Abstract of thesis entitled

An evidence based guideline of using chlorhexidine gluconate impregnated dressing in preventing catheter related bloodstream infections in hemato-oncology patients with central venous catheters

Submitted by

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Background:

Central venous catheter (CVC) is commonly inserted and maintained in hemato-oncology patients who require prolonged indwelling venous catheter for access for a certain period of time. The use of CVC can facilitate doctors and nurses for medical procedures, e.g. intravenous medications administration, fluid infusion, blood sampling taking, etc. The use of CVC would greatly reduce patients’ discomfort from frequent blood sample taking and intravenous access settings, which would result in a better patient’s outcome.

However, the use and maintenance of CVC are associated with substantial infection risk. For the hemato-oncology patients who are suffering from neutropenia after receiving chemotherapies or due to malignancies, they pose a higher risk of infections. Catheter-related bloodstream infection (CRBSI) is the most critical and life threatening complication that can occur in catheterization, which causing around 62,000 deaths every year in U.S.A.
Chlorhexidine gluconate (CHG) impregnated dressing, which contains a 2% (w/w) chlorhexidine gluconate aqueous-based gel, is introduced and evidence supported its application as an effective preventive measure of CRBSIs.

**Purpose:**

This written proposal aims to systematic evaluate the evidence on the use of CHG impregnated dressing in hemato-oncology patients with CVCs in preventing CRBSIs, assess the transferability and feasibility of implementation of the proposal guideline in a regional hospital in Hong Kong, and develop an implementation and evaluation plan for the implementation of the guideline.

**Method:**

A total of 5 eligible randomized control trials were selected from electronic databases, which looking into the effectiveness of CHG impregnated dressing concerning on catheter related infections. Data were summarized and scythed, and critical appraisals of each study were performed. After comparing the settings in selected studies and the target setting, the application of CHG impregnated dressing is found to be transferable and feasible to implement in the target setting in Hong Kong. An evidence-based guideline in details based on the level of evidence as retrieved and the grades of recommendations as according to the Scottish Intercollegiate Guidelines Network (SIGN) was developed.

Before launching the innovation, communication plan with different levels of stakeholders was developed and a quality improvement committee for managing CRBSIs was formed for guiding, monitoring and sustaining the proposed innovation.

A pilot study would be started to access the feasibility of innovation and identify barriers and difficulties encountered so to refine the program.
Finally, the innovation would be considered as effective based on different levels of outcome achievements. An evaluation plan with methods of taking measurements, length of follow up and methods for data analysis were well planned.

Conclusion:

The effectiveness of CHG impregnated dressing in preventing CRBSIs was well supported with evidence, and it is worthy to be adopted in clinical setting for hemato-oncology patients with CVC implementation.
An evidence based guideline of using chlorhexidine gluconate impregnated dressing in preventing catheter related bloodstream infections in hemato-oncology patients with central venous catheters

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Declaration

I declare that the thesis and the research work there of represents my own work, except where due an acknowledgement is made, and that has not been previously included in a thesis, dissertation or report submitted to this University or to any other institution for a degree, diploma or other qualifications.

Signed ______________________________

Chan Yuen Ying
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>APN</td>
<td>Advance Practicing Nurse</td>
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<tr>
<td>BSI</td>
<td>Bloodstream Infection</td>
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<tr>
<td>CBC</td>
<td>Complete Blood Count</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CFU</td>
<td>Colony-forming units</td>
</tr>
<tr>
<td>CHG</td>
<td>Chlorhexidine gluconate</td>
</tr>
<tr>
<td>COS</td>
<td>Chief of Services</td>
</tr>
<tr>
<td>CRBSI</td>
<td>Catheter-related bloodstream infection</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
</tr>
<tr>
<td>CVC</td>
<td>Central venous catheter</td>
</tr>
<tr>
<td>DOM</td>
<td>Department Operation Manager</td>
</tr>
<tr>
<td>GM(N)</td>
<td>General Manager (Nursing)</td>
</tr>
<tr>
<td>HA</td>
<td>Hospital Authority</td>
</tr>
<tr>
<td>HAI</td>
<td>Hospital acquired infection</td>
</tr>
<tr>
<td>HDU</td>
<td>High Dependence Unit</td>
</tr>
<tr>
<td>IC</td>
<td>In-charge</td>
</tr>
<tr>
<td>ICT</td>
<td>Infection Control Team</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
</tr>
<tr>
<td>IJV</td>
<td>Internal jugular veins</td>
</tr>
<tr>
<td>MDRO</td>
<td>Multiple drug resistance organism</td>
</tr>
<tr>
<td>Abbr.</td>
<td>Description</td>
</tr>
<tr>
<td>-------</td>
<td>-------------</td>
</tr>
<tr>
<td>MRSA</td>
<td>Methicillin resistance Staphylococcus Aureus</td>
</tr>
<tr>
<td>NICU</td>
<td>Neonatal Intensive Care Unit</td>
</tr>
<tr>
<td>PICC</td>
<td>Peripherally inserted central catheter</td>
</tr>
<tr>
<td>PICO</td>
<td>Patient, Intervention, Comparison, Outcomes</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized Control Trial</td>
</tr>
<tr>
<td>RN</td>
<td>Registered Nurse</td>
</tr>
<tr>
<td>SIGN</td>
<td>Scottish Intercollegiate Guidelines Network</td>
</tr>
<tr>
<td>SNO</td>
<td>Senior Nursing Officer</td>
</tr>
<tr>
<td>SPSS</td>
<td>Statistical Package for Social Sciences</td>
</tr>
<tr>
<td>VRE</td>
<td>Vancomycin Resistance Enterococcus</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
<tr>
<td>WM</td>
<td>Ward Manager</td>
</tr>
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</table>
CHAPTER 1

INTRODUCTION

1.1 Introduction

Central venous catheter (CVC) is a tunneled or non-tunneled catheter, which is passed through a vein to end up in the thoracic portion of the vena cava or in the right atrium of the heart (e.g. Hickman® and HemoStar® catheter), or through vein in the arm (which is also known as peripherally inserted central catheter (PICC)). CVCs are commonly inserted and maintained in hemato-oncology patients who required indwelling venous catheters for access for a certain period of time. CVCs would facilitate intravenous medication administration frequently, fluid infusion, blood product transfusion and blood sampling taking. The use of CVC can facilitate doctors and nurses for procedures. Moreover, the use of CVC would reduce patients’ discomfort from frequent blood sample taking and intravenous access setting. This would also greatly reduce the risk of intravenous extravasation in peripheral veins due to the administration of chemotherapies and certain types of intravenous medications, which would result in a better patient’s outcome.

However, the use and maintenance of CVC are associated with substantial infection risks, which leading to increase in mortality and morbidity (Blot, et al., 2005; Dimick, et al., 2001). Especially for the hemato-oncology patients who are suffering from neutropenia after receiving chemotherapies or due to their malignancies, they pose a higher risk of local and systematic infections (Guinan, et al., 2003). Catheter-related bloodstream infection (CRBSI) is the most critical and life threatening complication that could occur in catheterization,
which the mortality rate is up to 12-25%, causing around 62,000 death every year in U.S.A. (CDC, 2011).

Guidelines are developed and strategies are implemented previously to prevent the incidence of CRBSI. The migration of skin organisms at the insertion site of catheter with the colonization of the catheter tip is the most common route of infections for CVCs (CDC, 2011); thus, the key element in the prevention of CRBSI is preventing the pathogens colonization at the exit site of CVCs. Chlorhexidine gluconate (CHG) impregnated dressing, which contains a 2% (w/w) chlorhexidine gluconate aqueous-based gel, is introduced and applied as a preventive measure of CRBSIs. With broad-spectrum efficacy, substantivity for the skin, low irritation and low toxicity (McDonnell, & Russell, 1999), the application of CHG impregnated dressing is supported by evidence as a better choice of dressing material for both protection and security of CVC, and as an effective measure in prevention of CRBSIs.

1.2 Background

Potent neoplastic chemotherapies and advances in supportive care have prolonged the survival rates for patients with hemato-oncology malignancies (Guinan, et al., 2003). However, due to more severe and prolonged immunosuppression caused by the treatments and underlying malignancies, infections remained the major cause of morbidity and mortality among cancer patients (CDC, 2011; Maschmeyer, & Haas, 2008).

Patients with hemato-oncology malignancy often required the placement of indwelling intravenous access devices (i.e. CVCs), which increased the risk for infectious complications
CRBSI is one of the most frequent health-care-associated infections (HAIs) (Guinan, et al., 2003), which accounts for about 250,000 HAIs, causing around 62,000 deaths (mortality rate 12-25%) every year in the U.S.A. (CDC, 2011). In prospective surveillance studies, in adult cancer patients, 1.1 to 7.5 CRBSIs occurred in every 1,000 CVC days; where in hematology patients, the prevalence was much higher with 20.3 to 22.0 CRBSIs occurred in every 1,000 neutropenic days (Hentrick, et al., 2014). In the Department of Medicine of one of the regional acute hospitals in Hong Kong, the rate of CRBSIs in hematology patients ranged from 5.00 to 15.15% in between 2009 to 2014 (See Figure 1). Patients with CRBSI have to receive additional antibiotics and inotropes; due to the sepsis effects caused by CRBSIs, some cases even have to admit to intensive care units and undergo an additional period of mechanical ventilation support. Some of them even have to have the catheter change. All these would result in a longer period of hospitalization (Blot, et al., 2005). According to Dimick, et al. (2001)’s study, one single incidence of CRBSI was associated with an increase of HKD 432,486 in total hospital cost.

<table>
<thead>
<tr>
<th>CRBSI Rate (%)</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15.15</td>
<td>6.45</td>
<td>13.33</td>
<td>7.32</td>
<td>9.76</td>
<td>5</td>
</tr>
</tbody>
</table>

Figure 1: The rate of CRBSI in hematology patients (year 2009-2014) in a regional acute hospital in Hong Kong
The presence of indwelling venous catheters is one of the patient-related factors correlated with the development of bloodstream infections (BSIs) have been identified by large epidemiological analyses in Maschmeyer & Haas (2008)’s study. With the compromised immune system related to underlying malignancy treatment and the immune response, hemato-oncology patients, who receive treatment frequently via their CVCs that remain in place for a certain long period of time, would carry a higher risk of infecting the blood with bacteria (Guinan, et al., 2003). A strong correlation between the presence of CVC and HAI development was demonstrated in Guinan, et al. (2003)’s study. Infection of CVCs occurs from two routes. First is the extra-luminal colonization, where endogenous skin flora at the CVC insertion site migrated along the external surface of the catheter and colonized the intravascular tip; second would be the intra-luminal colonization, where pathogens from the contaminated hub moved along the internal surface of the CVC and colonized the lumen (Dimick, et al., 2001). The World Health Organization (WHO) and the Hospital Authority (HA) of Hong Kong have published guidelines on strategies for prevention of catheter-related infections, including the choice of catheter insertion sites, type of catheter material, hand hygiene and maximal sterile barrier precautions during the insertion of CVCs, and choices of skin disinfectants (HAHO, 2015; WHO, 2015), so to prevent the intra-luminal and extra-luminal colonization of CVC. Moreover, WHO has updated the guideline on caring for a patient with a CVC in 2015, where the importance of ‘scrub the hub’ with alcohol-based chlorhexidine-gluconate for at least 15 seconds was emphasized. The practice of ‘scrub the hub’ would greatly reduce the risk of hub contamination, which causing intra-luminal colonization, and effectively reduce CRBSI (Bjorkman & Ohlin, 2015).

However, the most common route of infections in CVC is the migration of skin organisms at the insertion site of CVC (CDC, 2011). In Luft, et al. (2010)’s randomized clinical trial
(RCT), skin colonization at the insertion site was a predictor of CVC-tip colonization and a predictor of BSI in hematology patients. Thus, other than the maximal sterile barrier precautions during the insertion of CVCs, the care of exit site of CVC would be another key consideration, and the disinfectant use for CVC exit site and the CVC exit site dressing would be the major means to prevent colonization of organisms and incidence of CRBSI.

Nurses would be the key holders to monitor the catheter site condition, apply measures to prevent catheter colonization and look for early signs and symptoms of CRBSIs.

1.3 Affirming the Need

For the disinfectants used in CVC dressing, WHO, the Centers for Disease Control and Prevention (CDC) and HA in Hong Kong have recommended the use of >0.5% chlorhexidine preparation with alcohol; if there is contraindication to chlorhexidine, use of tincture of iodine, an iodophor, or 70% alcohol as alternative of antiseptic (CDC, 2011; HAHO, 2015; WHO, 2015). However, there is still no standard guideline developed in local or international institutions on the catheter site dressing regimens. WHO, CDC and HA in Hong Kong have no standard recommendation on the dressing materials for CVC exit site. Sterile gauze, transparent dressing, semipermeable transparent dressings are all recommended for CVC care (CDC, 2011; HAHO, 2015; WHO, 2015), which result in inconsistent in daily practice. CHG impregnated dressing is developed and introduced as an effective measure in preventing catheter site colonization and reducing the rate of CRBSI (Guinan, et al., 2003). Researchers have looked into its effect and have evaluated its clinical and economic impacts.
CHG impregnated dressing is semi-permeable transparent polyurethane dressing with transparent aqueous-based gel, which containing 2% (w/w) chlorhexidine gluconate. It was developed for ease of inspection of skin condition, security, protection, with low toxicity and limited systemic or bodily absorption (WHO, 2009). Previous study also showed that the delivery of antiseptic in CHG impregnated dressing was up to 10 days (Karpanen, et al, 2011), which would greatly reduce the catheter colonization and incidence of CRBSIs. In previous studies, CHG impregnated dressing has demonstrated its broad-spectrum antimicrobial activity against coagulose-negative staphylococci, Staphylococcus aureus, enterococci and Candida supp. (Bhende, et al, 2004; Echague, et al, 2010; Kawamura, et al, 2014), which are the most common pathogens causing CRBSIs (CDC, 2011; Hentrick, et al., 2014). The application of CHG impregnated dressing has greatly reduced the rate of CRBSI by 60% in Roush (2009) and Wall, et al (2014)’s studies; and its efficacy in reducing the incidence of CRBSIs was further been proved in other studies (Garland, et al, 2001; Karpanen, et al, 2011; Ruschulte, et al, 2009; Timsit, et al, 2009; Timsit, et al., 2012). Moreover, it is supported by evidence that it is a safe practice to change the CHG impregnated dressing every 7 days with no significant increase in both the rate of local and systematic infections (Garland, et al, 2001; Roush, 2009; Rasero, et al, 2000), which would greatly reduce patient’s discomfort from changing dressing frequently, and this would also greatly reduce the workload of nursing staff. From Crawford, et al. (2004)’s RCT, the estimated potential annual net benefits from the use of CHG impregnated dressing ranged from HKD 2.15 billion to HKD 15.37 billion.

With the high demand use of CVC in hemato-oncology patients and the emphasis on the prevention of CRBSI, it is necessary to review the effectiveness of the use of CHG impregnated dressing as a standard dressing material for CVCs and the development of an evidence-based guideline of its use for hemato-oncology patients with CVCs.
1.4 Objectives and Significance

In response to the affirming needs, an evidence-based guideline of using CHG impregnated dressing in preventing CRBSIs in hemato-oncology patients with CVCs would be developed. The following objectives would be achieved in this dissertation.

1) To systematic evaluate the current evidence on the use of CHG impregnated dressing in hemato-oncology patients with CVCs in preventing CRBSIs.

2) To develop an evidence-based guideline of using CHG impregnated dressing in preventing CRBSIs in hemato-oncology patients with CVCs.

3) To assess the transferability and feasibility of implementing the evidence-based guideline in a regional hospital in Hong Kong.

4) To develop an implementation and evaluation plan for the implementation of the evidence-based guideline in a regional hospital in Hong Kong.

With the implementation of an effective evidence-based guideline, the incidence of CRBSIs would be greatly reduced. The use of CHG impregnated dressing, with changing every 7 days, was supported by evidence to be a safe practice, and it is effective in preventing catheter colonization, cost effective and also promote patients’ outcome in hemato-oncology patients. For health-care professionals, CHG impregnated dressing is user-friendly, no additional training would be needed for nurses, time could be saved and workload would also be greatly reduced with a reduction of frequency of dressing changing schedule (Olson, et al., 2008). Moreover, standardizing the care practice could greatly reduce the problems common with learning ‘on the job’ and reduce the variation in different practice. The development of evidence based guideline would provide information to the nursing staff and remind them the
important point in day-to-day patient care, which would result in better performance. For economic impact, the additional economic outcome associated with the incidence of CRBSI would be greatly reduced.
CHAPTER 2
CRITICAL APPRAISAL

2.1 Search Strategies

A comprehensive literature search was performed in three electronic databases, including PubMed, Medline and Cochrane Library from 1st August 2015 to 30th November 2015. Constraints were set for full text available studies with human species, publication date from 1st January 2000 to 30th November 2015. ‘Chlorhexidine gluconate impregnated dressing’, ‘chlorhexidine impregnated dressing’, ‘central venous catheter’, and ‘catheter related bloodstream infection’ were the keywords used in searching. After searching, titles and abstracts of the retrieved manuscripts would be screened carefully. For those satisfied the inclusion criteria, full text of paper would be reviewed for eligibility.

Inclusion criteria for study selection

For studies which meeting the following criteria would be included:

✓ Study was a RCT in all languages
✓ Characteristics of the study group:
  ➢ All age group, including pediatric patients
  ➢ With CVC (including the tunneled, non-tunneled, and PICC)
  ➢ In intensive care settings or general in-hospital settings
✓ Use of CHG impregnated dressing would be the study intervention of the intervention group
✓ Study outcome would mainly concern on catheter related infections (including catheter site colonization and CRBSI)
Exclusion criteria

For studies which meeting the following criteria would be excluded:

- Pilot studies, vitro studies, or studies concerned on economic impact of the use of CHG impregnated dressing
- Studies, which are looking for other factors, other than the dressing materials, related to CRBSI.
- Studies in out-patient settings

Full text of the eligible studies would be extracted for further analysis. Information about the study design, randomization and concealment methodology, intervention group and control group baseline characteristics, drop out rate, outcome measurements are analyzed.

2.2 Appraisal Strategies

The Scottish Intercollegiate Guidelines Network (SIGN) ‘SIGN 50’ framework would be used for critical appraisal of the each of selected literatures for grading their level of evidence. The SIGN methodological assessment is a reliable and valid assessment tool, which is ‘based on a number of criteria that focus on those aspects of the study design that research has shown to have a significant effect on the risk of bias in the results reported and conclusions drawn’ (SIGN, 2014, p.11). With the use of the SIGN methodology checklist, the risk of bias and the heterogeneity of each study could be evaluated; and thus the levels of evidence could be concluded. For RCTs, the level of evidence rank from 1- to 1++, where 1- is for RCTs with a high risk of bias, and 1++ if for high quality with a very low risk of bias (see Table 2: Levels of Evidence in Appendix III) (SIGN, 2014).
2.3 Result

The search was conducted from 1st August 2015 to 30th November 2015 in in three electronic databases, including PubMed, Medline and Cochrane Library. A total number of 1,589 RCTs were sorted out with using ‘chlorhexidine gluconate impregnated dressing’, ‘chlorhexidine impregnated dressing’, ‘central venous catheter’, and ‘catheter related bloodstream infection’ as keywords for searching. Total 48 articles were sorted out after primary screening of the topics, and 37 manuscript of which were excluded after secondary screening of the abstract. After final screening of the full text articles, only six out of eleven articles are achieving all the inclusive criteria. Kawamura, et al. (2014) was also excluded after looking into the study design and the evaluation methodology, which the sample size was too small (recruited only 32 patients in total), the subject assignment was done according to the date of admission, which was a poor randomization method, and the evaluation method was not clearly defined. Finally, five RCTs were selected (Garland, et al., 2001; Levy, et al., 2005; Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012). The mechanism of the search flow is showed in Figure 2: PRISMA flowchart.
Records identified through PubMed and Medline (n = 9,379)

Additional records identified through Cochrane (n = 907,952)

Records after duplicates removed (n = 1,589)

Records screened (n = 48)

Records excluded (n = 37)

Full-text articles assessed for eligibility (n = 11)

Full-text articles excluded, with reasons (n = 5)

Studies included in qualitative synthesis (n = 6)

Studies included in quantitative synthesis (meta-analysis) (n = 5)
Study Characteristics

The eligible five RCTs were conducted between 2001 and 2012, which two in France (Timsit, et al., 2009; Timsit, et al., 2012), one in Germany (Ruschulte, et al., 2009), one in U.S. (Garland, et al., 2001), and one in Israel (Levy, et al., 2005). All study protocols of the eligible studies were approved by either the ethics committee or the investigational review board of the regional institutions. Informed consents from the participants were obtained in all of the six studies.

All eligible studies were evaluating the effectiveness of the use of CHG impregnated dressing in reducing catheter-related infections.

Summary of methodology and quality assessment

Of the five eligible RCTs, after the methodology and quality assessment with the use of ‘SIGN 50’ framework, three of them have a high quality of evidence, which are graded of 1++ (Timsit, et al., 2009; Timsit, et al., 2012; Ruschulte, et al., 2009); two of which have an acceptable quality of evidence and are graded of 1+ (Garland, et al., 2001; Levy, et al., 2005). The table of evidence (see table 1) as the summary table of the eligible studies is attached in Appendix I, where the individual assessments of the methodology and quality of each study with the use of SIGN methodology checklist for controlled trials are attached in Appendix VIII.

All studies addressed an appropriate and clearly focused question in PICO (patient, intervention, comparison, outcome) format, which all were targeting to assess the effectiveness of the use of CHG impregnated dressing in reducing catheter-related infections.
For the randomization method, two studies were using web-based random-number generator to select permuted blocks of eight (Timsit, et al., 2009; Timsit, et al., 2012), one study’s subject assignment was done according to computer-generated identification numbers (Ruschulte, et al., 2009), one study in which the randomization was done by random number generator (Levy, et al., 2005), while another study was using computer-generator randomization codes developed by the study statistician, which were maintained by center pharmacists (Garland, et al., 2001).

For the method of concealment, four studies were used adequate concealment methods with the use of web-based random-number generator or computer-generator randomization codes (Garland, et al., 2001; Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012), while Levy, et al. (2005)’s study had not provided any information or details on the method of concealment.

For the ‘blinding’ levels, it was not feasible to ‘blind’ the patients and nurses, as the dressing materials were totally different in appearance, however, it is feasible to ‘blind’ the microbiologists who processing the skin and catheter culture and for the assessors too. Thus, single ‘blinding’ for the microbiologists was used in Levy, et al. (2005)’s study, and double ‘blinding’ for both the assessors and microbiologists was used in Timsit, et al. (2009) and Timsit, et al. (2012)’s trials. However, two of the five studies had not mentioned about ‘blinding’ for any levels (Garland, et al., 2001; Ruschulte, et al., 2009).

For the demographic characteristics reporting, all of the eligible studies have reported the baseline characteristics of both study groups. Three studies even performed the statistical analysis on baseline characteristics of both study groups (Garland, et al., 2001; Levy, et al.,
2005; Ruschulte, et al., 2009), giving the p-value of ≥ 0.05, which meant the baseline demographic characteristics of each study group did not affect the study results. In two trials, the demographic characteristics were fully reported in their papers, with no significant difference (Timsit, et al., 2009; Timsit, et al., 2012); however, the absence of statistical analysis would not be a good practice.

In four eligible studies, both the intervention group and control group were equally treated, including the choice of catheter insertion sites, type of catheter material, hand hygiene, maximal sterile barrier precautions during the CVCs insertion, and choices of skin disinfectants; expect the dressing material used for the CVC insertion site, which was the treatment under investigation (Levy, et al., 2005; Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012). However, in Garland, et al. (2001)’s trial, not only the dressing materials used on the CVC insertion site was different between the groups, the skin disinfectants used before CVC insertion were also different (70% isopropyl alcohol used in the intervention group and 10% povidine-iodine used in control group). Moreover, the frequencies on dressing change were also different (dressing change every seven days in the intervention group, while twice weekly in control group). All these factors would also affect the study result, and increase the risk of bias.

Of the five eligible studies, all relevant outcome evaluations were clearly defined and mentioned, including the method of collecting specimen and the definitions of evaluation criteria, which are all standard, valid and reliable methods.
For the ‘intention to treat’ analysis, four studies had mentioned in their papers (Garland, et al., 2001; Levy, et al., 2005; Timsit, et al., 2009; Timsit, et al., 2012). Only Ruschulte, et al. (2009)’s paper had not mentioned any information about ‘intention to treat’ analysis.

Three studies have reported 0% drop out before their studies were completed (Garland, et al., 2001; Levy, et al., 2005; Timsit, et al., 2012). Ruschulte, et al. (2009) reported only one patient (which the drop out rate was 0.17%) refused to further participate and receive the regular treatment. In Timsit et al. (2009)’s trial, 5.88 and 7.69% drop out in both the intervention group and control group reported respectively. The dropped out participates were mainly due to omission by intensive care unit (ICU) nurses, sudden death, accidental catheter removal and sample tube broken. However, the drop out rate was still within the acceptable range, thus Timsit, et al. (2009)’s study would not be downgraded.

2.4 Data Summary

The eligible studies were conducted between 2001 and 2012. The studies were conducted in France (Timsit, et al., 2009; Timsit, et al., 2012), in Germany (Ruschulte, et al., 2009), in U.S. (Garland, et al., 2001), and in Isral (Levy, et al., 2005).

Three of the five studies were multi-centered trials, which Timsit, et al. (2009) carried out their trial in seven ICUs in three university and two general hospitals, Timsit, et al. (2012)’s trial in twelve ICUs in seven university and four general hospitals, Garland, et al. (2001)’s study in six level III neonatal intensive care units (NICUs) in four university and two community hospitals. The generalizability of these three studies was higher. While the other
two carried their trials in one hospital or one medical center, in which generalizability was lower (Levy, et al., 2005, Ruschulte, et al., 2009).

For the sample size, all the five studies have showed the sample size calculation clearly in their studies with giving the value of $\alpha$ (type 1 error) and $\beta$ (type 2 error) in their calculation. 705 neonates were enrolled in Garland, et al. (2001)’s study, 601 patients were recruited in Ruschulte, et al. (2009)’s, 2095 patients were enrolled in Timsit, et al. (2009)’s study, 1879 patients were recruited in Timsit, et al. (2012)’s study. All these four trials’ sample sizes were large enough to show the intervention effect. In Levy, et al. (2005)’s trial, although the sample size calculation was clear, the sample size (only 71 patients were enrolled) was still too small to reflect the study result.

Three studies carried out in adult patients, with two studied in patients in ICU (Timsit, et al., 2009; Timsit, et al., 2012), one study conducted in high dependency unit (HDU) where patients undergoing chemotherapy for haematological or oncological malignancies (Ruschulte, et al., 2009); two studies carried out in pediatrics patients, which Levy, et al. (2005) studied in pediatrics cardiac ICU, where patients underwent invasive cardiothoracic procedures and Garland, et al. (2001) studied in NICU.

The median age in the five eligible trials ranged from 2.2 years old to 64 years old. Two studies enrolled similar percentage of both genders (Garland, et al., 2001; Ruschulte, et al., 2009), while Levy, et al. (2005) recruited a bit too many female patients (~63.6%) and the other two enrolled a bit too many male patients (64.3% - 66.8%) (Timsit, et al., 2009; Timsit, et al., 2012). Patients recruited in all eligible studies were all critically ill or immunosuppressed due to the treatment undergo. In these groups of patients, antibiotics are
commonly used for therapeutic or empirical purposes. However, only Garland, et al. (2001) had reported the types of antibiotics used in the participants, which is an important factor affecting the culture results, and the risk of bias. As the prevalence of multidrug resistant organisms (MDROs) is increasing steadily globally (Siegel, et al., 2006), screening for colonization of MDRO (including Methicillin resistant Staphylococcus aureus (MRSA), Vancomycin resistant enterococcus (VRE), Pseudomonas aeruginosa resistant to multiple antibiotics) for these groups of patients maybe necessary, as the colonization would also affect the study result.

The insertion sites of CVCs in four eligible studies included the internal jugular veins (IJV), subclavian veins and femoral veins (Levy, et al., 2005; Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012). Garland, et al. (2001) did not report any information on the insertion site of CVC. Tunneled, non-tunneled, single to triple lumen catheters were included in four trials (Garland, et al., 2001; Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012), while Levy, et al. (2005) had not reported on the types of catheter included in their study.

All five studies were investigating the effectiveness of CHG impregnated dressing as compared with sterile semipermeable transparent dressing in reducing catheter related infections. Three studies had the dressing change scheduled every seven days (Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012). In Garland, et al. (2001)’s trial, the dressing were changed every seven days in intervention group, and twice weekly in control group. All the four studies mentioned that the dressing would be changed due to lifted up for inspection control, mechanical complications, bleeding, oozing, or any signs of infections (including redness and pain) (Garland, et al., 2001; Ruschulte, et al., 2009; Timsit, et al.,
2009; Timsit, et al., 2012). No information regarding the schedule of changing dressing was reported in Levy, et al. (2005)’s study. Alcohol based povidine-iodine solution and alcoholic chlorhexidine were used as dressing lotions for CVC in Levy, et al. (2005), Timsit, et al. (2009) and Timsit, et al. (2012)’s studies. In Garland, et al. (2001)’s trial, 70% isopropyl alcohol was used for skin antisepsis in intervention group, while 10% povidone-iodine was used in control group. Ruschulte, et al. (2009) missed the information on the antiseptic solution used in their study.

Four eligible studies had clearly defined the diagnosis of skin colonization as based on the quantitative culture by roll-plate technique (Garland, et al., 2001; Levy, et al., 2005; Timsit, et al., 2009; Timsit, et al., 2012); however, the number of yielding colony-forming units (CFUs) per ml was various among the studies, which ranged from greater than or equal to 15 CFUs/ml up to 1,000 CFUs/ml. All the five eligible studies were defined the diagnosis of CRBSI based on clinical assessment, laboratory investigation and vivo culture technique.

2.5 Data Synthesis

For five eligible studies, they targeted patients from neonatal to adults, in all age and both genders, which supported the effectiveness of CHG impregnated dressing in CVC-related infection reduction. Two trials carried out in adult ICUs (Timsit, et al., 2009; Timsit, et al., 2012), while the other two trials were conducted in pediatric cardiac ICUs and NICUs (Garland, et al., 2001; Levy, et al., 2005). Patients in ICUs are usually found their immune system insufficient functioning due to their poor prognosis (Januszkiewicz, et al., 2007), which are similar to the hemato-oncology patients who are commonly found to be immunosuppressed due to the treatments received and their underlying malignancies. The
four selected studies showed the effectiveness of the CHG impregnated dressing in reducing catheter colonization and the incidence of CRBSI in this group of immunosuppressed patients (Garland, et al., 2001; Levy, et al., 2005; Timsit, et al., 2009; Timsit, et al., 2012). Ruschulte, et al. (2009)’s study further supported the evidence, in which the trial was conducted in HDUs where patients undergoing chemotherapies for hematological or oncological malignancies.

Four eligible studies demonstrated the effectiveness of using CHG impregnated dressing in reducing the catheter colonization in CVCs inserted in IJVs, subclavian veins and femoral veins (Levy, et al., 2005; Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012). The CHG impregnated dressing even showed its effectiveness in tunneled, non-tunneled, single to triple lumen catheters in four of the five selected trials (Garland, et al., 2001; Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012).

Alcohol based povidine-iodine solution, alcoholic chlorhexidine, 70% isopropyl alcohol and 10% povidone-iodine were used as dressing lotions for CVC in Garland, et al. (2001), Levy, et al. (2005), Timsit, et al. (2009) and Timsit, et al. (2012)’s trials. All these antiseptic are suggested in both the CDC (2011) and HA (2015)’s guideline in caring patients with CVCs.

Four trials have provided evidence supporting the practice in changing CHG impregnated dressing every 7 days as safe practice (Garland, et al., 2001; Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012). However, the frequency of dressing change would be increased by mechanical complications, bleeding, oozing, or signs of infections (including redness and pain), and nurses have to pay attention on this. Moreover, localized contact dermatitis is an adverse effect reported in Garland, et al. (2001) (reported 7 neonates), Timsit,
et al. (2009) (reported 8 patients) and Timsit, et al. (2012) (reported 22 patients)’s studies, regarding the use of CHG impregnated dressings. Thus, assessment and continuous monitoring the CVC site condition would be required with the application of CHG impregnated dressing.

In conclusion, the above evidences are sufficient to support the effectiveness of the use of CHG impregnated dressing in hemato-oncology patients with CVCs in preventing CRBSIs.
CHAPTER 3

IMPLEMENTATION POTENTIAL AND CLINICAL GUIDELINE

In the previous chapters, the impact of CRBSI has been discussed, and the effectiveness of CHG impregnated dressing in preventing CVC site colonization and CRBSI in both adult and pediatric patients have been supported by the evidence explored. In this chapter, the evidence would be translated into clinical practice. The implementation potential of the application of CHG impregnated dressing would be assessed based on target setting, target audience, transferability of the findings, and the feasibility, cost-benefit ratio of the proposed innovation.

3.1 Target setting

The target setting is a hemato-oncology unit of an acute public hospital with capacity of 2973 beds, managed by HA, situated in Hong Kong Island of Hong Kong.

3.2 Target audience

The target audiences include hemato-oncology patients who are

a) Aged 18 or above,

b) Having CVC implementation.
3.3 Transferability

All selected studies were conducted in developed countries, including France, Germany, U.S., and Isral, where having a similar economic background and medical development with Hong Kong. Three studies carried out in adult patients (Ruschulte, et al., 2009; Timsit, et al., 2009; Timsit, et al., 2012), while the other two in pediatrics patients (Garland, et al., 2001; Levy, et al., 2005). The median age of the study groups ranged from 2.2 to 64 years old, and the percentage of both genders recruited were similar. These supported the effectiveness of CHG impregnated dressing in reducing CVC-related infections in all age and in both genders.

Four of the five selected trials were carried out in ICUs (Garland, et al., 2001; Levy, et al., 2005; Timsit, et al., 2009; Timsit, et al., 2012). The immune systems of patients in ICU are usually found insufficient functioning due to their poor prognosis (Januszkiewicz, et al., 2007), while the hemato-oncology patients who are commonly found to be immunosuppressed due to the treatments they undergo and underlying malignancies. Both groups of patients are found to be similar. Moreover, all subjects in the selected studies were having CVC implementation, and their incidence rate of CRBSI was high too, which were commonly found in our target setting. All these four studies showed the effectiveness of CHG impregnated dressing in reducing catheter colonization and the incidence of CRBSI in immunosuppressed patients. Ruschulte, et al. (2009)’s study further supported this evidence, in which the trial was conducted in patients undergoing chemotherapy for hematological or oncological malignancies, which were as same as our target audiences.
3.3.1 The Philosophy of Care

The philosophy of care underlying the proposed innovation is also similar to that in our target hospital. Researchers in the eligible studies aimed at improving the standard of care and providing high quality of nursing care by utilization of evidence-based findings to promote clients’ health and improve clients’ quality of life. The objectives of the selected studies were all aimed at reducing CVC related infections by different measures, which shared the same core value of the target hospital, always concerning patients’ comfort and well-being as their prime concern by delivering high quality service. HA is having the mission of ‘Helping People Stay Healthy’, giving our patients life-saving treatments and empowering their health, the philosophy of care of this proposed innovation which preventing the incidence of CRBSI in hemato-oncology patients having CVC implementation, is congruent with that of the philosophy of care of HA.

3.3.2 Population Benefit from the innovation

From the statistics of our target hospital, a sufficient number of patients would be benefit from the proposed innovation. There were around 5,000 attendances admitted to the target unit annually, and which 30% of them were having CVC implementation. Therefore, there would be around 1,600 patients directly benefit from the proposed innovation. Moreover, as the service would be extended in the target hospital in the coming three years, the number of patients who can benefit from the innovation would be greatly increased in the near future.

3.3.3 Schedule of implementing the proposed innovation

Before the implementation, planning including drafting a detailed protocol, preparation and communication with the stakeholders would be taken twelve weeks. A twelve-week pilot trial
would be run for exploring the feasibility of the proposed innovation. A sixteen-week evaluation would be performed after the pilot trial. Therefore, it would take total forty weeks for the implementation and evaluation of the proposed innovation (Work Plan Schedule is to be seen in figure 3).

<table>
<thead>
<tr>
<th>Item/ Week</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; - 5&lt;sup&gt;th&lt;/sup&gt; week</th>
<th>6&lt;sup&gt;th&lt;/sup&gt; – 10&lt;sup&gt;th&lt;/sup&gt; week</th>
<th>11&lt;sup&gt;th&lt;/sup&gt; – 15&lt;sup&gt;th&lt;/sup&gt; week</th>
<th>16&lt;sup&gt;th&lt;/sup&gt; – 20&lt;sup&gt;th&lt;/sup&gt; week</th>
<th>21&lt;sup&gt;st&lt;/sup&gt; – 30&lt;sup&gt;th&lt;/sup&gt; week</th>
<th>31&lt;sup&gt;st&lt;/sup&gt; – 40&lt;sup&gt;th&lt;/sup&gt; week</th>
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<tr>
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<tr>
<td>(2) Preparation</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>(3) Briefing to all nurses</td>
<td></td>
<td></td>
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<tr>
<td>(4) Pilot run</td>
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<td></td>
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<tr>
<td>(5) Evaluation</td>
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</tbody>
</table>

*Figure 3: Work Plan Schedule*

After comparing the settings in selected studies in the previous chapter and our target setting, the application of CHG impregnated dressing is transferable as the proposed innovation is found to be fit our audience in the target setting.

### 3.4 Feasibility

There are several factors have to be considered while assessing the feasibility of the proposed innovation.

#### 3.4.1 Nursing Autonomy

Firstly, as nurse is the key profession in wound monitoring, prospering infection control to minimize the risk of infection, and also promoting wound healing by nursing knowledge in wound management, thus nurses would have to perform wound assessment regularly and choose the appropriate dressing lotion and dressing materials for the patients. Thus nurses would have the autonomy to carry out or terminate the use of CHG impregnated dressing for
the patients. Moreover, assessment of CVC exit site condition with the application of CHG impregnated dressing have to be performed regularly by nurses to look for any mechanical complications, such as bleeding, oozing or signs of infections and allergy. Therefore, the implementation of the proposed innovation will not interfere with current nursing functions.

3.4.2 Communication with the stakeholders

The administrative stakeholders, including nursing specialists, department and ward managers, and doctors are eager to promote the standard of care and reduce the risk of infections in patients. They are supporting the innovation, and they would also provide comments and information so to refine the proposal. On launching a new intervention in a clinical setting, a well-developed work plan could increase the feasibility. A working group would be formed to discuss the pro and cons, cost and benefit ratio, risk and challenges before the implementation of the proposed innovation. An evidence-based guideline would also be developed so to gain the consensus among nurses and other disciplines. Moreover, a detailed work plan schedule would be developed to assess and evaluate the whole progress.

3.4.3 Potential barrier

Nurses would carry out the proposed program, which does not involve other allied health care profession; thus, there would not be any collaborative problems with other disciplines. The CVC exit site care would be as same as the usual nursing care as before, the only difference and the difficulty is the additional assessment on the fitness of applying CHG impregnated dressing, including checking patients’ allergy history and CVC exit site skin condition. The CHG impregnated dressing is easy to handle and apply, which do not need to spend extra time and extra skill to apply. However, the potential predictable barrier while launching the innovation is the nurses may not willing to choose the new CHG impregnated
dressing, as they got not much idea about the proposed innovation and misunderstand its effectiveness. In order to overcome this barrier and let the nursing staff to get more idea and information about CHG impregnated dressing, before launching the program, there would be six identical lectures given to total 75 nursing staff during their handover period in wards, with each session lasts about 15 minutes, to explain the mechanisms and the application of the CHG impregnated dressing with demonstration performed. The lectures would be held twice a week, and lasted for three weeks so to allow all nursing staff to attend. The training materials would also be circulated among the involved parties for information sharing and referencing.

3.4.4 Resources Management

Furthermore, apart from the new dressing, there is no additional equipment necessary for the proposed innovation. The dressing could be easily purchased through the supplier in Hong Kong, and it is suggested to purchase according to the estimated number of target patients in our setting, while each patient would receive about 10 pieces of CHG impregnated dressing during their period of hospitalization (estimated that each patient would stay about 6 to 10 weeks for every admission). As in the previous chapters, there are strong evidence supporting the application of the CHG impregnated dressing is benefit to the target patients, nursing staff and also the hospital, thus, funding would be applied from the department for purchase.

3.4.5 Evaluation of the innovation

Evaluation would be conducted after twelve-week implementation so to gather information, including the nursing staff feedbacks, patients’ satisfactions, CVC exit site colonization rate and the incidence of CRBSI.
3.5 Cost-Benefit Ratio

The potential risk and benefits result from the implementation of the proposed innovation would be discussed as follow.

3.5.1 Potential risk of implementation of the use of CHG impregnated dressing

In the previous chapters, the evidence explored supported the application of CHG impregnated dressing in reducing CVC exit site colonization and preventing the incidence of CRBSI in hemato-oncology patients who are having CVC implementation. However, the complications of using CHG impregnated dressing were found to be ‘under-research’ and ‘under-investigated’. Localized contact dermatitis is a major complication reported in papers, around 1.49% - 5.9% cases reported of erosive contact dermatitis after applying CHG impregnated dressing (Garland, et al, 2001; Levy, et al., 2005; Timsit, et al, 2009; Timsit, et al, 2012). It is believed that skin lesion developed from contact dermatitis would provide a large entry port for the microorganisms and the risk of local and systematic infections would also be increased, especially in immunosuppressed patients (Weitz, et al., 2013). Moreover, patients would also suffer from severe pain due to the erosive dermatitis. To overcome this complication, nurses should check patient’s allergy history in advance and close monitoring of the CVC exit site condition is necessary to look for signs and symptoms of contact dermatitis. Immediate removal of CHG impregnated dressing is the treatment of contact dermatitis.
3.5.2 Potential benefits result from the implementation of the innovation

CHG impregnated dressing includes a transparent aqueous-based gel, which containing 2% (w/w) chlorhexidine gluconate, which demonstrated its persistent antimicrobial activity on human skin for up to ten days (Karpanen, et al., 2011). In the selected studies, it is found to be a safe practice to get the CHG impregnated dressing to be changed for every seven days with no significant increase the rate of local or systematic infections. Ruschulte, et al (2009)’s trial further demonstrated that the application of CHG impregnated dressing would greatly reduce the incidence of CVC-related infection by 46% in HDU patients undergoing chemotherapies for hematological or oncological malignancies. With such re-scheduling of changing dressing frequency would greatly reduce patients’ discomfort due to changing dressing and improve patients’ outcome. Moreover, as there is no additional training or skills is necessary for applying CHG impregnated dressing, it is easy to manage, and the reduction in changing dressing frequency would further relief nursing staff’s workload (Olson, et al., 2008).

3.5.3 Potential risk and cost of maintaining current practice

The cost of a piece of transparent permeable dressing is around HKD 3.5, while that of a piece of CHG impregnated dressing is approximately up to HKD 35.0. This seems to be not very cost effective, however, as a preventive treatment option, the potential cost saving (including prolonged patient’s length of stay due to infections, cost of extra medications, and admission of ICU for support, etc.) would be around HKD 26,600 to 175, 000 (Pfaff, et al, 2012; Roush, 2009); and from hospital perspective, the potential hospital net cost savings would be up to HKD 6,265,000 annually (Ye, et al, 2011). Furthermore, as no extra training is necessary for the proposed innovation, thus, no extra manpower or extra time needed to be
spared. The proposed innovation has showed to be a cost effective intervention (Ruschulte, et al, 2009; Timsit, et al, 2009).

To conclude the above discussion, the proposed innovation has a high transferability, feasibility, and cost-benefit ratio. An evidence-based guideline (see Appendix II) would be developed in details based on the level of evidence as retrieved in the previous chapter and the grades of recommendations according to the SIGN (SIGN, 2014) as follow.

3.6 Evidence-Based Practice Guideline

✓ Intended users of the proposed guideline
  o Nurses in the target unit

✓ Purpose of the proposed guideline
  o To provide an evidence-based guideline on application of CHG impregnated dressing
  o To build the consensus among nurses on application of CHG impregnated dressing
  o To guide and assist nurses in providing evidence-based care in reducing CVC colonization and incidence of CRBSI

✓ Target population of the proposed guideline
  o Hemato-oncology patients who are having the implementation of CVC
Rating scheme for the strength of the evidence and grades of recommendations

According to the SIGN (SIGN, 2014), the levels of evidence would be ranged from number 1++ to 4, which 1++ with the highest level of evidence with a very low risk of bias and 4 with the lowest as expert opinion; and the grades of recommendations would be ranged from capital alphabet A to E, which A having the highest evidence level and E having the lowest level and as recommended based on the clinical experience of guideline development group (see Appendix III and Appendix IV for details respectively).

Recommendations

- **Recommendation 1:** Assessment before the use of CHG impregnated dressing (Grade B)
  
  Assessment including checking the patient’s allergy history and the skin condition before the use of CHG impregnated dressing.

  Evidence: Patient would be excluded from the study if allergic reactions to chlorhexidine-impregnated foam were noted in Ruschulte, et al. (2009) (1++)’s trial.

- **Recommendation 2:** Assessment of patient’s skin condition before the application of CHG impregnated dressing (Grade A)
  
  Patient’s skin condition should be assessed before and during the application of CHG impregnated dressing. Dressing should be avoided for those skins that are found to be sensitive or fatigue.

  Evidence: The rate of contact dermatitis reported in pediatrics subjects (5.4 – 5.9%) (Garland, et al., 2001 (1+); Levy, et al., 2005 (1+)) were much higher
than that in adult subjects (0 – 2.3%) (Ruschulte, et al., 2009 (1++); Timsit, et al., 2009 (1++); Timsit, et al., 2012 (1++)). It is possible that the skin was found to be more sensitive to the CHG.

- **Recommendation 3**: Frequency of changing CHG impregnated dressing (Grade A)
  
  The CHG impregnated dressing should be changed every 7 days; mechanical complications, bleeding, oozing, leakage or soiling prompted immediate dressing change.


- **Recommendation 4**: Termination of the use of CHG impregnated dressing (Grade A)
  
  The CVC exit site should be inspected and palpated daily and when necessary. The use of CHG impregnated dressing should be terminated immediately when any signs and symptoms of suspected contact dermatitis or skin allergy was noted.

**Evidence:** 7 to 22 patients were reported with localized contact dermatitis in Garland, et al. (2001) (1+), Timsit, et al. (2009) (1++) and Timsit, et al. (2012) (1++)’s studies. And the lesions were resolved after the CHG dressing removed.
CHAPTER 4
IMPLEMENTATION PLAN

In the previous chapter, the guideline of using CHG impregnated dressing in preventing CRBSI in hemato-oncology patient with CVC is developed (see Appendix II) and supported with sufficient research evidence. This chapter will discuss the implementation plan of the proposed innovation, including the communication plan and a pilot study. An evaluation plan would also be finally discussed in this chapter.

4.1 Communication Plan

Communication plan of a proposed innovation would always start with identifying the stakeholders of the innovation and forming a communication team for getting support and sustaining the innovation.

A. Identifying the stakeholders

‘An efficient and effective policy-making process should not rely solely on higher-level decision makers but instead incorporate multiple stakeholders with vested interests, including those who actually implement the health care policy at the patient level as well as those the health care policies address.’ (Irvin, et al., 2007, p. 1031).

Thus, not only the management and administrative level of target hospital are being targeted, the users of proposed guideline (nurses and physicians) would also be targeted as the stakeholders.
1. **Users of the proposed evidence based guideline, who are the key persons required to understand the proposed innovation**

- Ward nurses who are working in the target unit, and would perform the assessment, apply the CHG impregnated dressing, and continuous monitor the CVC exit site condition.
- Physicians of the target unit are also included, as they are the ones managing patients who have got complications with the use of CHG impregnated dressing.

2. **Management level of the target department**

   Advanced practicing nurses (APN) of hematology, ward managers (WMs) Department Operations Managers (DOMs) of the Department of Medicine, are the key decision makers for supporting and approving the innovation.

3. **Administrative level of the target hospital**

   Senior Nursing Officer (SNO) of the Infection Control Team (ICT), General Manager (Nursing) (GM(N)) of the target hospital, the Consultant of Hematology, and the Chief of Service (COS) of the Department of Medicine are all the key persons who make changes of hospital policies as all proposed innovation must be approved by them before implementation.

B. **Communication Plan**

   The implementation of a new innovation was impeded by several (types of) barriers, including lack of agreement, barriers associated with leadership, issues related to evidence-based decision making (Borggreve & Timen, 2015). Therefore, to initiate a
new innovation, effective communication with the stakeholders is essential for gaining their collaboration and ensuring the success in the implementation.

1. **Communication with management and administrative staff**

   The first persons to communicate with would be management level of the target unit as they are the decision makers for the unit protocol. Presenting clinical data indicating less-than-optimal outcomes for patients may motivate practice change, and may simultaneously offer the opportunity to incorporate established guideline into practice (Dulko, 2007). Thus, in order to gain the support from management level of the unit, a formal meeting would be held for introducing the guideline, explaining the proposed innovation and significant of CRBSIs, objectives and content, feasibility and cost benefit of the proposed innovation, and also the implementation plan.

   Another formal meeting would be arranged for the administrative staff with a well-prepared written proposal including the implementation potential analysis and detailed time scheduling. The budget plan would also be explained in details in table 3.
<table>
<thead>
<tr>
<th>Items</th>
<th>Description</th>
<th>Estimated Cost</th>
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</thead>
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<td>Labour Cost</td>
<td>RN (n = 4)</td>
<td>HKD 70,000</td>
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<tr>
<td>Training Material</td>
<td>Assessment Forms</td>
<td>HKD 37.5/75 copies</td>
</tr>
<tr>
<td></td>
<td>Training Materials</td>
<td>HKD 60/3 copies</td>
</tr>
<tr>
<td>Material Costs</td>
<td>CHG impregnated dressing</td>
<td>HKD 8,750/250 pieces</td>
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<td></td>
<td>Evaluation Forms</td>
<td>HKD 200/400 copies</td>
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<tr>
<td></td>
<td>Blood culture sampling</td>
<td>HA</td>
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<td></td>
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<td>Total HKD 79,047.5</td>
</tr>
</tbody>
</table>

*Table 3: Estimated cost for the proposed innovation*

2. **Forming a Quality Improvement Committee for managing CRBSIs**

   After getting the approval from the managers and administrators, a quality improvement committee, which including one administrator and two registered nurses (RNs), would be formed for planning, launching the innovation, providing training workshops for the frontline staff and preparing for the implementation.

3. **Communication with all in-charge (IC) nurses and ward nurses of the target unit**

   The next step would be communicating with all the IC nurses of the target unit. They would be informed through internal electronic mails and briefing for the innovation, so they could facilitate the implementation of innovation. They would be updated with the progress of innovation through electronic mails bi-weekly.

   After the IC nurses received the information, they would spread the message to the other ward nurses of the unit in the briefing sessions in every shift. At the
same time, circular about the innovation with detailed schedule would be circulated and posted on the notice boards.

Training workshops on the application of CHG impregnated dressing would be provided to the frontline nurses of the target unit, as they are the main users of the proposed guideline. WMs would be invited to arrange the nurses to attend training workshops. Six identical 20-minutes workshops, which include the introduction on mechanism of CHG impregnated dressing with demonstration on application, would be conducted by the committee. Skills and knowledge of the participants would be assessed at the end of each workshop so to ensure their competency on applying the CHG impregnated dressing (see the assessment form being used for assessment on the application of CHG impregnated dressing in appendix V).

Training materials would also be circulated among the target unit for information sharing and referencing.

4. *Communication with the physicians of the target unit*

An electronic newsletter about the innovation would be send to all physicians of the target department. Information about the innovation and its benefit would be included in the newsletter.

The committee would also hold a briefing session to the physicians in order to convince them and gain their support for prescribing the CHG impregnated dressing to the patients. Circular about the innovation with the implementation
schedule would be posted on the notice boards; at the same time, a copy of the training material would also be circulated among the physicians for referencing.

4.2 Pilot Study Plan

A pilot study is a small-scale preliminary study for determining feasibility of the innovation, and the study result would be used to check the appropriateness of the proposed innovation, the assessment tools, acceptability by both the patients and the health care professionals, avoid unexpected difficulties, modify limitations before implementing the change in other units, and help to develop a comprehensive budget planning for a full-scale implementation.

A. Objectives of the pilot study

(i). To determine the feasibility of innovation
(ii). To identify barriers and difficulties encountered
(iii). To determine compliance of nurses with the innovation
(iv). To assess the appropriateness of the new innovation, assessment tools used
(v). To evaluate the level of satisfaction towards innovation among patients and nurses
(vi). To assess the acceptability by both the patients and health care professionals.

B. Period of pilot study

The pilot study would be conducted in the target unit after all nurses finished training workshops and completed the assessment on application of CHG impregnated dressing. This pilot study would be last for twelve weeks.
C. Target population and sample size

From the evidence-based guideline proposed in Chapter 3, we are targeting hematologic oncology patients who are (i) having implantation of CVC, and (ii) aged 18 or above.

Forty patients would be recruited in this pilot study and convenience sampling would be adopted. Patients would be recruited 20 from male ward of the target unit (Ward A) and 20 from female ward (Ward B). Both group of patients are similar in terms of patients’ characteristics, nurses’ background and patient’s management.

D. Outcome measures - Level of satisfaction assessment and Compliance Rate

To assess acceptability of the innovation, questionnaire would be given to patients of the intervention group on day 7 after applying CHG impregnated dressing so to assess their level of satisfaction towards the innovation by using a 5-point scale (See appendix VI). An open-ended question would also be included for their recommendations.

Apart from patients, nurses are also invited to provide comments about any barriers or difficulties encountered during launching the innovation. Questionnaire (see appendix VII) would also be given to nurses to assess their level of satisfaction, workload and job satisfactions towards the innovation.

Feedbacks have shown to promote adoption and improvements in practice behaviors and clinical outcomes (Dulko, 2007). Thus, all these questionnaire and comments would be collected and analyzed by the committee for identifying barriers and difficulties so to refine innovation.
E. **Cost and risk evaluation**

Actual cost, including all material and non-material cost used for this pilot study would be calculated. Information about unexpected costs (e.g. costs for managing complications caused by the use of CHG impregnated dressing) and time-consumption would be used for refinement of the innovation, and this data would also be used for estimating the feasibility in using a larger-scale population, such as 5,000 attendances in the target unit annually.

F. **Modification and approval of the innovation**

The nurse compliance rate of the innovation and the level of satisfaction towards the innovation among patients and nurses would be analyzed. A formal written report, including result of the pilot study, patient and staff satisfaction level, cost and risk evaluation, would be prepared for meeting with administrative and management staff. Recommendations from both patients and staff would also be discussed. Modification of the innovation would be discussed and approval would be sought for launching the full-scale implementation of the innovation.

4.3 **Evaluation Plan**

‘Accountability for process and outcome is likely the most vital part of a guideline implementation program’ (Dulko, 2007, p.203). Evaluation would be an important process when launching a new innovation, which identifying the achieved outcomes. The following parts would discuss about the evaluation plan of this innovation.
I. Identifying outcomes to be achieved

The outcomes would be measured based on patient outcomes, healthcare (staff) outcomes and system (hospital) outcomes.

- **Patient outcomes**
  
  As mentioned in the previous chapter, based on the reviewed evidence, the main patient outcome is to measure incidence of CRBSIs. Besides, patient’s level of satisfaction towards the innovation would also be assessed. The outcomes would be assessed, and analyzed by the committee to determine the effectiveness of innovation.

- **Staff outcomes**
  
  Nurses compliance rate on the innovation would greatly affect the effectiveness of innovation and patient’s outcome. Therefore, the committee would visit the target unit twice weekly to audit staff compliance.

  Moreover, staff satisfaction level towards the innovation would also be assessed by using the 5-point scale (see appendix VII) at the end of the implementation period.

- **Hospital outcomes**
  
  There would be several components to measure the hospital effectiveness. As mentioned in the previous chapter, a committee would perform the cost evaluation. Furthermore, the length of hospitalization of patients, usage of
antibiotics, admission rate to intensive care units for managing CRBSIs would also analyzed for the cost-benefit ratio.

II. Nature and number of clients to be involved

From the proposed guideline, we are recruiting (i) hemato-oncology patients, who are (ii) having CVC implantation, and (iii) aged 18 or above in the evaluation plan from 3rd October 2106 to 22nd January 2017 for 16 weeks.

Full-scale implementation is one group design with all clients receiving CHG impregnated dressing. Evaluation objective is to determine the effectiveness of CHG impregnated dressing in reducing incidence of CRBSI, while the incidence would be compared with previous years data in the target unit.

From previous data of the target unit, the incidence rate of CRBSI was about 13.33%, thus the null value ($P_0$) would be taken as 0.133. The actual value ($P$) would be taken as 0.063 (taking the evidence from Ruschulte, et al (2009)’s trial, which having the same target population as ours). By using the 2-tailed $\chi^2$ test for testing one population with the use of Java applets for power and sample size (2015) online software, the sample size would be at least 154 patients, with alpha of 0.05 and power of 0.80.

III. Methods of taking measurements and the length of follow up

As mentioned before, the innovation would be implemented from 3rd October 2016 to 22nd January 2017 for total 16 weeks. Measurements would be taken according to different outcomes to be achieved.
For patients, measurement of the incidence of CRBSIs would be done in the target unit. With the application of CHG impregnated dressing, daily CVC exit site assessment would be performed and documented by case nurse following the guideline practice (see appendix II). Daily blood specimens for inflammatory markers (including complete blood count (CBC) and C-reactive protein (CRP)) would be taken for laboratory assessments. If (i) clinical signs of tenderness, erythema or swelling around the CVC exit site, or (ii) elevated inflammatory markers levels which suggested infections, or (iii) patients was found febrile with body temperature equal to 38 degree Celsius or above, three sets (two from each lumen of CVC and one from peripheral venipuncture after skin being disinfected) of blood specimen for culture growth would be taken. Diagnosis of CRBSI would be made by physicians based on the clinical presentation and bacteria growth from the blood specimen.

Besides, patient’s level of satisfaction towards the innovation would also be measured. Questionnaire (see appendix VI) would be distributed to patients and collected by the committee on the day of their discharge.

For staff, nurse compliance towards the innovation would be assessed by the committee who would visit the unit three times per week randomly during the implementation period for auditing (see appendix V as the assessment form). Staff satisfaction level towards the innovation would also be measured by distributing questionnaire (see appendix VII), which would be collected at the end of implementation period (that would be 9th to 22nd January 2017). For intermediate
measurement, the committee would ask staff for comments and difficulties encountered in between the implementation period during their ward visit.

For hospital, expenses including material and non-material expense for the innovation implementation would be evaluated by the committee. Besides, as mentioned before, the additional expenses used for managing the adverse events caused by application of CHG impregnated dressing would also be reported. The analysis would be performed from 23th January to 12th February 2017.

IV. Methods of analysis

Descriptive statistics would be used for analyzing demographic data of the patients including age, gender, underlying diseases, neutropenia days and catheterization days. All outcomes including the incidence of CRBSIs, usage of antibiotics and length of stay would be statistically analyzed by a Statistical Package for Social Sciences (SPSS). All outcome measures would be compared with the previous data of target unit.

Besides, patient and staff satisfaction levels and comments on the innovation would also be collected and analyzed with identification of categories key themes and patterns.

2-tailed \(x^2\) test would be used for testing the change proportion, which would determine the effectiveness of innovation in reducing incidence of CRBSIs. Furthermore, length of stay and usage of antibiotics would be measured and compared with the previous data. The confidence interval would be taken as 95%.
Nurse compliance would be evaluated by auditing. 80% compliance with 100% critical items done would be counted as ‘Pass’ in the auditing. The assessment would be stopped once critical items were being violated. If the staff got ‘Fail’ in the first attempt, individual training session would be arranged to reinforce the staff’s knowledge on current CVC care and reassessment would be performed one month later so to allow the staff to practice.

4.4 Basis for Implementation

The innovation would be considered as effective based on the outcome achievements, including reducing incidence of CRBSI and enhancing satisfaction among patients and staff.

Patient’s outcome

Effectiveness of the innovation would be determined by comparing the findings between eligible studies and the target setting. From the reviewed evidence, incidence of CRBSI with the use of CHG impregnated dressing has showed to be reduced by 0.6 – 60% (Garland, et al. (2001), Levy, et al. (2005), Ruschulte, et al. (2009), Timsit, et al. (2009), Timsit, et al. (2012)). Thus the innovation would be considered as effective if the incidence of CRBSI was reduced by 40% when compared with the previous data of setting.

Patient and staff satisfactory level

More than 50% of participants rank 3 or above for satisfactory level among patients and staff towards the innovation by using the 5-point scales.
A formal written report would be sent to the administrative and management staff of the target hospital. Results would be presented in nursing management meetings and in the weekly department news so to appreciate and reinforce the staff for achieving the goal of reducing incidence of CRBSI. The evidence-based guideline would also be reviewed and updated every 18 months for any new evidence in reducing the incidence of CRBSI.

4.5 Conclusion

The implementation of proposed innovation involves several components. With smooth communication with stakeholders and involved parties, a well-planned work plan schedule and a pilot run which testing the feasibility of the innovation will lead to a success implementation. Evaluation would also needed for assessing the effectiveness of the innovation and refining the proposal.
References


[http://www.sign.ac.uk/pdf/qrg50.pdf](http://www.sign.ac.uk/pdf/qrg50.pdf)


Timsit, J.F., Mimoz, O., Mourvillier, B., et al. (2012) Randomized Controlled Trial of Chlorhexidine Dressing and Highly Adhesive Dressing for Preventing Catheter-related Infections in Critically Ill Adults, American Journal of Respiratory and Critical Care Medicine, 186(12), 1272-1278.


Table 1: Table of Evidence

<table>
<thead>
<tr>
<th>Citation / Design (Study quality)</th>
<th>Sample characteristics</th>
<th>Intervention</th>
<th>Control</th>
<th>Outcome measures (Assessment time)</th>
<th>Effect size (Intervention – Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timsit, et al. (2009) / RCT (1++)</td>
<td>1. ICU patients</td>
<td>Use of chlorhexidine gluconated-impregnated sponge dressing</td>
<td>Use of semipermeable transparent dressing</td>
<td>1. Catheter colonization Incidence (n per 1,000 catheter-days) Hazard ratio</td>
<td>1. -9.5 0.360 (95% CI, 0.280-0.460, p &lt; 0.001)</td>
</tr>
<tr>
<td></td>
<td>2. Median age = 62 yrs (IQR: 50-74)</td>
<td>(817 patients/ 1,953 catheters)</td>
<td>(819 patients/ 1,825 catheters)</td>
<td>2. CRBSI Incidence (n per 1,000 catheter-days) Hazard ratio</td>
<td>2. -0.9 0.240 (95% CI, 0.090-0.630, p = 0.004)</td>
</tr>
<tr>
<td></td>
<td>3. 1052 (64.3%) Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Remarks:

CRBSI = Catheter-related bloodstream infection; ICU = Intensive care unit;
CI = Confidence interval; IQR = interquartile range; n = number; p = p-value; RCT = Randomized controlled trial; yrs = years old
<table>
<thead>
<tr>
<th>Citation / Design (Study quality)</th>
<th>Sample characteristics</th>
<th>Intervention</th>
<th>Control</th>
<th>Outcome measures (Assessment time)</th>
<th>Effect size (Intervention – Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timsit, et al. (2012) / RCT (1++)</td>
<td>1. ICU patients</td>
<td>Use of transparent chlorhexidine-impregnated gel dressing (938 patients/ 2,108 catheters)</td>
<td>Non chlorhexidine impregnated dressing (941 patients/ 2,055 catheters)</td>
<td>1. Catheter colonization Incidence (n per 1,000 catheter-days) Hazard ratio</td>
<td>1. - 6.6 0.588 (95% CI, 0.306-0.556), p &lt; 0.0001</td>
</tr>
<tr>
<td></td>
<td>2. Median age = 64 yrs (IQR: 53 – 75)</td>
<td></td>
<td></td>
<td>2. CRBSI Incidence (n per 1,000 catheter-days) Hazard ratio</td>
<td>2. - 0.8 0.598 (95% CI, 0.186-0.868), p = 0.02</td>
</tr>
<tr>
<td></td>
<td>3. 1255 (66.8%) Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ruschulte, et al. (2009) / RCT (1++)</td>
<td>1. HDU patients undergoing chemotherapy for haematological or oncological malignancies</td>
<td>Use of chlorhexidine-impregnated sponge dressing (300 patients/ 300 catheters)</td>
<td>Use of standard sterile transparent wound dressing (301 patients/ 301 catheters)</td>
<td>1. CVC-related infections Relative risk</td>
<td>1. – 46 % 0.54 (95% CI, 0.31-0.94), p = 0.016</td>
</tr>
<tr>
<td></td>
<td>2. Mean age = 47 yrs (range: 18 – 73)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. 333 (55.4%) Male</td>
<td></td>
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</tr>
</tbody>
</table>

**Remarks:**

CRBSI = Catheter-related bloodstream infection; CVC = central venous catheter; HDU = high dependency unit; ICU = Intensive care unit; CI = Confidence interval; IQR = interquartile range; n = number; p = p-value; RCT = Randomized controlled trial; yrs = years old
<table>
<thead>
<tr>
<th>Citation / Design (Study quality)</th>
<th>Sample characteristics</th>
<th>Intervention</th>
<th>Control</th>
<th>Outcome measures (Assessment time)</th>
<th>Effect size (Intervention – Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levy, et al. (2005) / RCT (1+)</td>
<td>1. PCICU patients</td>
<td>Use of chlorhexidine-impregnated sponge dressing (74 patients/ 74 catheters)</td>
<td>Use of transparent polyurethane dressing (71 patients/ 71 catheters)</td>
<td>1. Catheter colonization Relative risk</td>
<td>1. -14.7 % 0.61 (95% CI, 0.37-1.0), p = 0.04</td>
</tr>
<tr>
<td></td>
<td>2. Mean age = 2.2 yrs</td>
<td></td>
<td></td>
<td>2. Rate of CRBSIs</td>
<td>2. 1.2% p = 1.00</td>
</tr>
<tr>
<td></td>
<td>3. 53 (36.4%) Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Use of chlorhexidine-impregnated sponge dressing (74 patients/ 74 catheters)</td>
<td>Use of transparent polyurethane dressing (71 patients/ 71 catheters)</td>
<td>1. Catheter colonization Relative risk</td>
<td>1. -14.7 % 0.61 (95% CI, 0.37-1.0), p = 0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Use of chlorhexidine-impregnated sponge dressing (74 patients/ 74 catheters)</td>
<td>Use of transparent polyurethane dressing (71 patients/ 71 catheters)</td>
<td>2. Rate of CRBSIs</td>
<td>2. 1.2% p = 1.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Garland, et al. (2001)/ RCT (1+)</td>
<td>1. PICU patients</td>
<td>Use of 70% isopropyl alcohol for skin antisepsis before CVC placement, and use chlorhexidine gluconate impregnated dressing (335 patients/ 335 catheters)</td>
<td>Use of 10% povidone-iodine (PI) for skin antisepsis before CVC placement, and use polyurethane dressing (370 patients/ 370 catheters)</td>
<td>1. Catheter colonization Relative risk</td>
<td>1. -9.0 % 0.6 (95% CI, 0.5-0.9), p = 0.004</td>
</tr>
<tr>
<td></td>
<td>2. Mean age = 2.6 yrs</td>
<td></td>
<td></td>
<td>2. Rate of CRBSI Relative risk</td>
<td>2. 0.6% 1.2 (95% CI, 0.5-2.7), p = 0.65</td>
</tr>
<tr>
<td></td>
<td>3. 401 (56.9%) male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remarks:</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

CRBSI = Catheter-related bloodstream infection; CVC = central venous catheter; PICU = pediatric intensive care unit; PCICU = pediatric cardiac intensive care unit; CI = Confidence interval; IQR = interquartile range; n = number; p = p-value; RCT = Randomized controlled trial; yrs = years old
I. Objectives

- To provide an evidence-based guideline on application of the CHG impregnated dressing
- To guide and assist nurses in providing evidence-based care in reducing CVC colonization and incidence of CRBSI

II. Materials

- Sterile dressing set on top of clean trolley
- Prescribed antiseptic solution, e.g. 2% Chlorhexidine in 70% alcohol, normal saline
- CHG impregnated dressing
- Absorbent sheet
- Paper rubbish bag

III. Procedure

a. Preparation
   i. Assessment on the fitness for the application of CHG impregnated dressing, including checking patient’s allergy history and skin condition.
   ii. Patient is explained of the procedure.
   iii. Place absorbent sheet under the working area.

b. Intervention
   i. Perform hand hygiene.
   ii. Open sterile dressing set with aseptic technique.
   iii. Remove the old dressing and assess the CVC exit site for any signs of infections, exposure of Dacron cuff, skin excoriation, swelling, catheter leakage or kinking. Inform doctor for any abnormalities noted.
   iv. Wash hands with anti-microbial soap and water thoroughly.
   v. Use aseptic techniques in wound dressing procedure.
vi. Cleanse the CVC exit site and adjacent 6cm-diameter of skin with antiseptic solution and allow it to air dry.

vii. Cleanse 6cm of the catheter extending from the exit site with antiseptic solution and allow it to air dry.

viii. Apply CHG impregnated dressing over the CVC exit site.

ix. Tape the catheter in position to patient’s chest or put it into a ready-made bag.

c. Documentation

i. Document CVC exit site condition in patient’s integrated progress sheet or CVC Record Book.

d. Continuous Nursing Care

i. The CHG impregnated dressing should be changed every 7 days; mechanical complications, bleeding, oozing, leakage or soiling prompted immediate dressing change.

ii. The CVC exit site under CHG impregnated dressing should be inspected and palpated daily and when necessary. The use of CHG impregnated dressing should be terminated immediately when any signs and symptoms of suspected contact dermatitis or skin allergy was noted.
## Table 2: Levels of Evidence

(Scottish Intercollegiate Guidelines Network, 2014)

<table>
<thead>
<tr>
<th>Levels of Evidence</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1++</td>
<td>High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias</td>
</tr>
<tr>
<td>1+</td>
<td>Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias</td>
</tr>
<tr>
<td>1-</td>
<td>Meta-analyses, systemic reviews, or RCTs with a high risk of bias</td>
</tr>
<tr>
<td>2++</td>
<td>High quality systematic reviews of case control or cohort studies High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal</td>
</tr>
<tr>
<td>2+</td>
<td>Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal</td>
</tr>
<tr>
<td>2-</td>
<td>Case control or cohort studies with a high risk of confounding and a significant risk that the relationship is not causal</td>
</tr>
<tr>
<td>3</td>
<td>Non-analytic studies, e.g. case reports, cases series</td>
</tr>
<tr>
<td>4</td>
<td>Expert opinion</td>
</tr>
</tbody>
</table>
Table 3: Grades of Recommendations

(Scottish Intercollegiate Guidelines Network, 2014)

<table>
<thead>
<tr>
<th>Grades of Recommendation</th>
<th>Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target populations; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results</td>
</tr>
<tr>
<td>B</td>
<td>A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+</td>
</tr>
<tr>
<td>C</td>
<td>A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++</td>
</tr>
<tr>
<td>D</td>
<td>Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+</td>
</tr>
<tr>
<td>E</td>
<td>Recommended best practice based on the clinical experience of the guideline development group</td>
</tr>
</tbody>
</table>
Target Hospital
Department of Medicine

Assessment on Central Venous Catheter Exit Wound Dressing

Staff particular: 
Name: ______________________  
Rank: _______________________________  
Ward: _______________________________

Assessor particular: 
Name and Rank: ______________________  
Signature: ___________________________  
Date of assessment: ___________________

Result: Pass / Fail

*Critical items must be done

<table>
<thead>
<tr>
<th>No.</th>
<th>Actions</th>
<th>Yes</th>
<th>NO</th>
<th>NA</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Instrument and materials are assembled.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2</td>
<td>Patient is explained of the reasons and procedure.</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Perform hand hygiene.</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4*</td>
<td>Remove the old dressing. Exit site is assessed for signs of infection, skin excoriation, swelling and leakage. Catheter is assessed for kinking, slippage or loose suture.</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>5</td>
<td>Wash hands with anti-microbial soap and water thoroughly.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6*</td>
<td>Use aseptic techniques in wound dressing procedure.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7*</td>
<td>Clean the exit site and adjacent 6cm diameter of skin with prescribed indicated dressing lotion and allow it to air dry.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>8*</td>
<td>Clean 6cm of the catheter extending from the exit site with prescribed indicated dressing lotion and allow it to air dry.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>9</td>
<td>Apply transparent or appropriate dressing.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Tape the catheter in position to patient’s chest or put it into a clean ready-made bag.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11*</td>
<td>Sign MAR form.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Document site condition in Patient Notes/ CVC Record Book.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Remarks:

Appendix V
Target Hospital
Department of Medicine

Patient Survey on the application of CHG-impregnated dressing

Dear participants,

You are invited to participate in this survey conducted by the Quality Improvement Committee for managing CRBSI. The aim of this survey is to evaluate the satisfactory levels. Thank you for your valuable comments and recommendations.

<table>
<thead>
<tr>
<th></th>
<th>1 = strongly disagree</th>
<th>2 = disagree</th>
<th>3 = neutral</th>
<th>4 = agree</th>
<th>5 = strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Satisfaction towards the guideline</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) I am satisfied with the application of CHG impregnated dressing</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2) The side effects of CHG impregnated dressing is minimal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) I would ask for CHG impregnated dressing during my hospitalization period</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Recommendations:**
Target Hospital
Department of Medicine

Questionnaire on application of CHG impregnated dressing
Staff Survey on evidence-based guideline of using CHG-impregnated dressing

Dear colleagues,

Thank you for your effort on achieving the goal of reducing the incidence of catheter-related bloodstream infection (CRBSI) with the use of evidence-based guideline of using CHG-impregnated dressing in patients with central venous catheter (CVC). You are now invited to participate in this survey conducted by the Quality Improvement Committee for managing CRBSI. The aim of this survey is to evaluate the satisfactory levels towards the innovation by mean of staff workload, staff satisfaction and job satisfaction.

<table>
<thead>
<tr>
<th>Workload</th>
<th>1= strongly disagree</th>
<th>2= disagree</th>
<th>3= neutral</th>
<th>4= agree</th>
<th>5= strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) The guideline has reduced my workload.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Staff Satisfaction to the guideline

| 1) I am satisfied with the training provided. |                      |             |            |          |                   |
| 2) I am satisfied with the structure and recommendation of the guideline |                      |             |            |          |                   |
| 3) The guideline is clear and concise |                      |             |            |          |                   |
| 4) The guideline is easy to follow |                      |             |            |          |                   |

Job Satisfaction

| 1) The guideline increase my job satisfaction |                      |             |            |          |                   |
| 2) The guideline improve my work autonomy |                      |             |            |          |                   |

Recommendations:
**Methodology Checklist 2: Controlled Trials**

**Study identification**  
Include author, title, year of publication, journal title, pages


**Guideline topic:**  
Key Question No:  
Reviewer:

**Before** completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+

2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

**Reason for rejection:** 1. Paper not relevant to key question  
2. Other reason (please specify):

### SECTION 1: INTERNAL VALIDITY

**In a well conducted RCT study...**

<table>
<thead>
<tr>
<th></th>
<th>Does this study do it?</th>
</tr>
</thead>
</table>
| 1.1 | The study addresses an appropriate and clearly focused question.  
*P:* Patients in ICUs requiring an arterial catheter, central-vein catheter, or both inserted for 48 hours or longer  
*I:* Use of a chlorhexidine gluconate-impregnated sponge dressing  
*C:* Use of semipermeable dressings (Tegaderm, 3M)  
*O:* Reduce catheter-related infections  

<table>
<thead>
<tr>
<th></th>
<th>Does this study do it?</th>
</tr>
</thead>
</table>
| Yes ☑ | No ☐  
Can't say ☐ |

| 1.2 | The assignment of subjects to treatment groups is randomised.  
Patients were randomly assigned to 1 of 4 treatment groups. The randomization schedule, stratified by ICU, was developed using a Web-based random-number generator to select permuted blocks of 8 patients each.  

<table>
<thead>
<tr>
<th></th>
<th>Does this study do it?</th>
</tr>
</thead>
</table>
| Yes ☑ | No ☐  
Can't say ☐ |

| 1.3 | An adequate concealment method is used.  
The randomization schedule, stratified by ICU, was developed using a Web-based random-number generator to select permuted blocks of 8 patients each.  

<table>
<thead>
<tr>
<th></th>
<th>Does this study do it?</th>
</tr>
</thead>
</table>
| Yes ☑ | No ☐  
Can't say ☐ |

| 1.4 | Subjects and investigators are kept ‘blind’ about treatment allocation.  
The study was not blinded for the investigators or ICU staff but was blinded for the microbiologists processing the skin and catheter cultures and for the assessors.  

<table>
<thead>
<tr>
<th></th>
<th>Does this study do it?</th>
</tr>
</thead>
</table>
| Yes ☑ | No ☐  
Can't say ☐ |

| 1.5 | The treatment and control groups are similar at the start of the trial.  
The characteristics of both treatment and control groups were listed out with similar baseline characteristics, however, missing the p value for statistical comparison.  

<table>
<thead>
<tr>
<th></th>
<th>Does this study do it?</th>
</tr>
</thead>
</table>
| Yes ☑ | No ☐  
Can't say ☒ |
### Section 2: Overall Assessment of the Study

<table>
<thead>
<tr>
<th>2.1</th>
<th>How well was the study done to minimise bias?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Code as follows</strong>:&lt;sup&gt;xi&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>High quality (++): ✓</td>
</tr>
<tr>
<td></td>
<td>Acceptable (+): ✓</td>
</tr>
<tr>
<td></td>
<td>Unacceptable – reject: 0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.2</th>
<th>Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>This study design was good with subjects assigned randomly with the use of a Web-based random-number generator. The concealment was adequate. The sample size calculation was clearly mentioned in the paper and the statistical data were clearly showed in the paper. The study was conducted in 7 ICUs in 5 different hospitals, which the generalizability of this study was high. Moreover, the main patient characteristics were clearly presented and simplified acute physiology score and sequential organ failure assessment were also done for baseline comparison, which showed that the overall effect were quite certain due to the study intervention.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2.3</th>
<th>Are the results of this study directly applicable to the patient group targeted by this guideline?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YES, as the target group patients characteristics were similar to our target group patients.</td>
</tr>
</tbody>
</table>

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1.6 The only difference between groups is the treatment under investigation.<sup>vi</sup>

Both the treatment and control groups would have the dressing being changed every 3 days, and standard wound care and covered with semipermeable transparent dressing on top. The only care difference was the use of chlorhexidine gluconate impregnated sponge dressing.

1.7 All relevant outcomes are measured in a standard, valid and reliable way.<sup>vii</sup>

The evaluation criteria were well defined according to French and US guideline, which all outcomes are measured in a standard, valid and reliable way.

1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?<sup>viii</sup>

7.69% patients in control group and 5.88% patients in treatment group were excluded from the study due to omitted by ICU nurse, sudden death, accidental catheter removal and sample tube broken.

1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).<sup.ix</sup>

The primary analysis was performed in the intention-to-treat population, which included all patients except those who withdrew their consent to participate, in accordance with French law.

1.10 Where the study is carried out at more than one site, results are comparable for all sites.<sup.x</sup>

The study recruited patients in 7 ICUs (2 medical, 2 surgical, 3 medical-surgical) in 3 university and 2 general hospitals in France.
2.4 Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.

Patients admitted to ICU were all critically ill, and most of them should be given antibiotics for treatment. However, the type of antibiotics and the length of antibiotics given were not mentioned in this study, which would highly affect the culture result.

Any screening done on the admission of ICU (including rectal swab for VRE/CRE screening, MRSA screening) was not mentioned in this paper, which would also affect the result of the culture taken for the catheter colonization samples.

Double blinding was not feasible in this study with the visually identical sponges with and without chlorhexidine, and this would somehow affect the study result.

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1. Unless a clear and well defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

2. Random allocation of patients to receive one or other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study.

3. Allocation concealment refers to the process used to ensure that researchers are unaware which group patients are being allocated to at the time they enter the study. Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%.

4. Blinding refers to the process whereby people are kept unaware of which treatment an individual patient has been receiving when they are assessing the outcome for that patient. It can be carried out up to three levels. Single blinding is where patients are unaware of which treatment they are receiving. In double blind studies neither the clinician nor the patient knows which treatment is being given. In very rare cases studies may be triple blinded, where neither patients, clinicians, nor those conducting the analysis are aware of which patients received which treatment. The higher the level of blinding, the lower the risk of bias in the study.

5. Patients selected for inclusion in a trial must be as similar as possible. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin, or co-morbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

6. If some patients received additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. If groups were not treated equally, the study should be rejected unless no other evidence is available. If the study is used as evidence it should be treated with caution.

7. The primary outcome measures used should be clearly stated in the study. If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected. Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

8. The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients dropped out, as well as how many. It should be noted that the drop out rate may be expected to be higher in studies conducted over a long period of time. A higher drop out rate will normally lead to downgrading, rather than rejection of a study.
In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contra-indications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to be maintained, however, patient outcomes must be analysed according to the group to which they were originally allocated irrespective of the treatment they actually received. (This is known as intention to treat analysis.) If it is clear that analysis was not on an intention to treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.

In multi-site studies, confidence in the results should be increased if it can be shown that similar results were obtained at the different participating centres.

Rate the overall methodological quality of the study, using the following as a guide: **High quality** (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+): Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.
**Methodology Checklist 2: Controlled Trials**

Study identification  *(Include author, title, year of publication, journal title, pages)*  

Guideline topic:  
Key Question No:  
Reviewer:

**Before** completing this checklist, consider:

1. Is the paper a randomised controlled trial or a controlled clinical trial? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a controlled clinical trial questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+.

2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

**Reason for rejection:** 1. Paper not relevant to key question  
2. Other reason (please specify):

**SECTION 1: INTERNAL VALIDITY**

**In a well conducted RCT study...**

<table>
<thead>
<tr>
<th>Key Question No</th>
<th>Does this study do it?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Yes ☑</td>
</tr>
</tbody>
</table>
| The study addresses an appropriate and clearly focused question.  
P: Critically ill Adults  
I: Chlorhexidine-gel impregnated Dressing  
C: Highly adhesive dressings and Standard dressings  
O: Preventing Catheter-related infections  
| Yes ☑   Can't say ☐      |
| 1.2             | Yes ☑                 |
| The assignment of subjects to treatment groups is randomised.  
Randomization was by a web-based random-number generator producing permuted blocks of eight, with stratification on ICUs.  
| Yes ☑   Can't say ☐      |
| 1.3             | Yes ☑                 |
| An adequate concealment method is used.  
Web-based random-number generator was used in this study, where the investigators were unaware of the block size and of the permutation procedure.  
| Yes ☑   Can't say ☐      |
| 1.4             | Yes ☑                 |
| Subjects and investigators are kept 'blind' about treatment allocation.  
Patients, and investigators were not blinded, but the assessors (microbiologists) and adjudication committee were blinded in this study.  
| Yes ☑   Can't say ☐      |
| 1.5             | Yes ☑                 |
| The treatment and control groups are similar at the start of the trial.  
By group baseline characterististics (both patient and catheter characterististics) were reported with both looked reasonably similar, however, the p-value was not given in the study.  
<p>| Yes ☑   Can't say ☐      |</p>
<table>
<thead>
<tr>
<th>Section</th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
<th>Can’t say</th>
<th>Does not apply</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.6</td>
<td>The only difference between groups is the treatment under investigation.</td>
<td>Yes</td>
<td>No</td>
<td>Can’t say</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>All patients were equally treated, following French recommendations for catheter insertion and care, which are similar to Centers for Disease Control and Prevention recommendations. The only different was dressing materials applied.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.7</td>
<td>All relevant outcomes are measured in a standard, valid and reliable way.</td>
<td>Yes</td>
<td>No</td>
<td>Can’t say</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>The assessment methodology was clearly defined, and the evaluation criteria were followed to French and American guidelines, and Centers for Disease Control and Prevention, in which the outcomes were measured in a standard, valid and reliable way.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.8</td>
<td>What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?</td>
<td>0% of drop out rate in this study.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.9</td>
<td>All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).</td>
<td>Yes</td>
<td>No</td>
<td>Can’t say</td>
<td>Does not apply</td>
</tr>
<tr>
<td></td>
<td>This study analyses were performed in the intent-to-treat population, which included all patients except those who withdrew their consent to study participation.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.10</td>
<td>Where the study is carried out at more than one site, results are comparable for all sites.</td>
<td>Yes</td>
<td>No</td>
<td>Can’t say</td>
<td>Does not apply</td>
</tr>
<tr>
<td></td>
<td>The study was conducted in 12 ICUs in 7 university and 4 general hospitals.</td>
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<td></td>
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</tbody>
</table>

**SECTION 2: OVERALL ASSESSMENT OF THE STUDY**

<table>
<thead>
<tr>
<th>Section</th>
<th>Question</th>
<th>High quality (+++</th>
<th>Acceptable (+)</th>
<th>Unacceptable – reject 0</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>How well was the study done to minimise bias?</td>
<td>High quality (+++)</td>
<td>Acceptable (+)</td>
<td>Unacceptable – reject 0</td>
</tr>
<tr>
<td></td>
<td>Code as follows.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.2</td>
<td>Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?</td>
<td>The sample size calculation was clearly mentioned in the paper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.3</td>
<td>Are the results of this study directly applicable to the patient group targeted by this guideline?</td>
<td>YES, it is because the characteristics of the patients in adult ICU are similar to the target group of our study, which the study result could directly applied in our setting.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.4 **Notes.** Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.

Patients admitted to ICU were all critically ill, and most of them should be given antibiotics for treatment. However, the type of antibiotics and the length of antibiotics given were not mentioned in this study, which would highly affect the culture result. Any screening done on the admission of ICU (including rectal swab for VRE/CRE screening, MRSA screening) was not mentioned in this paper, which would also affect the result of the culture taken for the catheter colonization samples.

---

xi Unless a clear and well defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

xi Random allocation of patients to receive one or other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study.

xi Allocation concealment refers to the process used to ensure that researchers are unaware which group patients are being allocated to at the time they enter the study. Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%.

xi Blinding refers to the process whereby people are kept unaware of which treatment an individual patient has been receiving when they are assessing the outcome for that patient. It can be carried out up to three levels. Single blinding is where patients are unaware of which treatment they are receiving. In double blind studies neither the clinician nor the patient knows which treatment is being given. In very rare cases studies may be triple blinded, where neither patients, clinicians, nor those conducting the analysis are aware of which patients received which treatment. The higher the level of blinding, the lower the risk of bias in the study.

xi Patients selected for inclusion in a trial must be as similar as possible. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin, or co-morbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

xi If some patients received additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. **If groups were not treated equally, the study should be rejected unless no other evidence is available.** If the study is used as evidence it should be treated with caution.

xi The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

xi The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients dropped out, as well as how many. It should be noted that the drop out rate may be expected to be higher in studies conducted over a long period of time. A higher drop out rate will normally lead to downgrading, rather than rejection of a study.

xi In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contra-indications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to be maintained, however, patient outcomes must be analysed according to the group to which they were originally allocated irrespective of the treatment they actually received. (This is known as intention to treat analysis.) If it is clear that analysis was not on an
intention to treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.

In multi-site studies, confidence in the results should be increased if it can be shown that similar results were obtained at the different participating centres.

Rate the overall methodological quality of the study, using the following as a guide: High quality (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. Acceptable (+): Most criteria met. Some flaws in the study with an associated risk of bias. Conclusions may change in the light of further studies. Low quality (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.
### Methodology Checklist 2: Controlled Trials

**Study identification**  
*Include author, title, year of publication, journal title, pages*


**Guideline topic:**  
**Key Question No:**  
**Reviewer:**

**Before** completing this checklist, consider:

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2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

**Reason for rejection:** 1. Paper not relevant to key question  2. Other reason  (please specify):

### SECTION 1: INTERNAL VALIDITY

**In a well conducted RCT study…**

<table>
<thead>
<tr>
<th></th>
<th>Does this study do it?</th>
</tr>
</thead>
</table>
| 1.1 | The study addresses an appropriate and clearly focused question.  
  *P*: Patients undergoing chemotherapy for haematological or oncological malignancies requiring central venous catheters expected to remain in place for at least 5 days  
  *I*: receiving a chlorhexidine gluconate-impregnated wound dressing  
  *C*: receiving a standard sterile transparent dressing  
  *O*: reducing catheter-related infections  

  *Yes ☑*  
  *No ☐*  
  *Can’t say ☐*

| 1.2 | The assignment of subjects to treatment groups is randomised.  
  *In the anaesthesia clinic, the patients were randomly assigned to the treatment group or the control group according to computer-generated identification numbers.*  

  *Yes ☑*  
  *No ☐*  
  *Can’t say ☐*

| 1.3 | An adequate concealment method is used.  
  *Patients were randomly assigned according to computer-generated identification numbers.*  

  *Yes ☑*  
  *No ☐*  
  *Can’t say ☐*

| 1.4 | The design keeps subjects and investigators ‘blind’ about treatment allocation.  
  *Neither blinding to the subjects nor investigators was mentioned in this paper, which the investigators could be blinded in the study.*  

  *Yes ☐*  
  *No ☑*  
  *Can’t say ☐*

| 1.5 | The treatment and control groups are similar at the start of the trial.  
  *Patient characteristics, underlying diseases and insertion sites were clearly mentioned in the paper with p value indicated that the baseline characteristics were no statically significant difference.*  

  *Yes ☑*  
  *No ☐*  
  *Can’t say ☐*
1.6 The only difference between groups is the treatment under investigation. Experienced board-certified anaesthesiologists inserted chlorhexidine and silver sulfadiazine-impregnated catheters in a special anaesthesiology clinic under monitored care. All catheter insertion followed a strict antiseptic regimen and was secured with clips and two skin sutures. The dressing materials used would be the one according to the study group that they belonged to. Neither anti-septic ointments nor filters were used. The wound dressings were changed regularly after 1 week or after they had been lifted up for inspection controls. Yes ☑ No ☐ Can’t say ☐

1.7 All relevant outcomes are measured in a standard, valid and reliable way. The outcome measurement tools, which were according to the Healthcare Infection Control Practices Advisory Committee, were clearly defined, which are in a standard, valid and reliable way. Yes ☑ No ☐ Can’t say ☐

1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? One patient (out of 601 participants) refused to further participate in the study and received the regular, i.e. control group, treatment at his catheter site. 0.17% drop out rate is acceptable. Yes ☑ No ☐ Can’t say ☐

1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis). No patient had to be excluded from the study as a consequence of allergic reactions to the chlorhexidine-impregnated foam and all patients were followed up in the study. A number-needed-to-treat calculation was performed based on the data of this study. Yes ☐ No ☐ Can’t say ☐ Does not apply ☑

1.10 Where the study is carried out at more than one site, results are comparable for all sites. The patients were from two high dependency units at a university hospital. Yes ☐ No ☑ Can’t say ☐ Does not apply ☑

SECTION 2: OVERALL ASSESSMENT OF THE STUDY

2.1 How well was the study done to minimise bias? Code as follows: High quality (++) ☑ Acceptable (+)☐ Low quality (-)☐ Unacceptable – reject 0 ☐

2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention? The sample size calculation was clearly presented in the paper, and the baseline characteristics of both study groups were clearly presented with statistical analysed. The overall effect was due to the study intervention.

2.3 Are the results of this study directly applicable to the patient group targeted by this guideline? YES, it is because the target group is the same as ours.
2.4 **Notes.** Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.

The study targeted the patients undergoing chemotherapy for haematological or oncological malignance, different types of underlying haematological diseases were under investigated for the correlation with the study interventions. However, other medical histories, including diabetes, renal impairment or history of MRSA infections, should be also under investigated in this study as they may alter the study result. Moreover, patients with neutropenia were often receiving intravenous or oral antibiotics for treatment or prophylaxis use, thus, the type, dosage and frequency of the antibiotics administration should be also under investigated in this study.

---

xi Unless a clear and well defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

xi Random allocation of patients to receive one or other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study.

xi Allocation concealment refers to the process used to ensure that researchers are unaware which group patients are being allocated to at the time they enter the study. Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%.

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xi Patients selected for inclusion in a trial must be as similar as possible. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin, or co-morbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

xi If some patients received additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. If groups were not treated equally, the study should be rejected unless no other evidence is available. If the study is used as evidence it should be treated with caution.

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xi The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients dropped out, as well as how many. It should be noted that the drop out rate may be expected to be higher in studies conducted over a long period of time. A higher drop out rate will normally lead to downgrading, rather than rejection of a study.

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However, patient outcomes must be analysed according to the group to which they were originally allocated irrespective of the treatment they actually received. (This is known as intention to treat analysis.) If it is clear that analysis was not on an intention to treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.

In multi-site studies, confidence in the results should be increased if it can be shown that similar results were obtained at the different participating centres.

Rate the overall methodological quality of the study, using the following as a guide: **High quality (++)**: Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable (+)**: Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality (0)**: Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.
**Study identification**  
*Include author, title, year of publication, journal title, pages*


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**Guideline topic:**

**Key Question No:**

**Reviewer:**

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### SECTION 1: INTERNAL VALIDITY

**In a well conducted RCT study…**

<table>
<thead>
<tr>
<th></th>
<th>Does this study do it?</th>
</tr>
</thead>
</table>
| 1.1 | The study addresses an appropriate and clearly focused question.  
P: Patients 0 – 18 years of age who were admitted to the pediatric cardiac intensive care unit and required a CVC for >48 hours  
I: Receiving a chlorhexidine gluconate-impregnated sponge (Biopatch) dressing covered by a transparent polyurethane dressing  
C: Receiving a transparent polyurethane insertion site dressing  
O: Determine the efficacy and safety of the prevention of CVC colonization and CRBSI | Yes ☑ No ☐ Can’t say ☐ |
| 1.2 | The assignment of subjects to treatment groups is randomised.  
Patients were randomized, by random number generator, to either control group or study group. | Yes ☑ No ☐ Can’t say ☐ |
| 1.3 | An adequate concealment method is used.  
No details about the concealment method is reported in the paper. | Yes ☐ No ☑ Can’t say ☐ |
| 1.4 | The design keeps subjects and investigators ‘blind’ about treatment allocation.  
The study subjects and the investigators were not mentioned whether they were ‘blinded’ in the study, but the microbiology laboratory personnel were blinded and could not identify to which group the CVC had been randomized. | Yes ☑ No ☐ Can’t say ☐ |
| 1.5 | The treatment and control groups are similar at the start of the trial. The baseline characteristics of the study group and the control group were clearly reported and analyzed in the study with p-value indicated that the data was no significant differences between the two groups. | Yes ☑ | No □ |
| 1.6 | The only difference between groups is the treatment under investigation. Patients were treated under same care, with the only different was the dressing used to cover the insertion site of the CVCs. | Yes ☑ | No □ |
| 1.7 | All relevant outcomes are measured in a standard, valid and reliable way. The outcome measures are well defined, which are in a standard, valid and reliable way. | Yes ☑ | No □ |
| 1.8 | What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? | 0% drop out in this study reported. | |
| 1.9 | All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis). Of the 251 patients who met the inclusion criteria, 106 were excluded from the study because of parental refusal to participate (n = 95) or technical reasons (n = 21) such as inadvertent or nonaspecific removal of catheter. | Yes ☑ | No □ |
| 1.10 | Where the study is carried out at more than one site, results are comparable for all sites. The study was conducted in the Pediatric Cardiac ICU (PCICU) of Schneider Children’s Medical Center of Israel between January 2002 and March 2003. | Yes ☑ | No □ |

**SECTION 2: OVERALL ASSESSMENT OF THE STUDY**

| 2.1 | How well was the study done to minimise bias? Code as follows: High quality (++): ☑ Acceptable (+): □ Low quality (-): □ Unacceptable – reject 0 □ |

| 2.2 | Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention? The sample size calculation was clearly mentioned, and the baseline characteristics of two patient groups were clearly analysed with statically indicated they were no significant difference, which indicated that the result of the study was mainly due to the intervention. |

| 2.3 | Are the results of this study directly applicable to the patient group targeted by this guideline? NO, it is because the study group is children and infants after cardiac surgery who are totally different with our target patients |

File name: Checklist 2 – Controlled Trials | Version 2.0 | 28/05/2012 |
Produced by: Carolyn Sleith | Page 22 of | Review date: None |
2.4 Notes. Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.

The main limitation of the study is the setting in a specialized pediatric cardiothoracic surgical unit, where patients undergo multiple invasive procedures and require multiple drains and venous and arterial catheters, and mechanical ventilation; which lower the generalizability of the study. The duration of catheterization is relatively short, and thus the risk would be lower than other population. The sample size was too small to determine the effect of the intervention. The use of prophylaxis antibiotics maybe affect the result of the study, which was not being under analyzed in this study.

XI Unless a clear and well defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

XI Random allocation of patients to receive one or other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study.

XI Allocation concealment refers to the process used to ensure that researchers are unaware which group patients are being allocated to at the time they enter the study. Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%.

XI Blinding refers to the process whereby people are kept unaware of which treatment an individual patient has been receiving when they are assessing the outcome for that patient. It can be carried out up to three levels. Single blinding is where patients are unaware of which treatment they are receiving. In double blind studies neither the clinician nor the patient knows which treatment is being given. In very rare cases studies may be triple blinded, where neither patients, clinicians, nor those conducting the analysis are aware of which patients received which treatment. The higher the level of blinding, the lower the risk of bias in the study.

XI Patients selected for inclusion in a trial must be as similar as possible. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin, or co-morbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

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XI The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients dropped out, as well as how many. It should be noted that the drop out rate may be expected to be higher in studies conducted over a long period of time. A higher drop out rate will normally lead to downgrading, rather than rejection of a study.

XI In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contra-indications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to be maintained, however, patient outcomes must be analysed according to the group to which they were originally allocated irrespective of the treatment they actually received. (This is known as intention to treat analysis.) If it is clear that analysis was not on an
intention to treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.

In multi-site studies, confidence in the results should be increased if it can be shown that similar results were obtained at the different participating centres.

Rate the overall methodological quality of the study, using the following as a guide: **High quality (++)**: Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable (+)**: Most criteria met. Some flaws in the study with an associated risk of bias. Conclusions may change in the light of further studies. **Low quality (0)**: Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies.

### Guideline topic:

Before completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+.

2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

**Reason for rejection:**
1. Paper not relevant to key question
2. Other reason (please specify):

### SECTION 1: INTERNAL VALIDITY

**In a well conducted RCT study...**

<table>
<thead>
<tr>
<th>1.1</th>
<th>The study addresses an appropriate and clearly focused question.</th>
</tr>
</thead>
<tbody>
<tr>
<td>P:</td>
<td>Neonates who require a central venous catheter (CVC) for prolonged vascular access in neonatal intensive care units</td>
</tr>
<tr>
<td>I:</td>
<td>Skin disinfection with 70% isopropyl alcohol and use of a novel chlorhexidine-impregnated dressing (Biopatch Antimicrobial dressing) on the CVC sites</td>
</tr>
<tr>
<td>C:</td>
<td>Skin disinfection with 10% povidine-iodine (PI) skin scrub, and dressed with a polyurethane dressing</td>
</tr>
<tr>
<td>O:</td>
<td>Prevention of catheter tip colonization, CRBSI, and bloodstream infection (BSI) without a source</td>
</tr>
<tr>
<td>Does this study do it?</td>
<td>Yes ☑️ No ☐ Can’t say ☐</td>
</tr>
</tbody>
</table>

| 1.2 | The assignment of subjects to treatment groups is randomised. |
| Does this study do it? | Yes ☑️ No ☐ Can’t say ☐ |

| 1.3 | An adequate concealment method is used. |
| Does this study do it? | Yes ☑️ No ☐ Can’t say ☐ |

| 1.4 | The design keeps subjects and investigators 'blind' about treatment allocation. |
| Does this study do it? | Yes ☐ No ☑️ Can’t say ☐ |

| 1.5 | The treatment and control groups are similar at the start of the trial. |
| Does this study do it? | Yes ☑️ No ☐ Can’t say ☐ |
### 1.6 The only difference between groups is the treatment under investigation.

Not only the dressing material used on the CVC insertion site was different, the skin disinfectants used before CVC insertion were different (70% isopropyl alcohol in intervention group while 10% povidine-iodine in control group). Moreover, frequencies of changing dressing were also different (every 7 days in intervention group while twice weekly in control group).

<table>
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<tr>
<th>Yes</th>
<th>No</th>
<th>Can’t say</th>
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</thead>
<tbody>
<tr>
<td></td>
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<td></td>
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</table>

### 1.7 All relevant outcomes are measured in a standard, valid and reliable way.

The culture techniques and the diagnostic definitions were clearly mentioned in the paper, which were subjectively reliable and valid.

<table>
<thead>
<tr>
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</table>

### 1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?

0%

### 1.9 All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis).

All findings were based on intention-to-treat analyses.

<table>
<thead>
<tr>
<th>Yes</th>
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<th>Can’t say</th>
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<td></td>
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### 1.10 Where the study is carried out at more than one site, results are comparable for all sites.

This study was conducted in 6 level III neonatal intensive care units, where 4 in university teaching hospitals and 2 in community hospitals.

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
<th>Can’t say</th>
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### SECTION 2: OVERALL ASSESSMENT OF THE STUDY

#### 2.1 How well was the study done to minimise bias?

**Code as follows:**

- High quality (++)
- Acceptable (+)
- Low quality (-)
- Unacceptable – reject

<table>
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#### 2.2 Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?

The sample size calculation was clearly mentioned in the paper and the sample size is large enough to reflect the study result. The study was carried out in 6 NICU in 6 different hospitals, which represented that the generalizability of the study is higher. Medications, also another important factor that affect the risk of infections, were also reported and statistically analysed in this paper. However, the overall effect may not only due to the application of CHG dressing, varies in the disinfectants and frequency of changing dressing are all affecting the study result.

<table>
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#### 2.3 Are the results of this study directly applicable to the patient group targeted by this guideline?

NO, this study was carried out in NICU, where the patients’ characteristics are totally different with the target group of our study.

<table>
<thead>
<tr>
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<th>Can’t say</th>
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Review date: None
2.4 **Notes.** Summarise the authors’ conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.

The author did not mention whether the disinfectants used before the insertion of CVC and the frequency of changing dressing materials would affect the study result and yet the catheter care were not standardized in both study groups which may contaminated the study result.

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