Verantwoording

Module Handhygiëne Clostridioides difficile

Inhoudsopgave

A systematic review of the literature was performed to answer the following question:

Which method is most suitable for hand hygiene of healthcare professionals treating patients with *Clostridioides difficile (C. difficile)*? Do you need to wash or disinfect your hands? Does the hand hygiene method differ in an outbreak situation?

P	Healthcare worker treating patients with *Clostridioides difficile*, or patients infected with *Clostridioides difficile*
I	Hand disinfection using hand disinfectant/alcohol
C	Washing hands using water and soap
O	Removing/reduction of *Clostridioides difficile* spores, hand hygiene compliance, incidence of *Clostridioides difficile*, infection with a secondary pathogen, outbreaks, transmission

Relevant outcome measures
The guideline development group chose removing/reduction of C. difficile spores as a critical outcome measure for decision making; and hand hygiene compliance, incidence of C. difficile, infection with a secondary pathogen, outbreaks, transmission as important outcome measures for decision making.

A priori, the working group did not define the outcome measures listed above but used the definitions used in the studies.

The working group defined the GRADE-standard limit of 25% difference for dichotomous outcomes (RR <0.8 or >1.25), and 10% for continuous outcomes as a minimal clinically (patient) important difference.

Search and select (Methods)
The databases Medline (via OVID) and Embase (via Embase.com) were searched with relevant search terms until 24 august 2022. The detailed search strategy is depicted under the tab Methods. The systematic literature search resulted in 286 hits. Studies were selected based on the following criteria: systematic reviews, randomized controlled trials, or comparative observational studies answering the research question. Seventy-six studies were initially selected based on title and abstract screening. After reading the full text, 72 studies were excluded (see the table with reasons for exclusion under the tab Methods), and 4 studies were included.

Results
Four studies (Jabbar 2010, Oughton 2009, Kundrapu 2014, Knight 2010) were included in the analysis of the literature. Important study characteristics and results are summarized in the evidence tables. The assessment of the risk of bias is summarized in the risk of bias tables.

Summary of literature
Description of studies
Jabbar (2010) conducted an experiment to count how many viable *C. difficile* spores that had been experimentally inoculated on hands of volunteers were retained after Alcohol-Based Hand Rub (ABHR) use and to determine the subsequent efficiency of their transfer

through physical contact. Included were ten healthy volunteers, all of them nonclinical research personnel. Before inoculation, volunteers cleansed their hands with a nonmedicated soap and water and dried them with paper towels. At that point, stamp sampling for preinoculation cultures was performed by applying a prereduced taurocholate-cycloserine-cefoxitin-fructose agar (TCCFA) plate against the hypothenar eminence of the right hand. *C. difficile* was seeded onto volunteers' bare hands by an inoculation of 100 mL of the spore suspension (500,000 CFU total or 250,000 CFU per hand) onto the palm followed by 15 seconds of bimanual palmar rubbing and 3 minutes of air drying. This high inoculum was necessary to yield a sufficient number of CFU to be counted in post-decontamination cultures and to show a difference between tested products. Participants then used 1 of 5 hand hygiene agents to clean their hands: chlorhexidine gluconate soap and water, 3 different ABHRs (Isagel, Purell, Endure) with a minimum alcohol concentration of 60%, or a water control. A post–hand hygiene stamp for culture of the right hand was then performed on a TCCFA plate. To determine potential transfer of spores 5 donor volunteers shook hands with 5 recipient volunteers before a post-hand hygiene stamp was performed.

Oughton (2009) conducted a randomized crossover comparison evaluating common hand hygiene methods for efficacy in removing *C. difficile*. Ten hospital laboratory workers volunteered for this study. A crossover format was used so that all volunteers would be exposed to all interventions once for each contamination protocol during the observation period of June–July 2007. The order of interventions for each volunteer was assigned by means of computer-generated random number lists. A total of 20 mL nontoxogenic strain of *C. difficile* was poured into a clean, tight-fitting nitrile glove. The hands were allowed to air dry for 1–2 minutes, prior to one of the hand hygiene interventions. The hand hygiene interventions studied were (1) warm (30 C) water with plain soap, (2) cold (15 C) water with plain soap, (3) warm (30 C) water with 2% chlorhexidine antibacterial soap, (4) antiseptic hand wipes with 40% vol/vol ethanol and 0.5% parachlorometaxylenol, (5) alcohol-based handrub with 70% vol/vol isopropanol, and (6) a no-wash negative control. All interventions were evaluated for mean reduction in colonyforming units (CFUs) under 2 contamination protocols: "whole hand" and "palmar surface."

Kundrapu (2014) conducted a prospective, randomized trial to compare the effectiveness of soap and water hand wash with alcohol hand rub for removal of C. difficile spores from hands of patients. Patients with CDI or asymptomatic carriers of toxigenic C. difficile identified through rectal surveillance cultures were randomized to perform hand hygiene using alcohol hand rub or soap and water hand wash with soap containing 0.5% triclosan. For alcohol hand rub, 10 mL of product was applied to hands for 30seconds. For soap and water hand wash, 2 mL of soap was applied, and hands were washed for 30 seconds. Hands were cultured before and after each hand hygiene episode. Subjects participated in a maximum of 4 hand hygiene assessments separated by at least 24 hours with randomization before each assessment. For each group, the frequency of hand contamination and the number of colonies recovered were compared

Knight (2010) conducted a retrospective chart review analysis to compare incidence rates of Clostridium difficile-associated diarrhea (CDAD) before and after implementation of the ABHR policy. Included were adult (age >18 years) patients with in-patient status. CDAD was defined as health care facility-onset, health care facility associated diarrhea with a positive assay for *C. difficile* toxin A, toxin B, or both. Throughout the study period, *C. difficile*

assays were performed using an enzyme immunoassay for the detection of toxins A and B. All in-patients with a diagnosis of CDAD were identified by ICD-9 code from our medical records database or by positive C difficile toxin. Hand hygiene, including appropriate use of ABHR and soap and water, was monitored after ABHR implementation. Before implementation, only a 2% chlorhexidine-based soap product was available in the hospital. At the time of implementation, all existing antimicrobial products were removed and replaced with the alcohol-based hand foam. Hand hygiene compliance before ABHR implementation was not routinely measured. Compliance data after ABHR implementation was compared to earlier data as a reflection of hand hygiene compliance before introduction of the new policy. The only soap product available was a lotion soap with no antimicrobial activity. Outcome was the incidence rate of CDAD calculated as the number of patients with a positive C difficile toxin assay per 10,000 patient-days and hand hygiene compliance.

Results

Removing/reduction of Clostridioides difficile spores

In total, 3 studies reported on removing/reduction of *Clostridioides difficile* (*C. difficile)* spores.

Jabbar (2010) compared a total of 120 observations (10 participants, 2 hands each, 5 interventions, and 1 negative control) in a pairwise fashion for the whole hand protocol. Jabbar (2010) found a mean $\log_{10}$ reduction of 0.90 $\pm$ 0.37 CFU/cm^2 on hands of volunteers following chlorhexidine gluconate soap–and-water washing compared to a mean $\log_{10}$ reduction of 0.11 $\pm$ 0.20 CFU/cm^2 (Mean difference (MD) = -0.79; 95% CI -0.87 to -0.71) after use of isagel, 0.37 $\pm$ 0.42 CFU/cm^2 (MD= -0.53; 95% CI -0.63 to -0.43]) after use of endure, and 0.14 $\pm$ 0.33 CFU/cm^2 (MD= -0.76; 95% CI -0.85 to -0.67) after use of purell. Overall, the use of chlorhexidine gluconate soap–and-water washing resulted in a higher mean $\log_{10}$ reduction compared to alcohol-based handrubs.

Oughton (2009) found that, using the whole hand protocol, water and plain soap compared to alcohol-based handrub resulted in a mean log reduction of $\log_{10}$ 2.08 CFU/mL (95% CI 1.69 to 2.47). Cold water and plain soap compared to alcohol-based handrub resulted in a mean log reduction of $\log_{10}$ 1.46 CFU/mL (95% CI 1.06 to 1.85). Overall, the use of water and plain soap resulted in a higher mean $\log_{10}$ reduction compared to alcohol-based handrub (MD = -0.62; 95% CI -1.10 to -0.14).

Kundrapu (2014) found that 6/30 (20%) positive cultures prior to the hand wash intervention were also positive after hand washing compared to 28/30 (93%) cultures before and after alcohol rub. The RR was 0.21 (95% CI 0.10 to 0.44) in favour of hand washing.

Incidence of Clostridioides difficile

Knight (2010) observed a total of 766 patients with health care facility associated CDAD were identified. A total of 270 cases of CDAD were identified before ABHR implementation, and 496 cases were identified after implementation. The rate decreased from 4.96 per 10,000 patient-days before ABHR implementation, to 3.98 per 10,000 patient-days after ABHR implementation (P = 0.0036).

Transmission

Jabbar (2010) found that residual spore counts for donors' hands after ABHR use ranged from 180 to 1,547 CFU. After shaking hands with the donors, recipients' hands had spore counts of 33 to 369 CFU, for a mean efficiency of transfer of 30.2% ± 17.4%.

Handhygiene compliance
Knight (2010) found that after implementation of the ABHR policy, compliance with hand hygiene, including both ABHR and soap and water, rose dramatically. Overall, compliance rose from 46% to 90%.

Infection with a secondary pathogen
No evidence was found regarding the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure infection with a secondary pathogen.

Outbreaks
No evidence was found regarding the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure outbreaks

Level of evidence of the literature
Removing/reduction of Clostridioides difficile spores
The level of evidence for observational studies starts 'low'. The quality of evidence regarding outcome measure 'Removing/reduction of *Clostridioides difficile* spores ' was downgraded by 1 level to GRADE very low because of risk of bias due to limitation in the study design (no screening up on admission or prior/between exposure experiments).

Transmission
The level of evidence for observational studies starts 'low'. The quality of evidence regarding outcome measure *'transmission'* was downgraded by 1 level to GRADE very low because only one study reported the outcome measure (imprecision).

Incidence of Clostrioides difficile
The level of evidence for observational studies starts 'low'. The quality of evidence regarding outcome measure '*Incidence of Clostrioides difficile*' was downgraded by 1 level to GRADE very low because only one study reported the outcome measure (imprecision).

Hand hygiene compliance
The level of evidence for observational studies starts 'low' the quality of evidence regarding outcome measure '*hand hygiene compliance*' was downgraded by 1 level to GRADE very low because only one study reported the outcome measure (imprecision).

Infection with a secondary pathogen
No evidence was found regarding the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure infection with a secondary pathogen.

Outbreaks
No evidence was found regarding the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure outbreaks

Conclusions

Very low GRADE	**Removing/reduction of *Clostrioides difficile* spores** The evidence is very uncertain about the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure 'removing/reduction of *Clostrioides difficile* spores'. *Sources: Jabbar, 2010; Oughton, 2009; Kundrapu, 2014*

Very low GRADE	**Transmission** The evidence is very uncertain about the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure 'transmission'. *Sources: Jabbar, 2010*

Very low GRADE	**Incidence of *Clostrioides difficile*** The evidence is very uncertain about the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure 'incidence of *Clostrioides difficile*' *Sources: Knight, 2010*

Very low GRADE	**Hand hygiene compliance** The evidence is very uncertain about the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure 'hand hygiene compliance' *Sources: Jabbar, 2010; Oughton, 2009; Kundrapu, 2014*

No GRADE	**Infection with a secondary pathogen** No evidence was found regarding the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure infection with a secondary pathogen.

No GRADE	**Outbreaks** No evidence was found regarding the effect of hand washing using water and soap compared to hand disinfectant or alcohol on the outcome measure outbreaks

Referenties

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Kundrapu S, Sunkesula V, Jury I, Deshpande A, Donskey CJ. A randomized trial of soap and water hand wash versus alcohol hand rub for removal of Clostridium difficile spores from hands of patients. Infect Control Hosp Epidemiol. 2014 Feb;35(2):204-6. doi: 10.1086/674859. Epub 2013 Dec 23. PMID: 24442089.

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Widmer AF, Frei R, Erb S, Stranden A, Kuijper EJ, Knetsch CW, Tschudin-Sutter S. Transmissibility of Clostridium difficile Without Contact Isolation: Results From a Prospective Observational Study With 451 Patients. Clin Infect Dis. 2017 Feb 15;64(4):393-400. doi: 10.1093/cid/ciw758. PMID: 28172613.

Bijlage 1. Evidence table for intervention studies

(randomized controlled trials and non-randomized *observational* studies [cohort studies, case-control studies, case series])[1]

Study reference	Study characteristics	Patient characteristics [2]	Intervention (I)	Follow-up	Outcome measures and effect size [4]	Comments
Jabbar, 2010	Type of study: prospective cohort Setting and country: volunteers, hospital, US Funding and conflicts of interest: The study was funded by The US Department of Veterans Affairs Research Service. two authors report receiving commercial funds.	Inclusion criteria: - Ten healthy volunteers, all of them nonclinical research personnel at Hines VA Hospital, Exclusion criteria: Not applicable N total at baseline: 10 Important prognostic factors[2]: *2/10* had preinoculation hand cultures positive for C. difficile, although the number of colonies was negligible (fewer than 3 CFU per plate).	Describe intervention: Hand washing using alcohol-based hand rub compared to Chlorhexidine Hand Wash	Length of follow-up: No follow-up Loss-to-follow-up: Not applicable Incomplete outcome data: Not applicable	Outcome measures: *Washing with gluconate soap–and-water:* Mean log10 reduction 0.90 + 0.37 CFU/cm2 *Washing with Isagel:* mean log10 reduction of 0.11 + 0.20 CFU/cm2 *Washing with Endure:* mean log10 reduction 0.37 + 0.42 CFU/cm2 a *Washing withPurell:* mean log10 reduction 0.14 + 0.33 CFU/cm2 *Transmission:* mean efficiency of transfer of 30.2% + 17.4%.after ABHR use	The authors conclude that hand washing with soap and water is significantly more effective at removing C. difficile spores from the hands of volunteers than are ABHRs. Residual spores are readily transferred by a handshake after use of ABHR
Knight, 2010	Type of study: Retrospective chart review	Inclusion criteria: Adult (age ≥18 years) patients with CDAD and in-patient status	Describe intervention: Implementation of AHBR policy	Length of follow-up: 7,5 years Loss-to-follow-up: Not applicable	Outcome measures: *Incidence rate prior to ABHR implementation:*	The authors conclude that the data provides no evidence of an

	Setting and country: patients with CDAD, hospital, US Funding and conflicts of interest: Authors declare no conflicts of interest.	at our institution between January 1, 2001, and June 30, 2008 Exclusion criteria: Not fulfilling inclusion criteria N total at baseline: 766 Important prognostic factors[2]: 270 cases of CDAD were identified before ABHR implementation, and 496 cases were identified after implementation		Incomplete outcome data: Not applicable	4.96 per 10,000 patient-days *Incidence rate prior to ABHR implementation:* 3.98 per 10,000 patient-days (P = 0.0036). *Compliance compliance rose from 46% to 90%.*	increased CDAD rate after implementation of an ABHR policy at our institution.
Kundrapu, 2014	Type of study: Prospective cohort study Setting and country: patients, hospital, US Funding and conflicts of interest: Study was supported by the Department of Veterans Affairs. All authors declare no conflict of interest	Inclusion criteria: Adult (age ≥18 years) patients with CDI or asymptomatic carriers of toxigenic C. difficile identified through rectal surveillance cultures Exclusion criteria: Not fulfilling inclusion criteria N total at baseline: 44 patients 121 hands	Describe intervention: hand hygiene using alcohol hand rub (Purell) or soap and water hand wash with soap containing 0.5% triclosan	Length of follow-up: Not applicable Loss-to-follow-up: Not applicable Incomplete outcome data: Not applicable	Outcome measures: Positive culture after hand wash 6/30 (20%) Positive culture after alcohol rub 28/30 (93%) RR = 0.21 (95% CI 0.10 to 0.44) in favour of hand washing.	The authors conclude that the hand washing was effective for reducing levels of C. difficile spores on hands

		Important prognostic factors[2]: 28 patients with CDI 16 asymptomatic carriers.				
Oughton, 2010	Type of study: Prospective randomized cross-over study Setting and country: patients, hospital, Canada Funding and conflicts of interest: Study was supported by the Canadian Institutes of Health Research and Bayer Healthcare (Canada). All authors declare no conflict of interest	Inclusion criteria: Ten hospital laboratory workers volunteered for this study Exclusion criteria: Not fulfilling inclusion criteria N total at baseline: 10 patients Important prognostic factors[2]: 120 observations whole-hand protocol 318 observations palmar surface protocol	Describe intervention: The hand hygiene interventions studied were (1) warm (30 C) water with plain soap (Hygenipak Instafoam, Deb Canada), (2) cold (15 C) water with plain soap (Hygenipak Instafoam, Deb Canada), (3) warm (30 C) water with 2% chlorhexidine antibacterial soap (Hygenipak 2% CHG foaming skin cleanser, Deb Canada), (4) antiseptic hand wipes with 40% vol/vol ethanol and 0.5% parachlorometaxylenol (Sani-dex antimicrobial hand wipes, PDI), (5) alcohol-based handrub with 70% vol/vol isopropanol	Length of follow-up: Not applicable Loss-to-follow-up: Not applicable Incomplete outcome data: Not applicable	Outcome measures: *water and plain soap compared to alcohol-based handrub* mean log10 reduction of 2.08 CFU/mL (95% CI 1.69 to 2.47). *Cold water and plain soap compared to alcohol-based handrub* mean log10 reduction of l1.46 CFU/mL (95% CI 1.06 to 1.85).	The authors conclude that handwashing with soap and water showed the greatest efficacy in removing C. difficile and should be performed preferentially over the use of alcohol-based handrubs when contact with C. difficile is suspected or likely

			(Manorapid, Antiseptica, Pulheim-Brauwiler), and (6) a no-wash negative control.			

Notes:

1. Prognostic balance between treatment groups is usually guaranteed in randomized studies, but non-randomized (observational) studies require matching of patients between treatment groups (case-control studies) or multivariate adjustment for prognostic factors (confounders) (cohort studies); the evidence table should contain sufficient details on these procedures
2. Provide data per treatment group on the most important prognostic factors [(potential) confounders]
3. For case-control studies, provide sufficient detail on the procedure used to match cases and controls
4. For cohort studies, provide sufficient detail on the (multivariate) analyses used to adjust for (potential) confounders

Bijlage 2 Risk of bias tables

Risk of bias table for interventions studies (cohort studies based on risk of bias tool by the CLARITY Group at McMaster University)

Author, year	Selection of participants Was selection of exposed and non-exposed cohorts drawn from the same population? Definitely yes, probably yes, probably no, definitely no	Exposure Can we be confident in the assessment of exposure? Definitely yes, probably yes, probably no, definitely no	Outcome of interest Can we be confident that the outcome of interest was not present at start of study? Definitely yes, probably yes, probably no, definitely no	Confounding-assessment Can we be confident in the assessment of confounding factors? Definitely yes, probably yes, probably no, definitely no	Confounding-analysis Did the study match exposed and unexposed for all variables that are associated with the outcome of interest or did the statistical analysis adjust for these confounding variables? Definitely yes, probably yes, probably no, definitely no	Assessment of outcome Can we be confident in the assessment of outcome? Definitely yes, probably yes, probably no, definitely no	Follow up Was the follow up of cohorts adequate? In particular, was outcome data complete or imputed? Definitely yes, probably yes, probably no, definitely no	Co-interventions Were co-interventions similar between groups? Definitely yes, probably yes, probably no, definitely no	Overall Risk of bias Low, Some concerns, High
Jabbar (2010)	*Definitely yes* Reason: Ten healthy volunteers, all of them nonclinical research personnel at Hines VA Hospital	*Definitely yes* Reason: 2/10 had minor CFU preincolation and 8/10 had no CFU preincolation indicating no infection	*Definitely yes* Reason: Outcome is based on direct culture following inoculation	*Not applicable*	*Not applicable*	*Definitely yes* Reason: Culturing on selective medium.	*Not applicable*	*Not applicable*	**Low**
Knight (2010	*Definitely yes* Reason: All patients fulfilling selection	*Definitely yes* Reason: All in-patients with a diagnosis	*Probably no*, Reason: There was no screening upon admission it was	*Not applicable*	*Not applicable*	*Definitely yes* Reason: Throughout the study period,	*Not applicable*	*No information*	**Some concerns**

	criteria were included	of CDAD were identified by ICD-9 code from medical records database or by positive C difficile toxin assay from the microbiology laboratory database.	unclear if patients were infected in hospital as a result of hospital transmission			C difficile assays were performed using an enzyme immunoassay			
Kundrapu, 2014	*Definitely yes* Reason: All were hospital patient that fulfilled inclusion criteria	*Definitely yes* Reason: Patients with CDI or asymptomatic carriers of toxigenic C. difficile identified through rectal surveillance cultures	*Definitely yes* Reason: Patients were only included if positive	*Not applicable*	*Not applicable*	*Probably no* Reason: Only 14/44 (32%) patients had positive hand cultures before hand hygiene meaning the outcome was not present prior to the intervention	*Not applicable*	*No information*	**Some concerns**
Oughton, 2009	*Definitely yes* Reason: Ten hospital laboratory workers volunteered for this study	*Definitely yes* Reason: Culturing on selective medium	*Probably no* Reason: No screening prior to exposure. Unclear is outcome was present at the beginning of the intervention or during repeated interventions.	*Not applicable*	*Not applicable*	*Definitely yes* Reason: each hand was placed into a new glove containing 20 mL of sterile brain-heart infusion broth, which was gently dispersed for	*Not applicable*	*No information*	**Some concerns**

						30 seconds. A 1-mL sample of the broth was removed via pipette for quantification by serial 10-fold dilution on CCFA-T and incubated anaerobically at 37 C for 48 hours.			

Footnotes

Selection of participants Example of low risk of bias: Exposed and unexposed drawn for same administrative database of patients presenting at same points of care over the same time frame

Exposure Examples of low risk of bias: Secure record (e.g. surgical records, pharmacy records); Repeated interview or other ascertainment asking about current use/exposure

Confounding Examples of low risk of bias regarding assessment: Interview of all participants; Self-completed survey from all participants; Review of charts with reproducibility demonstrated; From database with documentation of accuracy of abstraction of prognostic data.

Example of low risk of bias regarding analysis: Comprehensive matching (e.g. with propensity score) or adjustment for all plausible confounding variables

Assessment of outcome Examples of low risk of bias: Independent blind assessment; Record linkage; For some outcomes (e.g. fractured hip), reference to the medical record is sufficient to satisfy the requirement for confirmation of the fracture

Follow up Examples of low risk of bias: No missing outcome data; Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring is unlikely to introduce bias); Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; Missing data have been imputed using appropriated methods

Co-interventions Example of low risk of bias: Most or all relevant co-interventions that might influence the outcome of interest are documented to be similar in the exposed and unexposed

Bijlage 3. Table of excluded studies

Author and year	Reason for exclusion
Alcohol hand gels are not effective against C. difficile spores. Nursing Times. 2005; 101 (24) :2-2	Wrong publication type - Narrative review
Alcohol rubs surprisingly effective against C. diff: traditional hand washing still performs better. Hospital Infection Control. 2006; 33 (2) :17-17	I and C does not meet PICO
Combat C. difficile with better hand hygiene: stick with alcohol except in outbreak. Hospital Employee Health. 2006; 25 (6) :67-68	Wrong publication type - Narrative review
PURELL Skin Nourishing Foam Hand Sanitiser. British Journal of Cardiac Nursing. 2010; 5 (3) :154-154	I and C does not meet PICO
The handiwork of good health. Harvard Health Letter. 2007; 32 (3) :1-3	I and C does not meet PICO
Anonymous Hand hygiene is crucial to combat Clostridium difficile. Nursing older people. 2014; 26 (8) :15	I and C does not meet PICO
Aydın, Ayla İrem and Atak, Meryem and Nurcan, Nurcan Özyazıcıoğlu and Dalkızan, Vahit Hand dermatitis among nurses during the COVID-19 pandemic: frequency and factors. World Council of Enterostomal Therapists Journal. 2021; 41 (4) :10-14	P does not meet PICO
Barbadoro, P. and Martini, E. and Savini, S. and Marigliano, A. and Ponzio, E. and Prospero, E. and D'Errico, M. M. In vivo comparative efficacy of three surgical hand preparation agents in reducing bacterial count. Journal of Hospital Infection. 2014; 86 (1) :64-67	P does not meet PICO
Barker, A. K. and Zellmer, C. and Tischendorf, J. and Duster, M. and Valentine, S. and Wright, M. O. and Safdar, N. On the hands of patients with Clostridium difficile: A study of spore prevalence and the effect of hand hygiene on C difficile removal. American Journal of Infection Control. 2017; 45 (10) :1154-1156	P does not meet PICO
Bettin, K. and Clabots, C. and Mathie, P. and Willard, K. and Gerding, D. N. Effectiveness of liquid soap vs. chlorhexidine gluconate for the removal of Clostridium difficile from bare hands and gloved hands. Infection control and hospital epidemiology : the official journal of the Society of Hospital Epidemiologists of America. 1994; 15 (11) :697-702	P does not meet PICO
Blanckaert, K. and Barbut, F. and Coignard, B. and Grandbastien, B. and Astagneau, P. Clostridium difficile and hand hygiene. Medecine et Maladies Infectieuses. 2007; 37 :S63-S65	Wrong publication type - Narrative review
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