

Appendices

The following tables present detailed information on each study analysed.

Appendix table 1. Publications on the economic burden of adverse events

Publication	Perspective	Adverse events (AEs)	Sample characteristics	Cost data sources	Components of hospital costs	Cost calculation methods	Sensitivity analysis?
Cosgrove and al., 2005[24]	HCO*	MRSA† BSI†	1 tertiary university hospital, 630 beds, 40 000 average annual admissions, 348 MRSA infected patients	Total billed charges (Tariffs)	Gross estimation of average daily cost	1) Tariff-to-cost conversion; 2) IC [†] =total cost - cost from the diagnosis of AEs	No
de Lissovoy and al., 2009[25]	Not stated (HCO)	SSI** in various surgery categories	723 940 nationally representative stays, 6 891 SSI cases	Total billed charges (Tariffs)	Gross estimation of whole-stay cost	1) Propensity score of SSI for matching; 2) Tariff-to-cost conversion; 3) IC=linear regression	No
Dietrich and al., 2002[26]	HCO + public insurer	Healthcare associated pneumonia	1 hospital, 2 ICU ^{††} , 437 eligible patients, 37 pairs included	HCO financial services + medical records (volumes)	Average daily and total costs in both ICU and general ward	1) Resources consumption for diagnosis, treatment, nursing and stay; 2) Matched comparison of cases and controls	No
Eber and al., 2010[27]	HCO	BSI and Healthcare associated pneumonia	58 701 608 nationally representative stays, 557 967 cases of healthcare associated pneumonia or BSIs	Total billed charges (Tariffs)	Gross estimation of whole-stay cost	Matched comparison of cases and controls	Yes, on cost calculation methods
Gianino, and al., 2007[28]	HCO	Various HAIs ^{**}	Surveillance data from an Italian region	HCO financial services + medical records (volumes)	Average daily costs if LOS ^{†††} was prolonged or treatment and nursing charges if not	Stochastic linear model	No

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Graves and al., 2003[29]	Private insurer	All HAIs	a) 32 179 medical stays, 24 899 surgical stays from a single hospital group b) nationally representative sample of 162 879 medical stays and 245 130 surgical stays	a) HCO financial services; b) published data	Gross estimation of both average daily and average total cost	Mean cost=HAI incidence*extra LOS*opportunity cost (mean daily cost)	Yes, on input variables in cost calculation
Herwaldt and al., 2006[30]	Not stated (HCO)	Postoperative infections	1 tertiary university hospital, 3 surgical units, 3 864 eligible patients, 438 SSIs	Not stated (reference to published data)	Excess LOS, healthcare resource use (drugs, readmission), mortality Direct inpatient cost (not stated, reference to published data)	Not stated (reference to published data)	No
Hoonhout and al., 2009[31]	Not stated (HCO)	All types of AEs	Nationally randomized representative sample, 21 hospitals, 200 deceased and 200 non deceased patients from each hospital	Published (official) tables	Average daily costs + specific diagnostic and treatment procedures	1) AE during hospitalization: average costs*attributable LOS; 2) AE cause of in-hospital admission: average costs*national average LOS	Yes, on the estimation of the attributable LOS
Kilgore and Brossette, 2008[32]	Not stated (HCO)	BSIs	55 voluntary hospitals, 1 355 647 eligible stays, 12 578 cases of bloodstream infections	Laboratory and HCO financial services	Not stated	Absorbing (linear) regression	Yes, on the LOS
Kim and al., 2002[33]	HCO	SARM colonisation and infection	1 tertiary hospital, 16800 eligible stays, 94 cases included	HCO financial services + medical records (volumes)	Average daily cost from nursing time, diagnostic procedures, treatment (standardized method, fixed costs included)	1) AE during hospitalization: daily costs*attributable LOS; 2) AE cause of in-hospital admission: whole-stay costs	No

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Publication	Perspective	Adverse events (AEs)	Sample characteristics	Cost data sources	Components of hospital costs	Cost calculation methods	Sensitivity analysis?
Larue and al., 2009[34]	HCO	Healthcare associated SARM pneumonia	1 tertiary university hospital, 6 UCI, 23 cases of MRSA pneumonia (21 matched and included)	Official tables for medication + medical records (volumes)	Diagnostic/therapeutic procedures, surgical or invasive acts	Omega score+++ = $[(45(\Omega_1) + 106(\Omega_2) + 16(\Omega_3) + 4703K + 191)]^*$ 1,2), where Ω_i are diagnostic/therapeutic procedures used and $K = 1$ if surgical or invasive acts were performed. Values are given in euros.	No
Plowman and al., 2001[35]	Not stated (HCO)	All HAIs	1 secondary hospital (579 beds), 5 909 eligible stays (68% recruited), 309 HAI cases	HCO financial services + medical records (volumes)	Average daily cost from fixed and variable costs for diagnostic, treatment, nursing and accommodation	1) In the sample: multivariate linear regression; 2) Nationwide estimates = $NiC(r-1)$ where N =number of in-hospital stays, i =incidence of HAI, r =cost of infected/cost of non-infected patients ratio	No
Sanchez-Velazquez and al., 2006[36]	Not stated (HCO)	All HAIs in the ICU	1 tertiary hospital, 1 ICU, 695 eligible patients, 43 cases (94% successful matching)	Medical records (volumes); prices: not stated	Average daily cost in ICU and in general ward	Matched comparison of cases and controls	No
Sheng and al., 2005[37]	HCO	All HAIs	1 tertiary teaching hospital, 2 000 beds, 60 000 - 70 000 eligible stays/year. Inclusion of 50 % of the HAI identified	HCO financial services	Accommodation (emergency, general ward and ICU), diet, medication, medical devices, laboratory, nursing and procedures	Matched comparison of cases and controls	No
Vargas and al., 2003[38]	Not stated (HCO)	Medication associated AEs in surgical ICUs	1 hospital, 3 surgical units, 401 eligible patients, 37 included	Medical records	Attributable (extra) LOS	Extra LOS was not valued	N/A

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Weber and al., 2008[39]	HCO + patients	SSI	1 hospital, 3 surgical units, 6283 eligible stays, 183 cases included	HCO financial services	Average daily cost from fixed and variable costs for diagnostic, treatment, nursing and accommodation	Matched comparison of cases and controls	No
Wilson and al., 2004[40]	HCO	<i>Acinetobacter baumannii</i> in a burn unit	1 tertiary university hospital, 1 specialized burnt unit, 217 eligible stays, 34 cases of HAI	Total billed charges (Tariffs)	Average whole-stay costs	Matched comparison of cases and controls	Yes, on the tariff-to-cost conversion coefficient
Wisplinghoff and al., 2003[41]	Not stated (HCO)	BSI in adult neutropenic patients	1 hospital, 1 specialized medical unit, 417 eligible patients, 84 cases included	Total billed charges (Tariffs)	Average whole-stay costs	Not stated	No

*HCO: Healthcare organisation

†MRSA: Methicillin resistant *Staphylococcus aureus*

‡BSI: Blood stream infection (sepsis)

‡CLABSI: Central line associated blood stream infection

¶IC: Incremental cost

**SSI: Surgical site infection

††ICU: Intensive care unit

‡‡HAI: Healthcare associated infection

‡‡LOS: Length of stay

¶¶CAUTI: Catheter associated urinary tract infection

***VAP: Ventilator associated pneumonia

†††: Omega score is a validated tool that allows for estimating the average cost of standardized diagnostic and therapeutic acts. Detailed information on this score is described elsewhere. Chaix C, Durand-Zaleski I, Alberti C, et al. A model to compute the medical cost of patients in intensive care. *Pharmacoeconomics* 1999;15:573–82.

Appendix table 2. Publications on the cost of safety practices.

Publication	Perspective	Sample characteristics	Patient safety practices	Output measures	Cost categories	Cost data sources
Fukuda and al., 2008a[42]	HCO*	7 tertiary university hospitals	Various types of patient-safety actions ("patient safety systems") and infection control activities	Activity level	Personnel (time spent on patient-safety meetings or actions), rooms and material for staff meetings	Hospital financial services
Fukuda and al., 2008b[43]	HCO, public insurer	Risk managers and hygienists of the whole country's teaching hospitals (40.2% response rate)	Various types of patient-safety actions	Activity level	Personnel (time spent on patient-safety meetings or actions)	Hospital financial services
Stone and al., 2007[44]	Not stated (HCO)	40 volunteer hospitals from the CDC [‡] NNIS [¶]	Implementation of the 2002 CDC* recommendations for hand hygiene	Rate of compliance with guidelines	Hygiene products and other implementation costs (staff time, educational material)	Hospital financial services

*CDC=Centers for Disease Control and Prevention

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Appendix table 3. Complete economic evaluations of patient safety practices.

Publication	Adverse events (AE)	Sample characteristics	Patient safety practice	Evaluation method	Perspective	Outcome measure(s)	Efficacy data sources	Economic data sources and categories	Sensitivity analysis?
Brown and al., 2009[45]	All HAI*s	Multiple data sources: a) 15 experts opinions b) published data	Intensive cleaning of all hospital wards in a national level	Cost-utility and cost-benefit analysis	HCO+, public insurer	QALYs++ gained per HAI avoided, cost per HAI avoided, net cost of the strategy	Expert opinion	1) Strategy: official allocated amounts + NHS payments to HCO (opportunity costs); 2) HAIs: Published data	Yes, on the incidence of AEs, efficacy and input economic variables
Calugar and al., 2006[46]	Nosocomial pertussis outbreak	Survey of hospital Data collected in the hospital during the outbreak of the pertussis (17HCW, 307 patients).	Mandatory vaccination of in-hospital HCW (versus outbreak control)	Cost-effectiveness and cost-benefit analysis	HCO, HCW±	Cases and complications avoided amongst HCW and contacts, number of outbreaks avoided for the vaccination to be cost-neutral	Published data	Hospital direct (diagnosis, prophylaxis, treatment) and indirect (lost personnel working hours) costs: billing records; 2) Personnel direct (lost wages and uncompensated care expenses) and indirect (lost leisure time) costs: interviews + published data; 3) Vaccination: published data	Yes, on expositions to pertussis and contact rates, on HCW turnover
Harbrecht and al., 2006[47]	Postoperative respiratory complications in selected surgical wards	1 hospital, 1 surgical unit, 2230 stays before implementation of the action and 2805 stays after implementation.	Implementation of a RT-driven patient-assessment scale and protocolled interventions on postoperative patients	Cost-effectiveness analysis	HCO	Number of treatments, number of ICU ⁱ admissions, length of stay, mortality, total hospital costs and charges	Empirical data (from the implementation and 8 months on)	1) Resource utilization: medical records (standardized collection); 2) Valuation: HCO financial services	No

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Karnon and al., 2008[48]	Medication-associated AEs	Published data	Three patient safety practices were considered separately: CPOE¶, additional ward pharmacists and bar coding	Cost-utility and cost-benefit analysis	HCO, societal	Number of AEs averted, QALYs per AE averted, net benefits resulting from the three patient safety practices	Published data	Published data (total costs estimation with Markov modelling by Monte Carlo technique using the lower and upper borders of cost information)	No
Kopp and al., 2007[49]	Medication-associated AEs in surgical ICUs	1 tertiary university hospital (360 beds), 1 ICU, 129 individual interventions	Multiple interventions of a critical care pharmacists in an ICU	Cost-effectiveness analysis	HCO	Number of AEs averted, costs averted by each intervention	Expert opinion	Published data	No
Nuckols and Scarce, 2005[50]	All types of AEs	Published data	National reduction of medical residents work-hours load	Cost-benefit analysis	HCO, societal	Number of AEs averted, rate of AE reduction for the intervention to be cost-neutral	Published data	1) Frequency and costs of AEs: Published data; 2) Wages, work-hours reduction: official sources	Yes, on AEs incidence and costs, patient safety practice effectiveness, personnel wages / categories)

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Rapp and al., 2004[51]	All HAIs	1 tertiary hospital (430 beds), all admissions included	Single fluoroquinolone-use policy	Cost-effectiveness analysis	HCO	Susceptibility rates of multiple pathogens to the fluoroquinolone used, policy acceptance by the medical staff, costs to the hospital	Empirical data from the implementation and 1 year on	Hospital accounting system (costs of the fluoroquinolones before and after implementation)	No
Van Rijen and Kluytmans, 2009[52]	MRSA HAIs	1 tertiary university hospital (1370 beds), 39 943 patients/year and 282 585 hospitalization days/year (mean values)	Search and destroy policy (implemented in a national level)	Cost-benefit analysis	HCO	Multiple activity (output) indicators, MRSA infections averted	Comparison between actual incidence and published values	1) Hospital accounting system: fixed costs: pressure-controlled isolation rooms and the salary of an infection-control practitioner; variable costs: screening, diagnosis, isolation-associated costs (cases and contacts, amongst which HCWs administrative leaves); 2) Published data (counterfactual): treatment, costs of MRSA outbreaks if the policy is absent	No
Vriens and al., 2002[53]	MRSA** HAIs	1 tertiary university hospital, 1045 eligible "at risk" patients, 38 in hospital and 16 ambulatory patients included. 16 outbreaks.	Search and destroy policy (implemented in a national level)	Cost-effectiveness analysis	HCO	Multiple activity (output) indicators, MRSA infections averted	Comparison between actual incidence and published values	1) Hospital accounting system: variable costs only: screening, diagnosis, isolation-associated costs, replacement of HCWs on administrative leave, income loss for HCWs; 2) Published data (counterfactual): cancelled surgical procedures, wards/beds closure.	No

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Wang and all, 2003[54]	All types of AEs in primary care	Multiple data sources: a) primary care provider (2500 patients); b) Published data	Electronic medical records implementation	Cost-benefit analysis	Private insurer	Drug expenditure, improvement in utilisation of medication and radiology tests, total net benefit	Published data	1)Empirical data: implementation of the strategy (fixed material and software costs, loss of productivity); 2)Published data and experts opinion: averted costs	Yes, on the number of patients, capitation rate, averted costs, discounting rate
Weeks and al., 2001[55]	Medication-associated AEs	172 hospitals from the Veteran Affairs Administration, 27 volunteer units Multiple data sources: a) 1 hospital group (700 beds), 27800 stays (all the patients included), b) Published data	Staff training for improvement of medication prescription and administration	Cost-effectiveness analysis	Private insurer	Frequency of life-threatening medication associated adverse events	Insurer's surveillance system	1) Empirical data: staff meetings for educational purposes, litigation costs; 2)Published data: treatment costs	Yes, on the incidence of AEs, on the discounting rate
Wu and al., 2007[56]	Medication-associated AEs	Multiple data sources: a) 1 hospital group (700 beds), 27800 stays (all the patients included), b) Published data	Electronic ordering and administration system implementation	Cost-effectiveness analysis	HCO	Averted medication errors	Published data	1) Empirical data: hardware, training sessions, staff time; 2) Published data: AEs averted	Yes, on the incidence of AEs, on the effectiveness rate, on personnel costs

*HAI: Healthcare associated infection

†HCO: Healthcare institutions

‡HCW: Healthcare workers

‡ICU: Intensive care unit

¶CPOE: Computerized physician order entry

**MRSA: Methicillin resistant *Staphylococcus aureus*

††QALY: Quality adjusted life year