**Supplementary material**

**EFFECTIVENESS OF Chlorhexidine dressings to prevent catheter-related bloodstream infections: does one size fits all? A systematic literature review and meta-analysis**

Mireia Puig-Asensio, Alexandre R Marra, Christopher A Childs, Mary E Kukla,

 Eli N Perencevich, Marin L Schweizer

**Content**

-Appendix 1: Search strategy 2–6

-Appendix 2: Reasons for excluding full-text articles 7–8

-Appendix 3: Sample size and incidence of CRBSI in included studies 9–10

-Appendix 4: Definition of the outcomes as described in the included articles 11–12

-Appendix 5: Funnel plot of included studies 13–15

-Appendix 6: Subgroup analyses evaluating the effectiveness of CHG dressing 16–17

to prevent CRBSI

-References 18–25

***Appendix 1.* Search strategy used in the meta-analysis**

**PubMed Search (March 1, 2019)**

**Group 1: Chlorhexidine**

**"Chlorhexidine"**[Mesh] OR Chlorhexidine [tw] OR **"chlorhexidine gluconate"** [Supplementary Concept] OR chlorhexidine gluconate [tw] OR chlorhexidine bigluconate [tw] OR chlorhexidine digluconate [tw] OR **"Occlusive Dressings"**[Mesh] OR Occlusive Dressings [tw] OR Occlusive Dressing [tw] OR Occlusive Bandage [tw] OR Occlusive Bandages [tw] OR Biopatch\* [tw] OR chlorhexidine dressing\* [tw] OR chlorhexidine impregnated dressing\* [tw] OR chlorhexidine gluconate-impregnated sponge\* [tw] OR chlorhexidine-impregnated sponge\* [tw] OR chlorhexidine sponge\* [tw] OR no dressing\* [tw] OR polyurethane dressing\* [tw] OR standard polyurethane dressing\* [tw] OR Tegaderm CHG dressing\* [tw] OR transparent polyurethane dressing\* [tw]

**Group 2: Infections**

**"Bacteremia"**[Mesh] OR Bacteremia [tw] OR Bacteremias [tw] OR **"Catheter-Related Infections"**[Mesh] OR Catheter-Related Infections [tw] OR Catheter Related Infections [tw] OR Catheter-Related Infection [tw] OR Catheter-Associated Infections [tw] OR Catheter Associated Infections [tw] OR Catheter-Associated Infection [tw] OR catheter-related bloodstream infection\* [tw] OR CLABSI\* [tw] OR central line-associated bloodstream infection\* [tw] OR CRBSI\* [tw] OR central venous catheter-related bloodstream infections\* [tw] OR vascular catheter-related infection\* [tw]

**Group 3: Catheters**

**"Catheters"**[Mesh] OR Catheters [tw] OR Catheter [tw] OR **"Catheters, Indwelling"**[Mesh] OR Indwelling Catheters [tw] OR Indwelling Catheter [tw] OR In-Dwelling Catheters [tw] OR In Dwelling Catheters [tw] OR In-Dwelling Catheter [tw] OR Implantable Catheters [tw] OR **"Catheterization"**[Mesh] OR Catheterization [tw] OR Catheterizations [tw] OR **"Catheterization, Central Venous"**[Mesh] OR Central Venous Catheterization [tw] OR Central Catheterization [tw] OR Central Catheterizations [tw] OR Central Venous Catheterizations [tw] OR **"Central Venous Catheters"**[Mesh] OR Central Venous Catheters [tw] OR Central Venous Catheter [tw] OR Broviac catheter [tw] OR Hemocath catheter\* [tw] OR Hickman catheter\* [tw] OR Hemodialysis catheter\* [tw] OR long term central venous catheter\* [tw] OR PICC [tw] OR PICCs [tw] OR PICC Line\* [tw] OR peripherally inserted central catheter\* [tw] OR peripherally inserted central venous catheter [tw] OR short-term central venous catheter\* [tw] OR tunneled central venous catheters\*

**EMBASE Search (March 1, 2019)**

**Group 1: Chlorhexidine**

**'chlorhexidine'/exp** OR **'chlorhexidine gluconate'/exp** OR 'ab antiseptico':ti,ab OR 'chlorhexidine bigluconate':ti,ab OR 'chlorhexidine digluconate':ti,ab OR 'chlorhexidine gluconate':ti,ab OR **'occlusive dressing'/exp** OR 'occlusive bandage':ti,ab OR 'occlusive bandages':ti,ab OR 'occlusive dressing':ti,ab OR 'occlusive dressings':ti,ab OR 'biopatch\*':ti,ab OR 'chlorhexidine dressing':ti,ab OR 'chlorhexidine dressings':ti,ab OR 'chlorhexidine impregnated dressing\*':ti,ab OR 'chlorhexidine gluconate-impregnated sponge':ti,ab OR 'chlorhexidine gluconate-impregnated sponges':ti,ab OR 'chlorhexidine-impregnated sponge':ti,ab OR 'chlorhexidine-impregnated sponges':ti,ab OR 'chlorhexidine sponge':ti,ab OR 'chlorhexidine sponges':ti,ab OR 'no dressing':ti,ab OR 'no dressings':ti,ab OR 'polyurethane dressing':ti,ab OR 'polyurethane dressings':ti,ab OR 'standard polyurethane dressing':ti,ab OR 'standard polyurethane dressings':ti,ab OR 'transparent polyurethane dressing':ti,ab OR 'transparent polyurethane dressings':ti,ab OR 'tegaderm chg dressing\*':ti,ab

**Group 2: Infections**

**'bacteremia'/exp** OR 'bacillaemia':ti,ab OR 'bacillemia':ti,ab OR 'bacteraemia':ti,ab OR 'bacteremia':ti,ab OR 'bacteriemia':ti,ab OR 'haemorrhagic bacteremia':ti,ab OR 'hemorrhagic bacteremia':ti,ab OR **'catheter infection'/exp** OR 'catheter associated blood stream infection':ti,ab OR 'catheter associated blood stream infections':ti,ab OR 'catheter associated bloodstream infection':ti,ab OR 'catheter associated bloodstream infections':ti,ab OR 'catheter associated infection':ti,ab OR 'catheter associated infections':ti,ab OR 'catheter infection':ti,ab OR 'catheter related blood stream infection':ti,ab OR 'catheter related blood stream infections':ti,ab OR 'catheter related bloodstream infection':ti,ab OR 'catheter related bloodstream infections':ti,ab OR 'catheter related infection':ti,ab OR 'catheter related infections':ti,ab OR 'catheter-related infections':ti,ab OR 'central line associated bloodstream infection':ti,ab OR 'catheter-associated infection':ti,ab OR 'catheter-associated infections':ti,ab OR 'catheter-related bloodstream infection':ti,ab OR 'catheter-related bloodstream infections':ti,ab OR 'clabsi':ti,ab OR 'clabsis':ti,ab OR 'central line-associated bloodstream infections':ti,ab OR 'crbsi':ti,ab OR 'crbsis':ti,ab OR 'central venous catheter-related bloodstream infection':ti,ab OR 'central venous catheter-related bloodstream infections':ti,ab OR 'vascular catheter-related infection':ti,ab OR 'vascular catheter-related infections':ti,ab

**Group 3: Catheters**

**'catheter'/exp** OR 'catheter':ti,ab OR 'catheters':ti,ab OR 'catheter device':ti,ab OR **'indwelling catheter'/exp** OR 'catheter indwelling':ti,ab OR 'catheters, indwelling':ti,ab OR 'indwelling cannula':ti,ab OR 'indwelling catheter':ti,ab OR 'catheterization'/exp OR 'catherization':ti,ab OR 'catheter technique':ti,ab OR 'catheterisation':ti,ab OR 'catheterization':ti,ab OR 'microcatheterisation':ti,ab OR 'microcatheterization':ti,ab OR **'central venous catheterization'/exp** OR 'central vein catheterisation':ti,ab OR 'central vein catheterization':ti,ab OR 'central venous catheterisation':ti,ab OR 'central venous catheterization':ti,ab OR 'central catheterization':ti,ab OR 'central catheterizations':ti,ab OR **'central venous catheter'/exp** OR 'axera':ti,ab OR 'broviac':ti,ab OR 'cvp line':ti,ab OR 'groshong':ti,ab OR 'icy (device)':ti,ab OR 'leonard':ti,ab OR 'leonard catheter':ti,ab OR 'pediasat':ti,ab OR 'powerline (central venous catheter)':ti,ab OR 'vortex (central venous catheter)':ti,ab OR 'vortex port':ti,ab OR 'central intravenous catheter':ti,ab OR 'central line':ti,ab OR 'central vein catheter':ti,ab OR 'central venous catheter':ti,ab OR 'central venous catheters':ti,ab OR 'central venous line':ti,ab OR 'cv cath':ti,ab OR 'hemocath catheter\*':ti,ab OR 'hickman catheter':ti,ab OR 'hickman catheters':ti,ab OR 'hemodialysis catheter':ti,ab OR 'hemodialysis catheters':ti,ab OR 'long term central venous catheter\*':ti,ab OR 'picc\*':ti,ab OR **'peripherally inserted central venous catheter'/exp** OR 'lifecath picc expert':ti,ab OR 'powerpicc solo catheter':ti,ab OR 'spectrum turboject':ti,ab OR 'peripherally inserted central catheter':ti,ab OR 'peripherally inserted central venous catheter':ti,ab OR 'pic line':ti,ab OR 'picc line':ti,ab OR 'picc lines':ti,ab OR 'peripherally inserted central catheters':ti,ab OR 'peripherally inserted central venous catheters':ti,ab OR 'tunneled central venous catheter'/exp OR 'tunneled central venous catheter':ti,ab OR 'tunnelled central venous catheter':ti,ab OR 'tunneled central venous catheters':ti,ab OR 'tunnelled central venous catheters':ti,ab OR 'short-term central venous catheter':ti,ab OR 'short-term central venous catheters':ti,ab

**CINAHL Search (March 5, 2019)**

**Group 1: Chlorhexidine**

MH "Chlorhexidine" OR "Chlorhexidine" OR "chlorhexidine gluconate" OR "chlorhexidine digluconate" OR MH "Occlusive Dressings" OR "Occlusive Dressings" OR "Occlusive Dressing" OR "Occlusive Bandage" OR "Occlusive Bandages" OR "Biopatch" OR "chlorhexidine dressing" OR "chlorhexidine dressings" OR "chlorhexidine impregnated dressing" OR "chlorhexidine impregnated dressings" OR "chlorhexidine gluconate-impregnated sponge" OR "chlorhexidine gluconate-impregnated sponges" OR "chlorhexidine-impregnated sponge" OR "chlorhexidine-impregnated sponges" OR "chlorhexidine sponge" OR "chlorhexidine sponges" OR "no dressing" OR "no dressings" OR "polyurethane dressing" OR "polyurethane dressings" OR "standard polyurethane dressing" OR "standard polyurethane dressings" OR "Tegaderm CHG dressing" OR "Tegaderm CHG dressings" OR "transparent polyurethane dressing" OR "transparent polyurethane dressings"

**Group 2: Infections**

MH "Bacteremia" OR "Bacteremia" OR "Bacteremias" OR MH "Catheter-Related Infections+" OR "Catheter-Related Infections" OR "Catheter-Related Infection" OR "Catheter-Associated Infection" OR "Catheter-Associated Infections" OR MH "Catheter-Related Bloodstream Infections" OR "Catheter-Related Bloodstream Infection" OR "Catheter-Related Bloodstream Infections" OR "CLABSI" OR "CLABSIs" OR "central line-associated bloodstream infection" OR "central line-associated bloodstream infections" OR "CRBSI" OR "CRBSIs" OR "central venous catheter-related bloodstream infection" OR "central venous catheter-related bloodstream infections" OR "vascular catheter-related infection" OR "vascular catheter-related infections"

**Group 3: Catheters**

MH "Catheters+" OR "Catheters" OR Catheter" OR "Indwelling Catheters" OR "Indwelling Catheter" OR "In-Dwelling Catheter" OR "In-Dwelling Catheters" OR "Implantable Catheter" OR "Implantable Catheters" OR MH "Catheterization+" OR “Catheterization” OR "Catheterizations" OR MH "Catheterization, Central Venous+" OR "Central Venous Catheterization" OR "Central Venous Catheterizations" OR "Central Catheterization" OR "Central Catheterizations" OR MH "Central Venous Catheters+" OR "Central Venous Catheters" OR "Central Venous Catheter" OR "Broviac catheter" OR "Broviac catheters" OR "Hickman catheter" OR "Hickman catheters" OR "Hemodialysis catheter" OR "Hemodialysis catheters" OR "long term central venous catheter" OR "long term central venous catheters" OR "PICC" OR "PICCs" OR "PICC Line" OR MH "Peripherally Inserted Central Catheters" OR "Peripherally Inserted Central Catheters" OR "Peripherally Inserted Central Catheter" OR "peripherally inserted central venous catheter" OR "peripherally inserted central venous catheters" OR "short-term central venous catheter" OR "short-term central venous catheters" OR "tunneled central venous catheter" OR "tunneled central venous catheters"

***Appendix 2.* Reasons for excluding full-text articles**

|  |  |
| --- | --- |
| **Study** | **Reason for exclusion** |
| Ali, 20151 | Study design was not clear (probable cohort study) |
| Apata, 20172 **\*** | Incidence of CRBSI has not reported. Bloodstream infections are grouped together with tunnel-site infections  |
| Banton, 20023 | Incidence of CRBSI as counts (%) has not been reported and cannot be calculated |
| Camins, 20104 **\*** | Incidence of CRBSI has not been reported. Rates are expressed per dialysis session |
| Camins, 20135 | Incidence of CRBSI as counts (%) has not been reported and cannot be calculated |
| Eggimann, 20106Eggimann, 20117 | Incidence of CRBSI has not been reported. Results are reported grouping together all types of bloodstream infections or primary bacteremias |
| Gould, 20118 | The control group uses an antimicrobial-impregnated dressing. Two types of CHG dressings are compared |
| Gould, 20109 | The CHG dressing was implemented along with catheter care "bundle" practices. The control group used silver alginate patch for 3 months  |
| Hanazaki, 199910 | Incidence of CRBSI has not been reported. Skin colonization was the only variable assessed |
| Ivanova, 201611 | Incidence of CRBSI has not been reported |
| Karlnoski, 201912 | The control group uses an antimicrobial-impregnated dressing. A CHG impregnated sponge is compared to a silver-plated dressing |
| Karpanen, 201613 | Incidence of CRBSI has not been reported. Skin colonization and catheter tip colonization were the outcomes assessed |
| Kawamura, 201414 | Zero outcomes in each study arm |
| Krau, 2009 15 | Not a research article. This is a commentary |
| Loftus, 201416 | Incidence of CRBSI has not been reported |
| Lewis, 201817 | Not enough information to calculate the incidence of CRBSI  |
| Maki, 200018 | Overlapping data with another abstract |
| Miller, 201119 | Not enough information to calculate incidence of CRBSI. Only aggregated rates for CRBSI among different groups are shown |
| Onder, 200920 **\*** | CRBSI is defined as positive blood cultures obtained from the catheter  |
| Pedrolo, 201421 | Overlapping data with another article |
| Pfaff, 201222 | The control group uses an antimicrobial-impregnated dressing. Two types of CHG dressings (Biopatch® vs Tegaderm®) are compared |
| Richtmann, 201123 | Incidence of CRBSI as counts (%) has not been reported and cannot be calculated |
| Righetti, 201624 **\*** | Cross-over RCT in which analyses could not be adjusted for within-patient correlation |
| Scheithauer, 201425 | Incidence of CRBSI as counts (%) has not been reported and cannot be calculated |
| Schroeder, 201226 | Incidence of CRBSI has not been reported. Catheter exit-site colonization was the reported outcome |
| Sharma, 201327 | Not enough information to calculate incidence of CRBSI. The number of participants in the intervention and control group are unknown |
| Telli, 201528  | The CHG dressing was implemented along with changes in infection control measures (i.e., swab sticks with CHG, staff education). The effectiveness of CHG dressing alone cannot be determined  |
| Webster, 201629 | The control group is an antimicrobial-impregnated dressing. The CHG dressing (Biopatch®) is compared to a Foam disc |
| Webster, 201730 | The control group is an antimicrobial-impregnated dressing. The CHG dressing (Biopatch®) is compared to a Foam disc |
| Wong, 201231 | Descriptive study. No control group without CHG dressing |
| Unpublished RCT 32 | There are no results available. Authors were contacted with no response |
| Yu, 201533 | Overlapping data with another article |

Abbreviations: CHG, chlorhexidine dressing; CRBSI, catheter-related bloodstream infection; RCT, randomized controlled trial

**\***Studies performed in hemodialysis patients

***Appendix 3.* Sample size and incidence of CRBSI and exit-site/tunnel infections in the included studies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **First author, year, location** | **No. of catheters studied****(no. of patients if applicable)a** | **Mean catheter indwelling time (days)b** | **Catheter-related bloodstream infection** | **Exit-site/tunnel infections** |
| **n (%)** | **Rate****(1,000 catheter-days)** | **n (%)** | **Rate****(1,000 catheter-days)** |
| **CHG group** | **Control group** | **CHG group** | **Control group** | **CHG group** | **Control group** | **CHG group** | **Control group** | **CHG group** | **Control group** | **CHG group** | **Control group** |
| Arpa, 2013 | 63 | 60 | 7.7 | 7.8 | 0 (-) | 1 (1.7) | NR | 0 (-) | 1 (1.7) | NR |
| Arvaniti, 2012 | 150 | 156 | 7 | 7 | 3 (2)  | 2 (1.3) | 2.8 | 1.4 | 1 (0.7) | 2 (1.3) | NR |
| Biehl, 2016c | 307 | 306 | 19 (SD 12.1) | 18.5 (SD 12.1) | Definite CRBSI: 13 (4.2) | Definite CRBSI:24 (7.8) | Definite CRBSI: 2.2 | Definite CRBSI 4.5 | NR | NR |
| Chambers, 2005 | 58 (52) | 54 (43) | 140.8 (SD 100.5) | 146 (SD 109.8) | 0/58 (-) | 4/54 (7.4) | NR | 5/58 (8.6) | 23/54 (42.6) | NR |
| Chan, 2017 | 86 | 35 | 9.4 | 8.6 | 1 (1.2) | 0 (-) | NR | 2 (2.3) | 2 (6.0) | NR |
| Duzkaya, 2016 | 50 | 50 | 13.8 (SD 7.0) | 14.2 (SD 7.1) | 1 (2) | 5 (10) | NR | 1 (2.0) | 2 (4.0) | NR |
| Ergul, 2018 | 63 | 68 | 14.7 | 14.3 | 13 (20.6) | 18 (26.5) | NR | NR | NR |
| Garland, 2001 | 335 | 370 | 17.7 | 17.4 | 12/314 (3.8)c | 11/341 (3.2)c | NR | NR | NR |
| Gerceker, 2017d | 14 | 13 | 72.5 (SD 55.8) | 85.7 (SD 50.8) | Definite CRBSI 2 (14.3) | Definite CRBSI 0 (-) | Definite CRBSI 2.0 | Definite CRBSI - | 0 (-) | 2 (15.4) | - | 1.7 |
| Levy, 2005 | 74 | 71 | NR | NR | 4 (5.4) | 3 (4.2) | NR | NR | NR |
| Maki, 2000 | 665 (301)e | 736 (366)e | NR | NR | 8/665 (1.2) | 24/736 (3.3) | NR | NR | NR |
| Margatho, 2018 | 47 | 54 | 7.7 (SD 5.1) | 7.7 (SD 5.1) | 1/35 (2.9)f | 2/42 (4.8)f | NR | 7 (14.9) | 6 (11.1%) |  |
| O’Horo, 2013 | 1237 | 1348 | NR | NR | 51 (4.1) | 69 (5.1) | NR | 13 (1) | 28 (2) |  |
| Pedrolo, 2014 | 43 | 42 | 4.9 (SD 2.5) | 5 (SD 2.7) | 6 (14.0) | 5 (11.9) | NR | NR | NR  |
| Pivkina, 2018 | 30 | 30 | 9.5 | 7.3 | 2 (6.7) | 5 (16.7) | 6.9 | 20.6 | 0 (-) | 2 (6.7) |  |
| Roberts, 1998 | 20 (NR)g | 20 (NR)g | 7 (range 4­–2) | 6 (range 2–14) | 1/17 (5.9)with available data | 0/16 (-)with available data  | NR | NR | NR |
| Ruschulte, 2009 | 300 | 301 | 16.6 | 15.8  | 19 (6.3) | 34 (11.3) | NR | NR | NR |
| Timsit, 2009 | 1953 (817) | 1825 (819) | 6.7 | 6.7 | 6/1953 (0.3) | 17/1825 (0.9) | 0.4 | 1.3 | 9 (0.5) | 6 (0.3) | NR |
| Timsit, 2012 | 2108 (938) | 2055 (941) | 7.7 | 7 | 9/2108 (0.4) | 22/2055 (1.1) | 0.5 | 1.3 | NR | NR |
| Yu, 2019 | 259 (NR)h | 215 (NR)h | NR | NR | 8 (3.1) | 6 (2.8) | 5.7 | 4.9 | NR | NR |

 Abbreviations: CRBSI, catheter-related bloodstream infection NR, not reported; SD, standard deviation;

aIn some studies, patients could have received more than one catheter during the study period; they could have been enrolled multiple times in the study. For studies in which this information was not clearly mentioned, we assumed that the number of catheters and patients were the same; patients were only enrolled once during the study period.

bFor studies that reported the catheter indwelling time as a median [inter-quartile range (IRQ) or range], we estimated the mean as devised by Wan et al34

cNot all the catheters had the tip cultured to define an episode as CRBSI

dMultiple definitions of CRBSI are provided in the article. Here, we only report incidence and rates of definite catheter-related bloodstream infections

eNumber of patients per study arm obtained from another article published by the same senior author

fThere were 12 patients in each group from whom blood samples were not taken, and thus the sample size for CRBSI assessment was reduced

gA total of 40 catheters from 32 patients were included

hA total of 474 catheters from 304 patients were analyzed

***Appendix 4.* Definition of the outcomes as described in the included articles**

1. *Catheter-related bacteremia (CRBSI)*

Some articles could use more than one definition. If there was not mention whether the positive blood culture was drawn from a peripheral vein, we assumed that this was the case.

|  |  |
| --- | --- |
| **Definition** | **Articles**  |
| **Definite/confirmed CVC-related bacteremia** Growth of the same pathogen from blood culture of peripheral vein and catheter and one of the following:**35 36** * Catheter exit site exudate with the same pathogen isolated from the bloodstream
* Semiquantitative catheter tip culture yielded greater than 15 colony-forming units (CFUs) of the same pathogen or quantitative (>103 colony forming units) device culture
* Simultaneously quantitative cultures of blood samples showed a ratio of 3:1 of CFU between blood samples obtained through a catheter and peripheral vein, or the differential time to positivity was greater than or equal to 2 hours
 | **37-49 (\*)**  |
| **“Probable” CVC-related bacteremia** * Bloodstream infection in a patient with an intravascular catheter
* Signs of infection with no other recognized focus of infection apart from the catheter and
* ± Positive catheter-tip culture (same organism recovered from tip and blood, without mention to semiquantitative roll-plate culture)
 | **50-54**  |
| **CVC-associated bloodstream infection as defined by the Centers for Disease Control and Prevention (CDC)55**  |  **54** |
| **No definition provided or unclear** | **56 57** |

(\*) Of these articles, Timsit et al 201245 performed a posthoc analysis in which episodes where reclassified according to the CDC criteria. This information has not been included in this meta-analysis.

1. *Exit-site infection/tunnel infection*

|  |  |
| --- | --- |
| **Exit-site infection** (with or without concomitant bloodstream infection) | **Articles**  |
| Purulent discharge at exit site or at catheter removal | **38 40 44 57** |
| Redness, pain and tenderness within 2 cm of the catheter exit site  | **41 48 50 56** |
| Growth of ≥15 CFUs in the culture of the catheter end and find­ings of inflammation at the catheter insertion site in the absence of blood-borne infection | **46** |
| Infection at the catheter entry site (without other details) | **37** |

|  |  |
| --- | --- |
| **Tunnel infection** (with or without concomitant bloodstream infection) | **Articles**  |
| Tenderness, erythema and induration along over the subcutaneous tunnel > 2 cm from the catheter exit site | **41 50** |

1. *Adverse events*

|  |  |
| --- | --- |
| **Definition** | **Articles**  |
| Severe contact dermatitis (leading to permanent discontinuation of the study dressing) | **44 45** |
| Contact dermatitis (regardless of severity) | **47** |
| Skin allergic reaction | **37** |
| Skin irritation | **48 57** |
| Local erythema | **53** |
| Any of the following: Blisters, itchiness, skin tear, maceration, rash, erythema, bruise at device removal, others | **39 40 52** |

***Appendix 5.* Funnel plot of included studies**

*A. Twenty studies assessing CRBSI*



*B. Ten studies reporting exit-site and/or tunnel infections*



There is publication bias. This plot is asymmetric toward a large association between CHG dressing and reduced infections.

*C. Ten studies reporting adverse events*



There is publication bias. This plot is asymmetric toward a large association between CHG dressing and adverse events.

***Appendix 6.* Subgroup analyses evaluating the effectiveness of CHG dressing to prevent CRBSIs**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Subgroup analyses** | **No. of studies** | **No. of catheters****(CHG/control)** | **Pooled risk ratio (95% CI)** | **I2 test** |
| *All studies* | 20 | 7,826/7,764 | 0.71 (0.58–0.87) | 0% |
| **Study design** |  |  |  |  |
| RCTs37-50 52-54 57 | 18 | 6,526/6,348 | 0.65 (0.49–0.85) | 0% |
| Non-randomized trials51 56 | 2 | 1,300/1,416 | 0.80 (0.59–1.09) | 0% |
| **Definition of CRBSI** |  |  |  |  |
| Definite/confirmed CRBSI37-49 | 13 | 6,062/5,936 | 0.60 (0.44–0.82) | 0% |
| “Probable” CRBSI or CDC criteria is met50-54 | 5 | 497/450 | 0.88 (0.55–1.41) | 0% |
| **Maximal sterile barrier precautions during catheter insertion** |  |  |  |  |
| Precautions stated37 38 41-48 52-54 57 | 14 | 5,410/5,217 | 0.71 (0.52–0.99) | 0% |
| No precautions are mentioned39 40 49-51 56 | 6 | 2,466/2,597 | 0.65 (0.51–0.82) | 0% |
| **Skin antisepsis preparation before catheter insertion** |  |  |  |  |
| Povidone iodine (± alcohol)37 38 44 46 50 | 5 | 2,274/2,145 | 0.41 (0.17–1.00) | 0% |
| CHG (± alcohol)40 42 48 51 53 54 57 | 7 | 564/477 | 0.83 (0.51–1.34) | 0% |
| **Reason for drawing blood cultures** |  |  |  |  |
| Only if signs or suspicion of infection37-40 42 43 47 48 50-53  | 12 | 1,641/1,600 | 0.73 (0.55–0.98) | 0% |
| **Assessment of CRBSI outcomes in RCTs** |  |  |  |  |
| Researcher was blinded38 40 44 45 48 49 | 6 | 4,997/4,849 | 0.48 (0.26–0.88) | 0% |
| Researcher was not blinded or unknown37 39 41-43 46 47 50 52-54 57 | 12 | 1,529/1,499 | 0.70 (0.51–0.95) | 0% |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Subgroup analyses** | **No. of studies** | **No. of catheters****(CHG/control)** | **Pooled risk ratio (95% CI)** | **I2 test** |
| *All studies* | 20 | 7,826/7,764 | 0.71 (0.58–0.87) | 0% |
| **Type of dressing** |  |  |  |  |
| CHG-impregnated disc38 40 42-44 47 49 50 53 56 | 10 | 5,009/5,113 | 0.74 (0.57­–0.95) | 0% |
| CHG transparent dressing37 39 41 45 48 51 54 57 | 8 | 2,714/2,559 | 0.64 (0.44­­­­­–0.94) | 0% |
| **Study population and settings** |  |  |  |  |
| Adults38-40 42-45 48-50 52 54 56 57 | 14 | 7,178/7,108 | 0.67 (0.53–0.84) | 0% |
| ICU38 42 44 45 48 52 54 57 | 8 | 4,525/4,328 | 0.70 (0.41–1.18) | 0% |
| Onco-hematological patients39 43 50  | 3 | 665/661 | 0.54 (0.36–0.81) | 0% |
| Neonates and pediatric populations37 41 46 47 51 53 | 6 | 578/603 | 0.90 (0.57–1.40) | 0% |
| **Type of catheter** |  |  |  |  |
| Short-term CVCs37-39 43 46 48 51-54 57 | 11 | 1,374/1,341 | 0.67 (0.50–0.90) | 0% |
|  Length of catheterization > 7  days37 39 43 46 48 51 57 | 7 | 848/857 | 0.58 (0.42–0.81) | 0% |
|  Length of catheterization ≤ 7 days38 42 52 | 3 | 210/214 | 1.34 (0.54–3.32) | 6% |
| Long-term CVCs41 50 56 | 3 | 1,309/1,415 | 0.80 (0.22–2.95) | 33% |
| **Insertion site** |  |  |  |  |
| Studies including only short-term CVCs with jugular/subclavian insertion37 51-53 57  | 5 | 273/271 | 0.82 (0.51–1.32) | 0% |
| Studies including mainly short-term CVCs with femoral insertion (≥44% of the study cohort)33 38 46 | 3 | 459/421 | 0.84 (0.29–2.42) | 17% |
| **Frequency of dressing change** |  |  |  |  |
| Similar frequency of dressing change in study groups37-45 48 53 57 | 12 | 5,137/4,910 | 0.58 (0.42–0.82) | 0% |
| Different frequency of dressing change between study groups (7 days in the CHG group vs ≤3 days)46 49 51 52 54 | 5 | 1,080/1,115 | 0.73 (0.46–1.14) | 0% |

Abbreviations: CDC, Centers for Disease Control and Prevention; CHG, chlorhexidine dressing; CI, confidence interval; CRBSI, catheter-related bloodstream infection; CVC, central venous catheter; ICU, intensive care unit; RCT, randomized-controlled trial

**REFERENCES**

1. Ali SMM, Koul SS, Memon MI, Pasha TMU, Afghan S, Tahir F. Comparison of chlorhexidine based dressing versus simple occlusive dressing in preventing catheter related bloodstream infections at medical ICU in a resource constraint settings. *Intensive Care Med Exp* 2015;3.

2. Apata IW, Hanfelt J, Bailey JL, Niyyar VD. Chlorhexidine-impregnated transparent dressings decrease catheter-related infections in hemodialysis patients: a quality improvement project*. J Vasc Access* 2017;18:103-8.

3. Banton J, Banning V.Impact on catheter-related bloodstream infections with the use of the BIOPATCH dressing. *JVAD* 2002;7:27-32.

4. Camins BC, Richmond AM, Dyer KL, et al. A crossover intervention trial evaluating the efficacy of a chlorhexidine-impregnated sponge in reducing catheter-related bloodstream infections among patients undergoing hemodialysis. *Infect Control Hosp Epidemiol* 2010;31:1118-23.

5. Camins BC. Reducing Catheter-Related Bloodstream Infections in the ICU With a Chlorhexidine-Impregnated Sponge (BIOPATCH). 2013. <https://clinicaltrials.gov/ct2/show/NCT00548132>. Accessed June 24, 2019

6. Eggimann P, Joseph C, Thévenin M-J, Voirol P, Bellini C, Pagani J-L, Revelly JP. Impact of chlorhexidine-impregnated sponges on catheter-related infections rate. *Intensive Care Med* 2010;36:S128.

7. Eggimann P, Joseph C, Thévenin M-J, Bellini C,Voirol P, Pagani J-L, Revelly JP. Reduction of primary bacteremia following the introduction of chlorhexidine-impregnated sponges combined with transparent dressings on central venous catheters in a mixed ICU. *J Vasc Access* 2011;12:83.

8. Gould P. Transparent chlorhexidine (CHG) IV securement dressing vs. chlorhexidine (CHG) impregnated disk. *Am J Infect Control* 2011;39:E32.

9. Gould P, Ouddaker A. What impact does chlorhexidine gluconate transparent IV securement dressing have on central line-associated bloodstream infection (CLABSI) rates? *Am J Infect Control* 2010;38:E38-E9.

10. Hanazaki K, Shingu K, Adachi W, Miyazaki T, Amano J. Chlorhexidine dressing for reduction in microbial colonization of the skin with central venous catheters: a prospective randomized controlled trial. *J Hosp Infect* 1999;42:165-8.

11. Ivanova O, Simakina J, Oparina J, Goncharova E, Zubarovskaya L, Afanasyev B. Comparative analysis of different CVC dressing types convenience and economic effectiveness in allogeneic hemopoietic stem cell transplant recipients. *Bone Marrow Transplant* 2016;51:S534.

12. Karlnoski R, Abboud EC, Thompson P, Oxner AZ, Sinnott JT, Marcet JE. Reduction in Central Line-Associated Bloodstream Infections Correlated With the Introduction of a Novel Silver-Plated Dressing for Central Venous Catheters and Maintained for 6 Years. *J Intensive Care Med* 2019;34:544-9.

13. Karpanen TJ, Casey AL, Whitehouse T, Nightingale P, Das I, Elliott TS. Clinical evaluation of a chlorhexidine intravascular catheter gel dressing on short-term central venous catheters. *Am J Infect Control* 2016;44:54-60.

14. Kawamura H, Takahashi N, Takahashi M, Taketomi A. Differences in microorganism growth on various dressings used to cover injection sites: inspection of the risk of catheter-related bloodstream infections caused by Gram-negative bacilli. *Surg Today* 2014;44:2339-44.

15. Krau SD. Intravascular catheter dressings with chlorhexidine-impregnated sponges reduced infections in the ICU. *Evid Based Nurs* 2009;12:115.

16. Loftus MJ, Florescu CJ, Stuart RL. Staphylococcus aureus bacteraemia associated with peripherally inserted central catheters: the role of chlorhexidine gluconate-impregnated sponge dressings. *Med J Aust* 2014;200:317-8.

17. Lewis RT, Sese GB, Marinacci A, Scott J.Central venous catheter infection rate with use of chlorhexidine gluconate 2%. *Transfus Altern Transfus Med* 2018;58(Supplement 2 (101A-).

18. Maki DG, Narans LL, Knasinski V, Kluger D. Prospective, randomized, investigator-masked trial of a novel chlorhexidine-impregnated disk (biopatch®) on central venous and arterial catheters. *Infect Control Hosp Epidemiol* 2000;21:96.

19. Miller MR, Niedner MF, Huskins WC, et al. Reducing PICU central line-associated bloodstream infections: 3-year results. *Pediatrics* 2011;128:e1077-83.

20. Onder AM, Chandar J, Coakley S, Francoeur D, Abitbol C, Zilleruelo G. Controlling exit site infections: does it decrease the incidence of catheter-related bacteremia in children on chronic hemodialysis? *Hemodial Int* 2009;13:11-8.

21. Pedrolo E, Santos MC, Mingorance P, Reichembach Danski MT, Boostel R. Chlorhexidine-impregnated dressing for central venous catheter: pilot clinical trial. *Revista Enfermagem UERJ* 2014;22:760-4.

22. Pfaff B, Heithaus T, Emanuelsen M. Use of a 1-piece chlorhexidine gluconate transparent dressing on critically ill patients. *Crit Care Nurse* 2012;32:35-40.

23. Richtmann R SC, Baltieri S, Rodrigues T, Camolesi F, Quadrado E, Saito K, Andrade C. Use of chlorhexidine-impregnated dressing in neonates. *BMC Proc* 2011;5.

24. Righetti M, Palmieri N, Bracchi O, et al. Tegaderm CHG dressing significantly improves catheter-related infection rate in hemodialysis patients. *J Vasc Access* 2016;17:417-22.

25. Scheithauer S, Lewalter K, Schroder J, et al. Reduction of central venous line-associated bloodstream infection rates by using a chlorhexidine-containing dressing. *Infection* 2014;42:155-9.

26. Schroeder KM, Jacobs RA, Guite C, et al Use of a chlorhexidine-impregnated patch does not decrease the incidence of bacterial colonization of femoral nerve catheters: a randomized trial. *Can J Anaesth* 2012;59:950-7.

27. Sharma B, Shina V.Catheter related blood stream infections (CRBSI) in critical care set-up; role of chlorhexidine impregnated sponge at the entry site of CVC in preventiing infection. *Indian J Crit Care Med* 2013;17:43-4.

28. Telli G, Dizbay M, Güzel OT, et al. Prevention of catheter releated bloodstream infections by using swap sticks with chlorhexidine and chlorhexidine-lmpregnated transparent dressings. *Gazi Medical Journal* 2015;26:152-4.

29. Webster J, Marsh N, Larsen E, Choudhury A, Gavin N, Booker C, Paterson D. Biopatch™ or Kendall™ AMD foam disc to reduce the incidence of central-line-associated blood stream infection: A feasibility study. *Infection, Disease and Health* 2016;21:119.

30. Webster J, Larsen E, Marsh N, Choudhury A, Harris P, Rickard CM. Chlorhexidine gluconate or polyhexamethylene biguanide disc dressing to reduce the incidence of central-line-associated bloodstream infection: a feasibility randomized controlled trial (the CLABSI trial). *J Hospit Infect* 2017;96:223-8.

31. Wong E, Cook M, Ross-Smith M, Mount P. A study of haemodialysis catheter infection rates using the biopatch. *Nephrology* 2012;17:32.

32. Trial on the Efficacy of Tegaderm Chlorhexidine Gluconate (CHG) in Reducing Catheter Related Bloodstream Infections (TegaCHG). <https://clinicaltrials.gov/ct2/show/NCT01142934>. Accessed June 20, 2019

33. Yu K, Li Z, Wang J, Li H, Lu M. Effect and cost analysis of two kinds of transparent dressings on the bloodstream infection rate of central venous catheter. *Chin J Pract Nurs* 2015;31:2777-80.

34. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol* 2014;14:135.

35. Mermel LA, Allon M, Bouza E, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 Update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009;49:1-45.

36. Hentrich M, Schalk E, Schmidt-Hieber M, et al. Central venous catheter-related infections in hematology and oncology: 2012 updated guidelines on diagnosis, management and prevention by the Infectious Diseases Working Party of the German Society of Hematology and Medical Oncology. *Ann Oncol* 2014;25:936-47.

37. Arpa Y, Aygün H, YalçInbaş Y, San D, Ulukol A. Comparison of catheter related infection rates in pediatric cardiovascular surgery patients with use of transparent cover and transparent cover saturated with chlorhexidin gluconate in central catheter care. *Turkish Journal of Research & Development in Nursing* 2013;15:57-67.

38. Arvaniti K, Lathyris D, Clouva-Molyvdas P, et al. Comparison of Oligon catheters and chlorhexidine-impregnated sponges with standard multilumen central venous catheters for prevention of associated colonization and infections in intensive care unit patients: a multicenter, randomized, controlled study. *Crit Care Med* 2012;40:420-9.

39. Biehl LM, Huth A, Panse J, et al. A randomized trial on chlorhexidine dressings for the prevention of catheter-related bloodstream infections in neutropenic patients. *Ann Oncol* 2016;27:1916-22.

40. Chan RJ, Northfield S, Larsen E, et al. Central venous Access device SeCurement And Dressing Effectiveness for peripherally inserted central catheters in adult acute hospital patients (CASCADE): a pilot randomised controlled trial. *Trials* 2017;18:458.

41. Gerceker GO, Yardimci F, Aydinok Y. Randomized controlled trial of care bundles with chlorhexidine dressing and advanced dressings to prevent catheter-related bloodstream infections in pediatric hematology-oncology patients. *Eur J Oncol Nurs* 2017;28:14-20.

42. Roberts B, Cheung D. Biopatch--a new concept in antimicrobial dressings for invasive devices. *Aust Crit Care* 1998;11:16-9.

43. Ruschulte H, Franke M, Gastmeier P, et al. Prevention of central venous catheter related infections with chlorhexidine gluconate impregnated wound dressings: a randomized controlled trial. *Ann Hematol* 2009;88:267-72.

44. Timsit JF, Schwebel C, Bouadma L, et al. Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. *JAMA* 2009;301:1231-41.

45. Timsit JF, Mimoz O, Mourvillier B, et al. Randomized controlled trial of chlorhexidine dressing and highly adhesive dressing for preventing catheter-related infections in critically ill adults. *Am J Respir Crit Care Med* 2012;186:1272-8.

46. Duzkaya DS, Sahiner NC, Uysal G, Yakut T, Citak A. Chlorhexidine-Impregnated Dressings and Prevention of Catheter-Associated Bloodstream Infections in a Pediatric Intensive Care Unit. *Crit Care Nurse* 2016;36:e1-e7.

47. Garland JS, Alex CP, Mueller CD, et al. A randomized trial comparing povidone-iodine to a chlorhexidine gluconate-impregnated dressing for prevention of central venous catheter infections in neonates. *Pediatrics* 2001;107:1431-6.

48. Margatho AS, Ciol MA, Hoffman JM, et al. Chlorhexidine-impregnated gel dressing compared with transparent polyurethane dressing in the prevention of catheter-related infections in critically ill adult patients: A pilot randomised controlled trial. *Aust Crit Care* 2018.

49. Maki DG, Mermel ML, Kluger D,Narans L, Knasinski V, Parenteau S, Covington P. The efficacy of a chlorhexidine-impregnated sponge (BiopatchTM) for the prevention of intravascular catheter-related infection: A prospective, randomized, controlled, multicenter study*. ICCAC* 2000;40th:422.

50. Chambers ST, Sanders J, Patton WN, et al. Reduction of exit-site infections of tunnelled intravascular catheters among neutropenic patients by sustained-release chlorhexidine dressings: results from a prospective randomized controlled trial. *J Hosp Infect* 2005;61:53-61.

51. Ergul AB, Gokcek I, Ozcan A, Cetin S, Gultekin N, Torun YA. Use of a chlorhexidine-impregnated dressing reduced catheter-related bloodstream infections caused by Gram-positive microorganisms. *Pak J Med Sci* 2018;34:347-51.

52. Pedrolo E, Danski MT, Vayego SA. Chlorhexidine and gauze and tape dressings for central venous catheters: a randomized clinical trial. *Rev Lat Am Enfermagem* 2014;22:764-71.

53. Levy I, Katz J, Solter E, et al. Chlorhexidine-impregnated dressing for prevention of colonization of central venous catheters in infants and children: a randomized controlled study. *Pediatr Infect Dis J* 2005;24:676-9.

54. Yu K, Lu M, Meng Y, Zhao Y, Li Z. Chlorhexidine gluconate transparent dressing does not decrease central line-associated bloodstream infection in critically ill patients: A randomized controlled trial. *Int J Nurs Pract* 2019:e12776.

55. Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and Non-central Line Associated Bloodstream Infection). <https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf>. Accessed August 14, 2019

56. O'Horo SK, Corson D, Baum RA. Efficacy of biopatch™ in reducing catheter related infections in cuffed, tunneled central venous catheters. *JVIR* 2013;24:S127.

57. Pivkina AI, Gusarov VG, Blot SI, Zhivotneva IV, Pasko NV, Zamyatin MN. Effect of an acrylic terpolymer barrier film beneath transparent catheter dressings on skin integrity, risk of dressing disruption, catheter colonisation and infection. *Intensive Crit Care Nurs* 2018;46:17-23.