Economic impact of clinical decision support interventions based on electronic health records

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Abstract

Background Unnecessary healthcare utilization, non-adherence to current clinical guidelines or insufficient personalized care are perpetual challenges and remain potential major cost-drivers for healthcare systems around the world. Implementing decision support systems into clinical care is promised to increase quality of care and thereby yield substantial effects on reducing healthcare expenditure. In this article we evaluate the economic impact of clinical decision support (CDS) interventions which are based on electronic health records (EHR).

Methods We searched for studies published after 2014 using MEDLINE, CENTRAL, WEB OF SCIENCE, EBSCO, and TUFTS CEA registry databases that encompass an economic evaluation or consider cost outcome measures of EHR based CDS interventions. Thereupon, we identified best practice application areas and categorized the investigated interventions according to an existing taxonomy of front-end CDS tools.

Results and discussion Twenty-seven studies are investigated in this review. Of those, twenty-two studies indicate a reduction of healthcare expenditure after implementing an EHR based CDS system, especially towards prevalent application areas, such as unnecessary laboratory testing, duplicate order entry, efficient transfusion practice or reduction of antibiotic prescriptions. On the contrary, order facilitators and undiscovered malfunctions revealed to be threats and could lead to new cost drivers in healthcare. While high upfront and maintenance cost of CDS systems are a worldwide implementation barrier, most studies do not consider implementation cost. Finally, four included economic evaluation studies report mixed monetary outcome results and thus highlight the importance for further high quality economic evaluations for these CDS systems.

Conclusion Current research studies lack to consider comparative cost-outcome metrics as well as detailed cost-components in their analyses. Nonetheless, the positive economic impact of EHR based CDS interventions especially with regard to reducing waste in healthcare is highly promising.

Background

As stated in the 2017 OECD health report, the annual average growth rate in per capita health expenditure continued to increase 1,7% in Germany and 2,1% in the US in real terms since 2009.[1] Accordingly, healthcare expenditure per capita was estimated to be $5,551 in Germany, but was yet outspent by the United States with almost 80% higher spending per person.[1] The latest OECD Health Statistics 2019 report reconfirms these numbers on rising healthcare expenditure and yet reveals an increase of spending per person to $5,986 in Germany and $10,586 in the US, which is equal to 11.2% and 16.9% of total GDP, respectively.[2]

Unnecessary healthcare utilization, non-adherence to current clinical guidelines or insufficient personalized care are perpetual challenges and remain potential major cost-drivers for healthcare systems around the world.[3,4] For instance, a recent review estimated the annual cost of waste in the US healthcare system to range between $760 billion and $935 billion, which accounts for 25% of total healthcare spending.[3] Furthermore, Shrank et al.[3] approximated that $191 billion to $282 billion could be saved annually with the use of systematic interventions that address the reduction of waste in healthcare.

The benefits of electronic health records (EHR) culminate in the integration of computerized provider order entry (CPOE) systems and real-time, point of care clinical decision support (CDS) interventions. Introducing decision support systems into clinical care is promised to increase quality of care and thereby yield substantial effects on reducing healthcare expenditure.[5] In addition, the rising field of behavioral economics explores how different interventions, such as nudges or best-practice-alerts (BPA), influence and improve clinical decision making through various applicable concepts.[6,7]

The goal of this study is to understand the economic impact of EHR based CDS interventions and to identify a coherent research best practice approach for these clinical interventions from a cost outcome perspective. Finally, we seek to examine application areas for different medical risk factors that have meanwhile been explored to be cost-saving or cost-effective.

Methods

Search strategy

We conducted a systematic literature review to identify the current research progress regarding the economic impact and benefits of clinical decision support interventions which are based on EHR. Following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement,[8] we searched English-language literature indexed in the following databases (1) PubMed, (2) Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, (3) Web of Science, (4) EBSCO Business Source Complete, and (5) CEA Registry Tufts Medical Center Library. Additionally, we screened the reference lists of all included studies for eligibility. The final loop of the literature screening process was completed on January 10th 2020.

In order to achieve high sensitivity and precision we developed each search query based on three main pillars: (a) economic outcome (b) electronic health record (c) clinical decision support. These main terms are then further extended with specific terminology and synonyms using Boolean operators to complete the search strategy. Furthermore, we used MeSH terms for the search in PubMed (1) and comparable search terms in databases (2) – (4). For the basic CEA registry search(5) only rudimentary key search terms were used. A detailed summary of the developed search queries is listed in an additional file [see Additional file 2].

Inclusion criteria

We included all trials in which a monetary economic outcome of an implemented EHR based CDS system is reported. Thus, we considered all analyses of inpatient or ambulatory financial data measures as well as trial-based modelling predictions. With regard to decision-analytic modelling approaches, we also included all kinds of economic perspectives, i.e. societal, health insurances, health systems or user-centered perspective, in order to identify the complete economic dimension of an EHR based CDS intervention. We summarized the detailed inclusion and exclusion criteria of this systematic economic review in Table1.

Table 1: Inclusion and exclusion criteria

Pre-search showed that the timeframe until year 2014 is adequately elaborated by prior systematic reviews, and we therefore include only studies published from 2014 to present. During our search process, we found that the number of studies meeting the inclusion criteria increased tremendously in the past years, partially overlapping the present research question.[9-11] The most recent review by Jacob et al.[9] examined the cost and economic benefits of CDS systems restricted to cardiovascular disease prevention, but were unable to conclude whether this intervention was either cost-beneficial or cost-effective. Moja et al.[10] reviewed randomized controlled trials (RCTs) that examined the effectiveness of EHR based CDS systems with regard to mortality, morbidity and economic outcomes, and the authors report that EHR based CDS interventions resulted in only small differences in costs and health service utilization.

Front-end clinical decision support interventions

Wright et al.[12] developed a taxonomy of front-end CDS interventions available to EHR users which we adopt into this study. Front-end CDS tools, in contrast to back-end system capabilities, are defined by the authors as “the intervention types available to end-users created using specific clinical knowledge bases and application logic”.[12] Their taxonomy consists of fifty-three designed CDS front-end tools, i.e. interventions, that were further categorized into six categories:[12]

1. Medication dosing support
2. Order facilitators
3. Point-of-care alert or reminders
4. Relevant information display
5. Expert systems
6. Workflow support

We use this taxonomy in order to identify a current best practice approach in terms of exploiting application areas that yield potentials for major cost-savings. For this, we aim to prioritize and weight different EHR based CDS tools based upon their economic benefit, so that policy makers, clinic managers and other healthcare providers, who intend to implement equal health information technology, will gain a better understanding of valuable EHR based CDS interventions and their application areas.

Results

We screened in total 1,309 publications of which twenty-seven studies meet our inclusion criteria for this economic review.[5,13-38] The process of our literature search as well as the reasons for excluding a number of studies is provided within the PRISMA flow-diagram in Figure 1. Furthermore, an overview of the characteristics of included studies is listed in Table 2.

Table 2: Characteristics of included studies (n=27)

Generally, twenty-two studies (81%) [5,13-16,18,20-25,28-31,32,34-38] out of the included twenty-seven studies report cost savings after implementing an EHR based CDS intervention. Four studies (15%) [17,26,27,33] report a rise in cost expenditure. The remaining study (4%) [19] did not detect significant differences in cost outcomes. Furthermore, in the majority of included studies the main cost outcome measures were laboratory test cost.[15-17,20,21,25,28,29,31,32,38]

Exploitation of different front-end CDS intervention categories

According to the taxonomy by Wright et al.[12], we identified ten (37%) studies [5,13,15,20,22,23,26,36-38] which explored EHR based CDS interventions based on *point-of-care alerts or reminders* (category 3). In addition, three interventions (11%) [17,27,34] were *order facilitators* (category 2), while *medication dosing support, relevant information display* as well as *expert systems* (categories 1, 4 and 5) were each reported only once from an economic perspective (11%).[18,19,24] In eight studies (30%), [14,16,25,28,30,31,33,35] interventions from two different categories were explored in combination. Moreover, we found three studies (11%) [21,29,32] in which the option to place a certain order or test, e.g. a laboratory test, was removed from the EHR CPOE system or the clinician's laboratory ordering preference list. These restrictive frond-end CDS intervention types were not yet mentioned in the pre-defined categories by Wright et al.[12]. Thus, for this study we extend their taxonomy by a new category

7. Restriction of choice[39]

The removal of an order option ultimately resulted in less laboratory tests ordered, and therefore in a reduction of healthcare expenditure in all studies it was implemented [14,28,31]. Finally, we identified two different types of implemented hard-stops.[40] An interruptive intervention, which requires a clicking response from the physician before being able to move forward[30], and a restrictive hard-stop, which prevents the physician from ordering a test, e.g. by directing them to call the laboratory director in case they persist on the order.[14] We grouped studies regarding the interruptive alert to category 3 and the hard stop restrictive intervention to category 7.

Economic impact for prevalent application areas

In Table 3, we summarized our findings and created an overview of application areas and cost outcome measures in relation to the applied CDS intervention types. Due to the heterogeneity of included studies with regard to different types of cost outcomes reported and different intervention duration, it was not possible to conduct a subgroup analysis considering the economic impact of each CDS-front end category. A detailed evidence synthesis of all included twenty-seven studies as well as a brief description of their intervention types, their application area and the resulting economic impact is provided in an additional file [see Additional file 3].

Table 3: Application areas and cost outcome measures in relation to CDS intervention categories 1.-7.

Application areas for cost-savings: Thereupon, we identified four main application areas based on their investigated prevalence that resulted in cost-savings after EHR based CDS implementation. Firstly, two studies report on essentially reducing unnecessary Vitamin D routine testing that led to a decrease of laboratory test cost of $300,000[15] and $1,4mill.[28] per year.

Secondly, two studies addressed the economic outcomes of the reduction of waste in transfusion practice and red blood cell usage.[36,37] Acquisition product cost of red cell units were decreased with the help of EHR based CDS and resulted in cost savings of in total $4,821,000 within three years[36] and about $62,715 within one year[37] after implementation, respectively.

Thirdly, two cost-effectiveness-analyses modeled the cost outcome of reducing antibiotic prescriptions for acute respiratory infection as well as for acute bronchitis.[5,33] Gong et al.[5] include a full accounting of costs into their Markov model and explore that the implemented CDS intervention, called “suggested alternatives”, yielded more quality adjusted life years (QALYs) at a lower cost of $500,000 per 100.000 individuals over thirty years of implementation. Michaelidis et al.[33] on the other hand report a small increase in costs compared to a printed decision support system, i.e. posters. However, the outcome of the latter mainly results from a cost difference between the direct costs of poster printing and the computer programming cost.

Lastly, five studies[20,29,31,32,38] report on the potential for cost savings through reducing duplicate orders or laboratory tests by using hard-stops[32] or applying order frequency rules[20] to prevent ordering the same test within a certain timeframe. Reducing laboratory duplicate tests resulted in savings of $3,395 in three months for a small patient size cohort[38] and up to $315,565 within twenty-four month for a large patient size cohort.[29]

Application areas resulting in cost increase: Furthermore, we also identified risk areas, which possibly lead to a further increase in healthcare expenditure. One study found that after implementing a CPOE system with default settings, specialized HIV laboratory test cost increased by $14,000-$96,000 within six months.[17] Another study reports that an unplanned change of a pre-selected default order for ‘complete blood count’ to ‘complete blood count with differential’ lead to an average cost increase of $293.11 per day.[27] Finally, the implementation of order sets as decision facilitators possibly entail negative economic effects. One study found that only after the uncoupling of Vitamin B12 and serum folate joint orders within predefined order sets, laboratory test cost decreased by about $26,719 per year.[16] Similarly, another study removed the option to order daily routine tests from automated admission order sets and found savings of $26,416 after two months.[25]

Cost-effectiveness-analyses models

Table 4 encompasses an overview of studies which conducted a cost-effectiveness-analysis (CEA) of EHR based CDS interventions considering various cost data as well as economic outcome measures, such as the incremental cost-effectiveness ratio (ICER), which depicts the incremental change in costs divided by the incremental change in health outcome or effect.

Cost-effectiveness-analyses aim to reveal the trade-offs in resource-allocation decisions.[41] In this context, it is essential to investigate when and to what extend upfront and maintenance cost for an EHR based CDS system will be amortized by its benefits, which again can be measured either in health outcomes, such as quality adjusted life years (QALYs) saved or in reduction of unnecessary healthcare utilization.

Table 4: Overview of cost data and cost outcome of model-based studies (n=4)

Generally, two studies report an increase in healthcare expenditure from a societal perspective, [26,33] while the other two report cost savings from a societal perspective as well as the medical group's perspective.[5,35] Notably, the measurement of effectiveness was single study-based estimates in all four studies.

Regarding the consideration of upfront implementation cost, Gong et al.[5] include only base case consolidated cost data of $1.91 for a cohort of 100.000 individuals based on expert opinions. Sharifi et al.[26] include intervention start-up cost for EHR modification of $2.7mill. as well as other direct cost, such as professional care provider training. Michaelidis et al.[33] report implementation and maintenance cost data, which is physician education per hour and medical record and CDS programming per patient of $18 in the base case. Lastly, Forrester et al.[35] report CPOE CDS system cost as hardware, software and maintenance cost starting from $373,000 in year one to $92,000 after five years, as well as personnel, $555,000 in year one, and indirect cost as 3% of the total cost. Interestingly, the latter also include the HITECH Meaningful Use incentives in their model in order to simulate the financial incentives by the Centers for Medicare & Medicaid Services in the US.[35,42]

Lack of considering all cost components

Despite revealing major potentials for cost-savings, we could not asses the quality of included studies, because of the lack of cost information provided, or predominantly the lack of considering all relevant cost components. According to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement, most of the reported recommendations were not satisfied.[43] All twenty-three non-model studies (85%) only calculate the economic outcome based on financial data reported before and after intervention implementation, which for instance, ultimately results from the computation of price per healthcare resource utilization times the quantity of used healthcare resources or services. Thus, even though it was not intended in those studies, it is necessary to mention that only four of them adhered to sound economic evaluations as recommended by CHEERS.[5,35]

The challenge of heterogeneity for the CEA is also aggravated by considering different cost outcomes. Two studies do not directly report an incremental cost effectiveness ratio (ICER) for a predefined threshold, nor include comparative metrics.[33,35] Other standardized metrics, such as the return on investment or net present value , were also not examined in the included studies. Only one study reported the net monetary benefit (NMB) of the intervention in relation to a predefined threshold.[5,44]

Additional studies worth mentioning

Notably, five more studies [45-49] meet most of our inclusion criteria, but were excluded due to various, although little, deviations. Three studies [45-47] report cost-savings after a bundle of information technology was implemented simultaneously, but the economic benefit could not solely be attributed to the EHR based CDS intervention. The fourth publication is a NHS health technology assessment (HTA) report.[48] In this HTA, a RCT was conducted in 79 general practices in the UK in which a multicomponent intervention was installed using electronic health records in order to reduce antibiotic prescribing for respiratory infections. The authors perform a basic cost-analysis on whether the cost of healthcare utilization, that is the number of provider consultations, will increase during the time of the trial under the CDS intervention arm, and if patients more often re-consult the physician when not given a prescription. However, the authors explored no difference in cost outcome between the intervention and control period.

The last study worth mentioning compared retrospectively generated alerts by an advanced machine learning CDS system with alerts triggered through the home-grown EHR based CDS system.[49] The authors calculated the healthcare costs of potentially prevented adverse drug events and medication errors, and found that by using the advanced machine learning CDS system 68,2% of alerts were only fired by that new system resulting in cost savings of $60.67 per alert. After extrapolating these results to an local patient population of 747,985 over five years they estimated savings of $1,294,457.[49]

Discussion

Evaluating the economic impact of EHR based CDS interventions and its potential to increase value in healthcare remains a great challenge. Even though we found that twenty-two studies report cost savings, most of them do not include developing or maintaining costs. Therefore, we could not draw a sound conjunction between the costs of vendor-purchased or home-grown systems to their economic benefit. Nonetheless, this study reveals several use cases with coherent CDS tools that have proven to be cost-saving, and could therefore be eligible for other healthcare providers, clinic managers and researchers for implementation or further exploration.

With the majority of implemented CDS interventions based on point-of-care alerts the question remains how more algorithm-based expert systems and multiple interventions will have synergy effects on the economic impact. Considering then the amount of alerts and a healthcare provider’s time expense, a process-cost analysis, such as the time-driven activity based costing approach, could be combined with the CEA to achieve a better understanding of the whole cost cycle as well as productivity effects for healthcare entities.[50,51] Generally, cost outcome measures continue to require comparative metrics, for instance, as used by Mathias et al., the cost per useful alert.[52] In a simple model the authors introduce this measure to analyze how different parameters affect the cost of implementing EHR based CDS alerts for genomic precision medicine.[52] However, for future economic evaluations of EHR based CDS interventions a more specific approach with regard to individual application areas or medical risk factor focus might result in better cost and outcome comparisons in order to draw a meaningful conclusion.[9] Moreover, decision-analytic modelling techniques, e.g. Markov models, enable the evaluation of multiple income and outcome parameters, and address down-stream costs or savings that may have incurred due to the implementation of health information technology. These complex modelling approaches are necessary in order to consider various health outcomes, which result from EHR CDS systems, e.g. prevention of adverse events.[5]

Another economic challenge to consider are CPOE systems with default lists or opt-out options of orderable tests as well as predefined order sets. The automation of orders through such order sets or joint-order options could ultimately lead to an increase of costs and a decrease of value.[53, 54] For example, the rate of unnecessary lab tests can increase when healthcare professionals tend to accept the whole order set rather than de-selecting single order items.[17] This can be explained by alert fatigue, which must not directly be related to the order set, in combination with the 'button clicking syndrome', which explains the inducement of moving along inattentively.[17,54] Apart from the direct economic factors, other potential benefits of order sets and joint-order options, such as improved adherence to clinical guidelines or patient safety outcomes, are not sufficiently addressed by the included studies which again highlights the importance of further profound health economic evaluations.

Finally, one study also reported an increase in cost after an unplanned change of the CDS system had occurred.[27] Thus, malfunctions or unintended errors by newly integrated health information technology, also called 'e-Iatrogenesis'[55], may also lead to yet another cost-driver and possibly cause unpredictable economic damage.[56,57]

Transferability for other countries

All included studies where based on cost data and trials from the United States or Canada. Consequently, current research progress on the economic potentials of EHR based CDS systems on rising healthcare expenditure in Europe or worldwide cannot be derived. We found recent studies evaluating the cost-effectiveness of a stand-alone CPOE CDS system in the Netherlands,[58] or comparing the effectiveness of an EHR based CDS intervention in the US, UK, Republic of Korea and Belgium,[59] while another RCT explored the effectiveness of an EHR based CDS intervention for patients with atrial fibrillation and high risk of stroke in Sweden.[60] Yet we found no study that evaluated the potential for increasing value in this present highly promising field of health information technology outside of North America.

However, this study reveals promising cost savings for already implemented health information technology. Even though implementation cost was not considered, on a long-term view these results reveal the potential for cost-savings once implementation costs are amortized. Therefore, the sooner broad health information technology systems will be implemented in other countries around the world and evaluated economically, the earlier cost-benefits and return on investments can be realized.

Support from policy makers could accelerate economic benefits

Interestingly, Forrester et al.[35] include monetary incentives as provided by the Meaningful Use Initiative in the US in their CEA. This financial support covered only a small percentage of total implementation cost, as in their developed model incentive-eligible prescribers received $42,000 over five years, but this nevertheless contributed to the investigated cost-effectiveness of an EHR based CDS intervention compared to paper-based prescribing. Therefore, how policy makers worldwide intend to financially support EHR adoption and incentivize usage of embedded CDS systems is a critical factor for the economic success of such systems. High upfront implementation cost is a major burden for healthcare entities, especially for smaller to middle size practices and hospitals.[61] For instance, a systematic review of EHR embedded CDS systems for cardiovascular disease prevention derived the mean annual cost of development, implementation and ongoing cost of operations to be $102 per patient and $6,056 per practice for small practices, and $49 per patient and $35,201 per practice for medium-sized practices.[9]

Finally, achieving a decrease in healthcare expenditure should never influence a patient's quality of life nor disease treatment in a negative way. Even though eliminating a laboratory order option from a CPOE system led to cost-savings, the value and health outcome of each patient is of highest importance and should be individually assessed. Rather than proving to have effectively reduced laboratory test costs, future economic evaluation of EHR based CDS systems should focus more on the potentials of health benefits that could be achieved, such as through reduced antibiotic prescriptions or adverse drug events. In the end, competing on shifting costs will not change anything about the main goal of decision stewardship, and that is to increase value in healthcare.[62]

Limitations

There are some limitations to this study. Firstly, since we only considered English language literature in our economic review, we might not have included international publications in other languages that indeed report on the information technology progress made by other countries regarding the linkage of CDS systems to an existing EHR. Another limitation is the exclusion of EHR cost and price display interventions. This decision was based on another recent systematic review which found that cost display interventions in EHR CPOE systems do not affect the efficiency and effectiveness domain of healthcare quality.[63] We also excluded other non-monetary impact measures, such as length of stay, which essentially also refer to the economic impact of EHR based CDS implementation.

Overall, the results of our findings might be biased, since we included all types of studies as well as all kinds of monetary outcomes reported. Due to the lack of economic evaluations, included studies tended to declare high cost-savings, but did only consider little to none cost components of implementing such a complex information system. In addition, authors might have been tempted to calculate cost-savings only when the intervention proved to be effective. Finally, based on our inclusion criteria we cannot argue to have involved all existing studies that meet the inclusion criteria of this review. While conducting the study, we found that studies not necessarily report calculated economic outcomes in the title or abstract of their publication, and thus by the nature of following the PRISMA guidelines leading to an exclusion of that study.

Conclusion

Clinical decision support interventions based on electronic health records have an overall positive economic impact. Predominantly point-of-care alerts with regard to unnecessary laboratory testing, efficient transfusion practice, or reduction of antibiotic prescription emerged as application areas with already promising potentials for high cost-savings. Nonetheless, lack of cost data consideration as well as the need for comparative metrics continue to be the reason why the economic dimension of EHR based CDS interventions need to be further explored. Therefore, high quality cost-effectiveness or cost-utility analyses, which include more extensive cost data and consider different economic perspectives, are needed in order to draw a sound conclusion. Finally, introducing personalized health services based on peoples' electronic health records is yet another promising research field with great potentials for further increasing value in healthcare, and should therefore receive more attention in future research.

Abbreviations

ADE: Adverse drug events; BPA: Best-practice-alerts; CDS: Clinical decision support; CEA: Cost-effectiveness-analysis; CHEERS: Consolidated Health Economic Evaluation Reporting Standards; CPOE: Computerized provider order entry; CW: Choosing Wisely; EHR: Electronic health record; HTA: Health technology assessment; ICER: Incremental cost-effectiveness ratio; NMB: Net monetary benefit; QALY: Quality adjusted life years; RCT: Randomized controlled trial; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta Analyses.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

DL conceptualized the study. DL and AW conducted the literature searches, literature screening as well as the analyses. DL drafted the manuscript, and all authors contributed to refining all sections and critically editing the paper.

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Tables

Table 1: Inclusion and exclusion criteria

	Inclusion criteria	Exclusion criteria
Type of decision support intervention	Any real-time and near real-time (point-of-care) computerized clinical decision intervention based on an EHR	- Decision support via e-mail, telephone contact, expert training or workshop, non-computerized education materials, or other behavioral economics interventions, such as accountable justification, i.e., free text entry, or peer comparison via e-mail - Retrospectively generated EHR based CDS alerts, e.g., for retrospective comparison or estimation - Basic CPOE without any decision stewardship - Cost or price display in order to facilitate cost-consciousness - BPA for EHR based patient recruitment for clinical trials - CDS for transitional care to improve post-discharge utilization and discharge management, i.e., process management - CDS usage for resource management, e.g., nurse staffing - EHR based CDS usage support through pay4performance incentives
Economic outcome	Monetary outcome data reported through quantitative cost-calculations or estimated through clinical trial-based modelling techniques	Other economic outcome measures, e.g., length of stay, amount of emergency department visits or primary care consultations

Table 2: Characteristics of included studies (n=27)

*C*ategory	Number of studies (% of total, rounded)
Country	
United States	24 (89%) [5,13-18,20,22,23,25,26,27-38]
Canada	3 (11%) [19,21,24]
Year published	
2019	6 (22%) [13-18]
2018	6 (22%) [5,19-23]

2017	5 (19%) [24-28]
2016	2 (7%) [29,30]
2015	3 (11%) [31,33,34]
2014	5 (19%) [32,35-38]
Study design	
Cluster randomized trial	4 (15%) [5,19,26,33]
Cross-sectional	1 (4%) [28]
Retroprospective	9 (33%) [15,17,18,20,21,27,32,36,38]
Quasi-experimental	5 (19%) [14,16,22,24,35]
Comparative	1 (4%) [31]
Observational	1 (4%) [23]
Pre-post-intervention	6 (22%) [13,25,29,30,34,37]
Setting	
Inpatient	14 (51%) [14,16,17,20,22-25,27,31,32,34,36,38]
Outpatient	8 (30%) [5,13,15,19,26,30,33,34]
Inpatient & Outpatient	4 (15%) [21,28,29,37]
Emergency department	1 (4%) [18]
Type of economic evaluation	
Basic cost calculation	23 (85%) [13-25,27-31,32,34,36-38]
Model approach	4 (15%) [5,26,33,35]

Table 3: Application areas and cost outcome measures in relation to CDS intervention categories 1.-7.

Study	Size[1]	Application area	CDS intervention period *(in month)*	Change in cost outcome per year *(in US$, if not other stated)* [2] per patient	per activated alert
1. Medication (dosing) support					
Tamblyn [19]	Medium	Reduce out-of-pocket costs for patients with uncomplicated hypertension	60	*no difference*[4]	
2. Order facilitator					
Bolles [17]	Small	Inappropriate test ordering for specialized HIV laboratory testing	6	+$102 to +$670	
Schnaus [27]	Large	The order "complete blood count without differential" unintentionally changed to "complete blood count with differential"	23 days	+$8	
Shaha [34]	Small	CDS order sets for managing new-onset stroke patients	6	-$1,742 to -$4,280	
3. Point of care alerts or reminders					
Gong [5]	Medium	Inappropriate antibiotic prescribing for acute respiratory infection	18	-$0.16[3]	
Chen D [13]	Large	Reduce unnecessary imaging studies in patients with low back pain	12	-$30	
Chin [15]	Large	Decrease routine testing for 25(OH) vitamin D levels	12		-$65
Bejjanki [20]	Large	Reduce 17 frequently used duplicate laboratory tests	17	n/a	
Chen JR [22]	Small	Directing the physician to order penicillin allergy testing for patients receiving aztreonam	9	-$678	
Heekin [23]	Large	Adherence to 18 different Choosing Wisely (CW) alerts	36	-$944	
Sharifi [26]	Small	Clinical childhood obesity intervention	12	+$11[3]	
Goodnough [36]	Large	Reduce overutilization in blood transfusion procedure	36	-$308	
Razavi [37]	Small	Reduce unnecessary waste in transfusion practice and blood use of cardiothoracic surgeons	12	-$82	
Bridges [38]	Small	Reduce unnecessary acute hepatitis profile laboratory tests	3	-$20	
4. Relevant information display					
Fertel [18]	Small	Reduce the amount of frequent or high emergency department utilizers	24	-$24,672	
5. Expert systems					
Nault [24]	Large	Antimicrobial stewardship that facilitates the post-prescription review process	36	- CAD $10	
6. Workflow support					
none	-	-	-	-	
7. Restriction of choice					
MacMillan [21]	Large	Reduce unnecessary frequent red blood cell folate tests	43	- CAD $5	
Konger [29]	Large	Define order frequency rules and reduce duplicate tests	24	n/a	
Procop (b) [32]	Large	Reduce unnecessary, same day duplicate orders	24		-$8
Studies with combined multiple CDS intervention categories					
1. Medication (dosing) support & 3. Point of care alerts or reminders					
Stenner [30]	Large	ePrescribing tool for therapeutic interchange prescribing	18	-$17	
Forrester [35]	Medium	CPOE CDS vs. paper-based prescribing in reducing medication errors and adverse drug events (ADE)	10	-$6[3]	
2. Order facilitator & 3. Point of care alerts or reminders					
Goetz [16]	Large	Decrease serum folate laboratory testing	12	-$29	
2. Order facilitator & 6. Workflow support					

Michaelidis [33]	Medium	Reduce inappropriate antibiotic prescribing for acute bronchitis	6	+$8[3]
2. Order facilitator & 7. Restriction of choice				
Sadowski [25]	Medium	Reduce admission order sets, which allowed multiple routine tests to be ordered repetitively	2	-$55[5]
3. Point of care alerts or reminders & 7. Restriction of choice				
Marcelin [14]	Large	Reduce inappropriate gastrointestinal pathogen panel testing	15	n/a [6]
Felcher [28]	Medium	Reduce unnecessary Vitamin D testing	6	-$157
Procop (a) [31]	Medium	Unnecessary duplicate laboratory testing	12	Hard-Stop -$16.08 Smart-Alert -$3.52

[1] Size is defined as the following:

Number of patients or encounters involved

0-999	small size
1,000-10,000	medium size
>10,000	large size

If patient count was not reported, we applied this range of criteria to the amount of triggered alerts in total

[2] All cost outcomes were scaled and calculated to overall change in cost outcome per year and per patient or activated alert. Values (for > $1) are rounded to full integer numbers. Because of the predominantly short CDS intervention period time range, a discount factor is not used for calculation. The original reported cost data is mentioned in an additional file [see Additional file 3].

[3] Cost estimation based on model

[4] No statistically significant differences between control and intervention group regarding out-of-pocket costs per patient

[5] Estimated reduced cost per inpatient day per year after intervention 1

[6] No information regarding number of patients or alerts. Overall cost outcome per year: - $51,206

[7] No information regarding number of patients or alerts. Overall cost outcome per year: - $157,782

[8] No information regarding number of patients or alerts. Overall cost outcome per year: -$53,600

Table 4: Overview of cost data and cost outcome of model-based studies (n=4)

Study	Model time horizon (years)	Choice of model	Implementation and maintenance cost	Total budget impact	ICER
Gong et al. [5]	30	Markov model	$1.91 base case for 100,000 individuals [preexisting EHR]	CDS intervention $17.32 mill. Control $17.82 mill.	$99.8 per QALY in base case scenario Not directly reported
Sharifi et al. [26]	10	Monte Carlo micro-simulation	$23,542 per PCP group [preexisting EHR]	CDS intervention +$239 mill.	$237 per BMI unit reduction
Michaelidis et al. [33]	5	Decision analytic tree	$18 base case - medical record programming [preexisting EHR]	CDS intervention $2,802* Control (usual care) $2,768*	$51.51 per antibiotic prescription safely avoided Not directly reported
Forrester et al. [35]	5	Decision analytic tree	$1,773,000 five years CPOE system costs	CDS CPOE system $25 mill. Control (paper system) $43mill.	$110 per ADE averted†

* *Cumulative 5-year societal cost per five cases of acute bronchitis*

† Documented only for the explored modelling scenario no. 2: The Everett Clinic achieved no reduction in paper chart pulls throughout the 5-year time horizon, to explore the effect of inefficiency from running a paper and electronic system in parallel

Figures

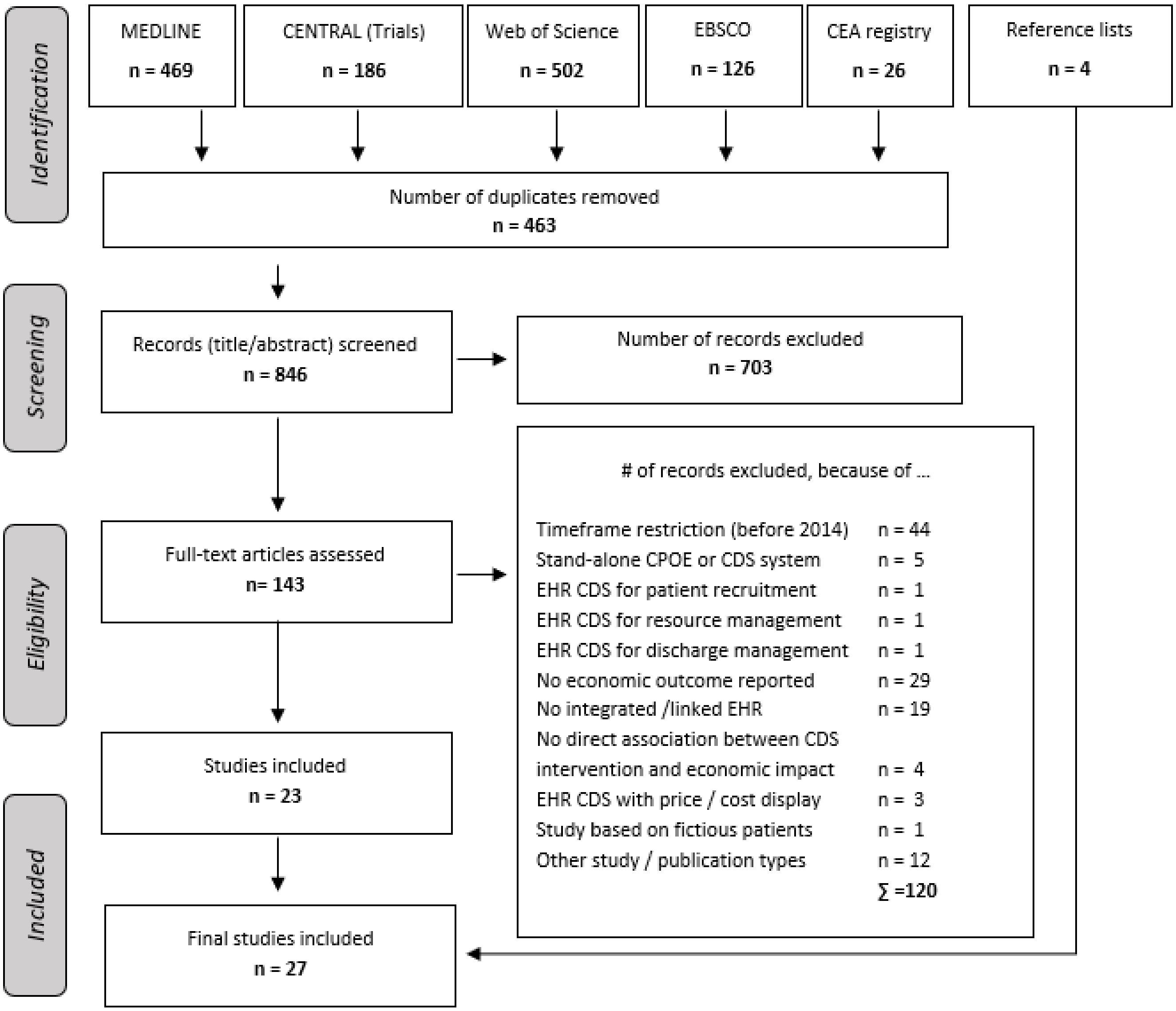

Figure 1

Flow-diagram of the search process (N = 1,309 publications screened)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1PRISMAchecklist.doc
- Additionalfile2Searchstrategy.docx
- Additionalfile3Summaryofincludedstudies.docx