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Advancing the discussion about Clinical Decision Support Systems to tackle Adverse Drug Events: a 'problematizing' approach

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ADVANCING THE DISCUSSION ABOUT CLINICAL DECISION SUPPORT SYSTEMS TO TACKLE ADVERSE DRUG EVENTS: A 'PROBLEMATIZING' APPROACH

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Research Paper

Abstract

Clinical decision support systems (CDSS) can prevent situations in which doctors prescribe a drug to a patient that causes a harmful reaction with another drug that a patient already takes (adverse drug events (ADE)). This can be achieved through generating medication alerts in the moment that a drug is prescribed. Researchers have paid considerable attention to how to design these alerts in the best possible ways, however, largely with inconclusive results. We tackle this body of literature using a 'problematizing' approach that enables to understand why research results are inconclusive by disclosing underlying assumptions in a body of literature that have over time shaped a scholarly debate into a particular direction. We uncover four problematic assumptions, offer alternatives to these assumptions and outline potentials to implement our ideas in future research projects.

Keywords: Clinical Decision Support, Healthcare, Adverse Drug Events, Variance, Process Research, Routines.

1 Introduction

There is a strong interest among reseachers in the area of healthcare IT (HIT) to better understand, design, and implement clinical decision support systems (CDSS) (Sen, al Kawam and Datta, 2019; Sutton *et al.*, 2020). CDSS are usually deployed within hospitals and integrate data from Electronic Medical Records or Electronic Health Records in order to improve clinical decision making (Sutton *et al.*, 2020). An important area where such improvements are sought is medication safety (i.e. Bardhan and Thouin, 2013). Its importance derives from the fact that particularly elderly people increasingly suffer from multiple chronic conditions (WHO, 2014) leading to these people having to take multiple drugs at the same time (Hogerzeil, 1995; Holloway *et al.*, 2003; WHO, 2014, 2019). Potential interactions between these drugs can have severe consequences as they can put a patient's life at risk while also driving healthcare-related spending (Tolley, Slight, *et al.*, 2018; Lowenstein *et al.*, 2020; Sutton *et al.*, 2020). These problems have made researchers aware of adverse drug events (ADE) commonly defined as "harmful event[s] which [coincide] with the use of […] pharmaceutical drug[s]" (Ammenwerth *et al.*, 2014, p. 337).

There is a rich literature on how to design effective CDSS to tackle ADEs scattered across medical informatics, biomedical informatics, as well as medicine (Akçura and Ozdemir, 2014; Baysari *et al.*, 2018; Marcilly *et al.*, 2018; Tolley, Forde, *et al.*, 2018; Lowenstein *et al.*, 2020). This literature has commonly focused on alerts that are sent by clinical decision support systems (CDSS) in order to make doctors aware that they should not prescribe a particular drug because it may create an ADE (Akçura and Ozdemir, 2014; Marcilly *et al.*, 2018). Throughout two decades, researchers have tried to find out how optimal alerts could be designed so that doctors would accept them (van der Sijs *et al.*, 2006; Seidling *et al.*, 2011; Horsky *et al.*, 2012; Nabovati *et al.*, 2017). However, research is inconclusive with

studies reporting positive impacts of certain designs on acceptance (Horsky *et al.*, 2012; Nabovati *et al.*, 2017) while others could not support this finding (Bryant, Fletcher and Payne, 2014; Phansalkar *et al.*, 2014; Kilsdonk, Peute and Jaspers, 2017; Edrees *et al.*, 2020). This inconclusiveness seems problematic given the overall efforts to optimize alerts for nearly two decades (Kawamoto *et al.*, 2005; Seidling *et al.*, 2011; Alagiakrishnan *et al.*, 2016; Jia *et al.*, 2016; Edrees *et al.*, 2020; Sutton *et al.*, 2020). In fact, scholars are now questioning the trajectory of this stream of research more fundamentally arguing that a shift in methods to design medication alerts and gauge their empirical impacts is due (Kilsdonk, Peute and Jaspers, 2017; Luna *et al.*, 2017; Shoolin, 2017; Marcilly *et al.*, 2018; Sutton *et al.*, 2020).

In this paper, we respond to the abovementioned call using a 'problematizing' approach (Sandberg and Alvesson, 2011; Alvesson and Sandberg, 2020). 'Problematizing' is an approach that discovers problems in a corpus of research by tracing them back to problematic assumptions that underlie a body of research (Alvesson and Sandberg, 2011). They key idea then is to question these assumptions and to offer alternatives that help reorienting a stream of literature by reflection upon extant research (Alvesson and Sandberg, 2020). In our case, we focused on articles seeking to design optimal medication alerts with the goal to offer to this literature fresh takes on how researchers could think of medication alerts and design them in new ways. Therefore, we compiled 43 articles using techniques of doing systematic literature reviews (vom Brocke *et al.*, 2009). This enabled us to detect how this literature sought to increase acceptance of alerts revealing inconclusiveness with regard to outcomes of medication alerts (Jia *et al.*, 2016; Kilsdonk, Peute and Jaspers, 2017; Nabovati *et al.*, 2017). We then used 'problematizing' in order to unpack four assumptions that guide this literature on a whole, to derive reasons for why these assumptions contribute to inconclusive empirical results, and to offer alternatives to these assumptions. In this paper, we keep the results of the systematic literature review brief and elaborate on our 'problematizing' of the literature. Finally, we specify our thinking by suggesting recent literature that links business process management (BPM) with organizational routines (Mendling *et al.*, 2021) as a basis to execute research about CDSS to tackle ADEs differently. Our overarching research question is thus '*what are problematic assumptions in research on IT-interventions in ADEs and how can these be overcome?'*

Our study offers two key contributions: First, we respond to calls to pivot the debate about CDSS to tackle ADEs (Ammenwerth *et al.*, 2014; Kilsdonk, Peute and Jaspers, 2017; Luna *et al.*, 2017; Shoolin, 2017; Marcilly *et al.*, 2018) and move it away from a variance logic toward a process logic. We do this in a fashion that accounts for both design of alerts and emergent behaviors by doctors. We believe that this offers a fresh insight into designing these systems more effectively. Second, we offer concrete suggestions for how our thinking can be executed in concrete design projects.

2 Literature Review: Background and subsequent 'Problematizing'

Our analysis of the literature about CDSS to tackle ADEs embraced two layers: a systematic literature review (vom Brocke *et al.*, 2009) and a problematizing review (Alvesson and Sandberg, 2020) on the analysed literature. The systematic literature review enabled us to summarize literature about optimal designs of medication alerts and to describe key findings, research gaps, as well as methodological developments. In short, this review described a cumulative body of research and, in our case, disclosed inconclusiveness of empirical results regarding optimal designs of medication alerts. The problematizing review was more analytic as problematizing is an approach that builds on the idea that scholarly work oftentimes evolves along a cumulative trajectory as part of which some assumptions become taken-for-granted (Alvesson and Sandberg, 2011). While this enables consistency across different publications within this literature, these publications also contribute to solidifying these assumptions rendering them unquestioned (Alvesson and Sandberg, 2011). The purpose of 'problematizing' is to identify and unpack those assumptions that have become taken-for-granted and, if necessary, offer alternatives to them (Alvesson and Sandberg, 2011, 2020). To this end, 'problematizing' complements systematic literature reviews as these tend to summarize research and

point out gaps (vom Brocke *et al.*, 2009; Leidner, 2016), whereas 'problematizing' encourages to question reified trajectories of research (Alvesson and Sandberg, 2011, 2020).

The method that we used to search for literature is consistent with the approach taken by (Sen, al Kawam and Datta, 2019): We searched across the Pubmed/Medline and Google Scholar databases because we wanted to generate a comprehensive sample covering different disciplines within which research on CDSS to tackle ADE had been done (Sen, al Kawam and Datta, 2019). We used the query "decision support system drug prescribing" to facilitate a far-reaching coverage of articles. Our initial sample included 798 articles, as visualized in Figure 1. Following procedures for doing literature reviews (vom Brocke *et al.*, 2009; Sen, al Kawam and Datta, 2019), we applied inclusion and exclusion criteria to our literature: First, papers had to treat medication alerts as components of CDSS as central part of their papers. This means that review papers and empirical studies were included were design of medication alerts were central.

Aggregated Keyword	**SLR**	**A1**	**A2**	**A3**	**A4**	**Min(Year)**	**Max(Year)**
Drug Administration	52	34	22	10	0	2011	2021
System	102	50	24	14	0	2007	2021
Safety	32	24	16	10	0	2011	2021
Technology	18	12	4	2	0	2007	2020
Medical Ward	6	4	0	0	0	2018	2021
Alert	20	10	6	4	0	2011	2020
Human Factors	28	14	8	6	0	2012	2020
Discipline	4	2	0	0	0	2011	2014
Knowledge	8	2	0	2	0	2014	2018
Design	12	8	8	8	0	2012	2018
Min(Year)	2007	2013	2014	2016	0		
Max(Year)	2021	2018	2018	2020	0		

Table 1. Categorized keywords of the reviewed literature depicted per generated assumption

Table 1 describes the used literature set with our own aggregation of the author-supplied keywords. We categorized keywords according to certain domains that they applied to and included the categories in the left columns. For instance, the category "Drug Administration" encompasses keywords such as "Adverse Drug Event", "Drug Interactions", "Drug Drug Interactions". The category "system" contains "Clinical Decision Support System" , "Computerized Pharmacist Order Entry System", and "Medical Order Entry System". Furthermore, we connected the key words to the four assumptions that we identified. Assumption four does not show any connection to keywords: The rationale is that all studies that we reviewed were carried in hospitals. The hospital setting seemed to be taken-for-granted in our sample while other settings such as care homes or doctors' offices did not play a role. We problematize this focus on hospitals below. Yet, because hospitals were so central, no study mentioned them as key word.

Subsequently, we focused on those papers were drug prescriptions were central and excluded papers that dealt with other areas of health care. This enabled us to narrow our search down to 43 papers that we deemed central for assessing (Leidner, 2016). Closely reading these articles disclosed to us that this research was inconclusive with regard to what would constitute effective designs of alerts.

Against this background we problematized the 43 articles (heavily influenced by two journals of medical informatics, (11x JAMIA, 5x IJMI)) to understand and reflect on *why* the literature generated inconclusive or "inconsistent" (Jia *et al.*, 2016, p. 14) results. Next, we first offer a brief recap of the literature that describes the results of our systematic literature review and then we unpack our problematizing of this literature.

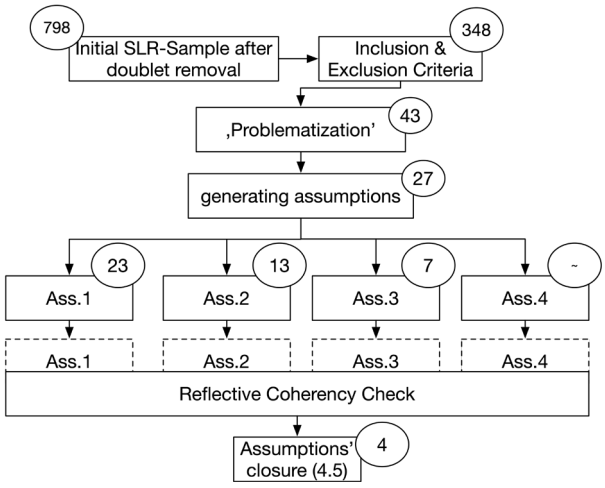

Figure 1. Executed literature review process with generated assumptions.

3 Literature about CDSS to tackle ADEs: A brief Recap

During qualitative analysis of the literature, it struck us that the key dependent variable that was studied in the reviewed articles was the acceptance of alerts of CDSS by healthcare professionals. The notion of 'alert fatigue' was introduced in this context and can be seen as an effect caused by "poor signal-to-noise-ratio" (van der Sijs *et al.*, 2006, p. 139; Sutton *et al.*, 2020), leading to persistent, habitual overrides of alerts regardless of their medical appropriateness (Phansalkar *et al.*, 2014). Table 2 summarizes the overarching outcome of the analytical stage. We grouped the independent variables that we found in various studies into two types of independent variables that summarize how researchers have tackled acceptance of CDSS alerts: quantitative and qualitative interventions.

Independent Variables	Examples
Quantitative interventions focus on what is presented	Reducing number of alerts (Bubp et al., 2019), modifying their frequency (Schreiber et al., 2017), prioritizing alerts (Bryant, Fletcher and Payne, 2014; Edrees et al., 2020) that are displayed to doctors
Qualitative interventions focus on how the knowledge is presented	Changing what information is presented (Chaparro et al., 2020), how it is presented (Baysari et al., 2018; Lowenstein et al., 2020), using methods of user-centered design (Horsky et al., 2017)

Table 2. Two Types Of Interventions Used To Increase Acceptance Of Alerts

An important explanation of alert fatigue that emanated from our sample was that doctors were overwhelmed by the alerts that CDSS would send. For example, many studies reported that the number of alerts sent was too high for doctors to meaningfully make sense of the alerts (Schreiber *et al.*, 2017; Tolley, Slight, *et al.*, 2018). They were extremely busy with treating patients while the IT confronted them with many detailed instructions about what to prescribe and what not (Meulendijk *et al.*, 2015; McEvoy *et al.*, 2017; Schreiber *et al.*, 2017). While vendors would sometimes justify the implementation of very many alerts (or prevent their deactivation) in their systems with the intent to be on the proverbial 'safe side' (Payne *et al.*, 2015; Schreiber *et al.*, 2017), situations such as these were reported to lead to doctors overriding alerts (Bryant, Fletcher and Payne, 2014; Payne *et al.*, 2015; Shoolin, 2017). Consequently, a set of studies has aimed to increase acceptance of alerts by reducing their frequency (Bryant, Fletcher and Payne, 2014; Horsky *et al.*, 2017; Schreiber *et al.*, 2017; Edrees *et al.*, 2020). Based on the idea of less alerts per time unit, the assumption was that reduced alert frequency would

lead to reductions in override rates (Bryant, Fletcher and Payne, 2014; Schreiber *et al.*, 2017; Edrees *et al.*, 2020). However, the effect could not be shown and override rates remained as high as 93 per cent (Bryant, Fletcher and Payne, 2014) or 95.7% (Edrees *et al.*, 2020). Another approach followed a similar logic and selected relevant interacting drug pairs to achieve "targeted DDI alert reduction", by lowering their alert priority (Schreiber *et al.*, 2017, p. 66). The idea was that better targeted alerts would reduce the time that doctors would have to study an alert (Schreiber *et al.*, 2017). While the effect was empirically demonstrated, it was modest (Schreiber *et al.*, 2017, p. 66). Similarly, the idea to better prioritize alerts and display to doctors only those alerts that were of high priority was introduced. Yet, an override rate of over 90 per cent even in high-severity alerts was found (Edrees *et al.*, 2020). Cumulatively, these approaches indicate attempts to reduce the number or frequency of alerts, or prioritizing them in some fashion (Seidling *et al.*, 2011; Bryant, Fletcher and Payne, 2014; Schreiber *et al.*, 2017; Tolley, Slight, *et al.*, 2018; Edrees *et al.*, 2020). Provided the focus on managing the amount of alerts, we group these as 'quantitative interventions' *not* to be conflated with the use of quantitative methods in empirical research.

In addition to works that focused on handling the number of alerts, a second stream of research has explored interventions into the content of the alerts that IT would send. The guiding idea here is that doctors' acceptance of alerts could be increased through changing content, design, and the overall representation of alerts. For example, acceptance of alerts has been shown to increase through changes in the textual information provided by an alert as well as how it was displayed (Seidling *et al.*, 2011; Baypinar *et al.*, 2017; Marcilly *et al.*, 2018; Chaparro *et al.*, 2020). Specifically, if textual information was specific (i.e., what drug-drug-interaction (DDI) was at risk leading to which outcome(s)) and actionable (i.e. what to do to avoid the DDI and when)), these factors were found to positively correlate with acceptance; even though the effect was stronger in inpatient settings compared to outpatient settings (Seidling *et al.*, 2011). These findings are echoed in review articles that highlight poor usability as barrier to acceptance of alerts and, in turn, stressed the importance of specific alerts that doctors can perceive of as valuable given the particular context that they are acting in (Horsky *et al.*, 2012; Nabovati *et al.*, 2017; Marcilly *et al.*, 2018; Tolley, Slight, *et al.*, 2018; Lowenstein *et al.*, 2020). Horsky et al. (2012) also stressed that to generate knowledge about these contexts and what doctors actually consider valuable, system designers and researchers would need to shift paradigms and make use of user-centered design when developing systems and context-sensitive methods such as ethnography when evaluating them (Horsky *et al.*, 2012; Luna *et al.*, 2017). Likewise, systems should be regularly reviewed with regard to the quality of the alerts that they sent in order to ensure acceptance of alerts over time (Horsky *et al.*, 2012; McEvoy *et al.*, 2017; Nabovati *et al.*, 2017). The promise of these suggestions could be seen in potentially illuminating how doctors' workflows actually unfold in practice (Nabovati *et al.*, 2017; Marcilly *et al.*, 2018; Chaparro *et al.*, 2020). Alagiakrishnan *et al.* (2016) engaged in participatory design – a variant of user-centered design – in order to design a system that would not negatively impact on existing workflows. However, still 50 per cent of users reported such interruptions (Alagiakrishnan *et al.*, 2016, p. 77 table 2). Further research on the impact of such design methods thus seems warranted, so that also other influential factors can be identified (Luna *et al.*, 2017)

Researchers have typically captured doctors' reactions to alerts as 'human factors' that design of alerts would need to account for. Integrating many of the insights that mattered for modifying content of alerts in order to increase acceptance, the specific design tool "I-MeDeSA" was developed in order to "assess compliance with nine human factor principles of DDI alerts" (Phansalkar *et al.*, 2014, p. e332). The 'I-MeDeSa' framework was catered to system developers "to improve alert design" and as decision criteria for managerial purchase decisions (Cho *et al.*, 2014). It was first reported by Zachariah et al. (2011) in a multinational study that ensured empirical validity of the presented, literature grounded principles aiming at increasing alert acceptance (Zachariah *et al.*, 2011). The framework was then picked up by Phansalkar et al., Cho et al., and others. While the human factors perspective of 'I-MeDeSa' is maintained in a newer review (Tolley, Slight, *et al.*, 2018), the tool is recently also criticized for "not reflecting the relative importance that end-users place on different aspects of alert design" (Lowenstein *et al.*, 2020, p. 564).

Taken together, work that relates to content of the alerts as independent variable typically tackles issues related to how information is presented to doctors. How texts were presented and what information they contained has been researched in several studies (Zachariah *et al.*, 2011; Horsky *et al.*, 2012; Luna *et al.*, 2017; Tolley, Slight, *et al.*, 2018; Chaparro *et al.*, 2020; Lowenstein *et al.*, 2020). Provided this focus on content of alerts and representation of information in alerts, we group these interventions into 'qualitative interventions' as key independent variable whose influence on acceptance of alerts has been studied.

Finally, drawing on both quantitative and qualitative interventions as independent variables, a set of recommendation articles have been published that promote prescriptions for how to design IT-interventions into ADEs. Phansalkar et al. gathered a US-based expert panel to identify which alerts to display to doctors and how (Phansalkar *et al.*, 2011). Other recommendation articles also stress that alerts need to be clearly prioritized, display actionable information, include complete information such as patient characteristics, and should be designed according to methods of user-centered design (Ammenwerth *et al.*, 2014; Tolley, Slight, *et al.*, 2018).

Despite varying in details, literature on CDSS to tackle ADEs reveals an overall tendency to try to find factors that affect as well as methods that can create fit between alerts and users. The articles that we reviewed reveal a common interest in acceptance of alerts as key dependent variable. A subset of articles attempts to increase acceptance through handling quantity of alerts whereas another subset targets their quality in terms of what content is displayed and how it is displayed. The gist of these works is that there need to be interventions into the design of the alerts so that they become accepted by doctors given their preferences and workflows. This is also true for articles that call for user-centered design as a method to generate alerts. User-centered design allows for incorporating doctors' expectations from the beginning on of a design process as opposed to subjecting doctors to a fully programmed and designed alert in a decision support system. However, this does not change that user-centered design is per se expected to increase acceptance of alerts. In turn, we conclude that literature on alerting behaviour of CDSS has generally developed a strong research interest on acceptance, that is into how these systems can integrate with their users in a better way.

4 Unpacking Assumptions in Literature on CDSS and ADE-alerts

Reviewing literature on CDSS and ADEs revealed to us a focus on acceptance of alerts in hospital settings but generated puzzling results overall. Why was this the case? 'Problematizing' (Alvesson and Sandberg, 2011, 2020) highlights that when research streams have developed into a cumulative but potentially problematic direction, unpacking the assumptions that guide these streams of research is helpful to change to the conversations that are going on within these streams. Next, we unpack four assumptions prevalent in discourse on CDSS to tackle ADEs and problematize those by drawing on wider literature from the information systems (IS) field.

4.1 Assumption 1: The knowledge that is codified in alerts should dominate the prescription decision

Many studies in our sample promoted that doctors' prescribing behavior should follow prescriptions emanating from alerts (Bryant, Fletcher and Payne, 2014; Payne *et al.*, 2015; Schreiber *et al.*, 2017; Edrees *et al.*, 2020). Reductions in the overall number of alerts (Schreiber *et al.*, 2017), their prioritization (Edrees *et al.*, 2020), modifications in design (Chaparro *et al.*, 2020; Lowenstein *et al.*, 2020) or efforts to match alerts with clinical work flows (Horsky *et al.*, 2013; Alagiakrishnan *et al.*, 2016; Luna *et al.*, 2017) all aimed at making doctors use alerts. This general orientation is interesting because it reveals an underlying logic in how researchers have treated different sources of knowledge that matter for prescribing drugs. One the one hand, alerts reflect knowledge as they are designed according to state-of-the-art evidence-based knowledge (Ammenwerth *et al.*, 2014; Schreiber *et al.*,

2017). On the other hand, there is individual expertise of doctors (Akçura and Ozdemir, 2014; Horsky *et al.*, 2017; Schreiber *et al.*, 2017). Doctors can draw on their individual knowledge to assess the situation of a patient and judge whether prescribing certain drugs may make sense or not. For example, prescriptions may be executed, although in potential conflict with strict evidence-based guidelines due to medically justified deviations based upon the prescriber's final decision ((Akçura and Ozdemir, 2014; Horsky *et al.*, 2017; Schreiber *et al.*, 2017; Edrees *et al.*, 2020). One puzzling example of such scenarios is representatively highlighted: "*combinations of interacting drugs are sometimes used intentionally with favorable effects"* (Luna *et al.*, 2017, p. 211). Here, the alert is actually a false-positive because medical sedation is necessary. In such a case, doctors have to deviate mindfully from otherwise standard treatments (Luna *et al.*, 2017; Tolley, Slight, *et al.*, 2018; Edrees *et al.*, 2020). Literature on alerts concerned with ADEs, however, suggests deviations are to be avoided, which is reflected in override rates as important dependent variable in many studies that we reviewed (van der Sijs *et al.*, 2006; Ammenwerth *et al.*, 2014; Bryant, Fletcher and Payne, 2014; Payne *et al.*, 2015; Edrees *et al.*, 2020). This suggests that research generally sees situations where drugs are to be prescribed as situations where the knowledge that is codified in alerts should dominate these decisions. Individual medical expertise is backgrounded or implicitly seen as much less important than knowledge codified in alerts.

There are several reasons why the assumption that knowledge codified in alerts should dominate prescriptions decisions is problematic. One important reason relates to data quality. This assumption calls for the systems that create alerts to build on data of very good quality. To create alerts that match well with the situation of patient, the alert needs to draw from the electronic medical record of the patient that, in turn, needs to contain complete data as well. This clashes with reality in many clinical settings that have reportedly shown insufficient data quality (Bubp *et al.*, 2019). For example, problems such as inconsistent medical records, non-machine-readable diagnoses (Middleton, Sittig and Wright, 2016) or problems with data transfers across health care institutions (El-Sappagh and El-Masri, 2014) cause that the data, which alerts build on, are oftentimes imperfect (see also Tolley, Forde, *et al.*, 2018). This is why calls for designing 'context-sensitive' systems (Ammenwerth *et al.*, 2014; Marcilly *et al.*, 2018; Tolley, Forde, *et al.*, 2018) have been put to the fore. Additionally, data quality problems clarify that there are good reasons why alert overrides may be 'appropriate' (Horsky *et al.*, 2017; Edrees *et al.*, 2020) and not something to be reduced per se.

A second reason why the abovementioned assumption can be criticized lies in the heterogeneity of medical professions. Professionals across sub-disciplines such as oncology, rheumatology, radiology, and others have specialized knowledge in their respective sub-fields that can be highly diverse (Oborn, Barrett and Davidson, 2011). It is striking that while alerts were studied in various units of hospitals such as intensive care units (Bakker *et al.*, 2021), emergency rooms (Patapovas *et al.*, 2013), oncology (Crespo *et al.*, 2018), geriatric & family medicine (Alagiakrishnan *et al.*, 2016), there have been little to no explicit take-aways for how the heterogeneity in medical expertise of alert users may matter. Doctors may assess situations differently according to their specialization and, indeed, doctors of different specialties have been shown to make use of electronic patient records differently without negatively affecting overall treatment successes (Oborn, Barrett and Davidson, 2011; Akçura and Ozdemir, 2014; Schreiber *et al.*, 2017). This means that doctors may have various reasons to override alerts or deviate from them deriving from their professional expertise.

Thirdly, a critical aspect related to what knowledge dominates prescription decisions relates to legal arguments. Vendors of systems that create alerts have been found to include some alerts mainly for legal reasons (Ridgely and Greenberg, 2012; Schreiber *et al.*, 2017) or prevent their local adaptation (Lowenstein *et al.*, 2020). The rationale is one of liability: If hazard arises from integration of too few alerts, vendors can be potentially held accountable whereas too many alerts may 'only' annoy doctors but not lead to legal consequences for the vendor (Ridgely and Greenberg, 2012; Payne *et al.*, 2015; Schreiber *et al.*, 2017). Yet the fact that some alerts are integrated into systems for liability reasons of vendors reinforces that it is important to take into account how doctors assess and judge the quality of information that an alert provides to them.

We highlighted reasons why the assumption of knowledge codified in alerts is problematic. Due to the problems identified, a productive alternative to this assumption is to lax the prerogative of knowledge codified in alerts. An alternative assumption could be that knowledge codified in the alert needs to interact[1] with knowledge of a focal medical professional to produce the prescription decision. Seen this way, neither of the two sources of knowledge gains dominance and 'override rates' appear in different theoretical light.

4.2 Assumption 2: Alerts are a Nuisance emanating from Decision Support Systems

It seems almost evident that, based on the literature we reviewed, alerts are to be conceived of as nuisance as they interrupt doctor's work. Because these interruptions seem justified to avoid ADEs, designing alerts in such ways that nuisance is minimized has become the primary interest of researchers working on IT-interventions into ADEs. This is reflected in basically all studies that we reviewed. Quantitative interventions searched for optimal amounts and priorities among alerts in order to reduce nuisance. Qualitative interventions targeted alert design so as to limit nuisance. Approaches such as user-centered design aimed at integrating doctors' perspectives from early on in the design process, which also reveals a method of trying to get nuisance into grip.

Provided the general orientation that alerts will annoy doctors it may seem counterintuitive to suggest otherwise. However, our reading of literature on CDSS's alerts and more general IS literature indicated alternatives to this assumption. In particular, literature commonly addresses alerts as part of decision support systems that build on electronic medical record systems (Davidson, Chismar and Davidson, 2007; Ammenwerth *et al.*, 2014; Schreiber *et al.*, 2017; Marcilly *et al.*, 2018; Tolley, Forde, *et al.*, 2018; Lowenstein *et al.*, 2020). IS research has generally highlighted that systems such as these are resisted by doctors (Lapointe and Rivard, 2005) or used in divergent ways by doctors (Davidson, Chismar and Davidson, 2007; Akçura and Ozdemir, 2014) as these systems often reflect economic ideals such as cost minimization and process standardization (Ammenwerth *et al.*, 2014; Jia *et al.*, 2016; Lewkowicz, Wohlbrandt and Boettinger, 2020; Sutton *et al.*, 2020). In case of alerts that target ADEs, various aspects enforce that alerts may be seen as nuisance. Some alerts may be created only to protect the vendor from liability issues (Ridgely and Greenberg, 2012; Schreiber *et al.*, 2017), other alerts may misfit clinical workflows (Luna *et al.*, 2017; Marcilly *et al.*, 2018; Chaparro *et al.*, 2020) or simply display information that doctors do not perceive of as useful (Luna *et al.*, 2017; Edrees *et al.*, 2020). It is logical that researchers have to some extent tried to ease the problems through diverse interventions into how to design alerts.

Subsequently, an important question is whether research and practice are on a promising track with trying to optimize alerts implemented in decision support systems further and further. An alternative to this trajectory to research would be to relax the assumption that alerts *have* to emanate from decision support systems and that these systems *have* to create alerts under any thinkable circumstances. In more detail, an alternative way to design IT-interventions into ADEs could be to question the conceptualization of these systems as decision support systems, which is only one possible "decision-making" strategy (Todd and Benbasat, 1999; Morana *et al.*, 2017, p. 33). Another approach would be to create guidance systems (Todd and Benbasat, 1999; Arnold *et al.*, 2004; Morana *et al.*, 2017, p. 33) that *guide* doctors through prescription decisions within which the system would also assume a different legal role. The authority to make the decision would rely solely within the doctor, who can consult with the guidance system but does not *have* to act upon an alert send by a CDSS. Designing these systems would then call for creation of customer and user journeys in the first place to derive what suggestive features are necessary to create meaningful guidance systems as IT-interventions into ADEs.

[1] "interact" in the context of this article implies that the healthcare professional's knowledge is on pair with the knowledge codified into the alert. This is currently not always the case, hence "unnecessary" alerts are results of a failed knowledge interaction between the system and it professional user in the concrete situation given.

4.3 Assumption 3: Design is everything

The literature in our sample shared a unanimous interest into design of alerts. Regardless of variation in how design was to be affected (i.e., through quantitative or qualitative interventions) or how articles suggested to design effectively (i.e., through user-centered design, participatory design, and the like), all articles wanted to increase acceptance of alerts by changing something that mattered for how they were designed. Overall, our literature could be summarized as 'design is the key independent variable and acceptance the key dependent variable'.

Notwithstanding the importance of design but the overall focus on *design only* creates a somewhat deterministic impression. As long as designers get the designs right, prescriptions will follow that are consistent with what alerts say. The quest of researchers then is to identify the best possible design of alerts. In turn, override rates or non-use of alerts become things that will be reduced or vanish (Alagiakrishnan *et al.*, 2016; Luna *et al.*, 2017). The crux is that this provides an overall image where the technology should determine what doctors in organizations do. This runs counter to the importance of medical reasoning and expert knowledge in making whatever treatment decision and prescribing drugs in particular (Horsky *et al.*, 2017; Schreiber *et al.*, 2017). Medical reasoning and expert knowledge may provide solid explanations for why doctors deviate from alerts or override them but literature on CDSS to tackle ADEs casts these more emergent behaviors as something to be avoided. Consequently, it seems that the more that researchers find emergent behaviors to occur in practice, the more researchers focus in improving design without questioning the overall orientation at design only.

Our suggestion here is to no longer see emergent behaviors as problematic and to be avoided. General IS literature has long highlighted that people oftentimes use systems in ways that deviate from designers' intents (Desanctis and Poole, 1994; Orlikowski and Iacono, 2001). In case of the alerts discussed in this paper, there may be good reasons why emergent behaviors occur and develop along pathways that deviate from prescriptions suggested by alerts. Doctors from different specialized fields may make use of an alert differently (Oborn, Barrett and Davidson, 2011; Akçura and Ozdemir, 2014), and doctors may well arrive at the judgement that some medicine may not apply well to a certain patient at hand (Luna *et al.*, 2017; Edrees *et al.*, 2020). Doctors may also well know that the data that the alert draws on is imperfect and, therefore, deviate from the alert (Kilsdonk, Peute and Jaspers, 2017). Consequently, an alternative way forward in research on IT-interventions into ADEs could be to give equal weight to design and emergence in order to trace their interplay over time and designing more effective alerts based on the insights derived from this interplay. We return to this issue below.

4.4 Assumption 4: Hospitals control CDSS' data

It struck us that all studies that we included into our review were carried out in hospitals. There are various reasons for why research on health care IT generally focuses on hospital settings (Baird Georgia, 2007) but this has important implications for how researchers treat alerts to avoid ADEs. Precisely, this research suggests that hospitals are those entities where CDSS to tackle ADEs are controlled and prescribing behavior occurs. This reinforces a general 'container view' (Winter *et al.*, 2014) of IS where all IS-related practices that matter happen in formal organizations despite the fact that computing is increasingly happening outside of formal organizations (Yoo, 2010).

A problem with this 'container view' in the context of CDSS to tackle ADEs is that patients may consult with various health care institutions including care homes, outpatient treatment facilities, or small physician practices (Baird, Davidson and Mathiassen, 2017). All of them generate information that is likely important for prescriptions of drugs and doctors in physician practices may actually prescribe drugs, too. Consequently, for the container view' to come to full fruition here it would be necessary that all information produced at diverse spots and through diverse behaviors of a patient is fed back into the systems of a hospital and made available for doctors there. Various technical issues place an obstacle on such far-reaching integration of information.

One way to address these problems could be to relax the assumption that hospitals need to be in control of all data needed for effective prescriptions. Specifically, patients move through various health care institutions including but not limited to hospitals. An alternative assumption could thus be to grant the control over ADEs to patients. This would imply to, for example, design a platform that provides interfaces to patients and doctors (for one exemplary approach see Wan *et al.*, 2020). Patients could have with them a client such as an app on smartphones into which diverse information that matters for treatments is fed. Doctors would use a different client to access the platform and access information relevant for prescribing from there. This would imply a noteworthy shift of control away from hospitals and doctors into the hands of patients.

4.5 Overcoming Variance Views in Research on CDSS-based ADE-alerts

In summary, the research we reviewed and problematized above suggests strong interest in improving our understanding of how design of alerts affects their acceptance. As stated, perhaps the single most interest in the research that we covered here, was the relationship between design as independent variable and acceptance as dependent variable. This has led to noteworthy progress in terms of how to manage quantity and quality of alerts as well as methods for more inclusive and effective ways of designing them. However, research remains inconclusive with regard to whether interventions into design of alerts really lead to the expected outcomes.

Our problematization revealed that the strong interest into how design would affect acceptance came at the cost of discounting more emergent and unforeseen aspects that may affect drug prescribing behaviors. For example, we highlighted that doctors have diverse individual knowledge that should interact with the knowledge codified in alerts in jointly producing prescriptions. However, this renders the outcome of the decision somewhat emergent. Likewise, our idea to shift from design of decision support systems to design of guidance systems also introduces emergence as it becomes tough to determine outcomes of prescriptions a priori. The importance of emergence amplifies when shifting the locus of control away from hospitals towards prescribers' (and patients') hands.

Overall, our review of the literature suggests that it was a strong tendency to develop knowledge through uncovering variance that is studying how changing an independent variable affects a given dependent variable (Seidling *et al.*, 2011; Nanji *et al.*, 2018; Tolley, Forde, *et al.*, 2018; Edrees *et al.*, 2020). Such generation of knowledge allows for understanding broad and widely applicable patterns in behavior (Ortiz de Guinea and Webster, 2017) yet comes at the cost of missing out on contextual and concrete observations that may explain why particular behaviors emerge to deviate away from the pattern (Langley, 1999; Langley *et al.*, 2013). Such emergence can best be covered through establishing a process mode of generating knowledge (Markus and Robey, 1988). Next, we offer some concrete ideas through which the aspects that problematized before can be executed in concrete research projects on IT-interventions into ADEs.

5 Advancing Research on CDSS-based ADE-alerts through Process Research

Research into processes generally is different from research into variance as research into processes suggests to understand impacts on certain dependent variables to emerge over time (Markus and Robey, 1988). This is why research on processes is generally seen as a complement to research on variance as research on processes is particularly insightful when research on variance yields results that are inconclusive (Ortiz de Guinea and Webster, 2017).

Our intent here is to build on more classical process theorizing that highlights the importance of explaining a particular dependent variable by (a) identifying the events that lead to an outcome; (b) identifying how they build upon another over time; (c) identifying the conditions under which this interplay happens, as well as (d) studying how variations in these interplays affect the outcome of interest (Markus and Robey, 1988). It should be noted though that there are many more understandings

of what constitutes a legitimate 'process view' (Wurm *et al.*, 2020; Mendling *et al.*, 2021) with 'strong process' views highlighting that any outcome of interest emerges and that social reality is to be explored through this lens and not a logic of 'dependent variable vs. independent variable' (Lynne Markus and Robey, 1988). In essence, this would deny to design systems since it would be conceptually incommensurate to treat the design as separate process (Leonardi, 2013). Our intent here is not to deny design but to bring it into balance with emergence. Likewise, our intent is not to contradict extant research on IT-Interventions into ADEs but to advance it in a meaningful way. This is why we draw on more classical views on process research in order to advance this discussion. Next, we discuss concrete means for carrying out our suggestions.

It is an important general insight that efforts to design digital technologies often focus on designing a certain artifact while the intent is to shape more emergent patterns of actions in which these artifacts are used (Pentland and Feldman, 2008; Holeman and Barrett, 2017). The same could be said of literature on CDSS to tackle ADEs. After all, the studies that we reviewed all explored ways to improve designs of alerts while indeed bemoaning that these would not be used in the ways that were intended by designers. An important challenge for research on CDSS to tackle ADEs thus is to strike a balance between design of alerts and emergence of the use of alerts in practice.

One promising approach to designing alerts in the context of ADEs is **business process management (BPM)** (de Ramón Fernández, Ruiz Fernández and Sabuco García, 2020; Mendling, Pentland and Recker, 2020). BPM is an engineering driven approach (Recker *et al.*, 2009) that sees organizational actions such as prescribing drugs as a sequence of logically interconnected activities that build upon another in order to produce an outcome that satisfies customers (Hammer, 2015). Moreover, the key interest in literature on BPM is how to design these processes so that they perform well (Dumas *et al.*, 2018). To this end, activities such as prescribing drugs should be modelled using business process modelling notation (BPMN) so that process diagrams can be created that reflect ideal ways in how the according activities will be carried out. An overarching BPM approach describing a generic drug prescription process from a doctor's perspective does to the best of our knowledge not yet exist (see two systematic literature reviews on BPMN (de Ramón Fernández, Ruiz Fernández and Sabuco García, 2020; Tomaskova and Kopecky, 2020)) even though there is literature that indicates that design of clinical decision support systems draws on principles that are similar to BPM (Cánovas-Segura *et al.*, 2016; Greenes *et al.*, 2018). A basic BPM diagram in the context of prescribing a drug could identify potential key activities: which information does the doctor retrieve (how, what, and from where), how and when is the intent to prescribe a drug entered into the system and how does a potential alert-dialogue with the system would affect prescribing. Different possibilities of acting within the process are included according to BPMN, so that the process diagram accounts for variation within the process (Hammer, 2015, p. 5).

Whereas literature about BPM emphasizes on design, literature on **organizational routines** emphasizes on emergence. An organizational routine is commonly defined as "repetitive, recognizable pattern of interdependent actions, involving multiple actors" and consists of ostensive and performative aspects (Feldman and Pentland, 2003, p. 96). The ostensive aspect encompasses standard operating procedures, such as guidelines, indeed process diagrams coded into software (Feldman and Pentland, 2003). The enactment of such diagrams is then referred to as performative aspect constituted by practices and potential improvisation (Feldman and Pentland, 2003). This perspective would highlight that doctors may deviate from the design of the alert or override it for various reasons. Moreover, these deviations would be captured by the performative aspect of the prescription process arising from expert knowledge, improvisation or other aspects that make doctors deviate from the performative aspects coded into the alert. Organizational routines thus highlight emergence as important part of everyday organizational reality (with Pentland and Feldman, 2008). Artifacts such as alerts or software in general are seen as containing "rules and written procedures" for the execution of the routine while acknowledging that this execution leaves way for deviation from the procedures (Pentland and Feldman, 2008, p. 241).

Researchers have recently come to see BPM and literature on business process management as two sides of the same coin (Mendling *et al.*, 2021). Both focus on concrete actions that are carried out in

organizations. Yet BPM looks at these actions as processes that can be designed and emphasizes on stable representations of these processes (Hammer, 2015). Organizational routines, in turn, focus on the same actions but conceptualize them as emergent and dynamic. Beverungen (2014) was among the first to draw on (Feldman and Pentland, 2003) to connect their view on routines with BPM. He argued that BPM creates the 'ostensive aspect' of a routine that is its abstract representation oftentimes explicated in standard operating procedures. When for example doctors draw on ostensive aspects, they use them in their practice but may diverge from that (Feldman and Pentland, 2003). Beverungen (2014) highlights that the interplay between ostensive and performative aspects offers a dynamic conception of design and emergence over time.

In terms of indicating how these insights could be used to design alerts, it makes sense to see that alerts exist in both perspectives. In a BPM logic, the alerts are an outcome of "rational engineering effort" (Beverungen, 2014, p. 195) reflected in many of the studies we reviewed before. The problem is that even literature on BPM enforces deterministic, top-down approaches where business processes and hence alerts are seen as key driver of outcomes. This is why under-performance of business processes is oftentimes associated with a flaw in their design (Recker *et al.*, 2010; Hammer, 2015). This is consistent with the literature that we reviewed as it displays the dynamic that under-performance of alerts called for more and more efforts to improve design. Yet the key insight emanating from literature on organizational routines is that alerts are open to agency of doctors who make use of alerts in a flow of activities that may or may not converge with the efforts to engineer alerts (see also, Feldman and Pentland, 2003). Combining these two views in future efforts to design IT-interventions into ADEs holds strong potentials to account for both design and emergence and to deliver more powerful insights into how, why, and under what conditions combinations of alerts and organizational routines lead to certain outcomes.

6 Discussion

CDSS to tackle ADEs are designed with the intent to improve medication safety (Akçura and Ozdemir, 2014; Ammenwerth *et al.*, 2014; Jia *et al.*, 2016; Tolley, Forde, *et al.*, 2018; Lowenstein *et al.*, 2020). Throughout two decades, researchers across different disciplines have focused on better understanding the role that alerts, which are generated by software, play for making doctors aware of potential ADEs in the moments when doctors prescribe drugs to patients (Kilsdonk, Peute and Jaspers, 2017; Nabovati *et al.*, 2017; Tolley, Forde, *et al.*, 2018). The single most important research interest in this body of work is how the design of alerts affects the acceptance of alerts by doctors (Kilsdonk, Peute and Jaspers, 2017; Luna *et al.*, 2017; Nabovati *et al.*, 2017). But the empirical results on this relationship are inconclusive leading to calls for fundamental pivots of how research of IT-interventions into ADEs is actually being done (Bryant, Fletcher and Payne, 2014; van Dort, Zheng and Baysari, 2019).

Our study responds to calls to redirect research on IT-interventions into ADEs away from a variance logic and more toward a processual logic (Ammenwerth *et al.*, 2014; Payne *et al.*, 2015; Kilsdonk, Peute and Jaspers, 2017; Hussain, Reynolds and Zheng, 2019; van Dort, Zheng and Baysari, 2019; Lowenstein *et al.*, 2020). We did this by introducing a viewpoint that brings into balance the design of alerts with their emergence in practice. This approach enables us to design alerts on the one hand through relying on established techniques of business process management and software engineering; in fact, corresponding with much of traditional literature on IT-interventions into ADEs (Davidson, Chismar and Davidson, 2007; Ammenwerth *et al.*, 2014; McEvoy *et al.*, 2017; Hussain, Reynolds and Zheng, 2019). Yet in sharp contrast to this traditional literature, which sees deviations from alerts as problem and casts emergent behaviors as challenge, we address emergence as natural part of alerts. Though viewing enactment of alerts as emergent organizational routines, we can begin seeing deviations and overrides as something to be effective, indeed productive (Feldman and Pentland, 2003; Pentland and Feldman, 2008). This is because we can learn from these deviations much about how and why professionals bring themselves and their knowledge into the setting of prescribing drugs. In our view, the design of alerts calls on traditional techniques of engineering and design in the sense of a functional

design process but the evaluation of alerts on techniques such as ethnography and deep qualitative inquiry to explicitly cater to the social construction process of the IT-artifact generating the alerts and its subsequent organizational performance. This interplay will, we argue, enable us to design more effective alerts in the future since this interplay emphasises the situated organizational use of the IT-artifact. Putting emphasisis on the situated organizational use implicates in practice to carefully structure the introduction of off-the-shelf systems, that is to explicity consider the organizational department from a healthcare professional perspective; i.e. systems in the emergency room or intensive care unit need to have a different alerting behaviour than systems in the general geriatric ward.

Furthermore, our study also identified one more fundamental problem that some articles on IT-interventions into ADE appear to have let the genuine key dependent variable – medication safety – out of sight while extensively studying means to increase doctors' acceptance of medication alerts: simple interventions, that is to turn off a certain alert and present this as a solution may reduce the quantitative alert burden, but this solution harms medication safety and renders such systems less utile to the healthcare professionals who deem such systems as generally useful, because they know ex-post (such an intervention) that at least one kind of alert is not thrown anymore.

Albeit quantitative interventions reducing the sheer number of alerts have been conducted, our approach of problematizing (Alvesson and Sandberg, 2011, 2020) in this systematic literature review is able to unpack underlying assumptions that lead to quantitative or qualitative interventions into ADE alerts: we highlighted that alerts are considered a nuisance rooted in decision support systems but that knowledge coded into alerts should simultaneously dominate prescription decisions. It almost follows that doctors will resist alerts, which leads to high override rates and situated general ignorance of alerts (Kilsdonk, Peute and Jaspers, 2017; van Dort, Zheng and Baysari, 2019; Edrees *et al.*, 2020). In turn, the widespread thwarting of alerts in practice has created ever more research into how to optimize their design, reduce their nuisance and improve the capabilities of hospitals to control ADEs. Over time, this has led to a discussion where normative acceptance has moved to the center of attention. Through the alternatives that we offered both in terms of accounting for professional heterogeneity, control over prescribing, and in terms of the systems to be designed (i.e., from decision support to guidance systems), we offered a new take that can guide us back toward designing for medication safety as well as measuring its development over time.

7 Limitations

Our article serves the purpose to offer research avenues on how CDSS could address Adverse Drug Events (ADE) from a new perspective. We did this by identifying problematic assumptions that underlie this corpus of literature and yet this may be seen as 'high level' exercise lacking empirical substantiation and evaluation. That is very true. Future research should indeed explore our assumptions in concrete research projects perhaps by testing alternative systems to enable medication safety as well as shifting control over ADE-alerts towards prescribers' hands. We offered concrete ideas for how this could be done by introducing a lens that combines business process management and organizational routines. As this lens brings into balance design and emergence of CDSS' ADE-alerts, it can be a powerful tool for future design of alerts in concrete projects; a statement which we hope future researchers will evaluate.

8 Concluding remarks

Adverse Drug Events (ADE) are a substantial threat in an age where patients increasingly suffer from multiple chronic conditions and may have to take multiple drugs at the same time. IT can serve as powerful intervention here, yet the according research in this area has moved into a trajectory focusing on acceptance of these systems. We worked towards getting this literature on a different track by unpacking four problematic assumptions that have led to this state, offering alternatives and suggestions to implement them in future research. While much remains to be done, our paper enables fresh and new ways to address CDSS-based ADE-alerts.

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