




Benefit of medication reviews by renal pharmacists in the setting of a computerized physician order entry system with clinical decision support

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Abstract

What Is Known and Objective: A ‘renal pharmacist consultant service’ (RPCS) reviewing patients' charts with renal impairment (RI) for drug-related problems (DRP) can foster patient safety. However, the benefit of this service in the new setting of a computerized physician order entry (CPOE)-system with a clinical decision support (CDS)-system is unknown. The aim of our study was to evaluate the general need for an RPCS on wards with a CPOE-CDS-system already in use and its effectiveness on prescription changes to ensure in-hospital patient safety.

Methods: Over a period of 3 months (02-04/2021), elective orthopaedic and trauma patients with $eGFR_{\text{absolute}}/CrCl < 60$ ml/min at a German University Hospital received a medication review by a renal pharmacist for all medication entered into the CPOE-system (Meona[®]) by the treating physicians. Written consultations explaining identified DRP and recommending interventions to solve them, for example, dose or drug adaptation, were shared with the physicians directly in the drug chart tab of Meona[®]. In complex cases, DRP were additionally discussed via phone. The prescription changes were evaluated retrospectively.

Results and Discussion: During 53 working days, 712 (30.5%) of 2331 screened patients were included with an $eGFR_{\text{non-indexed}}/CrCl < 60$ ml/min and a pharmacist-led medication review was performed for all medication presented in the CPOE-system (Meona[®]). In 79 of 712 (11.1%) patients, one or more DRP were detected (median 1 DRP (1–3) per patient) and written recommendations concerning 106 of 1090 (9.7%) drugs were shared via Meona[®]. In total, 104 DRP were identified, mostly caused by ‘dosage too high’ ($n = 55$, 52.9%), ‘dosage regime wrong’ ($n = 13$, 12.5%), and ‘contraindication’ ($n = 9$, 8.7%). Acceptance rate of recommendations was 74.0% ($n = 77/104$). In nine cases (8.7%), despite of specific recommendations, no adjustment of drugs was made because of lack of alternatives. In 11 (10.6%) cases,

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prescription remained unchanged for unknown reasons and in seven (6.7%) cases, the result was unknown due to discharge.

What Is New and Conclusion: In the setting of prescribing in a CPOE-CDS-system, that provides physicians with advice for drug or dose adaptation, the pharmacist-led medication reviews still identified DRP in orthopaedic and trauma patients with RI. A RPCS forwarding recommendations to solve DRP via the electronic medical record increased appropriate prescribing by physicians and, thus, may further improve patient safety.

KEYWORDS

CPOE-CDS-system, drug-related problems, pharmacist-led medication review, renal impairment, renal pharmacist

1 | WHAT IS KNOWN AND OBJECTIVE

Around 20% of all hospitalized patients have renal impairment (RI), defined as an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m².^{1–5} To stage the degree of RI, the calculation of eGFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation that estimates an eGFR indexed to a standard body surface area (BSA) in ml/min/1.73 m² is recommended.⁵ For drug dosing purposes, renal function estimated in ml/min should be used.^{6,7} Therefore, either the CKD-EPI equation eGFR_{relative} should be converted to an eGFR_{absolute} or the creatinine clearance by the Cockcroft & Gault equation should be used. Drug adjustment is usually necessary at an eGFR_{absolute} or CreaCl <60 ml/min.⁸

Because of the lack of drug therapy adjustments, patients with RI often have renal drug-related problems (DRP).^{3,4,9,10} The Pharmaceutical Care Network Europe Association (PCNE) defines drug-related problems as “any events or circumstances involving drug therapy that actually or potentially interfere with desired health outcomes”.¹¹ They concern treatment effectiveness or treatment safety, have a variety of potential causes like drug selection, drug form, dose selection, or treatment duration and can lead to one or more necessary interventions.¹¹ In hospitalized patients with RI, pharmacists have identified 8%–81% inappropriate prescriptions resulting in higher adverse drug reaction (ADR) rates, prolonged hospitalization, higher drug expenditure and elevated mortality.¹⁰ Recently, we found that 61% of urological RI-patients admitted to hospital presented one or more DRP.⁴ To avoid DRP and thereby foster patient safety, it is important to detect and solve DRP at hospital admission and to continuously follow changes in renal function during hospital stay. The acceptance of pharmacists' advice on renal DRP is stated in the literature to be up to 95%.¹² The clinical pharmacist as part of the multiprofessional team takes a key role in identifying and solving DRP and has a positive influence on the safety of the prescription practice.^{13,14} The implementation of a ‘renal pharmacist consulting service’ (RPCS) at urological wards of an university hospital, screening patients with RI for DRP significantly increased appropriate prescribing by physicians and, thus, patient safety.¹⁵ In this study as well as in many others evaluating a renal pharmacists' activities, paper charts were used in daily hospital routine.^{10,12,15} In this case, information sharing with the physician as paper chart inlays was the most effective way to inform about and solve DRP.¹⁵

In the recent decade, traditional paper charts have increasingly been substituted by an electronic medical record (EMR) which represents the digital version of the paper chart.^{16,17} These systems include a computerized physician order entry (CPOE)-system with a clinical decision support (CDS). CPOE-systems are software programs used for electronic prescription of medications to ensure adequate orders.^{16,18,19} CDS-systems are generally integrated to aid physicians in medical decisions connecting clinical knowledge and patient information. Basic CDS-systems provide advice for correct drug dosing or drug–drug-interactions. The user must connect this knowledge with the specific patient information. Advanced CDS-systems can additionally perform drug allergy-, drug laboratory value- and drug guideline-checks by taking patient-specific information into account.^{18–20} In the case of a necessary adaptation regarding the prescription, the ordering physician receives an immediate warning from the CDS-system.

By implementation of a CPOE system, the quality of the prescription documentation can be improved.²¹ Electronic prescribing strategies have been found to considerably decrease medication errors, dosing errors, and adverse drug events.^{16–18,22} However, the implementation of CPOE-CDS-systems can also be problematic regarding user skills, integration in the hospital system, high costs and alert fatigue when CDS-systems show too many or clinically irrelevant alerts.^{22,23}

Recently, a CPOE-CDS-system with an electronic medication record was introduced at our hospital, changing the prescription and documentation process for the physicians. It is currently unknown if the warnings of the CDS-system are being considered in clinical routine in patients with RI for evaluating new prescriptions or, for example, when renal function is changing during the hospital stay. Clinical pharmacists working directly on wards are still no routine service in Germany.²⁴ It is also unknown, if a RPCS results in any additional benefit for patient safety in this new setting by identifying and informing about DRP.

The goal of our study was to evaluate the general need for an RPCS on wards with a CPOE-CDS-system in use. Therefore, a pharmacist regularly performing medication reviews in patients with RI was implemented. We assessed if the pharmacist still identified unnoticed DRP in the setting of a CPOE-CDS-system and, further, determined retrospectively the prescription changes after pharmacist's consultation to assess the benefit for patient safety.



2 | METHOD

Between February 2021 and April 2021, we implemented a 'renal pharmacist consultant service' (RPCS) for patients with renal impairment (RI) in the setting of a computerized physician order entry (CPOE)-system. The system integrates an advanced clinical decision support (CDS)-system and warns about possible risks during prescribing. On weekdays, the RPCS supported the physicians of two wards caring for elective orthopaedic and trauma patients of a tertiary teaching hospital by screening all patients for renal impairment. For all patients, who were ≥ 18 years and had an $eGFR_{\text{absolute}}$ and/or $CrCl < 60$ ml/min, a medication review (chart round) was conducted by the pharmacist of all medication presented in the CPOE-CDS-system (Meona[®]). Identified drug-related problems (DRP) were shared as a bold written consultation/note in the electronic medication record of Meona[®]. The participating wards had been using Meona[®] for at least 6 months prior to the study.

2.1 | Data collection and assessment

Serum creatinine, $eGFR$ by CKD-EPI equation (ml/min/1.73 m²), weight, height, age, and sex were extracted from the CPOE-CDS-system (Meona[®]), patients' electronic health record (SAP-i.s.h.med, Cerner Corporation, North Kansas City, USA), and laboratory records. The body surface area (BSA) was calculated by the Mosteller's equation and the indexed $eGFR$ (ml/min/1.73 m²) was recalculated to the non-indexed $eGFR$ (ml/min) with the following equation: $eGFR_{\text{non-indexed}}$ (ml/min) = $eGFR_{\text{indexed}}$ (ml/min/1.73 m²)/1.73 m² \times BSA.^{6,25} Additionally, the creatinine clearance (CrCl) by Cockcroft & Gault formula was calculated.²⁶ If the body mass index (BMI) was ≥ 30 kg/m², the adjusted body weight was used to calculate the CrCl.²⁷

While reviewing a patient's medication, the pharmacist focused on DRP regarding renal function, for example, contraindications, missing drug adjustment or inappropriate drug choice. Additionally, the physicians were informed about other obvious DRP, such as interactions, double prescriptions or inappropriate treatment durations, for example, for antibiotics. To assess the correct dosage or a contraindication of a drug regarding the renal function, the equation displayed in the specific German Summary of Product Characteristics (SPC) was used [$CrCl$ (ml/min) = Cockcroft & Gault formula; $eGFR$ (ml/min) = non-indexed $eGFR$ by CKD-EPI-formula]. For analysis, the identified DRP were categorized as described in previous studies with regard to the 'PCNE classification'.^{4,11,15} Following the PCNE classification, the DRP were classified to concern treatment safety or treatment effectiveness and categorized in one main cause that may lead to one or more proposed interventions. The cause of the DRP were 'contraindication', 'drug dosage too high' or 'too low', 'dosage regime wrong', 'therapy duration too long', 'double prescriptions', and 'others' (e.g., 'suboptimal drug', 'missing medication in comparison to prehospital medication', 'drug combination potentially decreasing renal function', and 'therapy stopped but still in Meona[®]'). As intervention, the RPCS recommended 'drug change/drug stop', 'dosage

change', 'dosage regime change', 'set therapy duration', 'start new drug', and/or 'monitoring'. Monitoring only referred to control of adverse drug events (ADR) or serum blood levels (e.g., electrolytes, creatine kinase) during drug therapy since monitoring of serum creatinine and $eGFR$ is mandatory in this patient population.

The RPCS only forwarded manifest DRP to the physicians, which were presently of concern regarding the current renal function of the patient. Potential DRP, that could arise if renal function would decrease further, were not forwarded to avoid over alerting. When $eGFR/CrCl$ were close to necessary drug adjustments, the pharmacist followed up these potential DRP the next working days.

2.2 | Pharmacist's intervention—Information sharing with physicians via the CPOE-system

The pharmacist shared the identified DRP and the resulting recommended interventions as bold written consultation via the electronic medication record of the CPOE-CDS-system Meona[®]. The consultation was composed of the different calculated renal functions [indexed $eGFR$, non-indexed $eGFR$ and $CrCl$ (absolute or adjusted body weight)], drug name and short description of DRP, proposed interventions to solve DRP and a telephone number for further inquiries. The consultation was directly retained in the monitoring/drug chart tab (electronic medical record; EMR) of the CPOE-CDS-system where the physicians also record the daily report on the patient. Drug chart, monitoring chart, progress report chart and lab value tab are all in the first window of Meona[®] and are directly seen when opening the electronic patient chart.

When DRP was time sensitive due to, for example, bleeding tendency, further clinical data had to be considered, or when there was no action taken after one working day, the DRP was additionally discussed with the ward physician via phone.

Prior to the introduction of a RPCS, the concept of the service and the information delivery via Meona[®] were introduced to all physicians of the study wards.

2.3 | Evaluation of the benefit of pharmacist-led medication review in the setting of a CPOE-system

Acceptance rates of recommendations regarding DRP were retrospectively evaluated as number of changed prescriptions in patient's electronic chart. The prescription changes were classified as the status of DRP as 'Unknown (discharge)', 'Not solved', 'Consciously retained' (meaning that the problem was discussed with the physician but it was decided to only monitor the DRP because of the lack of better therapy alternatives), and 'Solved'.

2.4 | Ethical approval

Ethical approval was obtained from the ethics committee at Ludwig-Maximilians-University Munich, registration number 21-0743.

TABLE 1 Demographic data for all patients with $eGFR_{\text{absolute}}/CrCl < 60$ ml/min, who received medication reviews (chart rounds) by a pharmacist, and for the subgroups of patients with and without drug-related problems (DRP)

	All patients, who received medication reviews	Patients with DRP (Consultation via CPOE-system)	Patients without DRP	p-values
Total	712	79 (11)	633 (89)	
Females	546 (77)	62 (78)	484 (76)	0.689 ^a
Age (years)	85 (21–101)	86 (52–98)	85 (21–101)	0.183 ^b
BMI (kg/m ²)	23.4 (15.7–46.1)	23.9 (16.8–45.7)	23.4 (15.7–46.1)	0.245 ^b
Renal impairment				
$eGFR_{\text{non-indexed}}$ (ml/min)	48 (10–79)	37 (10–77)	50 (10–79)	<0.05 ^b
CrCl (ml/min)	39 (7–75)	31 (11–56)	40 (7–75)	<0.05 ^b
Number of drugs	8404	1090	7314	
	12 (2–25)	14 (4–23)	12 (2–25)	<0.05 ^b
Number of drugs with DRP	—	106 (10)	—	
		1 (1–3)		

Note: Data are quoted as the median (interquartile range) or *n* (%).

Abbreviations: BMI, body mass index; CPOE, computerized physician order entry; CrCl, creatinine clearance; $eGFR$, estimated glomerular filtration rate.

^aChi-square test (categorical variables).

^bMann–Whitney–U test (continuous variables).

Because of the retrospective design, patient informed consent was not requested and not obtained in accordance with the applicable statutory provisions under the Bavarian State Hospital Act (Art. 27 Para. 4 BayKrG).

2.5 | Statistical analysis

Descriptive statistics were used to characterize the patient population. Qualitative variables are presented with their frequency distribution. Quantitative variables are expressed as mean and standard deviation (SD) (normal distribution) or as median and interquartile range (without normal distribution). As test for normality in frequency, the Shapiro Wilk test was used. For comparison between groups, Chi square test was used for categorical variables and Mann–Whitney–U test (without normal distribution) for continuous variables. Statistical significance was accepted as $p < 0.05$. Data analyses and figures were completed with Microsoft Excel[®] 2016 (Seattle, WA, USA) and IBM SPSS Statistics[®] version 25.0 (Armonk, NY, USA).

3 | RESULTS

During 53 working days, 547 patients (female $n = 334$; 61.1%) were followed during their hospital stay by the pharmacist and daily screenings of patients' records were performed. The patients were followed in median 3 (1–29) days by the pharmacist. During the period, which was used for data collection, 25 patients were readmitted. In sum, a total number of 2331 screenings of patient records (female $n = 1503$; 64.5%) were done for RI with a mean of 44 ± 4 patients per day.

Of all 2331 screenings, an $eGFR_{\text{absolute}}/CrCl < 60$ ml/min was found in 712 (30.5%) and medication reviews (electronic chart review of all medication presented in Meona[®]) were performed by the pharmacist. The patients' characteristics of these 712 screenings are shown in Table 1. Compared to patients without DRP, patients with DRP presented with significantly lower $eGFR_{\text{absolute}}/CrCl$ values and higher number of drugs, but no difference in gender ($p = 0.689$), age ($p = 0.183$), and BMI ($p = 0.245$) was found (Table 1). In median, the medication of 13 (7–23) patients per working day were checked by the pharmacist.

In 79 (11.1%) of the 712 medication reviews, one or more DRP were found and shared with the attending physicians via Meona[®]. A median of one (0–5) consultations per working day were given to the physicians explaining DRP and interventions to solve them.

The 712 reviewed patients were prescribed a total of 1090 medications, from which 106 (9.7%) were identified with DRP. The detected DRP concerned 43 different substances. Figure 1 shows the affected drug classes (according to the Anatomic Therapeutic Chemical classification system). Antithrombotic agents ($n = 26$, 24.5%), antibacterials for systemic use ($n = 20$, 18.9%), diuretics ($n = 12$, 11.3%) and blood glucose lowering drugs, excl. insulins ($n = 8$, 7.5%) were most often associated with DRP.

The pharmacist identified in total 104 DRP leading to 120 intervention proposals (Figure 2). In median the patients showed 1 (1–3) DRP. Most DRP concerned the treatment safety ($n = 84$, 80.8%). The main causes of DRP were 'dosage too high' ($n = 55$, 52.9%), 'dosage regime wrong' ($n = 13$, 12.5%), and 'contraindication' ($n = 9$, 8.7%). The 120 interventions were proposed to physicians with the major recommendation 'dosage change' ($n = 65$, 54.2%), 'drug change/stop' ($n = 20$, 16.7%), and 'monitoring of serum blood levels or ADR' ($n = 16$, 13.3%).

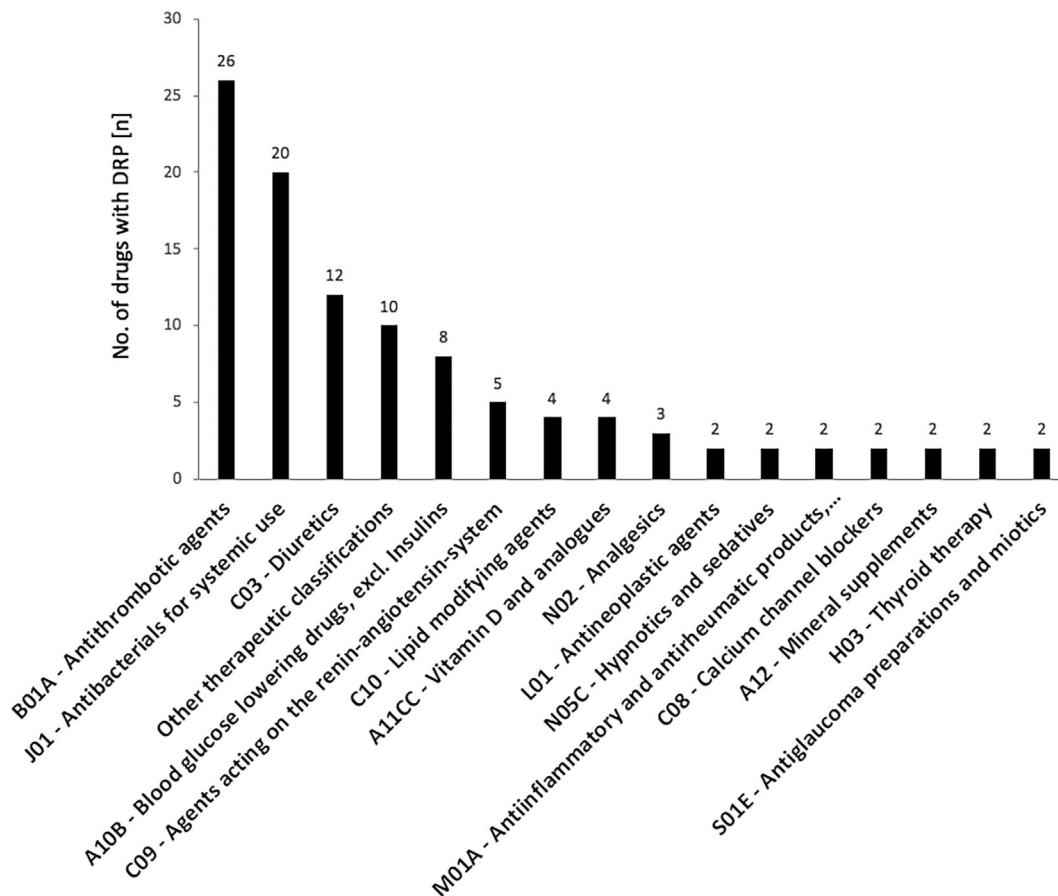


FIGURE 1 Drug classes (according to the Anatomic Therapeutic Chemical classification system) associated with drug-related problems (DRP) during the study period. In total 106 drugs showed 104 DRP ('Triple Whammy' interaction potentially decreasing renal function concerns three drugs per interaction and were counted separately)

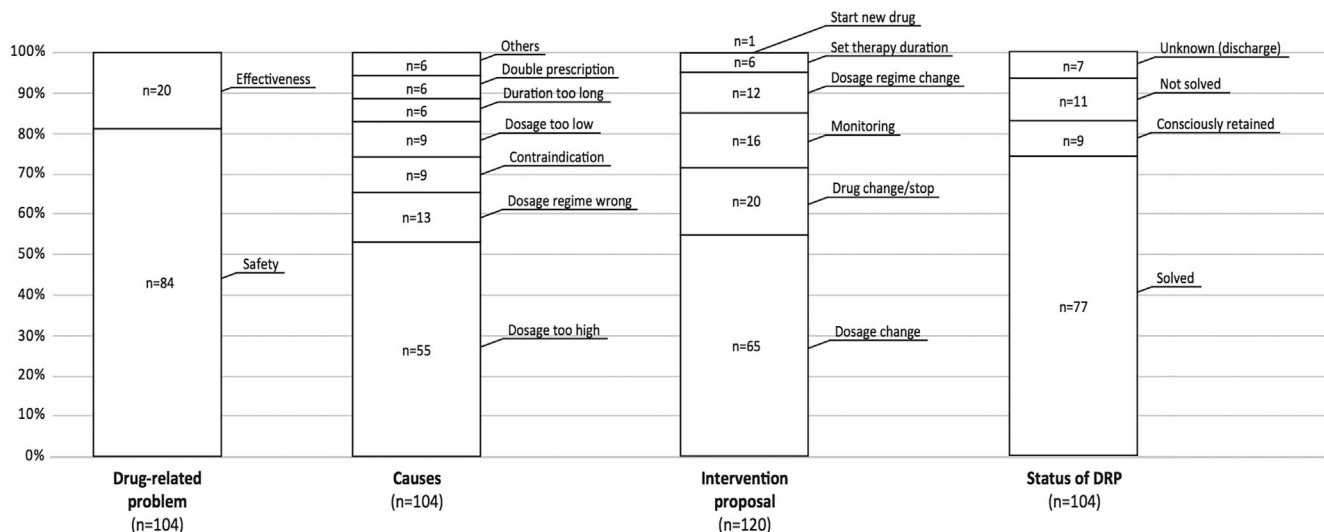


FIGURE 2 Identified drug-related problems (DRP; $n = 104$) in 79 (11.1%) of 712 patients with $eGFR_{\text{absolute}}/CrCl$ of <60 ml/min receiving a pharmacist-led medication review. The DRP of either treatment safety or treatment effectiveness is categorized in one main cause and more than one intervention might be necessary to solve DRP. Monitoring: refers to control of adverse drug events (ADR) or serum blood levels (e.g., electrolytes, creatine kinase). Consciously retained: means that the problem was discussed with the physician but the consensus decision was to only monitor the DRP because of the lack of suitable therapy alternatives for this patient's situation

The acceptance rate of recommendations was evaluated for all 104 DRP (Figure 2). In total, 77 of 104 recommendations (74.0%) were implemented by the physician in charge and the DRP was solved. In 9 cases (8.7%), the DRP was discussed with the responsible physician and was consciously retained because of the lack of better therapy alternatives and close patient monitoring. The possible prescription change of seven DRP (6.7%) could not be determined retrospectively because patients were already discharged. For 11 of 104 DRP (10.6%) the prescriptions remained unchanged for unknown reasons.

4 | DISCUSSION

Renal impairment is a well-known risk factor for drug safety and renal DRP occur in up to 81% of hospitalized patients.¹⁰ While implementation of a RPCS has been shown to improve prescribing in settings working with paper charts,¹⁵ appropriateness of drug therapy should per se improve when using CPOE-CDS-systems, which present computerized advice to the physician while prescribing. However, our study reveals that even in this setting, a RPCS has an additional benefit in terms of identification of DRP and adjustment of drug therapy to renal function, thereby improving patient safety. Renal impairment was found for 30.5% of the screened elective orthopaedic and trauma patients and in 11.1% of these patients one or more DRP were identified by a RPCS concerning 9.7% of all prescriptions. Importantly, by consulting the physicians digitally via EMR, 74.0% of the prescriptions were changed solving the DRP.

In the recent decade, EMR with CPOE/CDS-systems have been more and more implemented in clinical routine in Germany to enhance adequate prescribing and ensure patient safety. The workflow of physicians as well as pharmacists changed in this new setting. The prescribing systems are known to prevent medication and dosing errors and can positively affect guideline adherence, communication between wards and patient care.^{16–18,20,22,28} However, there is also evidence for alert fatigue due to too many or irrelevant warnings of the CDS-system and users distrust of CDS-system, leading to dismissal of the alerts regardless of its importance.^{22,23} Moreover, basic CDS-systems normally show general alerts that need to be evaluated for the specific patient situation. This evaluation requires expert knowledge and the RPCS can support in this process.

One important benefit of implementing an EMR/CPOE-CDS-system is easy access to the patient's complete treatment data that can be used from all departments and healthcare providers in the hospital.^{28,29} Indeed, this easy access to patient data enabled us to supervise two wards with daily screening for RI and medication reviews with only a 50% part-time pharmacist position.

When the pharmacist conducts medication reviews and identifies DRP that either the CDS-system did not recognize or the physician did not see or accept from the CDS-system, it is important that the shared information is available at the time of prescribing and can be adapted by the physician directly at this point of care. Therefore, to solve DRP we shared pharmaceutical advice directly in the

monitoring/drug chart tab of the EMR, where the physicians also record the patient's medical progress report. Hereby, the manual warnings are immediately recognized in clinical routine. In a review by Tesfaye et al., manual support as immediate concurrent feedback from a pharmacist was the most effective way to reduce inappropriate prescribing.¹⁰ That is the reason we decided to additionally discuss critical DRP directly with the physicians via phone.

Before the implementation of CPOE-CDS-systems, efforts to ensure adequate drug or dose adaption in patients with RI relied on pharmacist-based interventions alerting physicians about renal related DRP.¹⁹ Several studies show that a renal pharmacist can successfully support physicians with manual interventions in the complexity of drug therapy in patients with RI.^{10,12,15} Generally, clinical pharmacist services take a key role in ensuring the safety of the prescription practice.^{13,14} However, the use of CPOE-CDS-systems has been reported to reduce the amount of ADE in patients with RI.^{10,19,30} Although both computerized and manual pharmacist-based interventions have shown a reduction of inappropriate prescriptions, pharmacist-based interventions have been reported to lead to better improvement in clinical outcomes.^{10,30} This indicates the essential benefit of human-based interventions to improve patient safety. Of note, our study results also indicate that an additional pharmacist-led medication review still identifies inappropriate drug doses or contraindications within the setting of aCPOE-CDS-system. Additionally, it gives the opportunity to personally discuss necessary steps to solve DRP with the physicians.

Moreover, CDS-systems may make the dosage recommendation at the point of prescription and not continuously screen the correct drug dosing when renal function changes during hospital stay. To address this issue, the renal pharmacist daily screened the patient on the wards for renal impairment and manually reviewed all medications for DRP in patients with RI.

The acceptance for pharmaceutical advice regarding renal DRP is stated in literature to be up to 95%.¹² In a previous study on wards with paper charts, we detected an acceptance rate of 62.5% when using manual recommendations by a RPCS as written paper inlays.¹⁵ In the study presented here, the acceptance rate of manual recommendations in the setting of a CPOE-CDS-system was higher with 74.0%. In approximately 17%, we could not retrace the decision of the physician. Since the analysis of the real-life data was retrospective, it was not possible to distinguish the reasons for not solving the DRP due to incomplete documentation. In future studies, this aspect should be evaluated.

The retrospective study focused on rDRP but did not assess possibly related adverse drug reactions, which should be included in future evaluations.

Due to the retrospective design, it was also not possible to distinguish whether the CDS-system did not recognize the DRP or the physician did not see or accept the computerized advice. The system always refers to the latest renal function and it is not possible to determine which DRP were shown at a specific time with the GFR at this timepoint. Furthermore, we could not determine whether the DRP was present at the time of prescription or developed over time



because of decreased renal function. In the second scenario, the CDS-system could not have warned the physicians while prescribing. These aspects should be investigated in the future.

However, our pilot study gives a good insight into the clinical routine in a tertiary teaching hospital. The service was offered every day during weekdays and, hence, was able to recognize changes in renal function and thereby allowed to follow up on patients' progressions or potential DRP during hospital stay. According to the results of this study, a RPCS is still of benefit for patients with RI in the new setting with a CPOE-CDS-system and is an important support for physicians in improving patient safety.

5 | WHAT IS NEW AND CONCLUSIONS

After implementing a CPOE-CDS-system, that provides physicians with advice for drug or dose adaption during the prescription process, DRP were still identified by a renal pharmacist in 11% of elective orthopaedic and trauma patients with renal impairment. Following RPCS interventions by forwarding recommendations to solve DRP via the electronic medical record, 74% of inappropriate prescriptions were adjusted by physicians. This study shows that on orthopaedic and trauma wards using electronic medical prescribing records pharmacist-led medication reviews further increased appropriate prescribing compared to the sole implementation of a CPOE-CDS-system and, thus, may further improve patient safety.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

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