Review report of MTG25: The 3M Tegaderm CHG IV securement dressing for central venous and arterial catheter insertion sites

This medical technology guidance was published in July 2015.

All medical technology guidance is reviewed 3 years after publication according to the process described in the MTEP Interim addendum on guidance reviews.

This report is part of the information considered in the guidance review. It describes an update of the cost model so that it reflects any new relevant information including revising the cost and resource parameters to current values. The results from the updated cost model are used to estimate the current savings associated with the use of the technology.

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1. Background

The 3M Tegaderm CHG IV Securement Dressing is a sterile transparent semi-permeable polyurethane adhesive dressing with an integrated gel pad containing a 2% concentration by weight of chlorhexidine gluconate (CHG). It is designed for use in securing percutaneous devices and to cover and protect central venous and arterial catheter insertion site, aiming to act as a physical barrier against contaminant agents. The sponsor's submission claimed benefits of using the technology in the form of reduction in the incidence of catheter related bloodstream infection (CRBSI), reduction in the risk of mortality due to CRBSI, and reduction of the incidence of skin and catheter colonisation during time with catheterisation.

The technology was evaluated by NICE, and its corresponding assessment was executed by a collaboration between two of the external assessment centres (EAC) – Newcastle upon Tyne Hospitals (NUTH) and York Health Economics Consortium (YHEC). The assessment report was published as a NICE medical technology guidance (MTG25). An update of this assessment is planned and as part of the assessment review process, NICE has requested an update to the cost model.

The guidance development was based upon a *de novo* cost-consequence model elaborated and submitted by the sponsor. The original EAC assessment corrected the model and updated some of the parameters. The population was defined as critically ill adults in Intensive Care Units (ICUs) or High Dependency Units (HDUs). The analysis was made using a decision tree of two arms consisting in standard dressing and Tegaderm CHG. The model applied a short time horizon and considered a catheterisation time of 10 days with an NHS perspective. The key parameters of the model are baseline CRBSI incidence rate and hazard ratio for CRBSI when using Tegaderm CHG. The outcomes of the model were expected total cost for each arm. Scenario analysis was conducted varying the value of baseline CRBSI incidence rate using estimates from ICUs in England and Scotland. Univariate and probabilistic sensitivity analyses were undertaken by the EAC.

The results of the analysis in the base-case scenario indicated Tegaderm CHG is cost-saving even when considering the lower bound of CRBSI incidence rate. The cost-saving per patient was estimated to be £72.90 when considering an incidence rate of 1.48 per 1,000 catheter days reported on a national study of English ICUs. The estimated cost-saving when considering an incidence rate of 0.3 per 1,000 catheter days from the Scottish Critical Care Society Audit Group was £3.56 per patient. The EAC conducted univariate sensitivity analysis on the CRBSI determining Tegaderm CHG is cost incurring at a rate of 0.237 CRBSI infections per 1,000 catheter days. Other parameters impacting on the

magnitude of the cost-saving were the hazard ratio of CRBSI with Tegaderm CHG, catheter dwell time and CRBSI cost. Nonetheless none of these parameters changed the direction of the results when utilising English data. The PSA showed the results are robust resulting in cost-savings in 98% of the iterations.

The results obtained when considering the Scottish data have an impact on the robustness of the model. In the univariate sensitivity analysis, a number of variables have a non-marginal impact on the direction of cost difference (baseline incidence rate of CRBSI, hazard ratio of the intervention at preventing CRBSI, catheter dwell time, cost of CRBSI and mean number of dressings per patient). The probability that Tegaderm CHG is cost-saving decreases drastically to 58%.

2. Current validity of model

The cost-consequence model estimates the total expected costs by adding up the expected costs of complications plus the cost of the dressing in both treatment alternatives. Expected costs of CRBSI when using Tegaderm CHG are calculated by multiplying the cost of CRBSI episode by the size of the cohort, the baseline CRBSI incidence rate, the hazard ratio, and the length of stay with catheterisation. Similarly, expected costs of local site infection are calculated using the same methodology with the corresponding values for incidence rate and hazard ratio of Tegaderm CHG for preventing local site infections. The expected costs of dermatitis are estimated by multiplying cost of treating dermatitis by the relative risk of Tegaderm CHG, baseline risk of dermatitis and the cohort size. Expected costs of complications when using standard dressing are estimated using the same methodology only without applying hazard ratios or relative risk for CRBSI, local site infection and dermatitis. The model estimates the difference in expected total costs for standard dressing and Tegaderm CHG.

The EAC outlined the following structural assumptions for the de novo cost model in the original assessment report:

- There is no difference between the Tegaderm CHG and standard dressing group in the duration of additional length of stay for patients with CRBSI. Therefore, it was not included in the analysis.

- The short time horizon impedes the inclusion of long-term consequences in the analysis. Consequences after developing CRBSI are not included in the analysis.

- Risk of the different endpoints included in the analysis are independent.

- Organisation consequences between using Tegaderm CHG and standard dressing are equal (e.g. time to apply and remove dressing, wastage and training). Therefore, only unit cost of both alternatives and cost of complications were considered.

Most of the assumptions were made in the light of lack of clinical evidence. The EAC recognised them as a limitation of the analysis. Nevertheless, the EAC determined they were valid and will not represent a risk of significant bias to the total cost estimates in the original assessment report.

The EAC analysed the evidence provided by the manufacturer and the clinical experts consulted by NICE for this cost model update report. Two economic evaluations were identified comparing Tegaderm CHG against standard dressings employing alternative methodologies to estimate costs (Maunoury et al., 2015, Thokala et al., 2016).

Thokala et al. (2016) conducted a study to assess the economic impact of Tegaderm CHG in critically ill patients. They developed a decision analytical cost-consequence model defining the same structure outlined in the original assessment report. They compared estimated costs of Tegaderm CHG and standard dressing. The study differs from the methodology used in the original assessment report in the calculations of expected cost. Total costs are estimated by adding up average cost of dressing plus expected cost of complications. The average costs of both alternatives are estimated by multiplying the number of standard dressing required with the unit cost of the dressing. The number of dressings is estimated by dividing the average length of stay with catheterisation by the average dress duration. The expected costs of complications in each alternative do not take into account length of stay nor number of dressings.

Maunoury et al (2015) conducted a cost-effectiveness analysis utilising a Markov model with a time horizon of 30 days with daily cycles. The model estimates costs and number of CRBSIs avoided. The authors used a randomised control trial conducted in 12 ICUs in France to populate the model. The cost analysis undertaken in this study considered the following inputs: dressing cost per day, mean cost of treating contact dermatitis, mean episode cost of CRBSI, mean length of stay, additional length of stay due to CRBSI, cost of additional length of stay, cost per day in ICU due to CRBSI, and cost per catheter change. The authors estimated the cost per episode of CRBSI.

The EAC took into consideration the evidence identified and determined the assumptions made in the sponsor’s submission and validated by the original EAC are still valid, given that there is no evidence of changes to the current clinical pathway where this technology is used.

The EAC noted a mistake in the calculations of expected costs of CRBSI and expected costs of local site infection. The impact of the mistake was small as it appears in both arms. The original EAC assessment report considers incidence rates and hazard ratios in the calculation of risk of CRBSI and local site infection in both groups. The incidence rate must be converted to cumulative incidence rate, i.e. risk of event happening when using the intervention (Boyle, 1991). Such transformation is necessary in order to capture the risk at the time of exposure of an event, as oppose to rates that does not depend on time. The following formula can be applied:

$$Risk\ of\ event\ happening\ = 1 - exp\{-incidence\ rate * time\}$$

When considering the risk of event happening in the Tegaderm CHG group, the baseline incidence rate can be adjusted by multiplying it by hazard rate and the average length of stay with catheterisation as follows:

$$Risk\ of\ event\ happening\ with\ Tegaderm\ CHG = 1 - exp\{-baseline\ rate * hazard\ rate * length\ of\ stay\ with\ catheterisation\}$$

Given the absence of longer-term data from randomised clinical trials reflecting NHS practice, decision tree model was considered sufficient. Hence, the EAC considered the calculations in the cost-consequence model are valid and there is no need to further changes besides the outlined above and parameter update.

Although no changes within the current clinical pathway of the scope of the original assessment report were identified, following clinical expert consultation by NICE and manufacturer claims, the EAC acknowledges there is increasing evidence towards the utilisation of Tegaderm CHG to prevent CRBSI in different populations, e.g. non-intensive care IV services such as haemodialysis, chemotherapy, haematology, and infants (Biehl et al., 2016, Gerceker et al., 2017, Waters et al., 2019). Further analysis is to be undertaken in order to assess the cost-effectiveness of the technology in the different services as key parameters are likely to differ to those of the population evaluated under the scope of the original assessment report.

3. Updated input parameters

The parameters included in the original assessment report were retrieved from a variety of sources. The baseline rates of CRBSI used in the base-case scenarios are from the Matching Michigan study and from the Scottish Intensive Care Society Audit Group. The baseline local site infection was taken from NHS Wales whereas the study conducted by Timsit et al (2012) contributed with estimates of baseline risk of dermatitis, hazard rates of CRBSI and local site infection for Tegaderm CHG. Assumptions were made based upon the

manufacturer data for relative risk of dermatitis and mean number of dressings per patient. Costs of both alternatives were estimated using weighted averages from NHS supply chain costs. The cost of CRBSI was obtained from Hocknaull et al (2008). Estimates of length of stay with catheterisation and cost of dermatitis were based upon clinical expert advice.

The EAC complemented the evidence provided by the manufacturer and the clinical expert advice with a targeted literature review in order to update the model parameters. KiTEC retrieved evidence to update the following parameters and variables: baseline CRBSI rate, effectiveness of Tegaderm CHG for preventing CRBSI, and length of stay with catherization. Cost of Tegaderm CHG was updated based on data from the manufacturer. Other costs from the original assessment report were inflated to 2017-2018 prices using the hospital and community health services index (Curtis and Burns, 2018). Table 1 summarises the parameter values utilised in the updated base case scenario.

Baseline incidence rate of CRBSI, local site infection and dermatitis

The EAC identified the most recent update to the audit of critical care in Scotland used in the original assessment report (SICS, 2018). The authors reported in 2018 an incidence rate of 0.4 per 1000 central venous catheter days, a 0.1 unit increase from the estimate reported in 2013. The incidence rate for local and general catheter related infections is reported to be 0.28 per 1000 catheter days (95% CI: 0.1 – 1.0). The EAC also identified the assessment MTG44 CUROS FOR PREVENTING INFECTIONS WHEN USING NEEDLELESS CONNECTORS, utilises estimates of CRBSI incidence rate as part of the cost model (NICE, 2019). The guideline reported a wide range of baseline incidence rates of CRBSI within the literature and noted that the Scottish study may be an underestimate of the true CRBSI rate due to potential under-classification of blood stream infections. The value used in the base-case analysis for MTG44 is 1.48 CRBSIs per 1000 catheter days - the same as the figure used in the original assessment report. The baseline incidence rate of dermatitis was obtained from Eggimann et al (2019). The EAC undertook scenario analysis using the English incidence rate for CRBSI and the updated value from Scottish ICU.

Effectiveness of Tegaderm CHG for preventing CRBSI

The EAC identified a meta-analysis that assessed the effectiveness of utilising chlorhexidine-impregnated dressing for preventing central venous catheter related colonization and CRBIS (Safdar et al., 2014). The analysis included only prospective randomised control trials where CRBSI was based upon standardised microbiology definitions. Safdar et al (2014) conducted subgroup analysis allowing to assess the impact of CHG impregnated dressings in

critically ill adult patients. They reported a relative risk of 0.45 (95% CI 0.28 - 0.72) associated to the intervention group.

A more recent meta-analysis conducted by Dang et al. (2019) compared the effectiveness of 13 different antimicrobial dressings – including CHG impregnated dressings – to reduce the incidence rate of CRBSI. The study reports odds ratios of indirect comparisons among the different alternatives. The odds ratio of utilising CHG-impregnated dressing compared to transparent dressing is reported as 0.66 (95% CrI 0.02 - 0.62). This study incorporates evidence from all services within the hospital setting, falling outside the scope of the population determined in the original assessment report (Dang et al., 2019).

The manufacturer highlighted a study conducted by Eggimann et al (2019) assessing the effectiveness of Tegaderm CHG to reduce CRBSI as an enhancement of catheter bundle. The study design is a real-world design that evaluates the gradual implementation of chlorhexidine dressings. The authors reported a statistically significant 91% decrease in the incidence rate of CRBSI between no CHG dressing and full implementation of Tegaderm CHG. The incidence rate in the first period was 1.12 per 1,000 catheter days (95% CI 0.79 – 1.59) and 0.10 (95% CI 0.03 – 0.031) in the full implementation period (IRR of 0.089 95% CI 0.028 – 0.284) (Eggimann et al., 2019).

The EAC considered the most appropriate estimate for effectiveness of Tegaderm CHG to prevent CRBSIs is the figure reported in Safdar et al (2014). This meta-analysis incorporated only RCTs assessing the effectiveness specifically on the target population, including the reference used as the base-case value in the original assessment report. The measure of effectiveness was applied to baseline incidence rate in the three types of infection using the formula described in section 2, under the assumption relative risks and hazard ratios tend to be equal within a short period of time (Stare and Maucort-Boulch, 2019).

Length of stay with catheterisation

The EAC identified the MTG44 CUROS FOR PREVENTING INFECTIONS WHEN USING NEEDLELESS CONNECTORS utilises estimates of length of stay with catheterisation in ICU patients. The figure was based upon the estimate from Tan et al. (2009) and was varied upon clinical expert advice.

Cost of Tegaderm CHG

The manufacturer reported a decrease in the cost of Tegaderm CHG of 2% (£0.12). The EAC assumed this reduction was implemented in all sizes of Tegaderm CHG and estimated an updated weighted average using the sales

proportions from the original assessment report. The updated value is £6.14 per Tegaderm CHG dressing. The cost of Tegaderm CHG was varied using one-way sensitivity analysis.

Several studies have reported different values for the cost of treating an episode of CRBSI. The MTG 44 Curos for preventing infections when using needleless connectors identified 3 studies reporting estimates for this parameter published after the original assessment report. All of them, including the guideline itself, based their estimates of cost upon Hocknaull et al (2008). The EAC identified two additional studies reporting estimates of this parameter. Heimann et al (2018) conducted a cost and resource utilisation analysis in Germany and reported overall cost of treating CRBSI between €13,881 and €13,929 (Heimann et al., 2018). Maunoury et al (2014) reported an average cost of treating CRBSI of €12,391 using data from ICUs in France (Maunoury et al., 2015). The EAC considered it appropriate to uplift the figure used in the original assessment report inflating it to 2017-2018 prices.

Table 1. Updated cost model parameters

Model parameter	Value used in the original model	Updated value	Distribution and SE	Source of updated parameter
Baseline rate for CRBSI	0.3 per 1,000 catheter-days	0.28 per 1,000 catheter-days	Gamma (SE = 0.12)	Scottish Intensive Care Society Audit Group (2018)
Effectiveness of Tegaderm CHG to prevent CRBSI	0.402 (reported as hazard ratio)	0.45 (reported as relative risk)	Lognormal (SE = 0.11)	Safdar et al (2014)
Baseline local site infection rate	0.14 per catheter-days	0.4 per 1000 catheter-days	Gamma (SE = 0.12)	Scottish Intensive Care Society Audit Group (2018)
Baseline dermatitis rate	0.002 1-year probability	0.3 per 1000 catheter-days	Gamma (SE=0.70)	Eggimann et al (2019)

Length of stay with catheterisation	10 days	13 days	Gamma (SE=6.5)	NICE MTG44 Curos for preventing infections when using needleless connectors
Cost of Tegaderm CHG	£6.26	£6.14	Fixed	Estimated in the basis of cost reduction provided by manufacturer
Cost of standard dressing	£1.54	£1.72	Fixed	Uplifted from the original report
Cost of CRBSI	£9,990	£10,199.86	Gamma (SE=3000)	Uplifted from the original report
Cost of local site infection	£100	£103.03	Gamma (SE=30)	Uplifted from the original report
Cost of dermatitis	£6	£6.18	Gamma (SE=3)	Uplifted from the original report

4. Results from updates changes

As per the original assessment report, the updated base-case scenario was complemented by a sub scenario analysis using two alternative estimates of baseline incidence rate of CRBSI from English and Scottish ICUs. Table 2 summarises the base-case results per patient when utilising the English CRBSI incidence rate of 1.48 per 1,000 catheter-days. The use of Tegaderm CHG dressing generates a cost of £106.62 whereas standard dressing generates a cost of £199.69. The intervention generates a cost saving of £93.07. Similarly, when using the estimate of CRBSI baseline incidence rate from the Scottish Critical Care Society audit group (0.28 per 1,000 catheter-days), the cost difference between the two alternatives favours the utilisation of Tegaderm CHG although the magnitude of the savings decreases to £7.50 (see table 3).

Table 2. Deterministic base case results per patient using 1.48 per 1,000 catheter-days as baseline CRBSI incidence rate(English data).

	Costs of dressing	Costs of CRBSI	Costs of local site infection	Costs of dermatitis	Total
Standard	£4.76	£194.37	£0.53	£0.02	£199.69
Tegaderm CHG	£18.43	£87.93	£0.24	£0.02	£106.62
Incremental	£13.67	-£106.44	-£0.29	£0.00	-£93.07

Table 3. Deterministic base case results per patient using 0.28 per 1,000 catheter-days as baseline CRBSI incidence rate (Scottish data).

	Costs of dressing	Costs of CRBSI	Costs of local site infection	Costs of dermatitis	Total
Standard	£4.76	£37.98	£0.53	£0.02	£43.30
Tegaderm CHG	£18.43	£17.11	£0.24	£0.02	£35.80
Incremental	£13.67	-£20.87	-£0.29	£0.00	-£7.50

These cost differences are mainly driven by the estimates of baseline incidence rate of CRBSI, clearly illustrated in the sub-scenario analysis in the base case. In the deterministic sensitivity analysis, the tornado diagram from the base-case using English data suggests cost of treating CRBSI, the effectiveness of Tegaderm for preventing CRBSI infections, and catheter dwell time (length of stay with catheterisation) are the most important drivers of the cost difference. Nonetheless, none of these parameters have the sufficient impact to change the direction of the incremental cost estimate. In the sub-scenario analysis using Scottish data, mean number of dressing per patient and the unit cost of Tegaderm CHG also become important drivers of the cost difference. When considering extreme values of such parameters, the direction of the incremental cost changes and the use of Tegaderm CHG becomes cost-incurring.

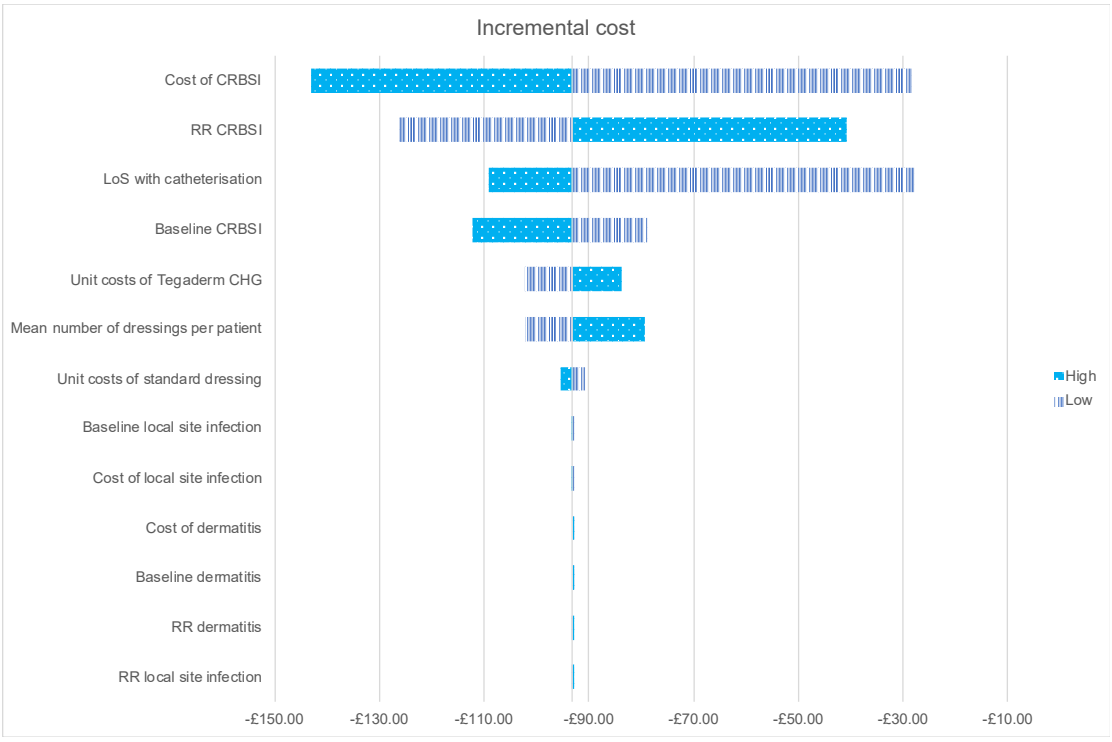

Figure 1.Tornado diagram of univariate sensitivity analysis using English data

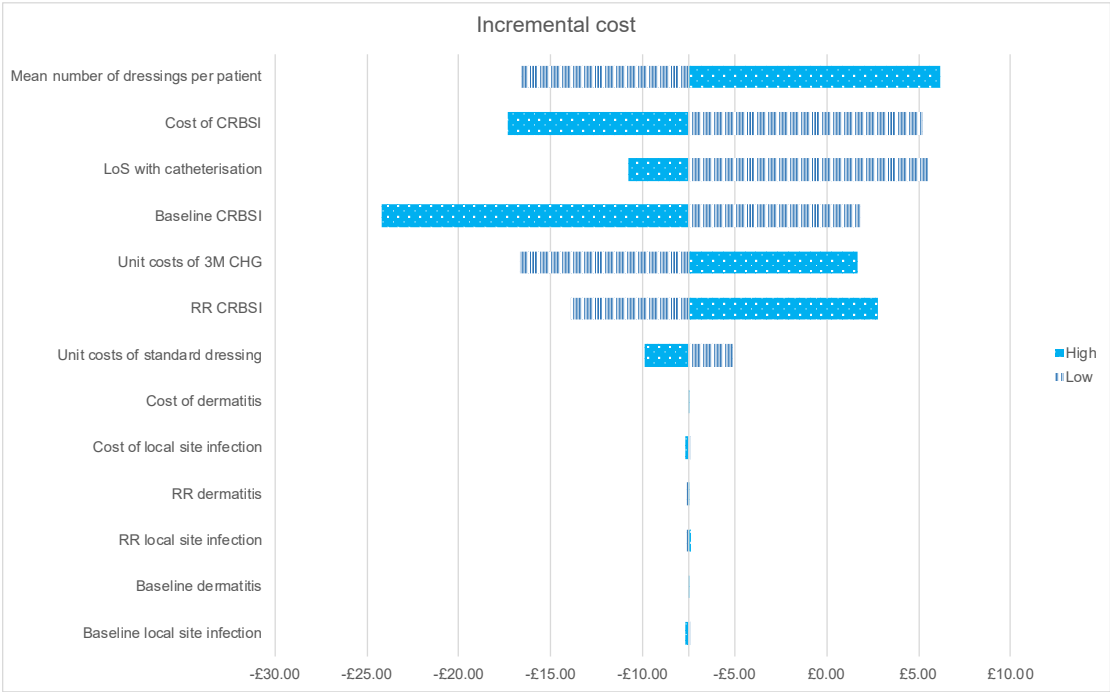

Figure 2. Tornado diagram of univariate sensitivity analysis using Scottish data

As per the original assessment report stated, there is a high degree of uncertainty around CRBSI incidence rate estimates. Therefore the EAC replicated the impact assessment of such parameter on the cost difference between standard dressings and Tegaderm CHG. The results of the univariate sensitivity analysis showed the model is robust as the cost difference favours the use of Tegaderm CHG even when the lower bound (Scottish CRBSI incidence rate estimate of 0.28 per 1000 catheter days) was used. Additionally, the analysis showed that a parameter value of 0.18 per 1,000 catheter days is the cut-off value to make the use of Tegaderm CHG cost-incurring in comparison to standard dressing.

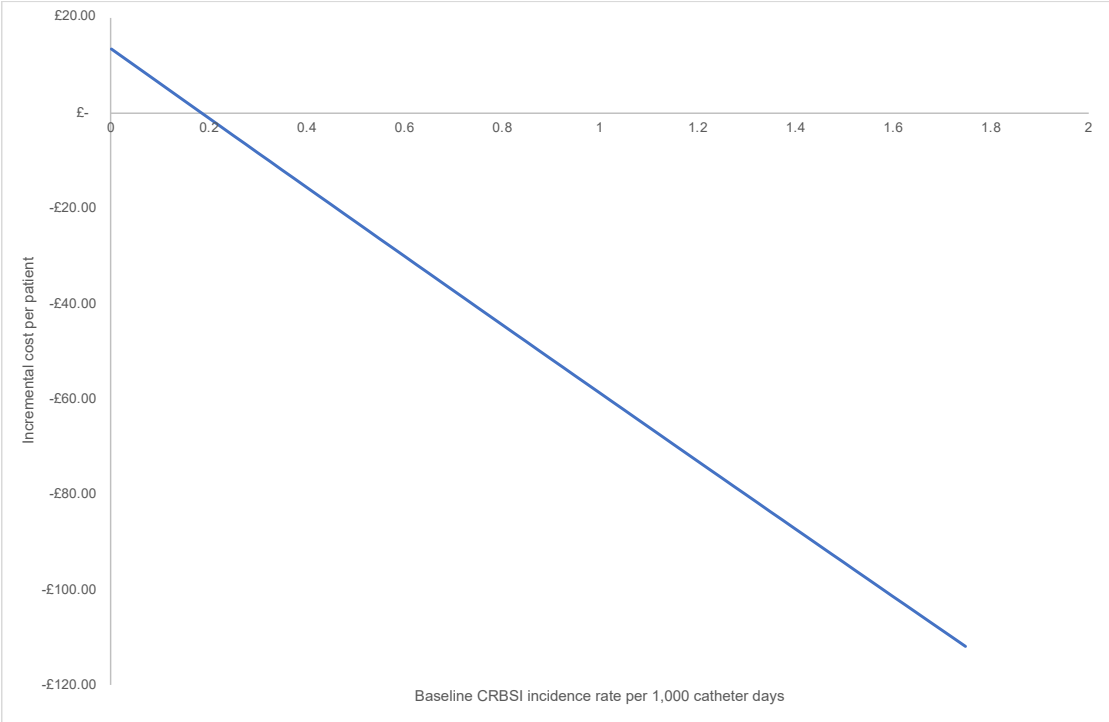

Figure 3. Univariate sensitivity analysis around baseline CRBSI incidence rate per 1,000 catheter-days

Given the uncertainty around the cost of Tegaderm CHG, the EAC conducted cost threshold analysis in order to estimate the break-even cost value in both base-case sub scenarios. Figure 3 shows the point estimate were Tegaderm CHG becomes cost-neutral is £8.64 when using the Scottish estimate of CRBSI incidence rate. The estimate of cost-savings of Tegaderm CHG are robust to the variation of the unit cost of the intervention in the base case, even when considering extreme values of that parameter. In order to make Tegaderm CHG under in the base case, its unit cost has to increase up to £37.16.

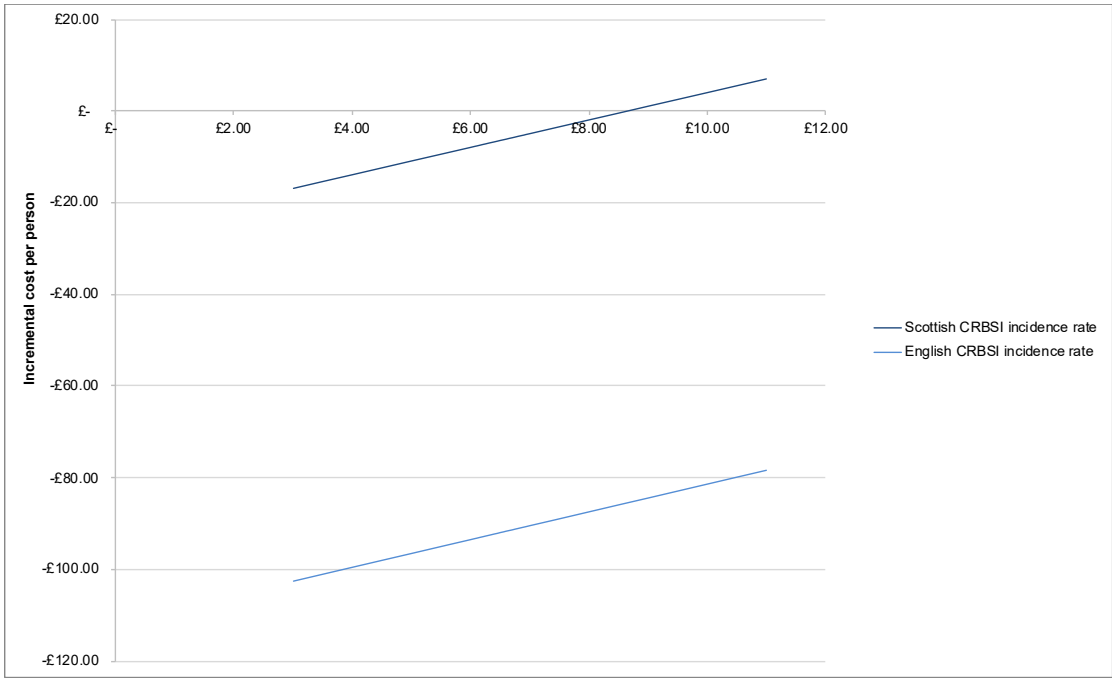

Figure 4. Univariate sensitivity analysis around unit cost of Tegaderm CHG

The PSA undertaken in this cost update was run using the ranges and distributions of the updated parameters specified in table 2. The rest of the parameters remained unchanged. The EAC replicated the analysis undertaken in the original assessment report. The results of the PSA are shown in table 5.

Table 4. Probabilistic sensitivity analysis

	English data	**Scottish data**
Probabilistic total cost per patient with Tegaderm CHG	£107.06	£44.34
Probabilistic total cost per patient with standard dressing	£199.19	£36.45
Probabilistic incremental total cost per patient	-£92.13	-£7.89
Probabilistic incremental total cost per patient	98.88%	50.30%

5. Conclusion

The new base case and sensitivity analyses with the updated parameters show that Tegaderm CHG is cost-saving within the time horizon considered in the calculations. Some differences were noted between the results obtained from this cost update analysis and the results contained in the original assessment report.

Firstly, the magnitude of the cost-savings is slightly larger than those estimated in the original assessment report. When utilising the lower bound of CRBSI incidence rate considered in this assessment (0.28 per 1,000 catheter-days retrieved from Scottish ICUs), the cost difference between Tegaderm CHG and standard dressing is £7.89, an additional saving of £4 in comparison to the estimates of the original assessment report. Correspondingly, when utilising the upper bound of CRBSI incidence rate estimate considered (1.48 per 1,000 catheter days from English ICUs), the cost difference between Tegaderm CHG and standard dressing is £92.13. In comparison to the estimate of cost difference reported in the original assessment, the updated value represents and additional saving of £20.

The value of CRBSI incidence rate to determine the use of Tegaderm CHG as cost-incurring also differed from the value estimated in the original assessment report. Considering all the parameter updates, the threshold to determine Tegaderm CHG as cost incurring shifted from 0.24 to 0.18 per 1,000 catheter-days.

The differences between the estimates of cost differences and breakeven value of CRBSI incidence rate between this cost updated analysis and the original assessment report are likely due to the increment in cost of infection and the increment in length of stay. Nonetheless, the findings in the cost update are consistent with the estimations from the original assessment report.

6. References

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