholic and aqueous CHG, rather than comparing the relative efficacy of CHG and PVI. We have also found that using a clinically relevant research question engages general practitioners and practice nurses and facilitates practitioner recruitment, as well as increasing the potential for translation into clinical practice[30].
Our surgical and wound management protocol was developed in consultation with participating doctors and practice nurses, which again increases the ownership and practicality of the project. Occasionally, scientific rigor may be compromised at the expense of pragmatism. For instance, in contrast with hospital-based research, it is simply not practically or financially feasible to have an independent outcome assessor assessing each wound at each of the three geographically dispersed practices. To compensate for this, infections will be photographed and assessed for infection by a second independent and blinded outcome assessor, who will re-assess every wound.

It is also not feasible to have an independent researcher to recruit patients. In our trial practice nurses will be responsible for recruitment. A number of provisions have been developed to assure informed consent. This is intended to minimise risk of perceived coercion, as nurses are somewhat less responsible for direct decisions regarding patient care than the patient's GP. The practice nurses are also responsible for data collection and are paid on a fee per service basis that compensates them for their time. The study involves very little extra work for the participating GPs – they are not responsible for any data collection, and were only required to have knowledge of the process involved in order to answer any possible queries.

The trial will provide guidance to GPs regarding skin antisepsis, and will inform current clinical guidelines and healthcare worker education. Although our study is conducted in a tropical rural setting and we are aware that our baseline infection rate is comparably high (6,7) we have no reason to believe that any relative risk reduction detected will not be generalizable to other settings. If we detect a measurable decrease in incidence of SSI with alcoholic CHG, this may result in a change in clinical practice, with an increase in use of alcoholic CHG, which could reduce SSI rates following clean surgery. As this is a pragmatic trial, the findings can potentially be immediately translated into clinical practice.

ACKNOWLEDGEMENTS

The authors thank Ms Debbie Kimber, Ms Julie O'Sullivan, Dr Sheldon Browning, Dr Luke Notely, Dr Andrew O'Neil, Dr Andrea Cosgrove.

Authors Contributions

CH conceived the study idea and oversaw the development of the study design and protocol. DC led the development of the study protocol. AH, MD, and JB assisted with the development of the study design and protocol. PB assisted with the sample size calculation and statistics. All authors contributed to the drafting of the manuscript.

COMPETING INTERESTS

None declared

FUNDING

James Cook University Honours program grant: $1000
Royal Australian College of General Practitioners PWH Grieve Award: $2 500
Royal Australian College of General Practitioners Family Medical Care Education and Research Grant: $13 500

The authors’ work is independent of this funding.

REFERENCES


SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

<table>
<thead>
<tr>
<th>Section/item</th>
<th>Item No</th>
<th>Description</th>
<th>Addressed on page number</th>
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<tbody>
<tr>
<td><strong>Administrative information</strong></td>
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<tr>
<td>Title</td>
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<td>Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym</td>
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<tr>
<td>Trial registration</td>
<td>2a</td>
<td>Trial identifier and registry name. If not yet registered, name of intended registry</td>
<td><strong>2</strong></td>
</tr>
<tr>
<td></td>
<td>2b</td>
<td>All items from the World Health Organization Trial Registration Data Set</td>
<td><strong>Supplementary Docs</strong></td>
</tr>
<tr>
<td>Protocol version</td>
<td>3</td>
<td>Date and version identifier</td>
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<tr>
<td>Funding</td>
<td>4</td>
<td>Sources and types of financial, material, and other support</td>
<td><strong>10</strong></td>
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<tr>
<td>Roles and responsibilities</td>
<td>5a</td>
<td>Names, affiliations, and roles of protocol contributors</td>
<td><strong>1,10</strong></td>
</tr>
<tr>
<td></td>
<td>5b</td>
<td>Name and contact information for the trial sponsor</td>
<td><strong>1</strong></td>
</tr>
<tr>
<td></td>
<td>5c</td>
<td>Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities</td>
<td><strong>10</strong></td>
</tr>
</tbody>
</table>
5d Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)

N/A

Introduction

Background and rationale

6a Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention

4,5,9,10

6b Explanation for choice of comparators

4,5,9

Objectives

7 Specific objectives or hypotheses

5

Trial design

8 Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)

5

Methods: Participants, interventions, and outcomes

Study setting

9 Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained.

5

Eligibility criteria

10 Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)

6

Interventions

11a Interventions for each group with sufficient detail to allow replication, including how and when they will be administered

5,6

11b Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)

N/A

11c Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)

6,7,10

11d Relevant concomitant care and interventions that are permitted or prohibited during the trial

6
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<td>Participant timeline</td>
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<td>Recruitment</td>
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<tr>
<td>Methods: Assignment of interventions (for controlled trials)</td>
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<tr>
<td>Allocation:</td>
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<td>Sequence generation</td>
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<td>Implementation</td>
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</tr>
<tr>
<td>Blinding (masking)</td>
<td>17a</td>
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<tr>
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<td>17b</td>
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</table>

Outcomes: Primary, secondary, and other outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (e.g., median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended.

Participant timeline: Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure).

Sample size: Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations.

Recruitment: Strategies for achieving adequate participant enrolment to reach target sample size.

Methods: Assignment of interventions (for controlled trials)

Allocation:

- Sequence generation: Method of generating the allocation sequence (e.g., computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (e.g., blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions.

- Allocation concealment mechanism: Mechanism of implementing the allocation sequence (e.g., central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned.

Implementation: Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions.

Blinding (masking): Who will be blinded after assignment to interventions (e.g., trial participants, care providers, outcome assessors, data analysts), and how.

If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial.

Methods: Data collection, management, and analysis
Data collection 18a Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

18b Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

Data management 19 Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol

Statistical methods 20a Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol

20b Methods for any additional analyses (eg, subgroup and adjusted analyses)

20c Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)

Methods: Monitoring

Data monitoring 21a Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed

21b Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial

Harms 22 Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct

Auditing 23 Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor

Ethics and dissemination
<table>
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<tr>
<th>Item</th>
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<td>24</td>
<td>Plans for seeking research ethics committee/institutional review board (REC/IRB) approval</td>
</tr>
<tr>
<td>25</td>
<td>Plans for communicating important protocol modifications (e.g., changes to eligibility criteria, outcomes, analyses) to relevant parties (e.g., investigators, REC/IRBs, trial participants, trial registries, journals, regulators)</td>
</tr>
<tr>
<td>26a</td>
<td>Who will obtain informed consent or assent from potential trial participants or authorized surrogates, and how (see Item 32)</td>
</tr>
<tr>
<td>26b</td>
<td>Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable</td>
</tr>
<tr>
<td>27</td>
<td>How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial</td>
</tr>
<tr>
<td>28</td>
<td>Financial and other competing interests for principal investigators for the overall trial and each study site</td>
</tr>
<tr>
<td>29</td>
<td>Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators</td>
</tr>
<tr>
<td>30</td>
<td>Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation</td>
</tr>
<tr>
<td>31a</td>
<td>Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (e.g., via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions</td>
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<tr>
<td>31b</td>
<td>Authorship eligibility guidelines and any intended use of professional writers</td>
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<tr>
<td>31c</td>
<td>Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code</td>
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**Appendices**

<table>
<thead>
<tr>
<th>Item</th>
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<tbody>
<tr>
<td>32</td>
<td>Model consent form and other related documentation given to participants and authorized surrogates</td>
</tr>
</tbody>
</table>
Biological specimens

33 Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable

N/A

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.*
Appendix 1: WHO trial registration dataset
Note: All of this information is included in the ANZCTR registry

<table>
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<tr>
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<th>Australian and New Zealand Clinical Trials Registry, registration number: ACTRN12615001045505.</th>
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<td>Secondary identifying numbers</td>
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</table>
| Sources of monetary or material support       | Royal Australian College of General Practitioners  
James Cook University |
| Primary Sponsor                               | James Cook University                                                                             |
| Secondary Sponsor                             | Dr Daniel Charles                                                                                 |
| Contact for public queries                    | Dr Daniel Charles  
C/- Mackay Clinical School  
College of Medicine and Dentistry  
James Cook University  
Level 1, Building K  
Mackay Base Hospital, 475 Bridge Rd  
Mackay QLD 4740 Australia  
Daniel.charles@my.jcu.edu.au |
| Contact for scientific queries                | Professor Clare Heal  
Contact details as per 'corresponding author' section |
| Public title                                  | Aqueous vs Alcoholic Antisepsis with Chlorhexidine for skin Excisions – the AVALACHE trial.       |
| Scientific title                              | Preoperative skin antisepsis with aqueous vs alcoholic chlorhexidine for the prevention of surgical site infection after minor skin excisions in general practice – a randomised controlled trial. |
| Countries of recruitment                      | Australia                                                                                         |
| Health conditions or problems studied         | Surgical Site Infection                                                                          |
| Interventions                                 | Intervention:  
Preoperative skin antisepsis with 0.5% chlorhexidine dissolved in 70% alcohol applied to the surgical site immediately prior to minor skin surgery in general practice.  
Control:  
Preoperative skin antisepsis with 0.5% chlorhexidine dissolved in water applied to the surgical site immediately prior to minor skin surgery in general practice.  
Application protocol for intervention and control:  
Approximately 30mL of antiseptic solution will be applied over skin surface at the site of the |
planned excision using a soaked gauze so as to cover an area 1cm greater at all borders than the area of skin exposed by the sterile drape which will be placed over the site of the excision.

### Key inclusion and exclusion criteria

#### Inclusion criteria
- All patients over the age of 18 undergoing minor skin procedures at the participating practices during the study period who:
  - have capacity to give informed consent and;
  - are able to return for removal of sutures
- Patients who are not presenting for:
  - excision of sebaceous cyst
  - suturing of lacerations
  - excisions not requiring sutures, such as shave biopsies
  - punch biopsies
  - excisions on body sites where adrenaline is contraindicated

#### Exclusion Criteria
- Allergy to alcohol or chlorhexidine
- Evidence of infection at or adjacent to the operative site
- Current use of antibiotics
- Clinical indication for antibiotic treatment following excision (besides SSI)
- Peri-ocular excisions
- Patients with a primary language other than English for which certified translation services for that language are not available

### Study details

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<td>Target sample size</td>
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<tr>
<td>Recruitment status</td>
<td>Recruiting</td>
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<tr>
<td>Primary Outcome(s)</td>
<td>Surgical Site Infection (SSI) diagnosed in accordance with a modified version of the CDC definition for superficial surgical site infection:</td>
</tr>
</tbody>
</table>
  - Infection occurs within 30 days after the excision, AND
  - Infection involves ONLY skin or subcutaneous tissue of the incision, AND
  - At least ONE of the following:
Purulent drainage with or without laboratory confirmation from the superficial incision
- At least one of the following signs or symptoms: pain or tenderness, localised swelling, redness or heat
- Diagnosis of superficial SSI by the GP

Stitch abscesses, characterised by minimal inflammation and discharge confined to the points of suture penetration, will not be included as SSIs.

| Key secondary outcomes | 1. Adverse reactions to the preoperative skin antiseptic agent, manifesting as any one of
|                        |   a. anaphylaxis
|                        |   b. skin irritation or contact dermatitis
|                        |   c. rash
|                        | 2. Microbiology of infected wounds with a purulent discharge, and any patterns of antibiotic resistance |
Appendix 2: Consent Form and Patient Information Sheet

Participant Informed Consent Form

Project: Aqueous Vs Alcoholic Antisepsis with Chlorhexidine for Skin Excisions – The AVALANCHE Trial

Principal Investigator: Dr Daniel Charles
Study supervisor: Professor Clare Heal
School: James Cook University School of Medicine and Dentistry

I understand that the aim of this research study is to compare alcoholic chlorhexidine and aqueous chlorhexidine to see if there are any differences between them in terms of how well they prevent wound infections when they are applied to surgical sites before skin excisions.

I consent to participate in this project; the details of which have been explained to me by the practice nurse, and I have been provided with a written information sheet to keep.

I understand that my participation in this study involves being randomly allocated to one of two groups. Depending upon the group I am allocated to, the site where my skin excision will take place will be cleansed using either alcoholic chlorhexidine or aqueous chlorhexidine. I also acknowledge that prior to giving consent to participate in this study, I will have no knowledge of which of these preparations will be used for my surgery.

I understand that aside from the surgical site cleansing, the doctors and nurses involved in my care will follow standard surgical and wound care protocols. I understand that, as per standard practice, my wound will be assessed for evidence of wound infection when I come back to my GP for removal of sutures, and if a wound infection is noted, I will be treated as per standard practice.

I also agree that the researcher may use the results from my participation as described in the information sheet.

I acknowledge that:

- any risks and possible effects of participating in this study have been explained to my satisfaction;
- taking part in this study is voluntary and I am aware that I can stop taking part in it at any time without explanation or prejudice and withdraw any unprocessed data I have provided;
- any information I give will be kept strictly confidential and that no names will be used to identify me with this study without my approval;
- my details will be kept in storage and will be accessible to the researchers only
- after I sign this consent form it will be retained by the researcher

Name: (printed)  
Signature:  
Date:

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
Participant Information Sheet

Project: Aqueous Vs Alcoholic Antisepsis with Chlorhexidine for Skin Excisions – The AVALANCHE Trial

Principal Investigator: Dr Daniel Charles
Study supervisor: Professor Clare Heal
School: James Cook University School of Medicine and Dentistry

We would like to invite you to take part in a research study that your doctor is participating in. The study is being carried out by an honours student studying the Bachelor of Medicine and Surgery course at James Cook University.

DO YOU NEED TO TAKE PART?
We would like to stress that you do not need to take part in this study unless you wish to. Your decision to participate or not will not impact upon the care you receive at this practice, nor will any additional cost be incurred regardless of your decision. If you choose to participate, you can stop taking part at any time without explanation.

WHAT ARE THE AIMS OF THE STUDY?
Before a surgical procedure is carried out, the area on the patient’s body where the procedure takes place (the surgical site) is routinely cleansed with a solution which kills bacteria on the skin (an antiseptic preparation). The aim of this process is to reduce the likelihood of infection at the surgical site (wound infection). As it stands, however, not enough research has been done to determine which antiseptic preparations are best at preventing wound infections. As such, this study aims to compare two different antiseptic preparations - alcoholic chlorhexidine, and aqueous chlorhexidine - to see which is most effective.

WHAT WILL HAPPEN IF YOU CHOOSE TO TAKE PART?
If you choose to take part in this study, the practice nurse will first take down some basic information from you, such as your height and weight, your basic medical history and the names of any medications you are taking. You will then be randomly allocated to either the alcoholic chlorhexidine group, or the aqueous chlorhexidine group.

Before your skin excision, the surgical site will be cleansed with whichever of these two solutions you have been randomly assigned to. The doctors and nurses involved in your procedure will then be using standard surgical techniques and following routine surgical protocols. They will thoroughly wash their hands, wear gloves, and use routine instruments and stitch materials to complete the surgery. After the skin excision, a dressing will be put over the wound and you will be given instructions about how to care for your wound.

WHAT WILL HAPPEN IF YOU GET A WOUND INFECTION?
As is routine, when you come back for removal of stitches, your doctor or nurse will look carefully for signs of wound infection, however if you believe that you have developed a wound infection before this, please feel free to come back earlier. There is always a small chance of developing a wound infection; they happen 9% of the time after skin excisions, and many factors effect whether or not patients develop wound infections besides the type of antiseptic preparation used. However, if you do develop a wound infection, it is unlikely to be a serious health issue; you may experience some mild pain and discomfort, but the infection is likely to be able to be simply and effectively treated.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY?
The risks of this study are minimal, as both of the solutions being used in this study are already routinely used in medical practices in the area. There is a risk of developing a wound infection, though, as mentioned above, this risk is always present after a skin excision, and your doctor will look carefully for wound infection and treat it if one is found. The only other major risk of the study is the risk of a skin reaction to one of the antiseptic preparations. These reactions are
uncommon, but if you have a known allergy to either chlorhexidine or to alcohol, we would ask that you inform the practice nurse, and we would request that you DO NOT take part in this study.

The major benefit of this study will be to hopefully clarify which antiseptic preparations are best at preventing wound infections and thereby help health workers to decide upon the best way to manage skin excisions in future.

**WILL YOUR INFORMATION BE CONFIDENTIAL?**

Yes, all information collected for the purposes of the study will be completely confidential. Only your GP, the practice nurse, and the main study investigators will have access to your information. The data from this study will be used in research publications and reports, but you will not be identified in any way in these publications.

**WHAT SHOULD YOU DO IF YOU DON'T WANT TO TAKE PART?**

If you do not wish to take part in this study, simply inform the practice nurse looking after you. If this is the case, your excision will take place as normal.

If you have any questions about the study, please contact the principal investigator, Dr Daniel Charles, or the supervisor for this project, Prof Clare Heal. Contact details are listed below.

<table>
<thead>
<tr>
<th>Principal Investigator:</th>
<th>Study Supervisor:</th>
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<tbody>
<tr>
<td>Dr Daniel Charles</td>
<td>Professor Clare Heal</td>
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<tr>
<td>School of Medicine and Dentistry</td>
<td>School of Medicine and Dentistry</td>
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<td>Email: <a href="mailto:clare.heal@jcu.edu.au">clare.heal@jcu.edu.au</a></td>
</tr>
</tbody>
</table>

**If you have any concerns regarding the ethical conduct of the study, please contact:**

*Human Ethics, Research Office*
*James Cook University, Townsville, Qld, 4811*
*Phone: (07) 4781 5011 (ethics@jcu.edu.au)*
Protocol for a randomised controlled trial comparing aqueous with alcoholic chlorhexidine antisepsis for the prevention of superficial surgical site infection after minor surgery in general practice: the AVALANCHE trial

C F Heal, D Charles, A Hardy, M Delpachitra, J Banks, M Wohlfahrt, Sabine Saednia and P Buettner

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