Research in Social and Administrative Pharmacy 18 (2022) 3980–3987

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

journal homepage: www.elsevier.com/locate/rsap

Cost-effectiveness of central automated unit dose dispensing with barcode-assisted medication administration in a hospital setting

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ARTICLE INFO

Keywords:
Medication errors
Patient safety
Medication administration errors
Barcode
Medication systems
Cost-effectiveness

ABSTRACT

Background: Central automated unit dose dispensing (cADD) with barcode-assisted medication administration (BCMA) has been shown to reduce medication administration errors (MAEs). Little is known about the cost-effectiveness of this intervention.
Objective: To estimate the cost-effectiveness of cADD with BCMA compared to usual care.
Methods: An economic evaluation was conducted alongside a prospective before-and-after effectiveness study in a Dutch university hospital. The primary effect measure was the difference between the rate of MAEs before and after implementation of cADD with BCMA, obtained by disguised observation in six clinical wards and subsequent extrapolation to the entire hospital. The cost-analysis was conducted from a hospital perspective with a 12-month incremental costing approach. The total costs covered the pharmaceutical service, nurse medication handling, wastage, and materials related to cADD. The primary outcome was the cost-effectiveness ratio expressed as costs per avoided MAE, obtained by dividing the annual incremental costs by the number of avoided MAEs. The secondary outcome was the cost-effectiveness ratio expressed as costs per avoided potentially harmful MAE (i.e. MAEs with the potential to cause harm).
Results: The intervention was associated with an absolute MAE reduction of 4.5% and a reduction of 2.7% for potentially harmful MAEs. Based on 2,260,870 administered medications in the entire hospital annually, a total of 102,210 MAEs and 59,830 potentially harmful MAEs were estimated to be avoided. The intervention was associated with an increased incremental cost of €1,808,600 annually. The cost-effectiveness ratio was €17.69 per avoided MAE and €30.23 per avoided potentially harmful MAE.
Conclusions: The implementation of cADD with BCMA was associated with a reduced rate of medication errors, including harmful ones, at higher overall costs. The costs per avoided error are relatively low, and therefore, this intervention could be an important strategy to improve patient safety in hospitals.

1. Introduction

Medication errors are a main cause of preventable patient harm.[1,2] Medication errors in hospitals may occur in the entire medication process – from prescription to administration.[3] Especially administration is a critical step because an error at this stage may directly harm a patient. Medication errors may lead to prolonged hospitalization, morbidity, mortality [1,3–6] and subsequently increased healthcare costs .[7,8] A systematic review found a widely varying incidence of adverse drug events caused by medication errors across individual studies, from 0.006 to 13.3 per 100 inpatients.[5] Medication administration errors (MAEs) have been found to occur in approximately 10% of medication administrations[9 10] (interquartile range 7.3%–21.7%[10]) in hospital settings. Adverse drug events are associated with extensive costs, roughly varying between €1,000 and €7,000 per event.[7] Thus, it is important to reduce MAEs and related healthcare costs.

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https://doi.org/10.1016/j.sapharm.2022.07.006
Received 18 January 2022; Received in revised form 14 May 2022; Accepted 10 July 2022
Available online 13 July 2022

Many different strategies, such as technological interventions and training programmes, have been explored for their potential to prevent MAEs.[11–14] Central automated unit dose dispensing (cADD) and barcode-assisted medication administration (BCMA) have been shown to be effective interventions to prevent MAEs, combined[15,16] as well as separately.[17–19]

In healthcare systems, scarce resources need to be prioritized, making economic evaluations of effective interventions valuable. Many interventions, including cADD and BCMA, designed to prevent MAEs are comprehensive and are associated with high direct investment costs.

To our knowledge, only two previous studies have examined the cost-effectiveness of the combined intervention in relation to prevented errors.[20] These Danish studies showed affordable cost-effectiveness ratios, i.e. between €19 and €30 per avoided MAE.[21,22] The intervention was associated with a decrease of MAEs as well as medication handling costs in clinical wards, but an increase of all other costs; i.e. costs related to wastage, pharmaceutical service, personal digital assistants, and delivered dose bags.

However, generalizability remains a concern in economic evaluations, because cost-effectiveness results may be affected by factors such as geographic location, hospital type, and available resources.[23] Differences in volume, procedures, unit costs as well as effectiveness parameters are expected to result in variation of estimated cost-effectiveness ratios.[23]

Because only limited evidence is available, we studied the cost-effectiveness of cADD with BCMA compared to usual care in a Dutch university hospital.

2. Methods

2.1. Study design

An economic evaluation was conducted in Erasmus MC, University Medical Center Rotterdam, a university hospital in Rotterdam, the Netherlands. The evaluation was based on data from our previously published before-and-after study on the effectiveness of cADD and BCMA, which was performed in six clinical wards (internal oncology, neurology, pulmonary medicine, hematology, neurosurgery, and hepatopancreatobiliary surgery).[24] Cost data were prospectively collected before and after implementation of cADD and BCMA. These data were collected from October 2018 through December 2018 pre-intervention and from September 2020 through December 2020 post-intervention. Further specifications are described in a later section. The Medical Ethics Review Committee of Erasmus MC waived approval for this study (reference number MEC-2018-1532). Data were handled confidentially according to the Dutch General Data Protection Regulation. The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) guideline was used for reporting.[25]

2.2. Study setting

2.2.1. Usual care

An electronic medical record (EMR) system, a computerized physician order entry (CPOE) system, and an electronic medication administration record (eMAR) system were already in place, using HiX® software version 6.1 (ChipSoft B.V.; Amsterdam, the Netherlands). An additional CPOE system, Practocol® version 2.0.9.3 and 2.1.5.1 (Practocol B.V.; Rotterdam, the Netherlands), was used for medication prescription and administration in chemotherapy protocols.

Each ward kept a ward-based medication stock in the medication room, consisting of emergency medication, commonly used medication, and patient-specific medication delivered by the central hospital pharmacy. Nurses in the clinical wards put the medication in the trays of the mobile medication carts.

The following products were returned to the hospital pharmacy when found eligible (i.e. intact packages, correct storage conditions, and at least 6 months till expiration): expensive medication, complete packages of parenteral medication, and complete packages of opioids. Other medications were discarded in the clinical ward or in the hospital pharmacy.

2.2.2. The intervention

The intervention, which was gradually implemented starting mid-2019 in the entire hospital, consisted of a pharmacy-based cADD and BCMA integrated with HiX®.

The two cADD devices, Pillpick® (Swisslog; Buchs, Switzerland), were integrated with the CPOE and delivered the barcoded, unit-dose medication, in plastic bags on patient-specific rings. Each plastic bag was filled with one unit of medication in its original package and contained a medication-specific barcode, medication name, strength, lot number, national article identifier, and expiration date. All medications for a specified period of time, between 12 and 24 h (based on ward preferences), were attached to a patient-specific ring that contained a printed label with general patient and medication information. The cADD system particularly contained oral pharmaceutical forms. Each cADD device had a storage capacity of 30,350 unit doses and maximum dispensing capacity of 1,000 doses per hour. Management data showed that approximately 70% of all medication orders were delivered by the cADD devices by August 2020.

After introduction of the cADD, medication cart filling (for 24 h on Mondays through Thursdays, or 72 h on Fridays) was performed in the hospital pharmacy for three of the six clinical wards, i.e. internal oncology, hematology, and hepatopancreatobiliary surgery. Procedures differed between wards because implementation of central cart filling for the three other wards was hampered by personnel shortages.

For return procedures, the main difference compared to usual care was that all intact cADD-medication bags were eligible for return. Intact cADD-medication bags solely needed to be placed by a pharmacy operator in the return conveyer of the cADD device. The cADD device automatically reviewed the placed bags on medication specifications and on expiration date to restock or reject the bags.

BCMA allows scanning of patient and medication barcodes, which produces visual alerts in the eMAR if erroneous medication (i.e. wrong medication, wrong dosage form, or wrong strength per unit) for the selected patient is scanned. The implemented HiX® version did not support automated dose checking (e.g. number of tablets scanned). Barcode scanners used by nursing staff were attached to mobile medication carts containing computers with HiX® access.

2.3. Outcomes

The main outcome of this study was the cost-effectiveness ratio expressed as the costs per avoided MAE, estimated by the annual incremental costs divided by the total number of avoided MAEs in the entire hospital. The secondary outcome was the cost-effectiveness ratio expressed as costs per avoided potentially harmful MAE.

2.4. Data collection

2.4.1. Measurement of effects

An MAE was defined as any deviation from medication orders used by the nursing staff to administer medication; a deviation from general medication administration protocols; and if local protocols were not available, a deviation from the medication information sheet provided by the manufacturer. Timing errors were not included, because they are generally considered not to have clinical consequences.[10] Procedural errors (e.g. documentation, hygiene, and labeling errors) were not considered an MAE.

The direct disguised observation method – the gold standard to detect medication administration errors – was used to collect data on medication administration.[26–28] Nursing staff were informed that the purpose of the observations was to study the medication process.

Trained observers shadowed nursing staff and recorded details of every medication administration on data collection forms. Afterwards, a pharmacist (JJ) reviewed whether an MAE had occurred. Based on literature and experience, the potential severity of each MAE was assessed by both a pharmacist (JJ) and hospital pharmacist (NH). The potential severity was classified using the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) severity index, which ranges from category A to I.[29] MAEs categorized in class E (an error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention) through I (an error occurred that may have contributed to or resulted in the patient's death) were considered potentially harmful. The data collection process is described in detail in Jessurun et al.[24]

To estimate the total number of MAEs in the entire hospital, the total number of administered medications in 2 months (pre-intervention) was extracted from HiX® and Practocol® by a pharmacist (JJ), which was extrapolated to an annual total.

2.4.2. Economic evaluation

A cost-effectiveness analysis was performed, using a 12-month time horizon before and after implementing the intervention. The hospital perspective and short term incremental costing approach was used. The cost model was designed to estimate the incremental costs compared to usual care. Data collection of 1–2 months per measurement period in such a dynamic environment is considered long enough to capture all meaningful differences in costs and effects. However, we have chosen to present the annual estimates, because decision makers generally use annual costs. Personnel costs related to the implementation and costs of MAEs or actual potential adverse drug events were beyond the scope and feasibility of this study. Personnel costs related to the implementation should be taken into account when initiating the implementation, but we believe that these costs in a single setting are tailored to the setting and therefore, not generalizable. Because costs of adverse drug events vary substantially between studies[7] and the current study did not measure actual harm, costs of adverse drug events were not included.

Costs related to the six investigated clinical wards (175 clinical beds) of the hospital were extrapolated to all general adult clinical wards (570 clinical beds) excluding wards that did not receive the same intervention, such as the intensive care units. Micro-level costing was used to accurately estimate unit costs of individual elements. Standard annuity methods were used to estimate costs of the dispensing device. The total costs, both pre-intervention and post-intervention, were the sum of pharmaceutical service costs, nurse medication handling costs, medication wastage costs, and materials and facilities costs (Table 1). Costs of medication were not expected to have changed due to the intervention. Where necessary, adjustments were made for down-scaling the number of total non-COVID-19 beds in the hospital. No adjustments seemed necessary for costs other than medication wastage because these were fixed costs (e.g. costs of the cADD devices) or costs assessed using the number of administered medications.

The post-intervention period was extended to July 2021 for nurse medication handling measurements because of personnel shortages to perform the observations.

2.4.3. Resource quantities and unit costs

2.4.3.1. Labor costs. Labor costs of staff members were obtained from the collective labor agreement for university hospitals, prevailing in 2019, and were based on the standard salary scales for the respective functions. The total labor costs included allowances such as the end-of the year and holiday bonuses, which complies with the prevailing Dutch guideline on economic evaluations in healthcare.[30] For all labor costs, the time spent on respective tasks was extrapolated to full-time equivalents per month and multiplied by the monthly labor costs and subsequently extrapolated to annual costs.

2.4.3.2. Pharmaceutical service. The costs of pharmaceutical services consisted of costs for medication order processing, dispensing medication, transporting medication from the pharmacy to the ward, and all tasks performed with regard to the cADD device.

Time spent on medication order processing was measured by observing pharmacy technicians for 2 h in daily clinical practice in each of the six clinical wards, both pre-intervention and post-intervention. The mean time needed to process one medication order was calculated by dividing the total time spent on medication order processing by the number of processed medication orders. This mean time was multiplied

Table 1
Input unit costs before and after implementation of central automated unit dose dispensing (cADD) and barcode-assisted medication administration (BCMA), based on an incremental costing approach.

Resource type	Resources pre-intervention	Performing member	Resources post-intervention	Performing member	Input unit costs of staff[a] or products (€)
Pharmaceutical service	Dispensing medication	Pharmacy member	Dispensing medication	Pharmacy member	2,210/month
	Double checking dispensed medication	Pharmacy technician	Double checking dispensed medication	Pharmacy technician	2,560/month
	Processing medication orders	Pharmacy technician	Processing medication orders	Pharmacy technician	2,560/month
	Transporting medication	Transport staff	Transporting medication	Transport staff	2,210/month
	–	–	Releasing of cADD batches produced	Pharmacist	3,680/month
	–	–	Operating the cADD devices	Pharmacy operator	2,210/month
Nurse medication handling	Performing medication related tasks	Nursing staff member	Performing medication related tasks	Nursing staff member	2,830/month
Materials and facilities	–	–	cADD devices (n = 2) including installation, interfaces, validation	–	2,251,000/year[b]
			Service and maintenance cADD		135,000/year[b]
			Disposable materials cADD[c] (e.g. rings and bags)		110,000/year[b]
	–	–	Materials, non-recurring (e.g. printers, transportation carts)	–	353,910 once
	–	–	Addition hospital area (375 m^2)	–	462,970/year
Wastage	Medication wastage	–	Medication wastage	–	National pharmacy purchase price

[a] Salary excluding allowances for one full time equivalent, i.e. 36 h per month.
[b] Costs excluding value added tax (21% in the Netherlands).
[c] Based on 2,500,000 unit doses annually.

by the total number of medication orders, generated from the EMR, in the entire hospital in the 2-month period pre-intervention.

The costs of pharmacy staff related to dispensing medication, transporting medication, and all tasks performed with regard to cADD device, were determined from the work schedules in the 2-month period retrieved from management staff.

Time spent on processing returned medication was registered by pharmacy staff on data collection forms for 2 months pre-intervention and 1 month post-intervention for cADD returns. However, due to the COVID pandemic, processing returns for non-cADD medication was not performed regularly in the planned period post-intervention. All costs related to processing returns were excluded from further analyses because they were considered negligible. The time spent on processing returns was 12 h per month pre-intervention and 3 h per month for cADD returns post-intervention.

2.4.3.3. Nurse medication handling. Time spent on medication handling by nurses was measured by shadowing nurses for at least 100 h during daily clinical practice, both pre-intervention and post-intervention. Observation periods were scheduled for 4-h during daytime (8 a.m.-12. p.m., 12 p.m.–16 p.m., 16 p.m.–20 p.m.) or 8 h at night (11 p.m.-7 a.m.). Observers registered the start and end time of all nursing activities during the observation. The time spent on medication tasks in the six clinical wards during daytime and night was extrapolated to the entire hospital by, respectively, the ratio of the number of medication administrations and the number of beds in the six clinical wards versus the entire hospital.

2.4.3.4. Medication wastage. Costs related to medication wastage were measured by collecting all medication wastage during a 1-month period in the clinical wards and in the pharmacy, both pre-intervention and post-intervention. Nursing and pharmacy staff were instructed to collect all medication wastage in dedicated bins. Parenteral medication was excluded because the examined intervention does not influence that particular distribution process. The wasted products were identified and counted. The costs of these products were calculated according to the standard national pharmacy purchase price, prevailing in March 2019 for the pre-intervention measurement and in April 2021 for the post-intervention measurement, because these prices were available at time of product identification. All costs were adjusted to 2019 using a price index of 1.6% for costs of 2018 and 1.2% for costs in 2020. The post-intervention costs were corrected for the number of blocked bed-hours (i.e. an average of 11% in a period of 1 month) in the six clinical wards due to the COVID-19 pandemic.

2.4.3.5. Materials and facilities. The costs of materials and facilities consisted of the costs of the two cADD devices and related services (i.e. validation, maintenance, and assistance), disposables, non-recurring investments related to the intervention (e.g. additional transportation carts, software applications), and costs for the additional hospital area.

The costs directly related to the purchase of the dispensing devices (i.e. two dispensing devices, installation, validation, service, maintenance, disposable materials) were collected from the manufacturer. It is difficult to estimate the lifespan of the dispensing devices, but the manufacturer guaranteed support for 10 years. A lifespan of 10 years was therefore chosen for the devices. Additional non-recurring investments were collected from investment reports used by management staff. Costs of disposables unrelated to the dispensing device were collected from the invoices in the 2-month period, but excluded because they were negligible and difficult to relate to intervention effects. These costs were initially considered because automated dispensing could result in decreased costs of other materials, such as labels and sealable disposable bags.

The costs of the additional hospital area needed were estimated by multiplying the number of square meters needed for the intervention by the costs per square meter per year calculated by the hospital.

2.5. Specific data collection periods

Details of the data collection periods are shown in Table 2.

2.6. Data analysis

The total number of avoided MAEs in the entire hospital annually was calculated by multiplying the estimated absolute difference in proportion of MAEs in the six clinical wards in each measurement period (pre-intervention and post-intervention) by the total number of administered doses in 2 months (pre-intervention) and by 6. The cost-effectiveness ratio was estimated by dividing the incremental costs by the estimated total number of avoided MAEs annually. The same analysis was used to calculate the cost-effectiveness ratio based on potentially harmful MAEs.

Sensitivity analyses for the cost-effectiveness ratios were conducted for different 1. pharmaceutical forms (oral and non-oral); 2. absolute MAE reduction rates (20%, 15%, 10%, 5%, 2%, and 1%) at the annual incremental cost; 3. increases in nurse handling times (i.e. a 100%, 50%, and 0%) at a constant MAE reduction rate; 4. annual incremental costs (20% increase or decrease) at a constant MAE reduction rate; and 5. number of administered doses (1,500,000 doses and 600,000 doses) at the annual incremental cost and different absolute MAE reduction rates (20%, 15%, 10%, 5%, 2%, and 1%). The variables included in the sensitivity analysis were chosen based on expected variations for different pharmaceutical forms [9,10] (oral and non-oral medication according to cADD delivery) and variations in different healthcare settings [23,31], leading to varying MAE reduction rates.[9,10,17], costs in general,[23] medication handling procedures, and the number of administered doses.

Data analysis was performed with SPSS Statistics® version 25 (IBM Corporation; Armonk, New York, United States). Descriptive statistics were used to determine MAE frequencies. Excel® 2016 (Microsoft Corporation; Redmond, Washington, United States) was used for all other analyses.

3. Results

3.1. Effect of cADD and BCMA

The rate of MAEs fell from 21.2% (316 MAEs in 1,490 medication administrations) pre-intervention to 16.7% (272 MAEs in 1,630 medication administrations) post-intervention in six clinical wards. A total of 376,810 medications were administered in the 2-month period. Based on 2,260,870 administered doses annually and an absolute MAE reduction of 4.5%, a total of 102,210 MAEs were estimated to have been avoided. The intervention was associated with a decrease in the rate of potentially harmful MAEs from 3.0% (44 MAEs in 1,490 medication administrations) to 0.3% (5 MAEs in 1,630 medication administrations). Based on 2,260,870 administered doses annually, a total of 59,830 potentially harmful MAEs were estimated to have been avoided.

3.2. Costs and cost-effectiveness

Input unit costs before and after implementation of cADD and BCMA are shown in Table 1. The annual incremental cost of the entire hospital was €1,808,600 higher after implementation of cADD and BCMA (Table 3). The costs of materials and facilities as well as costs of nurse medication handling had increased after implementation of cADD and BCMA, whereas other costs (i.e. of pharmaceutical service and medication wastage) had decreased. The total additional hospital area was 375 square meters, including storage areas.

The incremental comparison of the frequency of MAEs and costs annually as well as the cost-effectiveness ratios are shown in Table 4. An estimated total of 102,210 MAEs were avoided at a cost of €1,808,600

Table 2
Data collection periods.

Data type	Data type specification	Data collection period	Data type specification	Data collection period
	Pre-intervention	Pre-intervention	Post-intervention	Post-intervention
Effect data				
Number of medication administration errors		October 2018 until February 2019 [a]		September 2020 until December 2020
Total number of administered medications		October and November 2018		October and November 2018
Cost data				
Pharmaceutical service	Dispensing medication	October and November 2018	Dispensing medication	October until December 2020
	Double checking dispensed medication	October and November 2018	Double checking dispensed medication	October until December 2020
	Processing medication orders	November and December 2018	Processing medication orders	November and December 2020
	Transporting medication	October and November 2018	Transporting medication	October until December 2020
	–		Releasing of cADD batches produced	October until December 2020
	–		Operating the cADD devices	October until December 2020
Nurse medication handling	Performing medication related tasks	October until December 2018	Performing medication related tasks	October until December 2020 March until July 2021
Materials and facilities	–		cADD devices (n = 2) including installation, interfaces, validation -Manufacturer information 2019	Not applicable
			Service and maintenance cADD -Manufacturer information 2019	Not applicable
			Disposable materials cADD[c] (e.g. rings and bags) -Manufacturer information 2019	Not applicable
	–		Materials, non-recurring (e.g. printers, transportation carts) -Management information 2017	Not applicable
	–		Addition hospital area (375 m^2) -Management information 2019	Not applicable
Wastage	Medication wastage	October and November 2018	Medication wastage	October and November 2020

[a] Not during the holiday season (late-December until mid-January).

Table 3
Resource use and costs in the entire hospital (based on 570 clinical beds receiving the intervention) before and after implementation of central automated unit dose dispensing (cADD) and barcode-assisted medication administration (BCMA) annually, based on an incremental costing approach.

Resource type	Costs without cADD and BCMA (€)	Costs with cADD and BCMA (€)	Cost difference (€)
Pharmaceutical service	298,870	263,940	−34,930
Nurse medication handling	575,950	1,493,980	+918,030
Materials and facilities	Not applicable	1,042,980	+1,042,980
Wastage	204,950	87,470	−117,470
Total incremental costs	*1,079,770*	*2,888,370*	*+1,808,600*

annually, corresponding to a cost-effectiveness ratio of €17.69 per avoided MAE. A total of 59,830 potentially harmful MAEs were estimated to have been avoided, which corresponds to a cost-effectiveness ratio of €30.23 per avoided potentially harmful MAE.

3.3. Sensitivity analysis

Table 5 shows the incremental comparison as well as the cost-effectiveness ratios stratified by pharmaceutical form (oral forms and non-oral forms). For solely oral pharmaceutical forms, the cost-effectiveness ratio was €27.89 per avoided MAE and €70.00 per avoided potentially harmful MAE; and for non-oral forms the corresponding figures were €52.64 and €52.66.

The sensitivity analyses for the cost-effectiveness ratio for different scenarios are shown in Table 6.

With regard to different absolute MAE reduction rates, varying from 20% to 1% at constant costs, the cost-effectiveness ratios ranged from €4.00 to €80.00.

Cost-effectiveness ratios differed for the varying increases of nurse medication handling times (100%, 50%, 0% increase) at constant costs, i.e. €14.35, €11.53, and €8.71. A 20% increase or 20% decrease of total incremental costs at a constant MAE reduction rate would lead to a cost-effectiveness ratio of €21.23 or €14.16, respectively.

In the analysis with 1,500,000 administered doses annually at constant costs, the cost-effectiveness ratios ranged from €6.03 (20% absolute MAE reduction) to €120.57 (1% absolute MAE reduction), but ranged from €15.07 to €301.43 if 600,000 doses would be administered.

4. Discussion

The cost-effectiveness ratio of pharmacy-based automated unit dose dispensing with BCMA was €17.69 per avoided MAE and €30.23 per avoided potentially harmful MAE. Including solely oral pharmaceutical forms, which are the forms delivered by the cADD, the cost-effectiveness ratio was €27.89 per avoided MAE and €70.00 per avoided potentially harmful MAE.

These findings are in line with results of previous studies examining the cost-effectiveness of the combined intervention.[21,22] Two Danish studies, focusing on oral pharmaceutical forms, have shown similar cost-effectiveness ratios, i.e. €19.38 (95% confidence interval €15.83-€86.63) per avoided MAE[22] and between €21.98 and €30.39 per avoided MAE for three different scenarios.[21] One of these studies was a cost-effectiveness analysis of the intervention in hematological wards in a university hospital, using data from their controlled before-and-after study on effectiveness.[22] The other study compared this intervention

Table 4
The frequency of medication administration errors, costs, and cost-effectiveness ratio before and after implementation of central automated unit dose dispensing (cADD) with barcode-assisted medication administration (BCMA).

	MAE prevalence Data of the effectiveness study in 6 clinical wards	Incremental comparison (annually)[a]		Cost-effectiveness ratio
	n/N (%)	***Costs (€)***	***Estimated avoided MAEs (n) of N administrations***	***Costs per avoided medication administration error (€)***
All pharmaceutical forms (N = 2,260,870)				
All MAEs				
Without cADD and BCMA	316/1,490 (21.2)	Reference	Reference	Reference
With cADD and BCMA	272/1,630 (16.7)	1,808,600	102,210	17.69
Potentially harmful MAEs [b]				
Without cADD and BCMA	44/1,490 (3.0)	Reference	Reference	Reference
With cADD and BCMA	5/1,630 (0.3)	1,808,600	59,830	30.23

MAE, medication administration error.
[a] Extrapolated to the entire hospital (570 clinical beds receiving the intervention).
[b] *NCC MERP (National Coordinating Council for Medication Error Reporting and Prevention) class E (an error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention) or higher*[29]*; pre-intervention: n = 35, E; n = 7, F; n = 2, H and post-intervention: n = 5, E).*

to two different automated medication systems in acute medical wards (i.e. a non-patient specific system and a patient specific system with automated dispensing cabinets), using a model-based comparative analysis.[21] These studies are hardly comparable to the current study because they were performed in specialty wards and focused on fewer MAE types (e.g. medication handling errors were excluded) and solely on oral medication. This may also explain the considerably different results of the effectiveness measurement. Notably, in the study of Risor et al., 2017, the proportion of MAEs decreased from 0.04 to 0.02 in the intervention ward, whereas in the control ward, the proportion of MAEs increased from 0.02 to 0.12, leading to a very low odds ratio (0.06, 95% confidence interval 0.02–0.17) in favor of the intervention.[22] This same study calculated a 6-month incremental cost of €16,843, by estimating the dispensing machine costs for one ward. The costs were based on the number of delivered doses in that particular ward and the cost per dose bag (estimated using full production specifications and an annuity of 17 years for the cADD). In contrast, our study focused on the total incremental costs in the entire hospital, using a lifespan of 10 years for the cADD devices. This may explain the comparable cost-effectiveness ratios, even though parameter estimates were dissimilar.

The present study has some strengths. First, the cost-effectiveness analysis was based on a large sample size in six general clinical wards to assess the effectiveness of the intervention. Second, we used a robust method of data collection with regard to identifying MAEs and estimating costs. Real-life and real-time data were obtained from observation in daily clinical practice, using strict protocols. Third, to our knowledge, this is the first study examining the cost-effectiveness of this intervention attempting to include the clinical relevance of MAEs.

Table 5
The frequency of medication administration errors, costs, and cost-effectiveness ratio before and after implementation of central automated unit dose dispensing (cADD) with barcode-assisted medication administration (BCMA) stratified by pharmaceutical form (oral and non-oral).

	MAE prevalence Data of the effectiveness study in 6 clinical wards	Incremental comparison (annually)[a]		Cost-effectiveness ratio
	n/N (%)	***Costs (€)***	***Estimated avoided MAEs (n) of N administrations***	***Costs per avoided medication administration error (€)***
Oral pharmaceutical forms (N = 1,497,640)				
All MAEs				
Without cADD and BCMA	151/1,002 (15.1)	Reference	Reference	Reference
With cADD and BCMA	119/1,108 (10.7)	1,808,600	68,840	27.89
Potentially harmful MAEs [b]				
Without cADD and BCMA	20/1,002 (2.0)	Reference	Reference	Reference
With cADD and BCMA	3/1,108 (0.3)	1,808,600	25,840	70.00
Non-oral pharmaceutical forms (N = 763,250)				
All MAEs				
Without cADD and BCMA	165/488 (33.8)	Reference	Reference	Reference
With cADD and BCMA	153/522 (29.3)	1,808,600	34,360	52.64
Potentially harmful MAEs [b]				
Without cADD and BCMA	24/488 (4.9)	Reference	Reference	Reference
With cADD and BCMA	2/522 (0.4)	1,808,600	34,350	52.66

MAE, medication administration error.
[a] Extrapolated to the entire hospital (570 clinical beds receiving the intervention).
[b] *NCC MERP (National Coordinating Council for Medication Error Reporting and Prevention) class E (an error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention) or higher.*[29]

Notwithstanding the strengths, this study also has some limitations. First, observer bias, including a Hawthorne effect on the observed staff, may have occurred. This probability was minimized by using the disguised observation method to collect data on MAEs.[26,28] We used protocols and extensive training programmes for all real-life observations in daily clinical practice, but errors cannot be ruled out. For instance, observers stated that it can be difficult to classify some nursing tasks into medication-related tasks or non-medication related tasks – for example, when nurses read patient records. Nonetheless, with regard to the estimated costs, the material costs related to cADD were fixed costs and accounted for 58% of the cost difference. Second, uncertainties in economic evaluations and before-and-after studies are inevitable.

Table 6
Cost-effectiveness ratio of central automated unit dose dispensing (cADD) and barcode-assisted medication administration (BCMA) for different scenarios.

	Incremental costs (€)/year	Estimated avoided MAEs (n) of N administrations/ year N = 2,260,870	Costs per avoided MAE (€)
Cost-effectiveness (main analysis)	**1,808,600**	**102,210**	**17.69**
Different scenarios (sensitivity analysis)			
Absolute MAE reduction rates			
20%	1,808,600	452,170	4.00
15%	1,808,600	339,130	5.33
10%	1,808,600	226,090	8.00
5%	1,808,600	113,040	16.00
2%	1,808,600	45,220	40.00
1%	1,808,600	22,610	80.00
Nurse handling time			
100% increase	1,466,530	102,210	14.35
50% increase	1,178,550	102,210	11.53
No increase	890,580	102,210	8.71
Total incremental costs			
20% increase	2,170,330	102,210	21.23
20% decrease	1,446,880	102,210	14.16
Number of administered doses annually at constant costs and different absolute MAE reduction rates			
1,500,000 doses administered			
20%	1,808,600	300,000	6.03
15%	1,808,600	225,000	8.04
10%	1,808,600	150,000	12.06
5%	1,808,600	75,000	24.11
2%	1,808,600	30,000	60.29
1%	1,808,600	15,000	120.57
600,000 doses administered			
20%	1,808,600	120,000	15.07
15%	1,808,600	90,000	20.10
10%	1,808,600	60,000	30.14
5%	1,808,600	30,000	60.29
2%	1,808,600	12,000	150.72
1%	1,808,600	6000	301.43

MAE, medication administration error.

Therefore, different sensitivity analyses have been performed for different scenarios (i.e. related to MAE reductions as well as several costs). Data on MAEs obtained in six clinical wards were extrapolated to the entire hospital based on the estimated number of administered medications in the entire hospital, which may differ from actual numbers. Supporting our findings, the MAE reduction found in this study (4.5% absolute reduction) is similar to absolute reduction rates found in studies on technological interventions, including studies on BCMA or cADD.[11 17 19 32] Third, down-scaling the number of total non-COVID-19 beds in the hospital may have affected the results, e.g. due to different patient populations (non-COVID) or altered personnel staffing. We strived to adjust for the cost differences by adjusting wastage costs to the number of available beds. No adjustments seemed necessary for other costs because some of these were extrapolated using the number of administered medications, while other costs were fixed (e.g. costs of the cADD devices, hospital area, scheduled pharmaceutical personnel). Estimated costs related to nurse medication handling were also considered minimally affected by the down-scaling, because extrapolation was based on the number of administered medications for observations during the day and number of beds for observations at night. For the night observations, no adjustments were made, because the patient-to-nurse ratios of observed personnel were similar between measurement periods. Contrary to expectations, however, the estimated nurse medication handling cost was substantially higher in the post-intervention period. Scanning may have been responsible for the increase in the medication handling time (e.g. due to technical difficulties such as slow scanner response.[24,33,34]), but it is unlikely that this degree of increase can be attributed solely to the intervention itself .[21,35] Other contributing factors could be related to the COVID-19 pandemic and include slightly different patient populations, hygiene measures, or personnel-related factors like fatigue or staffing problems. Fourth, the use of statistical analysis to estimate the absolute MAE reduction was hampered because converting the odds ratio of the mixed-effects multivariable logistic regression analysis presented in the effectiveness study[24] (odds ratio 0.7, 95% confidence interval 0.51–0.96) would lead to an overestimation of the relative risk, as the MAE prevalence exceeds 10%.[36] Also, the adjusted risk reduction based on the odds ratio would not differ considerably from the unadjusted risk reduction (from 21.2% to 16.7%). Last, the monocenter setting may limit generalizability. However, the previous Danish studies, which show quite similar cost-effectiveness ratios, support the generalizability to similar settings –university hospitals in high-income European countries. Also, the marginal costing approach allows for assumptions on the generalizability to low-income or middle-income countries because many costs, such as personnel and material costs, in these countries are generally lower, probably leading to a cost-effectiveness ratio less than the estimated €17.69. Moreover, the costs per avoided potentially harmful MAE are much lower than the costs for adverse events, which range from roughly €1,000 to €7,000 per event.[7] Sensitivity analyses also showed that considerably lower absolute MAE reduction rates (e.g. 1%) or number of administered doses (e.g. 600,000 doses annually) compared to our study, would lead to substantially lower costs than the reported costs of adverse drug events. For instance, the worst case scenario (1% absolute MAE reduction and 600,000 doses administered annually at constant costs), would lead to a cost-effectiveness ratio of €283.55.

4.1. Implications for research and practice

This study showed that the investigated intervention comes with high direct investment costs, but a return on investment will be made in due course by preventing MAEs, including potentially harmful errors. Additionally, the intervention reduced the medication wastage in only one hospital by €117,470 annually, suggesting increased sustainability. However, the cADD device is associated with a higher use of plastic disposables (plastic unit dose bags and plastic rings).

The affordability and sustainability of this intervention might be increased by focusing on efficiency measures in addition to safety parameters during implementation by using comprehensive implementation and evaluation strategies. For instance, one cADD device would be sufficient to for the entire hospital, but our institution implemented two devices to have a backup in case of technical problems. An alternative and cost-saving solution would be to collaborate with surrounding hospitals with a similar cADD in case of emergency. It would be worthwhile to evaluate the effects of tailoring the intervention to the needs of different clinical wards (e.g. tailored delivery schedules) because this may also affect efficiency on ward level or pharmacy level.

To verify our hypothesis on generalizability and on identifying measures to increase the efficiency of the combined intervention, it might be interesting to focus on the cost-effectiveness in other settings, for example general hospitals or hospitals in low-income and middle-income countries.

5. Conclusion

In this study, the implementation of pharmacy-based automated unit dose dispensing with barcode scanning at patient bedside was associated with a reduced rate of MAEs, including harmful ones, at higher overall costs. The cost-effectiveness ratio of this intervention was €17.69 per avoided MAE and €30.23 per avoided potentially harmful MAE. Considering the relatively low costs per avoided error, this intervention could be an important strategy to improve patient safety in hospitals.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

The non-confidential data underlying this article will be shared on reasonable request to the corresponding author.

Declarations of competing interest

None.

Author statement

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Acknowledgements

We thank L.S.C. Nanda, S. Numanoğlu, and L.C. van Rijn (pharmaceutical students when conducting the study) for assistance with data collection. We thank Ko Hagoort (language editor, Erasmus MC) for proofreading/editing the article.

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