REME • Rev Min Enferm. 2022;26:e-1440
DOI: 10.35699/2316-9389.2022.38490

REVIEW

DISINFECTION OF INTRAVENOUS CATHETER HUBS AND CONNECTORS: SCOPING REVIEW

DESINFECÇÃO DE HUBS E CONECTORES DE CATETERES INTRAVENOSOS: REVISÃO DE ESCOPO

DESINFECCIÓN DE HUBS Y CONECTORES DE CATÉTERES INTRAVENOSOS: REVISIÓN DE ALCANCE

Camila Biazus Dalcin[1]
Sabrina de Souza[1]
Jane Cristina Anders[1]
Juliana Coelho Pina[1]
Andréia Cristina Feitosa do Carmo[2]
Bruna Figueiredo Manzo[3]
Patrícia Kuerten Rocha[1]

[1]Universidade Federal de Santa Catarina - UFSC, Enfermagem. Florianópolis, SC - Brazil.
[2]Universidade Federal de São Paulo - UNIFESP, Biblioteca Central. São Paulo, SP - Brazil.
[3]Universidade Federal de Minas Gerais - UFMG, Enfermagem. Belo Horizonte, MG - Brazil.

Corresponding Author: Camila Biazus Dalcin
E-mail: camilabiazus@hotmail.com

Authors' contributions:
Conceptualization: Camila B. Dalcin, Sabrina de Souza, Andréia C. F. Carmo, Patrícia K. Rocha; ***Data Collection:*** Camila B. Dalcin, Sabrina de Souza, Andréia C. F. Carmo, Patrícia K. Rocha; ***Investigation:*** Camila B. Dalcin, Sabrina de Souza, Andréia C. F. Carmo, Bruna F. Manzo, Jane C. Anders, Juliana C. Pina, Patrícia K. Rocha; ***Methodology:*** Camila B. Dalcin, Sabrina de Souza, Andréia C. F. Carmo, Bruna F. Manzo, Jane C. Anders, Juliana C. Pina, Patrícia K. Rocha; ***Project Management:*** Camila B. Dalcin; ***Resource Management:*** Camila B. Dalcin, Sabrina de Souza, Andréia C. F. Carmo, Patrícia K. Rocha; ***Supervision:*** Patrícia K. Rocha; ***Validation:*** Camila B. Dalcin, Sabrina de Souza, Andréia C. F. Carmo, Bruna F. Manzo, Jane C. Anders, Juliana C. Pina, Patrícia K. Rocha; ***Visualization:*** Camila B. Dalcin, Sabrina de Souza, Bruna F. Manzo, Jane C. Anders, Juliana C. Pina, Patrícia K. Rocha; ***Writing - Original Draft Preparation:*** Camila B. Dalcin, Sabrina de Souza, Andréia C. F. Carmo, Bruna F. Manzo, Jane C. Anders, Juliana C. Pina, Patrícia K. Rocha; ***Writing - Review and Editing:*** Camila B. Dalcin, Sabrina de Souza, Andréia C. F. Carmo, Bruna F. Manzo, Jane C. Anders, Juliana C. Pina, Patrícia K. Rocha.

Funding: *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* - CAPES - DOC-PLENO - Full Doctorate Abroad 2016, Number 88881.128573/2016-01 (Migrated - SICAPES3).

Submitted on: 06/15/2021
Approved on: 01/25/2022

Responsible Editors:
Allana dos Reis Corrêa
Luciana Regina Ferreira da Mata

ABSTRACT

Objective: to identify disinfection methods for intravenous catheter hubs and needleless connectors in hospitalized patients, as well as to verify the effectiveness of the interventions to prevent bloodstream infections associated with intravenous catheters. **Method:** a scoping review following the Joanna Briggs Institute recommendations. The search was conducted in the following electronic databases: PubMed, Embase, Cochrane Library, *Literatura Latino-Americana e do Caribe em Ciências da Saúde, Base de Dados Enfermagem and Bibliografía Nacional en Ciencias de la Salud Argentina*, as well as in studies indicated by experts. The search was conducted until September 2020. The review protocol was registered in the Open Science Framework. **Results:** a total of 27 studies were included, of which five were Guidelines and 22 were articles published in journals. There is a significant variety of disinfection methods for hubs and connectors. Chlorhexidine Gluconate, Isopropanol and Povidone-iodine were indicated for active disinfection; and Chlorhexidine Gluconate and Isopropanol, for passive disinfection. The disinfectant volume varied from 0.25 mL to 0.6 mL. Friction time in active disinfection ranged from five to 30 seconds, and contact time in passive disinfection varied from three minutes to seven days. The disinfectants' drying time was over five minutes. **Conclusion:** a variety of disinfection methods is verified, although with no consensus on the best indication. Studies that show the amount of disinfectant, pressure, friction and drying time are required. There is a need to conduct research studies with disinfection practices used in Brazil and randomized clinical trials.

Keywords: Catheter-Related Infections; Disinfection; Effectiveness; Disinfectants; Infection Control; Nursing, Practical.

RESUMO

Objetivo: *identificar métodos de desinfecção de hubs e conectores sem agulha dos cateteres intravenosos em pacientes hospitalizados e verificar a efetividade das intervenções para a prevenção de infecções de corrente sanguínea associada a cateter intravenoso.* ***Método:*** *revisão de escopo seguindo as recomendações de Joanna Briggs Institute. Busca realizada em bases de dados eletrônicas Pubmed, Embase, Cochrane Library, Literatura Latino-Americana e do Caribe em Ciências da Saúde, Base de Dados Enfermagem e Bibliografía Nacional en Ciencias de la Salud Argentina, e estudos indicados por experts. A busca foi atemporal até setembro de 2020. Protocolo registrado na Open Science Framework.* ***Resultados:*** *foram incluídos 27 estudos, sendo que cinco foram Guidelines e 22 foram artigos publicados em periódicos. Existe grande variedade de métodos de desinfecção de hubs e de conectores. Para a desinfecção ativa, foram indicados Gluconato de Clorexedina, Isopropanol e Iodopovedina; para a desinfecção passiva, Gluconato de Clorexedina e Isopropanol. A quantidade do agente desinfetante variou de 0,25 mL a 0,6 mL. O tempo de fricção na desinfecção ativa variou de cinco segundos a 30 segundos, e o tempo de contato na desinfecção passiva variou de três minutos a sete dias. O tempo de secagem de agentes desinfetantes foi superior a cinco segundos.* ***Conclusão:*** *verifica-se variedade de métodos de desinfecção; no entanto, não há consenso sobre a melhor indicação. Necessita-se de estudos que evidenciem a quantidade de desinfetante, a pressão e o tempo de fricção e o tempo de secagem. Pesquisas com práticas de desinfecção utilizadas no Brasil e ensaios clínicos randomizados são necessários.*

Palavras-chave: *Infecções Relacionadas a Cateter; Desinfecção; Efetividade; Desinfetantes; Controle de Infecções; Enfermagem Prática.*

RESUMEN

Objetivo: *identificar los métodos de desinfección de los hubs y conectores sin aguja de los catéteres intravenosos en pacientes hospitalizados, y verificar la eficacia de las intervenciones para la prevención de las infecciones del torrente sanguíneo asociadas a los catéteres intravenosos.* ***Método:*** *revisión del alcance siguiendo las recomendaciones del Instituto Joanna Briggs. Búsqueda realizada en las bases de datos electrónicas Pubmed, Embase, Biblioteca Cochrane, Literatura Latinoamericana y del Caribe en Ciencias de la Salud, Base de Datos de Enfermería y Bibliografía Nacional en Ciencias de la Salud Argentina, y estudios indicados por expertos. La búsqueda era atemporal hasta septiembre de 2020. Protocolo registrado en el Open Science Framework.* ***Resultados:*** *se incluyeron 27 estudios, cinco de los cuales eran Guidelines y 22 eran artículos publicados en revistas. Existe una gran variedad de métodos para la desinfección de hubs y conectores, siendo el gluconato de clorhexedina, el isopropanol y la yodopovedina*

How to cite this article:
Dalcin CB, Souza S, Anders JC, Pina JC, Rocha PK, Carmo ACF, Manzo BF. Disinfection of intravenous catheter hubs and connectors: scoping review. REME - Rev Min Enferm. 2022[cited ____ ___ __];26:e-1440. Available from: _____ DOI: 10.35699/2316-9389.2022.38490

los indicados para la desinfección activa, y el gluconato de clorhexedina y el isopropanol para la desinfección pasiva. La cantidad del agente desinfectante osciló entre 0,25 mL y 0,6 mL. El tiempo de fricción para la desinfección activa osciló entre cinco segundos y 30 segundos, y el tiempo de contacto para la desinfección pasiva osciló entre tres minutos y siete días. El tiempo de secado de los agentes desinfectantes fue superior a cinco segundos. ***Conclusión:*** *se comprueba la variedad de métodos de desinfección, aunque no hay consenso sobre la mejor indicación. Se necesitan estudios que evidencien la cantidad de desinfectante, la presión y el tiempo de fricción, y el tiempo de secado. Es necesario investigar las prácticas de desinfección utilizadas en Brasil y realizar ensayos clínicos aleatorios.*

Palabras clave: *Infecciones Relacionadas con Catéteres; Desinfección; Efectividad; Desinfectantes; Control de Infecciones; Enfermería Práctica.*

INTRODUCTION

Hospitalization is a predicting factor of Healthcare-Associated Infections (HAIs). Aware of this issue, the World Health Organization (WHO) emphasizes the importance of care measures focused on the prevention and control of infections, recommending a reduction of at least 30% in the HAI rates in health institutions worldwide.[1]

Among their many causes, the presence of invasive hospital devices is a factor associated with the occurrence of HAIs, especially due to contamination when handling them. Intravenous catheters stand out among these devices, as they are widely used in the hospital setting. A study conducted in public hospitals from Queensland, Australia, reported an approximate annual use of 2.75 million intravascular access devices.[2]

Given the above, high rates of infections related to these devices are reported in the literature. These infections, called Central Line-Associated Bloodstream Infections (CLABSI), present rates that vary from 0.38 to 4.58 episodes/1,000 days.[3] Complementary data reveals that, in a total of 1,236 cases of bacteremia, 414 were classified as CLABSI, of which 124 were related to the use of Peripheral Intravenous Catheters (PIVCs) and 110, to Central Vascular Access Catheters (CVADs).[4]

Such being the case, there is an urgent need for measures that contribute to the prevention of CLABSI, such as proper management of intravenous catheters, with emphasis on disinfection of their connectors.[5,6] If performed with an effective method, this disinfection can reduce CLABSI rates by up to 69%.[7] Corroborating the previous argument, a study conducted in the USA showed that disinfection of connectors was responsible for a 34% reduction in the infection rates and saved approximately US$ 3.2 million.[8]

Consequently, to understand the disinfection methods, it is important to discuss how they are implemented in the clinical practice; thus having active or passive disinfection. Active disinfection consists in "scrub the hub", that is, the mechanical friction performed by the health professional on the connector, such as through the use of wipes rubbing the connector from five to 60 seconds.[9-12] Passive disinfection is performed through the introduction of caps with disinfectants in the connector, which remain in contact with the connectors for a period of two minutes to seven days (according to the manufacturers' recommendations), being considered technological devices.[7,13,14]

In the Brazilian context, the recommendation regarding disinfection of connectors by the National Health Surveillance Agency (*Agência Nacional de Vigilância Sanitária*, ANVISA) is to use alcohol-based disinfectant solutions for a period of five to 15 seconds. However, it does not list the specific type and amount of the substance.[13] The recommendations of the international Guidelines vary in relation to the indication of the disinfectant agent, with the use of Isopropanol (IPA) 70%, Chlorhexidine Gluconate (CHG) from > 0.5% to 2% with 70% IPA and Povidone-iodine (PVPI) In relation to the time required for friction between the connector and the disinfecting agent, a number of studies also show variations from five to 60 seconds depending on the reference used to perform the active disinfection procedure. Regarding the contact time for passive disinfection, the Guidelines recommend following the manufacturer's instructions. Drying time is considered essential; however, the guidelines are unclear as to the time required to dry each disinfectant agent.[5,10-13,15]

Some studies have been conducted with the objective of comparing different disinfection methods. A study that analyzed the effectiveness of disinfection of needleless connectors (NDC) using CHG 2% wipes with 70% IPA, 70% IPA wipes or protective caps impregnated with 70% IPA to prevent CLABSI resulted in the indication of the use of CHG 2% wipes with 70% IPA and disinfection caps with 70% IPA.[14] Another study revealed that there was no consensus on the best practice regarding disinfection and there was lack of findings on the correct friction time in the disinfection process.[12]

A number of studies indicate the need for a scoping review to verify and update the main findings based on the disinfection methods.[12,14] Therefore, this scoping review aimed at identifying the disinfection methods for intravenous catheter hubs and needleless connectors in hospitalized patients, as well as to verify the effectiveness of the interventions to prevent CLABSI.

METHODOLOGY

A scoping review was carried out to identify knowledge gaps and describe the existing evidence in order to improve the practice.[16] The review followed the quality parameters set forth in the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).[17] The protocol was attached to the Open Science Framework (OSF) online platform on September 25th, 2020, with registration number d3be2, available at https://osf.io/d3be2/.

The following guiding question was defined to search and select the studies: Which are the disinfection methods for intravenous catheter hubs and needleless connectors in hospitalized patients? No time clipping was defined for the study, as the intention was to include all the publications in the knowledge area. Thus, all the studies published until September 2020 were included.

The data search strategy (Table 1) included the bibliographic survey conducted in the following databases: National Center for Biotechnology Information (PubMed-NCBI), Embase, Cochrane Library, *Literatura Latino-Americana e do Caribe em Ciências da Saúde* (LILACS), *Base de Dados Enfermagem* (BDENF) and *Bibliografía Nacional en Ciencias de la Salud Argentina* (BINACIS), in the Portuguese, English and Spanish languages. The search for data was also performed in sources external to the databases, through the indication of literature material by experts in the patient safety and intravenous therapy areas.

The sample included in the study was for convenience, with inclusion of all the studies found in the search strategy that met the inclusion criteria. The inclusion criteria focused on the selection of studies with hospitalized patients using NDC in a central or peripheral intravenous catheter, regardless of age and hospitalization time (population/participants), with the intervention to be analyzed based on the disinfection of the intravenous catheter hubs and connectors. The outcomes included in the study were the following: type of disinfection (active or passive), type of disinfecting agent, friction time (active), contact time (passive), amount of disinfectant, drying time, and effectiveness of the disinfection method. Studies with different designs that had data from primary research sources were included, as well as Guidelines indicated by experts.

Studies focused on the prevention of infection associated with insertion and removal of the intravenous catheter were excluded from the sample, as well as those with secondary data sources (such as reviews), studies with experts' opinions (such as a letters to the editor), and studies with data from more than one intervention to reduce infection rates other than hub or connector disinfection. If the study had more than one intervention but presented data that showed the effectiveness of the interventions separately, it was included in this review, provided that one of the interventions analyzed was disinfection of intravenous catheter hubs or connectors. Studies that did not present their full texts in the databases were excluded. Congress materials such as summaries published in conferences were also excluded.

The process to select the studies was conducted in two stages. The first consisted of two reviewers independently reading the titles and abstracts using the Rayyan QCRI online tool.[18] For the situations in which there was divergence between both reviewers, a third reviewer (judge) decided on inclusion or exclusion through a consensus meeting.

Table 1 - Search strategy in the databases

Database	Search strategy
PubMed	(decontamination OR disinfectants OR iodine OR Anti-Infective Agents, Local OR "chlorhexidine"[MeSH Terms] OR "chlorhexidine"[All Fields] OR "ethanol"[MeSH Terms] OR "ethanol"[All Fields] OR "alcohol"[All Fields] OR "alcohols"[MeSH Terms] OR "alcohols"[All Fields] OR disinfection) AND ("central venous catheters"[MeSH Terms] OR ("central venous catheters"[all fields] OR needleless connector[All Fields] OR "catheter-related infections"[MeSH Terms] OR "catheter-related infections"[All Fields] OR "catheter-related infections"[All Fields] OR ("catheter"[All Fields] AND "related"[All Fields] AND "infections"[All Fields]) OR "catheter related infections"[All Fields]) AND (safety procedures [tw] OR infection control)
Embase	(decontamination OR iodine OR alcohol OR 'antiinfective agent' OR chlorhexidine) AND ('catheters and tubes' OR catheterization OR 'intravenous catheter' OR 'vein catheterization') AND ('safety procedure' OR 'hygiene' OR 'infection control')
Cochrane Library	"decontamination" OR disinfectants OR iodine OR "anti-infective agents" OR chlorhexidine OR ethanol AND "needleless connector" OR "catheter-related infections" AND "safety procedures" OR "infection control"
LILACS/BDENF and BINACIS	(desinfecção OR desinfection OR decontamination OR iodine OR chlorhexidine OR alcohol) AND (cateter* OR catheter*) AND ("infection control" OR hygiene OR higiene OR "controle de infecção")

Source: The authors (2020).

Subsequently, in the second stage, the main reviewer separated the pre-selected articles and sent them in full to the other reviewers. Again, both reviewers made a second selection using the inclusion and exclusion criteria. For situations in which both reviewers did not reach consensus, the third reviewer (judge) was called upon again to decide on inclusion or exclusion through a consensus meeting. The *EndNote*® software, version X9, was used to manage the studies found in the databases.

To categorize the results, the studies were organized according to the eligible criteria. Categorization was performed independently by two reviewers. A number of meetings about the categorization stage were held in order to validate the data extracted. During data extraction, it was sought to maintain the terminology used in the studies, in order to preserve reliable data for analysis.

Data analysis was performed by describing the different disinfection methods available in the literature, using tables and charts to facilitate visualization of the results, following the Joanna Briggs Institute recommendations (Methodology for JBI Scoping Reviews).[16] The results were described and summarized according to their relationship with the research question of this study.

RESULTS

After removal of the duplicates, a total of 901 studies were identified in the databases and in the external information sources. Based on the analysis of the titles and abstracts, 825 studies were excluded. Thus, 76 were selected for full-text reading and eligibility analysis, with exclusion of 49. The remaining 27 studies were included in the research. The identification, selection, eligibility an inclusion process corresponding to the studies is illustrated in Figure 1 by means of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.[19]

In relation to the publication date of the studies, the year with the highest number of publications was 2017, accounting for 14.8% of the total. It is noticed that 55.5% of the eligible studies were published in the last five years, that is, from 2015 to September 2020. Regarding the countries where the studies were published, the USA is locus to most of the papers, accounting for 51.8% of the studies published. It is worth noting that only one study comes from Brazil, retrieved from external sources and included by the authors. United Kingdom (18.5%) and Australia (14.8%) are the second and third countries with the highest number of publications on the theme of disinfection of hubs and connectors.

In relation to the journals or platforms where the studies were published, the *American Journal of Infection Control* was the one with the highest number of studies published in the area, accounting for 33.3% of the publications. 29.6% predominance of *in vitro* studies was observed, with the Guidelines totaling 18.5% of the sample. Randomized Clinical Trials (RCTs) represented 7.4% of the sample, consisting of only two studies.[20,21] Both RCTs were published in 2020 and in Australian journals, one of which was considered a pilot RCT.[20] The characteristics of the research studies included in the scoping review are shown in Table 2.

The purpose of Table 3 is to present results such as first author, year of publication, objective, study design, disinfection method studied, main results and recommendations.

Table 4 summarizes the disinfection methods recommended in the studies. There was a search for diverse information on the type of disinfection, disinfectant agent, amount of disinfectant, pressure exerted on friction, friction time (active), contact time (passive) and drying time. Considering the types of disinfection, it is evidenced that 11 studies recommended active disinfection alone o passive disinfection alone (40.7%). Both disinfection methods were recommended in four studies (14.8%). A single study listed the use of an Ultraviolet Light-Emitting Diode (UV LED) for disinfection although it was not possible to classify it as passive or active disinfection according to the concepts established.

DISCUSSION

This scoping review allowed identifying the disinfection methods for intravenous catheter hubs and needleless connectors in hospitalized patients. It is noticed that the disinfection recommendations are varied and that the different disinfection methods are a challenge for the clinical practice, and this diversity of recommendations can generate questions about the best method to follow.[39]

Of the methodological designs carried out with hospitalized patients, most included the adult population, examples being E4, E8, E9, E15, E17, E20, E21 and E22.[7,8,20,21,27,36-38] The disinfection method was understood as a combination of components, namely: type

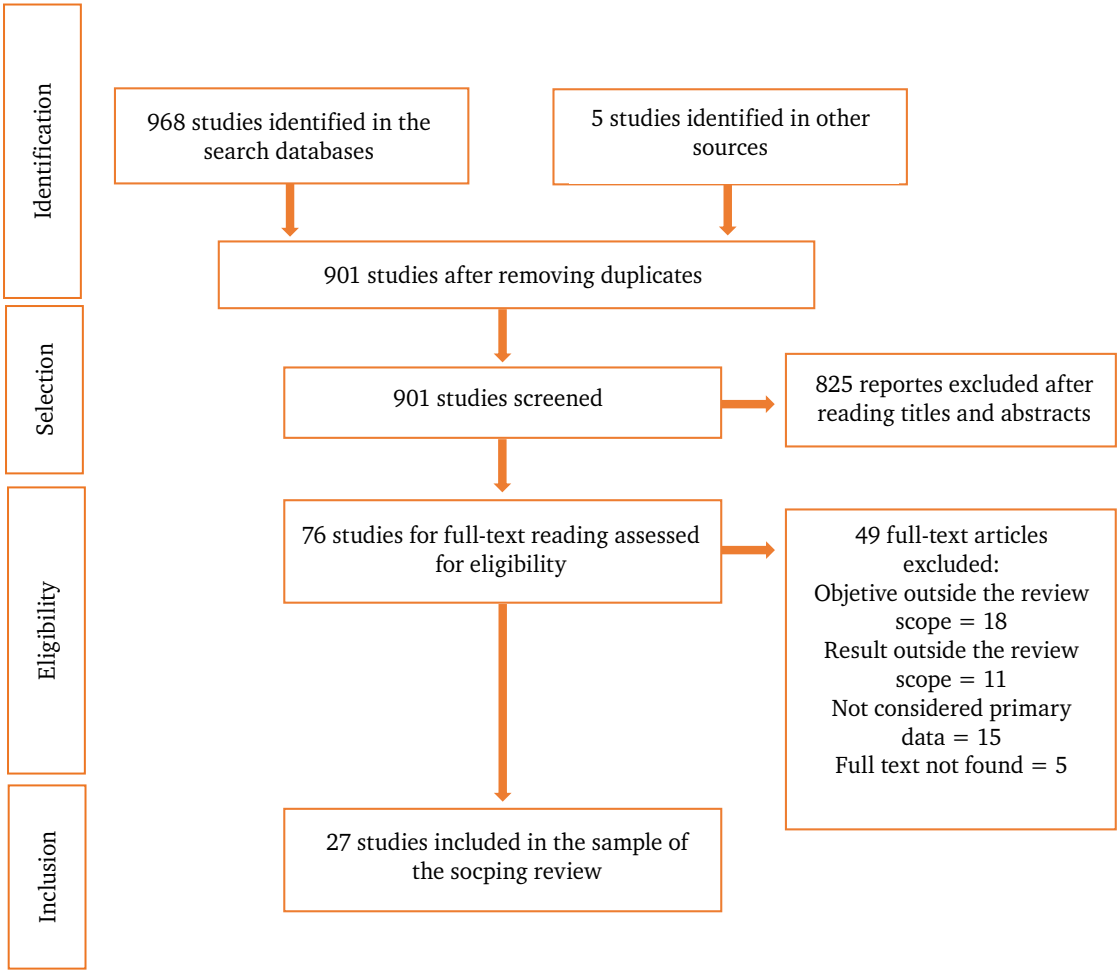

Figure 1 - Flowchart corresponding to the stages to select the articles
Source: Model adapted from the PRISMA Flowchart.[19]

of disinfection (active or passive), disinfecting agent, amount of disinfectant, friction pressure, friction time or contact time and drying time.

In relation to the type of disinfection, 11 studies only recommended active disinfection and another 11, only passive disinfection. Four studies (E15,[20] E25,[10] E26[15] and E27[13]) recommended both types, and one study recommended the use of UV LED.[26]. As for active disinfection, it is noticed that all the studies that had this analysis were based on the use of wipes/swab/pads, namely: E1, E2, E5, E6, E10, E15, E16, E17, E18, E19, E23, E24, E25, E26 and E27.[5,9-11,13,15,20,22,24,25,28, 33-35] These devices already contain the disinfectant and are sold in individual sachets. This set of international studies do not reflect the clinical practice of disinfecting hub connectors and catheters in some national hospitals since, in Brazil, disinfection is also performed with the introduction of a disinfectant agent in gauze or cotton by the health professional.

As for passive disinfection, studies E3, E4, E8, E9, E11, E12, E13, E14, E15, E20, E21, E22 E25, E26 and E27 used disinfection caps.[7,8,10,13,15,20,23,27,29-32,36-38] E3 used a disinfection cap with CHG 2% with 70% IPA[23] and revealed that the cap is effective, although it does not replace the use of alcohol wipes. On the other hand, in the search for innovations in the area of connector disinfection, study E2 presented the use of 2.5% CHG Spray[22] and E7 indicated the use of a 285 nm Ultraviolet Light-Emitting Diode (UV LED) at a distance of 0.5 cm to 1.5 cm.[26] It is known that the use of technologies is a

Table 2 - Characteristics of the research studies included in the review (N=27)

Characteristics	n	%
Year		
1997	1	3.7
2006	1	3.7
2008	1	3.7
2009	2	7.4
2011	1	3.7
2012	1	3.7
2013	2	7.4
2014	3	11.1
2015	3	11.1
2016	3	11.1
2017	4	14.8
2018	2	7.4
2019	1	3.7
2020	2	7.4
Country where the study was conducted		
Australia	4	14.8
Brazil	1	3.7
USA	14	51.8
Japan	1	3.7
United Kingdom	5	18.5
Sweden	1	3.7
Turkey	1	3.7
Type of study		
Cohort	1	3.7
Randomized Clinical Trial	2	7.4
Guideline	5	18.5
In vitro	8	29.6
Observational	2	7.4
Prospective	3	11.1
Quasi-experimental	6	22.2

Source: The authors (2021).

challenge due to the costs for their implementation in the health services, as well as to the need to carry out tests with these devices. Thus, effectiveness-efficacy (costs--benefits) studies are important for management of the health services.[7]

All 27 studies indicated at least one type of disinfection agent in their results. In other words, all the studies showed the effectiveness of one or more disinfection agents. The disinfectants indicated for active disinfection were the following: 70% IPA (seven studies), CHG 2% with 70% IPA (six studies), PVPI (four studies), CHG>0.5% with 70% IPA (two studies), CHG 5% (one study), CHG 3.15% with 70% IPA (one study), 2.5% CHG Spray (one study), 70% IPA with 2.5% CHG Spray (one study), PVPI 10% (one study), Alcohol (one study) and Alcohol-based disinfectant solution (one study). For passive disinfection, the studies recommended disinfecting agents CHG 2% with 70% IPA (three studies) and 70% IPA (nine studies). It is to be emphasized that some studies recommend more than one disinfection agent. It is believed that the large number of studies that used IPA, CHG with IPA and PVPI is due to their recommendation by international and national guidelines.[5,10,11,13,15]

Regarding the amount of disinfectant used and the friction pressure, most of the studies did not offer these data, and study E15 presented an amount of 0.6 mL of 70% IPA for active disinfection.[20] Studies E11 and E12 reported the use of 0.25 mL of CHG 2% with 70% IPA for passive disinfection.[29,30]

The friction time range in the studies was from five to 30 seconds for active disinfection. The variations in the contact time corresponding to the disinfection caps (passive disinfection) ranged from three minutes to seven days. The five-second friction time is advocated by some studies for reducing the number of microorganisms in hubs and connectors.[10,13,20] However, other studies show that only friction times of at least 15 seconds are effective for reducing microbial load and/or reducing BSI rates.[9,11,15,24,25,28,34] There is variation in the diverse evidence in relation to the recommendations for the disinfectant's friction time.

More investments are required in research studies aimed at the effect of friction itself, in order to verify the importance of this component in the disinfection process. It is important to evaluate the use of pressure, as well as the pressure exerted on the hub or connector during the friction used in active disinfection, and this aspect should be verified in future research studies. Only study E16[33] verified the pressure necessary for disinfection, showing that a force of 1 kg was sufficient for a time of two frictions. This study did not specify the time involved in two frictions.

Another component of the disinfection method is the drying time. There is a knowledge gap regarding the drying time of the disinfectant agents on the connectors. Only eight studies cited the need for drying as a disinfection component, and the indications varied from allowing to dry without mentioning the time,[10,11,15,20,24] or using a

Table 3 - Presentation of the studies

	Author, Year	Objective	Study design	Disinfection method	Main results/ Recommendations
E1	Bjorkman *et al.* (2015)[9]	To investigate if the disinfection of intravenous catheter hubs with alcohol wipes for 15 seconds can reduce the incidence of sepsis in a Neonatal ICU	Intervention study	CHG 5% Wipe for 15 seconds before connector access	Zero sepsis during the intervention (the risk was reduced by 1.5%). Introducing a CHG 5% Wipe for 15 seconds was effective. The evidence was considered weak by the author, an RCT is necessary
E2	Brown *et al.* (1997)[22]	To evaluate the use of Connecta Clava to reduce infection in NDC	*In vitro*	(a) 70% IPA Wipe; (b) CHG 2.5% Spray; (c) CHG 2.5% Spray + 70% IPA Wipe	There was no significant difference between disinfection with a 70% IPA wipe followed by a CHG spray or a 70% IPA wipe alone. Contamination was minimal when both methods were used together
E3	Buchman *et al.* (2009)[23]	To describe a new protective cap, the AB Cap, to reduce the risk of contamination in an *in vitro* model	*In vitro*	AB Caps (CHG 2% with 70% IPA)	AB Cap was been evaluated as a complete replacement for proper catheter cleaning techniques and other prevention strategies
E4	Cameron-Watson (2016)[7]	Effect of compliance and incidence of vascular access-related bacteremia following the introduction of a protective passive disinfection cap (Curos®)	A quasi-experimental study of the before-and-after type	Curos® (70% IPA disinfection cap)	Using Curos® reduced the CLABSI rate by 69%. There was an increase in the professionals' adherence and compliance to the new device by 53% and a reduction in hospital costs
E5	Devrim *et al.* (2019)[24]	To identify colonization of the connectors on the outer surface of CVADs and to measure the efficiency of 15 seconds of disinfection with 70% IPA	Prospective	15 seconds of disinfection with 70% IPA wipes	The results showed that the use of 70% IPA wipes for 15 seconds was effective in eliminating surface colonization
E6	Flynn *et al.* (2017)[25]	To investigate the comparative efficacy of three NDC decontamination methods and three different application times on different types of connectors	*In vitro*	(a) 70% IPA wipe; (b) 70% IPA disinfection cap; (c) CHG 2% wipe with 70% IPA	The CHG 2% wipe with 70% IPA was more effective than the 70% IPA wipe. When comparing the disinfection caps with the CHG 2% wipe with 70% IPA, the wipe had better performance. The ideal disinfection method would be: rubbing for 30 seconds with CHG 2% wipes with 70% IPA
E7	Hutchens *et al.* (2015)[26]	To evaluate the hypothesis that UV LED is sufficient to eliminate contamination in the connectors and contamination of the flow	*In vitro*	UV LED that emits a peak wavelength of 285 nm	The use of 285 nm UV LED is a viable source of disinfection for connectors at a distance of 0.5 to 1.5 cm
E8	Kamboj *et al.* (2015)[8]	To examine the impact of the routine use of passive disinfection caps on hemato-oncology patient catheter hubs	Prospective	70% IPA disinfection cap	Implementation of the cap reduced CLABSI rates by 34%. There was a 51%-63% reduction in the positive blood cultures
E9	Martino *et al.* (2017)[27]	To introduce a commercial alcohol-impregnated connector protective device for CVADs to reduce CLABSI in a Burns unit	Cohort	Use of Curos Cap 70% IPA disinfection cap	Reduction in CLABSI rates from 7.30 per 1,000 days of use of CVADs to the mean of 3.04 per 1,000 days of CVADs

Continued...

...Continuation

Table 3 - Presentation of the studies

	Author, Year	Objective	Study design	Disinfection method	Main results/ Recommendations
E10	Mazher *et al.* (2013)[28]	To evaluate the effect of three antiseptics and two disinfection techniques on microorganisms in NDC	*In vitro*	Antiseptics: (a) CHG 3.15% pad with 70% IPA, (b) 70% IPA pad; (c) PVPI 10% pad. Procedures: (a) friction on the septum and external threaded surfaces; (b) only the surface of the septum	It was concluded that PVPI 10% wipes and CHG 3.15% wipes with 70% IPA were more effective than wipes with only 70% IPA. In relation to the technique, it was noticed that friction was more important than cleaning, although this data was not significant
E11	Menyhay *et al.* (2006)[29]	To verify the effectiveness of a conventional pre-access alcohol disinfection method with a new connector protector on luer-activated valve connectors	*In vitro*	0.25 ml CHG 2% disinfection cap with 70% IPA	The 70% IPA wipe did not prevent microbial ingress (442-25,000 CFU). The sanitizer cap offered a high level of protection against microbial ingress
E12	Menyhay *et al.* (2008)[30]	To compare the effectiveness of standardized disinfection on luer-activated valve connectors with 70% IPA and the effectiveness of a new connector protector	*In vitro*	0.25 ml CHG 2% disinfection cap with 70% IPA	The disinfection cap is highly effective in preventing entry of microorganisms
E13	Merrill *et al.* (2014)[31]	To analyze the effect of an NDC with CLABSI rates and types, CLABSI costs using a central line bundle.	Quasi-experimental	Luer-lock protective cap with 70% IPA (Curos Disinfecting Port Protector)	The traditional disinfection methods should be substituted by new technologies, with a 40% reduction in the CLABSI rates
E14	Pavia *et al.* (2016)[32]	To verify the effect of innovative practices and technologies of CVAD bundles for the reduction of bloodstream infections in the pediatric population	Prospective and observational	70% IPA disinfection cap (SwabCap)	54.7% reduction in CLABSI rates after implementation
E15	Rickard *et al.* (2020)[20]	To generate viable data and pilots comparing wipes with 70% IPA, CHG 2% wipes with 70% IPA and connector protectors with 70% IPA	Randomized Clinical Trial (pilot)	(a) 70% IPA wipes, 0.6 ml; (b) 2% CHG wipes with 70% IPA, 0.6 mL; (c) 70% IPA disinfection cap (SwabCap)	Occurrence of CLABSI was 1/61 (2%) with 70% IPA wipe, 0/58 (0%) with CHG 2% wipe with 70% IPA, and 1/59 (2%) with 70% IPA disinfection caps. CLABSI was low in both groups using 70% IPA and was zero if it was the CHG 2% with 70% IPA combination
E16	Satou *et al.* (2018)[33]	To investigate the proper friction-scrub technique for NDC in order to minimize the contamination risk	*In vitro*	Friction direction: (a) 180 degrees once and in one direction; (b) straight line once and in one direction. Number of times: (a) rub once; (b) rub twice. Force applied: (a) 0.5 kg; (b) 1 kg; (c) 2 kg; (d) 3 kg	Higher bacterial clearance was achieved by rubbing the access port in a straight line with an alcohol wipe, applying a force that was nearly equal to an arterial compression hemostasis to the access port. It is recommended to repeat the procedure

Continued...

...Continuation

Table 3 - Presentation of the studies

	Author, Year	Objective	Study design	Disinfection method	Main results/ Recommendations
E17	Slater *et al.* (2020)[21]	To establish the most effective disinfection method, using 70% IPA or CHG 2% with 70% IPA, with decontamination times of 5, 10 and 15 seconds in an NDC in a Peripherally-Inserted Central Catheter (PICC) in the clinical setting	Randomized clinical trial	Type of disinfectant: (a)70% IPA wipe; (b) CHG wipe with 70% IPA. Friction times: (a) 5 s; (b) 10 s; (c) 15 s	There was no difference between 70% IPA wipe and CHG 2% with 70% IPA wipe for decontamination. There was no difference between the disinfection times. The study recommended using a 70% IPA wipe for 5 seconds or more
E18	Slater *et al.* (2018)[34]	To verify how long it takes for the NDC to dry after 15 seconds of "scrub the hub" disinfection in a hospital setting	Experimental, with comparison between the groups	(a) 70% IPA wipe; (b) CHG wipe with 70% IPA; (c) PVPI	NDC manufacturers should do tests with the drying time. The drying times varied between 5 seconds (70% IPA), 20 seconds (70% IPA with CHG 2%) and 6 minutes or more for PVPI
E19	Soothill *et al.* (2009)[35]	To verify CLABSI rates using 70% IPA with CHG 2% in catheter connectors	Observational, of the before-and-after type	CHG 2% wipe with 70% IPA Clinell wipes	Using a CHG 2% wipe with 70% IPA reduced CLABSI rates from 12 per 1,000 to 3 per 1,000 days of central catheter use
E20	Stango *et al.* (2014)[36]	To test whether the use of a connector protector with antiseptic products can impact on the CLABSI rates in a hospital setting, with an Oncology unit	Intervention study of the before-and-after type	SwabCap disinfection cap (70% IPA)	Using the disinfection cap reduced the CLABSI rates by 51%
E21	Sweet *et al.* (2012)[37]	To assess the effect of optimizing hub disinfection by using a quality improvement intervention to measure the CLABSI rates and positive blood cultures in adult cancer patients	Observational, of the before-and-after type	70% IPA disinfection cap (Curos)	Use of a disinfection cap and application of neutral pressure to the NDC significantly reduce CLABSI and positive blood culture rates
E22	Wright *et al.* (2013)[38]	To evaluate the *in vivo* performance of a connector protector for luer-access valve disinfection impregnated with a sponge saturated in 70% alcohol affixed to catheter hubs	Quasi-experimental	Disinfection cap (SwabCap), sponge and 70% IPA	Lumen contamination was reduced from 12.4% to 5.5%, and CLABSI reduction was from 16 CLABSI in 11,154 days to 13 CLABSI in 18,962 days of catheter use
E23	Loveday *et al.* (2014)[11]	To describe clinically effective measures to prevent infections in hospitals and other acute health care settings	Epic3 (Guideline)	–	CHG 2% with 70% IPA or PVPI in alcohol for patients allergic to CHG, with a friction time higher than or equal to 15 seconds. Cleaning and drying of the NDC is recommended
E24	O'Grady *et al.* (2011)[5]	To provide recommendations for the prevention of infections related to intravascular catheters	CDC (HICPAC) (Guideline)	–	Appropriate disinfectant (CHG>0.5% with 70% IPA, PVPI, or 70% IPA). Friction time not specified

Continued...

...Continuation

Table 3 - Presentation of the studies

	Author, Year	Objective	Study design	Disinfection method	Main results/ Recommendations
E25	Gorski *et al.* (2017)[10]	To offer a guide with standard practices for infusion therapy	INS (Guideline)	–	70% IPA, PVPI, or CHG>0.5% with 70% IPA. The recommended friction time is 5-15 seconds. Friction must be mechanical and vigorous, and should allow the disinfectant to dry. Passive disinfection caps can be used depending on the manufacturer
E26	RCN (2016)[15]	To support the care provided to adult patients undergoing infusion therapies	Royal College of Nursing (Guideline)	–	Antibacterial solution such as CHG 2% with 70% IPA, for a period of 15 seconds or more. The disinfectant should be allowed to dry. Passive disinfection caps can be used according to the local policy
E27	Anvisa (2017)[13]	To contribute to reducing the incidence of HAIs in health services, through availability of the main preventive measures and practices suitable to the Brazilian reality	Review of studies and regulating agencies (Guideline)	–	Alcohol-based disinfectant solution with application of movements that generate mechanical friction for 5 to 15 seconds. Disinfection caps can be used

Source: The authors (2021).

drying time of five to 30 seconds.[21,25,34] Only PVPI showed a drying time of more than six minutes,[34] which justifies its limited use for the disinfection of hubs and connectors in the clinical practice, as it makes the process time-consuming for health professionals.

As seen in previous reviews,[12,14] scarcity of RCTs in the area is noticed, with only two RCTs included in the study. Study E17 had a total of 258 patients[21] and study E15 was considered a pilot RCT with 178 participants.[20] It is noteworthy that these articles were published in 2020. RCTs are "gold standard" studies in the clinical practice, as they serve as a reference for the health professionals' decision-making.[40]

In order to discuss about best practices, the results of the RCTs were taken into account. Pilot RCT study E15 conducted with adult patients showed low occurrence of CLABSI in two groups using 70% IPA and zero occurrence of CLABSI when using CHG 2% with 70% IPA.[20] RCT study E17 revealed that there was no difference between 70% IPA wipes and CHG 2% wipes with 70% IPA for connector decontamination in the clinical environment, and there was also no difference between the disinfection times tested: five, 10 and 15 seconds.[21] Therefore, due to cost, compliance and low allergy risk, the study recommends using a 70% IPA wipe for at least five seconds.[21] It should be noted that this data must be interpreted in its context, as a drying time of 30 seconds was allowed, in which all disinfection components must be considered for its recommendation.

The effectiveness of the disinfection methods for the prevention of CLABSI can also be verified through a reduction in the sepsis rates,[9] a reduction in the bacterial load of connectors;[21,22,24-26,28-30,33] and a 34% to 69% reduction in the risk for CLABSI.[7,8,20,23,27,31,32,35-38] Therefore, studies that used risk reduction for CLABSI were focused on CLABSI. There is a clear need for research studies with reduction of the infection rates by means of effective disinfection on PIVC hubs and connectors. Of the total of 27 studies, a single research (E17)[21] was conducted on PIVC connectors, although the results were associated with effectiveness in connector decontamination and not in reducing CLABSI rates.

We highlight that the level of evidence of most of the studies included in the sample is not strong enough to drive changes in the clinical practice, as this review only included two RCTs. It is worth noting that another two studies from the sample (E11 and E12) presented very similar data.[29,30]

The study limitation was the non-identification of cross references that might be included in the sample.

Table 4 - Disinfection methods recommended in the studies

Recommendation	Type of disinfection	Disinfectant	Amount/ Pressure	(Active) friction or (passive) contact time	Drying time
E1[9]	Active	CHG 5%	-	15 s (F)	-
E2[22]	Active	70% IPA; 70% IPA + CHG 2.5% Spray; CHG 2.5% Spray	-	5 frictions (F); Not mentioned (Spray)	- Not mentioned (after F) - 2 minutes (Spray)
E3[23]	Passive	CHG 2% + 70% IPA	-	From 12 hours to 7 days (contact)	-
E4[7]	Passive	70% IPA	-	From 3 min to 7 days (contact)	-
E5[24]	Active	70% IPA	-	15 s (F)	Allow to dry
E6[25]	Active	CHG 2% + 70% IPA	-	30 s (F)	30 s
E7[26]	UV LED	UV LED (0.5 cm-1.5 cm distance)	285 nm	60 s	-
E8[8]	Passive	70% IPA	-	Up to 7 days (C)	-
E9[27]	Passive	70% IPA	-	From 3 min to 7 days (C)	-
E10[28]	Active	CHG 3.15% + 70% IPA; PVPI 10%	-	15 s (F)	-
E11[29]	Passive	CHG 2% + 70% IPA	0.25 mL	10 min (C)	-
E12[30]	Passive	CHG 2% + 70% IPA	0.25 mL	10 min (C)	-
E13[31]	Passive	70% IPA	-	From 3 min to 7 days (C)	-
E14[32]	Passive	70% IPA	-	-	-
E15[20]	Active and Passive	CHG 2% + 70% IPA (A); 70% IPA (A); 70% IPA (P)	0.6 mL (A)	5-15 s (F); 5 min (C)	Allow to dry (A)
E16[33]	Active	Alcohol	Force: 1 kg	2 frictions	-
E17[21]	Active	70% IPA	-	5 s (F)	30 s
E18[34]	Active	CHG 2% + 70% IPA; 70% IPA; PVPI	-	15 s (F)	5 s (IPA); 20 s (CHG + IPA); More than 6 min (PVPI)
E19[35]	Active	CHG 2% + 70% IPA	-	-	-
E20[36]	Passive	70% IPA	-	-	-
E21[37]	Passive	70% IPA	-	-	-
E22[38]	Passive	70% IPA	-	-	-
E23[11]	Active	CHG 2% + 70% IPA; PVPI	-	≥ 15 s (F)	Allow to dry
E24[5]	Active	CHG>0.5% + 70% IPA; 70% IPA; PVPI	-	-	-
E25[10]	Active and Passive	CHG>0.5% + 70% IPA (A); 70% IPA (A); PVPI (A); According to Manufacturer (P)	-	From 5 s to 15 s (F); According to Manufacturer (C)	Allow to dry
E26[15]	Active and Passive	Antibacterial solution such as 2% CHG + 70% IPA (A); According to Manufacturer (P)	-	≥ 15 s (F)	Allow to dry
E27[13]	Active and Passive	Alcohol-based disinfectant solution; According to Manufacturer (P)	-	From 5 s to 15 s (F); According to Manufacturer (C)	-

Source: The authors (2021). Key: (A): Active, CHG: Chlorhexidine Gluconate, (C): Contact, IPA: Isopropanol, (F): Friction, min: minutes, (P): Passive, PVPI: Povidone-iodine, s: seconds, (-): not mentioned.

FINAL CONSIDERATIONS

This study enabled the investigation of different disinfection methods for intravenous catheter hubs and needleless connectors recommended in the literature for hospitalized patients. The study sample included 27 studies available in online databases or accessed due to their nature of being guidelines for the clinical practice, such as Guidelines for international and national use.

The scoping review allowed identifying disinfection methods in primary outcome research studies, with predominance of the use of wipes (active disinfection) and disinfection caps (passive disinfection). However, there was lack of data reflecting the Brazilian hospital reality, where gauze and cotton are generally used as vehicles for the mechanical friction of disinfecting agents in intravenous catheter connectors.

The disinfectants indicated for active disinfection were the following: CHG 5%, CHG>0.5%-3.15% with 79% IPA, 2.5% CHG Spray, 70% IPA and PVPI up to 10%. For passive disinfection, the studies recommended CHG 2% with 70% IPA and 70% IPA. The use of alcohol-based solutions and UV LED was also indicated.

The disinfection components must be considered and analyzed in the context of the intervention. Therefore, not only the disinfecting agent should be considered, but also the recommended friction time in active disinfection, which varied from five to 30 seconds; and the contact time in passive disinfection, which varied from three minutes to seven days. Drying time of the disinfecting agents varied from five seconds to more than six minutes.

Effectiveness of the disinfection methods recommended by the studies and how they influence the reduction of microbial load, sepsis rates and CLABSI rates in a hospital environment became clear, and the studies were mostly carried out with adult populations.

More studies are required to outline the best disinfection practices, mainly for PIVCs, due to the lack of studies that assess the reduction of infection rates associated with this intravascular device. It is emphasized that there is scarcity of RCT methodological designs that may be used to evidence the best disinfection practices.

REFERENCES

1. World Health Organization. Infection prevention and control: Genova: WHO; 2020[cited 2020 Sept 28]. Available from: https://www.who.int/infection-prevention/en/

2. Tuffaha HW, Marsh N, Byrnes J, Gavin N, Webster J, Cooke M, *et al*. Cost of vascular access devices in public hospitals in Queensland. Aust Health Rev. 2019[cited 2021 Mar 19];43(5):511-5. Available from: https://pubmed.ncbi.nlm.nih.gov/30176985/

3. Dreesen M, Foulon V, Spriet I, Goossens GA, Hiele M, De Pourcq L, *et al*. Epidemiology of catheter-related infections in adult patients receiving home parenteral nutrition: a systematic review. Clin Nutr. 2013[cited 2021 May 15];32(1):16-26. Available from: https://pubmed.ncbi.nlm.nih.gov/22959630/

4. Tatsuno K, Ikeda M, Wakabayashi Y, Yanagimoto S, Okugawa S, Moriya K. Clinical Features of Bloodstream Infections Associated with Peripheral Versus Central Venous Catheters. Infect Dis Ther. 2019[cited 2020 Dec 19];8(3):343-52. Available from: https://pubmed.ncbi.nlm.nih.gov/31368046/

5. O'Grady NP, Alexander M, Burns LA, Dellinger EP, Garland J, Heard SO, *et al*. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis. 2011[cited 2020 Dec 19];52(9):e162-93. Available from: https://pubmed.ncbi.nlm.nih.gov/21460264/

6. Sato A, Nakamura I, Fujita H, Tsukimori A, Kobayashi T, Fukushima S, *et al*. Peripheral venous catheter-related bloodstream infection is associated with severe complications and potential death: a retrospective observational study. BMC Infect Dis. 2017[cited 2020 Dec 19];17(1):434. Available from: https://pubmed.ncbi.nlm.nih.gov/28623882/

7. Cameron-Watson C. Port protectors in clinical practice: an audit. Br J Nurs. 2016[cited 2020 Dec 19];25(8):S25-31. Available from: https://pubmed.ncbi.nlm.nih.gov/27126760/

8. Kamboj M, Blair R, Bell N, Son C, Huang YT, Dowling M, *et al*. Use of Disinfection Cap to Reduce Central-Line-Associated Bloodstream Infection and Blood Culture Contamination Among Hematology--Oncology Patients. Infect Control Hosp Epidemiol. 2015[cited 2020 Dec 19];36(12):1401-8. Available from: https://pubmed.ncbi.nlm.nih.gov/26394849/

9. Björkman L, Ohlin A. Scrubbing the hub of intravenous catheters with an alcohol wipe for 15 sec reduced neonatal sepsis. Acta Pediatr. 2015[cited 2020 Dec 19];104(3):232-6. Available from: https://pubmed.ncbi.nlm.nih.gov/25399485/

10. Gorski LA. The 2016 Infusion Therapy Standards of Practice. J Infus Nurs. 2017[cited 2020 Dec 19];39(1S):S1-159. Available from: https://source.yiboshi.com/20170417/1492425631944540325.pdf

11. Loveday HP, Wilson JA, Pratt RJ, Golsorkhi M, Tingle A, Bank A, *et al*. epic3: National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England. J Hosp Infect. 2014[cited 2020 Dec 19];86:S1-S70. Available from: https://pubmed.ncbi.nlm.nih.gov/24330862/

12. Moureau NL, Flynn J. Disinfection of Needleless Connector *Hubs*: Clinical Evidence Systematic Review. Nurs Res Pract. 2015[cited 2020 Dec 19];796762:1-20. Available from: https://pubmed.ncbi.nlm.nih.gov/26075093/

13. Agência Nacional de Vigilância Sanitária. Medidas de Prevenção de Infecção Relacionada à Assistencia à Saúde. Brasília: Anvisa; 2017[cited 2020 Dec 19]. Available from: http://www.riocomsaude.rj.gov.br/Publico/MostrarArquivo.aspx?C=pCiWUy84%2BR0%3D

14. Flynn JM, Larsen EN, Keogh S, Ullman AJ, Rickard CM. Methods for microbial needleless connector decontamination: a systematic review and meta-analysis. Am J Infect Control. 2019[cited 2020 Nov 17];47(8):956-62. Available from: https://pubmed.ncbi.nlm.nih.gov/30824388/

15. Royal College of Nursing. Standards for infusion therapy. London; 2016[cited 2020 Nov 17]. Available from: https://www.rcn.org.uk/professional-development/publications/pub-005704

16. Peters MDJ, Godfrey C, McInerney P, Munn Z, Tricco AC, Khalil H. Chapter 11: Scoping Reviews. In: Aromataris E, Munn Z, editors. JBI Manual for Evidence Synthesis. Australia Joanna Briggs Institute; 2020[cited 2020 Nov 17]. Available from: https://wiki.jbi.global/display/MANUAL/Chapter+11%3A+Scoping+reviews

17. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, *et al*. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. ACP J Club. 2018[cited 2020 Nov 17];169(7):467-73. Available from: https://www.acpjournals.org/doi/10.7326/M18-0850

18. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016[cited 2020 Sept 17];5(1):1-10. Available from: https://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-016-0384-4

19. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009[cited 2020 Nov 17];6(7):e1000097. Available from: https://www.bmj.com/content/339/bmj.b2535

20. Rickard CM, Flynn J, Larsen E, Mihala G, Playford EG, Shaw J, *et al*. Needleless connector decontamination for prevention of central venous access device infection: a pilot randomized controlled trial. Am J Infect Control. 2020[cited 2020 Nov 17];49(2):269-73. Available from: https://pubmed.ncbi.nlm.nih.gov/32735809/

21. Slater K, Cooke M, Fullerton F, Whitby M, Hay J, Lingard S, *et al*. Peripheral intravenous catheter needleless connector decontamination study -Randomized controlled trial. Am J Infect Control. 2020[cited 2020 Nov 17];48(9):1013-8 . Available from: https://www.ajicjournal.org/article/S0196-6553(19)31017-X/abstract

22. Brown JD, Moss HA, Elliott TS. The potential for catheter microbial contamination from a needleless connector. J Hosp Infect. 1997[cited 2020 Nov 17];36(3):181-9. Available from: https://pubmed.ncbi.nlm.nih.gov/9253699/

23. Buchman AL, Spapperi J, Leopold P. A new central venous catheter cap: decreased microbial growth and risk for catheter-related bloodstream infection. J Vasc Access. 2009[cited 2020 Dec 19];10(1):11-21. Available from: https://pubmed.ncbi.nlm.nih.gov/19340794/

24. Devrim İ, Demiray N, Oruç Y, Sipahi K, Çağlar İ, Sarı F, *et al*. The colonization rate of needleless connector and the impact of disinfection for 15 s on colonization: a prospective pre- and post-intervention study. J Vasc Access. 2019[cited 2020 Dec 19];20(6):604-7. Available from: https://pubmed.ncbi.nlm.nih.gov/30722715/

25. Flynn JM, Rickard CM, Keogh S, Zhang L. Alcohol Caps or Alcohol Swabs With and Without Chlorhexidine: An In Vitro Study of 648 Episodes of Intravenous Device Needleless Connector Decontamination. Infect Control Hosp Epidemiol. 2017[cited 2020 Dec 19];38(5):617-9. Available from: https://pubmed.ncbi.nlm.nih.gov/28137322/

26. Hutchens MP, Drennan SL, Cambronne ED. Calibration of optimal use parameters for an ultraviolet light-emitting diode in eliminating bacterial contamination on needleless connectors. J Appl Microbiol. 2015[cited 2020 Dec 19];118(6):1298-305. Available from: https://pubmed.ncbi.nlm.nih.gov/25801979/

27. Martino A, Thompson L, Mitchell C, Trichel R, Chappell W, Miller J, *et al*. Efforts of a Unit Practice Council to implement practice change utilizing alcohol impregnated port protectors in a burn ICU. Burns. 2017[cited 2020 Dec 19];43(5):956-64. Available from: https://pubmed.ncbi.nlm.nih.gov/28139260/

28. Mazher MA, Kallen A, Edwards JR, Donlan RM. An in vitro evaluation of disinfection protocols used for needleless connectors of central venous catheters. Lett Appl Microbiol. 2013[cited 2020 Dec 19];57(4):282-7. Available from: https://pubmed.ncbi.nlm.nih.gov/23710651/

29. Menyhay SZ, Maki DG. Disinfection of needleless catheter connectors and access ports with alcohol may not prevent microbial entry: the promise of a novel antiseptic-barrier cap. Infect Control Hosp Epidemiol. 2006[cited 2020 Dec 19];27(1):23-7. Available from: https://pubmed.ncbi.nlm.nih.gov/16418982/

30. Menyhay SZ, Maki DG. Preventing central venous catheter-associated bloodstream infections: development of an antiseptic barrier cap for needleless connectors. Am J Infect Control. 2008[cited 2020 Dec 19];36(10):S174.e1-5. Available from: https://pubmed.ncbi.nlm.nih.gov/19084153/

31. Merrill KC, Sumner S, Linford L, Taylor C, Macintosh C. Impact of universal disinfectant cap implementation on central line-associated bloodstream infections. Am J Infect Control. 2014[cited 2020 Dec 19];42(12):1274-7. Available from: https://pubmed.ncbi.nlm.nih.gov/25465256/

32. Pavia M, Mazza M. Adding innovative practices and technology to central line bundle reduces bloodstream infection rate in challenging pediatric population. Am J Infect Control. 2016[cited 2020 Dec 19];44(1):112-4. Available from: https://pubmed.ncbi.nlm.nih.gov/26769282/

33. Satou K, Kusanagi R, Nishizawa A, Hori S. Scrubbing technique for needleless connectors to minimize contamination risk. J Hosp Infect. 2018[cited 2020 Dec 19];100(3):e200-e3. Available from: https://pubmed.ncbi.nlm.nih.gov/29574119/

34. Slater K, Fullerton F, Cooke M, Snell S, Rickard CM. Needleless connector drying time-how long does it take? Am J Infect Control. 2018[cited 2020 Dec 19];46(9):1080-1. Available from: https://pubmed.ncbi.nlm.nih.gov/29880433/#:~:text=Drying%20time%20instructions%20on%20antiseptic,%3A%20Drying%20time%3B%20Needleless%20connector.

35. Soothill JS, Bravery K, Ho A, Macqueen S, Collins J, Lock P. A fall in bloodstream infections followed a change to 2% chlorhexidine in 70% isopropanol for catheter connection antisepsis: a pediatric single center before/after study on a hemopoietic stem cell transplant ward. Am J Infect Control. 2009[cited 2020 Dec 19];37(8):626-30. Available from: https://pubmed.ncbi.nlm.nih.gov/19616869/

36. Stango C, Runyan D, Stern J, Macri I, Vacca M. A successful approach to reducing bloodstream infections based on a disinfection device for intravenous needleless connector *hubs*. J Infus Nurs. 2014[cited 2020 Dec 19];37(6):462-5. Available from: https://pubmed.ncbi.nlm.nih.gov/25376323/

37. Sweet MA, Cumpston A, Briggs F, Craig M, Hamadani M. Impact of alcohol-impregnated port protectors and needleless neutral pressure connectors on central line-associated bloodstream infections and contamination of blood cultures in an inpatient oncology unit. Am J Infect Control. 2012[cited 2020 Dec 19];40(10):931-4. Available from: https://pubmed.ncbi.nlm.nih.gov/22575286/

38. Wright MO, Tropp J, Schora DM, Dillon-Grant M, Peterson K, Boehm S, *et al*. Continuous passive disinfection of catheter *hubs* prevents contamination and bloodstream infection. Am J Infect Control. 2013[cited 2020 Dec 19];41(1):33-8. Available from: https://pubmed.ncbi.nlm.nih.gov/23084024/

39. Rossini FP, Andrade D, Santos LCS, Ferreira AM, Tieppo C, Watanabe E. Microbiological testing of devices used in maintaining peripheral venous catheters. Rev Latinoam Enferm. 2017[cited 2021 Apr 28];25:1-8. Available from: https://pubmed.ncbi.nlm.nih.gov/28513768/

40. Hariton E, Locascio JJ. Randomised controlled trials - the gold standard for effectiveness research: study design: randomised controlled trials. BJOG. 2018[cited 2021 Apr 28];125(13):1-2. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6235704/