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Vision and challenges of Evidence-Based Health Informatics: A case study of a CPOE meta-analysis

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ABSTRACT

Objective: To discuss, taking the example of a meta-analysis on computerized physician order entry (CPOE) systems, the special challenges of Evidence-Based Health Informatics, defined as the conscientious, explicit and judicious use of current best evidence when making decisions about introduction and operation of information technology in a given health care setting.

Methods: We conducted a case study by performing a systematic review and meta-analysis of CPOE studies. We collected and discussed the challenges we addressed and how they could be overcome.

Results: Challenges comprise the correct identification of published health informatics evaluation studies, the low reporting and study quality of studies, the problem of combining evidence from heterogeneous studies, and the problem of publication bias in health informatics.

Conclusion: Based on our experiences while conducting the CPOE meta-analysis, we argue that we are still at the beginning of Evidence-Based Health Informatics. To overcome the discussed challenges, health informatics should strive for harmonized terminology, a study registry, reporting standards, financial or legal incentives for conducting studies, methods to combine evidence from quantitative and qualitative studies, and guidelines for conducting and publishing evaluation studies.

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1. Introduction

In the last years, an increasing number of publications reported on problems and unintended consequences after introduction of information technology (IT) in health care (see,

e.g. [1–3]). Some authors even report of an increase in mortality following (not necessarily caused by) IT introduction [4]. We summarized these problems under the label “bad health informatics can kill” [5]. Research has therefore been conducted on the notion of IT failure and how to prevent it [6–8].

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The increasing number of publications on IT failure shows a rising awareness of the fact that IT is an intervention that can largely affect quality, efficiency, costs and outcome of health care [9]. A more professional attitude concerning IT, regarding it as an important intervention into healthcare and not just as a question of infrastructure, is thus called for [10,11], and a rigorous evaluation is seen as important part of this professional attitude [12].

In this context, the term Evidence-Based Health Informatics (EBHI) has been introduced [13]. The idea of EBHI copies from the experiences with Evidence-Based Medicine (EBM) defined as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients” [14]. We therefore want to define EBHI as the conscientious, explicit and judicious use of current best evidence when making decisions about the introduction and operation of IT in a given health care setting. While EBM means integrating individual clinical expertise with the best available external clinical evidence from systematic medical research, EBHI means integrating individual IT expertise with best available external evidence from systematic health informatics research. It has been argued that Evidence-Based Health Informatics is an important step towards better healthcare IT [13,15].

Practically, this means that available evidence must be identified, read and analysed, critically assessed, synthesized, and applied to a given situation. As this is time-consuming and often not feasible in a day-to-day situation, systematic reviews are developed to facilitate the quick access to available evidence. Systematic reviews are also a core element of health technology assessments (HTAs), which are a comprehensive procedure to inform decision making at the population level concerning regulation of pharmaceuticals, devices, and services, reimbursement, research and development, education of health care providers, and consumers [16]. In contrast to merely narrative approaches, a systematic review using formal meta-analysis to statistically combining the results of studies can provide results about the overall magnitude and precision of effects. A further advantage is that heterogeneity across individual studies can be statistically examined and provide useful information of moderator variables [17,18]. In EBM, the Cochrane Collaboration initiates and collects such systematic reviews and meta-analyses (<http://www.cochrane.org>).

Accordingly, Evidence-Based Health Informatics has also to be built on published IT evaluation studies of sufficient quality. Following the idea of EBHI, this published evidence should be aggregated in the form of systematic reviews and meta-analysis, to provide the IT decision maker with quick, valid decision support. Until now, while a large number of unsystematic narrative reviews exists, fewer systematic reviews have been conducted on health care IT, and even less quantitative meta-analyses (e.g. on blood pressure control by home monitoring [19], on anticoagulant therapy management [20], on preventive reminders [21]). Also, the Cochrane Collaboration contains only a limited number of systematic reviews related to IT interventions in health care, such as a review on clinical decision support systems for neonatal care [22], on computerized advice on drug dosage [23], and on nursing record systems [24], to name some examples.

In general, authors that systematically review IT interventions in health care often find that the available evidence is too insufficient to come to valid conclusions, mentioning problems related to number of available studies, size and quality of published studies and reporting quality of publications themselves (e.g. [24–28]).

In this paper we take an interdisciplinary approach to explore and discuss the challenges when applying EBM methods such as systematic reviews and meta-analysis to health informatics. In particular, we want to discuss whether health informatics poses special challenges with regard to the following aspects:

1. Identification of published health informatics evaluation studies;
2. Study and reporting quality of health informatics evaluation studies;
3. Assessment of heterogeneity and evidence synthesis using meta-analysis;
4. Publication bias in health informatics.

2. Methods

We took an exploratory approach to address our research questions and conducted a case study where we developed a systematic review and meta-analysis on computerized physician order entry (CPOE). For our review, we defined CPOE as application systems supporting online medication ordering at the point of care. It is expected that CPOE systems can significantly reduce medication errors, thus improving patient safety [9,29].

We conducted a systematic literature search and determined the effect of CPOE on the risk of medication errors and adverse drug events (ADEs). The details of this systematic review and meta-analysis are published elsewhere [30]. Briefly, we included 27 controlled field studies and pretest–posttest studies that evaluated all types of CPOE systems, drugs and clinical settings. We assessed the study quality using an established instrument, performed sub-group analysis for categorical factors such as patient group, type of drug, or type of system, and generated funnel plots to assess publication bias.

While conducting the review, we paid special attention to the methodological problems and challenges we had to address, and how they may be related to the specificities of health informatics. We collected the issues we found and discussed them from an interdisciplinary perspective including the views of health informatics and IT evaluation (E.A.), EBM and HTA (P.S.-I. and U.S.), and biostatistics (U.S.).

3. Results

We want to present our experiences ordered to the above mentioned four research questions.

3.1. Identification of published health informatics evaluation studies

For the CPOE review, we conducted a comprehensive literature search in MEDLINE and EMBASE and other sources (e.g.

Cochrane, hand-search of major journals) to identify all studies that evaluated CPOE systems in a clinical setting. We identified 172 CPOE evaluation studies. Out of 172 found CPOE evaluation studies, 27 studies met all the inclusion criteria and were included in the detailed review. For details, see [30].

While doing this literature search, we found the identification of CPOE evaluation studies in the literature to be difficult. We had to combine MeSH terms, such as “Medical Order Entry Systems”, “prescriptions, drug”, “drug therapy, computer-assisted”, “evaluation studies” with general search terms such as “order entry”, “CPOE”, “POE”, “order communication”, “prescription system”, “drug prescription”, “prescribing”, “ordering”, “computerised reminders” or “evaluation”. Overall, the search comprised nearly 70 terms combined by AND or OR. Despite this extensive search, we first missed some papers that we only later identified by other sources such as hand-search of journals. Reasons for overlooking papers were, for example, that title, abstract, or MeSH headings did not make explicitly clear that the paper described an evaluation study on a CPOE system. Instead, other terms or synonyms were often used. For example, “outcome of...” within the title points to an evaluation study, “decision support for drug dosing” points to a CPOE system. Consequently, studies such as [31] are difficult to identify, as neither title, abstract nor MeSH terms point to the fact that the paper deals with electronic prescribing (here as part of an overall intensive care system). In general, MeSH headings and publication type seem to be often incomplete, misleading or not to be used consistently for health informatics evaluation studies. The problem to fully identify evaluation studies has also been noted by others. For example, Eslami et al. [26] noted that they may have missed CPOE systems in specific outpatient areas, or papers with limited evaluation focus.

In summary, substantial time must be invested in a literature search; however, published evidence may be overlooked, and an incomplete literature search may endanger the basis of EBHI.

3.2. Study and reporting quality of health informatics evaluation studies

While trying to extract data for evidence tables and the meta-analysis, we had to address several problems on reporting quality. For example, 6 studies included in our review could not be included in the meta-analysis because the reported data were insufficient for this purpose (e.g. number of orders was not reported and could not be derived from the reported data). Six studies did not specify inclusion or exclusion criteria of the participating institutions or patients. In 21 studies, baseline characteristics of institutions and/or patients and their comparability in intervention and control group was not reported. Twenty-two studies did not report about missing values or drop-outs. Eight studies did not clearly describe the measurement of endpoint of the study.

Thus, studies often do not provide sufficient information to adequately assess the comparability of the intervention and comparison groups and are therefore susceptible to confounding bias. About two-third of the studies did not attempt to adjust for potential confounding factors. Moreover, besides low reporting quality, many studies also used designs of lower

level of evidence such as observational designs including before–after comparisons or other quasi-experimental study designs (for a definition, see [32]). In these cases, it is unclear whether any context such as staffing or workflow of the study departments may have changed over time, in turn influencing the observed effects and leading to bias. The same is true for any non-randomised allocation of clinicians and/or patient to study groups. This all affects the validity of the analysed studies and the causal interpretation of the effect estimates.

Randomised controlled trials (RCTs) are considered as gold standard in EBM [14]. Only two studies in our review were randomised trials, and only seven studies had a parallel group comparison. Only in half of the studies, the outcome measurement could be considered as valid, and only in six studies, the outcome measurement was blinded. This reflects the situation in the whole field of EBHI. Most studies in health informatics are not RCTs. Eslami et al. [26] noted that results from non-randomised studies were more likely to report significant positive effects, which they see as possible indication for bias of such kind of studies. Another common situation in health informatics studies is that the data collected are clustered, that is, not independent and identically distributed (i.i.d.). IT-systems are very often deployed above the individual patient level, for example, a CPOE system will be implemented in at least one department of a hospital. This means that the outcomes of patients are not completely independent as assumed in some standard statistical methods. Ignoring the clustered data structure in the statistical analysis may affect the results. In particular, it is likely that reported *p*-values are underestimated and confidence intervals are too narrow [33–35]. Only 5 of the studies in our review accounted for clustering. Therefore, the precision of the estimates in most of the studies is likely to be overestimated.

3.3. Assessment of heterogeneity and evidence synthesis using meta-analysis

In our meta-analysis, we had planned to present a forest plot to present individual effects and the overall (pooled) effect estimate with confidence intervals. The included studies were focussing on the same outcome criteria, e.g. medication error rate, but the outcome measures used different denominators such as number of orders, number of patients, number of discharges, patient visits, patient days, or daily doses per bed-days. Even after contacting the investigators of the original studies, in some cases, it was not possible to recalculate data for a common denominator.

Besides the above mentioned heterogeneity, the studies were very heterogeneous in geographic setting, clinical setting, ordering workflow, included patients and drugs, and functionality of the introduced system. There are ways to allow for such heterogeneity in the statistical analysis (e.g. using a random effects model) or to formally investigate heterogeneity with the aim of explaining it (e.g. using sub-group analysis or meta-regression techniques) [17]. Nevertheless, it can be questioned whether pooling the effect sizes from such diverse locations and settings makes sense. For example, the summary estimate of the mean relative risk reduction on medication errors of all CPOE studies included in our review would have been 63%, with a confidence interval of 53–72%. One of

the advantages of meta-analysis is that by combining several studies, the statistical power is increased and a more precise estimate of the outcome can be obtained. But what does this number mean for heterogeneous health informatics studies? Can we combine a study of a commercial intensive care system with integrated CPOE including advanced decision support [36] with a home-grown CPOE with limited dosing advice in a paediatric unit where only the prescription of paracetamol and promethazine was evaluated [37]? Each study and each setting is quite unique. Is it helpful to aggregate and generalize the results of such heterogeneous studies into one statistical number? Does this help the IT decision maker when planning to introduce a CPOE system in his own hospital? We do not have a simple answer to this question. Heterogeneity is a basic challenge for any meta-analysis in any (medical) field. However, it may be that in health informatics, the heterogeneity of interventions (e.g. Electronic Patient Record) and of the overall setting (e.g. IT knowledge and motivation of staff, clinical workflow, quality of IT support, etc.) may often be even larger.

For our meta-analysis, we finally decided – after intensive discussion and also comments from reviewers – only to present a forest plot *without* a summary estimate. Additionally, we conducted sub-group analyses to further assess heterogeneity, e.g. on type of drug, type of CPOE system, or clinical setting. The problem of heterogeneity of health informatics applications has also been discussed by other authors of reviews such as by Chatellier et al. [20] (for computer-assisted anticoagulant management) and by Garg et al. [38] (for clinical decision support systems).

We want to stress another point that makes quantitative summary estimates as part of meta-analysis in health informatics difficult: A forest plot can only comprise evidence from quantitative trials. Qualitative evidence is completely omitted by this approach. This may lead to a simplified picture of reality. For example, for CPOE systems, qualitative research points to potential negative effects (e.g. [1,39]), and this seems not to be sufficiently reflected in quantitative reviews. Some may argue that only quantitative evidence is reliable evidence. However, quantitative reviews may not sufficiently answer questions as “what effects can occur”, questions that need to be answered [27]. Then, quantitative evidence from meta-analysis may not be as objective as expected, but may be interpreted differently by differently readers [40]. It has even already been argued that qualitative evidence should be included in systematic reviews [41], and first approaches have been discussed [42].

3.4. Publication bias in health informatics

In our CPOE meta-analysis, the funnel plot showed a slight asymmetry, which may indicate a potential publication bias. In an earlier study [43], we surveyed 136 health informatics academics and found that about half of all evaluation studies conducted by them have never been published, due to several reasons such as lack of time, lack of budget, lack of scientific interest, doubts on study quality, or political reasons. Research point to the fact that in general, published studies may describe a present positive effect more often than unpublished studies or studies from the grey literature [44–46]. This

may also be true for CPOE studies. What may be reasons for this?

First, substantial time and energy is invested to introduce CPOE, hoping to improve health care. Sponsors may not favor publishing evidence that is weak or not favoring their products. Authors therefore may tend to report only on selected variables showing a positive effect, and ignore negative results. Papers on negative effects (such as [4]) are often subject to intensive, critical discussion (see, e.g. [47,48]), while results of positive papers may be more likely to be accepted by the scientific community without critical questions.

Then, CPOE introduction is a long process of optimization of the system, the workflow, the organization and the support. It would not be surprising when researchers presented results only after the expected outcome has been reached and the hypotheses confirmed (see a corresponding example analysed in [49]). This would mean that CPOE systems are optimized as long as needed to achieve positive outcome. Although this real optimization process is formally not a bias, it will also contribute to the predominance of positive study results.

Furthermore, the majority of evaluated CPOE systems are non-commercial systems, developed and operated by organizations that have direct access to the underlying software. In our meta-analysis, more than half of the studies were on “home-grown” systems. This enables them to achieve maximum results, an observation also discussed by others [27].

Finally, as CPOE implementations are very complex endeavors, it is likely that implementations will first be done in those settings that provide optimal preconditions such as high motivation of the staff, low complexity of workflow, best information technology used. Rigby [50] calls this “alpha sites” and argues that those sites are atypical with regard to larger technical, emotional, and financial support.

All this may explain why published quantitative evidence shows mostly positive effects. In other words, published quantitative evidence may tend to present the maximum positive effects of CPOE (in favorable conditions), but not the range of possible (positive and negative) effects.

4. Discussion

Based on the findings of our case study, we want to discuss the following major challenges to EBHI and how they could be addressed in the future.

Health informatics seems to lack a clearly defined terminology or ontology that can be used to uniformly describe IT evaluation studies in health care (i.e., type of evaluated system, type of study). This terminology could be used in title and abstract, or to index evaluation papers, to facilitate identification of available papers. It should be harmonized with available MeSH Headings.

Finding of evaluation studies may also be supported by a uniformed study registry, where studies (or publications on studies) are collected and indexed with a clearly defined terminology. The evaluation database at <http://evaldb.umat.edu> contains more than 1200 papers and shows how such a system could look like. This registry could be extended to also cover planned or currently performed studies, to address the

problem of publication bias (see also an initiative presented in [51]).

To improve study quality, health informatics needs guidelines for good practice in designing, conducting and reporting an evaluation study. Such guidelines must take into account the specific situation in health informatics, in order to help to overcome frequent pitfalls (see also [52]), in particular those of quasi-experimental studies. Adequate outcome measures should be recommended by scientific societies in the field to facilitate comparability between studies. More randomised controlled trials, taking into account clustering of data, and studies from more (non-U.S., non-university, commercial) sites are needed to further improve the evidence and to identify the setting that those systems are most useful in. However, also evidence from qualitative studies is important, and we need approaches to combine quantitative and qualitative evidence to a more complete picture. To avoid publication bias, we need (financial or legal) incentives to publish negative trials. In addition, studies describing positive outcomes should be submitted to the same rigorous quality discussion than negative trials.

Finally, to improve publication quality of evaluation studies, health informatics needs reporting guidelines making recommendation on the structure, scope and form of reporting the results. Similar to the CONSORT statement [53] for randomised controlled trials, these guidelines should also cover non-RCT and qualitative trials. A recent initiative related to this issue is STARE-HI (Standards for Reporting of Evaluation Studies in Health Care), which has just been published [54].

4.1. Limitations of our approach

In this paper, we raised and discussed some challenges we found while conducting a CPOE meta-analysis. We discussed how they may be challenges for EBHI in general. The discussion points have been shaped mostly by (1) our experiences while conducting the quantitative CPOE review and meta-analysis, (2) discussions with reviewers and other colleagues, and (3) findings from the literature. Most importantly, our exploratory comments are based on the experiences from one case study. Our paper should therefore be seen as an initial exploratory step to initiate the discussion rather than a comprehensive review in the field of health informatics evaluation.

5. Conclusion

Based on our experiences while conducting a meta-analysis on CPOE, we argue that we are still at the beginning of Evidence-Based Health Informatics. Many of the discussed challenges are similar to other (medical) fields. However, health informatics is still a young discipline, and certain problems such as missing incentives for a critical technology assessment, high number of quasi-experimental trials, use of clustered data, limited reporting quality, publication bias, and over-criticism of published negative trials seem to be problems. In addition, research seems to be needed on methodologies to deal with the strong heterogeneity of study settings, and with the mix of quantitative and qualitative evi-

dence. Further research and development of methodologies, guidelines and tools are needed to advance Evidence-Based Health Informatics.

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