

Review

Antiseptic barrier cap effective in reducing central line-associated bloodstream infections: A systematic review and meta-analysis



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ABSTRACT

Background: Microorganisms can intraluminally access a central venous catheter via the catheter hub. The catheter hub should be appropriately disinfected to prevent central line-associated bloodstream infections (CLABSI). However, compliance with the time-consuming manual disinfection process is low. An alternative is the use of an antiseptic barrier cap, which cleans the catheter hub by continuous passive disinfection.

Objective: To compare the effects of antiseptic barrier cap use and manual disinfection on the incidence of CLABSI.

Design: Systematic review and meta-analysis.

Methods: We systematically searched Embase, Medline Ovid, Web-of-science, CINAHL EBSCO, Cochrane Library, PubMed Publisher and Google Scholar until May 10, 2016. The primary outcome, reduction in CLABSI per 1000 catheter-days, expressed as an incidence rate ratio (IRR), was analyzed with a random effects meta-analysis. Studies were included if 1) conducted in a hospital setting, 2) used antiseptic barrier caps on hubs of central lines with access to the bloodstream and 3) reported the number of CLABSI per 1000 catheter-days when using the barrier cap and when using manual disinfection.

Results: A total of 1537 articles were identified as potentially relevant and after exclusion of duplicates, 953 articles were screened based on title and abstract; 18 articles were read full text. Eventually, nine studies were included in the systematic review, and seven of these nine in the random effects meta-analysis. The pooled IRR showed that use of the antiseptic barrier cap was effective in reducing CLABSI (IRR = 0.59, 95% CI = 0.45–0.77, $P < 0.001$).

Conclusions: Use of an antiseptic barrier cap is associated with a lower incidence CLABSI and is an intervention worth adding to central-line maintenance bundles.

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What is already known about the topic

- To prevent central line-associated bloodstream infections (CLABSI), the catheter hub should be appropriately disinfected. However, the adherence to this time consuming manual disinfection process is low.
- *In vitro* studies suggest that an antiseptic barrier cap placed over IV needleless connectors decreases colonization of microorganisms on the connectors and thereby lowers the risk of CLABSI.

What this paper adds

- This systematic review and meta-analysis showed that use of antiseptic barrier caps reduced the risk of CLABSI.
- That is why the antiseptic barrier cap deserves to be added to central-line maintenance bundles and could improve nurses' work processes.

1. Introduction

Microorganisms can access central venous catheters (CVCs) via an intraluminal or an extraluminal route. An important route is intraluminally via the catheter hub (Salzman et al., 1993a).

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Microorganisms may be a source of central line-associated bloodstream infections (CLABSI), especially in patients with impaired immunity (e.g. patients who are on chemotherapy) and in patients admitted to the Intensive Care Unit (ICU) (Ziegler et al., 2015). Research has shown that a combination of interventions, known as central line insertion and maintenance bundles, is effective in preventing CLABSI in ICU settings and is cost saving (Blot et al., 2014; Ista et al., 2016; Ista et al., 2016). To prevent intraluminal contamination, important aspects of the bundles are ensuring a maximum sterile barrier during catheter insertion and adequate disinfection of the hub prior to intravenous medication administration (Salzman et al., 1993b). Adequate disinfection means rubbing the hub for 10 s with chlorhexidine, povidone iodine, an iodophor, or 70% alcohol followed by 30 s drying time, which is a time consuming procedure (O'Grady et al., 2011; Hong et al., 2013). However, the optimal duration of rubbing and drying is still unclear and is therefore not present in guidelines. A recently published meta-analysis showed that maximum compliance with maintenance bundles is hard to reach (Ista et al., 2016). Also, a study by Helder et al. showed that nurses' compliance with the 30 s drying time after hub disinfection was only 35% before and only 45% after a feedback intervention (Helder et al., 2016).

To protect the hub from contamination an antiseptic barrier cap was developed (Menyhay and Maki, 2006, 2008). Through continuous contact with the disinfectant, this device optimizes needleless connector disinfection through cleaning of the catheter hub without active scrubbing (Menyhay and Maki, 2006, 2008). The antiseptic barrier cap is placed onto an intravenous (IV) needleless connector and bathes the connector in 70% isopropyl alcohol. The single-use antiseptic barrier cap remains in place until the next catheter access. This design allows for direct safe access to the hub when the barrier cap is removed. *In vitro* studies suggest that an antiseptic barrier cap placed over an IV needleless connector reduces colonization of microorganisms on the connectors and thereby lowers the risk of CLABSI (Menyhay and Maki, 2006, 2008). With this systematic review and meta-analysis we aimed to answer the question: what is the effect of antiseptic barrier caps compared to manual disinfection on the incidence of CLABSI?

2. Methods

2.1. Search strategy

This systematic review and meta-analysis followed the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement (S1 file) (Moher et al., 2009). The study protocol was registered in the PROSPERO international register (registration number: CRD42016032303). A librarian devised and executed the search strategy. This included the terms CLABSI, catheter and infusion, in combination with disinfectant, in combination with a cap or hub. The full search strategy is presented in the S2 file. The following databases were searched until May 10, 2016: Embase, Medline Ovid, Web-of-science, CINAHL EBSCO, Cochrane Library, PubMed Publisher and Google Scholar. The search was not limited by language, date of publication, country, study methodology or patient characteristics.

2.2. Study selection

The following inclusion criteria were applied: 1) studies conducted in a hospital setting; 2) antiseptic barrier caps used on hubs of central lines with access to the bloodstream; and 3) reporting CLABSI per 1000 catheter-days with the use of the antiseptic barrier cap compared to manual disinfection. The

exclusion criteria were the following: 1) reviews – however, citations of reviews about prevention of CLABSI were hand-searched to identify additional studies; 2) studies about the barrier cap used on feeding tubes or used for other purposes without access to the bloodstream; 3) conference abstracts, letters to the editor and abstracts only; 4) studies with missing information about CLABSI per 1000 catheter-days after contacting the corresponding author. These inclusion and exclusion criteria served to select articles based on title and abstract and to select articles based on the full-text. Studies reporting both the number of CLABSI and the number of catheter-days were included in the meta-analysis. All selections were performed independently in duplicate by AV, OH, MV, LS, AH and EI; disagreements were discussed until consensus was reached.

2.3. Data extraction

We developed a data abstraction form, pilot-tested it on one randomly selected study and redefined it according to the outcomes of the pilot. The following data were collected: study methodology, study period, setting, country, study population, specific department(s) where study was conducted, usual care and compliance with usual care, barrier cap tested (name, manufacturer) and compliance with barrier cap use, CLABSI incidence per 1000 catheter-days before introduction of antiseptic barrier cap, CLABSI incidence per 1000 catheter-days after introduction of the antiseptic barrier cap, and estimated costs and savings. Data were extracted and checked by AV, OH, MV, LS, AH and EI. Disagreements were discussed by the extracting and the checking author; the study protocol stated that if no agreement could be reached a third author should decide. A third author judgement was not needed, however. The corresponding authors of the included articles were asked to verify whether the data were extracted correctly and to provide missing information where relevant.

The methodological study quality was estimated according to the 27-item scoring system of Downs and Black (Downs and Black, 1998). Studies with scores below 12 were considered of low quality; studies with scores of 12 and 13 were considered of moderate quality; studies with scores of 14 and higher were considered as of high quality. Low study quality was not an exclusion criterion.

2.4. Outcomes

With as intervention the antiseptic barrier cap and with as control manual disinfection, the primary outcome of this study was the incidence of CLABSI per 1000 catheter-days. The secondary outcomes were compliance with antiseptic barrier cap use, and costs and savings.

2.5. Statistical analyses

Study characteristics are summarized as frequencies and percentages. We quantitatively pooled the results of individual studies, where suitable. The primary outcome, expressed as an incidence rate ratio (IRR), was analyzed with a meta-analysis. Clinical heterogeneity was expected since the studies were performed in different countries and at different departments. Therefore a random effects model based on the method of DerSimonian and Laird was fitted (DerSimonian and Laird, 1986). Further, the I^2 statistic to quantify heterogeneity between studies was calculated. As suggested by Higgins et al. heterogeneity was classified as low (I^2 25–50%), moderate (I^2 50–75%), or high (I^2 > 75%) (Higgins et al., 2003).

For studies included in the meta-analysis, publication bias across studies was examined via the bias indicators Egger and

Begg-Mazumdar (Kendall's tau). Publication bias was assumed to be present if both bias indicators showed a significant result. Additionally, publication bias was examined visually with use of a funnel plot; asymmetry indicated publication bias. First, we performed a subgroup analysis for the two different brands of barrier caps used, CuroTM disinfecting port protectors (Curo, Ivera Medical, San Diego, CA) and SwabCap[®] disinfecting caps for needleless connectors (Excelsior Medical, Neptune, NJ). Second, a possible influence of study quality was examined in a sub-sample analysis. Third, studies conducted in cancer centers and studies which included only patients from cancer/hematology wards were analyzed separately. For all analyses, a *P*-value of <0.05 was considered statistically significant. All meta-analyses and calculations were performed using StatsDirect statistical software, version 3.0.171 (Altrincham, United Kingdom).

3. Results

3.1. Description of included studies

A total of 1536 articles were identified as potentially relevant (Fig. 1, S2 file). Additionally, we selected one article from the reference lists of 14 reviews about preventing CLABSIs in patients (Fig. 1). Screening of the titles and abstracts yielded 18 articles that met the eligibility criteria described in the Methods section when. After reading these 18 articles full-text, we eventually included nine articles (Ramirez et al., 2012; Sweet et al., 2012; Wright et al.,

2013; Devries et al., 2014; Merrill et al., 2014; Stango et al., 2014; Kamboj et al., 2015; Cameron-Watson, 2016; Pavia and Mazza, 2016) in this systematic review and seven of those (Ramirez et al., 2012; Sweet et al., 2012; Wright et al., 2013; Merrill et al., 2014; Stango et al., 2014; Kamboj et al., 2015; Cameron-Watson, 2016) in the meta-analysis (Fig. 1). Eight corresponding authors were asked to verify the extracted information and/or to provide additional information. For one study, contact information (i.e. email address) was not available (Cameron-Watson, 2016). Five out of eight authors responded and provided additional information (Sweet et al., 2012; Wright et al., 2013; Merrill et al., 2014; Stango et al., 2014; Kamboj et al., 2015). Two out of four studies of which the author could not be reached did not specify the number of CLABSIs and the number of catheter-days in the control and intervention periods and could not be included in the meta-analysis (Fig. 1) (Devries et al., 2014; Pavia and Mazza, 2016).

3.2. Study characteristics

Study characteristics are listed in Table 1. Eight of the nine included studies were conducted in the USA and one in the UK. The studies were conducted between 2009 and 2015. All nine studies were designed as prospective quasi-experimental before-after studies and one was a multi-center study (Wright et al., 2013). One study was conducted at the ICU (11.1%), two at hematology-oncology units (22.2%), and six were conducted at multiple departments (66.7%). Three studies used the Curo antiseptic

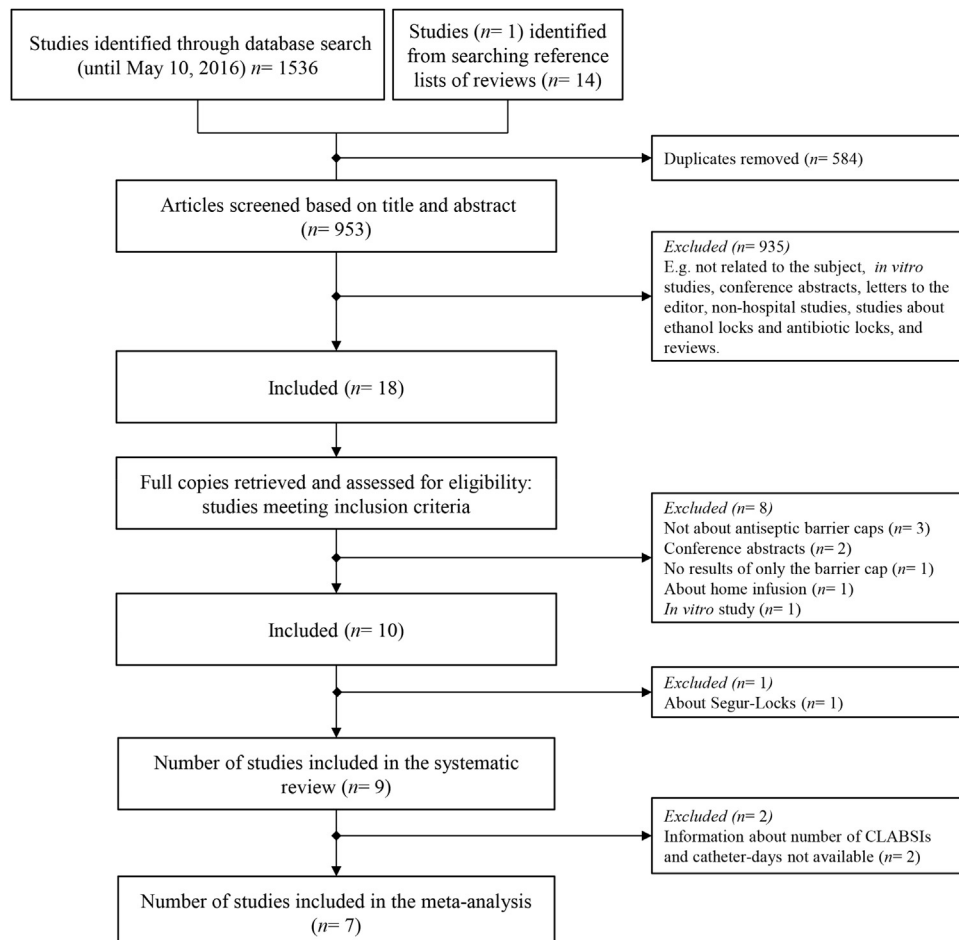


Fig. 1. Flow diagram of study selection.

Table 1

Characteristics of the 9 included quasi-experimental before-after studies.

First author, year, country	Setting	Brand	Type of Lines ^a	Pre-intervention period	Intervention period	CLABSI rate	Compliance ^b	Quality score ^c
Sweet et al. (2012), USA	Adult hematology and oncology unit	Curos	2	12 months	6 months	P: 2.34 I: 0.33	85%	13
Ramirez et al. (2012), USA	Two intensive care units at a 214-bed community hospital	Curos	1	12 months	12 months	P: 1.90 I: 0.50	73%	7
Wright et al. (2013), USA	All inpatient adult units at 4 acute care facilities	SwabCap	2	18 months	14 months	P: 1.45 I: 0.74	ND	13
Devries et al. (2014), USA	634-bed hospital	SwabCap	3	21 months	21 months	ND	ND	7
Merrill et al. (2014), USA	430-bed trauma center	Curos	3	12 months	12 months	P: 1.44 I: 0.87	ND	15
Stango et al. (2014), USA	520-bed acute care institution	SwabCap	1	21 months	21 months	P: 1.52 I: 0.83	85% ^d	14
Kamboj et al. (2015), USA	470-bed cancer center	SwabCap	1	16 months	16 months	P: 2.65 I: 2.02	ND	13
Cameron-Watson (2016), UK	Oncology, surgery, acute care of the elderly, critical care units	SwabCap	4	6 months	6 months	P: 4.30 I: 1.50	80%	11
Pavia and Mazza (2016), USA	97-bed urban pediatric post-acute care hospital	SwabCap	1	18 months	6 months	ND	ND	12

Abbreviations: ND = no data; USA = United States of America; UK = United Kingdom; P = CLABSI rate in pre-intervention period; I = CLABSI rate in intervention period.

^a 1 = Central venous lines; 2 = Central venous and PICC lines; 3 = Central venous and PICC and Peripheral catheters; 4 = Central venous and PICC and Peripheral and Central arterial lines.^b Compliance when using the barrier cap.^c 27-item scoring system developed by Downs and Black (1998).^d In medical/surgical units.

barrier cap (33.3%) and six the SwabCap (66.7%). Six out of the nine included studies described the manual disinfection procedure in more detail; with three studies using alcohol wipes (Sweet et al., 2012; Wright et al., 2013; Cameron-Watson, 2016), and three studies using an alcohol sponge (Ramirez et al., 2012), swab (Stango et al., 2014) or pad (Kamboj et al., 2015). The patient population was described in two articles (Sweet et al., 2012; Wright et al., 2013). The mean age of the patients in these studies ranged from 56.3 to 67.5 years, and between 41% and 49% of patients were men. Six studies (66.7%) used the Centers for Disease Control and Prevention (CDC) definition to define CLABSIs (Ramirez et al., 2012; Sweet et al., 2012; Wright et al., 2013; Merrill et al., 2014; Stango et al., 2014; Kamboj et al., 2015); the other three studies did not specify this (Devries et al., 2014; Cameron-Watson, 2016; Pavia and Mazza, 2016). Compliance with the antiseptic barrier cap was described by four studies (44.4%) (Ramirez et al., 2012; Sweet et al., 2012; Stango et al., 2014; Cameron-Watson, 2016); the median compliance rate was 82.5% (range 73–85%). In all four studies audits were used to assess compliance, and in two studies it was described that this was based on number of barrier caps *in situ* (Ramirez et al., 2012; Cameron-Watson, 2016). The median quality

index score of the nine included studies was 13 (range 7–15). Three studies (33.3%) were of low, four (44.4) of moderate, and two (22.2%) of high methodological quality. Overall, we considered the methodological quality as moderate.

Seven studies declared no conflicts of interest (77.8%) (Sweet et al., 2012; Wright et al., 2013; Merrill et al., 2014; Stango et al., 2014; Kamboj et al., 2015; Pavia and Mazza, 2016). For four of these, the manufacturer provided the antiseptic barrier caps but was not involved in any other way (Sweet et al., 2012; Devries et al., 2014; Stango et al., 2014; Kamboj et al., 2015). Two out of these seven studies acknowledged, however, that the manufacturer provided partial writing assistance for the article (Devries et al., 2014; Pavia and Mazza, 2016). For one study (11.1%), the possible conflicts of interest were not reported (Ramirez et al., 2012). The authors of one study (11.1%) stated that the study was supported by the manufacturer of the antiseptic barrier cap without declaring that the manufacturer had not been involved in study design, data collection, analysis, decision to publish or preparation of the manuscript (Cameron-Watson, 2016). The latter two studies were of low methodological quality (Ramirez et al., 2012; Cameron-Watson, 2016).

Table 2

Results of the random effects meta-analyses.

	No. of studies	Pooled IRR	95% CI	P value	Risk of publication bias				Heterogeneity	
					Egger	P value	KT	P value	I ²	95% CI
Total	7 (Ramirez et al., 2012; Sweet et al., 2012; Wright et al., 2013; Merrill et al., 2014; Stango et al., 2014; Kamboj et al., 2015; Cameron-Watson, 2016)	0.59	0.45–0.77	<0.001	–1.28	0.003	–0.33 [#]	0.239 [#]	27.1%	0–69%
Moderate/high quality	5 (Sweet et al., 2012; Wright et al., 2013; Merrill et al., 2014; Stango et al., 2014; Kamboj et al., 2015)	0.66	0.53–0.83	<0.001	–1.29	0.002	–0.80 [#]	0.017 [#]	15.1%	0–69%
Curos	3 (Ramirez et al., 2012; Sweet et al., 2012; Merrill et al., 2014)	0.48	0.24–0.95	0.04	NA	NA	NA	NA	11.5%	0–76%
SwabCap	4 (Wright et al., 2013; Stango et al., 2014; Kamboj et al., 2015; Cameron-Watson, 2016)	0.60	0.43–0.84	0.003	–1.66	0.05	–0.33 [#]	0.333 [#]	39.7%	0–79%
Hematology/oncology patients	2 (Sweet et al., 2012; Kamboj et al., 2015)	0.45	0.10–2.07	0.305	NA	NA	NA	NA	61.8%	NA

Abbreviations: IRR; incidence rate ratio, no; number, CI; confidence interval, NA; not available, too few strata included, KT; Kendall's tau, I; inconsistency.

[#] Low power because of low number of studies included.

3.3. Meta-analysis

Seven out of nine studies (77.8%) were included in the meta-analysis. The IRR of the individual studies ranged from 0.14 to 0.76 (Table 1). Three of these seven studies (42.9%) did not show a statistically significant result when comparing the antiseptic barrier cap to usual care. The pooled IRR showed that the antiseptic barrier cap was effective in reducing CLABSI (IRR = 0.59, 95% CI = 0.45–0.77, $I^2 = 27\%$, $P < 0.001$). Subgroup analysis showed that the Curo (IRR = 0.48, 95% CI = 0.24–0.95) and SwabCap (IRR = 0.60, 95% CI = 0.43–0.84) were equally effective. When excluding the studies of low methodological quality ($n = 2$), the IRR improved to 0.66 (95% CI = 0.53–0.83). Two studies were conducted in a cancer center or only included patients from oncology/hematology wards (Sweet et al., 2012; Kamboj et al., 2015). The pooled IRR showed that the barrier cap was also effective in this setting, albeit non-significant (IRR = 0.45, 95% CI = 0.10–2.07). The results of the meta-analyses are shown in Table 2; and Fig. 2 shows the forest plots.

Because of the low number of studies included, bias indicators Egger and Begg-Mazumdar (Kendall's tau) had low statistical power to detect differences. However, asymmetry of the funnel plots indicated publication bias (S3 file).

3.4. Costs and savings

Five out of nine studies (55.6%) described costs and savings (Ramirez et al., 2012; Wright et al., 2013; Merrill et al., 2014; Stango et al., 2014; Kamboj et al., 2015). Net savings ranged from \$39,050 to \$3,268,990. These figures are clearly dependent on the scale of the study and are partially calculated using cost estimates from secondary literature. Therefore we only calculated the mean device costs per avoided CLABSI, assuming no other costs are involved, such as training/implementation costs. These calculations showed that using the device is cost saving if the additional costs attributed to one CLABSI do not exceed \$1996–\$3556 (Table 3).

4. Discussion

4.1. Summary of evidence

We found evidence that the antiseptic barrier cap compared to manual disinfection is associated with a risk reduction of the incidence of CLABSI, also when excluding the two studies with possible conflicts of interest and low methodological quality. Further, both brands of barrier cap, the Curo and the SwabCap, are effective in reducing CLABSI. While use of the latter was more frequent, the Curo was associated with a lower IRR. However, confidence intervals were large and close to one as only few studies

were included in these subgroup analyses. The pooled IRR (0.45) of the two studies conducted in cancer centers or including only patients from hematology and oncology wards also indicated a reduction of the incidence of CLABSI with the use of the antiseptic barrier cap (Sweet et al., 2012; Kamboj et al., 2015). However, only two studies were included and the result was non-significant.

Overall, the median rate of compliance with the antiseptic barrier cap was 82.5%, which is high compared to the rates of compliance with manual disinfection. For many studies it was not clear how compliance was assessed, however, and almost half of the included studies did not describe compliance rates after the implementation of the antiseptic barrier cap. Still, it seems that implementation in daily practice is feasible.

Several studies have highlighted the importance of multimodal and multidisciplinary strategies for education and training of professionals or the use of non-pharmacological interventions to reduce healthcare-related infections (e.g. CLABSI) (Zingg et al., 2015; Helder et al., 2013). Most interventions programs have a strong focus on professional level, aimed at reducing individual barriers to adherence and stimulating positive attitudes. In addition, change of physical work process should be explored, to the effect that nurses and other healthcare workers are facilitated to help reduce infections.

In 2015, a research article warned that the SwabCap allowed significant amounts of alcohol to be injected (Sauron et al., 2015). The authors stated that the barrier cap must not be used for neonates without further research. The Curo and SwabCap antiseptic barrier caps differ in their designs (i.e. the flexibility of the sponge); this should be subject of further investigations.

4.2. Costs

All studies that described costs conclude that use of the device is cost-saving, i.e. the costs per avoided CLABSI outweigh the cost of using the device. However, caution is required while considering the net saving estimates. First, the net savings are reported in absolute terms and are thus dependent on the hospital/study scale. Second, the net savings are estimated from the actual costs of using the device plus secondary cost estimates for which transferability may be questioned. Third, it remains unclear whether the costs per avoided CLABSI relate to the incremental costs of CLABSI or the total costs attributed to the entire hospital admission. While the incremental costs, such as prolonged length of stay or additional tests, could be avoided, the total costs related to the entire hospital admission could not. As such, the net savings reported could be overestimated. To circumvent these limitations, we calculated at what incremental costs of a CLABSI the hospital would still achieve savings given the reported costs for the devices. For the cost studies under consideration, we found a range between \$1996 and \$3556.

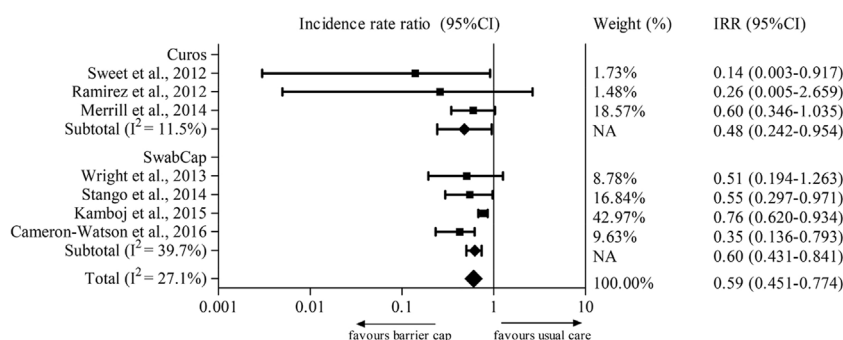


Fig. 2. Forest plot. Abbreviations: IRR = incidence rate ratio, 95% CI = 95% confidence interval.

Table 3
Results of costs-savings analysis.

Source	Annual estimated:		Costs of devices/reduction in #CLABSI
	Reduction in #CLABSI	Costs of devices	
Ramirez et al. (2012) ^a	3.0	\$10,000.00	\$3333.33
Wright et al. (2013)	21.0	\$60,233.00	\$2868.24
Stango et al. (2014)	10.8	\$21,560.00	\$1996.30
Merrill et al. (2014)	Not reported	\$192,160.00	NA
Kamboj et al. (2015)	57.0	\$202,706.56	\$3556.26

Abbreviations: NA; not applicable.

^a Reported costs of trial.

Note that these estimates are not inflation-adjusted and may be affected by hospital idiosyncrasies.

4.3. Limitations

A first limitation of this study is the heterogeneity between studies. Although all studies but one were conducted in the USA, patient populations differed (e.g. adult hematology patients, children, only ICU patients). This is why we corrected for heterogeneity by using a random effects model rather than a fixed effects model when analyzing the data. Second, funnel plots indicated that publication bias was present (S3 file). We urge researchers to publish their data even if no difference between the antiseptic barrier cap and usual care was observed or even if results showed that the barrier cap increased the risk of CLABSIs. A third limitation is the relatively low number of studies included, of which only one was a multi-center study and only one not from the USA. The results of this meta-analysis should therefore be interpreted taking into account the context of the included studies. For example the pediatric and neonatology departments are underrepresented. Fourth, for three out of nine studies (33.3%) the definition of CLABSI was unclear. The six other studies all used the CDC definition. A final limitation is that we only included quasi-experimental before-after studies, whereas the inclusion of randomized controlled trials (RCTs) would be preferable. Therefore, we could possibly have overestimated the true effect of the antiseptic barrier cap on the reduction of CLABSIs, since before-after studies are more prone to bias (Eccles et al., 2003). However, up until the completion of this systematic review no RCTs have been published.

4.4. Conclusions and implications

Our findings show that use of the antiseptic barrier cap can lower the occurrence of CLABSIs and is cost saving. That is why it could be added to central-line maintenance bundles and could improve nurses' work processes. However, there is still a need for RCTs to study the effectiveness of the antiseptic barrier cap. Further research should indicate whether the effect is also visible in other patient groups (e.g. neonates, children) and if the effect is also visible when using non-central lines. Also, use of the antiseptic barrier cap in home infusion settings (e.g. patients who use total parenteral nutrition) should be further studied.

Ethical approval

No.

Conflict of interest

Onno K. Helder PhD is a board member of the European Foundation for the Care of Newborn Infants (EFCNI). He has

obtained lecture and consultancy fees from 3M. All other authors report no conflict of interest relevant to this article.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.ijnurstu.2017.01.007>.

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