

# Criteri di scelta degli antiasettici

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**E' necessario disinfettare la cute  
prima del posizionamento di un  
accesso venoso?**

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Is it necessary to disinfect the skin before venous access placement?



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Results from 11 relevant papers



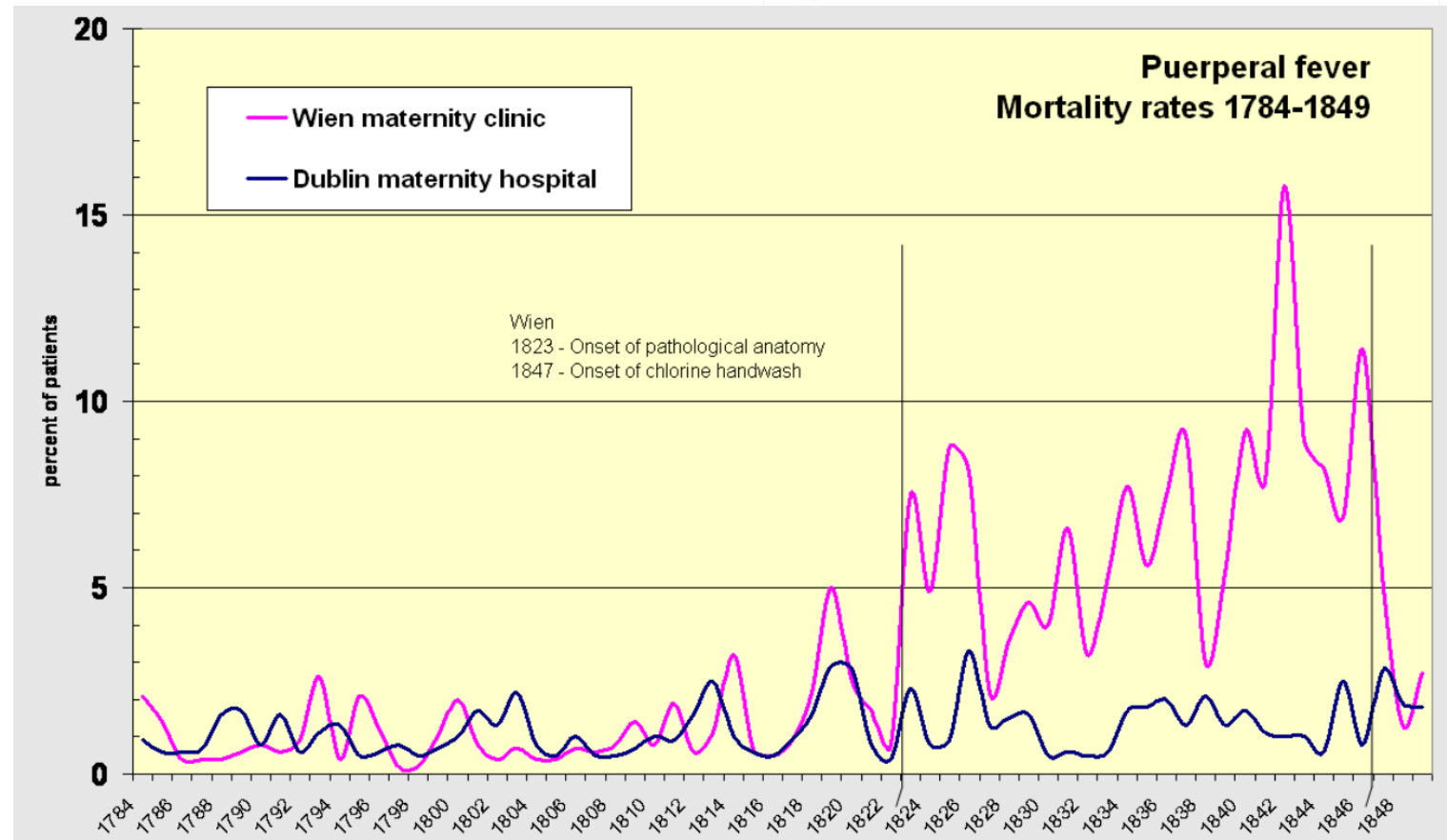
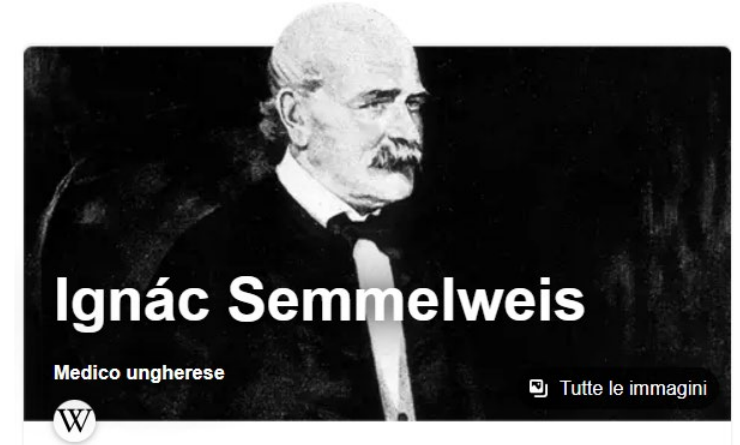
☒ **Yes** 100% · ☐ **Possibly** 0% · ☐ **Mixed** 0% · ☐ **No** 0%



Disinfecting the skin before venous access placement is crucial to prevent infections. The research consistently supports the use of antiseptics to reduce the risk of catheter-related infections.

# L'igiene delle Mani, cenni storici

- ▶ Semmelweis nel **1847** scoprì che, nelle cliniche ostetriche, l'alta incidenza di febbre puerperale poteva essere drasticamente ridotta mediante la **disinfezione delle mani**.
- ▶ I risultati furono sorprendenti: **la mortalità per febbre puerperale scese drasticamente, passando dall'11,4% all'1%** nelle sale operatorie gestite dai medici e questo gli valse l'appellativo di "salvatore delle mamme".
- ▶ Ma **il pregiudizio dei colleghi restò duro a morire** ed il giovane dottore austriaco trovò la dura opposizione dei suoi colleghi, anche quelli più rinomati, come Rudolf Virchow, il padre dell'istologia moderna. Semmelweis non riuscì a sopportare le ostilità dei suoi colleghi finendo per **essere ricoverato in un manicomio, luogo dove trovò la morte**, forse in seguito alle percosse subite dal personale dell'Istituto.

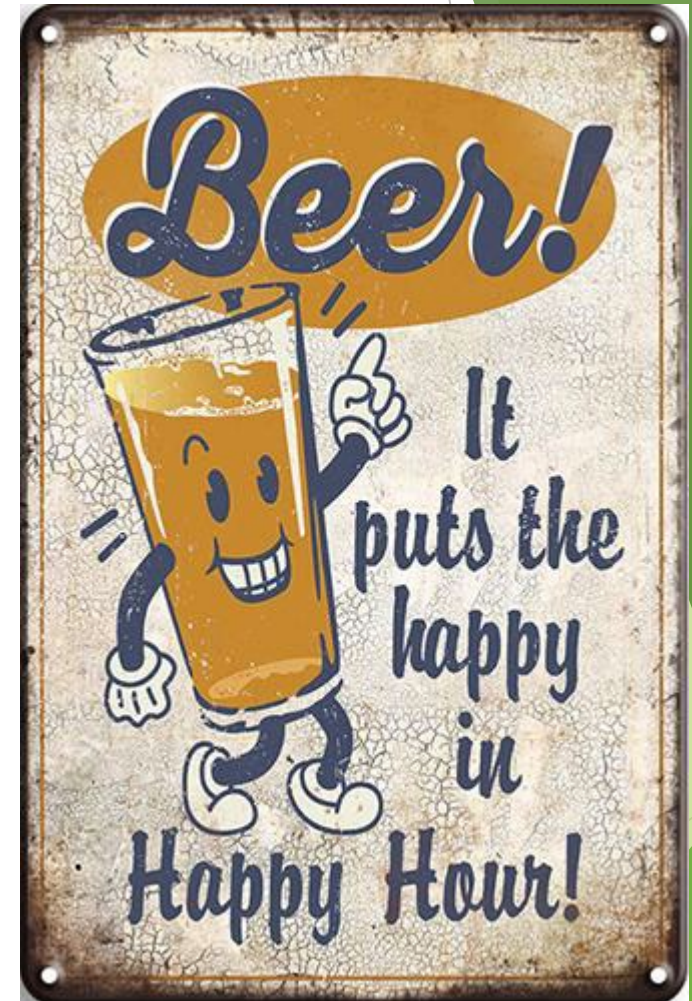




The Wine Buffs  
by Mike Payne



Mike Payne x



# La scoperta della Microbiologia, Pasteur

## Le grandi scoperte [\[ modifica \]](#) [\[ modifica wikitesto \]](#)

È significativo rilevare che tutte le grandi scoperte dello scienziato francese vennero realizzate affrontando i problemi più gravi, a metà dell'Ottocento, dell'agricoltura, dell'industria agraria, dell'allevamento. La successione delle stesse scoperte corrisponde a una successione di studi su problemi agricoli, agroindustriali, veterinari:

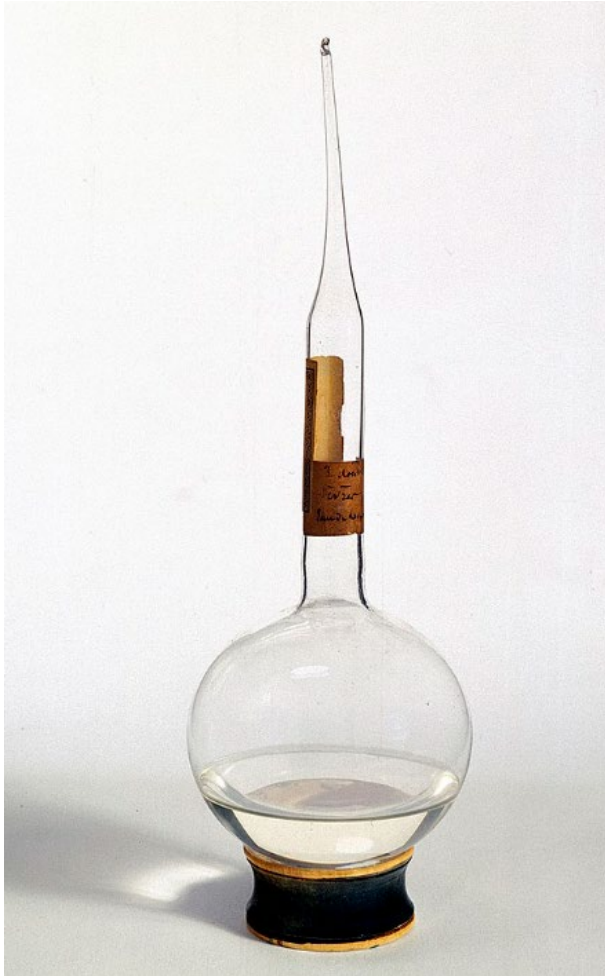
- Anomalie della fermentazione della birra (1854);
- Fermentazione del vino e dell'aceto (1861-62);
- Pastorizzazione (1862);
- Alterazioni del vino di origine fungina o batterica (1863-64);



Louis Pasteur



# La scoperta della Microbiologia, Pasteur



- **1864** - Louis Pasteur mette fine alla controversia sulla **generazione spontanea**, dimostrando scientificamente che i microrganismi sono incapaci di generarsi spontaneamente in un ambiente precedentemente sterilizzato e riparato da contaminazioni esterne.



Louis Pasteur





# L'inventore del metodo dell'antisepsi e, il padre della moderna chirurgia: Joseph Lister

- ▶ Nei secoli addietro il tasso di mortalità, conseguente ad un intervento chirurgico, era molto elevato, ben **oltre il 50%**, ciò era dovuto principalmente all'infezione delle ferite
- ▶ Lister effettuò diverse sperimentazioni e notò che il **fenolo** (o acido fenico), impiegato per ridurre l'odore dei rifiuti, poteva essere utilizzato anche come **antisettico**, in soluzione acquosa per la disinfezione della cute ed in soluzione oleosa per la medicazione delle ferite post-operatorie.
- ▶ Il primo utilizzo del fenolo come antisettico avvenne il 12 agosto **1865** presso il *Glasgow Infirmary* dove Lister applicò su una ferita post-operatoria di un ragazzo di sette anni una fasciatura imbevuta di acido fenico.
- ▶ L'antisettico veniva adoperato anche per **gli strumenti, il vestiario e le mani del chirurgo, ma anche l'aria atmosferica** in cui si eseguivano le operazioni era sottoposta ad irrorazione continua di acido fenico tramite l'ausilio di uno spruzzatore
- ▶ Il metodo adoperato da Lister venne reso noto grazie ad una pubblicazione su *Lancet* e, nonostante all'inizio non venne accettato, si constatò che, tra il **1865 ed il 1869, il tasso di mortalità chirurgica calò dal 45% al 15%.**



# L'inventore del metodo dell'antisepsi e, il padre della moderna chirurgia: Joseph Lister



- Listerine was developed in **1879** by Joseph Lawrence, a chemist in St. Louis, United States.

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RESULTS BY YEAR

16,408 results



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of 1,641



1897

1944: 0

2025



1897

1974: 9

2025

# **CDC GUIDELINE FOR HANDWASHING AND HOSPITAL ENVIRONMENTAL CONTROL, 1985**

(Originally published in November 1985)  
Supersedes Guideline for Hospital Environmental Control  
Published in 1981

*Revised by Julia S. Garner, RN, MN  
and*

*Martin S. Favero, PhD*  
Hospital Infections Program  
Center for Infectious Diseases  
Centers for Disease Control  
Public Health Service  
U.S. Department of Health  
and Human Services  
Atlanta, Georgia

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## Section Three: Infection Prevention and Control

### 17. HAND HYGIENE

2. Perform hand hygiene using an ABHR for 15 seconds or according to manufacturer's recommendations.<sup>3,7</sup>

clean body site on the same patient.

- B. Use an alcohol-based hand rub (ABHR) containing at least 60% ethanol or 70% isopropyl alcohol routinely for hand hygiene, unless the hands are visibly soiled or if the patient is suspected of having/or there is an outbreak of a spore-forming pathogen or norovirus gastroenteritis.<sup>1,3-7</sup> (I)
- D. Use chlorhexidine gluconate with caution for routine hand hygiene.<sup>10</sup> (II)





State of the Science Review

## Risks and benefits of using chlorhexidine gluconate in handwashing: A systematic literature review



Marcia Maria Baraldi RN, MSc<sup>a,\*</sup>, Juliana Rizzo Gnatta RN, MSc, PhD<sup>b</sup>, Maria Clara Padoveze RN, MSc, PhD<sup>c</sup>

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**Background:** Antimicrobial soaps containing chlorhexidine gluconate (CHG) are indicated for hand hygiene (HH) in specific situations. This study aimed to identify whether the continuous use of CHG for HH affects the reduction of healthcare-associated infections (HAI), the selection of microorganisms resistant to CHG, or hands skin damage.

**Methods:** Systematic review was performed using the protocol of the Joanna Briggs Institute, including clinical trials and observational comparative studies. Search was conducted via PubMed, Medline, CINAHL, LILACS, Embase, Cochrane Library, Scopus, Web of Science, ProQuest, Google Scholar, and gray literature. To evaluate outcomes, 3 independent reviews were conducted: HAI rates, presence of resistance genes or higher minimum inhibitory or bactericidal concentration, and damage to skin integrity.

**Results:** Studies showed no significant difference in HAI rates when using CHG for HH. Among 13 studies, 10 suggested an association with use of and tolerance to CHG. The use of CHG was associated with skin reaction events.

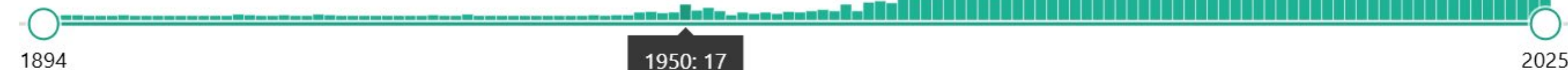
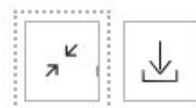
**Conclusions:** Strong evidence regarding the risks and benefits of CHG for HH is still lacking. Due to potential risk of selecting mutants carrying genes for cross-resistance to CHG and antibiotics, it is advisable to reserve the use of CHG for purposes other than HH.

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RESULTS BY YEAR

6,828 results

Page 1 of 683



1 : 6 - DI - 4' - CHLOROPHENYLDIGUANIDOHXANE  
("HIBITANE"\*) . LABORATORY INVESTIGATION OF A NEW  
ANTIBACTERIAL AGENT OF HIGH POTENCY

BY

G. E. DAVIES, J. FRANCIS,† A. R. MARTIN, F. L. ROSE, AND G. SWAIN

*From Imperial Chemical Industries, Limited, Biological and Research Laboratories, Hexagon House,  
Manchester, 9*

(RECEIVED JANUARY 7, 1954)

- ▶ La clorexidina fu sintetizzata per la prima volta nel 1950
- ▶ La clorexidina ha un'azione di tipo battericida; agisce, infatti, aumentando drasticamente la permeabilità della membrana cellulare batterica alterandone la struttura proteica.

## WATER OR ALCOHOL ?

SIR,—During an investigation of sepsis rates in a hospital, an interesting observation was made in a gynæcological ward. An outbreak of sepsis began in a ward where an old lady had undergone an operation for carcinoma of the vulva. Her vulval wound was infected with a strain of *Staphylococcus aureus* (phage type RTD 29/42E/47/54/83A/84/81) resistant to cloxacillin as well as to benzylpenicillin, tetracycline, and erythromycin; and she remained on the ward until her death, without ever being effectively isolated. At

THE LANCET, NOVEMBER 7, 1970

taining 70% ethanol, on the other hand, seems to have been an effective skin disinfectant.

Department of Microbiology,  
Central Middlesex Hospital,  
London N.W.10.

PAUL NOONE.

## Skin antisepsis for reducing central venous catheter-related infections (Review)

Lai NM, Lai NA, O'Riordan E, Chaiyakunapruk N, Taylor JE, Tan K

Lai NM, Lai NA, O'Riordan E, Chaiyakunapruk N, Taylor JE, Tan K.  
Skin antisepsis for reducing central venous catheter-related infections.  
*Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No.: CD010140.  
DOI: [10.1002/14651858.CD010140.pub2](https://doi.org/10.1002/14651858.CD010140.pub2).

- Comparison 1: povidone-iodine (in aqueous solution) versus no skin antisepsis ([Prager 1984](#)).
- Comparison 2: chlorhexidine (in aqueous solution) versus no skin antisepsis ([Tuominen 1981](#)).
- Comparison 3: alcohol versus no skin antisepsis ([Sadowski 1988](#)).



# Draft guideline for use of topical antimicrobial agents

Elaine Larson, R.N., Ph.D., FAAN

Baltimore, Maryland

**Table 2.** Characteristics of six topical antimicrobial ingredients

Agent	Mode of Action	GPB <sup>1</sup>	GNB <sup>2</sup>	MTb <sup>3</sup>	Fung <sup>4</sup>
Alcohols	Denaturation of protein	Excellent	Excellent	Good	Good
Chlorhexidine	Cell wall disruption	Excellent	Good	Fair	Good
Hexachlorophene	Cell wall disruption	Excellent	Poor	Poor	Poor
Iodine/iodophors	Oxidation substitution by free iodine	Excellent	Good	Good	Good
PCMX (chloroxylenol)	Cell wall disruption	Good	Fair*	Fair	Fair
Triclosan (Irgasan, DP-300)	Cell wall disruption	Good	Good (except for <i>Pseudomonas</i> )	Fair	Poor

<sup>1</sup>GPB = Gram-positive bacteria.

<sup>2</sup>GNB = Gram-negative bacteria.

<sup>3</sup>MTb = *Mycobacterium tuberculosis*.

<sup>4</sup>Fung = Fungi.

<sup>5</sup>Vir = Viruses.

\*Activity improved by addition of chelating agent such as EDTA.



## State of the Science Review

# Disinfection, sterilization and antisepsis: An overview

William A. Rutala PhD, MPH <sup>a,b,\*</sup>, John M. Boyce MD <sup>c</sup>, David J. Weber MD, MPH <sup>a,b,d</sup>

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<sup>c</sup> *J.M. Boyce Consulting, Boyce Consulting, LLC, Middletown, CT*

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A9

**Table 4**

Summary of advantages and disadvantages of disinfectants used as low-level disinfectants.

Disinfectant active	Advantages	Disadvantages
Alcohol	<ul style="list-style-type: none"><li>• Bactericidal, tuberculocidal, fungicidal, virucidal</li><li>• Fast acting</li><li>• Non-corrosive</li><li>• Non-staining</li><li>• Easy to use</li><li>• Used to disinfect small surfaces such as rubber stoppers on medication vials</li><li>• No toxic residue</li></ul>	<ul style="list-style-type: none"><li>• Not sporicidal</li><li>• Affected by organic matter</li><li>• Slow acting against non-enveloped viruses (eg norovirus)</li><li>• No detergent or cleaning properties</li><li>• Damage some instruments (eg harden rubber, deteriorate glue)</li><li>• Flammable (large amounts require special storage)</li><li>• Evaporates rapidly making contact time compliance difficult</li><li>• Generally, not used on large surfaces</li><li>• Outbreaks ascribed to contaminated alcohol<sup>83</sup></li></ul>

State of the Science Review

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<sup>c</sup> J.M. Boyce Consulting, Boyce Consulting, LLC, Middletown, CT



**Table 5**

Antimicrobial spectrum and characteristics of hand-hygiene antiseptic agents\*.

Group, typical Concentration	Gram-positive bacteria	Gram- negative bacteria	Myco- bacteria	Fungi	Viruses enveloped	Viruses non- enveloped	Speed of action	Residual activity	Comments
Alcohols, 60-70%	+++	+++	+++	+++	+++	++	Fast	No	Optimum conc 60%-95%
Chlorhexidine (0.5%-4% aqueous)	+++	++	+	+	++	+	Intermediate	Yes	Rare allergic reactions; not compatible with some anionic and nonionic detergents; ototoxicity
Iodophors	+++	+++	++	++	++	++	Intermediate	Contradictory	Less irritating than iodine
Phenol derivative (eg chloroxylenol)	+++	+	+	+	+	±	Slow	Contradictory	Not compatible with nonionic detergents; ecologic concerns
Triclosan	+++	++	±	±	?	?	Intermediate	Yes	FDA has banned use in the US.
Quaternary ammonium compounds (eg benzethonium chloride)	++	+	±	±	+	?	Slow	No	Not compatible anionic detergents

NOTE: +++ = excellent; ++ = good; + = fair; - = no activity of not sufficient activity; +/- = product activity varies from fair to none; PCMX-para-chloro-meta-xyleneol. In concentrations listed, the antiseptic agents are not sporicidal.

\*Modified from Boyce JM, Pittet D. Healthcare Infection Control Practices Advisory Committee. Guideline for hand hygiene in health-care settings.MMWR.2002;51(RR-16):1-48<sup>76</sup> and World Health Organization Guidelines on Hand Hygiene in Health Care, 2009. 270 pages.<sup>85</sup>



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# American Journal of Infection Control

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Infection Control



State of the Science Review

## Disinfection, sterilization and antisepsis: An overview

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<sup>d</sup> *Infection Prevention, University of North Carolina Medical Center, Chapel Hill, NC*

### Iodophors

- Bactericidal, mycobactericidal, virucidal
- Not flammable
- Used for disinfecting blood culture bottles
- Not sporicidal
- Shown to degrade silicone catheters
- Requires prolonged contact to kill fungi
- Stains surfaces
- Used mainly as an antiseptic rather than disinfectant
- Outbreaks ascribed to contaminated iodophor<sup>83</sup>

2002

# Guidelines for the prevention of intravascular catheter-related infections

Naomi P. O'Grady, MD<sup>a</sup>  
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E. Patchen Dellinger, MD<sup>c</sup>  
Julie L. Gerberding, MD, MPH<sup>d</sup>  
Stephen O. Heard, MD<sup>e</sup>  
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Henry Masur, MD<sup>a</sup>  
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Michele L. Pearson, MD<sup>d</sup>  
Issam I. Raad, MD<sup>i</sup>  
Adrienne Randolph, MD, MSc<sup>j</sup>  
Robert A. Weinstein, MD<sup>k</sup>

The Healthcare Infection Control Practices Advisory Committee\*

Bethesda, Maryland; Cambridge, Worcester, and Boston, Massachusetts; Seattle, Washington; Atlanta, Georgia; Madison, Wisconsin; Providence, Rhode Island; Houston, Texas; and Chicago, Illinois

**Background:** Although many catheter-related bloodstream infections (CR-BSIs) are preventable, measures to reduce these infections are not uniformly implemented.

**Objective:** To update an existing evidenced-based guideline that promotes strategies to prevent CR-BSIs.

**Data sources:** The MEDLINE database, conference proceedings, and bibliographies of review articles and book chapters were searched for relevant articles.

**Studies included:** Laboratory-based studies, controlled clinical trials, prospective interventional trials, and epidemiological investigations.

**Outcome measures:** Reduction in CR-BSI, catheter colonization, or catheter-related infection.

**Synthesis:** The recommended preventive strategies with the strongest supportive evidence are education and training of healthcare providers who insert and maintain catheters; maximal sterile barrier precautions during central venous catheter insertion; **use of a 2% chlorhexidine preparation for skin antisepsis**; no routine replacement of central venous catheters for prevention of infection; and use of antiseptic/antibiotic impregnated short-term central venous catheters if the rate of infection is high despite adherence to other strategies (i.e. education and training, maximal sterile barrier precautions and 2% chlorhexidine for skin antisepsis).

**Conclusion:** Successful implementation of these evidence-based interventions can reduce the risk for serious catheter-related infection. (Am J Infect Control 2002;30:476-89.)



Is 2% chlorhexidine the best disinfectant before venous access placement?



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## Consensus Meter Beta



Results from 12 relevant papers



Yes 58% · Possibly 8% · Mixed 0% · No 33%



2% chlorhexidine, especially when combined with alcohol, is considered one of the most effective disinfectants for skin preparation before venous access placement, outperforming alternatives like povidone-iodine.

Is 2% chlorhexidine gluconate in 70% isopropyl alcohol the best disinfectant before venous access placement?



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## Consensus Meter

Beta



Results from 6 relevant papers



Yes 67% · Possibly 0% · Mixed 0% · No 33%



The use of 2% chlorhexidine gluconate in 70% isopropyl alcohol (CHG-IPA) is a common antiseptic for skin disinfection before venous access placement. However, whether it is the best option remains a topic of investigation.



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## Brief Report

### Is 2% chlorhexidine gluconate in 70% isopropyl alcohol more effective at preventing central venous catheter-related infections than routinely used chlorhexidine gluconate solutions: A pilot multicenter randomized trial (ISRCTN2657745)?



Margaret McCann MSc, FFNMRC SI, PhD <sup>a,\*</sup>, Fidelma Fitzpatrick MD, FRCPI, FRCPath <sup>b,c</sup>, George Mellotte FRCPI, MSc, MB <sup>d,e</sup>, Michael Clarke PhD <sup>a,f</sup>

<sup>a</sup> School of Nursing and Midwifery, Trinity College Dublin, Dublin, Ireland

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<sup>d</sup> School of Medicine Trinity College Dublin, Dublin, Ireland

<sup>e</sup> Trinity Kidney Health Centre, Tallaght Hospital, Dublin, Ireland

<sup>f</sup> Northern Ireland Network for Trials Methodology Research, Queen's University Belfast, Belfast, UK

#### Key Words:

Hemodialysis  
central venous catheters  
chlorhexidine gluconate  
skin cleansing  
infection prevention  
clinical trial

A pilot randomized trial in 3 Irish outpatient hemodialysis units compared 2% chlorhexidine gluconate (CHG) in 70% isopropyl alcohol with routinely used CHG solutions for central venous catheter exit site antisepsis. **We found no significant difference between the groups for the prevention of catheter-related bloodstream infections (1/53 vs 2/52; relative risk [RR], 0.49; 95% confidence interval [CI], 0.05-5.25;  $P = .55$ ) and catheter-associated bloodstream infections (1/53 vs 4/52; RR, 0.25; 95% CI, 0.03-2.12;  $P = .16$ ).**

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# 2% chlorhexidine–70% isopropyl alcohol versus 10% povidone–iodine for insertion site cleaning before central line insertion in preterm infants: a randomised trial

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## ABSTRACT

**Objective** To determine whether 2% chlorhexidine gluconate–70% isopropyl alcohol (CHX–IA) is superior to 10% aqueous povidone–iodine (PI) in preventing catheter-related blood stream infection (CR-BSI) when used to clean insertion sites before placing central venous catheters (CVCs) in preterm infants.

**Design** Randomised controlled trial.

**Setting** Two neonatal intensive care units (NICUs).

**Patients** Infants <31 weeks' gestation who had a CVC inserted.

**Interventions** Insertion site was cleaned with CHX–IA or PI. Caregivers were not masked to group assignment.

**Main outcome measures** Primary outcome was CR-BSI determined by one microbiologist who was masked to group assignment. Secondary outcomes included skin reactions to study solution and thyroid dysfunction.

**Results** We enrolled 304 infants (CHX–IA 148 vs PI 156) in whom 815 CVCs (CHX–IA 384 vs PI 431) were inserted and remained in situ for 3078 (CHX–IA 1465 vs PI 1613) days. We found no differences between the groups in the proportion of infants with CR-BSI (CHX–IA 7% vs PI 5%,  $p=0.631$ ), the proportion of CVCs complicated by CR-BSI or the rate of CR-BSI per 1000 catheter days. Skin reaction rates were low (<1% CVC insertion episodes) and not different between the

## What is already known on this topic?

- ▶ International guidelines on the prevention and management of catheter-related blood stream infection make no recommendation on the solutions to use when inserting central venous catheters in newborns.
- ▶ There is no good quality evidence to support practice and randomised controlled trials are recommended.

## What this study adds?


- ▶ Adverse skin reactions to both 2% chlorhexidine–70% isopropyl alcohol and aqueous 10% povidone–iodine are uncommon.
- ▶ Infants whose skin is cleaned with povidone–iodine are at significant risk of thyroid dysfunction.

infection (CR-BSI) is the most common complication associated with CVCs in preterm infants. Late-onset sepsis (LOS) (ie, after 3 days of life) occurs



## Use of 2% chlorhexidine gluconate in 70% isopropyl alcohol for skin disinfection during central catheter insertion in premature neonates

Antonella Capasso<sup>1</sup> , Andrea Paonessa<sup>2</sup>, Teresa Ferrara<sup>1</sup>, Fiorentino Grasso<sup>1</sup>, Letizia Capasso<sup>1</sup>, Fiorella Migliaro<sup>1</sup>, Achille Illiano<sup>1</sup>, Serena Salome<sup>1</sup>, Maria Zollo<sup>1</sup>, Annapaola Amitrano<sup>1</sup>, Melania Rachiglia<sup>1</sup> and Francesco Raimondi<sup>1</sup>

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1–6  
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### Abstract

**Background and aim:** 2% Chlorhexidine gluconate in 70% isopropyl alcohol (2% CHG in 70% IPA) is the recommended skin antiseptic for adult and children during central venous catheter (CVC) insertion but neonatal data are limited. We assessed skin toxicity of 2% CHG in 70% IPA for vascular catheter site preparation in preterm neonates using sterile disposable pre-measured devices.

**Study design:** Monocentric, retrospective, observational study conducted in tertiary level NICU on 146 neonates less than 32 weeks gestational age (GA) and younger than 15 days.

**Methods:** Infants were stratified in Group I (GA ≤ 28 weeks) and Group II (GA = 29–32 weeks) and received skin disinfection with 2% CHG in 70% IPA for either umbilical venous catheters or epicutaneous caval catheters. We evaluated the incidence of skin lesions in preterm neonates who received skin disinfection 2% CHG in 70% IPA with the Neonatal Skin Condition Score. Numeric thresholds ≤ 5, 5–7, and > 7 were used to define mild, moderate, and severe skin infection respectively. The rate of central line associated bloodstream infection (CLABSI) was also calculated.

**Results:** Two hundred implanted catheters (100 per group) from 146 neonates were reviewed. While two cases of severe skin lesions occurred locally on the abdomen of two 24 weeks babies, no lesion was reported in Group II infants. We found a CLABSI rate of 16% with a rate of 17 infections per 1000 catheter days.

**Conclusion:** The use of 2% CHG in 70% IPA for skin disinfection during CVC implantation in preterm infants over 24 weeks GA does not lead to severe skin lesions.



## 31. VASCULAR ACCESS SITE PREPARATION AND SKIN ANTISEPSIS

### Standard

31.1 Skin antisepsis is performed prior to vascular access device (VAD) insertion.

31.2 The intended VAD insertion site is visibly clean prior to application of an antiseptic solution; if visibly soiled, the intended site is cleansed with soap and water prior to application of antiseptic solution(s).

### Practice Recommendations

- A. Remove excess hair at the insertion site if needed to facilitate application of VAD dressings. Use single-patient-use scissors or disposable-head surgical clippers; do not shave, as this may increase the risk for infection.<sup>1,2</sup> (I)
- B. Evaluate patient history of any allergy or sensitivity to skin antiseptics (see Standard 52, *Catheter-Associated Skin Injury*).<sup>3,4</sup> (I)
- C. Perform skin antisepsis using alcoholic chlorhexidine gluconate (CHG) as the preferred antiseptic solution.<sup>4-14</sup> (I)
  1. Use an alcoholic CHG solution containing at least 2% chlorhexidine gluconate.<sup>10,15</sup> (I)

# Infusion Therapy Standards of Practice

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## SHEA/IDSA/APIC Practice Recommendation

# Strategies to prevent central line-associated bloodstream infections in acute-care hospitals: 2022 Update

Niccolò Buetti MD, MSc, PhD<sup>1,2,a</sup> , Jonas Marschall MD, MSc<sup>3,4,a</sup> , Marci Drees MD, MS<sup>5,6</sup> ,  
Mohamad G. Fakih MD, MPH<sup>7</sup> , Lynn Hadaway MEd, RN, NPD-BC, CRNI<sup>8</sup>, Lisa L. Maragakis MD, MPH<sup>9</sup>,  
Elizabeth Monsees PhD, MBA, RN, CIC<sup>10,11</sup> , Shannon Novosad MD MPH<sup>12</sup>, Naomi P. O'Grady MD<sup>13</sup>,  
Mark E. Rupp MD<sup>14</sup> , Joshua Wolf MBBS, PhD, FRACP<sup>15,16</sup> , Deborah Yokoe MD, MPH<sup>17</sup> and  
Leonard A. Mermel DO, ScM<sup>18,19</sup> 

7. **Use an alcoholic chlorhexidine antiseptic for skin preparation** (Quality of Evidence: HIGH)<sup>42,129–134</sup>
  - a. Before catheter insertion, apply an alcoholic chlorhexidine solution containing at least 2% chlorhexidine gluconate to the insertion site.
    - i. The antiseptic solution must be allowed to dry before making the skin puncture.
    - ii. Alcoholic chlorhexidine for skin antisepsis to prevent CLABSI in NICU patients should be used when the benefits are judged to outweigh potential risk.



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Systematic Review

# Effect of skin antiseptic solutions on the incidence of catheter-related bloodstream infection: a systematic review and network meta-analysis

T. Masuyama<sup>a,†</sup>, H. Yasuda<sup>b,c,\*,†</sup>, M. Sanui<sup>a</sup>, A.K. Lefor<sup>d</sup><sup>a</sup> Department of Anaesthesiology and Critical Care Medicine, Jichi Medical University Saitama Medical Centre, Saitama, Japan<sup>b</sup> Department of Emergency and Critical Care Medicine, Jichi Medical University Saitama Medical Centre, Saitama, Japan

## S U M M A R Y

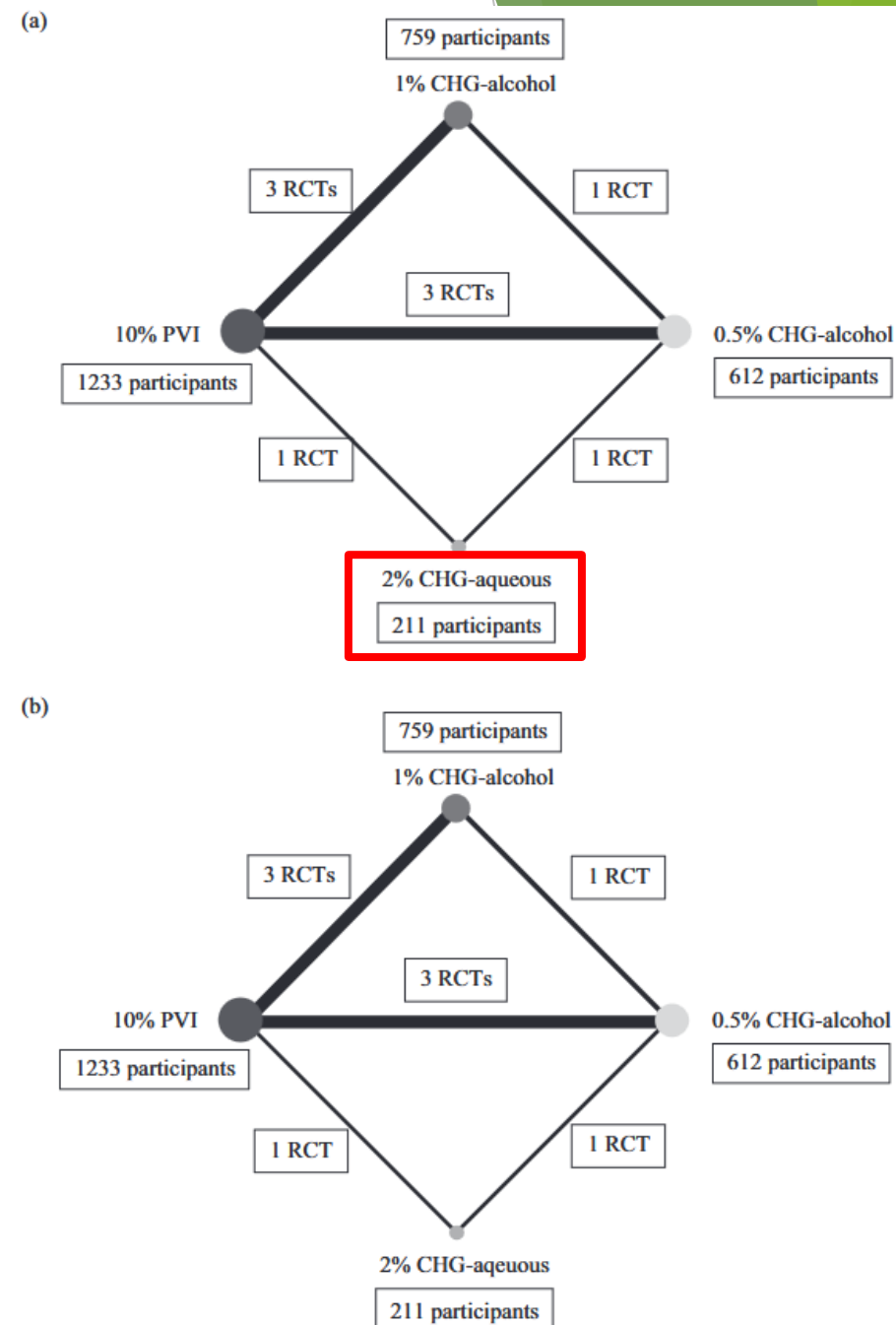
**Background:** The most effective skin antiseptic solution to reduce the incidence of catheter-related bloodstream infections (CRBSI) remains unknown.

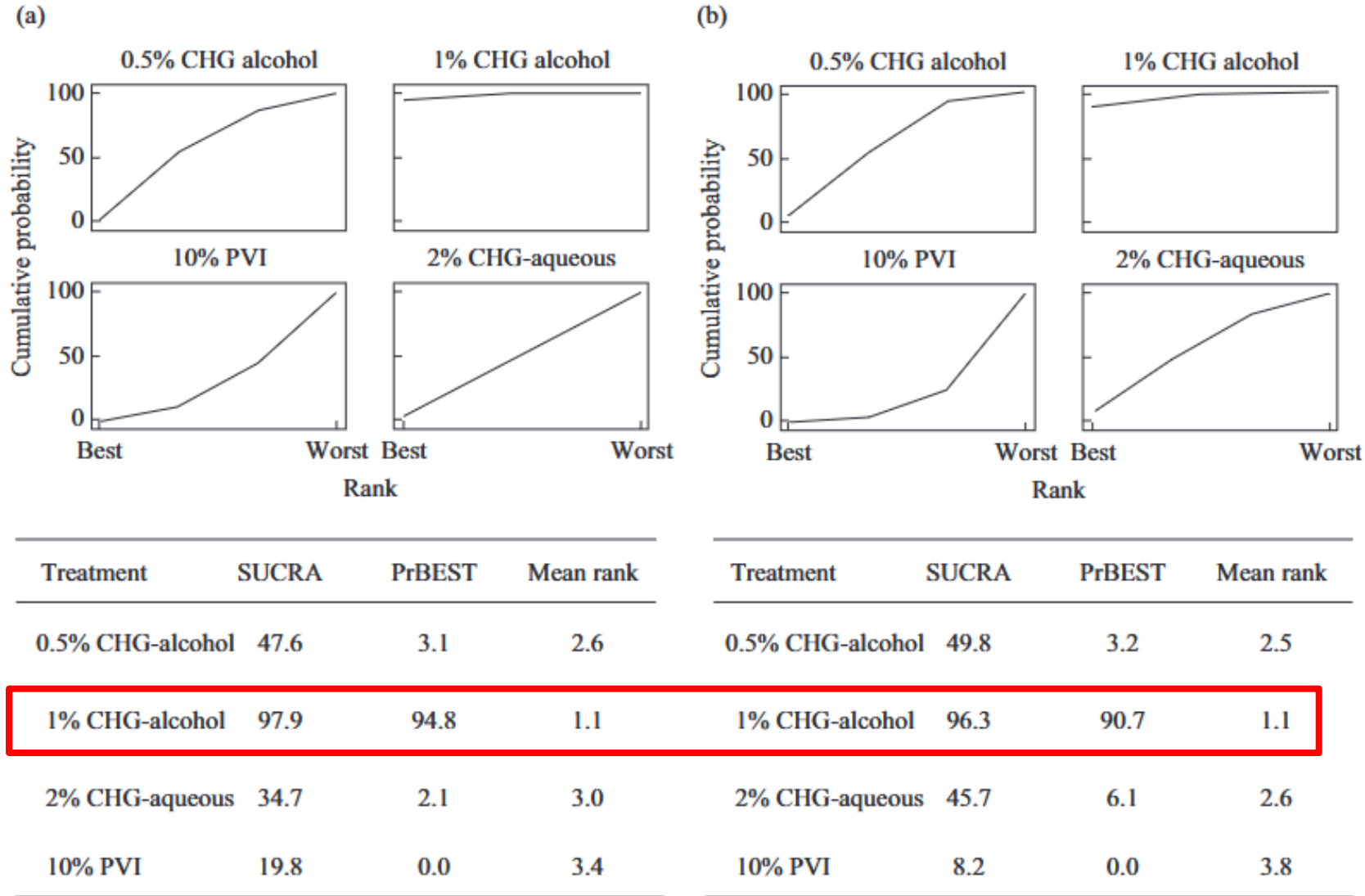
**Aim:** To compare solutions with different chlorhexidine (CHG)-based concentrations and povidone-iodine (PVI) in adults with a central venous catheter (CVC) or arterial catheter, and identify an association with the incidence of CRBSI.

**Methods:** This study evaluated randomized controlled trials comparing CHG and PVI antiseptic agents in patients aged  $\geq 18$  years with an underlying illness and a CVC or arterial catheter. The primary outcome was CRBSI rate. Network meta-analysis was performed by a frequentist-based approach with multi-variate random effects meta-analysis, and the effect size was expressed as relative risk (RR) with 95% confidence interval (CI).

**Findings:** The search yielded 1511 records, of which five studies (2815 catheters) were included in the network meta-analysis. The risk of CRBSI was significantly lower with 1% CHG-alcohol than with 0.5% CHG-alcohol (RR 0.40, 95% CI 0.16–0.98; high certainty) or 10% PVI-aqueous (RR 0.31, 95% CI 0.15–0.63; high certainty). There was no significant difference in the risk of CRBSI between 1% CHG-alcohol and 2% CHG-aqueous (RR 0.35, 95% CI 0.12–1.04; moderate certainty) or other antiseptic solutions. The hierarchy of efficacy in reducing CRBSI was 1% CHG-alcohol, 0.5% CHG-alcohol, 2% CHG-aqueous and 10% PVI-aqueous.

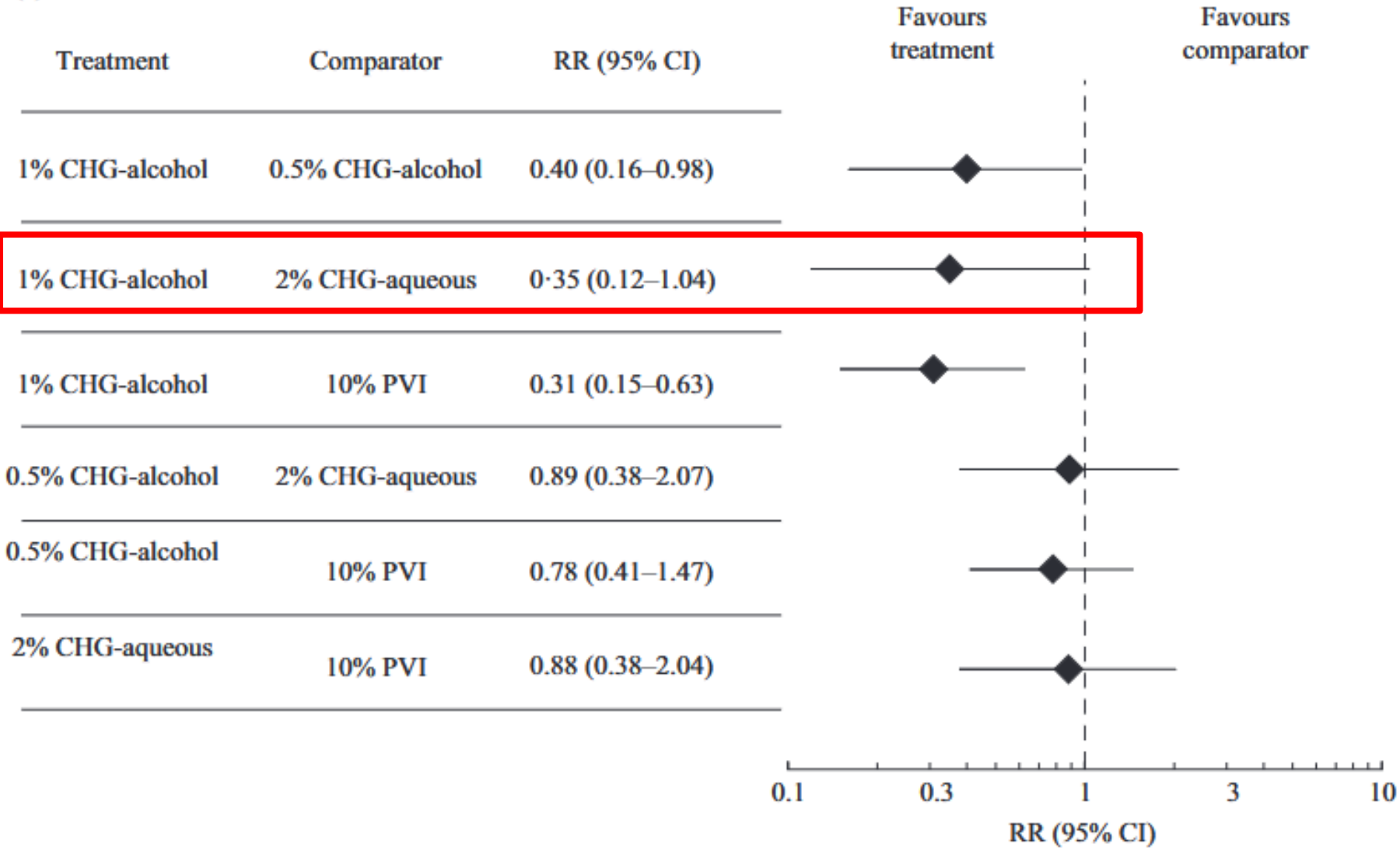
**Conclusion:** Antiseptic agents containing 1% CHG-alcohol were more strongly associated with reduced risk for CRBSI compared with agents containing 0.5% CHG-alcohol or 10% PVI-aqueous.





**Figure 3.** Surface under the cumulative ranking of each antiseptic solution for (a) catheter-related bloodstream infection and (b) colonization. CHG, chlorhexidine gluconate; PVI, povidone-iodine; PrBEST, probability of being ranked as the best SUCRA, surface under the cumulative ranking curve.

(a)







# 2% chlorhexidine gluconate aqueous versus 2% chlorhexidine gluconate in 70% isopropyl alcohol for skin disinfection prior to percutaneous central venous catheterisation: the ARCTIC randomised controlled feasibility trial

Paul Clarke ,<sup>1,2</sup> Aung Soe ,<sup>3</sup> Amy Nichols ,<sup>1</sup> Helen Harizaj ,<sup>3</sup> Mark A Webber ,<sup>2,4</sup> Louise Linsell ,<sup>5</sup> Jennifer L Bell ,<sup>5</sup> Catherine Tremlett ,<sup>6</sup> Priyadarsini Muthukumar ,<sup>1</sup> Santosh Pattnayak ,<sup>3</sup> Christopher Partlett ,<sup>5</sup> Andrew King ,<sup>5</sup> Ed Juszcak ,<sup>5</sup> Paul T Heath ,<sup>7</sup>

**Conclusions** A definitive comparative efficacy trial is feasible, but the very low catheter colonisation rate would make a large-scale RCT challenging due to the very large sample size required. ARCTIC provides preliminary reassurance supporting potential safe use of 2% CHG-70% IPA and 2% CHG-aqueous in preterm neonates.

## Original research

**Table 1** Summary efficacy outcomes for bacteriology and sepsis including primary outcome

	2% CHG-70% IPA (n=79)	2% CHG-aqueous (n=27)	All (n=106)
Positive exit site skin swab at catheter removal before disinfection, n (%)	11 (15.1)	4 (16.7)	15 (15.5)
Missing	6	3	9
Positive exit site skin swab at catheter removal after disinfection, n (%)	1 (1.4)	1 (4.3)	2 (2.1)
Missing	7	4	11
Culture-positive catheter segment at removal†, n (%)	3 (4.1)*	2 (8.3)	5 (5.2)
Positive tip alone	1 (1.3)	1 (3.7)	2 (1.9)
Positive proximal segment alone	2 (2.5)	0	2 (1.9)
Both tip and proximal segment positive	0	1 (4.2)	1 (1.0)
Missing	6	3	9
Definite catheter-related sepsis‡, n (%)	1 (1.5)	1 (4.5)	2 (2.3)
Missing	13	5	18
Catheter-associated sepsis§, n (%)	10 (13.7)	3 (12.5)	13 (13.4)
Missing	6	3	9
Total number of PCVC days	653	223	876
Definite catheter-related sepsis, n (rate per 1000 PCVC days)	1 (1.5)	1 (4.5)	2 (2.3)
Catheter-associated sepsis, n (rate per 1000 PCVC days)	10 (15.3)	3 (13.5)	13 (14.8)

\*Primary outcome: 3/73 (4.1%) with 95% confidence interval of 0.9% to 11.5%.

†Catheter colonisation: a catheter that at the time of removal has either one or both segments culture positive.

‡Definite catheter-related sepsis: a peripheral BC plus any catheter segment (i.e. proximal and/or tip) positive with the same organism, based on bacterial culture, antibiotic sensitivity and molecular typing, from a neonate who had an indwelling PCVC and clinical signs of sepsis but no other focus of sepsis.

§Catheter-associated sepsis: clinical signs of sepsis and an accompanying positive BC in the period between catheter insertion and 48 hours post removal but with no other focus of sepsis and with both catheter segment cultures negative.

BC, blood culture; CHG, chlorhexidine gluconate; PCVC, percutaneous central venous catheter.

ORIGINAL ARTICLE

SEVEN-DAY PROFILE PUBLICATION

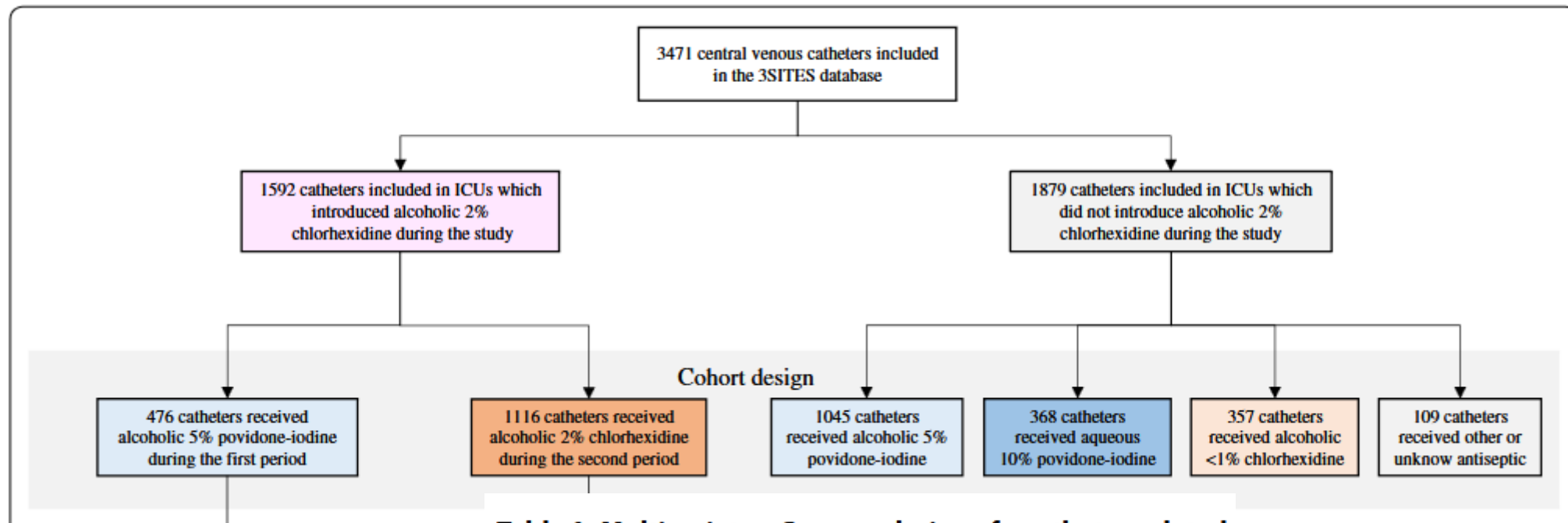


## Intravascular Complications of Central Venous Catheterization by Insertion Site

Jean-Jacques Parienti, M.D., Ph.D., Nicolas Mongardon, M.D.,  
Bruno Mégarbane, M.D., Ph.D., Jean-Paul Mira, M.D., Ph.D.,  
Pierre Kalfon, M.D., Ph.D., Antoine Gros, M.D., Sophie Marqué, M.D.,  
Marie Thuong, M.D., Véronique Pottier, M.D., Michel Ramakers, M.D.,  
Benoît Savary, M.D., Amélie Seguin, M.D., Xavier Valette, M.D.,  
Nicolas Terzi, M.D., Ph.D., Bertrand Sauneuf, M.D.,  
Vincent Cattoir, Pharm.D., Ph.D., Leonard A. Mermel, D.O.,  
and Damien du Cheyron, M.D., Ph.D., for the 3SITES Study Group\*

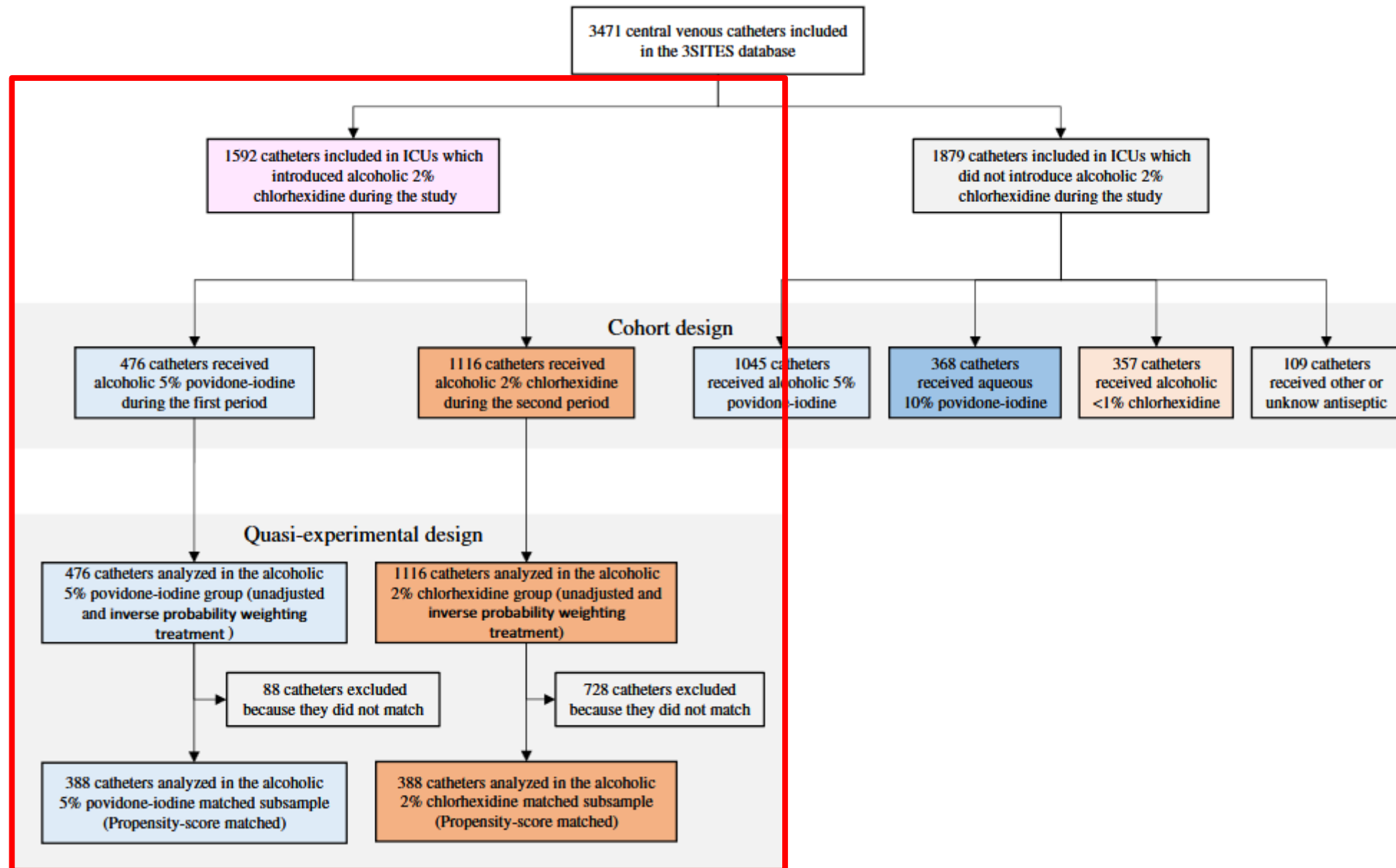
## Comparison of alcoholic chlorhexidine and povidone–iodine cutaneous antiseptics for the prevention of central venous catheter-related infection: a cohort and quasi-experimental multicenter study

Justine Pages<sup>1</sup>, Pascal Hazera<sup>2</sup>, Bruno Mégarbane<sup>3</sup>, Damien du Cheyron<sup>4,5</sup>, Marie Thuong<sup>6</sup>,  
Jean-Jacques Dutheil<sup>1</sup>, Xavier Valette<sup>4</sup>, François Fournel<sup>1</sup>, Leonard A. Mermel<sup>7</sup>, Jean-Paul Mira<sup>8</sup>,  
Cédric Daubin<sup>4</sup>, Jean-Jacques Parienti<sup>1,5,9\*</sup> and 3SITES Study Group

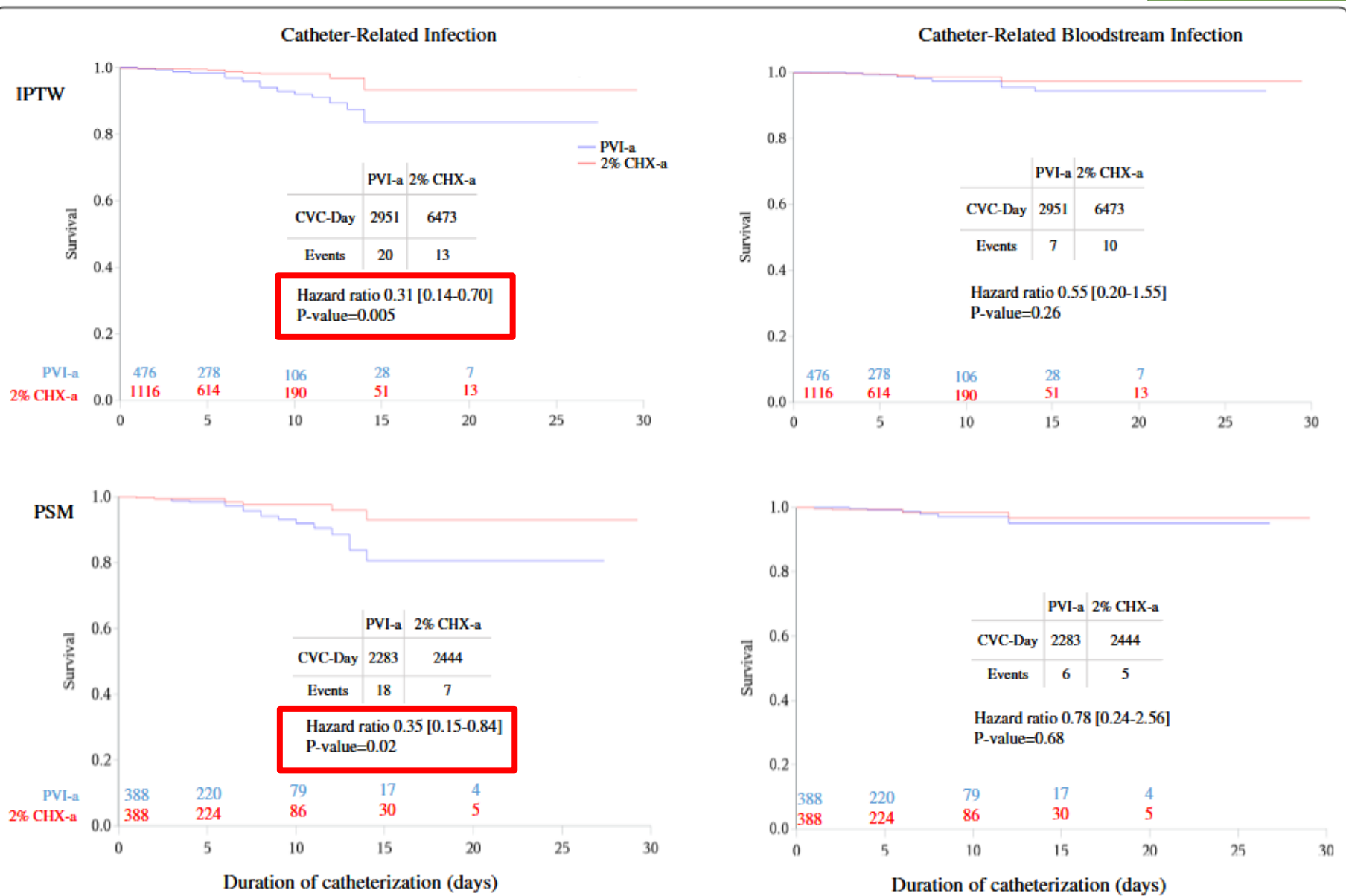


**Table 1 Multivariate Cox analysis of catheter-related infection (CRI) and catheter-related bloodstream infection (CRBSI) in the 3SITES cohort study ( $n = 3471$ )**

	CRI		CRBSI	
	aHR (95 % CI)	<i>p</i> value	aHR (95 % CI)	<i>p</i> value
<b>Antiseptic<sup>a</sup></b>				
5 % PVI-a (4-step)	1 [reference]		1 [reference]	
2 % CHX-a (1-step)	0.51 (0.28–0.96)	0.037	0.83 (0.38–1.79)	0.63
<1 % CHX-a (4-step)	0.73 (0.36–1.48)	0.37	0.93 (0.37–2.37)	0.94
10 % PVI (4-step)	1.50 (0.85–2.64)	0.16	1.17 (0.49–2.81)	0.73
Other or unknown	0.82 (0.21–3.18)	0.82	0.87 (0.12–6.31)	0.89



**Fig. 1** Flow chart of the study



**Fig. 2** Kaplan–Meier curves of time to catheter-related infection (left) and catheter-related bloodstream infection (right) by CHX-a and PVI-a groups in the quasi-experimental study. CVC central venous catheters, HR hazard ratio, CI confidence interval, IPWT inverse probability weighting treatment model, PSM propensity score matched





## Chlorhexidine plus alcohol versus povidone iodine plus alcohol, combined or not with innovative devices, for prevention of short-term peripheral venous catheter infection and failure (CLEAN 3 study): an investigator-initiated, open-label, single centre, randomised-controlled, two-by-two factorial trial

Jérémy Guenezan, Nicolas Marjanovic, Bertrand Drugeon, Rodérick O'Neill, Evelyne Liuu, France Roblot, Paola Palazzo, Vanessa Bironneau, Frederique Prevost, Julie Paul, Maxime Pichon, Matthieu Boisson, Denis Frasca, Olivier Mimos, on behalf of the CLEAN-3 trial investigators\*

	Entire population (n=989)	Antiseptic groups		Adjusted relative risk
		CHG group (n=496)	PVI group (n=493)	
Infectious complications				
Catheter colonisation*	74/846 (9%)	4/431 (1%)	70/415 (17%)	0.06 (0.05 to 0.06)
Local infection	6 (1%)	0	6 (1%)	0.45 (0.26 to 0.99)
Catheter-related bloodstream infections	0	0	0	..
All-causes bloodstream infections	21 (2%)	8 (2%)	13 (3%)	0.59 (0.40 to 1.07)

**Findings** 1000 patients were recruited between Jan 7, and Sept 6, 2019, of whom 500 were assigned to the chlorhexidine plus alcohol group and 500 to the povidone iodine plus alcohol group (250 with innovative solutions and 250 with standard devices in each antiseptic group). No significant interaction was found between the two study interventions. Local infections occurred less frequently with chlorhexidine plus alcohol than with povidone iodine plus alcohol (0 [0%] of 496 patients vs six [1%] of 493 patients) and the same was observed for catheter colonisation (4/431 [1%] vs 70/415 [17%] catheters among the catheters cultured; adjusted subdistribution hazard ratio 0.08 [95% CI 0.02–0.18]).

The Comparative Efficacy of Chlorhexidine Gluconate and Povidone-iodine Antiseptics for the Prevention of Infection in Clean Surgery

A Systematic Review and Network Meta-analysis

Ryckie G. Wade, MSc,\*†✉ Nicholas E. Burr, MBBS,‡§ Gordon McCauley, MBBS,\*† Grainne Bourke, MB,\*† and Orestis Efthimiou, PhD¶

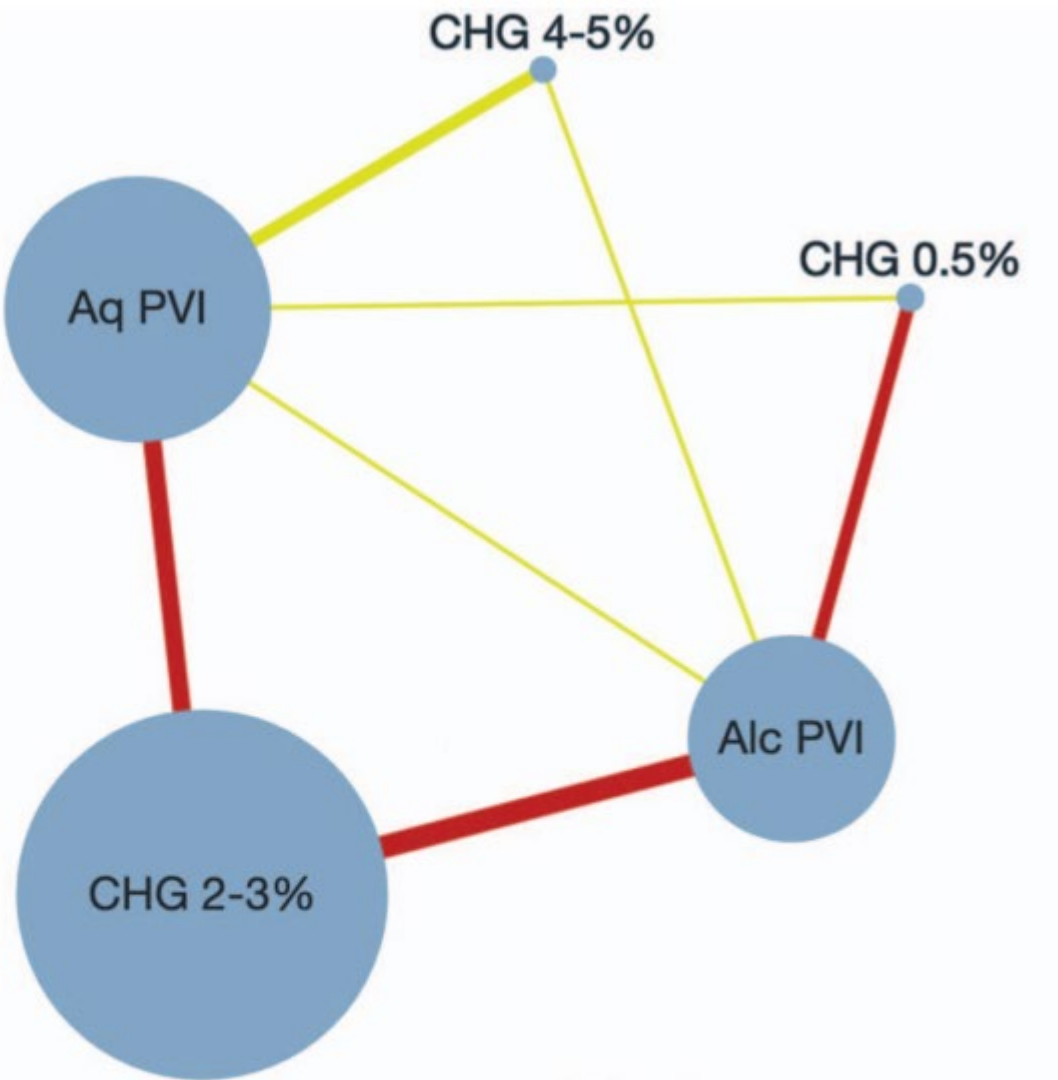


FIGURE 1. Network plot of studies included in the analysis. The size of the nodes correspond to the number of patients, the thickness of the connecting lines corresponds to the number of studies and the color of the lines corresponds to the average risk of bias assessment (yellow = unclear or moderate risk, red = high risk). NRS indicates nonransomized studies; RCT, randomized controlled trias.

Antiseptic	Label	Number of studies		Number of patients	Number of events
		RCT	NRS		
Alcoholic Chlorhexidine 4-5%	CHG 4-5%	3	3	412	18
Alcoholic Chlorhexidine 2-3%	CHG 2-3%	4	2	5628	98
Alcoholic Chlorhexidine 0-5%	CHG 0-5%	1	3	433	4
Alcoholic Povidone-Iodine	Alc PVI	4	6	3147	158
Aqueous Povidone-Iodine	Aq PVI	5	2	4041	100

# The Comparative Efficacy of Chlorhexidine Gluconate and Povidone-iodine Antiseptics for the Prevention of Infection in Clean Surgery

## A Systematic Review and Network Meta-analysis

Ryckie G. Wade, MSc,\*†✉ Nicholas E. Burr, MBBS,‡§ Gordon McCauley, MBBS,\*† Grainne Bourke, MB,\*† and Orestis Efthimiou, PhD¶

**TABLE 1.** League Table of Pairwise Comparisons in Network Meta-analysis for the Relative Risk of Surgical Site Infection With 95% Confidence Intervals

CHG 4%–5% ( <i>P</i> -score 0.91)	.	0.49 (0.08, 2.85)	0.50 (0.23, 1.09)	.
0.67 (0.29, 1.55)	CHG 2-3% ( <i>P</i> -score 0.68)	0.72 (0.42, 1.23)	0.78 (0.46, 1.32)	.
0.51 (0.21, 1.27)	0.77 (0.46, 1.27)	Alcoholic PVI ( <i>P</i> -score 0.35)	.	0.73 (0.32, 1.69)
0.49 (0.24, 1.02)	0.74 (0.45, 1.21)	0.96 (0.49, 1.89)	Aqueous PVI ( <i>P</i> -score 0.30)	3.20 (0.31, 32.9)
0.44 (0.14, 1.42)	0.66 (0.26, 1.64)	0.86 (0.39, 1.90)	0.89 (0.33, 2.40)	CHG 0.5% ( <i>P</i> -Score 0.26)

The best treatment is shown in the top left cell, whilst the worst is in the bottom right. Antiseptics are ordered according to their ranking, based on the *P*-score; the *P*-score is a value between 0 and 1, with a higher score indicating a better treatment. Estimates in the upper triangle are direct comparisons (ie, from studies comparing treatments head-to-head); estimates on the bottom triangle are from the network meta-analysis. CHG indicates alcoholic chlorhexidine gluconate; PVI, povidone-iodine.

# The ChloraPrep™ range

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John S. Hibbard, PhD  
Gayle K. Mulberry, MS  
Ann R. Brady, AS

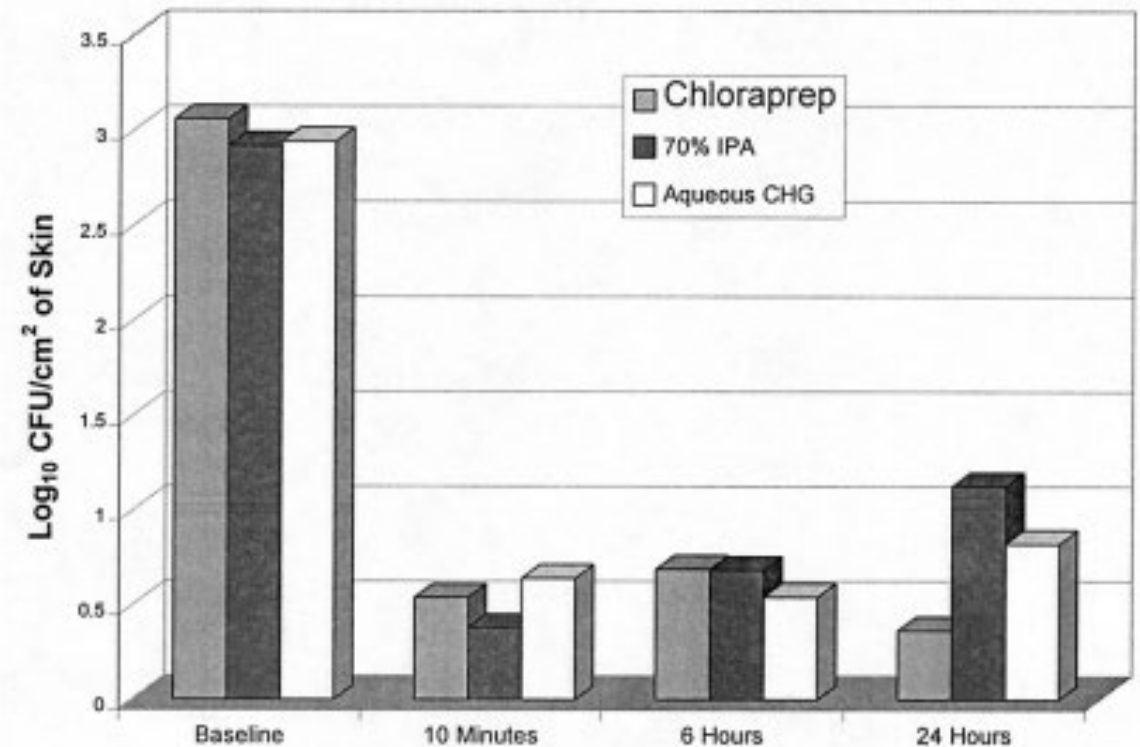
## A Clinical Study Comparing the Skin Antisepsis and Safety of Chloraprep, 70% Isopropyl Alcohol, and 2% Aqueous Chlorhexidine

**TABLE 1**

### Study Demographics

Variable	Number
Subjects in the test phase of study	106
Age (mean years)	56
Gender	
Males	32
Female	74
Race	
White	96
Black	9
Asian	1

**Mean Log<sub>10</sub> Microbial Counts on Abdominal Skin**





- D. Use a single-use applicator containing an antiseptic solution.<sup>4,8,21</sup> (V)
1. Follow manufacturers' directions for use to determine appropriate product application and dry times; always allow product to naturally dry completely without wiping, fanning, or blowing on skin.<sup>8,9</sup> (V)
  2. Adhere to Aseptic Non Touch Technique (ANTT®) while performing skin antisepsis. (see *Standard 19, Aseptic Non Touch Technique [ANTT®]*) .<sup>8,9</sup> (V)

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## Original Article

BD Chloraprep™ (“2 % chlorhexidine with 70 % isopropyl alcohol”) versus povidone iodine plus alcohol, for prevention of blood culture contamination at children: An investigator-initiated, open-label, single centre, randomized controlled trial

İlker Devrim<sup>a,b</sup>, Şahika Şahinkaya<sup>a</sup>, Miray Yılmaz Çelebi<sup>a,\*</sup>, Pelin Kaçar<sup>a</sup>, Ela Cem<sup>a</sup>, Ceren Sözen<sup>c</sup>, Yakup Yaman<sup>c</sup>, Fahri Yüce Ayhan<sup>d</sup>, Süleyman Murat Barman<sup>a</sup>

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## A B S T R A C T

**Introduction:** One of the important problems that lower the diagnostic value of blood culture is contamination with skin organisms. The povidone-iodine, alcohol, and chlorhexidine gluconate alcohol are used for disinfection prior to blood sampling for culture.

**Methods:** The investigator-initiated, open label, single centre, randomised trial compared blood culture contamination rates between two groups of patients in which using a povidone iodine skin-preparation process with the contamination rate for using “2 % chlorhexidine with 70 % isopropyl alcohol” skin-disinfection. The patients who required sampling for blood cultures were included in the study and study period was from 15 March 2023 to 15 July 2023.

**Results:** A total of 400 blood cultures were obtained during the study, including 133 in the study group and 267 in the control group. In the total blood cultures, 11.75 % (n = 47) had microorganism isolation. Among them 39 (9.75 %) were contaminants and 8 (2 %) of them were true pathogens. The contaminant microorganisms were as following; 34 coagulase-negative Staphylococci, 3 *Micrococcus* spp, and 2 Streptococci viridans. The blood culture contamination rate in the study group was 5.3 % (n = 7) and 12.0 % (n = 32) in the control group, and significantly lower in the study group (p = 0.033). There is no significant difference regarding skin related side effects between two groups.

**Conclusions:** This study, showed that 2 % chlorhexidine gluconate in 70 % isopropyl alcohol is more efficacious in children than 10 % povidone-iodine preparations for disinfecting the skin prior to blood specimen collection for prevention of blood culture contamination.



## Randomized study of antiseptic application technique in healthy volunteers before vascular access insertion (TApAS trial)

Yolène Carre<sup>a,\*</sup>, Bertrand Moal<sup>b</sup>, Christine Germain<sup>b</sup>, Eric Frison<sup>b</sup>, Marielle Dubreuil<sup>c</sup>, Céline Chansel<sup>d</sup>, Valérie Berger<sup>e</sup>, Hélène Boulestreau<sup>a</sup>, Agnès Lasheras-Bauduin<sup>a</sup>, Anne-Marie Rogues<sup>a,c</sup>

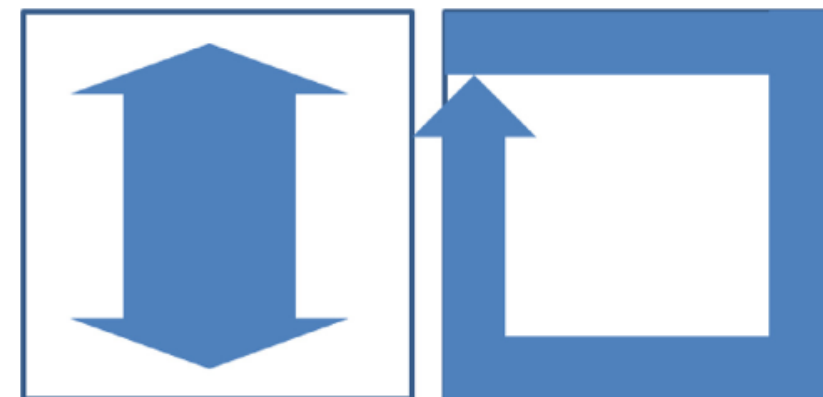
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<sup>e</sup> CHU Bordeaux Care and human sciences research unit, F-33000 Bordeaux France



1st step for 30 seconds

2nd step on the last move

Fig. 1. The Back-and-forth application technique – TApAS trial.



Fig. 2. The Concentric circle application technique – TApAS trial.

**Interpretation:** There was no clinically difference in reduction of microorganisms between the concentric circle and back-and-forth techniques at the bend of the healthy volunteer's elbow, after the 30 s of drying of the antiseptic. These findings have a significant impact on time required to achieve antiseptic applica-



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# Evaluation of the antiseptic activity of 5% alcoholic povidone-iodine solution using four different modes of application: a randomized open-label study

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<sup>a</sup> Burn Care Center, Plastic Surgery Department, University of Ghent, Belgium

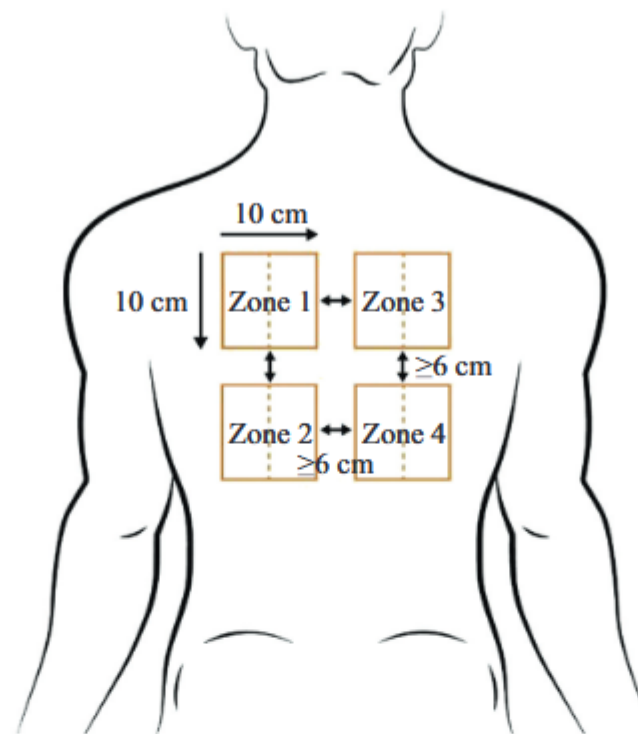
<sup>b</sup> Hospital Hygiene Department and Lab EE 1701 S MiHAR, Nantes University Hospital, Nantes, France

<sup>c</sup> Infection Control Groupe, Hôpital de Jolimont, La Louvière, Belgium

<sup>d</sup> Cardiovascular Surgery, University Hospital Amiens-Picardie (CHU Amiens-Picardie), Amiens, France

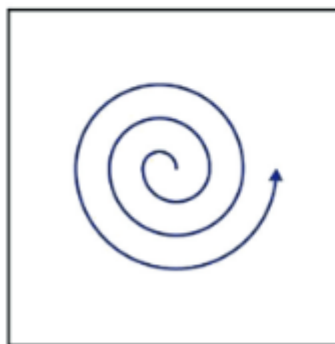
<sup>e</sup> Meda Pharma GmbH & Co. KG, A Viartis Company, Bad Homburg, Germany

<sup>f</sup> Meda Pharma S.p.A. A Viartis Company, Monza, Italy



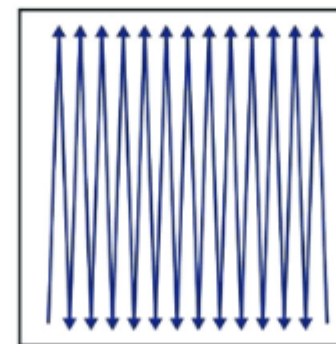
b

## Concentric circle method

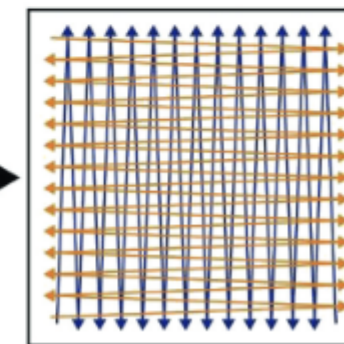


Spiral movements starting in the centre of the zone

## Back-and-forth friction method



First set of back-and-forth movements



Second set of back-and-forth movements, perpendicular to the first one



## Evaluation of the antiseptic activity of 5% alcoholic povidone-iodine solution using four different modes of application: a randomized open-label study

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<sup>b</sup> Hospital Hygiene Department and Lab EE 1701 S MIHAR, Nantes University Hospital, Nantes, France

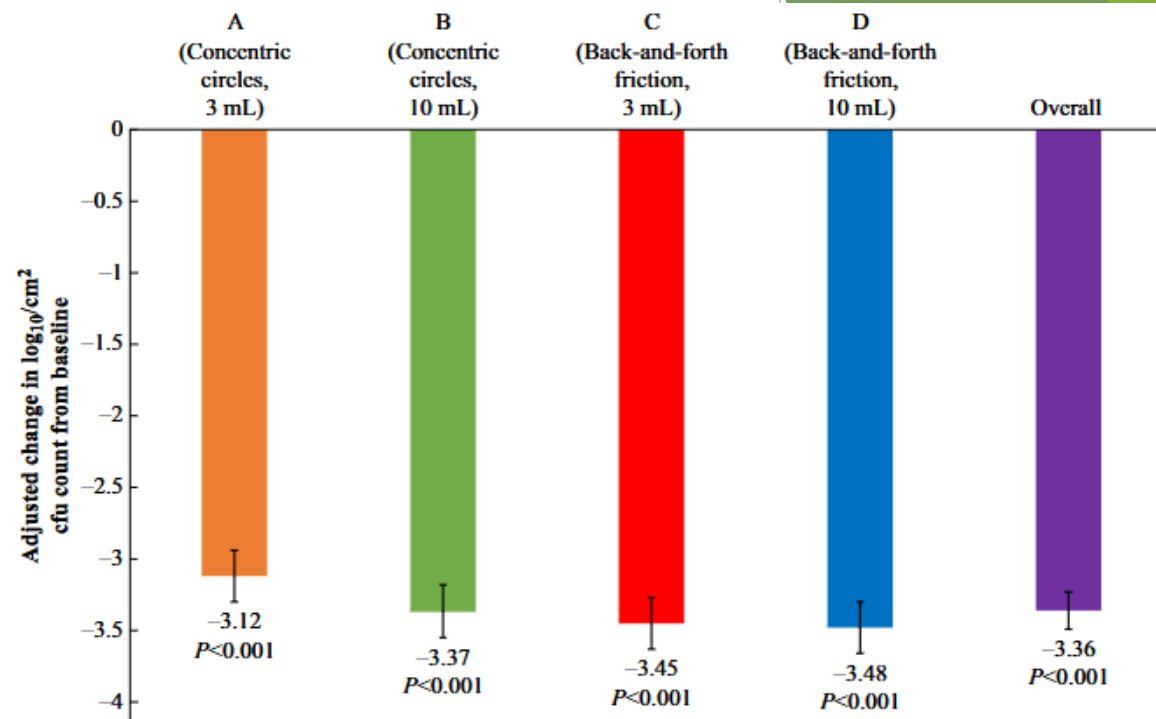
<sup>c</sup> Infection Control Groupe, Hôpital de Jolimont, La Louvière, Belgium

<sup>d</sup> Cardiovascular Surgery, University Hospital Amiens-Picardie (CHU Amiens-Picardie), Amiens, France

<sup>e</sup> Meda Pharma GmbH & Co. KG, A Viartis Company, Bad Homburg, Germany

<sup>f</sup> Meda Pharma S.p.A. A Viartis Company, Monza, Italy

**Conclusions:** Alcoholic PVP-I demonstrated high antiseptic activity for all modes of application. Greater efficacy was achieved with back-and-forth friction versus concentric circles, showing that application technique may influence antiseptic activity; these find-



**Figure 3.** Covariate adjusted change in colony-forming units (cfu) count (log<sub>10</sub>/cm<sup>2</sup>) from baseline — per protocol population. Data shown are mean (90% CI). For an exploratory study of this size, P<0.1 or 90% confidence interval excluding 0 is a notable result.

**Table I**

Adjusted mean change in colony-forming unit (cfu) count (in log<sub>10</sub>/cm<sup>2</sup>) from baseline, per application method and volume

Effect	Adjusted mean change in log <sub>10</sub> /cm <sup>2</sup> cfu count from baseline (SE)	90% CI	P <sup>a</sup>
<b>Application method</b>			
A vs. C (concentric circle vs. back-and-forth friction for 3 mL)	0.32 (0.13)	0.11, 0.53	0.012
B vs. D (concentric circle vs. back-and-forth friction for 10 mL)	0.11 (0.13)	-0.1, 0.33	0.372
Concentric circle vs. back-and-forth friction overall (i.e., AB vs. CD)	0.22 (0.09)	0.07, 0.37	0.017
<b>Volume</b>			
A vs. B (3 mL vs. 10 mL, concentric circle)	0.24 (0.13)	0.03, 0.46	0.062
C vs. D (3 mL vs. 10 mL back-and-forth friction)	0.03 (0.13)	-0.17, 0.24	0.789
3 mL vs. 10 mL overall (AC vs. BD)	0.14 (0.09)	-0.01, 0.29	0.129

CI, confidence interval; SE, standard error.

<sup>a</sup> For an exploratory study of this size, P<0.1 or 90% CI excluding 0 is a notable result.





Letter to the editor

Response to Monstrey *et al.*  
'Evaluation of the antiseptic  
activity of 5% alcoholic povidone-  
iodine solution using four  
different modes of application: a  
randomized open-label study'



studies. First, the sample localization: the bend of the elbow in TApAS and the back for Monstrey *et al.* Our study sampled an area frequently used for vascular access installation. Skin colonization is different depending on skin site, the bend of the elbow being a wet area unlike the back which is a sebaceous area [4]. Second, the volume of 5% alcoholic povidone-iodine solution used was 5 mL for TApAS versus 3 mL and 10 mL for Monstrey *et al.*'s study. The choice of the volume of 5 mL was justified in TApAS by the recommendations for use of

## 2020 Carrè et al.

- ▶ 132 pazienti
- ▶ Simile **baseline** contaminazione batterica
- ▶ Tampone al **gomito** un'area umida
- ▶ Volume di **5 ml**
- ▶ Tempo di asciugatura **standardizzato**
- ▶ Terreno di cultura più grande

## 2022 Mostrey et al

- ▶ 32 pazienti
- ▶ Assenti dati al base line
- ▶ Tampone alla **schiena** area sebacea
- ▶ Volume di **3 ml e 10 ml**, le differenze statisticamente significative sono sul volume **di 3 ml**
- ▶ Tempo di asciugatura **non standardizzato**
- ▶ Terreno di cultura più piccolo

## Standardized testing with chlorhexidine in perioperative allergy – a large single-centre evaluation

M. S. Opstrup<sup>1,2</sup>, H.-J. Malling<sup>2</sup>, M. Krøigaard<sup>2</sup>, H. Mosbech<sup>2</sup>, P. S. Skov<sup>2</sup>, L. K. Poulsen<sup>2</sup> & L. H. Garvey<sup>2</sup>

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### Abstract

**Background:** Perioperative allergic reactions to chlorhexidine are often severe and easily overlooked. Although rare, the prevalence remains unknown. Correct diagnosis is crucial, but no validated provocation model exists, and other diagnostic tests have never been evaluated. The aims were to estimate (i) the prevalence of chlorhexidine allergy in perioperative allergy and (ii) the specificity and sensitivity for diagnostic tests for chlorhexidine allergy.

**Methods:** We included all patients investigated for suspected perioperative allergic reactions in the Danish Anaesthesia Allergy Centre during 2004–2012. The following tests were performed: specific IgE (Immunocap<sup>®</sup>; Phadia AB, Sweden), histamine release test (HR) (RefLab ApS, Denmark), skin prick test (SPT) and intradermal test (IDT). Positivity criteria were as follows: specific IgE >0.35 kUA/l; HR class 1–12; SPT mean wheal diameter ≥3 mm; IDT mean wheal diameter ≥ twice the diameter of negative control. Chlorhexidine allergy was *post hoc* defined as a relevant clinical reaction to chlorhexidine combined with two or more positive tests. Based on this definition, sensitivity and specificity were estimated for each test.

**Results:** In total, 22 of 228 patients (9.6%) met the definition of allergy to chlorhexidine. Estimated sensitivity and specificity were as follows: specific IgE (sensitivity 100% and specificity 97%), HR (sensitivity 55% and specificity 99%), SPT (sensitivity 95% and specificity 97%) and IDT (sensitivity 68% and specificity 100%).

**Conclusions:** In patients investigated for suspected perioperative allergic reactions, 9.6% were diagnosed with allergy to chlorhexidine. Using our definition of chlorhexidine allergy, the highest combined estimated sensitivity and specificity was found for specific IgE and SPT.

## ORIGINAL ARTICLE Clinical Allergy

## Dynamics of plasma levels of specific IgE in chlorhexidine allergic patients with and without accidental re-exposure

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### Summary

**Background** Chlorhexidine is an effective disinfectant, which may cause severe allergic reactions. Plasma level of specific IgE to chlorhexidine (ImmunoCAP<sup>®</sup>) has high estimated sensitivity and specificity when measured within 6 months of allergic reaction, but knowledge of the dynamics over longer time periods is lacking and it is unknown whether levels fall below <0.35 kUA/L in patients with previously elevated levels. It is also unclear whether re-exposure influences levels of specific IgE.

**Objective** To investigate the dynamics of specific IgE in chlorhexidine allergic patients with and without re-exposure.

**Methods** All patients diagnosed with chlorhexidine allergy in the Danish Anaesthesia Allergy Centre January 1999 to March 2015 were invited to participate. The study included blood samples from the time of reaction and time of investigation and blood samples drawn prospectively over several years.

**Results** Overall, 23 patients were included. Specific IgE within hours of reaction was available in eight patients and was >0.35 kUA/L in six of these. During allergy investigations, usually 2–4 months later, specific IgE was >0.35 kUA/L in 22 of 23 patients. In the following months/years specific IgE declined <0.35 kUA/L in 17 of 23 patients (most rapidly within 4 months). Nine re-exposures in the healthcare setting were reported by seven patients (35%). Most re-exposures caused symptoms and were followed by an increase in specific IgE. Two patients with specific IgE <0.35 kUA/L reacted upon re-exposure.

**Conclusions & Clinical Relevance** Time from reaction should be considered when interpreting specific IgE results. Specific IgE is >0.35 kUA/L in most patients at time of reaction but should be repeated after a few weeks/months if negative. The optimal sampling time seems to be >1 month and <4 months. A value <0.35 kUA/L neither excludes allergy nor implies loss of reactivity in previously sensitized patients. Re-exposures are common, often iatrogenic, and can cause a rebound in specific IgE.

# Survey Infezioni catetere relate

