Evidence-Based Clinical Decision Support

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Summary

Background: Clinical decision support (CDS) is a key tool for enabling evidence-based medicine and improving the quality of healthcare. However, effective CDS faces a variety of challenges, including those relating to knowledge synthesis, capture, transformation, localization and maintenance. If not properly addressed, these challenges can limit the effectiveness of CDS, and potentially risk inaccurate or inappropriate interventions to clinicians.

Objectives: (1) To describe an approach to CDS development using evidence as a basis for clinical decision support systems that promote effective care; (2) To review recent evidence regarding the effectiveness of selected clinical decision support systems.

Method: Review and analysis of recent literature with identification of trends and best practices.

Results: The state-of-the-art in CDS has advanced significantly, and many recent trials have shown CDS to be effective, although the results are mixed overall. Issues related to knowledge capture and synthesis, problems in knowledge transformation at the interface between knowledge authors and CDS developers, and problems specific to local CDS design and implementation can interfere with CDS development. Best practices, tools and techniques to manage them are described.

Conclusions: CDS, when used well, can be effective, but further research is needed for it to reach its full potential.

Keywords

Clinical decision support system, practice guideline, evidence-based medicine

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1 Introduction

The concept of *evidence-based medicine* (EBM) has been promoted and largely accepted over the past two decades bringing with it new methods and tools for distilling knowledge and preference from the biomedical literature, accumulated clinical experience, and patient values [1]. Clinical decision support (CDS) is a key tool for enabling EBM. Osheroff et al. define CDS as "[providing] clinicians, staff, patients or other individuals with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and health care"[2]. CDS systems are diverse, ranging from drug interaction checks and dosing support, screening reminders and order sets though to sophisticated protocol-based care plans and diagnostic systems [3].It may seem self-evident that CDS should be "evidence-based" but for a variety of reasons this may not be the case. Problems in knowledge synthesis, capture, transformation, localization, or maintenance may contribute to inaccurate or inappropriate decision support. And non-adherence continues to be an issue even when high-quality evidence is produced [4].

We consider two major areas where EBM intersects with clinical decision support. In the first, we describe how evidence can be used to serve as a basis for clinical decision support systems that promote effective care; in the second, we review recent evidence regarding the effectiveness of clinical decision support itself. Our summary is not intended to be comprehensive nor is our literature review systematic. Rather, we describe an approach to CDS development we have found to be useful and highlight selected recent advances. As such, our manuscript is more of an "update" than a "review" of what's happened in the area of evidence-based clinical decision support in the last few years.

2 Using Evidence to Develop Clinical Decision Support

We can classify issues incident to the development of evidence-based decision support into 3 categories: issues related to knowledge capture and synthesis, problems in knowledge transformation at the interface between knowledge authors and CDS developers, and problems specific to local CDS design and implementation.

2.1 Knowledge Synthesis

The biomedical literature is massive, multilingual, burgeoning, and continuously changing. Although this raw knowledge is well indexed and is increasingly available to all who need it [5], distilling and summarizing the literature is resource-intensive and dependent on evidence-based medicine skills and tools that are not uniformly distributed. Moreover, in spite of the volume of new knowledge that is being produced, for many—if not most—issues in clinical care, the evidence basis is of low quality or simply absent.

Evidence quality is defined as "the extent to which all aspects of a study's design and conduct can be shown to protect against bias and inferential error" [6]. Evidence quality determines our confidence in the validity of a single study or a body of evidence. It depends on study type (with randomized controlled trials—RCTs—generally being considered as the highest quality), careful appraisal of how the study was conducted, and the study's applicability to the question at hand. Results of individual studies must be aggregated with careful consideration of their applicability and consistency.

Yet RCTs may not provide the most accurate information for all patients. For example, people with multiple morbidities

represent an increasing component of Western populations. In Holland, 4 or more chronic diseases are present in 30% of 65-74 year olds and 55% of those over age 75 [7]. But patients with multiple morbidities are often systematically excluded from RCTs. Similarly, children and pregnant women (and sometimes even women of childbearing age) have been regularly excluded from RCTs. In such cases, RCT results may not be applicable to the populations that were excluded.

Implementers of guideline knowledge require a clear understanding of what must be done and when. In addition, a number of factors intrinsic to a particular guideline are associated with impediments to successful implementation. The GLIA instrument has been useful in highlighting threats to implementability and defining characteristics of implementable guideline recommendations [8]. These include:

- Members of the intended audience execute the recommended action in a consistent way.
- Members of the intended audience agree when the recommendation should be applied.
- The recommendation is identifiable as such and its discussion is concise.
- Adherence to the recommendation is measurable.
- Outcomes of following the recommendation are measurable.
- Justification for the recommendation is stated explicitly.
- Quality of supporting evidence and recommendation strength are indicated.
- Patient or practice considerations that require individualization are specified.

When used with tools that appraise guideline quality (such as the AGREE II instrument [9] or the Conference on Guideline Standardization checklist [10]), guideline implementers can compare and choose to implement the highest quality, most implementable recommendations.

Raw knowledge can be summarized effectively in rigorously conducted systematic reviews and meta-analyses [11]. Such reviews make clear what the evidence is that addresses a clinical question, but generally do not take the next step of deciding how the evidence should be applied to make decisions about appropriate care. Creating recommendations is best accomplished using methodologies defined for practice guideline development.

2.2 Generation of Clinical Practice Guidelines

Evidence-based practice guidelines represent repositories of the most current knowledge about best clinical practices. When developed by trusted authors using transparent and rigorous methods, guidelines can help reduce the delivery of inappropriate care and support the introduction of new knowledge into clinical practice.

In 2011, the IOM issued a report entitled *Clinical Practice Guidelines We Can Trust* [12], that redefined guidelines as "statements that include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of benefits and harms of alternative care options." This focus on recommendations is important because guidelines describe and prescribe *actions* to be undertaken under specific conditions. Many guideline developer organizations recognize shortcomings in their guideline development processes that limit transparency, allow bias and non-currency, and result in poor articulation of recommendations [13]. By highlighting a set of aspirational goals, the IOM has set a high bar.

Guideline recommendations are based on factual evidence about what benefits and harms can be expected when users adhere to the guidance and judgments about the desirability (and undesirability) of those outcomes. The best guidelines clearly articulate a course of action, define precisely the circumstances under which the action is appropriate, clarify the reasoning that justifies the recommendation, and provide an indication of the authors' intended *strength of recommendation*. Strength of recommendation is particularly important to guideline implementers since it helps to define both prioritization of recommendations and rigor of enforcement. Only the strongest recommendations should be selected for development of quality measures. Yet indicators of strength of recommendation are available in fewer than half of guideline recommendations [14].

Because the process of developing guideline recommendations can be specified prospectively, investigators at Yale have created a wizard application called BRIDGE-Wiz that is intended to produce clearer, more implementable recommendations that describe benefits and harms, which may be anticipated when a recommendation is followed [15]. The program leads a panel of developers through a series of questions to focus attention on WHEN (i.e., under what circumstances), WHO (in the guideline's Intended Audience), OUGHT (with what level of obligation), to do WHAT, to WHOM (in the guideline's Target Population), HOW, and WHY. It makes use of controlled natural language to assist authors in developing clearly articulated statements [16].

Knowledge maintenance for guidelines represents another serious challenge. Continuous or interval review of the dynamically changing biomedical literature is necessary to assure currency. When substantive changes in understanding a problem arise, modification of systems that depend on this knowledge, such as CDS, must be undertaken.

2.3 Knowledge Formalization

Knowledge formalization is a process that takes a natural language knowledge source such as a clinical guideline, which is written for clinician-experts, and transforms it in a stepwise manner into a symbolic representation that allows for automated interpretation and execution by computers [17]. For many organizations, the process of knowledge formalization remains ad hoc despite the efforts of many investigators to define a standardized procedure.

Balas and Boren showed that it takes 17 years for the findings of research to reach clinical practice [18]. Moreover, the process of transforming guideline text into decidable and executable rules has not been either systematic or replicable. Efforts to create decision support systems from textual guidelines demonstrated significant inconsistencies and potential to deliver wrong advice [19, 20].

Funded by the US Agency for Healthcare Research and Quality, the GLIDES Project (GuideLines Into Decision Support) is a collaboration of guideline developers, disseminators, and implementers working to design, develop, implement, and demonstrate clinical decision support using systematic and replicable processes for knowledge transformation and CDS design. Since its beginnings in 2008, GLIDES multi-site collaborators have worked to develop an approach and suite of tools to facilitate the acquisition of evidence-based knowledge and deliver it in effective computer-mediated decision support (see http://medicine.yale.edu/cmi/glides/index.aspx).

Guideline recommendations are often not stated clearly. Guideline authors are accustomed to writing in nuanced prose, which may be interpreted inconsistently by guideline users. Underspecification and frank ambiguity may result when committees of subject matter experts draft statements that attempt to accommodate the knowledge and values of all panel members. Vagueness may also be introduced deliberately when evidence is limited, when consensus cannot be achieved, when authors worry about setting a legal standard, and when economic considerations may not justify resource-intensive interventions.

Knowledge transformation of narrative guidelines into a format that can be used in a CDS is facilitated by using an intermediate knowledge representation (see Figure 1). Narrative guideline recommendations can be parsed into the ANSI-standard Guideline Elements Model [21] using the GEM Cutter editor (available from http://GEM.med.yale.edu).

GEM is a hierarchical model whose high-level elements include concepts related to a guideline's identity, purpose, developer, method of development, intended audience, target population, knowledge components, testing, revision, and implementation plan. As an XML file, a GEM-ified guideline document can be read by humans but processed in multiple ways by machines (see below). Clear linkages to the source text are maintained providing an audit trail. The resulting "*semi-structured*" XML natural language representation of the recommendations is further transformed into "*semi-formal*" IF… THEN rules. Concepts representing conditions and actions are linked to standardized vocabulary codes. This semiformal representation is useful to developers of quality measures as well as CDS implementers.

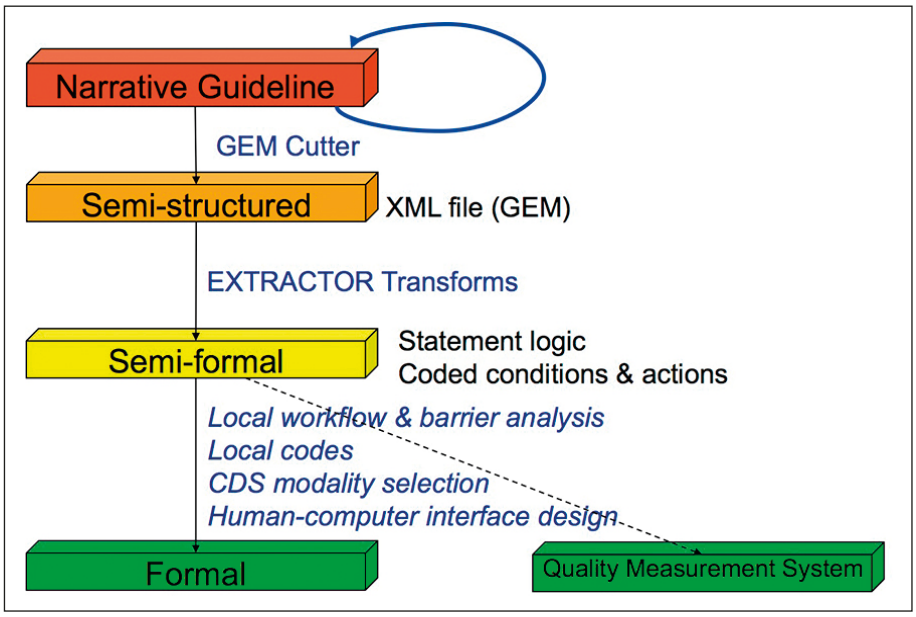

Fig. 1 Four stage process for knowledge formalization. Semi-formal representation can be transformed into CDS or quality measures.

There is a limit to how much can be accomplished centrally by guideline authors and the work that must be completed at a local level. The process of transforming guideline prose into a semi-formal representation can be performed centrally by guideline producers or disseminators. However, the final step in formalization—knowledge localization—requires clear understanding of local factors. Central specification of all aspects of CDS design is unlikely to be able to adapt to local requirements. Often, the final design requires accommodation to limitations in the host EHR system [22].

2.4 Knowledge Localization

The final step in this systematic approach to knowledge formalization is to embed the coded knowledge in a clinical decision support system integrated with an electronic health record. Proceeding from recommendations expressed in statement logic—with conditions and actions encoded in standardized vocabularies—to functional decision support is a complex, multifaceted process. Although several groups have offered guidance regarding keys to successful implementation including [23-25], no single approach defines the best path through implementation.

The process requires an understanding of system functionality and limitations, local barriers and facilitators, and application of principles of effective human computer interface design. Decision support can be offered in a wide variety of formats—not simply as alerts and reminders. These formats include displays of relevant information arranged so as to facilitate appropriate care, calculators of various forms that manipulate text and numbers to simplify and improve the accuracy of computation, order sets, documentation templates that prompt the user to collect appropriate information, algorithms, and infobuttons that provide context-sensitive information when requested. In addition, the modality by which advice is delivered (prescriptive or critiquing) affects its ultimate acceptance [26, 27].

Local workflow and barrier analysis is necessary to demonstrate decision support "origins," i.e., when in the course of clinical care, each decision variable is likely to have

been instantiated, and "insertions," i.e., when in the course of clinical care it is appropriate for the decision support to appear. Similar considerations will also dictate to whom the decision support should be addressed.

A cornerstone of decision support design is to involve end-users in the development of tools and systems they will use. As Elson and Connelly have noted, just as in real estate the key is "location, location, location", in decision support design the key is "workflow, workflow, workflow" [28]. Systems that do not accommodate or effectively reengineer workflow are destined to fail.

In addition to local workflow considerations, CDS implementers must also integrate their knowledge transformation tools and processes with local systems development and maintenance methodologies.

Post-implementation evaluation is a vital component of implementation that is often overlooked and underfunded. Knowing what works—and what does not—must be accompanied by inquiry that determines why a given project succeeds or fails.

3 Evidence of CDS Effectiveness

In the last several years, a considerable body of evidence has been added regarding the effectiveness of clinical decision support, as well as best practices for decision support. Effectiveness is a critical dimension of quality. The Institute of Medicine (IOM) defined effectiveness as "providing services based on scientific knowledge to all who could benefit and refraining from providing services to those not likely to benefit" [29]. When combined with other attributes of high-quality care—particularly safety, patient-centeredness, and efficiency—it becomes clear that clinical decision support can contribute mightily to healthcare quality.

3.1 Systematic Reviews and Epidemiologic Evidence of CDS Effectiveness

In 2012, Bright et al. published a new systematic review of the effect of CDS on clinical outcomes [30]. They reviewed 148 randomized trials of clinical decision support systems, and found significant improvements in three areas: preventive services (combined OR = 1.42), ordering clinical studies (combined OR = 1.72) and prescribing therapies (combined OR = 1.57). This work builds on earlier systematic reviews by Kawamoto et al. [31], Garg et al. [32], Hunt et al. [33], Chaudhry et al. [34], and others, all of which found positive effects of CDS. That said, many of the studies included in these systematic reviews showed an effect of CDS only on process measures. Demonstrating effects on hard clinical outcomes, such as mortality and disease progress, has been more elusive.

Many of these systematic reviews included a large number of studies from a small number of academic medical centers [34]. A key differentiator of the Bright study was the identification of a larger number of positive studies from sites beyond the set of historical CDS leaders.

The Cochrane Collaboration also recently released an evidence review focused on point of care reminders [35]. They included 28 high-quality studies in their review, and found a median improvement in processes of care of 4.2% across the studies, with most studies having only modest effects on outcome measures. The effect size Cochrane found was lower than in other systematic reviews, likely because their inclusion criteria were stricter and they focused on outcome rather than process measures. Consistent with prior reviews, they noted that a small number of institutions with self-developed clinical information systems contributed a large number of positive studies.

To shed further light on the question of evidence for CDS, in 2011, Jaspers et al. conducted a synthesis of 17 high quality systematic reviews (out of a total of 35 systematic reviews they identified) [36]. Their conclusions were mixed: they found that the evidence does suggest the possibility that CDS can have important effects on quality; however, they also concluded that most studies of CDS have not shown significant improvements in patient outcome, possibly due to limited power associated with small sample sizes and limited duration of study. Similar results were found in a 2012 systematic review by Cheung et al. [37].

An additional and quite significant contribution to the knowledge base about CDS evidence came from a special issue of the journal *Implementation Science* in 2011 entitled "Computerized Clinical Decision Support Systems: How Effective Are they?" and edited by R. Brian Haynes. The issue consisted of six reviews covering clinical decision support for therapeutic drug monitoring [38], drug prescribing [39], diagnostic test ordering [40], primary prevention [41], chronic disease management [42] and acute care management [43]. The results of these reviews were decidedly mixed. The first, focused on therapeutic drug monitoring, analyzed 33 trials and found that the available studies were generally small, of uneven quality and showed limited benefit. The review on drug prescribing identified more and higher quality studies which showed some benefits in process measures, but few improvements in outcomes. The diagnostic test ordering review found several positive studies, including four successful trials focused on reducing test ordering behavior, while the review on primary prevention found that most studies were positive, with particularly strong evidence for dyslipidemia screening and management. The chronic disease management review, likewise, found that just over half of studies demonstrated improvement on process measures, with a smaller number demonstrating improvement on surrogate outcomes. The final review, on acute care management, also demonstrated that most trials showed improvements in process measures, but outcome measures were infrequently measured.

Romano and Stafford took an epidemiologic approach to studying the effect of CDS on outcomes [44]. They studied the relationship between use of CDS and quality of care in the longitudinal National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) datasets. They found that, for 19 of 20 quality indicators, there was no association between use of CDS and quality of care. This is in contrast to the findings of Samal et al. who, also using the NAMCS dataset, showed a modest relationship between use of CDS and improved control of systolic blood pressure [45] (Romano and Stafford looked only at blood pressure measurement, but not at control).

3.2 Recent Trials of CDS

A key limitation of these systematic reviews is even the most recent among them, (by Bright et al.) only included studies indexed through January, 2011. However, a number of high quality studies on CDS have been released since then. Consistent with the prior systematic reviews, the results were mixed, but several studies broke new ground and we discuss some of them here.

In a before-after study, Litvin et al. [46, 47] showed a significant reduction in the inappropriate use of broad-spectrum antibiotics for patients with acute respiratory infections after implementing a CDS tool; however, there was no difference in overall use of antibiotics. A randomized trial by Foy et al. from the UK showed some improvement in three areas of diabetes managements: glycemic control, foot examination and blood pressure management, but no difference in cholesterol management [48]. Tamblyn et al. conducted a randomized trial in Canada of a CDS alert focused on reducing potentially harmful medication use in the elderly, and found that physicians modified therapy in response to 24.6% of the alerts they provided, leading to a predicted reduction in risk of fall-related injury of 1.7 fewer falls per 1,000 patients per year [49]. Carroll et al. tested a decision support tool to identify maternal depression during pediatric visits – the identification rate in the CDS-assisted arms (2.4%) was double the rate in the non-CDS arms (1.2%) [50].

Several CDS trials also showed effectiveness for CDS in the nursing domain. In a study published in *JAMA*, Dykes et al. reviewed the effects of a multi-faceted fall prevention decision support tool and showed a statistically significant difference in falls (3.15 vs 4.18 falls per 1,000 patient days in the intervention and control groups, respectively) [51]. A randomized trial in Belgium by Beeckman et al. on decision support for pressure ulcer prevention showed mixed results: participants in the intervention arm were more likely to provide appropriate prevention for pressure ulcers, and had more positive attitudes about the importance of pressure ulcer prevention; however, there was only a reduction in Category I pressure ulcers (non blanchable erythema) and no reduction in more severe ulcers [52].

CDS can also be used for improving the quality of problem lists. After noting clinically significant omissions on the problem lists of patients at the Brigham and Women's Hospital in Boston (BWH) [53-55], one of the authors (AW) and colleagues developed a decision support intervention, which identifies patients who are likely to have a particular problem (e.g. diabetes based on HbA1c results and medications, or hypertension based on antihypertensive therapy and blood pressure measurements), but do not have that problem on their problem list. The patients' physicians were alerted to this possible omission and given the opportunity to correct it. In a randomized trial, there was a three-fold increase in the number of problems documented by physicians receiving this alert [56].

AW and colleagues also showed some preliminary evidence of effective CDS for patients. In a randomized trial conducted at BWH, patients were shown clinical reminders in their personalized health records. Patients in the intervention arm were significantly more likely to receive appropriate influenza vaccinations and mammograms; however, no difference was found for bone densitometry, cholesterol testing, Pap smears or pneumococcal vaccination [56]. This is consistent with the findings of the systematic review by Kawamoto et al., who found that CDS provided directly to patients is particularly effective [31].

3.3 Best Practices and Recent Trends in CDS Research

Several other papers were released in the last few years with guidance and best practices for clinical decision support. Some papers looking at the best methods for using Web 2.0 technologies in support of CDS development [57] as well as best practices for governance in clinical decision support initiatives [58]. Phansalkar et al. released a national consensus set of high-priority drug-drug interaction pairs which we anticipate will be highly influential in alleviating alert fatigue associated with interruptions for low priority interactions [59].

In addition to these developments in the evidence for clinical decision support, several important trends have emerged. There has been an increased focus on service-oriented models for delivering clinical support. This trend was first noted in 2007 [60] it has accelerated since then. The Clinical Decision Support Consortium, based at the Brigham and Women's Hospital in Boston, Massachusetts has assembled a consortium of healthcare providers, electronic health record vendors, clinical decision support vendors and many others across Europe, Asia and North America and has developed and demonstrated technical approaches to providing clinical decision support using web services [61]. OpenCDS, another international consortium, has developed standards to support open-source CDS [62]. Many other standards development activities are also underway, and are nicely summarized in a recent review by Kawamoto et al. [63]

Another trend has been an increased focus on clinical decision support by policymakers, particularly in the United States. The US Centers for Medicare & Medicaid Services (CMS) created an incentive program for "meaningful users" of certified EHR technology [64-66]. In the first stage, providers were required to implement one CDS rule and also to use computerized drug-drug interaction checking [64]. In the second stage, the requirement to use a CDS rule was replaced with a broader requirement to "implement five clinical decision support interventions related to five or more clinical quality measures at a relevant point in patient care for the entire EHR reporting period" [67]. Although the number of CDS interventions required increased from 1 to 5, the requirement is still quite basic, and we anticipate that most eligible professionals and hospitals will be able to meet it with ease. It is more difficult to predict what effect, if any, this requirement will have on quality – although early data suggest that meaningful use has significantly increased adoption of EHRs, there is not yet evidence that it has had any effect on quality, and such an effect may not be likely until the later stages of the program. In addition to the meaningful use CDS requirements, the US government also sponsors Health eDecisions, an effort to develop consensus standards and implementation guidance for CDS in EHRs [68].

The importance of human factors issues related to CDS has also drawn recent attention. Karsh et al. developed a report for the US Agency for Healthcare Research and Quality on CDS and workflow [69] and also published a viewpoint paper on "fallacies and sober realities" pertaining to design and implementation [70]. The federally-funded National Center for Cognitive Informatics and Decision Making in Houston, Texas is carrying out a series of projects to study and improve the alignment of CDS and cognitive processes, including the development of a unified framework for assessing the usability of CDS and EHRs [71] and a series of projects on summarization of EHR data as a form of CDS [72-75]. Horsky et al. laid out a set of design principles for CDS interventions in the prescribing domain [76] and Zachariah and Phansalkar developed the i-MeDeSa instrument for assessing human factors issues in medication-related CDS [77].

Another recent area of attention has been best practices for CDS in community settings. Ash et al. published a series of such practices based on a large qualitative study [78] which identified ten themes, including the importance of workflow, the criticality of good human-computer interaction and the role of special people. The theme of human-computer interaction was also addressed by Saleem et al. when they reported on the re-design of a reminder system for colorectal cancer [79] to improve usability. McGreevey published a series of best practices for order sets in *Chest* [80], with a focus on how the order set development process interacts with the system of care.

Finally, considerable recent work in CDS has focused on unintended consequences of CDS interventions. Key studies by Ash identified the risk of such unintended consequences [81, 82] and more recent work has focused, in particular, on the issue of alert fatigue. Embi et al. showed a downward trend in response rates over time for an alert pertaining to clinical trial eligibility [83] and Murphy et al. studied the volume of alerts received by primary care providers, concluding that providers receive such a large volume of alerts that accurately filtering them may be challenging [84]. In an unintended but informative natural experiment, Landman et al. found that when a link from a hospital EDIS to PACS was broken due to a browser upgrade, image viewing fell by a quarter, further underscoring the importance of workflow [85]. Further work has also been done on methods for assessing the appropriateness of alerts [86] and potential legal implications of CDS [87].

4 Conclusion

In conclusion, the past few years of evidence have shown that CDS has the potential to improve the quality of care. However, it has not been universally effective, and some of the cases where it has been effective have shown only a modest improvement. As a complex sociotechnical endeavor, CDS must be, itself, effective, but also must be used effectively and be based on effective and current evidence. Over the last few years, considerable research, technology development, and policy work have been undertaken to lay the foundation for more effective use of CDS. Spurred in large part by these efforts we have, encouragingly, seen the first signs of effective widespread deployment of CDS outside of the small number of academic medical centers that have, historically, had the most success with CDS. We are at a pivotal moment in the adoption of CDS. Now is the time for healthcare providers, clinical information system vendors and clinical content providers to take advantage of these recent lessons and accelerate adoption of effective CDS. In parallel, CDS researchers, developers and policymakers should continue to improve all facets of the CDS process, from gathering and assessing evidence-based clinical knowledge to implementation of CDS at the point of care and rigorous evaluation [88]. These parallel efforts will best ensure that CDS achieves its full potential and widespread adoption in support of improved care.

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