Computerized Physician Order Entry (CPOE) in pediatric and neonatal intensive care

Recommendations how to meet clinical requirements

I Castellanos1; G Rellensmann2; J Scharf3; T Bürkle4

1Anästhesiologische Klinik, Universitätsklinikum Erlangen, Germany;
2Klinik und Poliklinik für Kinder- und Jugendmedizin, Allgemeine Pädiatrie, Universitätsklinikum Münster, Germany;
3Kinder- und Jugendklinik, Universitätsklinikum Erlangen, Germany;
4Lehrstuhl für Medizinische Informatik, Universität Erlangen-Nürnberg, Germany

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Inpatient, inpatient CPOE, critical care and emergency, pediatrics, neonatology, clinical documentation and communications, requirements analysis and design, intensive care, workflow

Summary
Objective: To identify and summarize the requirements of an optimized CPOE application for pediatric intensive care.
Methods: We analyzed the medication process and its documentation in the pediatric and neonatal intensive care units (PICU/NICU) of two university hospitals using workflow analysis techniques, with the aim of implementing computer-supported physician order entry (CPOE).
Results: In both PICU/NICU, we identified similar processes that differed considerably from adult medication routine. For example, both PICU/NICU prepare IV pump syringes on the ward, but receive individualized ready-to-use mixed IV bags for each patient from the hospital pharmacy on the basis of a daily order. For drug dose calculation, both PICU/NICU employ electronic calculation tools that are either incorporated within the CPOE system, or are external modules invoked via interface.
Conclusion: On the basis of this analysis, we provide suggestions to optimize CPOE applications for use in the pediatric and neonatal intensive care unit in the form of three catalogues of desiderata for drug order entry support.

Correspondence to:
Dr. med. Ixchel Castellanos
Anästhesiologische Klinik, Universitätsklinikum
Krankenhausstr. 12
91054 Erlangen
Germany
E-Mail: ixchel.castellanos@kfa.imed.uni-erlangen.de

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I. Castellanos, G. Rellensmann, J. Scharf, T. Bürkle. CPOE in pediatric and neonatal intensive care
1. Introduction

In pediatric intensive care, fluid and drug therapy differs from adult intensive care in numerous aspects. Patient length, body weight, renal and hepatic function vary significantly and frequently. These factors must be considered by the physician. Fluid balance, caloric intake and electrolytes must be closely monitored. Usually individual syringes are prepared for weight-adjusted standard flow rates (for example 1 mL/hr for an adrenaline pump, corresponding to 0.10 microgram adrenaline per kg bodyweight per minute) aimed at preventing fluid overloading. In adult medicine, in contrast, a weight-independent standard concentration (e.g. 5 mg adrenaline/50 mL) is used.

Complex dosing computations may generate medication errors [8]. In a large prospective study involving 113 intensive care units (ICU) Valentin et al. [19] detected 74.5 medication errors per 100 patient days. Fortunately, 71% of those medication errors did no harm to the patient, but 0.9% caused permanent damage or death.

The use of electronic tools aimed at avoiding such medication errors has been recommended as a standard e.g. [11] for adult patients. On the other hand, these electronic tools have been reported to cause medication errors [12] and even increased mortality in children [4]. Other researchers described the successful use of computer supported physician order entry (CPOE) applications [7, 9, 10, 15, 20].

A potential problem of CPOE or ICU specific Patient Data Management Systems (PDMS) is that pediatric drug order requirements may be insufficiently represented. We therefore compared both the requirements and the existing CPOE applications of two university hospital pediatric ICUs with the goal of answering the following questions:

● What are the user requirements for pediatric drug CPOE in intensive care?
● To what extent can these user requirements be met with current CPOE applications?

2. Study environment

We analyzed two pediatric/neonatal intensive care units (PICU/NICU) in two German university hospitals. Both PICU/NICU provide regional tertiary care for very premature infants and newborns with congenital malformations and/or organ failure.

The combined PICU/NICU of hospital A is an interdisciplinary neonatal and pediatric ICU with 16 beds treating 350 patients per year. This hospital operates a commercial Hospital Information System (HIS) AGFA ORBIS® OpenMed, but no specific PDMS for the PICU/NICU. Pediatric drug ordering was done on paper sheets with the help of an MS Word document containing calculation macros.

Hospital B has a combined pediatric/pediatric-cardiologic ICU with 12 beds treating 800 patients a year and a separate neonatal ICU with 14 beds treating 290 patients per year. This hospital operates a commercial HIS Siemens Soarian Clinicals and introduced the PDMS Dräger ICM first into the PICU and later, when our analysis was finished, into the NICU. Drug ordering was done on paper sheets with the help of MS Excel Spreadsheets.

In both hospitals there was and is no data-transmission between CPOE and the paper based (hospital A) or digital (hospital B) medication chart.

3. Methods

Preparatory activities for a new CPOE application in hospital A were begun with a systematic workflow analysis using methods suggested in [3, 17]. This bottom up method is divided into seven steps:

1. Structural analysis
2. Forms analysis
3. Data analysis
4. Task analysis
5. Workflow analysis
6. Communication analysis
7. Weakness analysis
Structural analysis comprises examination of roles, responsibilities, locations etc, resulting e.g. in organizational diagrams. Forms analysis identifies the existing paper forms and their purpose. In contrast, data analysis deals with data processing applications and data storage. Task analysis collects and describes elementary tasks and activities within the workflows. Workflow analysis composes those elementary tasks in different workflows. Communication analysis examines communication activities necessary to perform the workflows and finally weakness analysis looks for shortcomings and problems in workflows.

Analysis steps 1 to 5 have been performed before change of documentation methods in both hospitals using observation methods and semi-structured interview techniques with feedback. In hospital A the workflow analysis performed by corresponding author IC took six weeks. Its results led to development of a CPOE module for pediatric drug orders within the AGFA HIS. Interview partners included one senior physician, three junior physicians and three intensive care registered nurses.

In hospital B a configuration team consisting of two physicians (one senior, one junior) and two nurses (ward sister plus registered nurse) was responsible for the adaptation of the commercial PDMS into PICU and a second team for NICU. A six month configuration period preceded PDMS implementation in the PICU. The configuration team used results from a previous evaluation study in the surgical adult patient ICU [1] and performed a participating analysis of local documentation activities with regard to future NICU use. Many problems in neonatal drug order entry requirements were detected. Thereafter, the pediatric configuration of the commercial PDMS was adapted, drug order spreadsheets implemented in the system and the system finally introduced successfully in the NICU as well [2].

4. Results

4.1 What are the user requirements for pediatric drug CPOE in intensive care?

4.1.1 Results of structural analysis

The structural analysis concentrates on the departments involved, staff groups, and staff roles. The drug prescribing workflow was analyzed in both hospitals, and comparable working environments were found. In both hospitals, the medical staff is responsible for the planning of infusions, drug and nutrition therapy for the following 24 hrs. Three main ward rounds are performed by nurses, junior and senior physicians during the day to check and change the medication regime, the first one around 8.00 a.m. Most orders are initiated by junior physicians, usually after discussion with senior physicians/registrars. At the end of the morning round the junior physician in charge examines the patient and interprets the results of current laboratory investigations. She / he then calculates drug dosages and draws up the patient’s individual daily drug therapy plan (valid from 6:00 pm in hospital A and 3:00 pm in hospital B).

Unlike German adult intensive care, where IV solutions and syringes are usually prepared by nursing staff in the ICU, we found that in both hospitals the pharmacy receives a medication order by facsimile and prepares individual pediatric IV solutions/mixtures. The individualized mixed IV bag with all ingredients is prepared by a pharmaceutical technical assistant or pharmacist and returned to the PICU that afternoon. Short turnover times are mandated by the dynamics of intensive care treatment, the need for frequent dose adjustments and the elevated risk of microbial contamination of solutions. In contrast, syringes for IV-pumps are prepared by nursing staff in a special drug preparation room in the PICU. The responsibility for the administration and documentation of all drugs lies with the nurses.
4.1.2 Results of forms analysis

We detected a number of similarities in the drug-prescribing process. In hospital A two forms are used for drug therapy:

- **\( <a> \)** the drug request sheet (a copy of which is sent to the pharmacy) and
- **\( <b> \)** the daily medical patient chart for documentation purposes

The drug request sheet **\( <a> \)** consists of different sections and is completed by physicians. It is completed and printed from a MS Word document (see section 4.1.3). Sheet **\( <a> \)** contains the therapy plan, and remains on the ward. It is consulted by nurses for the preparation and administration of medications. A copy of the third section of sheet **\( <a> \)** however is sent to the pharmacy where it is used to prepare the individual patient’s IV bag. This section contains patient identification data such as patient ID, case number, name, date of birth, ward ID, patient actual weight and length (daily updated in growing neonates) and the amount and composition of the patient’s individual infusion bag for 24 hrs. Drugs ordered and administered are entered in the patient chart **\( <b> \)** and taken into account for fluid and caloric balancing. This medical chart **\( <b> \)** exists on paper only and is completed mostly by nurses. The four forms used in hospital B are:

- **\( <a> \)** the drug therapy treatment plan (‘Medikamentenplan’) for all patients plus either
  - **\( <a1> \)** The parenteral nutrition treatment plan for pediatric intensive-care patients (‘DTI Pädiatrie’) or
  - **\( <a2> \)** The parenteral nutrition treatment plan for neonatal patients (‘DTI Neonatologie’) plus
- **\( <b> \)** the daily medical patient chart for documentation

In hospital B for a regular postoperative PICU/NICU stay, only the drug therapy treatment plan **\( <a> \)** and the daily chart **\( <b> \)** is used. Complex intensive care patients require the parenteral nutrition treatment plan **\( <a1> \)** or **\( <a2> \)**. Forms **\( <a> \)**, **\( <a1> \)** and **\( <a2> \)** are printed from computer see section 4.1.3 The drug amount administered, together with nutrition in both hospitals are documented in the respective patient chart **\( <b> \)**, which was initially paper based and later mirrored in the PDMS.

4.1.3 Results of data analysis

In both hospitals, we found basic computer-based support of pediatric drug therapy even before specific applications such as CPOE or PDMS had been introduced.

In hospital A a Microsoft Word 6.0 application had been designed internally, which supported drug dose calculation with 120 Visual Basic Word Macros. The application was invoked once a day for each patient to produce the drug request sheet **\( <a> \)** described in section 4.1.2.

In hospital B, electronic data processing support prior to PDMS-introduction consists of three different Microsoft Excel spreadsheets designed internally to produce the three forms **\( <a> \)**, **\( <a1> \)** and **\( <a2> \)** for medication ordering described in section 4.1.2. These spreadsheets comprise lists of different standard nutrition components as well as numerous dose calculations, and can be combined in accordance with the clinical needs of the respective patient. Printouts **\( <a> \)** and **\( <a1> \)** respectively **\( <a2> \)** are sent by facsimile to the pharmacy.

4.1.4 Results of task analysis

Task analysis aims to identify the elementary tasks. Here we found comparable elementary tasks in both hospitals:

- Daily measurement of length and weight, calculation of body surface
- Oral nutrition order plus calculation of IV calories
- IV pump orders for catecholamines, anesthesia and other short-acting drugs
- Calculation of the required total fluid and electrolyte intake, including infusions, IV pumps and enteral and parenteral nutrition
- Oral drug orders
- Calculation of ingredients and composition for the 24hr individualized mixed IV bag prepared in the hospital pharmacy
- Preparation of the drug request sheet for this mixed IV bag
- Calculation of substance concentration and flow rate for the IV pump syringes
Balancing of conflicting aims such as
- fluid restriction
- administration of all required drugs
- adequate nutrition
- limited osmolarity for peripheral drips
- drug-drug interactions
- medications incompatible with electrolytes (e.g. Calcium)

With regard to these tasks, we detected some fundamental differences between the two hospitals. In hospital A, total fluid intake, expressed either as mL/kg/day or mL/m²/day or simply in mL/day, is the primary parameter for drug and infusion therapy. All subsequent prescriptions are based on this predefined total fluid intake, which must not be exceeded. In hospital B, in contrast, total fluid intake is a result of all previous order steps, with no specific fluid intake monitoring mechanism implemented in the calculation tool.

4.1.5 Results of workflow analysis

Workflow analysis is based on the previous analysis steps and delivers flow diagrams of interlinked elementary respectively composite tasks. Figure 1 shows the top-level drug therapy workflow, which at this level is similar in both hospitals. The top level workflow starts with the composite task one “Pre-planning of medication and nutrition” (Fig 1 step 1). This normally takes place during the night shift, and is continued during the morning round (Fig 1 step 2). The next composite task is the daily completion of the drug therapy plan by the physician. It comprises elementary tasks such as the oral nutrition orders, IV pump orders and oral drug orders, and leads directly to the completion of the drug request sheet for the pharmacy. In the pharmacy the individualized mixed infusion bags are prepared and sent to the ward (Fig 1 steps 7a and 8).

Tasks performed by nursing staff run (to some extent) in parallel, e.g. preparation of oral drugs and IV drugs plus IV pump syringes (Fig 1 step 5). Next, medications are allocated to individual patients and administered in accordance with the drug therapy plan (Fig 1 steps 9, 10). Finally, all doses and units administered, as well as IV flow rates, are documented in the patient chart (Fig 1 step 11). Although the top-level workflow diagram of both hospitals is similar, there are several differences in task sequence in the detailed workflow diagrams.

Hospital A

In hospital A, total fluid intake is the primary parameter for drug and infusion therapy and therefore all following steps depend on this. Furthermore, the sequence of subsequent tasks is more rigid than in hospital B. In hospital A, the following tasks are performed:
- defining total fluid intake
- prescribing of oral nutrition or tube feeding
- prescribing of oral drugs,
- prescribing of IV-drugs (e.g. single dose medications)
- prescribing of IV-pumps
- prescribing of individualized mixed IV bag. This comprises
  - selection of a basic (pediatric) solution from a catalogue
  - adding a highly concentrated glucose solution. The amount of this glucose solution is calculated in accordance with the desired parenteral carbohydrate supply.
  - adding the desired amount of 10% amino acid-solution to provide the desired parenteral protein.
  - Sodium, potassium, calcium and magnesium are added as required.
  - Adding of fat solutions to meet the desired caloric fat supply
  - Checking drug respectively nutrient interaction
  - Checking line precipitation risks, osmolarity

At each step, all the respective fluid quantities are deducted from the previously defined total fluid intake in order not to exceed it. The amount of each of these substances (glucose, amino acids, lipids, electrolytes etc.) can be entered in mL/day, g/kg bodyweight or kcal/kg bodyweight, as necessitated.
by the specific clinical situation or the individual preferences of the ordering doctor. For practical reasons, doctors first select all desired ingredients and make the final adjustments to the concentration of glucose in the mixed IV bag such as to provide both the desired amount of glucose and the pre-specified volume of fluid.

**Hospital B**

In hospital B, the procedure is similar, but divided into two tasks supported by two different Excel sheets: drug therapy planning <a> and (for some patients only) daily parenteral nutrition planning <a1> (pediatric) respectively <a2> (neonatal) see section 4.1.2.

In an initial step, drug therapy is planned and the total amount of fluids is calculated. This amount is deducted from the planned total amount of fluid intake over the next 24 hrs. The difference is the amount of fluid needed to be administered via the individualized mixed IV bag. In the simplest case, this might be a single glucose infusion, which would be entered in the drug-therapy planning spreadsheet <a> simply as an additional drug. In those cases requiring parenteral nutrition, one of the parenteral nutrition planning Excel spreadsheets is used (<a1> for pediatric patients, <a2> for neonatal patients). In these cases, the next step is to manually enter the amount of fluid to be administered by mixed IV bag. Then, planning of the mixture begins and is supported by a drop-down list offering an assortment of standard nutritions, additives and various calculation schemes. Although the planning is a bit more complicated (due to less sophisticated input options and computation support), the final result is very similar in both hospitals. Marked differences were found only in the time scheduling of the workflow.

In hospital B steps 1–4 have to be completed by 11 am, and the drug-request sheet has to be sent by facsimile to the pharmacy by 12 o’clock. The mixed IV bag is returned to the ward by 2:00 pm for administration to the patient from 3:00 pm onward. This extremely tight time schedule is problematic when an error occurs, leading to delayed infusion of the novel solution. In an extreme delay the pharmacy might have closed and the IV bag would have to be prepared by nursing staff on the ward (dotted line in Fig 1). On the other hand, hospital B starts the administration of drugs in the dayshift what can have advantages if adverse events occur and is the main reason for the tight time schedule. In hospital A, in contrast, the new therapy plan is valid from 6:00 pm onwards, leaving more time for consideration of new laboratory results and necessary revisions, but having potential disadvantages concerning adverse events which may occur during nightshift.

Another difference found concerns the rounding of the calculated quantity of substances in syringes e.g. catecholamines such as adrenaline. In hospital B, the rounding is done by the person who prepares the syringes in accordance with practical needs. This results in changing substance-concentrations in the syringes and might be a source of errors. And it is less precise than the rounding in hospital A, which is software supported using an algorithm to calculate manageable substance-amounts. Nevertheless, no clinical disadvantages seem to result from this difference.

### 4.2 To what extent can these user requirements be met with current CPOE applications?

#### 4.2.1 CPOE and remaining problems in hospital A

Following the analysis, a CPOE module for drug therapy planning was developed in hospital A using tools provided by the ORBIS® OpenMed HIS. The forms generator [13, 14] is a HIS component for the end user to define new documents and create local applications. It supports a paper-like approach where online “documents” mimic their paper equivalents.

The OpenMed CPOE module replaced the existing MS Word drug request sheet <a>. Fig 2 shows a partial screenshot of the new module, which is divided into three sections:

Section one contains patient name, date of the order, patient age, length, weight and body surface area. Body weight and length are entered manually, age and body surface area are calculated automatically. There are a number of fields to order patient monitoring, for example the frequency of central venous pressure monitoring and the assignment of normal pressure ranges and alarm limits for vital parameters. The primary information is the selected total fluid intake per day. The volume of the first infusion solution is automatically adjusted to achieve the desired total volume. If the ad-
justed result indicates a negative volume, a warning is displayed and must be corrected. In addition, there are fields for displaying the previous day’s fluid balance.

The second section contains fields to prescribe oral and IV-drugs and infusions. For each medication dosage, the administration route and timing must be entered. Standard IV pumps are selected from a drop down list indicating either total or weight-adjusted dose. Automated calculation functions support the definition of flow rates and active ingredient per mL or per kg body weight. Additional drug information can be accessed via an info button.

The third section (fig 2) has two purposes. It is used to complete the orders of mixed IV fluids (administered by volumetric infusion pump) and replaces the former third section of the paper drug request sheet for the pharmacy (see 4.1.2). As described in 4.1.5 IV fluids can be ordered beginning with a basic pediatric IV solution and adding further ingredients up to full parenteral nutrition. Calculation functions prevent exceeding of the total fluid intake and support such calculations as fluid, caloric and electrolyte balances. A printout (of this part) is sent by facsimile to the hospital pharmacy, because it has no access to the OpenMed HIS. Fig 2 shows the recalculation of total fluid intake at the stage when sodium is added.

In hospital A, intensive care documentation remained predominantly paper based, only some functionalities have been covered within the HIS. Post implementation, the following problems persist:

- Drug calculation is not a part of the documentation chart (double work, transcription errors).
- Printouts must still be archived in the paper-based chart
- There is no electronic charting
- The implementation for the drug order CPOE supports only a fixed number of typical pediatric infusions
- The person implementing the HIS module has left the hospital and long-term support and adaptation is uncertain.

A verification process was completed before the new HIS based drug order module went live. Two medical specialists performed the technical evaluation using 25 typical drug therapy plans from printed patient records. Each drug therapy plan was entered in the MS Word application and in the new ORBIS® module. Besides the therapy plan was calculated by hand using a pocket calculator. Deviating calculatory values observed in this process were closely examined and the correct result determined based on the two medical specialists and their manual calculation as a gold standard. In this formative evaluation process calculation procedures and mathematic formulas have been double checked in both the MS Word application and the ORBIS® module. Especially when calculating divisions with small amounts it became obvious that rounding presented a real problem which had not been fully considered in the MS Word application. As a consequence, for the HIS module a two stage rounding mechanism was implemented which led to a higher consistency with the manual process especially for small children. The technical evaluation was continued until both specialists agreed with the ORBIS® module for all 25 drug therapy plans.

4.2.2 CPOE and remaining problems in hospital B

In hospital B, a commercially available PDMS ICM (Dräger) was rolled out subsequently to the PICU and later to the NICU. This PDMS had been configured for ward-specific requirements – including the definition of orders and order sets. Frequency of drug administration, dosing standard, application route, nutritional, electrolyte and fluid balancing information has been defined. When ordering a drug, the PDMS supports basic calculation of substance amount per kg body weight. The administration of each drug dose is confirmed by nursing staff. The daily patient medication chart (form <b>) and its workflows such as confirming drug administration by nurses were replaced by the PDMS medication chart. Mixed infusions however are only entered into this chart as “mixed infusion” without further decomposition.

While configuring the PDMS (before implementation in NICU) it quickly became apparent that the following functions were inadequate for the needs of our clinicians:

- Calculation of mixed IV bags within the PDMS and their composition was inadequate.
- Calculation of mixed IV bags could be performed only once at the time of ordering.
Dynamically varying solution composition and the effect on caloric, electrolyte and fluid balance was not supported.

Specific pediatric drugs and pediatric drug dosages had to be configured manually – including balance calculation information.

Automated calculation functions particularly for caloric and electrolyte balance, were either inadequate, or not available.

Initially, body surface area could not be integrated into dose calculations.

Paper copy or electronical communication of the parenteral nutrition planning spreadsheet for the pharmacy was not supported.

To allow fast track PDMS implementation in the NICU, a two-step approach was adopted to ensure adequate functionality. In a first step, a simple integration of the three existing Excel spreadsheets (see 4.1.3) into the PDMS was realized. Pediatric drug information was added to the PDMS medication data base. A paper copy of the parenteral nutrition planning spreadsheets (<a>, <a1> and <a2>) can be made using MS Excel functions.

Fig 3 shows a current screenshot. Only basic patient data (name, date of birth, weight and length) is transmitted once from the PDMS into the MS Excel spreadsheet when starting the calculation. Results are not transferred back into the PDMS electronic chart. In the electronic chart the mixed IV bag is just documented as one IV drug. A verification process for the Excel calculations was not performed because the identical Excel spreadsheets were in continuous use before and after the implementation of the PDMS.

A second more comprehensive step led to a development partnership with the PDMS provider. In this partnership a range of change requests, for example regarding drug dosing based on body surface area calculations and specific pediatric drug dose calculations, were created. Meanwhile, those change requests have been partially realized in new PDMS software releases. Current goals include integrating an improved drug data model including drug/drug substance links and references to external drug information systems into the PDMS. Intelligent functions are being added to the PDMS to support advanced drug calculations, drug interaction warnings and other functions based on Arden syntax [5].

4.2.3 From problems to recommendations: Relation to tables 1 to 3

Normally we would expect that a commercial PDMS is immediately able to support pediatric CPOE needs with minimal adaptations. Taking our experiences we noted that major adaptations were needed. Table 1 lists basic requirements for ICU drug order entry not yet specific for pediatric orders. Table 2 derives the specific requirements found in our workflow analysis (compare e.g. 4.1.4) which are typical for PICU/NICU drug orders. Contents of Table 1 and 2 are, according to our analysis, a must for pediatric drug order entry. Table 3 goes beyond, listing those desirable characteristics, which we would expect from a modern PDMS delivering decision support for order entry.

5. Discussion

According to Koppel et al. [12] each year approximately 770,000 persons in the USA are seriously harmed by, or die from drug side effects. 28% of these side effects can be attributed to errors in the drug order process and therefore can potentially be avoided. Most errors were found in the drug order process itself, e.g. lacking or faulty dosage information, lacking or incorrect application route and errors in the frequency of drug administration. In a review-paper, Kaushal et al. reported a reduction in drug order errors in several of the studies included, when electronic drug order systems were used, and in particular in those cases in which electronic decision support for drug therapy was available [9]. In the PICU environment Kadmon et al. described similar results when using CPOE [7]. Smith et al. [18] summarized the potential benefits of computerized prescribing:

- All prescriptions include the drug name, dose, route and frequency (system prompts prescriber for these data elements)
- Prescriptions are legible and the prescriber is always identifiable
- Information about the patient is available to the prescriber at the time of prescribing
Information about the drug is available to the prescriber at the time of prescribing

Prescribers are alerted to anomalous dose and frequency selections

Prescriptions are checked for allergies, drug-drug interactions, drug-laboratory interactions, contraindications or cautions in the patient, and the prescriber is alerted

All relevant data about the patient and their drug regimen are available at one point

Adverse effects can be documented and reported, audit and pharmacovigilance are facilitated

Adverse drug events may be detected by capturing the use of antidotes such as vitamin K (Warfarin overdose) or glucagon / glucose (insulin overdose), allowing review of events which led to their use

Relevant prescribing guidelines can be built into the prescribing system, helping achieve optimal treatment

On the other hand, Koppel et al. [12] report that the drug order error rate may even increase when electronic drug order systems are used. This may happen, for example, when not all drug order data are displayed on a single screen, when the data displayed are ambiguous and drug stock figures are misread as dosing advice, when over-complicated drug order screens facilitate wrong drug dosing, or when there are no monitoring functions to prevent duplicate orders. Even increased mortality on a PICU following the introduction of a CPOE system has been described [4].

From the point of view of patient safety, such contradictory reports necessitate the adoption of a critical stance towards electronic support of the drug order process. Adequately workflow-integrated electronic drug order systems with advanced decision support for the order process have the potential to improve patient safety. Longhurst et al. described decreased hospital mortality following implementation of CPOE [15]. In contrast, mediocre systems that take insufficient account of workflow requirements can potentially endanger the patient. A poorly designed or incorrectly functioning electronic ordering system can be just as dangerous as poorly handwritten orders. A lack of standards, non-uniform user interfaces, non-standardized drug data bases, manual transmission steps, complex calculations and complicated communication processes can result in an error-prone drug order process.

Our analysis has shown similar top level drug order entry workflows among two institutions, amenable to standardized electronic data processing support. In general, the drug order process is organized according to current textbooks for pediatric infusion therapy [e.g. 6, 16]. We have oral reports from other PICU/NICU confirming this approach. Specifics of the PICU/NICU drug order workflow include a very rigid adherence to weight- and size-dependent dosing, with a small tolerance for variation, and a unit dose procedure with respect to the preparation of individualized ready-to-use mixed IV bags in the hospital pharmacy. The latter requires additional daily communication between ward and pharmacy. In contrast, IV pumps and other drugs are prepared on the ward by nursing staff, as is the case with German adult intensive care.

We detected few medication workflow variations between the two hospitals. In contrast, we saw more differences regarding the level of electronic data processing support for this workflow. In hospital A, electronic drug order entry was implemented within the regular HIS, using sophisticated tools of the HIS supplier. A motivated HIS configuration team at the hospital developed a tailor-made solution to fit the drug order workflow and to give maximum support for the clinician making dose calculations. Drawbacks arise because the drug order application itself is not part of the standard HIS modules and no support from the HIS vendor is available. As mentioned before, long-term support is uncertain.

In hospital B an ICU-specific PDMS has been introduced that supports many more functions and replaces the need to handwriting patient charts. PDMS are costly to acquire and maintain and create a high level of dependence on their proper functioning. Nevertheless, it was of interest to note that this PDMS – which is established not only in more than 40 ICU but also in other PICU – initially did not meet all requirements of the pediatric drug order workflow.

In section 4.2.3 we defined a set of desiderata for CPOE drug ordering in intensive care environments, distinguishing between

- basic requirements valid for all ICU environments (table 1)
- specific additional requirements for the PICU/NICU environment (table 2)
- and additional extended PICU/NICU requirements (table 3).

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These tables are intended on one hand as checklists for physicians involved in PDMS selection and purchase who may want to check if the selected product covers those features. On the other hand they may serve as a guideline for PDMS vendors who have the intention to cover PICU/NICU environments with regard to required functionalities.

The study has some limitations. Our focus is clearly restricted on PICU/NICU environments, based on only two sites and we do not present a formal pretest-posttest approach. Therefore we do not know if error rates in pediatric drug order have improved after introduction of the new functionalities in any of the two examined sites. The algorithms for drug dose calculation have only been evaluated in hospital A. Our analysis method might not cover all potential clinical requirements. It would have been desirable to compare more sites in different countries.

The requirements listed in Table 1 to 3 summarize the individual experiences of two sites, again with no formal evaluation. As mentioned above, it is possible that replacing simple tools with complex tools induces new problems. A prospective analysis of a system implementation covering the mentioned requirements would be desirable. Portability to other environments needs to be tested. Dosing recommendations and calculation methods should be endorsed by a pediatric physician society.

6. Conclusion and Perspectives

We discovered many similarities in the drug therapy workflow among different PICUs at two German university hospitals. A mixture of drugs prepared for IV pumps directly on the ward and individualized mixed IV bags prepared for the patient on a daily basis in the hospital pharmacy were available in both hospitals, and is one of the distinctions to adult intensive care. In both institutions, computer applications were regularly used to support the frequent and complicated drug dose calculations. Pre-existing calculation tools in MS Word and MS Excel have been either successfully incorporated into the PDMS (hospital B) or replaced by a new HIS module (hospital A). Despite the variability between electronic data processing tools and their features, we believe that the supported ordering and documentation process is similar and has the potential to be standardized. From our findings, we extracted basic ICU, specific PICU/NICU and extended PICU/NICU desiderata for a potential standard CPOE application to fulfill the needs of neonatal and pediatric ICUs. If such a standard could be established within some major software solutions aiming at CPOE support in the PICU, it would be a big step towards improving medication safety in intensive care and would be instrumental in putting pressure on other software vendors. Our experience in recent years justifies the belief that such a standard is realistic, and that every effort should be made to achieve it.

Clinical Relevance Statement
Pediatric and neonatal ICU medication order requirements are complicated and some medical information systems have difficulties to support them adequately. Since this cannot be attributed to completely different treatment workflows, it is desirable to identify common aspects with the aim of defining a set of requirements that would enable the stepwise optimization of a pediatric medication order regime. In selecting an information system for a pediatric or neonatal ICU it is recommended that clinicians examine available information systems for their ability to meet the set of requirements as identified and set out in the present paper.

Conflict of Interest
The Lehrstuhl für Medizinische Informatik received a grant from Dräger for improving some PDMS functions in a development partnership.

Human Subjects Protections
This was an observational study comparing workflows and electronic data processing support in two hospitals with the aim of drawing conclusions for an optimized CPOE application. No formal intervention was performed. No additional patient data was collected. In accordance with German Bavarian Hospital Law (BayKrg §27) observational studies which do not collect additional patient data beyond routine documentation may use anonymized patient documentation without additional patient consent.
Fig. 1 Diagram of top-level workflow for pediatric drug therapy (mostly identical for both hospitals) (white: physician tasks, blue/dotted: teamwork tasks, dark grey/narrowly dotted: nursing tasks, bright green/boxed: pharmacy tasks). The dotted lines show the workflow in hospital B in the event of an error in step 1, 2 or 3. In these error-cases, due to the short delivery-cycle, the individualized IV bags can not be prepared in the pharmacy and must be prepared in the ICU (step 7b), steps 6, 7a and 8 are ommitted.
Fig. 2 Part of the OpenMed drug order application in hospital A. Section three is shown. This is the digital equivalent of the former paper drug request sheet. It has a paper like look, but contains structured data fields. All fields with white background are input/output data fields. Entering or altering a number within one of the data fields e.g. 2 mmol/kg sodium (German Natrium) triggers automated calculation activities in other fields, e.g. remaining basic solution “Basis 1”, caloric information, osmolarity etc. (recalculated fields are highlighted with frames).
Fig. 3 Pediatric drug order entry and drug dose calculation in hospital B. The pre-existing Excel spreadsheets have been integrated and are invoked from the PDMS (highlighted center box). Patient information such as name, birth date, weight and length are automatically transferred from the PDMS (here anonymized). Calculation is done solely within MS Excel. There is no information flow back to the PDMS, it has to be printed for the patient chart and the pharmacy. In the PDMS only a "mixed IV bag" and its flow rate is documented manually. This is an intermediate solution to be resolved when further functionality is available in the PDMS.
Table 1 Basic requirements for ICU drug order entry

- Automatic transfer and takeover of patient demographic data from the HIS
- Electronic (long term-) archiving of documents concerning prescriptions
- Automatic takeover of data from previously completed prescription forms
- Automated copying from previous care plans
- Automated handover of calculation-results into the electronic chart
- Work list for nurses displaying all prescriptions for each patient per shift
- Selection of drugs from a standardized (external) drug database
- Well-arranged and complete presentation of all administered and planned prescriptions
- Avoidance of double-prescriptions by automatic checking of previous prescriptions. This should also cover prescription of two drugs from the same drug class
- Standardized electronic interfaces with pediatric drug databases
- Standardized communication with pharmacy electronic data processing applications
- Simple-to-maintain catalogues of standard infusions
- Communication with critical incident reporting systems
- Long-term support and adaptation
- Basic drug statistics for accounting and billing purposes

Table 2 Specific requirements for drug order entry in the PICU/NICU

- Fast and simple adjustment of drug dose to rapidly changing parameters such as weight or body surface
- Definition of a daily total fluid intake e.g. in different units such as mL/day, mL/kg bodyweight/day, mL/m² body surface/day.
- An accurate updated specific pediatric drug database containing standard pediatric IV drugs and IV nutrition solutions and oral nutrition solutions
- Easy maintenance of this pediatric database to facilitate rapid changes when needed
- Display of all drug therapy relevant parameters (e.g. potassium, sodium, triglyceride, blood-glucose) and medications (e.g. insulin, antibiotics), previous fluid-balances at a single glance during the planning process.
- Management of long-term parenteral nutrition schemes including supportive parenteral nutrition
- Automated consideration of electrolytes, fat, caloric content, carbohydrates and osmolality of IV solutions for balance sheets and IV drips
- Ordering and documentation options for pediatric and neonatal mixed infusions and additional ingredients such as phosphate, potassium, sodium
- Automated calculation of ordered sodium, potassium, calcium and phosphate supply using appropriate units (e.g. mL/day, mmol/kg body weight and g/kg bodyweight according to selected component)
- Automated calculation of planned caloric balance split into the components (carbohydrates, fat and proteins) and their percentage amounts within the nutrition scheme
- Implementation of a pharmacy drug request sheet for individualized pediatric mixed IV bags either with printed barcode or electronic communication to the hospital pharmacy
- Support easy to use iterating calculation of various mixed infusions to determine the best component regimen
- Automated calculation of drug substance concentration in standard IV pumps, considering the current patient weight vs standard drug concentrations
- Automated rounding of calculated drug substance amounts to practical concentrations
- Consideration of different IV pump syringe volumes, e.g. 10 mL, 25 mL, 50 mL
- Automated current documentation of mixed IV bag ingredients in the patient chart (after start of infusion)
- Temporal graphic illustration of parameters such as bodyweight, body surface etc. relative to percentiles
Table 3 Extended requirements in the PICU/NICU – desirable decision support

- Structured import and consideration of all laboratory data, calculation of effects on drug therapy
- Permanent monitoring and drug dose adjustment for essential organ functions (e.g. liver, kidney) based on this data
- Automated monitoring of patient maximum daily drug doses based on specific pediatric drug data
- Automated monitoring of drug interactions
- Advanced statistics permitting analysis of drug data to improve patient therapy, e.g. scientific trend analysis and data mining approaches
- Recommendations for drug timing and pharmacokinetic drug monitoring
- Advanced drug statistics for accounting purposes, e.g. specific additional monetary reimbursement
References