Appendix 1. Included studies (n=30) about automated- and semi-automated drug distribution systems sorted by distribution type and GRADE.[d]

Reference	Country & setting	Objectives	Design & GRADE	Materials and Methods	Keyfindings*
DECENTRALIZED DRUG DISTRIBUTION SYSTEM (n=19)					
Tsao et al., 2014[14]	Canada: Hospital setting	To summarize and evaluate the existing literature reporting the clinical and economic impacts of using decentralized ADDs in hospitals.	Systematic review HIGH	A literature search was conducted in MEDLINE, Embase, and other key databases for 1992-2012 to identify English-language articles (randomized controlled trials, observational studies, before-and-after studies, time series analyzes, cost-effectiveness and cost–benefit analyzes, and review articles) on the use of ADDs in hospital wards (n=175). Pharmacy-based ADDs were excluded. Results (n=8) were categorized according to the outcomes of interest (ME rates, efficiency, cost). All different type of outcomes including safety (ME rates), efficiency (the time pharmacists, pharmacy technicians and/or nurses spent performing medication-related activities) and costs (arge capture rates, personnel time).	**Positive outcomes:** ADDs were found to be effective in reducing 1) medication storage errors and 2) the time that nurses spent taking inventory of narcotics (e.g. from 107 to 48s) and controlled substances. ADDs have limited potential to decrease MEs and increase efficiencies, but impact is highly institution-specific. Use of technology requires proper integration into an institution's medication distribution process. **No definitive evidence** that using ADDs increased the time that nurses or pharmacists spent with patients, reduced MEs resulting in patient harm, or reduced costs in hospitals (e.g. extra-cost: $250,000 annually, savings: $2,08million/5 years, $80,910/year). Pharmacy technicians spent more time stocking the machines.
Chapuis et al., 2010[13]	France: 2 medical ICUs in the same department of a 2,000-bed university hospital.	To assess the impact of an ADS on the incidence of MEs related to picking, preparation, and administration of drugs in a medical ICU, and also evaluate the clinical significance of errors and user satisfaction.	Pre- and post-intervention study involving a control and an intervention medical ICU. MODERATE	Errors were identified by direct observation (1,476 medication for 115 patients). Two-month observation periods were performed before and after implementation of the ADS, preceded by a 15-day run-in period. User satisfaction was assessed three times using self-administered stuctured questionnaires (A 4-point Likert scale). **Data analysis:** Descriptive statistics.	**Positive outcomes:** ADS reduced 1) MEs (from 18.6%TOE to 13.5%) largely related to picking, preparation, and administration of drugs and 2) storage (27.7% to 0.7%) and dose errors (3.8% to 0.5%). Most errors caused no harm. ADS did not reduce errors that could cause harm. **Nurses satisfaction:** Nurses favored the new drug dispensation organization with a tendency for greater satisfaction over time, especially regarding time saved and working conditions. The majority of nurses wished to continue using ADS (96.7%). Working conditions improved (from1.0 +/- 0.8 to 2.5 +/- 0.8).
Dib et al., 2006[27]	Saudi Arabia: five nursing units within a 390-bed tertiary care hospital	To evaluate the impact of an ADDS implementation on cost containment and MAE occurances.	Observational pre- and post-implementation study MODERATE	An ADDS replaced the traditional UD cassette-exchange and open floor-stock medication systems in 5 nursing units. Data collection for MAEs 3 months before and after the implementation, and for cost containment 1 month after implementation. **Data analysis:** Descriptive statistics and time series analysis.	**Positive outcomes:** An ADDS improved the efficiency of drug distribution, assisted in cost containment, and decreased the total number of ADEs by 27%. **Other:** MAEs increased (33%) and other MEs decreased (12-61%). **The overall medication issuance** decreased by an average of 43%, corresponding to overall medication cost reduction by $9,932 (42%). Estimated savings in hemodialysis and six intensive care units $193,000/1 year.

Reference	Country & setting	Objectives	Design & GRADE	Materials and Methods	Keyfindings*
Fanning et al., 2016[29]	Australia: The original and new EDs within a 377-bed public teaching hospital	To assess the impact of ADCs on 1) medication selection and preparation errors, and the types and severity of MEs within the ED.	Observational pre- and post-intervention study MODERATE	Direct observations of 89 nurses completing medication related activities before and after the implementation of ADCs over 3 months (A total of 2087 medication selections and preparations among 808 patients pre-(1139) and post-intervention (864). Medication selection and preparation error rates were calculated and compared. Secondary end points included the impact on ME type and severity. No clinical pharmacy service or pharmaceutical review of medication charts was provided during either of the data collection periods. **Data analysis:** Descriptive statistics.	**Positive outcomes:** There was an observed reduction in medication selection and preparation error rates pre- and post-intervention (24, 1.96% and 6, 0.69%). ADCs resulted in a 64.7% reduction in medication selection and preparation errors. All ME types were reduced in the post intervention study period. **No impact** on ME severity as all errors detected were categorised as minor.
Franklin et al., 2007[30]	United Kingdom: A 28-bed surgical ward in a teaching hospital	To assess a closed-loop EP, automated dispensing, BC patient identification and eMAR system on prescribing and administration errors, confirmation of patient identification and staff time.	Before-and-after intervention study MODERATE	Data were collected 3–6 months before and 6–12 months after the intervention. The pharmacist identified (by observing) prescribing errors during a 4-week period. Timing and documentation errors were excluded. It was recorded whether or not patients' identity was checked while administering medication. Time spent prescribing and providing a ward pharmacy service and nursing time on medication tasks was studied. **Data analysis:** Descriptive statistics.	**Positive outcomes:** Reduction in prescribing errors (3.8 to 2.0%) and MAEs (7.0 to 4.3%). Non-IV MAEs reduced by 39%, predominantly reducing wrong dose and omission errors. Increased confirmation of patient identity before administration (not checked for 82.6% of doses (pre) and 18.9% (post)). **Changes in time spent on medication-related tasks:** Increase Prescribing a regular inpatient drug: 15 seconds pre-intervention phase, 39 s afterwards; time spent providing a ward pharmacy service increased (from 68 min to 98 min/day); nursing time on medication tasks outside of drug rounds (21.1% to 28.7%). Decrease: time per drug administration round (from 50 min to 40 min).
Franklin et al., 2008[31]	United Kingdom: A 28-bed general surgery ward in a teaching hospital.	To assess the impact of an ADD system consisting of a closed-loop EP, automated dispensing, BC patient identification and eMARs on the safety and quality of medication administration.	Before-and-after intervention study MODERATE	Data were collected by observing medication administration 3 months before and 1 year after introducing a closed-loop system. Aspects observed: MAE rates for ward-stocked and non-ward-stocked drugs, accuracy of medication administration documentation, timeliness of administration, administration of medication from unlocked areas and supervision of patients taking oral medication by nursing staff. **Data analysis:** Descriptive statistics, chi-square test, 95% CI.	**Positive outcomes:** Reductions in MAEs occurred for both ward-stocked (6.4 and 2.3%) and non-ward-stocked (14.6 and 13.7%) drugs. Timeliness of administration improved post-intervention, as did administration of medication from unlocked areas (CI 4.7 to 7.3%) and supervision of patients taking oral medication (CI 17 to 23%). **Negative outcomes:** documentation discrepancies increased from 5 (0.2%) clinically significant documentation discrepancies pre-intervention to 33 (2.0%) afterwards.

Reference	Country & setting	Objectives	Design & GRADE	Materials and Methods	Keyfindings*
Skibinski et al., 2007[39]	United States: General medical and medical ICUs.	To measure the effect of the implemented technology (a pharmacy computer system, ADCs and point-of-care products) on the processes and safety of the medication-use system.	pre- and post-implementation study MODERATE	Data were collected by interviewing healthcare professionals of the wards involved in the study. Interviews were conducted using a scripted questionnaire focusing on assessing the personnel's impressions of the safety of the dispensing and the medication administration processes occurred over 3 months before and after implementation. The hypotheses were that errors in each phase of the process would decrease by 50% with the implementation of each technological application and that workload measures would increase. **Data analysis:** Logistic regression analysis.	**Positive outcomes:** The new technology standardized the medication administration processes, decreased turnaround time for processing medication orders, and increased the accuracy of medication administration to patients (omissions -39%). The transition from a patientspecific cartfill to stock dispensing for the automated cabinets was a system change that simplified the dispensing function. **Negative outcomes:** The staffing of nurses and pharmacists increased.
Cottney, 2014[2]	United Kingdom: A 21-bed acute adult inpatient ward in mental health hospital.	To assess the benefits of ADCs with regard to reducing MAEs errors and reducing nurse time spent administering medication.	Observational study design MODERATE	Nurses were observed administering medication before and after the implementation of an ADC. Any administration errors that were observed were classified by type. 60 medication rounds were observed. There were 1895 ob-served opportunities for error, 137 errors were made. **Data analysis:** Descriptive statistics, unpaired t-test.	**Positive outcomes:** The ADC was found to improve the efficiency of the medicines-use process. The time that nurses spent administering medication reduced (from 2.94 min per dose to 2.37 min per dose), it generated free nursing time (66min/day). **No impact** on MAE rates (from 8.9% to 7.2%, not significant). The types of MAEs remained largely unchanged from beforehand.
Chapuis et al., 2015[25]	France: At the 2,000-bed University Hospital in 3 surgical ICUs (12, 12 and 9 beds).	To evaluate the economic impact of ADSs in surgical ICUs.	Cash flow analysis MODERATE	ADSs were implemented to replace the traditional floor stock system. Costs were estimated before and after implementation on the basis of floor stock inventories, expired drugs, and time spent by nurses and pharmacy technicians on medication-related work activities. The incidence of missing medications was measured prior to and after implementation over a one month period. Direct observations were performed, over a period of 10 days. **Data analysis:** A financial analysis included operating cash flows, investment cash flows, global cash flow and net present value.	**Positive outcomes:** nurses spent less time on medication-related activities (14.7 hours per day /33 beds). Pharmacy technicians spent more time (3.5 hours per day) on floor-stock activities. The cost of drug storage was reduced (€44,298). A reduction in the number of missing medications (56 %) was found. Expired drugs were eliminated (€14,772) due to a rotation of drug stocks and the regular monitoring of expiration dates. Five years after the investment, the global cash flow was €148,229 and the net present value of the project was positive by €510,404.
Barber et al., 2007[24]	United Kingdom: A 28-bed surgical ward in a teaching hospital	To evaluate an integrated (closed loop) EP, automated dispensing (ADC), BC patient identification and eMAR system designed to improve patient safety.	A qualitative observational study LOW	To use an evaluation framework based on socio-technical theory. Assessment of technical performance, developed attitudes to the new system, changes to delivery of care and work practices. A qualitative approach was adopted for data collection, complementing the quantitative study. Interviews (n=26) were held and a focus group session was held 9 months after the system went live. **Data analysis:** Discourse analysis.	**Implementation phase:** At the beginning technical problems showed. Over time, staff attitudes changed being more balanced and the potential benefits of the system became clearer. **Posite outcomes:** The system structured the work of staff (the drug round). *Doctors write more complete prescriptions. *Patients are considered one by one. *Patient identification through BCs and recording administration. *Medicines are systematically collected together. *Pharmacists review more prescriptions and detect more errors. *Time spent on medication-related tasks increased.

Reference	Country & setting	Objectives	Design & GRADE	Materials and Methods	Keyfindings*
Rodriguez-Gonzalez et al., 2012[36]	Spain: 2 gastro-enterology units (30 and 29 beds) in a 1537-bed tertiary teaching hospital.	To identify the frequency of medication preparation and administration errors and their potential risk factors in two clinical units using a CPOE program and profiled ADCs.	A prospective observational study LOW	MEs were measured using the disguised observation technique (2314 administrations to 73 patients). Types of MEs and their potential severity were described. The correlation between potential risk factors and MEs was studied to identify potential causes. The error rate was calculated. **Data analysis:** Univariate and multivariate logistic regression analyzes were performed to study the association between potential risk factors and the occurrence of errors. All p values were two-tailed. Statistical significance was set at p<0.05.	**Occurence of errors:** 509 errors (22.0%) were recorded, 13.4% in pre-paration and 86.6% in administration. The most frequent errors were: wrong administration techniques (especially concerning food intake), wrong reconstitution/ dilution, omission, and wrong infusion speed. **The main reason for a high error rate** was the lack of correct nursing working procedures. Neither the CPOE nor the ADCs provide information about which medicines need to be administered on an empty stomach.
Hull et al., 2010[32]	United States: a 246-bed district hospital, a 24-bed step-down unit in a progressive care unit	To examine the impact of automated medication cabinets installed outside patient rooms on nursing and pharmacy workflow.	Prospective study including survey LOW	To measure data before and after installation of the medication cabinets (n= 10), and compare the number of nurses' steps, trips to ADC and how many times ADC was busy, nursing frustration (with the medication delivery processs), and impact on pharmacy workflow. Prior to the installation of the storage cabinets, baseline data were collected. At the end of the study, participants completed a separate survey (a 7-point Likert scale) providing general feedback on the use of the cabinets. **Data analysis:** Descriptive statistics.	**Positive outcomes:** The cabinets outside the patient rooms decreased nursing visits to the automated medication dispen-sing system. Nurses reported fewer episodes wai-ting to access the system when it was busy. **No effect:** The system did not result in fewer nursing steps. **Negative outcome:** Pharmacy technicans spent more time delivering medications (from 25.4min to 30.9min) and the cabinets added to their workload.
Roman et al., 2016[37]	Australia An emergency and trauma centre in a major adult referral hospital without an electronic medication management system.	To examine the change in medication retrieval times, number of medications retrieved and staff perceptions before and after the installation of ADMs.	Time and motion study combined with the qualitative survey. LOW	The time spent retrieving medications from the medication room for administration to patients was measured before and after the installation of two ADMs. The number of medications retrieved, the regulatory schedule and retrieval location (open shelf, locked medication safe or ADM) of each medication were recorded. A qualitative survey (a 5-point Likert scale) was conducted pre- and post-implementation to identify the perceived impact on clinical practice. **Data analysis:** Student's t-test, Wilcoxon Rank- Sum test). Statistical significance was defined as $p < 0.05$.	**Recorded outcomes:** The mean number of medications per retrieval increased slightly (+5.7s) in the post implementation period. The medication retrieval process was slower with ADMs for less restricted medications (+18.4s), but faster for more restricted medications (such as opioid analgesics -36.1s). **Perceived impact on practice:** The staff believed ADMs save time. Staff perceptions were that ADMs improved knowledge of medications and reduced medication retrieval time.
Ardern-Jones et al., 2009[22]	United Kingdom: General hospital ED, which is attended by over 65 000 patients each year.	To assess the attitudes of ED staff to stock control and replenishment prior to and after automation (MVS) installed within the ED.	Pre- and postimplement ation survey LOW	All ED staff (n=68) were sent pre-piloted, semi-structured questionnaires and reminders, before and after automation of medicines stock control (response rates: the before survey 77.9%, n=53/68 and the after survey (83.9%) (52/62). **Data analysis:** A Spearman's correlation and a Mann-Whitney test). A P-value of <0.05 was considered statistically significant.	**Positive outcomes:** Automation improved medicines storage, security and stock control. The study did not find that staff had issues with access to the MVS, in terms of queuing or speed of access, in comparison with the previous, key-controlled storage units. The system was also perceived by almost 90% of staff to be easy to use. Improvement was reported in stock replenishment and storage of stock injections and oral medicines.

Reference	Country & setting	Objectives	Design & GRADE	Materials and Methods	Keyfindings*
Rochais et al., 2014[35]	Canada: A mother-child University hospital Center with 5000 beds. 7 ADCs were introduced in 3 critical care units, neonatology (n = 3), ICU (n =2) and ED (n = 2).	To evaluate how nursing staff felt about the impact of ADCs on the safe delivery of health care and workplace ergonomics, and to identify the main issues and to describe the corrective measures implemented.	Cross-sectional descriptive study with quantitative and qualitative components. LOW	The first phase: a stuctured survey to the nursing staff of the 3 care units where the ADCs were implemented (response rate 46%, n=172 out of 375 nurses). A questionnaire consisted of 33 statements about ADC. The second phase: a focus group (5 members) discussion. To discuss the results of the survey. **Data analysis:** Quantitative and qualitative analysis.	**Positive outcomes:** The nurses were satisfied with the use of ADC: They considered the introduction of ADC made their work easier (level of agreement of 90%), helped to safely provide patients with care (91%), and helped to reduce medication incidents (81%). Nursing staff were particularly satisfied with the narcotic drugs management with the ADCs. **Negative outcomes:** Nursing staff were not satisfied with the additional delays in the preparation (52%) and administration (54%) of a medication dose and the inability to prevent a medication from being administered when stopped on the medication administration record (48%).
Zaidan et al., 2016[16]	Qatar: 2 tertiary care specialty teaching hospitals with unit-based ADCs.	To assess nurses' perceptions of and satisfaction with the use of ADCs.	A cross-sectional study LOW	Study was conducted using a piloted, validated, anonymous online survey targeted to all 503 nurses (response rate 80%, n=403/503). The questionnaire consisted of four parts: nurses' sociodemographic and practice characteristics, 21 questions about their perceptions, one question about their overall satisfaction, and one about the system's ease of use. **Data analysis:** Descriptive and inferential statistics (chi-square test, independent t-test, one-way analysis). The significance level $p<0.05$. Open-ended questions: qualitative content analysis.	**Positive outcomes:** At 6 months, the overall satisfaction rate was 91 %. Of the nurses, 94% perceived that they were able do their job more safely and 87% that they were able to administer medication more efficiently with the ADC system than before, e.g. 90 % nurses agreed that they now spent less time waiting for medication from the pharmacy than they did before the ADCs.
Balka et al., 2007[23]	Canada: a large tertiary care facility	To identify and solve problems related to the introduction of the ADS, while improving professional practice.	Action research LOW	The data was primarily collected (2 months) through daily field observations and interviews during and after implementation, with regular follow-up visits to the field site. Observations were conducted on all units that moved to the new building. **Data analysis:** All collected data were qualitative analyzed reflecting relevant theoretical literature.	**Introducing systems** requires work process redesign and leaves space for the new work practices. It was found that work practices compromised patient safety. Many staff initially experienced frustration with the ADS, over time staff appear to have accepted the ADS. Changes had to be made to the work processes of nurses and pharmacy staff.

Reference	Country & setting	Objectives	Design & GRADE	Materials and Methods	Keyfindings*
Rodriguez-Gonzalez et al., 2015[8]	Spain: 2 gastro-enterology units (59 beds) in a 1381-bed public tertiary hospital	To evaluate the causes of preventable ADEs during the medication administration process with CPOE and profiled ADCs in order to prioritize interventions that need to be implemented and to evaluate the impact of specific interventions.	Failure mode, effects and criticality analysis study. LOW	A multidisciplinary consensus committee comprised of pharmacists, nurses and doctors evaluated the process of administering medications. By analysing the process, all failure modes were identified and criticality was determined by rating severity, frequency and likelihood of failure detection on a scale of 1 to 10, using adapted versions of already published scales. Safety strategies were identified and prioritized. The riskiness of each element was expressed as a risk priority number, which is calculated as the product of the severity, occurrence and detectability scores. The number identifies those elements that are the most likely contributors to medically serious failures.	**Outcomes:** The CPOE and profiled ADCs reduce the critical index arising from prescription and dispensing activities. Study showed 8 processes and 40 failure modes, of which 20 were classified as high risk. 21 different potential causes were found resulting in 24 recommendations: e.g. the development of an eMAR and BCMA technology. 60.7% of the risk was related to subprocesses other than drug administration itself. The drug administration is a high-risk process with many potential failure modes.
Romero et al., 2005[38]	United States: Five units in a tertiary care hospital with 655 beds.	To evaluate the overall reporting of ADEs and the accuracy of the ADE reports that are generated from the ADMs. And to compare the accuracy rates between 2 institutions.	Retrospective chart review LOW	ADMs were set up to use the tracer-drug system. ADE reports were collected by requiring nurses on units to select a reason for removing tracer drugs (dextrose injection 50% [D50] and naloxone) from an ADS. The accuracy of the ADE reports during a period of 4.5 months was evaluated. The sensitivity, specificity, positive and negative predictive value of the reports were calculated. **Data analysis:** chi-square test, A *p*-value ≤0.05 considered significant.	**Positive outcome:** ADM helped to generate more ADE reports than did the traditional method during the same time period. A review of 61/32 D50/naloxone transactions found that the appropriate reason for removal was selected by nursing staff 62%/88% of the time. The sensitivity and specificity of the ADE reports for D50/naloxone were 55.9%/95,2% and 70.4%/72,7%, respectively.
CENTRALIZED DRUG DISTRIBUTION SYSTEM (n=6)					
Al Adham et al., 2011[41]	Self-governing Palestinian territory: 2 main departments (medical and surgical) of 2 hospitals with different DDS.	To assess which DDS was more appropriate based on comparison between a hospital using the UD DDS and another using ward-stock DDS.	Quantitative, comparative cross-sectional design LOW	Medical records (n = 327) were collected and observations (n=1096) were made in the selected departments. The study compared which system was safer by calculating the rates of MAEs. Sturctured interview of pharmacists and head nurses (n=92, response rate 94.6%) concerned perceptions and practices to drug dispensing and management. It also assessed the level of clinical pharmacy interventions and staff perceptions about the systems. **Data analysis:** Descriptive statistics and bivariate analysis (cross-tabulations, chi-squared test, student t-test). The significance level p<0.05.	**Positive outcomes:** Unit-dose DDS: The number of missing units per drug item dispensed (t=2.5) and MAEs per patient (t=2.1) were lower. The UD DDS appeared to be safer, was more positively perceived by staff (interview: 80%) and was more supportive of good clinical pharmacy practice (time to check patients' charts). Unused drugs also returned to the pharmacy more often. **Negative outcomes:** In ward-stock DDS extra staff were needed (interview: 59%) and time scales were longer.

Reference	Country & setting	Objectives	Design & GRADE	Materials and Methods	Keyfindings*
Rochais et al., 2013[1]	Canada: A mother-child University Hospital Center with 500 beds.	To evaluate how nursing staff felt about the impact of medication carts on the safe delivery of health care and workplace ergonomics. And to identify the main issues involved in the use of the technology	Quantitative and qualitative cross-sectional study LOW	The questionnaire with 33 statements (a 4-point Likert scale) was administered to nurses and an organized focus group (nurses and pharmacists), pre- and post introduction of 68 decentralized medication carts. A total of 195 nurses (40%) completed the questionnaire. The second analysis involved setting up a focus group (7 participants) after delivering the questionnaire and a subsequent analysis of the responses to the questionnaire. **Data analysis:** Qualitative and quatitavive analysis.	**Positive outcomes:** Nurses were satisfied with medication carts. 80 % of the nurses agreed that medication carts made their work easier and 64% agreed that it helped to reduce medication incidents/accidents. Users were satisfied with the safety of the carts that restrict access to medications for patients and parents and make it possible to reduce the risk of medication theft.
Temple et al., 2010[40]	United States: A 471-bed tertiary care hospital.	To optimize workflow, control inventory, and improve dispensing accuracy after implementation of CDT at a university medical center pharmacy.	Pre- and post-implementation study LOW	An evaluation of CDT was conducted in 3 phases; preimplementation, implementation and postimplementation phase. The data collected were used to compare pre- and post-implementation time studies, labor requirements, inventory turns, and accuracy rates. **Data analysis:** Descriptive statistics were used to report time standards and accuracy rates. Inventory carrying costs and the number of inventory turns were reported for the pre- and post-implementation periods.	**Positive outcomes:** CDT improved accuracy of medication dispensing in a pharmacy (from 99.02% to 99.48%). Workflow efficiencies achieved in ADC refill, first-dose dispensing, supplemental cartfill, and the medication procurement process allowed for a reduction in the amount of technician labor required to support the medication distribution process, and reallocate technician labor to other areas. The estimated labor savings comparing the pre- and post-implementation time studies totalled 2.6 full-time equivalents. The inventory carrying cost reduced ($25,059).
Oldland et al., 2015[34]	United States: A 553-bed academic medical center	To measure the effects associated with sequential implementation of ADC and BC technologies on pharmacy technical accuracy and rates of potential medication dispensing errors.	A prospective observational study LOW	During four 28-day periods of observation, pharmacists recorded all technical errors identified at the final visual check of medicine prior to dispensing. Technical filling errors involving deviations from order-specific selection of product, dosage form, strength, or quantity were documented when dispensing medications using (a) UD system, (b) UD/ADC, (c) UD/ADC/BC1 and (d) UD/ADC/BC2. **Data analysis:** Descriptive statistics (%, RR). Incidence rates were compared by construction of 2×2 contingency tables and statistical tests (chi-square or Fisher's exact probability). The significance level $p<0.05$.	**Outcomes:** Pharmacy ADCs and BC systems provide complementary effects that improve technical accuracy and reduce the incidence of potential medication dispensing errors if this technology is used with comprehensive personnel training. Technical errors varied according to the study period from 0.157% during the (a) phase to 0.135%, 0.137%, 0.050% (RR=0.32, significant) during the (b), (c) and (d) phase. Subsequent changes in product labeling and intensified staff training in the use of BC systems was associated with a decrease in the rate of technical error to 0.050%.
Dussart et al., 2009[28]	France: A military teaching hospital with 296 beds.	To assess the user satisfaction with an individualized dispensing system, to improve the quality of pharmaceutical care practice and to facilitate its adaptation to the needs of the users.	A cross-sectional survey LOW	Questionnaires (including 14 stuctured and 1 open-ended questions) were administered anonymously to 57 users: physicians (n=18), nurses (n=29), pharmacy staff (n=10). A survey was repeated after several years. **Data analysis:** Groups of variables were compared using anova or Kruskal-Wallis tests. Parameters were determined with 95% CI and 5% accuracy. The answers to the open questions were categorized by topic and ranked by frequency of quotation.	**Positive outcomes:** Satisfaction scores about the system was positive. The pharmaceutical service was not rated negatively. The workload felt clearly improved from before. **Negative outcomes:** The computer system was rated negatively. Also the satisfaction of pharmaceutical information decreased.

Reference	Country & setting	Objectives	Design & GRADE	Materials and Methods	Keyfindings*
Lahtela et al., 2010[21]	Finland: University hospital	To study how the medication management process can be improved by a user-centric, computer-based ADDS.	Participative observation method and workshops VERY LOW	The data was collected during 8 months of an examination phase. Participative observation method and workshops were used as data collection methods. The information flow and medication management process was also modeled when ADDS was implemented into the hospital pharmacy.	**Positive outcomes:** Dispensing error rate was low, 0,013%. The medication management process improved. Costs and time stayed at the same level as before the implementation. **Other advantages of ADDS:** hygienic patient individual medication doses printed with all the necessary information, smaller medication warehouses. Patient safety improved by reducing the number of ADEs.
HYBRID STUDIES (n=5)					
Acheampong et al., 2014[17]	Ghana: Hospital setting	To systematically review the research literature on the various interventions for providing medication safety in hospitals.	Systematic literature review HIGH	8 databases were searched for research articles written in english (n=2239). References of included articles were also searched (n=4). Full research papers (n=56) were reviewed to determine whether they met the inclusion criteria. Papers involving delivery of interventions in hospitals with the aim of preventing or reducing MEs and ADEs were examined (n=42). Quality of studies was assessed.	**Positive outcomes:** Automated dispensing technology is useful in evaluating charging, improving workflow, inventory control, pharmacy workload, and reducing the potential for MEs. Pharmacy automation decreases dispensing errors and reduces preventable ADEs. Computer assisted delivery including BC technology reduces errors.
Lathrop et al., 2014[33]	United States: A 561-bed academic medical center (university hospital) that uses a hybrid medication distribution model.	To implement a thrice-daily cartfill to reduce medication returns and waste, improve efficiency, and facilitate reallocation of pharmacy technician time to enable an expansion of pharmacy services without additional resource utilization.	Observational pre- and post-implementation study MODERATE	15% are patient-specific i.v. or oral doses, 70% of doses are dispensed from the central pharmacy automation, and 15% from unit-based ADCs. The transition from a once-daily to a thrice-daily medication cartfill model designed to better align pharmacy operations with patterns of medication ordering, delivery, and order discontinuation. Lead times, storage and worktime was evaluated. **Data analysis:** 6 weeks of pre- and post-implementation data were extracted, normalized, and analyzed. This information was then used to calculate the ratio of cartfill doses to first doses during both periods. The impact of thrice-daily cartfill and all ancillary changes were evaluated through a pre-post assessment.	**Benefits** of the thrice-daily cartfill: decrease in the mean daily number of extemporaneously prepared oral doses, 55-65% reduction in lead times for three out of four peak delivery periods. The frequency of requests for missing medication doses through the EMR system increased (26.5%); improved nurse adherence to EMR protocols. Implementation resulted in increase in cartfill doses dispensed, decrease in first doses dispensed, and decrease in the number of medications returned to the central pharmacy. This resulted in a reduction in waste within pharmacy operations and allowed for redeployment of two technician full-time equivalents (-4.7%) to expand pharmacy services.
Cousein et al., 2014[26]	France: 40-bed short stay geriatric unit within a 1800-bed general hospital	To assess the impact of an automated drug distribution system on MEs. And to assess the efficacy of a daily UD DDS on discrepancies between what is prescribed and what is administered to the patient.	Before-after observational study MODERATE	Administration rounds were observed and compared with prescribed drugs, before and after the system changed from a WSS (n= 28 rounds) to a UD dispensing system (n=31 rounds), integrating a UD dispensing robot and ADC. MAEs were classified and MAE rates were calculated and compared between the periods. Type of errors, seriousness of errors and risk reduction for the patients were also studied. **Data analysis:** Descriptive statistics and statistical tests (95% confidence interval (CI), relative risk, Student's t-test, chi-square test, Fisher's exact). Statistical testing was performed at the he two-tailed α level of 0.05.	**Positive outcomes:** The implementation resulted in a 53% reduction in MAEs. All error types were reduced in the UD DDS period compared with the WSS period. Wrong dose and wrong drug errors were reduced by 79.1% and 93.7%, respectively. The number of patients subjected to one or more MAEs also significantly decreased. An automated system combining a UD dispensing robot and ADCs could reduce discrepancies between ordered and administered drugs, improving medication safety. One out of every 10 patients who were switched from WSS to UD DDS avoided a ME.

Reference	Country & setting	Objectives	Design & GRADE	Materials and Methods	Keyfindings*
Jiménez Muños et al., 2011[3]	Spain: A tertiary-care centre with 1800 beds.	To determine MEs rates for each phase (prescription, trans-cription and adminis-tration) of the pro-cess and to compare them between the 3 different medication prescription-dispensation systems.	Observational study LOW	The administration of medicinal products was observed directly and compared with medical and nursing prescriptions. Errors and adverse events were classified by a consensus of experts. All MEs were described and analyzed as to their relationship with the type of prescription and dispensing systems (traditional, single dose and EP). **Data analysis:** Statistical tests (student's t-test, chi square test, 99% CI).	**Outcomes:** In the traditional system the error prevalence rate was highest (13.59%; MAEs 1.5%). In the single dose system it was 6.43% (MAEs 0.36%) and in the EP system it was 8.86% (MAEs 0.47%). The highest error rates in all phases were found in the traditional system. The phase affected by most errors in all 3 models was transcription, and the least affected was administration, except for the single dose system, in which prescription was the worst. ADD systems reduce error rates and the severity of their effects.
Gray et al., 2013[18]	United States: A 561-bed university hospital. Time studies were performed on a medical unit and a surgical unit.	To estimate the human resource and cost implications of changing the medi-cation distribution model. To analyze the hybrid and decentra-lized medication distribution system, and to develop a model to simulate a decentralized medi-cation distribution system.	Comparison study LOW	Study was conducted to evaluate alternatives to the existing hybrid distribution model (64% of doses dispensed via cartfill and 36% via ADCs). An assessment of nurse, pharmacist, and pharmacy technician workloads within the hybrid system was performed through direct observation, with time standards calculated for each dispensing task; similar time studies were conducted at a comparable hospital with a decentralized medication distribution system involving greater use of ADCs. **The time study data** were then used in simulation modeling of alternative distribution scenarios: one involving no use of cartfill, one involving no use of ADCs, and one heavily dependent on ADC dispensing.	**Outcomes:** As the modeled percentage of doses dispensed from ADCs rose, the calculated pharmacy technician labor requirements decreased, with a proportionately greater increase in the nursing staff workload. Nurses are a higher-cost resource compared to pharmacy technicians, the projected human resource opportunity cost of transitioning from the hybrid system to a decentralized system similar to the comparator's facilities was estimated at $229,691 per year. A transition from the existing hybrid medication distribution system to a more ADC-dependent model would result in an unfavorable shift in staff skill mix and corresponding human resource costs at the medical center.

*The key findings in the table are selected from the presented studies in relation to the focus of the systematic literature search.

[d]ADD = automated drug dispensing, ME = medication error, ADS = automated dispensing system , ICU = intensive care unit, TOE = total opportunities for error, ADDS = automated drug dispensing system, UD = unit dose, MAE = medication administration error, ED = emergency department, ADC = automated dispensing cabinet, EP = electronic prescription, BC = bar code, eMAR = electronic medication administration record, ADE = adverse drug event, CPOE = computerized prescription order entry, ADM = automated dispensing machine, MVS = medicines vending system, DDS = drug dispensing system, CDT = carousel dispensing technology, EMR = electronic medical record, WSS = ward stock system