Using Chlorhexidine vs. Povidone Iodine in Reducing Surgical Site Infections (SSIs) An Evidenced-based Practice Using the John Hopkins Nursing Evidenced-based Practice Model

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Introduction

With the introduction of quality assurance in health care delivery, there has been a proliferation of research studies comparing patient outcomes for similar conditions among many health care delivery facilities. Since the 1990s, increasing interest has been placed in the incorporation of clinical adverse events as quality indicators in hospital quality assurance programs. Adverse postoperative events, especially Surgical Site Infection (SSI) rates after specific procedures, gained popularity as hospital quality indicators in the 1980s, and are currently some of the most widely used hospital quality indicators worldwide.

Surgical Site Infections (SSIs) continue to occur and remain a significant cause of disability among operated patients, in spite of the substantial advances in our understanding of its epidemiology, pathogenesis and prevention. While advances have been made in infection control practices, including improved operating room ventilation, sterilization methods, barriers, surgical technique, and availability of antimicrobial prophylaxis, SSIs remain a substantial cause of morbidity and an associated mortality rate of 3%. Of this, 75% of the mortality rate has been directly related to the SSIs. In 2010, an estimated 16 million operative procedures were performed in the United States. A recent prevalence study found that SSIs were the most common healthcare-associated infection, accounting for 31% of all HAIs among hospitalized patients. The National Healthcare Safety Network (NHSN) data for 2006-2008 (16,147 SSIs following 849,659 operative procedures) showed an overall SSI rate of 1.9% (CDC, 2013). Moreover, De Lissovoy G., et al, 2009 asserted in their study, “Surgical Site Infection: Incidence and Impact on Hospital Utilization and Treatment Costs”, among the 723,490 surgical hospitalizations as samples, 6,891 cases of SSI were identified (1%). On average, SSI extended length of stay by 9.7 days while increasing cost by $20,842 per admission. These cases of SSI were associated with an additional 406,730 hospital-days and hospital costs exceeding $900 million. This significant economic burden in terms of extended length of stay and increased costs of treatment is alarming to note despite the fact that the cause can be prevented.

In the Philippines, a number of retrospective and prospective studies had been undertaken since 1982 and had demonstrated surgical site infection rate ranging from 0.12 percent to 14.4 percent (NNICG, 1995).

Most SSIs are believed to be acquired during surgery. This is supported by the success of SSI prevention measures directed towards activities in the operating theater and a few reports demonstrating matching strains of pathogens from the surgeon’s fingers and postoperative infection. However, despite much research on SSIs, there are currently no data on the actual proportion acquired in the operating theater versus post-operative care in the wards. Similarly, within the subgroup of SSIs acquired during surgery, the proportion originating from the patient versus that transmitted by the surgical staff, operating theater procedure or the environment remains unknown (Uckay, I. et al 2010).

At present, four preventive measures are considered having a high level of evidence according to major evidence-based guidelines: surgical hand preparation, appropriate antibiotic prophylaxis, postponing of an elective operation in the case of active remote infection and hair clipping before
surgery was considered grade IA evidence in the 1999 CDC guidelines. However, this is now a matter of debate.

Skin preparation in the operating theater immediately before surgery is routinely implemented in daily clinical practice worldwide, based on expert opinion. However, even with optimal preparation, true sterilization of the skin is impossible. To the best of our knowledge, there is no consensus on the best antiseptic agent to be used. The development of bacterial resistance (mostly among staphylococci and *Pseudomonas aeruginosa*) to some antiseptic solutions like the chlorhexidine has been acknowledged and its clinical impact is the subject of ongoing studies. Skin preparation in concentric circles versus a back-and-forth motion has no significant impact on SSI, and surgical site marking does not affect antisepsis of the surgical field (Uckay, I. et al 2010).

We have been using antiseptic solutions 50 years ago to reduce or totally eliminate the normal microflora that are present in the skin to prevent impending infection. Povidone Iodine or polyvinyl pyrrolidone-iodine is an iodophor and a broad spectrum antimicrobial agent delivered in many forms including powders, gels, lotions, ointments, sprays and mousses. Compared to other similar compounds povidone iodine is highly soluble and less toxic making it widely suitable for surgical asepsis and wound dressing. Chlorhexidine Gluconate is used as a topical antiseptic skin scrub in hospital and household settings. It is used for general skin cleansing, as a surgical scrub, and as a pre-operative skin preparation. It is often used as a rubbing agent prior to the use of hypodermic or intravenous needles in place of iodine.

Scrubbing of the hands and forearms with a brush and antiseptic agents has been the standard for surgical practice. However, it has been increasingly recognized that brush scrubbing may provoke side effects and that an alcohol-based hand antiseptic used in conjunction with a scrub agent enhances its effectiveness. Since the patient’s skin is a major source of pathogens that cause surgical site infection, optimization of preoperative skin antisepsis may decrease postoperative infections (Darouiche, RO, 2010).

Members of the healthcare industry were trained to deliver optimum care to their patients. We practice based from the latest evidence we have to meet the demands of our clientele, reduce hospital stay and financial burden to our patients and to meet the standards of quality care and hospital management. If so, is it proper then to question the proficiency of a particular nurse in the occurrence of any hospital acquired infection or surgery site infection despite the presence of colonizing microorganisms in the skin? Is it always the nurse to be blame notwithstanding the fact that he followed all necessary measures in the prevention of infection and maintenance of sterility of instruments and items in the operating theater? Sometimes, what is being practiced in the past tends to be the accepted thing to do. Thus, I am posting this particular question and try to elucidate the efficacy of these antiseptics we are using at present if they are really an anti sepsis agents.

**Statement of the Problem**

The clinical question posed for query is: For admitted patients, does using chlorhexidine gluconate v. povidone-iodine reduces the microorganisms present in the skin?

- P – Admitted patients
- I – Chlorhexidine Gluconate
- C – Povidone-Iodine
- O – Reduction of microorganisms present in the skin

**Note:** To further enhance the clinical question and to have a better outlook of what is being asked, the researcher uses the Question Development Tool of the John Hopkins Nursing Evidenced-Based Practice Model.

**Review of Evidence**

In an effort to resolve this dilemma, a literature search was conducted using COCHRANE, CINAHL, PUBMed, ELSIVIER, GOOGLE SCHOLAR and NCBI.
Review of Evidence

| Research studies matching search terms | Number | 115 |
| Research studies identified through alternate means | | 44 |
| Research studies rejected at the title stage | | 67 |
| Research studies rejected at the abstract stage | | 26 |
| Research studies retrieved and copied for review | | 55 |
| Research studies rejected at first reading | | 22 |
| Research studies scored | | 20 |
| Research studies meeting cutoffs | | 13 |

Reasons for Rejection:
- Some research studies talk about hospital personnel and other health care providers who use antiseptic solutions before they perform particular procedure.
- Other studies compare different antiseptic solutions with chlorhexidinegluconate and/or povidone iodine.
- There were no clear numerical data presented to support the findings.
- Minimal background pertaining to data collection, results and interpretation.
- Some studies are weak evidences.

SUMMARY OF RESEARCH STUDIES APPRAISED USING THE JOHN HOPKINS NURSING EVIDENCE-BASED PRACTICE RESEARCH EVIDENCE APPRAISAL

<table>
<thead>
<tr>
<th>Study, Author, Date</th>
<th>Population (age, sex, location, condition)</th>
<th>Intervention or Test Treatment (no. studied)</th>
<th>Control Treatment (no. studied)</th>
<th>Outcome</th>
<th>Critical Appraisal Comments, Strengths of the Study, Conclusions</th>
<th>Evidence Level</th>
</tr>
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<tbody>
<tr>
<td>Systematic Review And Cost Analysis Comparing Use Of Chlorhexidine With Use Of Iodine For Preoperative Skin Antisepsis To Prevent Surgical Site Infection</td>
<td>Nine RCTs with a total of 3,614 patients</td>
<td>Meta-analysis revealed that chlorhexidine antisepsis was associated with significantly fewer SSIs (adjusted risk ratio, 0.64 [95% confidence interval, [0.51-0.80]) and positive skin culture results (adjusted risk ratio, 0.44 [95% confidence interval, 0.35-0.56]) than was iodine antisepsis.</td>
<td>Preoperative skin antisepsis with chlorhexidine is more effective than preoperative skin antisepsis with iodine for preventing SSI and results in cost savings.</td>
<td>IA: Meta-analysis of RCT, consistent results, adequate research studies appraised and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference</td>
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<tr>
<td>Study Title</td>
<td>Study Design</td>
<td>Sample Size</td>
<td>n=409</td>
<td>n=440</td>
<td>Results</td>
<td>IA:</td>
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| Chlorhexidine-Alcohol versus Povidone-Iodine for Surgical-Site Antisepsis | Darouiche RO, Wall MJ Jr, Itani KM, Otterson MF, Webb AL, Carrick MM, Miller HJ, Awad SS, Crosby CT, Mosier MC, Alsharif A, Berger DH. 2010 Jan | 849 subjects |       |       | - The overall rate of surgical-site infection was significantly lower in the chlorhexidine-alcohol group than in the povidone-iodine group (9.5% vs. 16.1%; P=0.004; relative risk, 0.59; 95% confidence interval, 0.41 to 0.85).  
- Chlorhexidine-alcohol was significantly more protective than povidone-iodine against both superficial incisional infections (4.2% vs. 8.6%, P=0.008) and deep incisional infections (1% vs. 3%, P=0.05) but not against organ-space infections (4.4% vs. 4.5%).  
Preoperative cleansing of the patient’s skin with chlorhexidine-alcohol is superior to cleansing with povidone-iodine for preventing surgical-site infection after clean-contaminated surgery. | Experimetal Study (RCT); consistent results, sufficient sample size, adequate control and definitive conclusions; consistent recommendations based on extensive scientific evidence |
| Prospective, Randomized Trial Of Two Antiseptic Solutions For Prevention Of Central Venous Or Arterial Catheter Colonization And Infection In Intensive Care Unit Patients | Surgical-Surgery Trauma Intensive Care Unit (ICU) In A University Hospital | Surgical-University Hospital |       |       | - The rate of significant catheter colonization (i.e., > or = 10(3) colony-forming units [cfu]/mL by quantitative culture), and catheter-related sepsis (as defined by sepsis abating following catheter removal per 1,000 catheter-days), were significantly lower in the chlorhexidine group (12 vs. 31, relative risk 0.4, 95% confidence interval 0.1 to 0.9, The 4% alcohol-based solution of 0.25% chlorhexidinegluconate and 0.025% benzalkonium chloride was more effective than 10% povidone iodine for insertion site care of short-term central venous and arterial catheters. This effect appeared related to a more efficacious prevention of infections with Gram-positive bacteria. | Experimetal Study (RCT); consistent results, sufficient sample size, adequate control and definitive conclusions; consistent recommendations based on extensive scientific evidence |
p < .01] and 6 vs. 16 [relative risk 0.4, 95% confidence interval 0.1 to 1, p = 0.5], respectively).

- The rate of central venous catheter colonization and central venous catheter-related sepsis per 1,000 catheter-days were also significantly lower in the chlorhexidine group (8 vs. 31 [relative risk 0.3, 95% confidence interval 0.1 to 1, p = .03] and 5 vs. 19 [relative risk 0.3, 95% confidence interval 0.1 to 1, p = .02], respectively).

- The rate of arterial catheter colonization per 1,000 catheter-days was significantly lower in the chlorhexidine group (15 vs. 32 [relative risk 0.5, 95% confidence interval 0.1 to 1, p = .05]), whereas the rate of arterial catheter-related sepsis per 1,000 catheter-days was similar for the two study groups (8 in the chlorhexidine group vs. 10 in the povidone iodine group [relative risk 0.8, 95% confidence interval 0.1 to 2.2, p = .6]).

- The 0.25% chlorhexidine solution was superior to the 10% povidone iodine solution in preventing catheter colonization and
catheter-related sepsis due to Gram-positive bacteria (5 vs. 20 \(p < .001\), and 2 vs. 10 \(p < .001\), respectively), whereas the activity of the 0.25% chlorhexidine solution was nonsignificantly superior in preventing Gram-negative infections (7 vs. 4 \(p = .5\), and 4 vs. 2 \(p = .8\), respectively).

Chlorhexidine Versus Povidone Iodine In Preventing Colonization Of Continuous Epidural Catheters In Children: A Randomized, Controlled Trial

Kinirons B, Mimoz O, Lafendi L, Naas T, Meunier J, Nordmann P.
2001 Feb

Children requiring an epidural catheter for postoperative analgesia longer than 24 hours 100 randomly assigned patients, 96 were evaluable

- Catheters inserted after skin preparation with chlorhexidine were one sixth as likely and less quickly to be colonized as catheters inserted after skin preparation with povidone iodine (1 of 52 catheters [0.9 per 100 catheter days] vs. 5 of 44 catheters [5.6 per 100 catheter days]; relative risk, 0.2 [95% confidence interval, 0.1-1.0]; \(P = 0.02\)).

Compared with aqueous povidone iodine, the use of alcoholic chlorhexidine for cutaneous antisepsis before epidural catheter insertion reduces the risk of catheter colonization in children.

IA: Experimental Study (RCT); consistent results, sufficient sample size, adequate control and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific evidence.

Alcohol-Based Chlorhexidine Vs. Povidone Iodine In Reducing Skin Colonization Prior To Regional Anesthesia Procedures

Krobbuaban B, Diregpoke S, Prasan S.

Patients requesting regional anesthesia. 100 patients

- The proportion of subjects with a positive skin culture immediately after skin disinfection differed significantly between the povidone iodine and alcohol-based

For skin disinfection prior to the neuraxial blockade procedure, the use of alcohol-based chlorhexidine compared with the use of povidone iodine lowered the incidence of insertion-site colonization.

IA: Experimental Study (RCT); consistent results, sufficient sample size, adequate
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Title</th>
<th>Methodology</th>
<th>Findings</th>
<th>Conclusions</th>
</tr>
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<tbody>
<tr>
<td>Thanomsat M, Kumkeaw S.</td>
<td>Surgical Hand Antisepsis To Reduce Surgical Site Infection</td>
<td>Randomized controlled trials comparing surgical hand antisepsis of varying duration, methods and antiseptic solutions. 10 trials (1 trial - 4387 patients)</td>
<td>• Fourth trial found 4% chlorhexidinegluconate scrubs more effective than chlorhexidine in 70% alcohol rubs. • Three trials found chlorhexidinegluconate scrubs were significantly more effective than povidone iodine scrubs. • Four trials compared the effect of different durations of scrubs and rubs on the numbers of CFUs on hands. One trial found no difference after the initial scrub but found subsequent three minute scrubs using chlorhexidine significantly more effective than subsequent scrubs lasting 30 seconds.</td>
<td>Alcohol rubs used in preparation for surgery by the scrub team are as effective as aqueous scrubbing in preventing SSIs however this evidence comes from only one, equivalence, cluster trial which did not appear to adjust for clustering. Four comparisons suggest that alcohol rubs are at least as, if not more, effective than aqueous scrubs though the quality of these is mixed and each study presents a different comparison, precluding meta analysis. There is no evidence to suggest that any particular alcohol rub is better than another. Evidence from 4 studies suggests that chlorhexidinegluconate based aqueous scrubs are more effective than povidone iodine based aqueous scrubs in terms of the numbers of CFUs on the hands. There is limited evidence regarding the effects on CFUs numbers of different scrub durations. There is no evidence regarding the effect of equipment such as brushes and sponges.</td>
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### Table

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<tr>
<th>A RandomizedTrial</th>
<th>Chlorhexidine and povidone iodine</th>
<th>n=23</th>
<th>n=27</th>
<th>Among the first set of intraoperative Chlorhexidinegluconate was more effective than control</th>
</tr>
</thead>
</table>
### That Compared Povidone Iodine and Chlorhexidine As Antiseptics For Vaginal Hysterectomy

Culligan PJ, Kubik K, Murphy M, Blackwell L, Snyder J. 2005 Feb

| Povidone Iodine for cleansing the operative field for vaginal surgery. 50 patients | specimens (which were obtained 30 minutes after the surgical scrub), 63% of the cultures (17/27) from the povidone iodine group and 22% of the cultures (5/23) from the chlorhexidine group were classified as contaminated (P = .003; relative risk, 6.12; 95% CI, 1.7, 21.6). | Povidone iodine in decreasing the bacterial colony counts that were found in the operative field for vaginal hysterectomy. |

### A Randomized Trial Comparing Povidone Iodine To A Chlorhexidine Gluconate-Impregnated Dressing For Prevention Of Central Venous Catheter Infections In Neonates


| Neonates who require a central venous catheter (CVC) for prolonged vascular access experience high rates of catheter-related bloodstream infection (CRBSI). 705 neonates | n=335 | n=370 |

- Neonates randomized to the antimicrobial dressing group (chlorhexidine-impregnated dressing) were less likely to have colonized CVC tips than control neonates (15.0% vs 24.0%, relative risk [RR]: 0.6 95% confidence interval [CI]: 0.5-0.9). Rates of CRBSI (3.8% vs 3.2%, RR: 1.2, CI: 0.5-2.7) and BSI without a source (15.2% vs 14.3%, RR: 1.1, CI: 0.8-1.5) did not differ between the 2 groups. | The novel chlorhexidine-impregnated dressing, replaced weekly, was as effective as cutaneous disinfection with 10% PI and redressing the site every 3 to 7 days for preventing CRBSI and BSI without a source in critically ill neonates requiring prolonged central venous access. The risk of local contact dermatitis under the chlorhexidine dressing limits its use in low birth weight infants who require prolonged central access during the first 2 weeks of life. | IA: Experimental Study (RCT); consistent results, sufficient sample size, adequate control and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific evidence |
### Influence Of Preoperative Showers On Staphylococcal Skin Colonization: A Comparative Trial Of Antiseptic Skin Cleansers

Kaiser AB, Kernodle DS, Barg NL, Petracek MR. 1988 Jan

Patients scheduled for an elective cardiac operation or coronary artery angioplasty were assigned to shower with one of the study skin cleansers.

- The chlorhexidine skin cleanser consistently reduced staphylococcal colony counts at both the subclavian and inguinal sites before the procedure. This reduction was significant for patients showering both evening and morning (p less than 0.05).
- The use of the povidone-iodine skin cleanser inconsistently affected skin flora.
- Patients using lotion soap either experienced no change or had an increase in colony counts.

Chlorhexidine is more effective than povidone-iodine in diminishing skin colonization with staphylococci in patients before operation. Repeated applications of chlorhexidine are superior to a single shower with this agent.

### A Randomized Controlled Trial Of 1% Aqueous Chlorhexidine Gluconate Compared With 10% Povidone-Iodine For Topical Antiseptic In Neonates: Effects On Blood Culture Contamination Rates

Nuntnarumit P, Sangsuksawang N. 2013 Apr

Neonates with birth weight greater than or equal to 1,500 g that compared 1% aqueous chlorhexidine gluconate (CHG) with 10% povidone-iodine (PI) as a topical antiseptic.

- We found 1% CHG to be more effective than 1% PI in reducing blood culture contamination rates, and no contact dermatitis was observed.

### Chlorhexidine Compared With Povidone-Iodine Solution For Vascular Catheter-Site Care: A Meta-Analysis

Chaiyakunapruk

All studies were conducted in a hospital setting, and various catheter types were used.

- The summary risk ratio for catheter-related bloodstream infection was 0.49 (95% CI, 0.28 to 0.88) in patients whose catheter sites were These results suggest that incidence of bloodstream infections is significantly reduced in patients with central vascular lines who receive chlorhexidinegluconate versus povidone-iodine for insertion-site skin disinfection. Use

Chlorhexidine is more effective than povidone-iodine in diminishing skin colonization with staphylococci in patients before operation. Repeated applications of chlorhexidine are superior to a single shower with this agent.
<table>
<thead>
<tr>
<th>N. Veenstra DL, Lipsky BA, Saint S.</th>
<th>Eight studies involving a total of 4143 catheters</th>
<th>Disinfected with chlorhexidine gluconate instead of povidone-iodine. Among patients with a central vascular catheter, chlorhexidine gluconate reduced the risk for catheter-related bloodstream infection by 49% (risk ratio, 0.51 [CI, 0.27 to 0.97]). Chlorhexidine gluconate is a simple and effective means of reducing vascular catheter-related infections.</th>
<th>Appraised and definitive conclusions; consistent recommendations based on extensive literature review that includes thoughtful reference to scientific evidence</th>
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<td>2002 Jun</td>
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**Comparison Of Bactericidal Properties Of Alcohol-Based Chlorhexidine Versus Povidone-Iodine Prior To Amniocentesis**

Adler MT, Brigger KR, Bishop KD, Mastrobattista JM. 2012 Jun

Cleansing the gravid abdomen prior to amniocentesis, University of Texas Women's Clinic in Houston, Texas. 50 study participants

- No statistically significant difference was detected between baseline colony counts between the left and right side of each patient's abdomen (p = 0.33) prior to cleansing.
- **Postcleansing colony counts** were evaluated, and a statistically significant difference was identified, favoring chlorhexidine as a more efficacious abdominal cleanser (p <0.001).

We demonstrated that 2% chlorhexidine with 70% isopropyl alcohol had excellent bactericidal efficacy and was superior to povidone-iodine for cleansing the maternal abdomen.

**A Comparison Of Chlorhexidine-Alcohol Versus Povidone-Iodine For Eliminating Skin Flora Before Genitourinary Prosthetic Surgery: A Randomized Controlled Trial**

Yeung LL, Grewal S, Bullock A, Lai HH, Brandes SB. 2013 Jan

Patients undergoing initial genitourinary prosthetic implantation. 100 patients

- Pre-preparation cultures were positive in 79% of the patients. Post-preparation cultures were positive in 8% in the chlorhexidine-alcohol group compared to 32% in the povidone-iodine group (p = 0.0091).
- Coagulase-negative staphylococci were more frequently eradicated with povidone-iodine compared to chlorhexidine-alcohol (p = 0.0001). Chlorhexidine-alcohol was superior to povidone-iodine in eradicating skin flora at the surgical skin site before genitourinary prosthetic implantation. There does not appear to be any increased risk of urethral or genital skin irritation with the use of chlorhexidine-alcohol.

Chlorhexidine-alcohol appears to be the optimal agent for skin preparation before genitourinary surgery.
the most commonly isolated organisms in post-preparation cultures in the povidone-iodine group (13 of 16 patients) as opposed to propionibacterium in the chlorhexidine-alcohol group (3 of 4 patients).

- Clinical complications requiring additional operations or device removal occurred in 6 patients (6%) with no significant difference between the 2 groups. No urethral or genital skin complications occurred in either group.

prosthetic procedures.

recommenda
dions based on extensive literature review that includes thoughtfu l reference to scientific evidence

**Conclusion**

Based from the research studies that were appraised using the John Hopkins Nursing Evidenced-Based Practice Research Evidence Appraisal, I therefore conclude that ChlorhexidineGluconate is more effective than Povidone Iodine in reducing the number of microorganisms present in the patients’ skin thereby lessening the chance of having surgical site infection or other procedure-related infections. The protection span of ChlorhexidineGluconate when used as antiseptic agent for cleansing the skin prior to a particular procedure is also longer compared to its counterpart thus, the possibility of contamination is lesser.

**Recommendation**

As part of the Evidence-Based Practice Process, I strongly recommend the use of ChlorhexidineGluconate in disinfecting the skin of patients prior to a particular procedure. This modification of using this type of antiseptic solution is beneficial to both the patients and the hospital to reduce hospital morbidity and mortality rates associated with surgery and other types of procedure. Lesser disease complication because of high protection rate is evident and possible. It also reduces the hospital expenses incurred for antiseptic solutions because ChlorhexidineGluconate is far economical than Povidon Iodine and other antiseptics purchased. In the part of the patient, reduction in the number of days of hospital confinement is of great advantage to lessen the financial burden and other crisis brought by the hospitalization and the disease per se.

A simple action plan was made to introduce the result of this research and the importance of evidence-based nursing practice. This is recommended to the Ilocos Training and Regional Medical Center, San Fernando City, La Union, to examine and crack the common practice when it comes to antiseptic solutions. This could be a good commence to assure the delivery of efficient, effective quality services to all patients catered.
References


12. Lee, I. et al. (2010), Systematic Review And Cost Analysis Comparing Use Of Chlorhexidine With Use Of Iodine For Preoperative Skin Antisepsis To Prevent Surgical Site Infection. Infect Control Hospital Epidemiology.


15. Mimoz, O. et al. (1996). Prospective, Randomized Trial Of Two Antiseptic Solutions For Prevention Of Central Venous Or Arterial Catheter Colonization And Infection In Intensive Care Unit Patients.