Office of Evidence Based Practice (EBP) – Critically Appraised Topic: Dry Time of Surgical Site Preparation Solutions

Specific Care Question

For the patient who will be undergoing a surgical procedure, does the dry time of the products used for skin disinfection impact the risk of surgical site infection (SSI)?

Recommendations Based on Current Literature

No recommendation is can be made for or against optimal dry time of surgical site preparation agents, based on expert review of current literature by the Department of EBP. The overall certainty in the evidence is very low[d]. Only one randomized controlled study (Yasuda et al., 2015) was identified that compared surgical site preparation agents and there was no difference in site infections when comparing the group that did not have a wait time, to the group that had an approximate 5 minute wait time. When there is a lack of scientific evidence, standard work should be developed, implemented, and monitored (see Summary by Outcome for substantiation of this recommendation).

Literature Summary

Background. Skin antisepsis is the pre-operative treatment of intact skin in the operating room to reduce the microbial load on the patient's skin prior to making the surgical incision (WHO, 2018). Products used for skin antisepsis can be categorized as aqueous based or alcohol based (Armstrong, Patrick, & Erstad, 2001). Aqueous products are iodophor formulations, while alcohol-based products are formulations of isopropyl alcohol combined with iodophors or chlorhexidine (WHO, 2018). Alcohol based skin antiseptic agents are recommended for most surgeries (Berrios-Torres et al., 2017; WHO, 2018; AST, 2008), but these agents **should not** be used on mucous membranes (AST, 2008). Although alcohol-based products are valued for their quicker drying time (Armstrong et al., 2001; Magalini et al., 2013), they have been implicated in operating room fires (Jones et al., 2017; Weber, Hargunani, & Wax, 2006). This review will summarize identified literature on the topic.

Study characteristics. The search for suitable studies was completed on May 7, 2019. L. Harte, PharmD, CPHQ reviewed the seven titles and/or abstracts found in the search and identified six articles believed to answer the question. After an in-depth review one article, an RCT, answered the question (Yasuda et al., 2015). The Center for Disease Control (CDC) guidelines (Berrios-Torres et al. (2017) and the Association of Surgical Technologists (AST, 2008) are the primary source of information for this analysis. Additionally, one case study (Weber et al., 2006) and one *in vitro* study (Jones et al., 2017) were identified on risk of fire with solutions used for surgical preparation (prep).

Summary by Outcome

Infection. Yasuda et al. (2015) compared no wait time after application of povidone iodine (PVI) versus 5-minute wait time (approximate) after application of PVI and measured the outcomes of Positive Cultures and SSI (N = 89). The odds of having a positive culture were significantly less in the wait time group OR = 0.16, p = .008, 95% CI [0.04, 0.61]. For the outcome SSI, there was no difference in the number of SSI based on the wait time versus no wait time. There is very low certainty in this finding. The risk of bias is unclear, as randomization was not clearly reported, nor was blinding of subjects, personnel, or outcome assessors (see Figure 2). The evidence is indirect as only culture from the wound edge were reported, and a sample size calculation was not reported to know if enough subjects were recruited into the study. Finally, since only one study is included in this review, imprecision of the finding is serious (see Table 1).

Other. Although other trials were not identified that compared antiseptic dry time of various products with the outcome risk of SSI, the following points can be made:

- The CDC (Berrios-Torres et al., 2017) and the AST (AST, 2008) recommends that alcohol-based products be used for skin prophylaxis in preparation for surgery. However alcohol-based products should not be used on mucous membranes, rather aqueous iodophor products, such as PVI, are recommended for this surgery type (AST, 2008).
- Dry times (in seconds) of alcohol-based products and iodophor products are significantly less than dry times of iodophor products (see Figure 3):
    - ChlorPrep (alcohol based) vs. PVI (aquaeous based), MD = -53.0, 95% CI [-70.18, -35.82] (Magalini et al., 2013)

  - DuraPrep (alcohol based) vs. PVI,(aquaeous based), *MD* = -31.8, 95% CI [-57.82, -5.78] (Armstrong et al., 2001)
- Weber et al. (2006) reported a case study of an operating room fire in a hirsute 62-year old male after surgical prep with DuraPrep. The operative field was draped after the patient's neck was shaved and the surgical prep solution was allowed to dry for at least 3 minutes. After skin incision and retraction, the electrocautery device was activated, and a flameless, smokeless fire occurred. Recommendations from this paper include:
  - Avoid the use of DuraPrep in the hirsute patient, collection of the agent on hair bearing skin can slow the dry time
  - The pooling of alcohol prep solution for any reason should be avoided
  - Oxygen deliver during skin antisepsis should be a the minimal level to meet patient's need
- In an animal model, Jones et al. (2017) applied both alcohol (4% CHG with 70% isopropyl alcohol (IPA); plain IPA (70%); iodine-IPA, (0.7% iodine povacrylex and 74% IPA) and nonalcohol-based (4% CHG or 1% PVI paint) skin preps to porcine skin samples. Electrocautery was performed, with an electrosurgical pencil, immediately after application and after at least a 3-minute dry time.
  - Nonalcohol-based skin preps did not cause a fire for either dry times.
  - Alcohol-based skin preps did cause a fire in 22% (13/60) with no time allowed for prep to dry and 6% (10/60) where at least a 3-minute dry time was allowed.
  - Pooling of chlorhexidine-IPA created more fires
    - No time for prep dry there were 10% (2/20) fires in the no pooling group and 19/20 (95%) in the pooling group, $p < .001$
    - Time for prep to dry group there were 15% (3/20) fires in the no pooling group and 75 % (15/20) in the pooling group, $p < .001$

Identification of Studies

Search Strategy and Results (see Figure 1)

PubMed: surgical site infection AND skin preparation AND (dry OR timing)
Records identified through database searching *n* = 6
Additional records identified through other sources *n* = 7

Studies Included in this Review

Citation	Study Type
Yasuda et al. (2015)	RCT

Studies Not Included in this Review with Exclusion Rationale

Citation	Reason for exclusion
Armstrong et al. (2001)	Does not address antiseptic drying time and SSI
AST (2008)	Does not address antiseptic drying time and SSI
Berrios-Torres et al. (2017)	Does not address antiseptic drying time and SSI
Hemani and Lepor (2009)	Does not address antiseptic drying time and SSI
Hibbard, Mulberry, and Brady (2002)	Does not address antiseptic drying time and SSI
Hibbard (2005)	Does not address antiseptic drying time and SSI
Johnson et al. (2016)	Does not address antiseptic drying time and SSI
Jones et al. (2017)	Does not address antiseptic drying time and SSI
Magalini et al. (2013)	Does not address antiseptic drying time and SSI
Moen, Noone, and Kirson (2002)	Does not address antiseptic drying time and SSI

Sidhwa and Itani (2015)	Does not address antiseptic drying time and SSI
Weber et al. (2006)	Does not address antiseptic drying time and SSI
WHO (2018)	Does not address antiseptic drying time and SSI

Methods Used for Appraisal and Synthesis

[a]The Appraisal of Guidelines Research and Evaluation II (AGREE II) is an international instrument used to assess the quality and reporting of clinical practice guidelines for this analysis (Brouwers et al. 2010).

[b]Rayyan is a web-based software used for the initial screening of titles and / or abstracts for this analysis (Ouzzani, Hammady, Fedorowicz & Elmagarmid, 2017).

[c]Review Manager (Higgins & Green, 2011) is a Cochrane Collaborative computer program used to assess the study characteristics as well as the risk of bias and create the forest plots found in this analysis.

[d] The GRADEpro Guideline Development Tool (GDT) is the tool used to create the Summary of Findings table(s) for this analysis (see Table 1).

[e]The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram depicts the process in which literature is searched, screened, and eligibility criteria is applied (Moher, Liberati, Tetzlaff, & Altman, 2009).

[a]Brouwers, M.C. et al. for the AGREE Next Steps Consortium. (2010) AGREE II: Advancing guideline development, reporting and evaluation in healthcare. *Canadian Medical Association Journal, 182*, E839-842. Retrieved from https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf

[b]Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan-a web and mobile app for systematic reviews. *Systematic Reviews, 5*(1), 210. doi:10.1186/s13643-016-0384-4

[c]Higgins, J. P. T., & Green, S. e. (2011). *Cochrane Handbook for Systematic Reviews of Interventions [updated March 2011]* (Version 5.1.0 ed.): The Cochrane Collaboration, 2011.

[d]GRADEpro GDT: GRADEpro Guideline Development Tool (2015). McMaster University, (developed by Evidence Prime, Inc.). [Software]. Available from gradepro.org.

[e]Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097 **For more information, visit www.prisma-statement.org.**

Question Originator
Lory Harte, PharmD, CPHQ
Medical Librarian Responsible for the Search Strategy
Keri Swaggart, MLIS, AHIP
EBP Scholar's Responsible for Analyzing the Literature
Erin Lindhorst, MS, RD, LD
EBP Team Member Responsible for Reviewing, Synthesizing, and Developing this Document
Nancy Allen, MS, MLS, RD, LD, CPHQ

Acronyms Used in this Document

Acronym	Explanation
AST	Association of Surgical Technologists
CAT	Critically Appraised Topic
CDC	Centers for Disease Control
CHG	Chlorhexidine
CMH	Children's Mercy Hospital
CPG	Clinical Practice Guideline

EBP	Evidence Based Practice
IPA	Isopropyl Alcohol
MD	Mean Difference
OR	Odds Ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
Prep	Preparation
PVI	Povidone Iodine
RCT	Randomized Controlled Trial
SSI	Surgical Site Infection
WHO	World Health Organization

Date Developed/Updated

July 2019

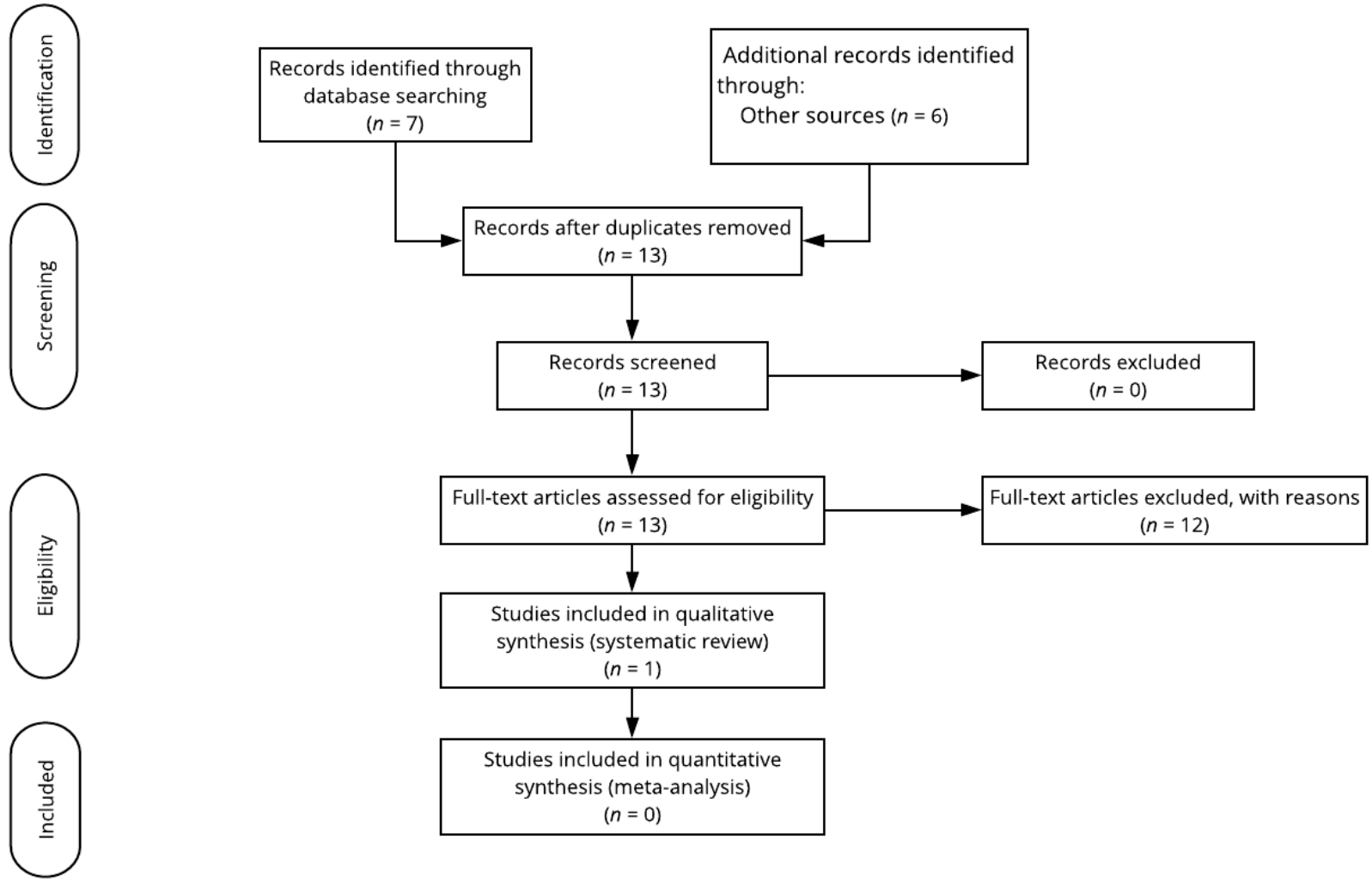

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA)[e]

AGREE II[a] Summary for the CDC Prevention of SSI Guideline (Berrios-Torres et al., 2017)

Domain	Percent Agreement
Scope and purpose	86%
Stakeholder involvement	81%
Rigor of development	81%
Clarity and presentation	93%
Applicability	46%
Editorial independence	94%
Overall guideline assessment	90%
Team's recommendation for guideline use	Yes with modifications

Note: Four EBP Scholars completed the AGREE II on this guideline.

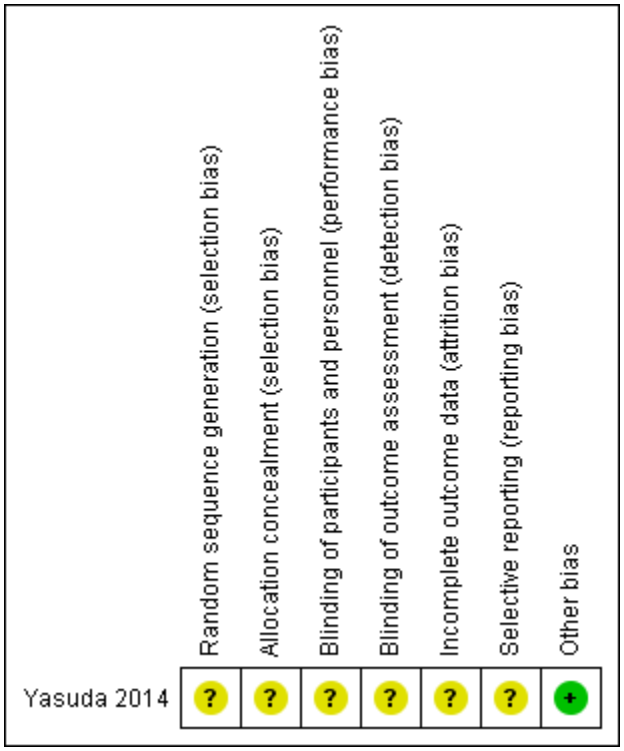

Figure 2. Risk of Bias Summary

Table 1

Summary of Findings Table: Wait Time vs. No Wait Time for Surgical Site Preparation Solution

Certainty assessment							Summary of findings				
№ of participants (studies) Follow-up	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Publication bias**	**Overall certainty of evidence**	**Study event rates (%)**		**Relative effect (95% CI)**	**Anticipated absolute effects**	
							With no wait time	**With Wait time**		**Risk with no wait time**	**Risk difference with Wait time**
Positive Cultures											
89 (1 RCT)	serious [a]	not serious	serious [b]	serious [c]	none	⨁◯◯◯ VERY LOW	13/43 (30.2%)	3/46 (6.5%)	***OR* 0.16** (0.04 to 0.61)	**302 per 1,000**	**237 fewer per 1,000** (from 285 fewer to 93 fewer)
SSI Infection											
89 (1 study)	serious [a]	not serious	serious [b]	serious [c]	none	-	0/43 (0.0%)	2/46 (4.3%)	***OR* 4.89** (0.23 to 104.76)	**0 per 1,000**	**0 fewer per 1,000** (from 0 fewer to 0 fewer)

Notes:
a. Reporting on randomization; allocation concealment; blinding of participant, personnel, and outcome assessors is poorly reported;
b. Cultures were only collected from the wound edge;
c. It is a single study with 89 subjects.

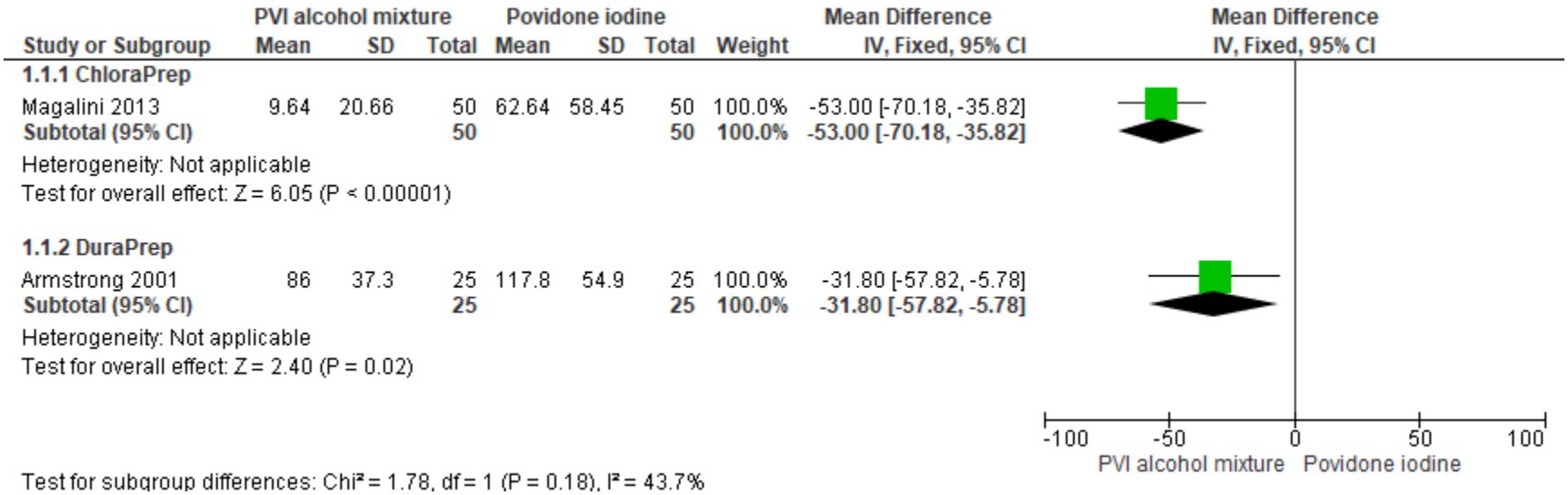

***Figure 3*. Comparison of PVI alcohol mixture vs. PVI/iodophor, Outcome: Dry time**

Characteristics of Studies

Armstrong 2001

Methods	Clinical Trail (not randomized)
Participants	**Participants:** • Twenty-five operating room personnel • Twenty-five subjects (patient volunteers) **Setting:** College of Pharmacy, Arizona, US **Participated in study:** *N = 50* • **Group 1, Operating room personnel*:** *n* = 25 ○ Povidone iodine paint and scrub (7.5% povidone iodine, 10% water, Operand; APlicare, Inc., Branford CT ○ Duraprep (0.7% iodophor, 74% isopropyl alcohol; 3M Health Care plus Ioban in combination ○ Prevail (5% povidone iodine, 62% alcohol; Allegiance Health care Corp., McGaw Park, IL ○ LiquiDrape not FDA approved at time of the study, Tradmark for this product has been abandoned https://trademark.trademarkia.com/liquidrape-75404162.html July 2 2019 • **Group 2, Patient volunteers:** *n = 25* **Completed Study:** *N = 50* • **Group 1, Applied surgical prep*:** *n* = 25 • **Group 2, Had surgical prep applied:** *n* = 25 **Gender, males (as defined by researchers):** • Not reported **Race / ethnicity or nationality (as defined by researchers):** • Not reported **Age:** • Not reported **Inclusion Criteria:** • Both groups - greater than or equal to 18 years of age • Both groups - free of known hypersensitivity to povidone iodine or alcohol • Operating room personnel - at least six months experience assisting in pre-operative patient preparation **Exclusion Criteria:** • Patient volunteer - rash, open sores, or pre-existing skin conditions on the lower extremities
Interventions	• Operating room personnel applied the four skin prep formulations to the lower extremity of the patient volunteers. There were two rounds of application. The first round, two products were applied, one to each leg from the knee to the ankle. The product was allowed to dry and then removed. The process was repeated with the remaining skin prep products for the second round. • Patients were not required to shave their legs • Operating room personnel read the product insert instructions prior to application.

Outcomes	**Primary outcome(s):** • Product application • Drying time • Removal time • Overall satisfaction

Magalini 2013

Methods	Observational study
Participants	**Participants:** Surgeons performing elective and emergency surgeries (medium and major operations). **Setting:** Hospital, Italy **Number enrolled into study:** *N* = 100 • **Group 1, Povidone iodine (PVI):** *n* = 50 • **Group 2, ChloraPrep:** *n* = 50 **Number completed:** *N* = 100 • **Group 1:** *n* = 50 • **Group 2:** *n* = 50 **Gender, males: N**ot reported **Race / ethnicity or nationality (as defined by researchers):** • Not reported **Age:** Not reported **Inclusion criteria:** • Surgeon approval for observation • Use of either PVI or ChloraPrep **Exclusion criteria:** • None listed **Covariates identified:** not reported
Interventions	**Both:** Every surgeon (27 unique surgeons were observed) performed their own surgical field and uses the two different approaches defined below they start from the middle of the surgical field and swabbing out. When the field is almost dry they may use a paper towel to complete the drying. All surgeons identified that they had received product training. • **Group 1:** PVI is poured on the skin and gauze/clamp used • **Group 2:** ChloraPrep applicator
Outcomes	**Primary outcome(s):** • Comparison of IPV and ChloraPrep in supplies used • Comparison of IPV and ChloraPrep in time for application, drying*, and total time needed for disinfection (defined as from the beginning of painting to placing of drapes) **Secondary outcome(s)** • Surgeons opinion from the questionnaire *Outcomes of interest to the CMH CPG or CAT development team

Yasuda 2014

Methods	Prospective, Randomized, controlled study
Participants	**Setting:** Department of Orthopaedic Surgery, Hamamatsu University of Medicine **Randomized into study:** N = 89 • **Group 1: No wait time for povidone-iodine applied,** *n* = 43 • **Group 2: Wait time povidone-iodine applied**, *n* = 46 **Completed study:** *N* = 89 • **Group 1:** *n* = 43 • **Group 2:** *n* = 46 **Gender, males:** • **Group 1:** *n* = 21 • **Group 2**: *n* = 23 **Race / ethnicity or nationality (as defined by researchers):** • Not reported **Age, years (mean):** • **Group 1:** 61.9 • **Group 2**: 58.1 **Inclusion criteria:** • Patients scheduled for spinal surgery **Exclusion criteria:** • Not reported **Power Analysis:** • Not reported
Interventions	**Both**: • In all cases, the surgical field was sealed with an antimicrobial plastic adhesive wound drape just before starting the surgery. • Culture samples were collected by rubbing a cotton swab at the wound edge just before wound closure and then they were incubated at 37-degree Celsius for 5 to 7 days. • Cefazolin was administered three times on the day of surgery, before surgery, one hour after surgery, and six hours after surgery, and two times on the next day as a prophylactic antibiotic. **Group 1:** povidone-iodine was applied to the surgical site just before skin incision, after the surgeon's hands were scrubbed. **Group 2:** povidone-iodine was applied before the surgeon's hands were scrubbed. Expected Wait time 5 minutes.
Outcomes	**Primary outcome:** • Culture results **Secondary outcome:** • SSI infection
Results	• In Group 1, coagulase negative *Staphylococcus aureus* was identified in one culture. In Group 2, three different bacteria (*streptococcus, staphylococcus epidermidis*, and *coagulase negative staphylococcus*) were identified in the culture.

	• Two cases of SSI (deep infection) (2 out of 46 patients, 4.3%) were identified in group 2 four weeks after surgery, and cultures from the wound edge intraoperatively were negative. There was no case of SSI in Group 1 after the surgery. • Because bacteria on the skin appeared significantly reduced by allowing povidone-iodine to dry for several minutes prior to surgery, the researchers recommend this approach to reduce the incidence of postoperative infections. The recommended drying time prior to surgery is 10 minutes. • A limitation of this study is that only analysis of cultures from the wound edge was conducted.

Risk of bias table

Bias	Scholars' judgment	Support for judgment
Random sequence generation (selection bias)	Unclear risk	Patients were randomly allocated into 2 groups, however how they were randomized was not indicated.
Allocation concealment (selection bias)	Unclear risk	Insufficient information to determine
Blinding of participants and personnel (performance bias)	Unclear risk	The study did not address this outcome
Blinding of outcome assessment (detection bias)	Unclear risk	Insufficient information to determine
Incomplete outcome data (attrition bias)	Unclear risk	All patients enrolled were analyzed. Although, no power analysis performed
Selective reporting (reporting bias)	Unclear risk	SSI infections not tested for significance
Other bias	Low risk	The study appears to be free of other sources of bias.

References

Armstrong, E. P., Patrick, K. L., & Erstad, B. L. (2001). Comparison of preoperative skin preparation products. *Pharmacotherapy, 21*(3), 345-350. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/11253858

Berrios-Torres, S. I., Umscheid, C. A., Bratzler, D. W., Leas, B., Stone, E. C., Kelz, R. R., . . . Healthcare Infection Control Practices Advisory, C. (2017). Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. *JAMA Surg, 152*(8), 784-791. doi:10.1001/jamasurg.2017.0904

Hemani, M. L., & Lepor, H. (2009). Skin preparation for the prevention of surgical site infection: which agent is best? *Rev Urol, 11*(4), 190-195. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/20111631

Hibbard, J. S. (2005). Analysis comparing the antimicrobial activity and safety of current antiseptic agents: A review. *Journal of Infusion Nursing, 16*(2), 195.

Hibbard, J. S., Mulberry, G. K., & Brady, A. R. (2002). A clinical study comparing the skin antisepsis and safety of ChloraPrep, 70% isopropyl alcohol, and 2% aqueous chlorhexidine. *J Infus Nurs, 25*(4), 244-249. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/12131506

Johnson, M. P., Kim, S. J., Langstraat, C. L., Jain, S., Habermann, E. B., Wentink, J. E., . . . Bakkum-Gamez, J. N. (2016). Using Bundled Interventions to Reduce Surgical Site Infection After Major Gynecologic Cancer Surgery. *Obstet Gynecol, 127*(6), 1135-1144. doi:10.1097/AOG.0000000000001449

Jones, E. L., Overbey, D. M., Chapman, B. C., Jones, T. S., Hilton, S. A., Moore, J. T., & Robinson, T. N. (2017). Operating Room Fires and Surgical Skin Preparation. *J Am Coll Surg, 225*(1), 160-165. doi:10.1016/j.jamcollsurg.2017.01.058

Magalini, S., Pepe, G., Panunzi, S., De Gaetano, A., Abatini, C., Di Giorgio, A., . . . Gui, D. (2013). Observational study on preoperative surgical field disinfection: povidone-iodine and chlorhexidine-alcohol. *Eur Rev Med Pharmacol Sci, 17*(24), 3367-3375.

Moen, M. D., Noone, M. B., & Kirson, I. (2002). Povidone-iodine spray technique versus traditional scrub-paint technique for preoperative abdominal wall preparation. *Am J Obstet Gynecol, 187*(6), 1434-1436; discussion 1436-1437.

Organization, W. H. (2018). *Global guidelines on the prevention of surgical site infection*. WHO Retrieved from https://www.who.int/gpsc/appendix8.pdf

Sidhwa, F., & Itani, K. M. (2015). Skin preparation before surgery: options and evidence. *Surg Infect (Larchmt), 16*(1), 14-23. doi:10.1089/sur.2015.010

Association of Surgical Technologists. (2008). AST standards of practice for skin prep of the surgical patient. Retrieved from http://www.ast.org/uploadedFiles/Main_Site/Content/About_Us/Standard_Skin_Prep.pdf

Weber, S. M., Hargunani, C. A., & Wax, M. K. (2006). DuraPrep and the risk of fire during tracheostomy. *Head Neck, 28*(7), 649-652. doi:10.1002/hed.20396

Yasuda, T., Hasegawa, T., Yamato, Y., Kobayashi, S., Togawa, D., Arima, H., & Matsuyama, Y. (2015). Optimal Timing of Preoperative Skin Preparation with Povidone-Iodine for Spine Surgery: A Prospective, Randomized Controlled Study. *Asian Spine J, 9*(3), 423-426. doi:10.4184/asj.2015.9.3.423