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Are educational interventions to prevent catheter-related bloodstream infections in intensive care unit cost-effective?

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SUMMARY

Background: There is increasing interest in evidence-based educational interventions in central venous catheter care. It is unclear how effective these are at reducing the risk of bloodstream infections from the use of intravascular catheters (catheter-BSIs) and the associated costs and health benefits.

Aim: To estimate the additional costs and health benefits from introducing such interventions and the costs associated with catheter-BSIs.

Methods: A comprehensive epidemiological and economic review was performed to develop the parameters for an economic model to assess the cost-effectiveness of introducing an educational intervention compared with clinical practice without the intervention. The model follows the clinical pathway of cohorts of patients from their admission to an intensive care unit (ICU), where some may acquire catheter-BSI, and estimates the associated costs, mortality and life expectancy.

Findings: The additional cost per catheter-BSI episode was £3940. The results of this model demonstrate that introducing an additional educational intervention to prevent catheter-BSI improved patient life expectancy and reduced overall costs.

Conclusion: Introducing evidence-based education is likely to reduce the incidence of catheter-BSI and the model results suggest that the cost of introducing the interventions will be outweighed by savings related to reduced ICU bed occupancy costs.

Introduction

Bloodstream infections resulting from the use of intravascular catheters (catheter-BSIs) are the most frequent infection in intensive care unit (ICU).[1] Catheter-BSIs increase patients' length of stay in hospital and their risk of health complications and death. They also impose an associated burden on health

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services resources.[1] However, there is growing evidence that these infections are preventable through the use of evidence-based educational interventions, potentially leading to best practice being employed by ICU staff. The Keystone ICU project, a multi-component educational intervention conducted in 103 ICUs predominantly in Michigan, USA, more than halved catheter-BSI incidence.[2] The intervention was a central venous catheter care (CVC) bundle that encompassed education together with five elements: optimal hand hygiene, chlorhexidine skin antisepsis, maximal barrier precautions for catheter insertion, choice of optimal insertion site, and prompt catheter removal. This approach has since been replicated with similar initiatives in the UK (Matching Michigan) and Australia (CLAB ICU project).[3,4]

The evidence for the effectiveness of single and multi-module interventions to prevent catheter-BSI has recently been reviewed, but uncertainty remains around the likely costs and health benefits associated with bundle interventions.[5] An economic model is a simplified mathematical representation of the clinical pathway and is a useful tool to synthesize evidence on health consequences and costs from many different sources in order to inform health decision-makers about clinical practices and healthcare resource allocations.[6,7] This article describes the model developed for the UK Health Technology Assessment Programme to synthesize the health and cost consequences of introducing a multi-component educational intervention (CVC care bundle) to catheter-BSI prevention.

Methods

Economic model

As no previous relevant economic model existed, we developed a model to estimate the costs, health benefits and cost-effectiveness of implementing a CVC care bundle for preventing catheter-BSI in adult patients in ICUs in England and Wales compared with current clinical practice. The CVC care bundle in this analysis replicated the original US Keystone ICU project approach, with data parameters from the Matching Michigan programme in the UK, and the CLAB ICU project.[2–4] Current clinical practice was defined as clinical care that did not implement all elements in the CVC care bundle.

The decision-analytic model follows hypothetical cohorts of patients, who receive the CVC care bundle or receive current clinical practice, from ICU admission for the remainder of their lifetime, and estimates the costs during hospital stay and the subsequent life expectancy and quality of life.[7] The economic evaluation was from the perspective of the UK National Health Service (NHS). The health benefits were discounted to give a time preference to costs and health outcomes that happen in the near rather than distant future, at 3.5% per year, as recommended by the National Institute for Health and Clinical Excellence.[8] The base price year for the costs was 2011. Where necessary, costs were inflated to that year using the Inflation Indices from the Unit Costs of Health and Social Care.[9]

The numbers of ICU patients infected with catheter-BSI depend upon the incidence rate, the proportion of patients with a CVC and the effectiveness of the intervention (CVC care bundle or current clinical practice) for preventing infections. Patients may die during their hospital stay and the risk of mortality is greater for those with catheter-BSI. Furthermore, patients' length of stay (LOS) in hospital is greater for those with catheter-bloodstream infection (BSI). This model estimates the number of people who contract catheter-BSI, those who die in hospital and the total LOS for the two cohorts. The long-term survival of patients after discharge from the ICU is estimated using a simple Markov model with states for alive and dead.[7] Quality of life is included in the model by estimating quality-adjusted life years (QALYs) by adjusting lifetime survival using patient health-state utility values, which vary between 0 for death and 1 for perfect health.[7] The model is used to calculate costs for each cohort, including those for hospital stay, the treatment and diagnosis of the catheter-BSI infections and the costs of implementing the CVC care bundle.

Several simplifying assumptions were made in the model structure due to lack of data. For the purposes of the model, we assumed that catheter-associated BSI (CABSI) and catheter-related BSI (CRBSI) were synonymous and were collectively referred to as catheter-BSI.[10] It was assumed that the catheters were inserted or removed mainly within the ICUs and that no multiple catheterizations existed. The consequences of catheter-BSI were also assumed not be dependent on age, disease severity or causative micro-organisms. It was assumed that mortality rates during the hospital stay following intensive care discharge, and after hospital discharge, did not differ between patients who had catheter-BSI in the ICU and those who did not.

One-way deterministic sensitivity analyses were performed by varying one parameter at a time, from its base case value, leaving all other variables unchanged. The ranges used were from the confidence intervals from the primary data. The sensitivity analyses investigated the effect of uncertainty around the model assumptions, structure and parameter values on the cost-effectiveness results, in order to highlight the most influential parameters and to test the robustness of the cost-effectiveness results.

Multi-parameter uncertainty in the model was addressed using probabilistic sensitivity analysis (PSA).[11] In the PSA, probability distributions were assigned to point estimates of all parameters used in the base case analysis. The model was run for 1000 iterations, with a different set of parameter values for each iteration, by sampling parameter values at random from their probability distributions. The parameters included in the PSA, the distribution used for sampling each parameter, and the upper and lower limits assumed for each variable are reported in Table I.

Data sources

Data used in the economic model were identified through a systematic review of the clinical effectiveness of the educational intervention, literature searches, and through discussion with clinical experts (Table II).[5] For the purposes of our analyses, we have used the baseline incidence of catheter-BSI in the model to reflect clinical practice without implementation of the CVC care bundle for the most recent UK period available, i.e. before the introduction of the Matching Michigan intervention.[3]

The effectiveness of a CVC care bundle was based upon a systematic review.[5] There were no UK data available, at the time of the analysis, and we considered the 'CLAB ICU' study in Australia to be the most appropriate for use in the economic model, as it was a good methodological study with multiple centres, specifically intended to replicate the original US

Table I
Parameters included in the model

Parameter name	Base case	Source
Catheter-BSI incidence rate, per 1000 catheter-days for current clinical practice	3.7	Matching Michigan[3]
ICU mortality, no catheter-BSI	0.169	ICNARC, 2011[16]
Relative risk for ICU mortality due to catheter-BSI	3.25	Lambert *et al.*[15]
Proportion of patients with a CVC	0.71	ICCTG[a]
Ward bed-day (£)	246	HRG 2010/11[18]
ICU bed-day (£)	1440	HRG 2010/11[18]
Catheter-BSI diagnosis and treatment costs (£)	518	Halton *et al.*[19]
CVC care bundle (per ICU patient) (£)	15.48	Matching Michigan[3]
Bundle effectiveness (relative risk)	0.4	Burrell *et al.*[4]
Additional ICU LOS for catheter-BSI (days)	1.5	Lambert *et al.*[15]
Additional ward LOS for catheter-BSI (days)	5.13	Warren *et al.*[25]
Relative risk for mortality outside ICU, first year	2.9	Williams *et al.*[17]
Relative risk for mortality outside ICU, year 2+	1.5	Williams *et al.*[17]

BSI, bloodstream infection; ICU, intensive care unit; ICNARC, Intensive Care National Audit and Research Centre; CVC, central venous catheter; HRG, Healthcare Reference Group; LOS, length of hospital stay.

[a] Irish Critical Care Trials Group, Intensive Care Society of Ireland, Health Protection Surveillance Centre, Health Service Executive Critical Care Program. Catheter-related infection in Irish intensive care units – a pilot surveillance study. 2011 (http://www.hpsc.ie/hpsc/A-Z/MicrobiologyAntimicrobialResistance/InfectionControlandHAI/Surveillance/20102011NationalCatheter-RelatedInfectionPilotStudy/File,12711,en.pdf).

Keystone ICU project approach in a different national setting.[2,4] The CLAB ICU study used the definition of central line-associated bacteraemia (CLAB) from the New South Wales Department of Health surveillance definition and the definition of the US Centers for Disease Control and Prevention.[12,13]

The increased LOS and excess mortality attributed to catheter-BSI varied widely in the literature according to the methodology used, with some studies overestimating these outcomes. The appropriate method to estimate these parameters is to use a multistate or longitudinal model that accounts for the time of the infection, and of these, Lambert *et al.*'s study was considered the most relevant and appropriate.[14,15]

General population data for patients in UK ICUs were taken from the Intensive Care National Audit and Research Centre (ICNARC).[16] As with LOS, we considered the study by Lambert *et al.* to be the most appropriate for estimating additional risk of mortality attributable to catheter-BSI.[15] Their findings suggest that catheter-BSI trebles the risk of mortality for patients in the ICU. The long-term survival of patients after discharge from the ICU was estimated based on England and Wales population mortality. The general population mortality rates were multiplied by the relative risks of mortality reported by Williams and Dobb.[17]

Table II
Model results for cohorts of 100 adult patients admitted to intensive care

Result	Current practice	CVC care bundle	Difference
Patients with catheter-BSI in intensive care	1.31	0.53	0.79
Total mortality, ICU unit	17.40	17.10	0.30
Total survivors, hospital discharge	74.30	74.60	0.30
Additional ICU LOS for catheter-BSI	1.97	0.79	−1.18
Additional ward LOS for catheter-BSI, days	6.74	2.70	−4.04
Discounted life-years	879	883	3.55
Discounted QALYs	674	677	2.72
Additional inpatient bed-day cost (£)	£4494	£1798	−£2697
Cost diagnosis + treatment catheter-BSI (£)	£681	£272	−£408
Intervention cost (£)	£0	£1548	£1548
Total cost (£)	£5175	£3618	−£1557
Cost per catheter-BSI infection	£3940	£3940	–
Cost-effectiveness (£/LYS)			−£439
Cost-effectiveness (£/QALY)			−£573
Cost per catheter-BSI averted			−£1976

CVC, central venous catheter; BSI, bloodstream infection; ICU, intensive care unit; LOS, length of stay; LYS, life-year saved; QALY, quality-adjusted life year.

The costs included in the model were ICU and ward bed-day costs, catheter-BSI diagnostic and treatment costs, and the cost of the CVC care bundle. ICU and ward bed-day costs were taken from UK NHS Healthcare Reference Group (HRG) costs.[18] The cost of the CVC care bundle used in the model refers to the additional costs (above those of current clinical practice) of implementing the bundle. For the purposes of the analysis the costs of current clinical practice are assumed to be zero. The cost of the CVC care bundle was estimated by combining the costs of the national management programme (from Matching Michigan) at £9.76 per ICU patient, and local implementation costs to the number of patients treated in ICU at £5.72 per ICU patient. The national management programme included central training days and the development of web-based collection tools. The local training costs were calculated based on clinical advice we received about the implementation of Matching Michigan in one local centre.[3] These primarily consisted of the cost of employing extra nurses to train ICU health professionals to implement the CVC care bundle.

Results

Table III shows the cost-effectiveness results for hypothetical cohorts of 100 adult patients aged 60 years admitted to the ICU. The analysis evaluates a CVC care bundle compared to remaining with current practice. Results are presented for costs and long-term survival and QALYs for the CVC care bundle cohort and the current clinical practice cohort, with outcomes discounted at 3.5%. The base case results show that for every 100 patients

Table III
Deterministic sensitivity analysis for the additional costs for cohorts of 100 adult ICU patients compared with base case results

Name	Input parameters			Distribution used in PSA	Additional costs, £		Additional QALYs	
	Base case	Higher estimate[a]	Lower estimate[a]		Higher estimate	Lower estimate	Higher estimate	Lower estimate
Catheter BSI incidence rate	3.7	5	1.3	Log normal	−£2648	£457	3.67	0.96
Additional ICU LOS for catheter BSI	1.5	2.5	0.001	Triangle	−£2692	£144	2.72	2.72
CVC care bundle effectiveness	0.4	0.67	0.22	Log normal	−£160	−£2488	1.50	3.53
Additional ward LOS for catheter BSI	5.13	8.68	1.58	Log normal	−£2245	−£869	2.72	2.72
Proportion of patients with CVC	0.71	0.96	0.49	Beta	−£2650	−£595	3.68	1.88
CVC care bundle cost (per ICU patient) (£)	£15.48	£20.13	£10.84	Gamma	−£1092	−£2021	2.72	2.72
ICU mortality due to catheter BSI, relative risk	3.25	3.6	2.7	Log normal	−£1557	−£1557	3.14	2.05
ICU mortality, no catheter BSI	0.169	0.2028	0.1352	Beta	−£1557	−£1557	3.26	2.17
ICU bed-day cost (£)	£1440	£1171	£1657	Gamma	−£1239	−£1814	2.72	2.72
Ward bed-day cost (£)	£246	£295	£197	Gamma	−£1756	−£1358	2.72	2.72
Catheter BSI diagnosis and treatment (£)	£518	£622	£415	Gamma	−£1639	−£1475	2.72	2.72

QALYs, quality-adjusted life-years; PSA, probabilistic sensitivity analysis; BSI, bloodstream infection; LOS, length of stay; CVC, central venous catheter; ICU, intensive care unit.
[a] Higher and lower estimates are used as the 95% confidence intervals to estimate the standard errors of the PSA distribution.

admitted to intensive care, the CVC care bundle cohort has 0.8 fewer catheter-BSIs than the current clinical practice cohort, and 0.3 fewer deaths during intensive care, which leads to an increased survival of 3.6 years and 2.7 QALYs. The additional cost for each catheter-BSI was £3940. The CVC care bundle is more effective and less costly (−£1557) than current practice, with an additional cost per life-year saved of −£439 and a cost per QALY gained of −£573. The cost savings are largely as a result of the savings from reduced length of stay in the ICU. The additional cost per catheter-BSI averted was −£1976.

Table I shows the results of the deterministic sensitivity analyses for changes to the input parameters, presented in terms of the difference in additional costs and QALYs between the CVC care bundle and the current clinical practice for cohorts of 100 patients. There was an increased health benefit for all sensitivity analyses (range: 0.96–3.67 QALYs). The additional cost of the CVC bundle varies between −£2692 and £457 for all analyses. With the exception of the catheter-BSI incidence rate and the additional ICU length of stay for patients with catheter-BSI, the CVC care bundle is cheaper for all parameter values, and the model results are most sensitive to changes in these two parameters. Changes to these two parameters produced cost-effectiveness estimates that remained within acceptable limits.

The scatterplot for the PSA is shown in Figure 1. In the majority of iterations (83%) the results show that the bundle is cost-saving compared with current clinical practice. The cost-effectiveness of the bundle was less than £5000 per QALY gained for all simulation results.

Discussion

Our economic evaluation is the only published example of an assessment of the cost-effectiveness of educational interventions for prevention of catheter-BSI in the UK, based on a systematic review of cost-effectiveness studies that identified three economic evaluations of educational interventions to prevent catheter-BSI. One study did not include the cost associated with the care bundle in the analysis; another study used a trial-based cohort analysis to derive estimates of the costs and benefits associated with a simulation-based education intervention in a hospital in the USA; whereas the third study did not consider long-term health benefits beyond the hospital stay.[19–21] It was not possible to conclude from any previous study what the likely cost-effectiveness of the intervention would be.

The model developed in this study estimates the cost-effectiveness of a CVC care bundle versus current clinical practice to prevent catheter-BSI and was developed following a structured and objective process in accordance with standard modelling practice.[22] Sensitivity analyses were used to test all assumptions made in the model for their effect on the model results. PSAs were also completed to describe the full uncertainty around the model parameters; these analyses confirmed the deterministic results.

Through the development of this model, we have used the latest literature on the epidemiology, clinical outcomes and costs associated with CRBSI. We have estimated the cost of a CRBSI episode to be £3940. We consider this cost estimate to be based upon more reliable evidence than previous estimates.[1,23] Estimates for the UK are based upon a study conducted by Plowman *et al.* in 1994–1995 for hospital-acquired infections.[23] This study considered several types of hospital-acquired infections, and there were only a few cases of bloodstream infection ($N = 4$). The study used in our analysis by Lambert *et al.* had a considerably larger sample size, and was conducted according to the European standard protocol for surveillance of healthcare-associated infections.

Despite the strengths of our analysis, the economic evaluation has some limitations. Due to lack of data, it was necessary to make some simplifying assumptions within the model. We estimated the effect of the intervention on a hypothetical cohort of ICU patients, and did not consider the consequences of catheter-BSI on different age groups, disease severity or causative micro-organisms. Data sources with different definitions of catheter-BSI were also included, and it was assumed that patients who had a catheter-BSI had no worse survival than other ICU patients after discharge from the ICU.

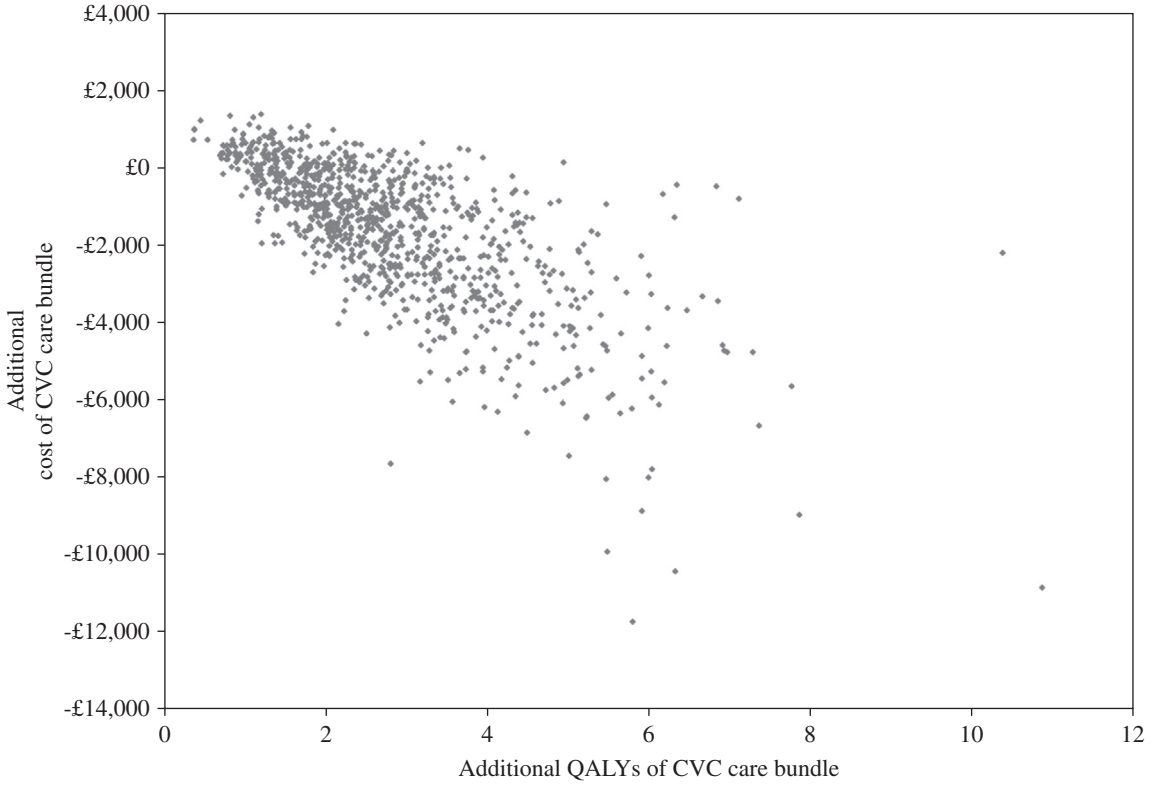

Figure 1. Scatterplot of probabilistic sensitivity analysis results. QALY, quality-adjusted life-year; CVC, central venous catheter.

There is limited reporting on some of the aspects of the CLAB-ICU trial, for example the critical care specialty of the 37 ICUs in their study, the type of CVCs (antimicrobial coated/non-coated CVCs), the changes in other infection control and hospital-acquired infection rates during the study period.[4] Furthermore they have not reported who validated each episode of CLAB. The implementation of components of the education intervention is likely to vary widely in practice between ICUs, both before and after the introduction of the CVC care bundle. This variability was also present among practices of the ICUs in the CLAB ICU study by Burrell *et al.*, on which estimates of the clinical effectiveness of the CVC care bundle were based.[4] This variation in implementation was not reported in the primary studies and cannot be directly quantified. However, the model captures the effect of this variability as a hypothetical average effect.

There was some uncertainty around the model parameters. The primary research studies for educational interventions were uncontrolled before—after studies that may not convincingly distinguish intervention effectiveness from background secular trends.[24] However, recently the results of the Matching Michigan study have been published and these are consistent with those of CLAB-ICU. For adult ICUs, the mean CVC-BSI rate decreased over 20 months by 60% for all clusters combined.[24] The estimates of the additional risk of mortality and additional ICU length of stay for patients with catheter-BSI may be confounded. It is possible that, in fact, very sick patients suffer catheter-BSI and therefore these patients would have worse mortality and additional ICU length of stay. Lambert *et al.* have attempted to adjust their data for these factors.[15] Our model results suggest that even if there were lower attributed health consequences to catheter-BSI, introducing the CVC care bundle would be cost-effective. More robust primary studies of clinical effectiveness are needed, however, to clarify cause and effect to ensure that model input parameters for clinical effectiveness truly reflect intervention impacts rather than secular trends.

In conclusion, implementation of a multi-component educational intervention, based on those CVC care bundles developed in the US Keystone ICU project, are likely to prevent catheter-BSI within ICU. We developed a model to investigate the likely consequences of implementing these CVC care bundles. The model showed that by preventing catheter-BSI within ICU, the CVC care bundles not only reduce the patients' risk of mortality, but also reduce their ICU length of stay, leading to considerable health resource savings. The model specifically addresses clinical practices in ICUs in England and Wales, but the results are likely to be generalizable within the UK and probably beyond.

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Conflict of interest statement
None declared.

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References

1. Tacconelli E, Smith G, Hieke K, Lafuma A, Bastide P. Epidemiology, medical outcomes and costs of catheter-related bloodstream infections in intensive care units of four European countries: literature- and registry-based estimates. *J Hosp Infect* 2009;**72**:97—103.
2. Pronovost P, Needham D, Berenholtz S, *et al*. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Eng J Med* 2006;**355**:2725—2732.
3. Richardson A. Minimising central venous catheter-associated bloodstream infections — 'Matching Michigan' in England. *Nurs Crit Care* 2009;**14**:105—106.
4. Burrell AR, McLaws ML, Murgo M, Calabria E, Pantle AC, Herkes R. Aseptic insertion of central venous lines to reduce bacteraemia. *Med J Aust* 2011;**194**:583—587.
5. Frampton G, Harris P, Cooper K, *et al*. Educational interventions for preventing vascular catheter bloodstream infections in critical care: evidence map, systematic review and economic evaluation. *Health Technol Assess* 2013 (in press).
6. Sculpher MJ, Claxton K, Drummond M, McCabe C. Whither trial-based economic evaluation for health care decision making? *Health Econ* 2006;**15**:677—687.
7. Briggs A, Sculpher M. An introduction to Markov modelling for economic evaluation. *Pharmacoeconomics* 1998;**13**:397—409.
8. National Institute for Health and Clinical Excellence. *Guide to the methods of technology appraisal*. London: NICE; 2008.
9. Curtis L. *Unit costs of health and social care*. Canterbury: University of Kent; 2011. Personal Social Services Research Unit.
10. Tomlinson D, Mermel LA, Ethier MC, Matlow A, Gillmeister B, Sung L. Defining bloodstream infections related to central venous catheters in patients with cancer: a systematic review. *Clin Infect Dis* 2011;**53**:697—710.
11. Briggs A, Sculpher M, Claxton K. *Decision modelling for health economic evaluation*. Oxford University Press; 2006.
12. McLaws ML, Taylor PC. The Hospital Infection Standardised Surveillance (HISS) programme: analysis of a two-year pilot. *J Hosp Infect* 2003;**53**:259—267.
13. O'Grady NP, Alexander M, Dellinger EP, *et al*. Guidelines for the prevention of intravascular catheter-related infections. Centers for Disease Control and Prevention. *MMWR Recomm Rep* 2002;**51**:1—29.
14. Wolkewitz M, Beyersmann J, Gastmeier P, Schumacher M. Modeling the effect of time-dependent exposure on intensive care unit mortality. *Intensive Care Med* 2009;**35**:826—832.
15. Lambert ML, Suetens C, Savey A, *et al*. Clinical outcomes of health-care-associated infections and antimicrobial resistance in patients admitted to European intensive-care units: a cohort study. *Lancet Infect Dis* 2011;**11**:30—38.
16. Intensive Care National Audit & Research Centre. *CMP case mix and outcome summary statistics*. London: ICNARC; 2011.
17. Williams TA, Dobb GJ, Finn JC, *et al*. Determinants of long-term survival after intensive care. *Crit Care Med* 2012;**36**:1523—1530.
18. Department of Health. *NHS reference costs 2009—10*. London: DoH; 2011.
19. Halton KA, Cook D, Paterson DL, Safdar N, Graves N. Cost-effectiveness of a central venous catheter care bundle. *PLoS ONE* 2010;**5**:1—11.
20. Cohen ER, Feinglass J, Barsuk JH, *et al*. Cost savings from reduced catheter-related bloodstream infection after simulation-based education for residents in a medical intensive care unit. *Simuln Healthcare* 2010;**5**:98—102.
21. Bond WF, King AE. Modeling for the decision process to implement an educational intervention: an example of a central venous catheter insertion course. *J Patient Safety* 2011;**7**:85—91.
22. Philips Z, Ginnelly L, Sculpher M, Claxton K, Golder S, Riemsma R. Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technol Assess* 2004;**8**:iii—iv. , ix—xi, 1—158.
23. Plowman R, Graves N, Griffin MA, *et al*. The rate and cost of hospital-acquired infections occurring in patients admitted to selected specialties of a district general hospital in England and the national burden imposed. *J Hosp Infect* 2001;**47**:198—209.
24. Bion J, Richardson A, Hibbert P, *et al*. 'Matching Michigan': a 2-year stepped interventional programme to minimise central venous catheter-blood stream infections in intensive care units in England. *BMJ Qual Saf* 2013;**22**:110—123.
25. Warren DK, Quadir WW, Hollenbeak CS, Elward AM, Cox MJ, Fraser VJ. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. *Crit Care Med* 2006;**34**:2084—2089.