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Research article

Bedside check of medication appropriateness (BED-CMA) as a risk-based tool for bedside clinical pharmacy services: A proof-of-concept study at the trauma surgery ward

Greet Van De Sijpe [a,b,*,1], Wencke Hublou [a], Peter Declercq [a,b,2], Willem-Jan Metsemakers [c,3], An Sermon [c,4], Minne Casteels [b,5], Veerle Foulon [b,6], Charlotte Quintens [a,b,7,8], Isabel Spriet [a,b,8,9]

[a] Pharmacy Department, University Hospitals Leuven, Leuven, Belgium
[b] Clinical Pharmacology and Pharmacotherapy, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Leuven, Belgium
[c] Department of Trauma Surgery, University Hospitals Leuven, Leuven, Belgium

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ABSTRACT

Background: Bedside clinical pharmacy prevents drug-related problems, but is not feasible in many countries due to limited resources. Hence, clinical rules using structural information in the electronic health record can help identifying potentially inappropriate prescriptions (PIPs). We aimed to develop and implement a risk-based clinical pharmacy service and evaluate its impact on prescribing at the trauma surgery ward.

Methods: The proportion of residual PIPs per day, i.e. the number of PIPs that persisted up to 24 h after pharmacist intervention divided by the number of PIPs at T0, was evaluated before and after implementation of the intervention in an interrupted time series analysis. The pre-intervention cohort received usual pharmacy services, i.e. a 0.3 FTE clinical pharmacist trainee. Fifteen clinical rules, targeting antimicrobial, anticoagulant and analgesic therapy were implemented in the post-intervention period. The pre-intervention period was compared to two post-intervention scenarios: A) clinical rule alerts reviewed by a 0.3 FTE clinical pharmacist trainee; and B) clinical rule alerts reviewed daily for approximately 1 h by a clinical pharmacist trainee.

Results: Pre-intervention, a median proportion of 67% (range 0%−100%) residual PIPs per day was observed. Scenario A showed an immediate relative reduction of 14% ($p = 0.72$) and scenario B a significant immediate relative reduction of 85% ($p = 0.0015$) in residual PIPs per day. In scenario A, recommendations were provided for 19% of clinical rule alerts, of which 67% was accepted by the surgeon within 24 h. In scenario B, recommendations were given for 56% of alerts, of which 84% was accepted.

Conclusions: Using clinical rules is an effective approach to organize bedside clinical pharmacy services and improves prescribing at the trauma surgery ward. Advanced training and daily follow-up of the clinical rules are two requirements to be considered.

Abbreviations: BED-CMA, Bedside check of medication appropriateness; CI, Confidence interval; CMA, Check of medication appropriateness; FTE, full-time equivalent; IR, Incidence rate; IRR, Incidence rate ratio; ITS, Interrupted time series; LMWH, Low molecular weight heparin; NOAC, Non-vitamin K oral anticoagulant; PIP, Potentially inappropriate prescription; SD, Standard deviation; UZ Leuven, University Hospitals Leuven.

* Correspondence to: University Hospitals Leuven, Pharmacy Department, Herestraat 49, 3000 Leuven, Belgium.
E-mail address: greet.vandesijpe@uzleuven.be (G. Van De Sijpe).
[1] ORCID 0000–0003-1475–6178
[2] ORCID 0000–0002-6338–2355
[3] ORCID 0000–0002-4114–9093
[4] ORCID 0000–0001-6295–9127
[5] ORCID 0000–0001-9401–5489
[6] ORCID 0000–0002-4053–3915
[7] ORCID 0000–0002-6072–2596
[8] *Shared last authorship
[9] ORCID 0000–0001-6342–0676

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1. Background

Drug-related problems, encompassing all patient-related issues involving drug therapy that actually or potentially interfere with desired health outcomes, continue to pose a significant threat to patient safety. [1,2] They are common in hospitalised patients and can lead to increased length of stay, morbidity, mortality and costs.[3] Prescribing errors, which occur during drug selection, prescription and therapy monitoring, are an important cause for drug-related problems.[3,4]

Patients admitted to surgical wards are especially vulnerable to drug-related problems, due to the prescription of high-risk medications, including antimicrobials, antithrombotic therapy and analgesics.[5–11] Additionally, many orthopaedic surgery patients are elderly and have multiple co-morbidities, elevating the risk for adverse drug events. [11–13] Next to these challenges, the care for trauma surgery patients often falls under the responsibility of junior physicians, with limited oversight from attending surgeons, who are frequently pressed for time. [11]

Bedside clinical pharmacy services were implemented in many hospitals to reduce drug-related problems, and have proven to be effective. [14–18] A large prospective intervention study performed by Bos et al. showed that education and support of the surgeon by a pharmacist led to a significant and clinically relevant benefit for patients and a reduction in clinically relevant drug related problems, including death, disability and increased length of hospital stay, without generation of additional costs.[11] Other studies showed that involving pharmacists in a multidisciplinary team at a surgery ward prevented serious adverse drug events and reduced overall costs.[13,19]

Because of limited resources for clinical pharmacy services in many European countries, clinical pharmacists are often only present at a small number of high-risk wards, and commonly not on a full-time basis. [20,21] Due to time constraints, conducting a medication review for every admitted patient is simply not possible. Consequently, patients at risk for drug-related problems might be missed.

Hence, a risk-based selection of patients with higher risk for drug-related problems would be of great benefit to tackle this problem. Clinical rules, which make use of structural information available in the electronic health record, such as patient characteristics, drug prescriptions and laboratory values, can help identify potential high-risk situations.[22–27] We hypothesize that clinical pharmacists can increase their efficiency at the ward by structuring their work and giving priority to reviewing patients identified by the clinical rule alerts.

The aim of this study was to develop and implement a risk-based clinical pharmacy service using clinical rules, called 'Bedside Check of Medication Appropriateness (BED-CMA)' and evaluate its impact on potentially inappropriate prescriptions (PIPs) at the trauma surgery ward.

2. Methods

2.1. Study design and setting

A quasi-experimental interrupted time series (ITS) study was performed to evaluate the impact of the BED-CMA. The ITS design is characterized by a series of measurements over time, interrupted by an intervention, i.e. the implementation of the BED-CMA service at the trauma surgery ward. The primary outcome was the daily proportion of residual PIPs, i.e. the number of PIPs that persisted up to 24 h after pharmacist intervention divided by the number of initial PIPs at baseline (T0). A PIP was defined as a prescription or an omission that both have the potential to cause harm. Data collection at multiple time points before and after the implementation of the intervention allows to evaluate both the effect over time (trend) of each period and the abrupt change in level as a result of the intervention (immediate effect of the intervention).[28]

The study was carried out at the 58-bed trauma surgery ward of the University Hospitals Leuven (UZ Leuven), a 1995-bed tertiary academic hospital in Belgium. In UZ Leuven, computerized physician order entry supported by clinical decision support systems is used for prescribing. In addition, a centralized clinical pharmacy service, called Check of Medication Appropriateness (CMA), comprising a rule-based screening for PIPs followed by a medication review performed by a back-office clinical pharmacist is implemented hospital-wide.[22, 25–27, 29, 30] The trauma surgery ward mainly consists of patients with musculoskeletal injuries. The study was approved by the Ethics Committee UZ/KU Leuven (S65024). The BED-CMA was implemented as a quality improvement project, and informed consent was not deemed necessary.

All inpatients admitted to the trauma surgery ward except palliative patients were eligible for study enrolment. The pre-intervention cohort received usual bedside pharmacy services. The post-intervention cohort was exposed to usual bedside pharmacy services and the BED-CMA.

2.2. Pre-intervention

Bedside clinical pharmacy services were performed by a hospital pharmacist trainee, i.e. a graduated pharmacist, running the 3-year training program for hospital pharmacist. The pharmacist was present at the trauma surgery ward on a 0.3 full-time equivalent (FTE) basis, i.e. three half-days per week. The pharmacist attended the ward rounds, performed medication reconciliation and medication review, and was available for questions from both physicians and nursing staff. If deemed necessary after medication review, a pharmacotherapeutic recommendation was provided by adding a note in the patient's electronic health record. Moreover, the recommendation was discussed verbally with the treating surgeon.

2.3. Set-up of BED-CMA

A joined meeting with a team of clinical pharmacists with expertise concerning trauma surgery was conducted. A set of 15 clinical rules targeting antimicrobial, anticoagulant and analgesic therapy was formulated based on bedside clinical pharmacy experience, a retrospective analysis of provided recommendations and relevant literature (Table 1, Supplementary Table 1).[31–38] These clinical rules were developed to specifically target drug-related problems occurring at the trauma surgery ward, in addition to the more general clinical rules embedded in the hospital-wide CMA service. Two trauma surgeons (WJM and AS) reviewed and validated the content of the clinical rules. A standardised flowchart was developed for each clinical rule which could be used by the clinical pharmacist during medication review, ensuring a consistent and uniform handling of inappropriate prescriptions.

The clinical rules were incorporated in the hospital information system as 'if-then' algorithms, using real-time structured data available in the electronic health record (e.g. patient characteristics, medication prescriptions, laboratory and microbiological data).[22]

The technical performance of the clinical rules was evaluated between February and August 2021, by manually checking 60 medical records of patients hospitalized at the trauma surgery ward to detect false negative and false positive results. The positive predictive value, negative predictive value, sensitivity and specificity were calculated. Clinical rules were adapted accordingly to increase their performance.

2.4. Implementation of BED-CMA

The validated BED-CMA service was implemented at the trauma surgery ward on September 1, 2021. Screening ran continuously on real-time patient data. The results of the screening, i.e. the clinical rule alerts, were compiled on a structured worklist in the hospital information system for review by the pharmacist. If deemed necessary after medication review, a pharmacotherapeutic recommendation was provided by adding a note in the patient's electronic health record. Moreover, the recommendation was discussed verbally with the treating surgeon.

Table 1
Clinical rules implemented at the trauma surgery ward.

	Clinical rule, screening for:
Anticoagulation management	Immobile or surgery patients not receiving thrombosis prophylaxis
	Not restarting of oral anticoagulation 72 h after surgery
Antimicrobial therapy	Excessive duration of surgical antibiotic prophylaxis
	Incorrect rifampicin dose for treatment of orthopaedic and trauma device-related infection
	Liver function abnormalities associated with rifampicin treatment
	Not starting rifampicin for treatment of orthopaedic and trauma device-related infection, when indicated
	Starting treatment with rifampicin when not indicated
	Continuation of meropenem treatment, when de-escalation to narrow spectrum antimicrobials is possible based on susceptibility data
	Continuation of piperacillin-tazobactam treatment, when de-escalation to narrow spectrum antimicrobials is possible based on susceptibility data
	Continuation of vancomycin treatment, when de-escalation to narrow spectrum antimicrobials is possible based on susceptibility data
	Treatment of osteomyelitis or orthopaedic and trauma device-related infection with orally administered flucloxacillin
	Incorrect dosing of vancomycin based on therapeutic drug monitoring levels
	Starting levofloxacin for high-inoculum Staphylococcal infection (i.e. within 14 days after positive culture)
	Treatment with linezolid
Analgesics	Treatment with opioids without a prescription for paracetamol

2.5. Data collection

Two ITS analyses were performed to evaluate the impact of the BED-CMA: (scenario A) the pre-intervention period compared to post-intervention period A, and (scenario B) the pre-intervention period compared to post-intervention period B. The pre-intervention period took place from September 2019 to January 2021. Two post-intervention periods were selected to further investigate necessary requirements for successful implementation of BED-CMA.

In post-intervention period A (September 2021 to January 2022), the clinical rule alerts of the BED-CMA were reviewed by a hospital pharmacist trainee on a 0.3FTE basis, who received basic training in the clinical rules. Basic training included one practical session to perform the trauma-focused BED-CMA, i.e. to use the software, to perform the medication review and to provide patient-tailored pharmacotherapeutic recommendations. In post-intervention period B (February to June 2022), alerts were reviewed once daily on weekdays for about 1 h by a hospital pharmacist trainee who received advanced training in the clinical rules. Advanced training included multiple practical sessions to perform the trauma-focused BED-CMA, as well as 4 months of field training at the trauma surgery ward. As the hospital pharmacist trainees rotated regularly between disciplines during their internship, they were not same in both periods.

For a sample of randomly chosen weekdays, the daily number of initial and residual PIPs was recorded. In the pre-intervention period, an initial PIP (PIP at T0) was identified by running the clinical rules on retrospective patient data, followed by a manual review of the alert to assess its relevance. When deemed relevant and actionable, it was defined as an initial PIP. Then, if the PIP persisted after T0 + 24 h, it was considered a residual PIP. In the post-intervention period alerts were generated prospectively by running the clinical rules on real-time patient data. Each alert was reviewed for relevance and in case of an initial PIP (PIP at T0) the pharmacist formulated a recommendation for which the acceptance by the physician within 24 h was recorded. A residual PIP was defined as a PIP that was still present at T0 + 24 h, due to non-acceptance of the recommendation. Acceptance was defined as an adaptation of the medical therapy or a follow-up of clinical and/or laboratory parameters based on the pharmacist's recommendation. Additionally, residual PIPs at T0 + 48 h were documented for both the pre- and post-intervention period.

Next to the ITS analyses, an observational study was performed for post-intervention period A and B. The number of alerts generated by BED-CMA, the number of pharmacists' recommendations and the physicians' acceptance rate were documented. The type, number and acceptance rate of non-clinical rule-based recommendations, i.e. medication recommendations given by the pharmacist independent of the clinical rules, were also documented.

2.6. Statistical analysis

A segmented Poisson regression model was used with the estimated effects expressed as incidence rate ratios (IRR)(Table 2).[28] The incidence rate (IR) was defined as the ratio of the number of residual PIPs to the number of initial PIPs. The IRR quantified the relative increase or decrease of the IR as a result of the intervention and/or time.

A sample size calculation was performed considering a mean number of 2.45 residual PIPs per day, based on an exploratory analysis. To detect a decrease of 50% in residual PIPs with a power of 90%, a minimum of 29 data points in each period were required. To ensure a stable estimate of the underlying secular trend, 85 data points were analysed in each period. A timeline of the study is presented in Fig. 1.

All statistical analyses were carried out with SAS software version 9.4 for Windows. Estimated effects with 95% confidence interval (CI) were calculated.

3. Results

3.1. Set-up of BED-CMA

The positive predictive value, negative predictive value, sensitivity and specificity of the clinical rules were 90.0%, 99.5%. 81.8% and 99.8%, respectively. The lower sensitivity was caused by two clinical rules, which were adapted accordingly to increase their performance.

3.2. Interrupted time series analysis

Baseline characteristics are shown in Table 3. For the 85 data points in the pre-intervention period, 249 initial PIPs and 153 residual PIPs per day were observed. The median proportion of residual PIPs at T0 + 24 h was 67% (range: 0–100%) with a median number of 1 residual PIP

Table 2
Equation of the segmented Poisson regression model. The shape of the formula is $Y_t = \exp[\beta_0 + \beta_1 *\text{time}_t + \beta_2 *\text{intervention}_t + \beta_3 *\text{time after intervention}_t] + \varepsilon_t$.

Y_t	the value of the dependent variable (IR) in month t
time	continuous variable indicating time in months at period t whereby time is centered at the intervention; hence taking a value of 0 months at intervention, positive values in the post-intervention period and negative values in the pre-intervention period.
intervention	an indicator for time t occurring before or after the implementation of BED-CMA
time after intervention	a continuous variable counting the number of months after the intervention at time t
β_0	estimate of the pre-intervention IR of residual PIPs at the beginning of the time series
β_1	estimate of the pre-intervention trend
β_2	estimate of the immediate change in level of the IR of residual PIPs after the intervention was implemented
β_3	estimate of the change in the trend after implementation of the intervention
ε_t	estimate of the random error

BED-CMA, bedside check of medication appropriateness; IR, incidence rate; PIP, potentially inappropriate prescription

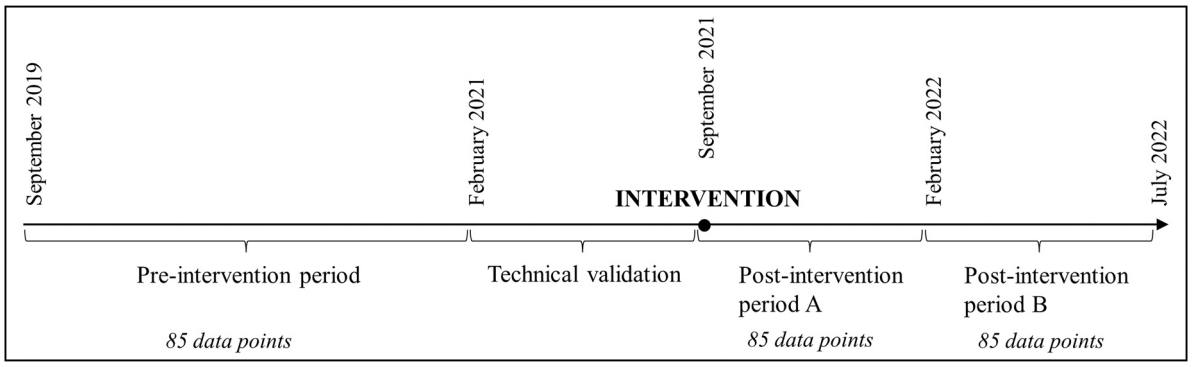

Fig. 1. Timeline of the study.

(range: 0–8) per day. After implementation of BED-CMA the median proportion of residual PIPs decreased to 45% (range: 0–100%) and 0% (range: 0–100%) in scenario A and B, respectively (Table 3, Fig. 2A, Fig. 2C).

Fig. 2 presents the proportion of residual PIPs (panel A and C) and the estimated IR with 95% CI over time and by period (panel B and D). The pre-intervention IR at the time of the intervention was 60% (β_0 0.60). In scenario A, the IRR for level change due to the intervention was 0.86 (β_2), meaning that the post-intervention IR was 86% of the pre-intervention IR. The BED-CMA showed a 14% immediate relative reduction in residual PIPs per day ($p = 0.72$). There was no evidence for an underlying time trend pre-intervention (β_1 0.99) nor post-intervention (0.97); there was neither a significant difference when comparing pre- and post-intervention trends (β_3 0.97) (Table 4, Fig. 2B). In scenario B, the IRR for level change due to the intervention was 0.15 (β_2), meaning that the BED-CMA showed a significant immediate relative reduction of 85% in residual PIPs per day ($p = 0.0015$). There was no evidence for an underlying time trend pre-intervention (β_1 0.99) and post-intervention (1.21) and there was no significant difference when comparing pre- and post-intervention trends (β_3 1.21) (Table 4, Fig. 2D). The impact of BED-CMA at T0 + 48 h is presented in Supplementary Fig. 1 and Supplementary Table 2.

3.3. Observational study

During post-intervention period A, 238 clinical rule alerts were evaluated in 109 days. Recommendations were provided by the pharmacist in 46 cases (19%), of which 67% and 69% were accepted within 24 h and 48 h, respectively. In addition, 45 non-clinical rule based recommendations were provided, of which 74% were accepted within 24 h. In post-intervention period B, 299 clinical rule alerts were reviewed in 108 days. Recommendations were given in 167 cases (56%) of which 84% and 93% were accepted within 24 h and 48 h, respectively. Additionally, 86 non-clinical rule based recommendations were provided, of which 66% and 71% were accepted within 24 h and 48 h, respectively.

Table 5 shows the top 3 most provided clinical rule based and non-clinical rule based recommendations and their acceptance rate within 24 h. An overview of all recommendations is shown in Supplementary Table 3 and 4.

Table 3
Baseline characteristics.

Characteristic	Pre-intervention period	Post-intervention period A	Post-intervention period B
Data points (days), n	85	85	85
Initial PIPs at T0, n	249	107	157
Number initial PIPs per day, median (range)	2 (0–11)	1 (0–6)	1 (0–7)
Residual PIPs at T0 + 24 h, n	153	51	22
Proportion residual PIPs per day, median (range)	67% (0–100%)	45% (0–100%)	0% (0–100%)
Number residual PIPs per day, median (range)	1 (0–8)	0 (0–4)	0 (0–3)
Patients with a PIP, n	182	80	110
Age (years), mean ± SD	67.3 ± 18.5	63.5 ± 21.0	68.3 ± 19.7
Female, n (%)	100 (54.9)	30 (37.5)	63 (57.3)

PIP, potentially inappropriate prescription; SD, standard deviation

4. Discussion

Our study demonstrates the effectiveness of the clinical rule based BED-CMA in streamlining bedside clinical pharmacy services, which resulted in a significant impact on prescribing at the trauma surgery ward. Potentially inappropriate prescriptions were reduced with 85% when alerts were reviewed daily by a hospital pharmacist trainee with advanced training in the clinical rules. A large proportion of the clinical rule alerts led to a recommendation (56%) of which 84% were accepted by the trauma surgeon.

We demonstrated that the BED-CMA has an added value on top of usual clinical pharmacy services. This can be explained by the magnitude of the trauma surgery ward (i.e. 58 beds) and the limited presence of the pharmacist (0.3 FTE). These constraints make it impossible to review the pharmacotherapy of every admitted patient. The BED-CMA lists possible drug related problems on a structured worklist, increasing the efficiency of the pharmacist and leaving more time for other clinical pharmacy activities such as medication reconciliation, comprehensive medication reviews and discharge counselling.[39]

We evaluated the impact of BED-CMA using two different scenarios that fit for implementation in clinical practice. A difference was observed between these two scenarios in the reduction of residual PIPs and the number of provided recommendations, with a greater impact in scenario B. This difference can be attributed to (i) a lack of experience and/or self-confidence of the hospital pharmacist trainee who did not receive advanced training; and (ii) an inadequate time frame to address the clinical rule alerts, resulting in some PIPs being missed. Therefore, two requirements should be taken into account when using BED-CMA in order to significantly impact inappropriate prescribing: (i) thorough training of pharmacists concerning the clinical rules and pharmacotherapy of surgery patients; and (ii) daily follow-up of clinical rule alerts.

Recommendations following BED-CMA alerts were communicated to the treating surgeon by providing an electronic note in the electronic health record. In addition, recommendations were discussed verbally with the surgeon whenever possible. This resulted in a high acceptance rate of 84% within 24 h (scenario B). This is consistent with previously reported studies that showed an enhancement in adherence to

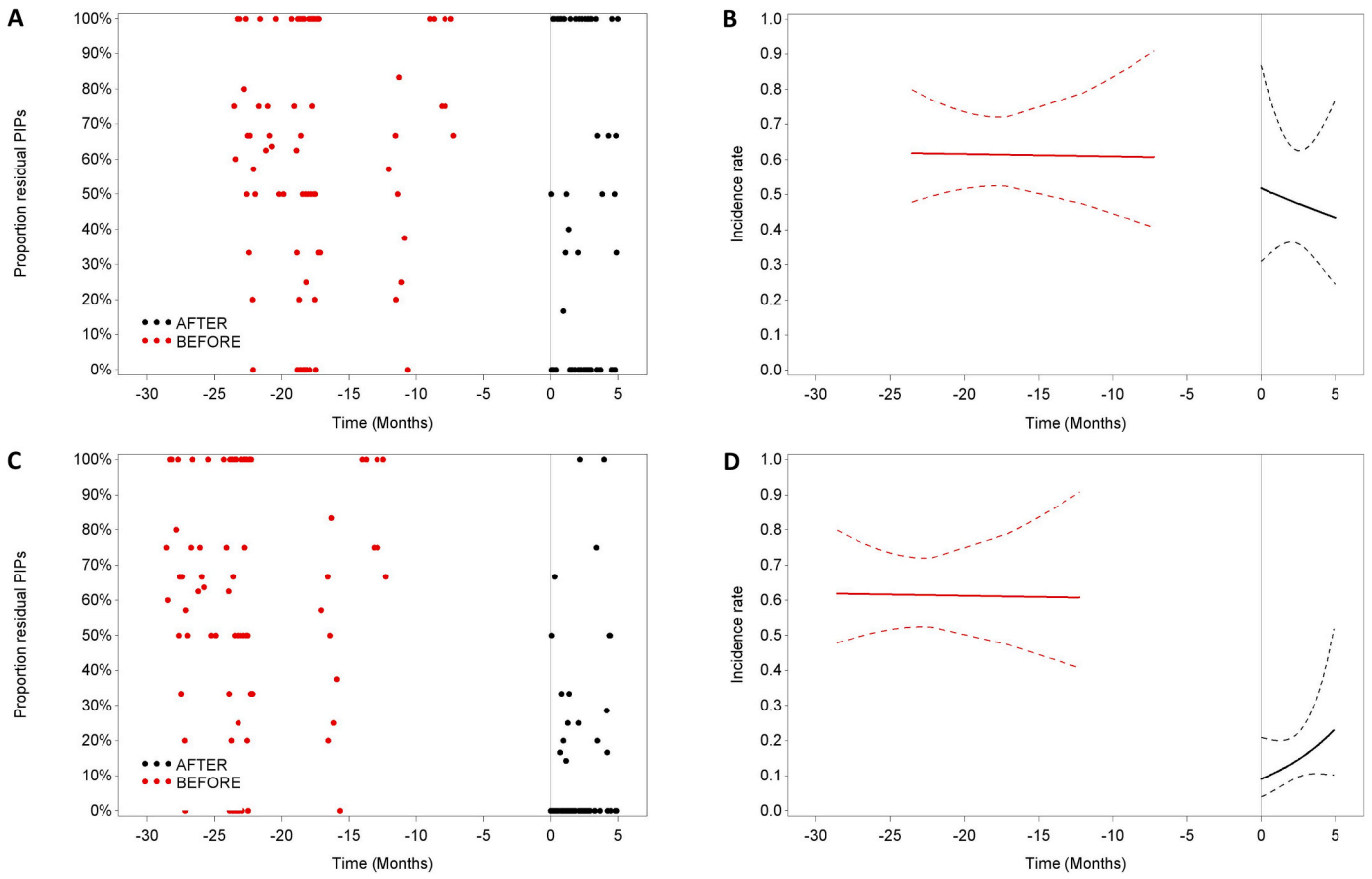

Fig. 2. Interrupted time series analyses. Time is centred at the intervention, taking a value of 0 months at intervention, negative values in the pre-intervention period and positive values in the post-intervention period. **Panel A**: Observed proportions of residual potentially inappropriate prescriptions per day at T0 + 24 h for the 85 data points in the pre-intervention period (September 2019 - January 2021) (red) and for the 85 days in the post-intervention period A (September 2021 - January 2022) (black). **Panel B**: Estimated incidence rate (with 95% confidence intervals) of residual potentially inappropriate prescriptions at T0 + 24 h over time and by period showing the difference between the pre-intervention period (red) and post-intervention period A (black). **Panel C:** Observed proportions of residual potentially inappropriate prescriptions per day at T0 + 24 h for the 85 data points in the pre-intervention period (September 2019 to January 2021) (red) and for the 85 days in the post-intervention period B (February 2022 - June 2022) (black). **Panel D**: Estimated incidence rate (with 95% confidence interval) of residual potentially inappropriate prescriptions at T0 + 24 h over time and by period showing the difference between the pre-intervention period (red) and post-intervention period B (black) PIP; potentially inappropriate prescription.

recommendations in case of verbal interaction with treating physicians. [29,40]

Three clinical rules, i.e. 'Treatment with opioids without a prescription for paracetamol', 'Incorrect dosing of vancomycin based on therapeutic drug monitoring levels' and 'Not restarting of oral anticoagulation 72 h after surgery', accounted for most alerts and recommendations in both scenarios A and B. The first two clinical rules are based on strongly recommended principles in clinical practice.[37,41] The relatively low acceptance rate of the third clinical rule may be explained by the trauma surgeon's reluctance to restart oral anticoagulation for fear of possible bleeding. However, risk factors such as any active bleeding or poor wound healing are reviewed by the pharmacist.[42] Not restarting oral anticoagulation during hospitalization increases the risk of duplicate therapy with both a low molecular weight heparin (LMWH) and a non-vitamin K oral anticoagulant (NOAC) after discharge, which is why switching during admission is so important.

We developed the BED-CMA as a tool to help pharmacists organize their bedside clinical pharmacy services. The alerts are compiled on a worklist used by the pharmacist, who interprets them for clinical relevance and communicates to the treating physician when deemed necessary.[43] Another approach would be to show alerts directly to the treating physician. However, it is known that the majority of safety alerts are ignored in clinical practice due to lack of time, lack of integration in the workflow or alert fatigue. This was recently shown in the SENATOR randomized controlled trial, in which the primary endpoint was not met due to a very limited uptake of 15% of software-generated medication advice.[44] Also in our study, not all alerts were deemed actionable, as (only) 56% of alerts led to a pharmacist's recommendation (scenario B). We therefore believe it is important that alerts are verified by specified trained person who has dedicated time for reviewing these alerts and can communicate to the treating physician when deemed necessary, thereby minimizing alert fatigue of physicians. [43]

Two observational studies describing the development and evaluating the effectiveness of clinical rules used by bedside clinical pharmacists in the prevention of potential adverse drug events have been published so far.[23,24] Rommers et al. investigated the rule effectiveness and positive predictive value of alerts in a 5-month study on six different internal medicine and cardiology wards. Only for 10% of alerts, the pharmacist contacted the physician or nurse, which led to an actual recommendation in 76%.[23] In this study, clinical rules ran only once daily during the night rather than in real-time, as in our study, which could explain the large amount of false positive alerts. More recently, Ibáñez-Garcia et al. investigated the effectiveness of safety alerts during a 6-month study on medical, surgical and critical care wards. Similar to our results, recommendations were provided in 51% of cases, of which 66% was accepted.[24]

Our study has two important strengths. First, this is the first quasi-

Table 4
Parameter estimates (with 95% confidence intervals), standard errors and *P* values for the segmented regression analysis of the impact of BED-CMA on the incidence rate of residual potentially inappropriate prescriptions at T0 + 24 h.

	Estimate (95% CI)	Standard error	*P* value
Post-intervention period A			
Intercept β_0	0.603 (0.318–1.145)	0.3266	0.122
Pre-intervention trend β_1	0.999 (0.965–1.034)	0.0178	0.955
Change in level after BED-CMA β_2	0.858 (0.377–1.953)	0.4195	0.715
Post-intervention trend	0.999 (0.965–1.035)		0.955
Change in trend after BED-CMA β_3	0.967 (0.799–1.170)	0.0974	0.727
Post-intervention period B			
Intercept β_0	0.600 (0.267–1.352)	0.4140	0.218
Pre-intervention trend β_1	0.999 (0.965–1.034)	0.0178	0.955
Change in level after BED-CMA β_2	0.151 (0.047–0.484)	0.5936	**0.0015**
Post-intervention trend	1.208 (0.904–1.615)		0.202
Change in trend after BED-CMA β_3	1.209 (0.903–1.620)	0.1491	0.202

BED-CMA, bedside check of medication appropriateness; CI, confidence interval

Table 5
Top 3 most provided clinical rule based and non-clinical rule based recommendations, and their acceptance rate in post-intervention period A and B.

	Number of reviewed alerts	Number of recommendations	Acceptance rate (%)
Post-intervention period A			
Clinical rule based recommendations			
Not restarting of oral anticoagulation 72 h after surgery	43	17	31
Incorrect dosing of vancomycin based on therapeutic drug monitoring levels	62	12	100
Treatment with opioids without a prescription for paracetamol	40	8	100
Non-clinical rule based recommendations			
Correct dosing of LMWHs		8	88
Antibiotics – switch of antimicrobial therapy based on susceptibility results		6	50
Antibiotics: vancomycin – perform TDM of vancomycin; switching from intermittent to continuous infusion; changing of posology		5	100
Post-intervention period B			
Clinical rule based recommendations			
Treatment with opioids without a prescription for paracetamol	95	69	89
Incorrect dosing of vancomycin based on therapeutic drug monitoring levels	68	40	97
Not restarting of oral anticoagulation 72 h after surgery	40	26	52
Non-clinical rule based recommendations			
Correct dosing of LMWHs/ NOACs		11	100
Antibiotics – switch of antimicrobial therapy based on susceptibility results		9	38
Tapering drugs (benzodiazepines, corticosteroids, PPIs)		8	57

LMWH, low molecular weight heparin; NOAC, non-vitamin K oral anticoagulant; PPI, proton pump inhibitor; TDM, therapeutic drug monitoring

experimental study, to our knowledge, evaluating the impact of clinical rule based screening on inappropriate prescribing. This approach was found to be effective, with added value on top of usual clinical pharmacy services, and is useful for all countries with limited resources for front-office clinical pharmacy services. Secondly, we investigated two feasible scenarios in clinical practice to determine requirements for successful implementation of BED-CMA.

Our study has the following limitations. First, we did not measure clinical outcomes, e.g. occurrence of adverse drug events, but only investigated the impact on inappropriate prescribing. However, we screen for drug related problems, for which an effect on clinical outcome has already been proven, such as (i) the detrimental effect of supra-therapeutic vancomycin concentrations on kidney function; (ii) the occurrence of pancytopenia during linezolid therapy; and (iii) increased risk of deep vein thrombosis after orthopaedic and trauma surgery when appropriate anticoagulation in lacking. Secondly, the shorter post-intervention period of five months limited the evaluation of the sustainability of this intervention. The estimated IR over time showed a visual increasing trend in post-intervention period B, yet this trend was not statistically significant and is therefore attributed to chance. Additional data points would be necessary to estimate a more reliable effect on time. Conversely, a visual decreasing trend was observed for the same plot at T0 + 48 h (Supplementary Fig. 1). Finally, this was a mono-centric study performed in an academic hospital, limiting the generalizability of the results. Meanwhile, the BED-CMA is already implemented and used in two other non-academic acute care Belgian hospitals.

In the future, it might be advisable to assess the long-term sustainability of the intervention in a follow-up study with a longer post-intervention period. Furthermore, we aim to expand the set of clinical rules at the trauma surgery ward, to evaluate this risk-based tool in other hospitals, and to implement and evaluate BED-CMA on other wards in our hospital.

5. Conclusion

Using of clinical rules is an effective approach to perform and organize bedside clinical pharmacy services with a significant impact on PIPs at the trauma surgery ward. This approach increases the efficiency of the clinical pharmacist and buys more time for other clinical pharmacy activities. Advanced training and daily follow-up of the clinical rules are two requirements to be considered.

Declarations

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Author statement

None to declare.

CRediT authorship contribution statement

GVDS, CQ and IS conceptualized and designed the study. GVDS, PD, CQ and IS formulated the clinical rules. GVDS and WH collected the data. GVDS and WH analyzed the data. WJM and AS validated the clinical rules for content. GVDS wrote the manuscript. All authors reviewed and edited the manuscript. CQ and IS supervised the study.

Declaration of Competing Interest

All authors declare that they have no conflict of interest related to this work.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.csbj.2023.10.017.

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