

Appendix 3: Key elements of the included studies

Source	Setting	N	Mean age, years (range)	% women	Study design	Study focus
Valentin et al. ⁹	205 ICUs, 29 countries	1913 patients	62 (18–99)	39	Cross-sectional survey	Risk factors
Cullen et al. ⁷	5 ICUs and 6 general care units, 2 tertiary care hospitals	4031 patients	NR	NR	Prospective cohort	Risk factors
Sinopoli et al. ¹⁰	20 ICUs, USA	1353 incidents	> 65 (44%)	43	Retrospective cohort	Risk factors
Calabrese et al. ¹¹	5 ICUs, USA	851 patients	NR	NR	Prospective cohort	Risk factors
Tissot et al. ¹²	1 academic MICU	26 patients	NR	NR	Prospective cohort	Risk factors
Rothschild et al. ³	1 MICU and 1 CCU, tertiary care academic hospital	391 patients	64	43	Secondary analysis of a prospective cohort	Risk factors
Landrigan et al. ¹³	1 MICU and 1 CCU, tertiary care academic hospital	581 patients	64	46	Randomized controlled trial	Physician work schedule
Shulman et al. ¹⁴	General ICU, UK	387 drug charts 3465 prescriptions	NR	NR	Before and after	CPOE
Colpaert et al. ¹⁵	1 SICU, Belgium	90 patients 2510 prescriptions	58 (37–71)	NR	Cross-sectional survey with concurrent controls	CPOE
Weant et al. ¹⁶	Neurosurgical ICU	88 medication errors	NR	NR	Before and after	CPOE
Evans et al. ¹⁷	1 MICU, USA	1681 patients	47	41	Before and after	CDSS
Rothschild et al. ¹⁸	2 CSICU and 2 step-down units	800 patients	67	34	Prospective time series	Smart pumps
Nuckols et al. ¹⁹	SICUs and MICUs, 2 hospitals, USA	4604 patients	NR	NR	Before and after	Smart pumps
Leape et al. ²⁰	1 MICU and 1 CCU, tertiary academic hospital	275 patients	NR	NR	Before and after with non-equivalent control	Pharmacists in the ICU
Pronovost et al. ²¹	1 SICU, USA	NR	NR	NR	Before and after	Medication reconciliation
Wasserfallen et al. ²²	1 MICU and 1 SICU, academic hospital, Switzerland	434 patients	NR	NR	Before and after with non-equivalent control	Standardization
McMullin et al. ²³	1 multisystem ICU, Canada	430 patients	66	42	Prospective longitudinal intervention study	Standardization

Note: CCU = critical care unit, CDSS = clinical decision support system, CPOE = computerized physician order entry, CSICU = cardiac surgical intensive care unit, ICU = intensive care unit, MICU = medical intensive care unit, NR = none reported, SICU = surgical intensive care unit, UK = United Kingdom, USA = United States of America.

Appendix 3b: Summary of Included Studies

Source (con't)	Recruitment Method & Sampling/Data Sources	Allocation	Blinding	Attrition of Participants	Outcomes	Statistical Analyses
Valentin et al. 2006 (9)	All patients staying in participating ICUs during 24 hour study period	N/A	None	Sampling frame not reported	Questionnaire of select sentinel events	Multivariable logistic regression
Cullen et al. 1997 (7)	ADEs screened for six months by direct reporting, soliciting information from health care workers and chart review	N/A	None	NR	Two physicians independently evaluated all potential ADEs clinically (important, serious, life threatening)	Univariable & multivariable linear regression analyses
Sinopoli et al. 2007 (10)	Safety reports from voluntary, anonymous, Web-based ICU Safety Reporting System (ICUSRS)	N/A	None	229 reports excluded due to missing data or duplication	Voluntary incident reports (ranging from family dissatisfaction to death)	Chi-square test, multivariable logistic regression
Calabrese et al. 2001(11)	Pharmacist selection of admitted non-consecutive weekday patients during 3 month period	N/A	None	NR	Pharmacist observation of medication errors (no harm, harm, death)	Medication error counts & proportions
Tissot et al. 1999 (12)	2 nurses randomly selected daily for observation	N/A	None	NR	Pharmacist observation of medication preparation and administration errors (minor, significant, life-threatening, fatal)	Medication error counts & proportions
Rothchild et al 2005(3)	Consecutive admitted patients followed until transfer, unit discharge or death	N/A	Suspected errors & AEs rated by two blinded MDs	NR	Direct continuous observation of on-call intern & chart review for errors & AE (severity & preventability rated)	Fisher's exact test, Wilcoxon rank-sum test, Student's t-test
Landrigan et al. 2004 (13)	Consecutive admitted patients followed until transfer, unit discharge or death	Interns randomised to one of two work schedules	Suspected errors & AEs rated by two blinded MDs	NR	Direct continuous observation of on-call intern & chart review for errors (intercepted, nonintercepted) & AEs (preventable, nonpreventable)	Fisher exact test, Wilcoxon rank-sum test, Student's t-test
Shulman et al. 2005 (19)	9 days observation during hand-written prescribing & 17 days during CPOE	CPOE implemented during study period	None	NR	Prospective recording of errors by pharmacist (minor, moderate, major)	Chi-squared test for trend, Student's t-test
Colpaert et al. 2006 (20)	Consecutive admitted patients to 3 units of a SICU over a 5 week period	2 paper-based units & 1 CPOE based unit within SICU	Panel blinded to patient & prescribing method	NR	SICU pharmacist reviewed all prescriptions for error & independent panel evaluated severity (minor, intercepted, serious)	Kruskal-Wallis, Mann-Whitney U test, Fisher's exact test, Chi-squared test, Spearman rank correlation
Weant et al 2007 (21)	Consecutive medication errors reported for 1 year before and 1 year after CPOE implementation	CPOE implemented during study	None	NR	Voluntary reporting of medication errors using online reporting system – clinical consequences	Paired Student's t test

		period			not reported	
Evans et al. 1998 (25)	Consecutive admitted patients over a 3 year period (2 year period before CDSS & 1 year period after)	CDSS implemented during study period	None	NR	Prospective surveillance for ADEs (severity not reported)	Chi-square test, Mann-Whitney U test, Fisher's exact test, multivariable linear regression
Rothschild et al. 2005 (27)	Consecutive admitted patients followed during four 8-week pump periods	Study periods 1 & 3 - decision support on Study periods 2 & 4 - decision support off	None	56 admissions excluded due to missing data logs	Pump software logs, medical record review, two physician review of AEs (preventable vs. nonpreventable; intercepted vs. nonintercepted).	Chi square test, Fisher's exact test, Wilcoxon rank-sum test, Student's t-test, Poisson regression
Nuckols et al. 2007 (28)	Examined 20,000 bed-days of care	Conventional pump study period & smart-pump study period	None	NR	ADEs (preventability) abstracted from medical records by study nurses & rated by two physicians	Poisson regression
Leape et al. 1999 (29)	Patients randomly sampled from four groups; 75 patients before & after intervention, 50 control patients before & 75 control patients after	Random number generator to sample patients before & after pharmacist participation in ICU	Physician reviewers & investigators blinded to patient assignment	NR	ADEs abstracted from medical records by nurse & pharmacist, rated by two blinded physicians for severity and preventability	Unpaired t test
Pronovost et al 2003 (31)	Audit of approximately 10% of patient discharges from ICU per week for 11 months	Medication reconciliation tool	None	NR	Medical record audits for medication errors in the discharge orders – clinical consequences not recorded	Medication error counts & proportions
Wasserfallen et al. 2004 (32)	Patients hospitalized for >24 hours in the study ICUs & prescribed antibiotics during 2 study periods totaling 5 months	Standardized order sheet implemented in the SICU during study period	None	NR	Study pharmacist reviewed antibiotic prescriptions according to American Society of Hospital Pharmacists' criteria for safety (safe vs. unsafe)	Chi-square test
McMullin et al. 2006 (33)	Consecutive ICU patients \geq 18 years of age who were admitted for >48 hours	Baseline usual practice period; 5 behavior change strategies period; follow up observation period	Practicing clinicians blinded to study	NR	Research coordinators abstracted medical record for VTE prophylaxis and VTE	Kruskal-Wallis test, Chi-square test, multiple variable logistic regression

Note: ICU; intensive care unit, NR; none reported, N/A; not applicable, MICU; medical intensive care unit, CCU; coronary care unit, SICU; surgical intensive care unit, CPOE; Computerized Physician Order Entry, CDSS; Clinical Decision Support Systems, ADE; adverse drug event, CSICU; cardiac surgery intensive care unit, VTE; venous thromboembolism