

Should *tunnelled* central venous catheters be covered by chlorhexidine dressings?

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Until now, chlorhexidine is the only antimicrobial agent used in catheter dressings. According to our knowledge there are two types of chlorhexidine dressings, i.e. Biopatch^R and TegadermTM. All trials included in this review investigated Biopatch^R. No trials were found comparing Biopatch^R with TegadermTM.

The systematic review on the effect of chlorhexidine dressings consists of two parts which are published separately on the website of the WIP.

Part I: Should non-tunnelled CVCs be covered by chlorhexidine dressings?

Part II: Should tunnelled CVCs be covered by antimicrobial dressings?

The following question was answered by a systematic review of the literature:
Should tunnelled central venous catheters (CVCs) be covered by chlorhexidine dressings versus standard dressings to reduce the occurrence of catheter-related bloodstream infection (CRBSI)?

Study population: patients with tunnelled CVCs

Comparison: chlorhexidine dressing versus standard dressing

Outcome: CRBSI

Methods

Data sources

Publications were retrieved by a search of Medline and the Cochrane Library up to 31 March 2010. The search strategy in Cochrane was: (central venous catheter* OR tunnelled intravascular catheter* OR catheter-related) AND (antimicrobial OR antiseptic* OR chlorhexidine* OR Biopatch OR disinfectant*) AND (dressing* OR sponge OR Biopatch). To identify randomised controlled trials in Medline the following search strategy was used: ((randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR "clinical trial" [tw] OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND

(mask* [tw] OR blind* [tw])) OR "latin square" [tw] OR placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp] OR comparative study [mh] OR evaluation studies [mh] OR follow-up studies [mh] OR prospective studies [mh] OR cross-over studies [mh] OR control* [tw] OR prospectiv* [tw] OR volunteer* [tw]) NOT (animal [mh] NOT human [mh]) AND (central venous catheter* OR tunnelled intravascular catheter* OR catheter-related) AND (antimicrobial OR antiseptic* OR chlorhexidine* OR Biopatch OR disinfectant*) AND (dressing* OR sponge OR Biopatch). In addition, the lists of references of all identified trials were checked for more trials.

Selection criteria

All randomised and quasi-randomised trials comparing antimicrobial dressings versus standard dressings for tunnelled central venous catheters and catheter-related bloodstream infection as the outcome measure were included. Studies in neonates were excluded.

Assessment of trial quality

Three reviewers assessed trial quality independently by evaluating each study to determine concealment of treatment allocation, double blinding, completeness of follow-up, use of intention-to-treat analysis, selective reporting of events and premature discontinuation of the trial due to benefit. Central randomization, sealed envelopes or a similar method was assumed to yield adequate randomization. The description of dropouts was considered adequate if the number of patients lost and reasons why patients were lost were reported according to allocation to treatment. Disagreements were resolved by consensus.

Review methods

Data were extracted by three reviewers independently and compared. Disagreements were resolved by consensus. Data from the original publications were used to calculate the overall incidence-density ratio (IDR) with a 95% confidence interval (CI) and the incidence-density difference (IDD) with a 95% CI by using Review Manager (Version 5.0). The incidence density was calculated by dividing the total number of CRBSIs by the total catheter days of follow up. The number of catheterisation days needed to treat (NNT) is calculated as the inverse of the IDD. Data were combined in the analysis where appropriate, using a random-effects model. The quality of evidence for CRBSI was assessed by using the Grade approach¹.

Results

Seventy six potentially relevant studies were initially identified by our search. By judgment of titles and abstracts, ten studies appeared to fulfil the selection criteria. Out of the ten studies, nine papers were excluded after reading the whole article. The reasons for exclusion are listed in Table 1. One parallel-group randomised controlled trial was included in the review ².

Excluded studies

See Table 1

Assessment of trial quality

See Table 2

Study population, interventions and outcome definitions

See Table 3

Summary estimates of associations between treatment and control group

See Figure 1 to 5

Summary of Findings table (GRADE)

See Table 4

Table 1 Excluded studies

	Reasons for exclusion
Crawford ³	NOT RCT
Garland ⁴	Neonates
Hanazaki ⁵	Another question was answered
Ho ⁶	Systematic review: included neonatology; included an article which was not published; pooled too heterogeneous data;
Levy ⁷	Another question was answered
Roberts ⁸	Another question was answered
Roush ⁹	Not primary study
Ruschulte ¹⁰	Another question was answered
Timsit ¹¹	Another question was answered

Table 2 Quality assessment

	Concealment of allocation	Placebo-controlled	Description of dropouts (%)	Analysis by intention-to-treat	Stopping trial early to benefit	Selective reporting of events
Chambers 2005	Adequate* (catheters were randomised)	No	Adequate 2%	No	No	No

* Information requested from the original author by mail

Table 3 Study populations, interventions and outcome definitions

	Setting	Treatment (T) and control group (C)	Duration of catheterisation	End of study protocol	Outcome n / N
Chambers 2005	Neutropenic in- and outpatients* undergoing chemotherapy via a tunnelled cuffed CVC; 114 CVCs in 95 patients; the CVCs were cuffed with a vitacuff antimicrobial cuff.	T (58 CVCs): BIOPATCH™ around the catheter covered by a adhesive dressing (Opsite IV3000) after the exit site was dry and free from ooze C (54 CVCs): no dressing Note: 1) After insertion all catheters were treated with a sterile gauze and porous adhesive dressing until the exit site was dry and free from ooze; 2) CHX dressing were changed weekly and as necessary	Mean T: 113 days C: 107 days Median T: 71.5 (9 - 411) C: 62.5 (10 - 449)	Catheter removal; infection	Bloodstream infection: Defined as positive blood culture during febrile episodes; blood drawn from CVC or peripheral catheter. T: 41 / 6573 catheter days; C: 60 / 5778 catheter days Exit-site or combined exit-site / tunnel infections: Defined as redness, pain and tenderness at the exit site to warrant antimicrobial therapy as judged by the attending medical team. T: 5 / 58 C: 23 / 54 Premature removal of catheter for documented

infection:

T: 6 / 58

C: 20 / 54

Premature removal of catheter overall:

T: 19 / 58

C: 21 / 54

Note: the reason for removal was judged by the attending clinical team at the time of removal

Vancomycin treatment because of suspected infection:

T: 30 / 58

C: 29 / 54

Adverse events:

We assume that there were no adverse events due to chlorhexidine, but authors did not state this explicitly.

* Information requested from the original author by mail

Figure 1 Summary estimates of association between antimicrobial dressings covered by standard dressings and no dressings at all for central venous catheters expressed as incidence density ratio (IDR) and 95% confidence interval (CI); outcome: bloodstream infection

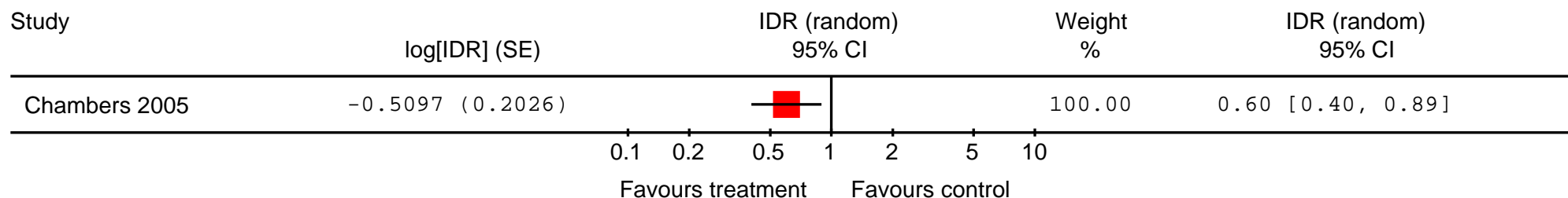


Figure 2 to 5 Summary estimates of association between antimicrobial dressings covered by standard dressings and no dressings at all for central venous catheters expressed as relative risk (RR) and 95% confidence interval (CI)

Figure 2 Outcome: exit-site or combined exit-site / tunnel infections

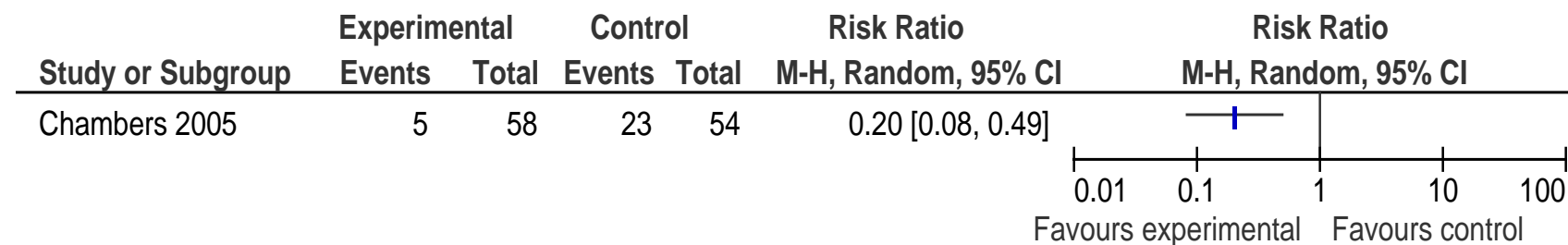


Figure 3 Outcome: premature removal of CVC for documented infection.

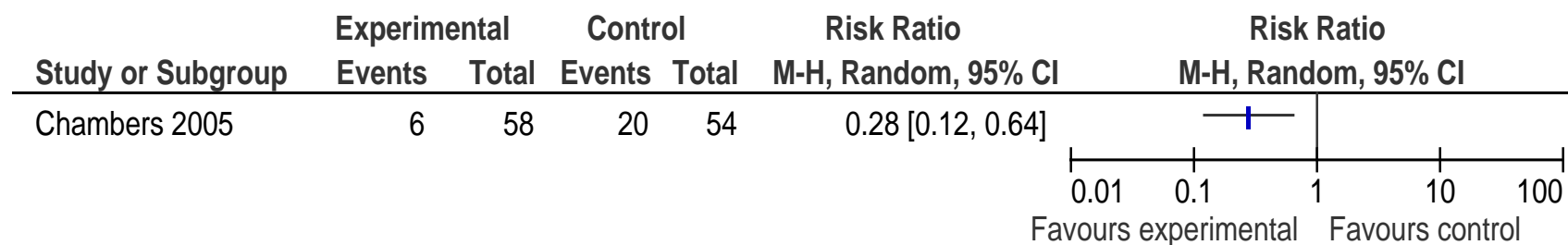


Figure 4 Outcome: premature removal of CVC overall.

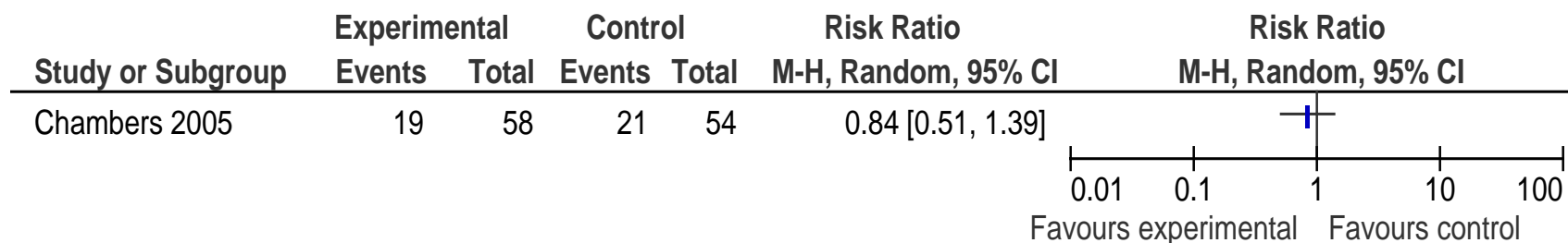
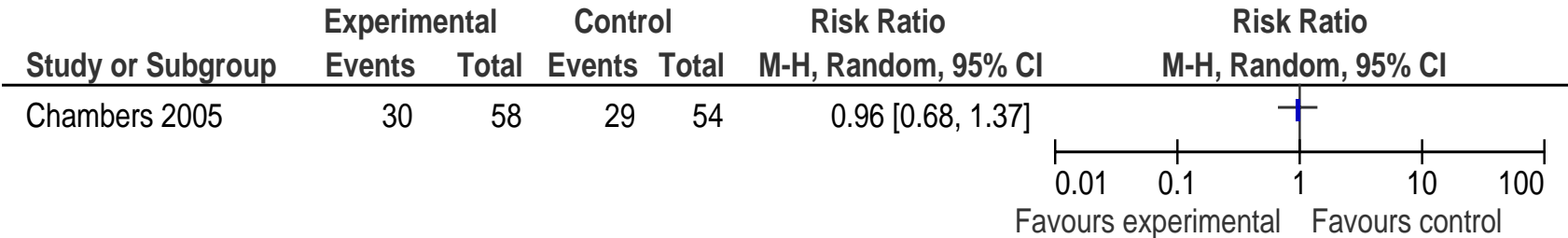


Figure 5 Outcome: vancomycin treatment because of suspected infection



Comment

Authors measured bloodstream infection, not catheter-related bloodstream infection.

Table 4 Summary of Findings table (GRADE)

antimicrobial dressing compared to no catheter site dressing for patients with tunnelled CVC						
Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk no catheter site dressing	Corresponding risk antimicrobial dressing				
Bloodstream infection	10 per 1000¹	6 per 1000 (4 to 9)¹	IDR 0.60 (0.4 to 0.89)	12351 (1 study)	very low^{2,3}	
Exit-site or combined exit-site / tunnel infection Follow-up: mean 100 days	426 per 1000⁴	85 per 1000 (34 to 209)⁴	RR 0.20 (0.08 to 0.49)	112 (1 study)	very low^{2,3}	
Premature removal of catheter for documented infection Follow-up: mean 110 days	370 per 1000⁴	104 per 1000 (44 to 237)⁴	RR 0.28 (0.12 to 0.64)	112 (1 study)	very low^{2,3}	
Premature removal of catheter overall Follow-up: mean 110 days	389 per 1000	327 per 1000 (198 to 541)	RR 0.84 (0.51 to 1.39)	112 (1 study)	very low^{2,3,4}	
Catheters treated with vancomycin Follow-up: mean 110 days	537 per 1000⁴	516 per 1000 (365 to 736)⁴	RR 0.96 (0.68 to 1.37)	112 (1 study)	very low^{2,3}	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio;

Very low quality: We are very uncertain about the estimate.

¹ Catheter days

² Not placebo-controlled; analysis not by intention to treat

³ Total number of events is low; small sample size

Conclusion

The evidence of the benefit of antimicrobial dressings in oncologic patients with tunnelled, cuffed (vitacuff) CVCs for chemotherapy and a mean duration of catheterisation of about 110 days is very uncertain. A single small trial compared chlorhexidine-impregnated dressings covered by standard catheter site dressings after the exit site was dry and free from ooze to no catheter site dressing at all and found that antimicrobial dressings were of benefit regarding bloodstream infection (IDR 0.60; 95% CI 0.40 – 0.89); exit-site or combined exit-site / tunnel infection (RR 0.20; 95% CI 0.08 to 0.49); premature removal of catheter because of documented infection (RR 0.28; 95% CI 0.12 to 0.64); it was uncertain whether antimicrobial dressings were of benefit or harm with regard to premature removal of CVC overall (RR 0.84; 95% CI 0.51 to 1.39) and vancomycin treatment because of suspected infection (RR 0.94; 95% CI 0.68 to 1.37). However, the quality of the available evidence of antimicrobial dressings is low because of serious limitations in trial quality and imprecision.

Reference list

1. Atkins D, Best D, Briss PA *et al*. Grading quality of evidence and strength of recommendations. *BMJ* 2004; **328**: 1490.
2. 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.
3. Crawford AG. Cost-benefit analysis of chlorhexidine gluconate dressing in the prevention of catheter-related bloodstream infections. 2004

4. Garland JS. A randomized trial comparing povidone-iodine to a chlorhexidine gluconate-impregnated dressing for prevention of central venous catheter infections in neonates. 2001
5. Hanazaki K. Chlorhexidine dressing for reduction in microbial colonization of the skin with central venous catheters: a prospective randomized controlled trial. 1999
6. Ho KM. Comment on: Use of chlorhexidine-impregnated dressing to prevent vascular and epidural catheter colonization and infection: a meta-analysis. 2010
7. Levy I. Chlorhexidine-impregnated dressing for prevention of colonization of central venous catheters in infants and children: a randomized controlled study. 2005
8. Roberts B. Biopatch--a new concept in antimicrobial dressings for invasive devices. 1998
9. Roush K. Drug-impregnated sponges for preventing catheter-related infections. 2009
10. Ruschulte H. Prevention of central venous catheter related infections with chlorhexidine gluconate impregnated wound dressings: a randomized controlled trial. 2009
11. Timsit JF. Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. 2009