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Major Article

# Chlorhexidine-containing dressings in the prevention of central venous catheter-related bloodstream infections: A cost and resource utilization analysis

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*Key Words:*
Chlorhexidine-containing gel pad
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Cost savings

***Background:*** A recent study reported a reduction in probable/definite central venous catheter (CVC)-related bloodstream infections (CRBSIs) in neutropenic high-risk patients using CVC dressings with a chlorhexidine-containing gel pad.

***Methods:*** Based on published data, a health-economic analysis was performed to analyze the economic effect of using CVC dressings with a chlorhexidine-containing gel pad compared to non-chlorhexidine control dressings. A micro-costing approach was used to determine CRBSI-related direct treatment cost factors.

***Results:*** Between February 2012 and September 2014, 356 patients (178 patients in both groups) were analyzed. Distribution of probable and definite CRBSI in the chlorhexidine group and control group were 12 (7%) vs. 18 (10%) and 9 (5%) vs. 21 (12%), respectively ($P = .011$). Median overall length of stay (25 vs. 27.5 days; $P = .630$) and days on treatment with antibacterials (10 vs. 12 days; $P = .140$) were similar between the chlorhexidine and control groups. The most important cost driver in both groups was treatment on general ward (€4275 [US$ 5173], interquartile range [IQR]: €592 - €6504 [US$ 716 - US$ 7871] vs. €4560 [US$ 5518], IQR: €1,227 - €8,567 [US$ 1485 - US$ 10,367]; $P = .120$), resulting in median overall direct treatment costs of €13,881 (US$ 16,798) [IQR: €10,922 - €25,457 (US$ 13,217 - US$ 30,807) vs. €13,929 [US$ 16,856] [IQR: €11,295 - €23,561 (US$ 13,669 - US$ 28,512); $P = .640$]).

***Conclusion:*** Our study shows similar results in overall direct treatment costs, meaning that higher acquisition costs of chlorhexidine-containing dressings did not translate into higher costs. Expenses were primarily outweighed by a lower rate of probable/definite CRBSI and reduced associated costs.



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## BACKGROUND

Neutropenic patients with hematologic conditions receiving intensive chemotherapy are at high risk of developing hospital-acquired infections.[1,2] Central venous catheter (CVC)-related bloodstream infections (CRBSIs) are one of the leading complications during their hospitalization, resulting in prolonged hospital stay, increased mortality, and additional treatment costs between €15,000 and €25,000 per patient.[3-5] Recently published studies from the United States reported more than 60,000 CRBSIs from US hospitals each year, resulting in overall costs of US$ 1.85 billion.[6,7]

Since pathogenic skin colonization is associated with catheter colonization and, consequently, increased risk for CRBSI, effective hygiene measures are needed to minimize the risk of developing a CRBSI. A recently published study analyzed the use of chlorhexidine gluconate (CHG)-containing CVC dressings (3M Tegaderm CHG IV; 8.5 x 11.5 cm) compared to non-chlorhexidine CVC dressings (3M Tegaderm Advanced IV; 8.5 x 11.5 cm) in neutropenic patients.[8] Biehl et al. demonstrated a significantly lower incidence rate of pooled definite and probable CRBSI in patients using CHG IV. These findings support the current AI (highest category of evidence level) recommendation of the Infectious Disease Working Party (AGIHO) of the German Society of Hematology and Medical Oncology (DGHO) supporting the application of CHG dressings in cancer patients.[9] In brief, the recommendation by the AGIHO-DGHO for prevention of CVC-related infections by using specific catheter site dressings were primarily based on a randomized controlled trial by Timsit et al., which demonstrated a significant reduction of CRBSI in patients with chlorhexidine-impregnated CVC dressings compared to patients with standard non-chlorhexidine dressings.[10] Two additional previously published randomized controlled trials showed similar efficacy of chlorhexidine-impregnated dressings.[11,12] However, many institutions may still hesitate to implement CHG dressings, due to higher acquisition costs and limited information regarding cost-effectiveness of this preventive strategy.

Based on the dataset of the Biehl et al. trial, we conducted a health economic evaluation to analyze the economic effect of CHG IV. The primary study objective was to analyze direct treatment costs of patients who received 3M Tegaderm CHG IV compared to patients who received 3M Tegaderm Advanced IV. Further objectives were to compare patients' overall length of stay (LOS), rate of probable and definite CRBSI, patient outcome, and the duration and type of anti-infective treatment between both groups.

## MATERIAL AND METHODS

### *Setting*

Our health-economic evaluation included only patients who were treated at the University Hospital of Cologne (UHC), a tertiary-care, 1500-bed hospital with 62,000 annual inpatient stays. All included patients from the UHC were treated in the first Department of Internal Medicine, one of the major providers of hematology and oncology services in Germany.

### *Data source*

Patient data (e.g., patient characteristics and type of CRBSI) were primarily extracted from the dataset by Biehl et al.,[8] and no further inclusion or exclusion criteria were applied. Therefore, for definition of CRBSI, the AGIHO-DGHO criteria used by Biehl et al. were used.[13] In contrast to the study by Biehl et al., who included information up to 14 days after onset of CRBSI, our study included relevant health-economic data until the end of inpatient stay. Furthermore, no detailed cost items were collected for the previously published study, such that additional direct treatment cost-relevant information was extracted from the internal hospital information system and the Cologne Cohort of Neutropenic patients (CoCoNut; ClinicalTrials.gov identifier: NCT01821456). This included CRBSI-related costs for medical measures, such as dose, duration, and route of administration of antibacterial agents, CVC dressings, and treatment on different hospital wards.

### *Health economic analysis*

Our analysis was performed from the German societal perspective as recommended by national guidelines,[14] whereby indirect costs were disregarded due to the severity of underlying diseases. The following direct treatment cost factors were included to compare patients who received 3M Tegaderm CHG IV (CHG group) and patients who received 3M Tegaderm Advanced IV (control group): (i) treatment on general ward, (ii) treatment on intermediate care unit, (iii) treatment on bone marrow transplant ward, (iv) treatment on intensive care unit (ICU), (v) mechanical ventilation, (vi) imaging, (vii) diagnostic measures, (viii) laboratory tests, (ix) CVC dressings, (x) antibacterial agents, (xi) antifungal agents, and (xii) antiviral agents. Non-CRBSI-relevant medical measures, such as surgery, were excluded from our analysis.

Direct treatment cost factors (i) – (viii) were calculated based on the System on the German Diagnosed Related Groups InEK matrix and included personnel and material costs (e.g., medical, nursing, and medical technical service).[15] Costs for anti-infective agents (cost factors [x] – [xii]) were calculated by using the cheapest manufacturer price extracted from the WEBAPO LAUER-TAXE, a database offering comprehensive pharmaceutical product information.[16] For calculation of CVC dressings (cost factor [ix]), information from our internal cost unit accounting was used. For all direct treatment cost factors, annual variations were considered. Furthermore, due to an observed timeframe of >1 year, discounting of all costs with an annual discount rate of 5% was performed. All costs were expressed in € (Euro) and US$ (January 1, 2015, exchange rate: €1 = US$ 1.21), based on year 2015 values. For statistical analysis, IBM SPSS Statistics software version 23.0 (IBM Corp., Armonk, New York) was used. Mann-Whitney-U test, Welch's bootstrapped t-test, and Pearson's chi-squared test (2-sided) were applied to test significance of normally and non-normally distributed data, and a $P$ value <.05 was considered statistically significant. Non-significant $P$ values were rounded to the nearest hundredth. Bootstrapping was performed for 10,000 samples, and starting point for the Mersenne Twister was at 1000. For descriptive purposes, patient data, treatment durations, and cost data are presented as median and range or interquartile range (IQR) and/or mean and 95% confidence interval where appropriate. For sensitivity analysis of overall direct treatment costs, the recommended discount rate of 5% per year[14] was replaced by annual discount rates of 0%, 3%, and 10% to improve robustness of cost analysis.

### *Ethical considerations*

For the previously published randomized trial by Biehl et al.,[8] an approval of the Ethics Commission of Cologne University's Faculty of Medicine was obtained, and the study was registered at ClinicalTrials.gov (NCT: 01544686). All patients included in the study signed a written informed consent. Furthermore, with respect to data extraction from the CoCoNut, the cohort was registered at ClinicalTrials.gov (NCT: 01821456) and also approved by our local Ethics Commission.