Computerized Physician Order Entry – effectiveness and efficiency of electronic medication ordering with decision support systems
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Health political background
Adverse drug reactions or events (ADR or ADE) cannot be avoided entirely as they are a calculated risk of any drug therapy. However, ADE which result from a non-application of knowledge, e.g. on drug interactions, can be prevented. Drug interactions are, for the most part, described in the summary of product characteristics. However, their consideration is difficult to include in the medical routine due to the abundance of information. In addition, contraindications and allergies can lead to side effects which are not always recognized immediately. The use of clinical decision support systems (CDS-system) during electronic prescription using a computerized physician order entry (CPOE) in the in- and outpatient setting could help to assure the maximum effectiveness and safety of pharmaceuticals.

In Germany, various vendors offer CPOE-/CDS-systems for hospitals and physicians’ offices. These systems have mostly been developed during the last five to ten years, some of the projects are still in the pilot phase or are in the process of being further developed.

Scientific background
ADE are defined as any injury caused to a patient during drug treatment. ‘Avoidable ADE’ are differentiated from ‘unavoidable ADE’. Avoidable ADE are events caused by a medication error and could have been avoided had the patient been treated lege artis. Medication errors are errors that occur in the process of ordering, transcription, dispensing, administration or monitoring drugs. They do not necessarily lead to an ADE; even ‘potential ADE’ can often be recognized and corrected soon enough or the administration of an incorrect drug does not cause any sequela in a patient. In the US, as well as the UK, Norway and Denmark, more people die per year due to ADE than due to traffic accidents. In the US, an estimated 770,000 patients experience an ADE during their hospital stay. Valid data for Germany do not exist, however, it has to be assumed that the situation is similar to that in the US. Generally, errors can occur at any step of the medication process in the hospital or the physician’s office: while ordering, transcribing the order into the medication plan, dispensing the drug, administrating the drug to the patient, or because of erroneous intake by the patient. Among ordering errors, failure to take into account allergies, clinically relevant interactions and contraindications play a role besides choosing a wrong dose (e.g. due to a lack of consideration of the patient’s weight or renal insufficiency). Despite physicians’ competence and diligence, such inadequate prescriptions occur and are probably the most frequent reason for avoidable ADE.
To reduce the number of medication errors, different strategies and technologies are suggested. The integration of pharmacists into the team responsible for patient care, the installation of satellite-pharmacies at particular wards (e.g. intensive care units), the encouragement of team work and open communication within the team, as well as training of personnel regarding correct medication can prevent medication errors. Apart from CPOE-systems, possible technologies that help to reduce the number of medication errors are electronic medical records (EMR), portable devices (tablet-PC, notebook, palms), automated medication dispensing machines, electronic medication administration records and barcode-technology. These technologies support the prevention of errors at different steps of the medication process and are often used combined with each other. At the steps of ordering and transcription, CPOE-systems, EMR and portable devices are primarily used.

CPOE-systems are computer programs which allow electronic prescription of medications; they make it possible to comfortably search for pharmaceuticals (brand name, active ingredients, indication, price comparison), select a drug from a pull-down menu together with a suggested dose, and directly access individual patient data (age, weight, diagnosis, comedication, renal function etc.). CPOE-systems exist since the 1970’s. CPOE-systems usually provide order sets (prepared prescriptions for a specific diagnosis and treatment) which help to avoid errors caused by incomplete or illegible information or transcription errors. In general, CDSS are integrated in the CPOE-system. CDSS provides warnings, reminders, clinical guidelines, diagnostic support, tools for clinical processes, reports on patient data and documentation templates.

According to the system, the CDSS can review if the indication specific dose and application frequency is correct with regard to organ function (including laboratory values). In addition, the system automatically checks for clinically relevant interactions with other drugs the patient is taking, as well as for allergies and contraindications. In case a change of dose is necessary, the physician receives a warning.

By linking the CPOE-system to other information systems of the hospital, physicians can also enter, access, monitor and search for laboratory or radiology orders, and clinical consultations. Treatments can be standardised, the communication between wards improved, transfer of patients facilitated and data collection for management, research and quality control be made possible.

Despite this, only a few hospitals have implemented CPOE-systems (USA: 4.3 % to 15 %). In Germany, these systems have been implemented during the last five to ten years, some of the projects are still in the pilot phase or are in the process of being further developed. Apart from the university hospital in Heidelberg, CPOE-systems are also used in Saarbrücken, Frankfurt and Bottrop.

The implementation of a CPOE-/CDS-system is a complex process. The success of a CPOE-system strongly depends on the willingness to change and on the organisational and structural pre-requisites of the individual hospital (project management, personnel resources, technical circumstances). A detailed analysis of the organisational structure of the institution and of the work-flow affected by the implementation of the CPOE-system should be undertaken before implementation. Furthermore, the selection and adaptation of the CPOE-system according to the circumstances of the institution, sufficient financial and technical resources, distinct leadership, user training and support before and after implementation of the system, as well as a sufficient number of prepared order sets are crucial for a successful imple-
mentation. A step-wise implementation has been proven to increase the success rate. The way information is provided by the CDSS also influences the use of the respective systems. Only systems oriented on the physicians' judgement of risks and clinical relevance are accepted and modify the prescription habits of physicians in the long run. An abundance of irrelevant warnings and notices can lead to the fact that users start to ignore important and relevant warnings as well.

Research questions
This report aims to answer the following questions:
- Which parameters are useful to evaluate the effects of CPOE-systems?
- What are the effects of CPOE-systems in regard to these parameters?
- What is the cost-effectiveness of CPOE-systems?
- What ethical, social and legal aspects need to be considered?

Only CPOE-systems used in the inpatient setting and for the prescription of medications with an integrated clinical decision support system are assessed.

Methods
This HTA-report was prepared by applying the methods for a systematic literature review. The systematic literature search was conducted on October 4, 2007 and includes German and English publications since 2002. Of the 791 abstracts that the systematic literature search (in the DIMDI-HTA-superbase and HTA- and Cochrane-databases) yielded, eight medical and four economic publications were included following a two-part selection process according to standard, predefined criteria. 49 publications were added by hand search. A total of 180 publications are used as background literature (including publications on social, ethical and legal aspects), 139 publications are excluded. For the discussion of legal aspects, relevant texts of law are also used. Data extraction and assessment of included publications follow predefined criteria.

Results
The medical studies assessed evaluate different settings, interventions and time frames. Therefore, it is difficult to compare their results. The lack of transparency and documentation of some studies exacerbates this problem. All reviews and primary studies included in the present report show a reduction of the medication error rate. Minor errors (e.g. errors due to incomplete information) can be eliminated almost entirely by using CPOE-/CDS-systems, as they ensure the completeness and legibility of orders. The positive correlation between the number of prescribed drugs and the occurrence of medication errors can also be avoided by the CPOE-system. With regard to the rate of ADE, the results in two recent studies are contradictory. Additional possible effects of the use of CPOE-systems are the better adherence to standards of care and treatment (e.g. an earlier removal of catheters that have become unnecessary), however, an improvement of treatment results (e.g. less urinary tract infections) cannot be demonstrated. Length of stay is usually not affected by the use of CPOE-systems. In one study, improved communication of personnel is emphasised as the major benefit of the
CPOE-system, another study shows that personnel satisfaction can be increased by using the CPOE-system.

The settings, interventions and time frames evaluated in economic studies also differ between studies. For this reason it is difficult to compare the results. In addition, the documentation often is not fully transparent. All four studies assessed measure costs and effects from the perspective of a hospital or hospital affiliation. Three studies financially balance these costs and effects against each other and come to the conclusion that net savings are to be expected by implementing the respective CPOE-system. Among the effects are, for example, cost savings due to reduced or more efficient use of drugs, more efficient work flow or a shorter length of stay due to a reduced ADE-rate.

The fourth study implies that the prevention of medication errors and, consequently, of ADE, results in an immaterial benefit per se for the hospital. The study calculates the costs which have to be paid for each ADE prevented by the implementation of CPOE. However, at 12,700 USD per prevented ADE, they are considerably higher than the cost savings presumably expected from a prevented ADE. From the perspective of the entire health system, the effects of CPOE-implementation in all or the majority of hospitals have a much broader scope, as potential effects in other areas of the health system have to be considered as well. From an economic point of view, effects such as shorter production downtime due to a shorter length of stay or less sequela due to a reduced ADE-rate need to be considered. From a patient's point of view, an increase in life quality or a gain in life years are relevant if ADE – which may lead to death – are prevented.

In three studies, the CPOE-system is compared to a paper-based system. In one study, it is a (partly implemented) electronic medication ordering system without clinical decision support. The results do not allow conclusions regarding a comparison of CPOE-/CDS-systems and other options of medication error prevention, such as the recruitment of additional pharmaceutical personnel.

Considering the limitations of the study results and their inconsistency, the transferability of the results to the German health system or to German hospitals can only be discussed in principle: regarding the (medical) effectiveness of CPOE-/CDS-systems to prevent ADE, different organisational structures of hospitals need to be considered, particularly if it is a small, general hospital or a large, highly specialized one. Regarding the costs of CPOE-system-implementation and the evaluation of cost savings of a hospital in particular, differences between health care systems need to be considered. According to the knowledge of the authors, a comprehensive evaluation of costs and benefits is not planned to be undertaken at any hospital in Germany.

Concerning social aspects, the literature points at changes (e.g. regarding responsibilities and work flow) the implementation of CPOE-systems may cause. How the effects of these changes influence the acceptance of the CPOE-system by users is evaluated. An underestimation of the importance of the socio-organisational context may cause problems in the implementation of CPOE-systems.
Discussion

CPOE-/CDS-systems are able to reduce the rate of medication errors when ordering medications. Using the available data, it cannot be assessed conclusively to what extent CPOE-systems or the reduction of medication errors have an impact on the ADE-rate - which clinically is more relevant -, or on mortality.

Apart from effects on medication errors, CPOE-systems can also have a positive effect on the adherence to guidelines, communication, patient care, and personnel satisfaction. A systematic review published after the period of literature selection arrives at the same conclusions.

Apart from positive effects of CPOE-/CDS-systems, negative effects are also reported. In one study, mortality significantly increases after the implementation of a CPOE-system in a pediatric hospital. Other authors also emphasise that new errors can be generated by CPOE-systems.

These types of errors inherent to the system demonstrate the importance of continuously reviewing CPOE-/CDS-systems. An additional potential source of errors is the lack of integration of the CPOE-system with other computerized systems, e.g. the pharmacy- or laboratory system of the hospital. A lack of knowledge regarding medications and regarding how to enter specific medications into the system, as well as a general lack of familiarity with the system can lead to errors especially when users are inexperienced. This points to the importance of training regarding medication as an effective quality assurance measure. In addition, sufficient training of users before and support during the implementation of a CPOE-system needs to be provided. In order to assure the effectiveness of a CDSS, the triggers for warnings need to be sufficiently sensitive and the warning itself needs to be specific. Otherwise, warnings are often ignored. Furthermore, the data used by the system to support the decision making process need to be continuously updated. Thus, all patient data need to be available which emphasises the importance of a complete anamnesis at admission. As warnings regarding necessary dose-changes are only delivered during the ordering process, a daily, automated review of the medication a patient receives concerning current laboratory values is necessary. In order to identify the reasons for medication errors, a standardized error-detection-system is needed using precise definitions of medication errors and UAE.

CPOE-systems have a great impact on the organizational culture of and clinical work-flow in an institution; therefore, it needs to be adjusted to the computerized systems already in place and to the needs of the respective institution.

Regarding the cost-benefit-ratio from the hospital perspective, the two qualitatively best economic studies arrive at contradictory conclusions. A positive cost-benefit-ratio for an individual hospital can therefore not be assumed, particularly as the results cannot be generalised. From the perspective of the health care system or from an economic point of view, additional positive effects, e.g. an increase in life quality, need to be considered provided that the number of ADE is reduced. No quantitative evaluations exist on this topic. Regarding a comparison of CPOE-/CDS-systems with other options for medication error prevention, e.g. recruiting additional personnel, literature is lacking as well.
Conclusions/recommendations

If the implementation of CPOE-/CDS-systems is well planned and conducted, the system adapted to the needs of the institution and continuously reviewed, and data used are updated on a regular basis, the rate of medication ordering errors can be reduced considerably by using CPOE-/CDS-systems. However, it is not clear how this results in a reduction of ADE. Prospective, systematic multi-centre evaluation-studies with clear methodology, which include an analysis of the user-friendliness and of social and technical aspects of the system are needed. Such studies should evaluate the impact a CPOE-/CDS-system has on the ADE-rate and mortality. A detailed description of the system used and of the hospital evaluated is essential. If possible, costs and cost effects should be surveyed and documented transparently.

A quantitative evaluation of the economic effects of implementing a CPOE-/CDS-system in (all) hospitals in Germany seems to be bold: the reliability of study results regarding relevant endpoints is only limited so far. They rarely allow a clear assignment of the results to individual measures and functionalities of the systems, or to other options; conclusions in regard to another context are only possible when data presentation is highly transparent. Structured interviews at selected hospitals with and without CPOE-/CDS-systems or using other measures to prevent medication errors could provide important input and help to appraise the need for further research.