GSASA Forschungsprojekt nationaler Tragweite 2014

Verschreibungsfehler in der Pädiatrie:
Welchen Einfluss hat die Einführung einer elektronischen Verordnung mit einem intelligenten klinischen Entscheidungsunterstützungssystem?

Statusbericht vom April 2015

Das ursprünglich eingereichte Forschungsprojekt war als Diplomarbeit FPH Spitalpharmazie vorgesehen. Um vereinzelte Schwächen im Projekt zu optimieren, wurde ein revidierter Projektbeschrieb (datiert vom 20.06.2014) an den Vorsitzenden der AG Forschung (Prof. P. Bonnabry) eingereicht und von ihm gutgeheissen. Entsprechend wird das Forschungsprojekt nun von einer Apothekerin mit Erfahrung im Bereich Spitalpharmazie als Dissertation in Zusammenarbeit mit der Universität Basel (Prof. C. Meier) durchgeführt wird.

Start der Dissertation am 1. April 2015

Die Dissertationsstelle wurde im Sommer 2014 ausgeschrieben. Ab 1. Oktober 2014 wurde Aylin Satir im Pharmazeutischen Dienst des Kinderspitals Zürich für ein halbes Jahr eingearbeitet. Sie konnte während dessen an diversen Sitzungen der Arbeitsgruppe „Elektronische Verordnung“ teilnehmen und sich mit den Kinderspital-internen Gegebenheiten vertraut machen, welche für die Durchführung des Forschungsprojekts relevant sind. Am 1. April 2015 begann Aylin Satir offiziell mit ihrer Dissertation (60%-Pensum) resp. der Arbeit am Forschungsprojekt, zu 40% arbeitet sie weiterhin als Apothekerin im Pharmazeutischen Dienst.

Gesuch Kantonale Ethikkommission

Da es sich um ein Forschungsprojekt mit medizinischen Personendaten handelt, muss für die Durchführung des Projekts eine Bewilligung der Kantonalen Ethikkommission Zürich vorliegen. Dieses Gesuch wurde am 15. April 2015 eingereicht.

Projekt elektronische Verordnung im Kinderspital Zürich

Die Kinderspital-interne Arbeitsgruppe „Elektronischen Verordnung“ trifft sich regelmässig, um die Implementierung des Tools „elektronische Verordnung“ im Programm Phoenix der Firma CGM (Compu Group Medical) voranzutreiben. Die notwendigen Funktionalitäten werden dort festgelegt, getestet und optimiert sowie auch der genaue Projektablauf und die zeitlichen Dimensionen bestimmt.

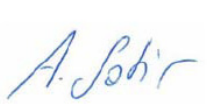
Weiteres Vorgehen

Das Tool „elektronische Verordnung“ muss weiter getestet und optimiert werden, bevor voraussichtlich Ende Jahr ein Pilotversuch gestartet werden kann. Gleichzeitig wird eine Literaturrecherche als Bestandteil der Dissertation durchgeführt und die genaue Methodik für die Durchführung der Medication Reviews soll festgelegt werden. In den folgenden Monaten (nach Eintreffen der Bewilligung der Kantonalen Ethikkommission) werden die Daten für den Zeitraum vor Einführung der elektronischen Verordnung (pre-CPOE – handschriftliche und halbstrukturierte Verordnungen) erfasst und analysiert.

Aktueller Zeitplan

Elektronische Verordnung:	
Mai 2015	Tests des CPOE[1] mit CDSS[2]
Juni - Sept 2015	Weiterentwicklung des CPOE
Okt 2015	Weitere Tests des CPOE mit CDSS
Nov – Dez 2015	Pilotphase
Ab Feb 2016	Implementierung
Studie:	
Mai 2015 – Feb 2017	Retrospektive Medication Review
März – Nov 2017	Datenanalyse
Dez 2017 – März 2018	Dissertation (Schreiben und Publikation)

Zürich, den 17. April 2015



Aylin Satir
Dissertandin / Apothekerin
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Beilage
Antrag Forschungsprojekt nationaler Tragweite, revidierte Version vom 30.06.2014

[1] CPOE: Clinical physician order entry (Tool für die elektronische Verordnung)
[2] CDSS: Clinical decision support system (klinisches Entscheidungsunterstützungssystem)

Forschungsprojekte nationaler Tragweite
Vorlage für das Einreichen eines Projekts

Ausschreibung No 4

Die Beschreibung des Projekts darf nicht länger als 5 Seiten sein

Titel des Projekts	Prescribing errors in children: What is the impact of a computerized physician order entry with a sophisticated clinical decision support system?		**Datum** 18. April 2014 (revidierte Version vom 30.06.2014)
Projektverant-wortlicher	Name, Vorname Funktion Institut Adresse Telefon E-mail	Vonbach Priska, Dr. phil. nat. Abteilungsleiterin Pharmazeutischer Dienst Kinderspital Zürich, Steinwiesstrasse 75, 8032 Zürich 044 266 78 17 priska.vonbach@kispi.uzh.ch	
Weitere Teilnehmer	Namen, Vornamen Funktionen Institute E-mail	Christoph Meier, Prof. Dr. phil. nat. Chefapotheker Spital-Pharmazie, Universitätsspital Basel, Spitalstrasse 26, 4031 Basel christoph.meier@usb.ch Caduff Angela, Dr. phil. nat. Stv. Abteilungsleiterin Pharmazeutischer Dienst Kinderspital Zürich, Steinwiesstrasse 75, 8032 Zürich angela.caduff@kispi.uzh.ch Remo Minder, Dr. med., Exc. MBA HSG Leitender Arzt und KLinikmanager Medizin Kinderspital Zürich, Stienwiesstrasse 75, 8032 Zürich remo.minder@kispi.uzh.ch Dissertand/in (möglichst mit Erfahrung in klinischer Pharmazie)	
Identifiziertes Problem und Bedeutung des Problems in der Schweiz	In the current health care system medication errors are an important source of morbidity and mortality. Pediatric patients are one of the most sensible groups regarding medication errors. The American Academy of Pediatrics recommends (among other interventions) the implementation of a computerized physician order entry (CPOE) with clinical decision support system (CDSS) to reduce medication errors in children. In Switzerland, the safety of drug therapy in pediatric care is an ongoing problem. In most hospitals, CPOE with pediatric CDSS is not yet established. However, in 2008 the pharmaceutical service of the University Children's Hospital Zurich began to develop a highly structured database which is published on the website www.kinderdosierungen.ch since 2012. Today it contains up-to-date drug information about around 330 different active substances. Furthermore, the website offers the possibility to automatically calculate required dosages for any child according to age, weight and / or body surface area of the patient. This database		

	and the corresponding calculator could be used as a CDSS in a CPOE.

Literatur **Analyse von Literaturdaten**	In the current health care system, especially in neonatal and pediatric intensive care, medication errors are an important source of morbidity [1, 2, 3, 4, 5, 6, 7] and efforts for improvement are paramount. Children are a challenging group of patients because of the increased need of dose calculations and special preparations of medicines and the fact that a lot of medications are in the off label use. It is known that dose calculation errors are the most common error source in neonatal and pediatric patients [8]. Kaushal et al reported that the rate of potential adverse drug events (ADEs) resulting from medication errors was threefold higher for children than for adults [3]. A review estimates that 5 to 27% of medication orders for children contain an error somewhere along prescribing, dispensing and administering. The review also estimates that there are 100 to 400 prescribing errors per 1000 patients. This review of the literature on medication errors in children highlights without question the prioritization of implementation of medication error reduction strategies. [9] The American Academy of Pediatrics recommends interventions which have the capacity to prevent medication errors in the pediatric inpatient setting: computerized physician order entry (CPOE) with clinical decision support systems, ward-based clinical pharmacists, educational programs for all hospital and medical staff in calculating, prescribing, preparing and administering medications, reporting of adverse medication events (critical incident monitoring system) and drug-use evaluation program. [10] The evaluation of CPOE in adults and children yielded conflicting results. In adult intensive care the introduction of CPOE was associated with a reduction in the proportion of medication errors. However, it introduced new types of error that may be more serious [11]. In a general adult hospital, CPOE decreased potential ADEs more than errors that actually resulted in an ADE [12]. The results of a systematic review [13], analyzing 27 studies, indicate that CPOE seems to be a useful intervention for reducing the risk of medication errors and ADEs. 25 studies reported on the risk of medication errors. 23 of these showed a significant relative risk reduction, with a risk ratio between 0.01 and 0.87. Nine studies reported on the risk of ADE. Six of these studies showed significant relative risk reduction with a risk ratio between 0.02 and 0.65. Unfortunately, less evidence is available for such systems outside the U.S. There are limited data evaluating the impact of CPOE on medication errors in the pediatric population. Fortescue et al showed that CPOE with clinical decision support reduced medication errors but not ADEs in pediatric inpatients [14]. King et al observed a significant decrease in the rate of medication errors but not adverse drug events in pediatric inpatients after implementation of CPOE [15]. In two studies performed in pediatric intensive care unit (PICU) it has been shown that the mortality did not increase after implementation of CPOE and that the introduction of CPOE was associated with a significant reduction in medication administration variances [16, 17]. In a study performed in PICU and pediatric ward beds, it could be shown that the rate of incomplete/wrong order errors declined after CPOE implementation but the rate of dosing errors did not decrease [18]. These findings are substantially different from those in adults for whom the introduction of CPOE was followed by a significant reduction in medication errors [12]. In another study,

	only errors that occur during the medication ordering process were analyzed [19]. This study focused on ADEs, medication prescription errors or rule violations and could show that all three categories were reduced after CPOE implementation. References 1. Bordun LA, Butt W. Drug errors in intensive care. J Paediatr Child Health 1992; 28:309-311 2. Folli HL, Poole RL, Benitz WE, et al. Medication error prevention by clinical pharmacists in two children's hospitals. Pediatrics 1987; 79:718-722 3. Kaushal R, Bates DW, Landrigan C, et al. Medication errors and adverse drug events in pediatric inpatients. JAMA 2001; 285:2114-2120 4. Raju TN, Kecskes S, Thornton JP, et al. Medication errors in neonatal and paediatric intensive care units. Lancet 1989; 2:374-376 5. Ross LM, Wallace J, Paton JY. Medication errors in a paediatric teaching hospital in the UK: five years operational experience. Arch Dis Child 2000; 83:492-497 6. Vincer MJ, Murray JM, Yuill A, et al. Drug errors and incidents in a neonatal intensive care unit. AJDC 1989; 143:737-740 7. Wilson DG, McArtney RG, Newcombe RG, et al. Medication errors in paediatric practice: insights from a continuous quality improvement approach. Eur J Pediatr 1998; 157:769-774 8. Conroy S, Sweis D, Planner C, et al. Interventions to reduce dosing errors in children: a systematic review of the literature. Drug Saf 2007; 30:1111-25 9. Miller MR, Robinson KA, Lubomski LH, et al. Medication errors in paediatric care: a systematic review of epidemiology and an evaluation of evidence supporting reduction strategy recommendations. Qual. Saf. Health Care 2007; 16:116-126 10. American Academy of Pediatrics. Prevention of medication errors in the pediatric inpatient setting. Pediatrics 2003; 112:431-436 11. Shulman R, Singer M, Goldstone J, et al. Medication errors: a prospective cohort study of hand-written and computerised physician order entry in the intensive care unit. Critical Care 2005; 9:R516-R521 12. Bates DW, Leape LL, Cullen DJ, et al. Effect of computerized physician order entry and a team intervention on prevention of serious medication errors. JAMA 1998; 280:1311-1316 13. Ammenwerth E, Schnell-Inderest P, Machan C, et al. The effect of electronic prescribing on medication errors and adverse drug events: systematic review. J Am Med Inform Assoc. 2008; 15:585-600 14. Fortescue EB, Kaushal R, Landrigan CP, et al. Prioritizing strategies for prevention medication errors and adverse drug events in pediatric inpatients. Pediatrics 2003; 111:722-729 15. King WJ, Oaice N, Rangrej J, et al. The effect of computerized physician order entry on medication errors and adverse drug events in pediatric inpatient. Pediatrics 2003; 112:506-509 16. Keene A, Ashton L, Shure D, et al. Mortality before and after initiation of a computerized physician order entry system in a critically ill pediatric population. Pediatr Crit Care Med 2007; 8:268-271 17. Taylor JA, Loan LA, Kamara J, et al. Medication administration variances before and after implementation of computerized physician order entry in a neonatal intensive care unit. Pediatrics 2008, 121:123-128 18. Walsh KE, Landrigan CP, Adams WG et al. Effect of computer order entry on prevention of serious medication errors in hospitalized children. Pediatrics 2008; 121:e421-e427 19. Potts AL, Barr FE, Gregory DF, et al. Computerized physician order entry and medication errors in a paediatric critical care unit. Pediatrics 2004; 113:59-63
Zielsetzungen des Projekts **Hypothese** **Begründung** **Erwartete Ergebnisse** **Auswirkung für die Praxis**	The purpose of our study is to evaluate the impact of the implementation of a pediatric CPOE with a sophisticated CDSS on medical and surgical wards. The number and the type of prescribing errors before (pre-CPOE) and after (post-CPOE) the implementation of CPOE with CDSS will be compared. In addition, the benefit of a semi-structured order compared with hand-writing forms as well as the possible benefit of CPOE with CDSS compared with a semi-structured order form will be evaluated. Before 2013 drug ordering was done in hand-writing forms (pre-CPOE). Then, between 2013 and the implementation of the COPE a semi-structured order form was used. In first quarter of 2015, the implementation of a novel pediatric-adapted CPOE software (Phoenix G3 Application for children, developed by Compu Group Medical in close collaboration with the AllKids-children's hospitals: Basel, St. Gallen and Zurich) is planned. This CPOE interoperates with the calculator and the drug dosage database, both provided by the Children's hospital Zurich. Therefore dosages specified by indication and based on patient's age and weight or surface area are proposed. In addition, all information from the database about drug safety issues will be available directly in the CPOE software at the time of prescription.

	The implementation of any CPOE with CDSS should increase the medication safety. However, there are limited data evaluating the impact of CPOE on medication errors in the pediatric population and the results do not prove a predictable benefit.
Beschreibung der Methode **Protokoll, Methode, Analyse der Ergebnisse, Statistik**	Design Retrospective observational study Setting Medical and surgical wards of a university children's hospital, totally 119 beds, annual patient admission numbers: 2'700 patients on the medical and 3'600 patients on the surgical wards Power calculation The sample size was estimated by a power calculation based on results of a previous study (Glanzmann C et al, unpublished) on medication prescribing errors in the intensive care unit of the Children's Hospital Zurich. (reduction of prescribing errors from 14% (before CPOE and hand-writing forms) to 9% (with CPOE) of all prescriptions, power 0.9, one-sided test; results in a number of 3'500 prescriptions per group, or around 700 patients per group) Data collection Data are retrospectively collected in the first period (hand-writing forms, April to September 2012) and in the second period (semi-structured order, both before CPOE with CDSS implementation, April to September 2014) from 700 randomly selected patient charts (350 medical and 350 surgical charts). Post CPOE data collection will also be done in n randomly selected patients (n/2 medical and n/2 surgical charts) about three month after implementation of CPOE, presumably in April 2015 and September 2015. Patient data are collected in all analyses on demographic parameters (age, sex, nationality, mother tongue, weight, height, body surface and creatinine clearance. Creatinine clearance is estimated according to the simplified formula of Schwartz. Length of stay on the medical or surgical ward and diagnosis will also be recorded. All medications (first prescrptions) are included in this analysis except the following: parenteral nutrition (PN), lipids and solutions for dialyse. A well-trained clinical pharmacist (certificate degree in clinical pharmacy and/or hospital pharmacy) checks all orders one a specific day after hospitalization on errors such as wrong dose, inappropriate dosage adjustment for renal function, wrong interval, wrong units, wrong dosage form, allergy, drug-drug interactions and missing information. Review process A senior pharmacist independently reviews all original medication orders for 10% of randomly selected patients in both pre-CPOE groups and in the post-CPOE group to determine the level of agreement with the master student. Agreement between reviewers will be calculated (reliability, kappa). Statistics Summary measures are given as medians, means or percentage as appropriate. The denominator is the total number of the drugs ordered or the number of patients. Differences between the two groups are analysed by unpaired t-test, Mann-Whitney test, chi squared test or Fisher's exact test, as appropriate.
Ort (e) der Studie **Institute, die am Forschungsprojekt teilnehmen**	Children's hospital Zurich, Pharmaceutical service, in collaboration with the medical and surgical wards

Outcomes **Erwartete Hauptergebnisse**	Number and type of prescribing errors before (hand-writing form and semi-structured order) and after implementation of a pediatric-adapted CPOE with CDSS
Nationale Tragweite **Aspekte hervorheben, die einen nationalen Impact rechtfertigen (z.B. Bedeutung der Ergebnisse, multizentrisch, interdisziplinär)**	The CPOE software was developed by Compu Group Medical in close collaboration with the three AllKids-children's hospitals: Basel, St. Gallen and Zurich). The CDSS (calculator) and the pediatric dosage database was developed by the Children's hospital Zurich and is used over whole Switzerland since November 2012. Within one year 37 health care institutions and more than 9'000 single users were registered. The pediatric CPOE with CDSS will be introduced first in the Children's hospital Zurich. However, every Swiss pediatric health care institution will be able to use our CDSS application by a web interface or by an in-house installation, without any further development regarding automatic dosage calculation. Therefore, we think, the question of the impact of a CPOE with CDSS should be answered before implementation in other institutions.
Planung **Vorgesehener Zeitplan Etappen (milestones)**	CPOE: May 2014 — first test of the CPOE/CDSS June - Sept 2014 — further developments of the CPOE Oct 2014 — second test of the CPOE/CDSS Nov – Dec2014 — pilot phase from Feb 2015 on — implementation Study: March 2015 – February 2016 — retrospective review of the charts March – November 2016 — Analysis of the data December 2016 – May 2017 — Doctoral thesis (writing and publication)
Finanzierung **Notwendiger Betrag Verwendung Andere Finanzierungsquellen**	This study will be done by a well-trained clinical pharmacist (doctoral thesis): salary for 36 months (20%, based on 13 months/year): CHF 54'597.50 additional 17% for employers' contribution: CHF 9'281.60 total: **CHF 63'879** other financial source: Children's Hospital Zurich conflict of interest: none