The effects of clinical decision support system for prescribing medication on patient outcomes and physician practice performance: A systematic review and meta-analysis

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Abstract

Background: The clinical decision support systems (CDSSs) for prescription medications is one of the technologies aimed at improving physician practice behavior and patient outcomes by reducing drug prescription errors. This study, thus, was conducted to investigate the effect of various CDSSs on physician practice behavior and patient outcomes.

Methods: This systematic review was conducted by searching in PubMed, EMBASE, Web of Science, Scopus and Cochrane Library from 2005 to 2019. Two researchers independently evaluated the studies. Any discrepancies over the eligibility of the studies between the two researchers were then resolved by consulting a third researcher. Finally, we extracted data from the articles. Then, we conducted a meta-analysis based on medication subgroups and outcome categories; we also presented a narrative form of the findings. Meanwhile, we applied random-effects model to estimate the effects of CDSS on patient outcomes and physician practice performance with 95% confidence interval. Q statistics and I^2 was then used to measure heterogeneity.

Results: Based on the inclusion criteria, 46 studies were considered eligible for the analysis in this review. The CDSS for prescription medications had been used for various diseases such as cardiovascular diseases, hypertension, diabetes, gastrointestinal and respiratory diseases, AIDS, appendicitis, kidney disease, malaria, high blood potassium, and mental disease. Meanwhile, other cases such as the concurrent prescription of multiple drugs for patients and its effects on the above-mentioned outcomes were evaluated. The analysis shows that in some cases the application of CDSS provides positive effects on patient outcomes and physician practice behaviors. The effect was statistically significant (std diff in means =0.114, 95% CI: 0.090 to 0.138) as overall. It was also statistically significant for outcome groups such as those showing improved outcomes on physician practice performance and patient outcome or both. No significant difference was observed in comparison between some other cases and conventional methods. We think that this could be due to the disease type, the quantity, and the type of CDSS requirements that influenced the comparison.

Conclusions: Our findings suggest that positive effects of the CDSS are due to factors such as user-friendliness, compliance with clinical guidelines, patient and doctor cooperation, integration of electronic health records, CDSS and pharmaceutical systems, consideration of the views of physicians in assessing the importance of CDSS alerts, and their real-time alerts in the prescription.

Background

Prescription errors and drug interactions are among the common medical errors; thus, no need to mention that eliminating such errors is of utmost importance in order to prevent the side effects of drugs and associated implications [1]. One of the most important medical errors that can result in morbidity, mortality, and extended hospital stay is an inappropriate prescription medication [2]. Typically, due to a lack of accurate documentation in medical records and also a lack of data recording and reporting systems, we think that the main reason for most medication prescribing errors is a lack of adequate patient or medication information [3]. Thus, Clinical Decision Support System (CDSS) technology is used to reduce prescription errors and overcome these deficiencies. CDSS provides reminders and alerts that result in a reduction in prescription errors, while improving physician performance and patient outcome [4]. Based on patient conditions, CDSS for prescription can work strongly in managing complex activities from initiation to supervision and completion of medical treatment as well as providing suggestions to doctors [5].

Different types of instructional systems based on clinical guidelines, alerts, reminders and recommendations may be listed in this study, among other types of CDSS [6]. The advantages of CDSS include reducing and prevention of prescription errors through using alerts and immediate reminders, automatic dosage error checking, and drug interaction. Meanwhile, these advantages will help save the physicians' time which consequently leads to improving the overall efficiency of healthcare system [7]. Also, CDSS can have a mutual connection with pharmaceutical systems and electronic health records that enhance patient care with greater efficiency [13].

In this regard, most studies have shown an upward trend with respect to the use and effectiveness of CDSSs, compared to usual clinical practices. Relevant literature on CDSS for prescription have shown an increase in physician practice performance, but the impact of these systems on patient outcomes was yet unknown [2, 8-10]. Due to the fact that CDSSs are known to be effective tools for reducing prescription errors; thus, we considered all type of CDSSs for prescription from 2005 according to the inclusion criteria in this study. To this end and given the significance of CDSSs, we in the present study examine the effects of CDSSs on physician prescription performance and patient outcomes.

Methods

The method used in this study was a systematic review and meta-analysis. The method section is divided into some subsections, namely Search strategy, Inclusion/exclusion criteria, Screening and data extraction, Quality assessment, data synthesis and statistical analysis. Each subsection is described in more details, as follows.

Search strategy

The initial search was conducted in PubMed in this systematic review to identify the keywords. We used Medical Subject Headings (MeSH) in PubMed, Emtree in EMBASE and other words/phrases used in similar articles as the basis of search strategy. Then, we carried out the search in PubMed, EMBASE, Web of science, Scopus and Cochrane Library. We conducted the search in 2018 and used the approach designed for each database without language restrictions. Alerts have been used to access published articles after the search date. All of databases alerts were reviewed to July 2019. Also, reference tracking and citation search were used to augment the retrieval of eligible studies. An example of the full search strategy is given below:

(("clinical decision support system*" OR "clinical Decision Support*" OR "computerized decision support tool*" OR "Information System*" OR "hospital information system*" OR "computerized medical record system*" OR "point-of-care system*" OR "medical order entry system*" OR "computer-assisted decision making" OR "computerized medical record system*" OR "reminder system*" OR "computer-assisted diagnosis" OR "clinical informatic*")) AND ("medical mistake*" OR "medical error*" OR "therapeutic error*" OR "diagnostic error*" OR "drug interaction*" OR "drug dose-response relationship" OR "drug administration schedule" OR "drug monitoring").

Registration number on PROSPERO is CRD42018079936 which is available online at: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=79936 [11].

Inclusion/exclusion criteria

This research included randomized CDSS-based clinical trial articles such as alert-based, recommendation, instructional, and reminder-based systems to evaluate their effects on the behavior of patients and providers. In selecting an article for this study, we provided a list of questions whose answers are the main inclusion criteria. Here are the questions:

- Does the study focus on evaluating the decision support system?
- Has the study been a randomized clinical trial in which patient care has been compared with and without a decision support system?
- Have these studies been used by physicians, specialists, and residents in the decision support system?
- Does the decision support system evaluate patient-specific information in the form of management or probability options or recommendations for physicians?
- Has clinical efficacy been described as a measure of the care process, or the outcome of patients with any improvement in the study?

Screening and data extraction

The papers were screened in three different stages based on title, abstract, and full text. Evaluation was conducted by two authors of this study, (S.T) and (F.V). All phases of selection and screening of the articles were independently conducted in order to avoid bias. Any discrepancies between researchers were resolved by consulting an expert in this field, (F.S).

Quality assessment

We assessed quality of studies by Jadad scale, the Oxford research methods scoring system for bias in clinical trials [12, 13]. Finally, we reached the conclusion that the results of the quality assessment were acceptable.

Data synthesis and statistical analysis

We extracted the data from eligible articles through using a structured data extraction process. The results of studies were then presented in a descriptive-narrative form. We conducted meta-analysis with Comprehensive Meta-Analysis (CMA) statistical software [14]. Also, we used PRISMA checklist as a reporting guideline in our study. PRISMA checklist is a known standard checklist for systematic review reports [15]. For all the outcomes analyzed, measures of both CDSS and Control groups were summarized as mean standard deviation for each study and as comparisons of pooled estimates within the intervention group versus the control group. An effect size of std diff in the means of change in outcomes between groups was presented as standard error, and 95% CI. An effect size with a lower limit greater than 0 indicates that the intervention group has positive affection on the outcome; otherwise, if lower limit slower than 0; then, CDSS group has no impact in the outcome compared with the control group. Also, if std diff in means equals 0, it indicates that the change in outcomes was similar between the CDSS and control groups. The meta-analysis by using a random-effects model was conducted to estimate the physician practice behaviour and patient outcome. Q statistics and I^2 was used for calculating heterogeneity (I^2 greater than 50% is considered to heterogeneity). Sensitivity analysis was also performed to define and reduce the source of heterogeneity. In the next step, the funnel plot was used to assess publication bias. Funnel plot is a useful tool for assessing possible visual bias in publishing [16].

Results

The evaluation of the reviewed studies provided us with enlightening information with respect to the aims of the research, types of electronic prescribing systems, illness types, and patients. The findings also showed that in several diseases such as cardiovascular disease, high blood pressure, and diabetes, or cases such as simultaneous prescription of drugs, the effect of CDSS was evaluated. Findings from the analyzed studies are presented in the following tables in which * stands for p values and indicates a statistically significant difference. Also, the results of the quest are shown in Figure 1.

The number of studies based on multiple evaluation results and types of studies are shown in Figures 2 and 3, respectively. Figure 4 shows the meta-analysis results for each sub group of medication scope and the total analysis. The pooled std diff in means of p values showed a significant difference between the CDSS and the control group (std diff in means = 0.091, 95% CI: 0.072 to 0.109, standard error = 0.010). 95% CI for the effectiveness was drawn for each study in the horizontal line format (Q = 209.2, df = 45, p value = 0.0002, I^2 = 78.492, Tau^2: 0.004). Due to the high heterogeneity of results, sensitivity analysis was performed with excluded Bruxvoort, K. et al [50]; Ackerman, S. et al [35]; Avansino, J. et al [42] and khonsari, S. et al [24]studies. We omitted these trials because of the limited number of patients; they were also the only study of one medication field. The findings indicate that heterogeneity improved considerably after sensitivity analysis (Figure 5). (Q = 164.8, df = 41, p value = 0.0001, I^2 = 75.136, Tau^2: 0.003). After this change, the overall effects of clinical decision support system for prescribing medication on patient outcomes and physician practice performance based on the random effect model was determined to be (std diff in means = 0.84, 95% CI: 0.067 to 0.102) that showed significant difference.

The effect of CDSS on cardiovascular diseases

For patients admitted to the hospital, the level of venous thromboembolism prophylaxis and the proportion of prescribed prophylaxis increased from 6 to 24 hours after admission for clinicians allocated to venous thromboembolism reminder CDSS [17]. In another study, differences among physicians over the thromboprophylaxis treatment effect decreased with the help of CDSS providing treatment recommendation (p value = 0.02) [18]. In other studies, alert-based CDSSs have been effective in physician behavior and progressive treatment improvement in anti-inflammatory drugs and lipid-lowering drugs, which has also been statistically significant [19-21]. As stated in another study, by following medical recommendations, doctors in the intervention group were able to improve the prescribing level of secondary preventive medication with the help of a regular CDSS [22]. Also, in the other trials, the short message of the program in patient outcomes had a positive effect on patient adherence to medication, diet, and cardiovascular disease (p value<0.01) [23, 24]. Table 1 shows the result briefly.

Table 1. Data extracted for CDSS trials of cardiovascular diseases

Author/year	No. of hospitals/physicians/patients	Type of computer system	Outcome	P value
Eckman [18] 2014	15 /-/1493	CDSS providing treatment recommendation	Reducing disagreement among physicians	*0/02
Beeler [17] 2014	-/-/15736	Computerized system equipped with reminder to prevent intravenous thromboembolism	Increasing the ratio of prescribing prophylaxis 6-24 hours after admission/transfer	P <0/0001 value * *0/03
Du [61] 2018	58/-/patients	CDSS in mobile devices	Increasing secondary preventive prescriptions after 15 months in the intervention group	From 73/7 to 86/8 percent
Karlsson [19] 2016	43 /-/14134	CDSS equipped with alerts for patients with atrial fibrillation	Increasing the prescription of anticoagulation after 12 months	*0/01
Mazzaglia [20] 2014	-/197 /-	Alert-based CDSS for patients using cardiovascular drugs	Increasing prescription of anti-blocking drugs	*P value<0/001
Nielsen [22] 2014	-/-/191	CDSS to regulate the rate of warfarin use	Increasing the time outcome in the scope of treatment	0/67 Percent
Patel [21]	23 /178/-	Framework for	Increasing the	*P value

2011		the UK Medical Research Council (MRC)	number of anti-inflammatory/lipid-lowering drugs	<0/001
Akhu-zaheya [23] 2016	-/-/160	Short message reminder system in adherence to a healthy nutritional diet, drugs, cessation of smoking	Increasing prescriptions in the short message group	*0/001
Khonsari [24] 2014	-/-/62	Web-based software equipped with text reminders for patients with chronic coronary syndrome	Increasing adherence to drug usage	*P value<0/01

The effect of CDSS on hypertension

In one study, the electronic monitoring and recall program had no effect on blood pressure reduction and the admission of patients [25]. However, in another study, the patient outcome improved after the implementation of the CDSS [26]. Table 2 shows the result briefly.

Table 2. Data extracted for CDSS trials on hypertension

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Christensen [25] 2009	-/-/398	Reminder in patient admission and blood pressure control	Reducing blood pressure after 12 months	0/06
Luitjes [26] 2008, 2010	16/-/532 at pre implementation phase,-/-/1762 at post implementation phase	Innovative strategy including decision support system, audit and feedback	For the control group, reducing the secondary outcome of infant morbidity after implementation	*P <0/0001 value

The effect of CDSS on diabetes

In some studies, the Real Time Medication Monitoring (RTMM) system, equipped with a short message reminder, improved precision of patients' compliance and taking forgotten dosages [27-30]. In another study, HbA1c and group differences were greater in the intervention group using recommendation CDSS than in the control group [31]. The use of statins (p value = 0.03) and the problem areas in diabetes (PAID) (p value=0.01) improved in another study for intervention group that used CDSS [28]. Table 3 shows the result briefly.

Table 3. Data extracted for CDSS trials on diabetes

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Buhse [27] 2019	22/-/363	ISDM-P program composed of CDSS and sessions	Reduction in faulty knowledge causing risk	*P value <0/001
Perestelo-pérez [28] 2015	14/29/168	The CDSS selects statin with an estimate of cardiovascular disease risk	Increasing satisfaction of decision making	*0/009
Sáenz [31] 2012	66/-/697	The CDSS including patient data, glucose profile and recommendation for physician	Increasing long-term blood sugar using between group differences	*0/01
Vervloet [29] 2008	-/-/161	Real-time monitoring system for drug use by applying short message for diabetic patients	Increasing adherence in the group receiving short messages	*P value <0/001
Vervloet [30] 2008	-/-/104	Real-time medication monitoring system equipped with short message reminder for patients with type two diabetes	Increasing the drug dosage in one hour during a six month period	*0/003

The effect of CDSS on digestive diseases

In all studies, the CDSS had an effect on prescribing non-steroidal anti-inflammatory drugs, proton pump inhibitors, and increasing the standard use of oral rehydration solution without any difference in other results [32-34]. The alert-based CDSS was also able to improve the quality of patient care to some degree in the other study [33]. Table 4 shows the result briefly.

Table 4. Data extracted for CDSS trials on digestive diseases

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Geurts [32] 2010	-/-/222	Recommendation decision support system	Increasing the standard use of oral rehydration solution	*P value <0/05
Gill [33] 2007	27/119/5234	CDSS equipped with alert functionality and integrated with electronic health record and clinical guidelines	Increasing the receiving care on the basis of instructions for patients with low-dose aspirin use (25%)	1/30
Petersen [34] 2013	General physicians	CDSS equipped with risk notification service	Increasing the drug prescription in patients with risk above 5 percent	*0/01

The effect of CDSS on pulmonary diseases

In some trials, the use of CDSS integrated with electronic health record, learning or prediction rules resulted in a decrease in the prescribing of antibiotics and macrolides; thereby, it helped minimize the inappropriate use of antibiotics (p value = 0.0005), decrease the resistance to antibiotics (p value = 0.04), and enhance primary care [35-39]. The patients had adhered to the reminder message of using their medication in another study; however, the messages did not affect therapy success [40]. Table 5 shows the result briefly.

Table 5. Data extracted for CDSS trials on pulmonary diseases

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Bourgeois [36] 2010	-/112/-	Chronic obstructive pulmonary disease pattern in electronic health records	Reduced antibiotic prescriptions in visits by using templates	*0/02
Jusuzik [37] 2015	-/79/-	Electronic health records combined with databases of Electronic medical records such as links to clinical practice research data	Reducing unnecessary prescription of antibiotics	*0/04
Mcdermott [38] 2014	-/103/-	DSS and electronic learning	Increasing physicians self-efficacy	*0/02
Mcginn [39] 2010	-/-/984	A real time and unified CDSS during care combined with integrated clinical prediction rules	Reduced antibiotic prescription	*0/008
Mohammed [40] 2011	-/-/2207	Short message as a two-way reminder	Inability to be effective in treatment success rate	0/76
Ackerman [35] 2010	-/29/33	CDSS in Electronic Health Records	Reducing excess prescription of antibiotics	*0/003

The effect of CDSS on AIDS

In the reviewed study, it was shown that the reminder systems for short text messages had a positive effect on the treatment process for antivirus. The length of the messages also required more attention from the physicians, but had no significant effect on patient compliance rates (p value = 0.12) [41]. Table 6 shows the result briefly.

Table 6. Data extracted for CDSS trials on AIDS

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Pop-eleches [41] 2007	-/-/428	Short-message reminder systems (daily and weekly) in the antivirus treatment process	Reducing the number of treatment interruptions in both groups receiving weekly messages	*0/02

The effect of CDSS on appendicitis

This study showed that the system's systematically developed order set, which used clinical guidelines, increased system usability (p value=0.05) and reduced system-related problems related to unfamiliarity with the system (p value=0.05). This is a result of Computerized Provider Order Entry (CPOE) improved efficiency, quality and safety [42]. Table 7 shows the result briefly.

Table 7. Data extracted for CDSS trials on appendicitis

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Avansino [42] 2009	-/7/-	Systematically developed order set for using the decision support system	Increasing the follow-up clinical guidelines for systematic prescriptions compared to case prescriptions	*0/003

The effect of CDSS on kidney diseases

One study showed the positive effect of multipurpose intervention on creatinine value estimation and dose adjustment to reduce the insufficient dosage of primary care drugs [43]. In the other study, the appropriate prescription rate for kidney problems was rather low, contrary to the results of the former study. Furthermore, the effectiveness of the CDSS, equipped with physician guidelines, has been increased, especially for new versions [44]. Table 8 shows the result briefly.

Table 8. Data extracted for CDSS trials on kidney diseases

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Awdishu [44] 2012	-/514/1278	DSS Warning	An increase in not taking medication or changing dose of inadequate drugs	*P value<0/0001
Erler [43] 2007	-/44/404	Software including a database in coronary resection	Reduction in the amount of medication received in the intervention group in excess of the prescribed dose	*0/04

The effect of CDSS on taking multiple medications

In one study, 194 hard-alerted CDSSs resulted in delayed drug treatment for four patients requiring immediate treatment, suggesting that adverse events of these systems need to be evaluated and monitored [45]. In another study, the CDSS improved the primary dose of medication, time intervals for drug use, and drug concentration, which is to be injected intravenously compared to standard doses [46]. Also in another study, the average number of readmission days for each patient and the combination of re-hospitalization and emergency ward visits in the 30 days after hospital discharge was not different in the intervention group using Recommendation CDSS with control groups [47]. In some trials, there was no discrepancy between the outcomes of the dosage rate and the Modified Medication Appropriateness Index (MMAI), improper medication prescribing (p value = 0.48), the Medication Regimen Complexity Index, and the mean pain outcome difference after 6 months (p value = 0.13) and 9 months (p value =

0.78) between the intervention group using alert or reminder CDSS and the control group [48, 49]. Table 9 shows the result briefly.

Table 9. Data extracted for CDSS trials on taking multiple medications

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value

Cox [46] 2009	-/-/216	The CDSS with medication order entry in order to determine the initial drug dosage	An increase in the number of prescriptions for initial drug use	*P value <0/0001
			An increase in the conformity of prescribed medication percentage with the suggested medication	*P value <0/00001
Muth [48] 2017	-/71/465	Reminder-based CDSS	Ineffectiveness of drug prescriptions after 6 and 9 months	0/31, 0/18
Strom [45] 2006	-/1981/-	Computerized drug prescribing systems equipped with hard-alerted CDSSs	Increasing the percentage of appropriate alerts that have been responded to by physicians in the intervention group compared to the control group	57/2 vs. 13/5
Strom [49] 2007	-/1963/-	Computerized medication order entry system equipped with various alerts	Reduction in the appropriate response of physicians to alerts during 17 months	*0/007
Elliott [47] 2016	-/-/110	Prescribing CDSS for creating drug	Reducing the average number of days	*0/007

The effect of CDSS on Malaria

The use of text messages in the study did not affect the behavior of patients in completing the course of medication for the full duration of treatment. However, if the side effects were low (p value = 0.02), it had effects on the continuous use of the medication. In addition, text messages had an effect on the physicians' knowledge in using medication with fatty foods (p value<0.0001) [50].

		treatment recommendations such as drug-drug and drug-gene interaction	re-hospitalized 60 days after discharge	
			Reducing the combination of re-hospitalizations, emergency ward visits and morbidity 60 days after discharge	*0/005

Table 10 shows the result briefly.

Table 10. Data extracted for CDSS trials on Malaria

Author/year	Population	Type of computer system	Outcome	P value
Bruxvoort [50] 2012	82/-/-	Text message reminders for Malaria treatment	Physicians' knowledge in using Lumefantrine orthometer	*P value <0/0001

The effect of CDSS on increasing the level of blood potassium

In one study, there is no statistical difference in terms of following alerts and patient compliance rate between the control and intervention groups. The doctors' compliance rate improved at the medium potassium level from 3 to 3.9 (mili-equivalents/liter) (p value<0.01) [51]. Due to the rapid response of the physicians to program reminders and alerts for high potassium levels in the intervention group, the positive effect of the system on physician behavior was evident in another study (p value = 0.01) and a high level of potassium (p value = 0.05). Thus, patient safety could be increased [52]. In another study, the time lapse in hyperkalemia monitoring (p value = 0.20) and the incidence rate of hyperkalemia (p value = 0.22) did not differ significantly even with the use of three different kinds of reminder and alert-based CDSSs [53]. Table 11 shows the result briefly.

Table 11. Data extracted for CDSS trials on increasing blood potassium

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Beeler [53] 2014	29/-/4861	Three types of CDSSs including reminder, high potassium and calcium alerts	An increase in the average monitoring time of potassium level	*P value <0/001
Duke [51] 2011	-/1029/-	Drug-drug interaction alerts for patients in danger of high potassium level	A decrease in the conformity rate in normal risk patients for increased potassium	*P value <0/01
Eschmann [52] 2014	15/-/37000	Electronic health records equipped with alerts and reminders systems	A decrease in the reaction time of reminders for physicians monitoring alerts of potassium level	*0/04

The effect of CDSS on medication prescription for patients

Based on the results of some studies, the regular or alert based CDSSs resulted in better drug prescriptions for the proton pump inhibitor and a reduction in abbreviation prescriptions [4, 54]. Also, in the other studies, the overall utilization of system functionalities, system utilization between two time laps (p value<0.0001), number of users (p value<0.0001), and physician compliance regarding drug recommendations given by the CDSS improved drug prescriptions, which eventually resulted in reduced side effects (p value = 0.02) and harm to patients due to the lower number of errors regarding the alert-based CDSS [5, 55]. There was no difference in drug prescription among physicians in one study (p value=0.14); However, the percentage of skill questions answered for the intervention group, equipped with training CDSS (p value = 0.01) improved [56]. In another study, alert-based CDSSs have been effective in identifying evidence-based pharmacotherapies (EBP). Meanwhile, the compliance with treatment by health care managers have had no effect on the outcome of patients [57]. Table 12 shows the result briefly.

Table 12. Data extracted for CDSS trials on medication prescription for the patient

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Curtain [4] 2009	185/-/-	CDSS for drug distribution in treatment with proton pump	Reduction in the approved percentage of inhibitor intervention proton pump which is registered by the pharmacologist	*P value <0/001
Turchin [5] 2008	-/3703/-	Hard alert systems to facilitate medication services	Increasing overall efficiency of system functionalities prior to admission	*P value <0/0001
Griffey [55] 2006	-/-/1407	CDSS for recommending drug dosage	Increasing the number of prescriptions by recommending the determined system dose	*P value <0/0001
Myers [54] 2006	-/59/-	Computerized alerts for manual or automatic correction of medical abbreviation	Reducing the significant number of inappropriate abbreviations	*0/02
Van Stiphout [56] 2014	2/115/1094	CDSS integrated with training session	More efficient medical summary	*0/03
Willis [57] 2009	-/-/2219	CDSS alerts for the primary care clinic	A lack of difference in the rate of patient	

			adherence to treatment, drug treatment significance, economic and clinical outcomes in three groups	

The effect of CDSS on mental disorders

DSS alerts resulted in reduced risk of injury and reduced dose of antipsychotics and anticoagulants (p value = 0.03) from the beginning of the study up to year 1. Therefore, the CDSS reduced the risk of injury (p value = 0.02) [58]. Table 13 shows the result briefly.

Table 13: Data extracted for CDSS trials on mental disorders

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P value
Tamblyn [58] 2008 to 2010	-/81/5628	DSS equipped with three types of alerts	Reduction in dose of drugs after one year for antipsychotics	*0/02

Subgroup analysis

The subgroup analysis showed a significant difference between CDSS and control groups for medication scopes such as hypertension: (std diff in means = 0.187, 95% CI: 0.102 to 0.272); increasing blood potassium: (std diff in means = 0.036, 95% CI: 0.006 to 0.066); multiple medications: (std diff in means = 0.208, 95% CI:0.084 to 0.332); AIDs: (std diff in means = 0.241, 95% CI:0.038 to 0.444); kidney disorders: (std diff in means = 0.133, 95% CI:0.073 to 0.193) diabetes: (std diff in means = 0.381, 95% CI:-0.223 to 0.539); cardiac: (std diff in means = 0.073, 95% CI:0.035 to 0.111); mental disease: (std diff in means = 0.062, 95% CI:0.010 to 0.114); medication prescription for patients: (std diff in means = 0.157, 95% CI:0.094 to 0.219); pulmonary disease: (std diff in means = 0.079, 95% CI:0.014 to 0.144). Also, there was no significant difference between the intervention and control group for digestive disease: (std diff in means = 0.182, 95% CI: -0.072 to 0.437). Figure 5 shows the forest plot for subgroup meta-analysis. However, Malaria and appendicitis diseases are eliminated due to the decrease of heterogeneity between studies, they have been described in narrative results.

Evaluation for publication bias

Funnel plot and Egger’s regression were performed to evaluate the publication bias regarding the effect of CDSS on patient outcomes and physician performance [59, 60]. There was no significant difference with respect to publication bias (std diff in means = 0.054, CI 95%: 2.116 to 2.941, p value:0.000001). Figure 6 shows that the X-axis shows std diff in mean in the funnel diagram, and the Y-axis reflects standard error.

Discussion

The aim of this systematic review is to establish the effect of CDSS on patient outcomes and physician performance. Figures 7 and 8 show the number of studies associated with each country and type of CDSS. The effect of CDSS was measured using different methods in included studies. In most cases, the effect of these programs on physician performance and patient outcomes was positive, and in others, it was ineffective.

The results show that the use of CDSSs in cardiovascular patients has positive effects on physician performance through increasing the prescription of anticoagulants, anti-inflammatory drugs, anti-thrombotic drugs, lipid-lowering drugs, blood pressure drugs, cardiovascular drugs recommended for the reduction of cardiovascular diseases in patients with diabetes, observing clinical guidelines, and improving the quality of patients [17, 19, 20, 61]. The results of the current study are consistent with the results of Brokel et al. and Duke et al. in reducing inadequate prescriptions and enhancing the process of observing clinical guidelines in the positive effect of CDSS [51, 62]. The system's user-friendliness and low running cost of CDSS resulted in system efficiency in the care delivery process [17, 19, 20, 61].

However, the study results showed that using CDSSs for cardiac patients did not affect the physician performance in a number of outcomes such as physician conduct in prescribing drugs, the warfarin treatment system, minimizing dissatisfaction with guidelines for antithrombotic diagnosis, and job satisfaction [18, 20-22]. The results of this study are also consistent with Byrnes and Lazaro studies that discussed that clinical factors and treatment issues were the reasons for physicians' disagreement with system recommendations [63, 64]. The main reason that no change was found in medical guidance disputes was the difficulty of clinical conditions which could increase the risk of patient injury and hinder the decision-making process [18, 20-22].

The results of this study indicate that the use of CDSSs in cardiovascular patients has a positive effect on a number of outcomes such as adherence to drug use by patients and following a nutrition-based diet in the Mediterranean [23, 24]. Similarly, according to clinical guidelines and reminders, the Schedlbauer et al.’s study evaluated the effect of CDSS on cardiovascular patient outcome as positive [65]. The reason for low Mediterranean diet adherence was the delivery of a short message outlining the advantages of the Mediterranean diet, which resulted in an improved conformity level [23, 24].

The study also showed that the use of CDSS in cardiovascular patients did not affect patient outcomes such as readmission rate, mortality or smoking cessation [23, 24]. Similarly, the findings of Simpson et al.'s study indicate that accurate compliance with the Short Message System (SMS) reduces mortality risk and has improved health outcomes in close relationship with patients [66]. One of the reasons for the negligible reduction in mortality is the short duration of the study, small sample size, and inability to identify causes of mortality [23, 24]. Study results show that using CDSS in patients with hypertension in adherence to clinical guidelines and laboratory tests has a positive effect on physician behavior [26]. Zwart et al.'s study, which is consistent with the results of this study, assessed the impact of CDSS on adherence to clinical guidelines. The study reported effective results about the treatment for pregnant women with hypertensive disorders [67]. In addition, physicians' awareness about special care during pregnancy for hypertension resulted in more patient care and adherence to CDSS [26].

Based on the results of this research, the use of CDSS in diabetic patients has a positive effect on physician performance in a number of outcomes such as adjusting the form of insulin and improving the quality of decision-making about statin prescription [27, 28, 31]. The findings of Den Ouden et al.'s and Mann et al.'s studies are consistent with the results of our research which suggest physicians' strong adherence to CDSS, enhanced statin prescribing, and improved quality of care [68, 69]. In fact, the CDSS can dynamically recommend the insulin dose based on the rounds of previous days, the type of insulin injected, and the glucose level of the patient on the day before [27, 28, 31].

The results of this study indicate that the use of CDSS in diabetic patients has a positive effect on a variety of patient outcomes such as adherence to the nutritional diet of patients with diabetes type two and taking the missed dose of medication [29, 30]. Meanwhile, the results of this study are consistent with Vervloet et al.'s and Krishna et al.'s systematic review on the positive effect of CDSS fitted with alerts on patients with diabetes [70, 71]. The main reason for the effect of CDSS on improving patient adherence seems to be due to the fact that it raises awareness in patients in taking medication [29, 30].

Also, the results of this study show that the use of CDSS in digestive disorders has a positive effect on the physician performance in a variety of outcomes such as the standard use of oral rehydration solution, the prescription of non-steroidal anti-inflammatory drugs and proton pump inhibitors in normal and high-risk patients, and the provision of care services in line with the guidelines for primary care [32-34]. The results of this study are also consistent with the findings of Nicastro, reporting the positive effects of the system on the behavior of physicians such as adherence to clinical guidelines and prescription of drugs [72]. The reason for the positive effect of CDSS on the prescription of non-steroidal anti-inflammatory drugs and proton pump inhibitors in healthy and high-risk patients and the use of oral rehydration solution was the systems' recommendations relating to the above-mentioned drugs and their previous knowledge [32-34].

The results of this study also showed that the use of CDSS in respiratory patients has a positive effect on physician performance and reduced antibiotic prescription [35-39]. The results of this study are thus consistent with the findings of Mcdermott et al.'s and Butler et al.'s results on the positive effect of CDSS on the self-efficacy of physicians in managing chronic respiratory patients and reducing prescription of antibiotics [73, 74]. We think that the reason for the system's positive effect on the self-efficacy of physicians was their tendency to cooperate on decision-making and not to receive mandatory CDSS recommendations [35-39].

With respect to respiratory patients, the results of this study show that the use of CDSS has a positive effect on some patient outcomes such as reduced antibiotic resistance and a reduction in antibiotic prescription [35, 40]. Similarly, Steinman and Hebert studies show reduced antibiotic resistance [75, 76]. The explanation for the effect of CDSS on reducing irrational prescription of antibiotics and reducing resistance was the patient-physicist collaboration with the aid of CDSS guideline which played a significant role in the prescription of drugs [35, 40].

When it comes to appendicitis, the results of our study indicate that the use of CDSS has a positive effect on the physician performance in certain outcomes such as performance, quality, and safety with the aid of physicians’ computerized order entry [42]. The results of this study are in line with Holden's report, which explores how doctors, who use the order entry system, get more up-to-date information and boost the system's ability [77]. Although prescriptions are not strong in terms of content, errors are reduced as they cause physicians to think about the cases [42].

The results also show that the use of CDSS in kidney patients has a positive effect on the behavior of physicians in some outcomes such as reduced dosage of inadequately prescribed drug and improved rate of adequate prescription [43, 44]. Such findings are consistent with Bates et al.’s and Chertow et al.’s studies which show the positive effect of CDSS alerts in modifying insufficient prescriptions and increasing the recommended level of inadequate dosage [78, 79]. Timeline of CDSS alerts was the main reasons for the success of CDSS in prescribing adequate drugs and correct dosage [43, 44].

Based on the results of our study, the use of CDSS in patients with a high level of blood potassium has a positive effect on the behavior of physicians in some outcomes such as the faster response of physicians in the intervention group to system alerts and reminders [52]. Our research results are consistent with Paterno et al.’s and Helmous et al.’s reports which show that physicians’ adherence to alerts improved by 19 percent [80, 81]. A main reason for the success of CDSS on the positive effect of physician behavior was uninterrupted alerts and reminders [52].

Results of the study showed that the use of CDSS in prescribing drugs for patients has a positive effect on physician performance in certain outcomes such as drug prescription for proton pump inhibitors, CDSS productivity and usability, reducing side effects of drugs, and improving the learning rate and skills of physicians [4, 5, 54-56]. The results of this study are consistent with the results of Curtis and Shah et al.’s study indicating that relevant CDSS, while providing users with performance-related information, reduces patients' harms and errors, and increases physicians’ enhanced knowledge and skills [82, 83]. One of the main reasons for the proton pump's enhanced medication performance was the monitoring of physicians’ prescribed drug dose as well as equipping pharmacies with CDSS with hard alerts which reduce costs and improved usability [4, 5, 54-56].

Results show that the use of CDSS in prescribing a number of drugs has a positive effect on the physicians performance in some outcomes such as number of emergency ward visits, number of re-hospitalizations, and determination and supervision of the amount of drugs including the initial dose [46, 47]. The results are consistent with Vincent and Cordero's research which demonstrates that combining the computerized order entry process with an alert system saves time in prescribing and optimizing the dosage of drugs [84, 85]. The reason for CDSS' positive effect on the number of re-hospitalizations, emergency ward visits, and reduced morbidity rate was due to the fact that CDSS had knowledge base in pharmacogenetics and was equipped with drug interaction alerts [46, 47].

Analysis of the results of the reviewed studies shows that the use of CDSS in prescribing a number of drugs has no effect on the physician performance in outcomes such as drug prescription rates with drug suitability index, average functional status outcome, and drug complexity index [45, 48, 49]. Our study results are consistent with Olsson's study which suggest that CDSS for elderly people, who use multiple types of medicines, has no effect on important outcomes [86]. We think that the unexpected findings of our research could be attributed to the lack of information for patients with serious infections who require immediate care and the lack of relevance of the checklist given for the drug problems of patients [45, 48, 49].

Outcome analysis

Figure 9 shows the meta-analysis results for outcome categories and the total analysis. The pooled std diff in means of p values did not show a significant difference between CDSS and the control group (std diff in means = 0.0110, 95% CI: 0.086 to 0.138, standard error = 0.013). 95% CI for the effectiveness was drawn for each study in the horizontal line format (Q = 209.2, df = 45, p value= 0.0003, I^2 = 78.492, Tau^2: 0.004). The findings indicate that heterogeneity improved considerably after sensitivity analysis (Fig10). (Q = 164, df = 41, p value = 0.0002, I^2 = 75, Tau^2: 0.003). After this change, the overall effects of clinical decision support system for prescribing medication on patient outcomes and physician practice performance based on the random effect model was determined to be: (std diff in means = 0.114, 95% CI: 0.090 to 0.138) that is significantly different.

The outcome analysis showed a significant difference between CDSS and control groups for the categorization of outcomes such as patient outcome improved: (std diff in means = 0.435, 95% CI: 0.122 to 0.747); physician practice performance improved: (std diff in means = 0.105, 95% CI: 0.78 to 0.133); physician practice performance and patient outcome improved: (std diff in means = 0.196, 95% CI: 0.111 to 0.281); physician practice performance didn't improve: (std diff in means = 0.131, 95% CI: 0.040 to 0.222). The outcome analysis did not show a significant difference between CDSS and control groups for the category of patient outcome which didn't improve: (std diff in means = 0.064, 95% CI: -0.038 to 0.165).

Conclusion

This systematic review study was conducted with the aim of identifying the effect of CDSS on patient outcomes and physician performance. The results show that the use of CDSS in some diseases has positive effects on the outcomes of patients and physician performance, while it has no significant effect on others. In addition, the type of outcomes and the effects of CDSS on the diseases are different. Using this technique in some cases yields positive results for patients and physician, while in some other cases it demonstrates no significant difference compared to those of conventional methods. The positive effect of CDSS seems to be due to factors such as user-friendliness of the system, the number of patients requiring treatment, the rate of observance of clinical guidelines, conformity of clinical guidelines and data registry, the rate of patients' accurate adherence to messages of the system, usefulness of short messages, the existence of algorithms with dynamic functioning based on patient data, existence of patient medical records, and the relationship between electronic health records with CDSS and timely alerts of the system in the prescribing process. In addition, the positive effect of CDSS depends on a number of other factors such as having an instruction section, not being confronted with mandatory recommendations, patient and physician cooperation with the help of CDSS guidelines, not lagging between alerts where the alert is of low importance, the identification of important alerts, equipping pharmacies with CDSS and system applicability, and considering the opinions of physicians when assessing the value of alerts and notifications for drug interaction.

Abbreviations

CDSS: Clinical Decision Support System; MeSH: Medical Subject Headings; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; MRC: UK Medical Research Council; RTMM: Real Time Medication Monitoring system; PAID: Problem Areas in Diabetes; MMAI: Modified Medication Appropriateness Index; SMS: Short Message System; RCT: Randomized Control Trial

Declarations

Ethics approval and consent to participate

Before collecting the data for the present study, authors obtained the Code of Ethics from Ethics Committee for University Research, Iran University of Medical Sciences.

All stages of research were conducted by two independent researchers.

During the research project, all papers related to the accuracy of the method were identified and analyzed.

Consent to publish

There is not any individual person's data in any form in this research.

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

The authors declare that *there is no* financial and non-financial competing interests associated with this research.

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Authors' contributions

TM and FV searched the literature, extracted the information, and discussed it. FS convinced the PRISMA result, reviewed the contradictions and organized the entire outcome. SP helped analyze the clinical outcomes. The statistical analysis and meta-analysis was performed by TM. SE assisted in the writing process and language editing. All authors read and approved the final manuscript.

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Figures

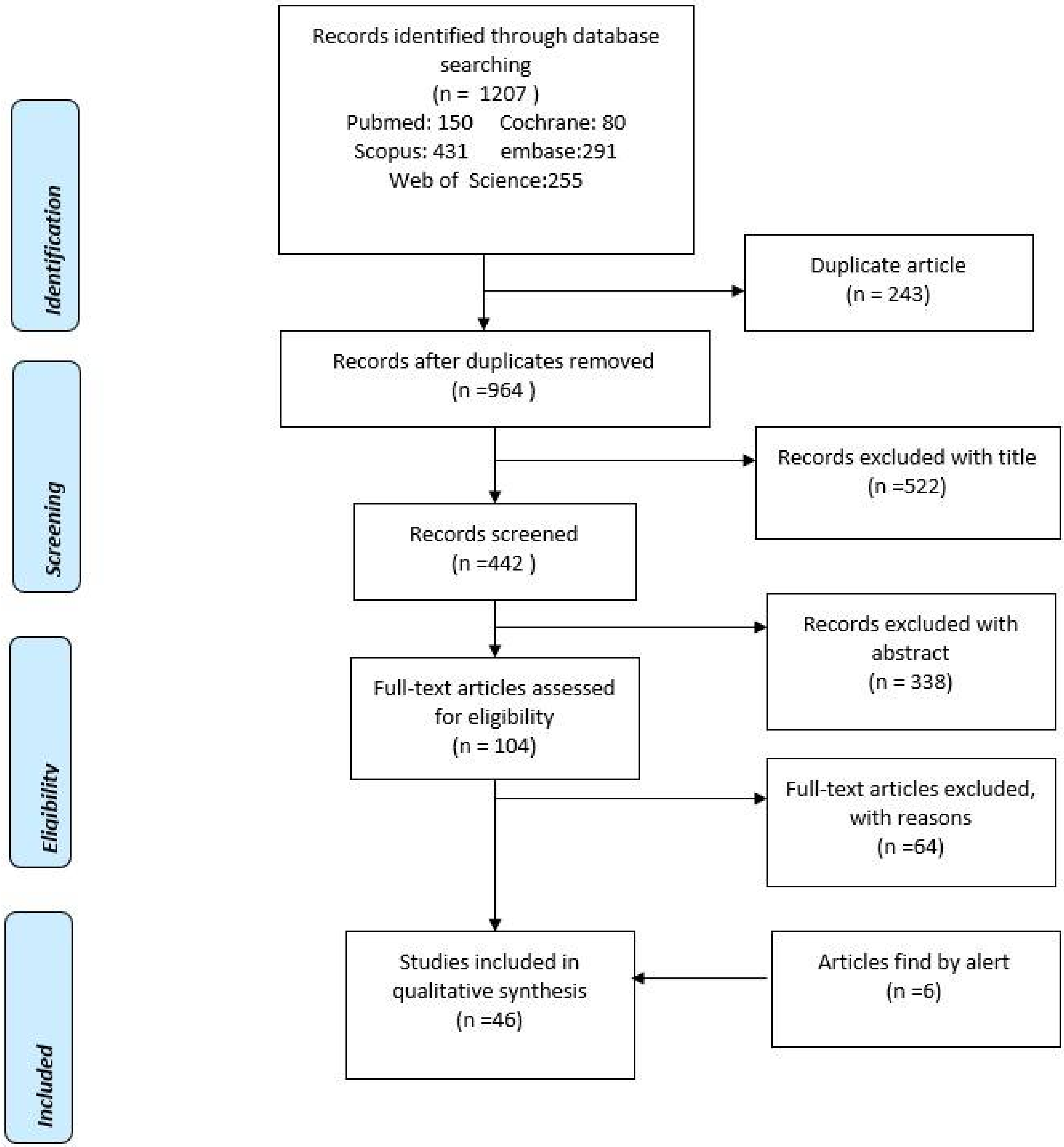

Figure 1

Algorithm of screening articles based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

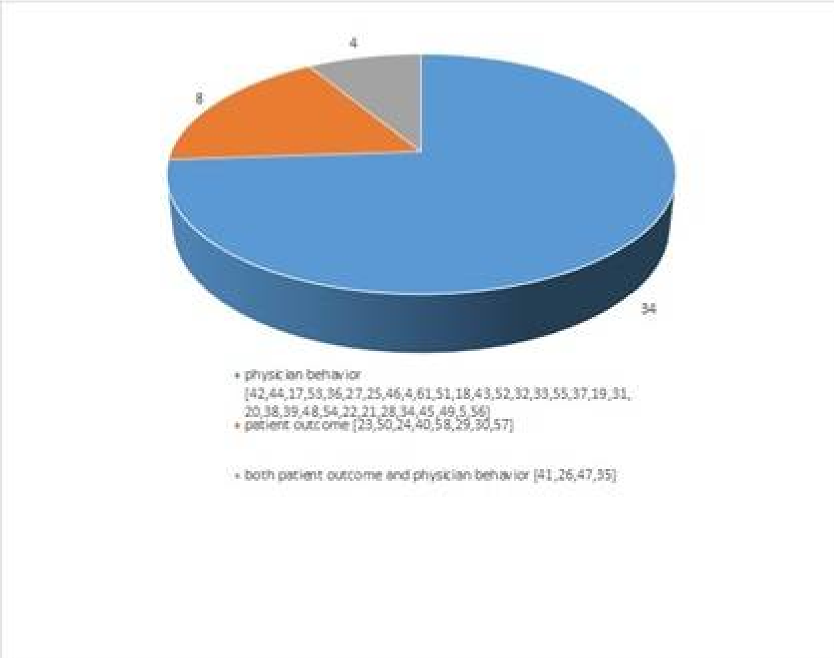

Figure 2

The number of studies based on several evaluating outcomes

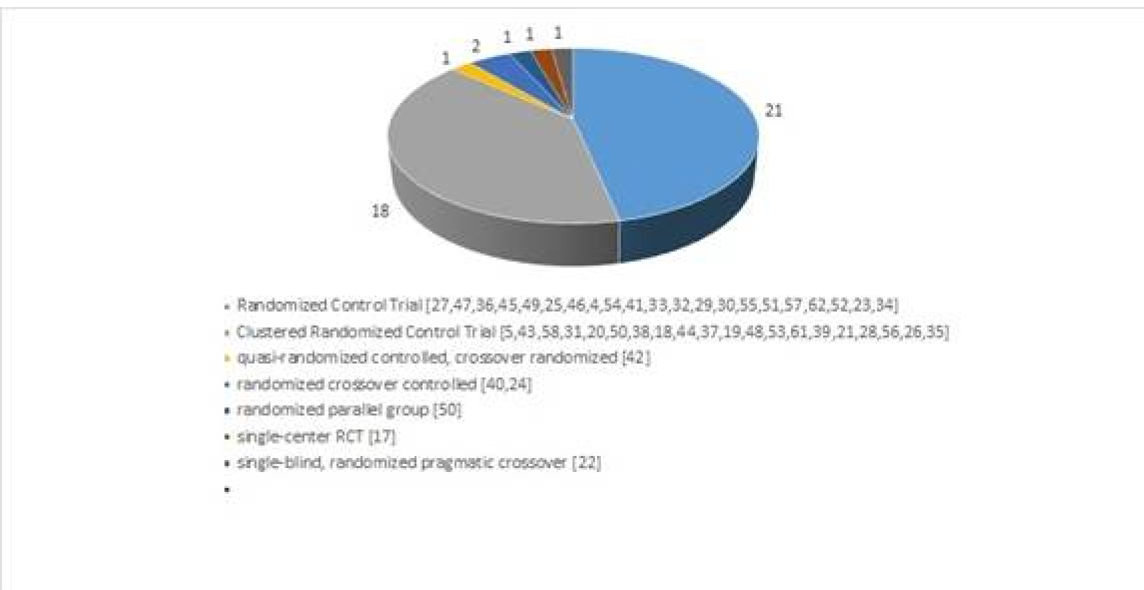

Figure 3

Type of included studies

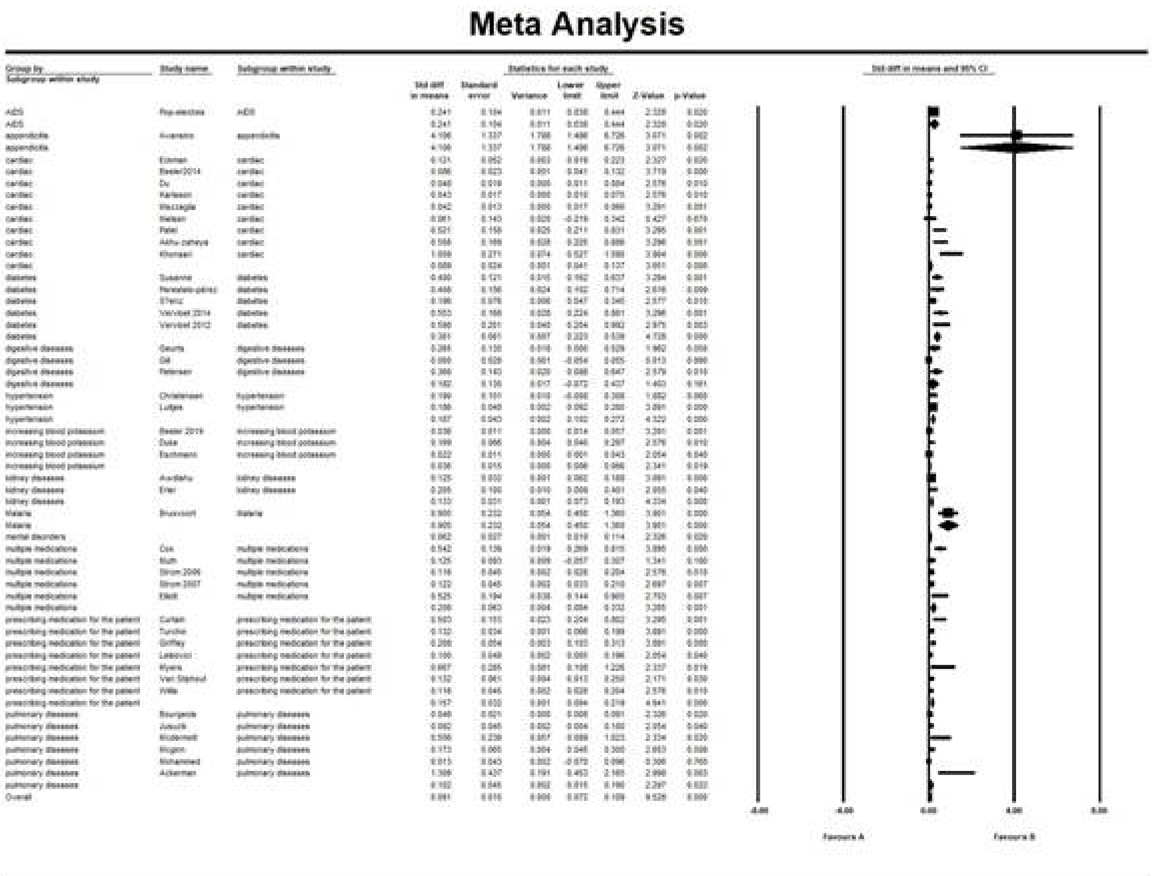

Figure 4

Forest plot of the overall effect of CDSS for prescribing on physician practice performance and patient outcome based on subgroup analysis. CI: confidence interval.

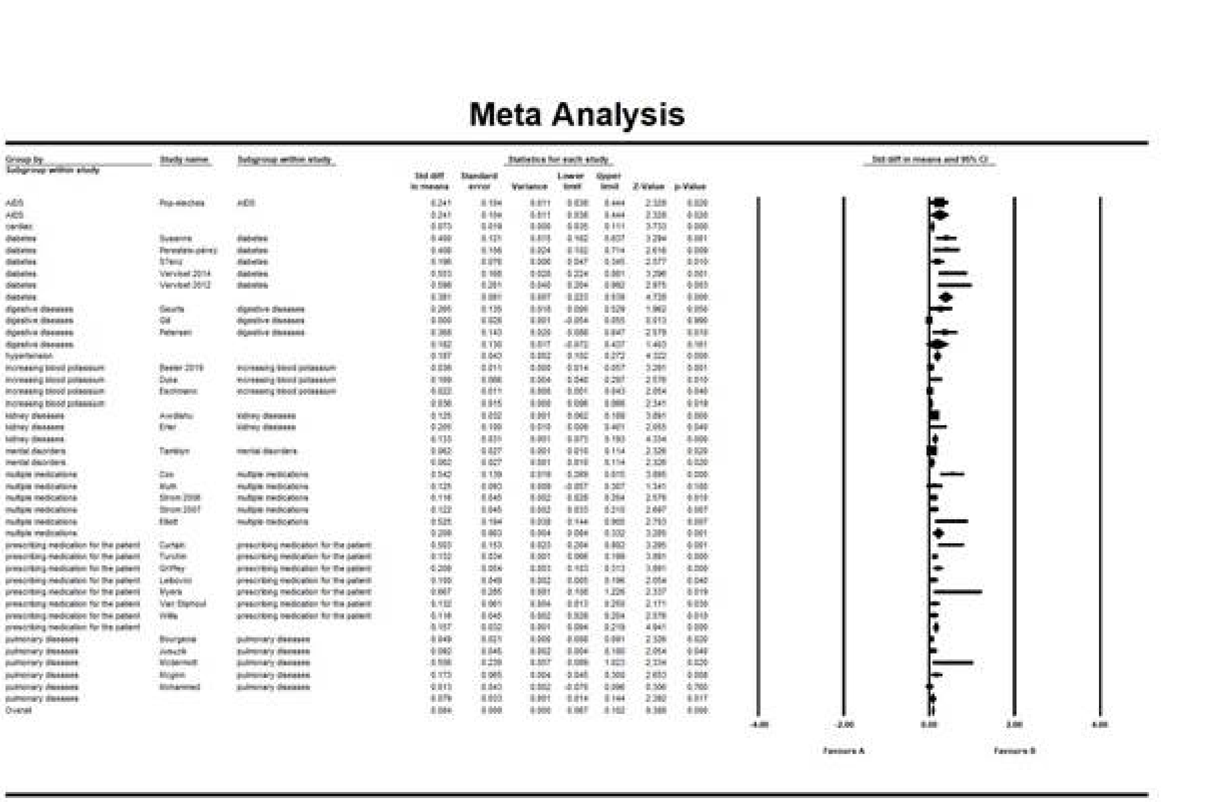

Figure 5

Forest plot of the overall effect of CDSS for prescribing on physician practice performance and patient outcome based on subgroup analysis. (excluded Bruxvoort, K. et al; Ackerman, S. et al; Avansino, J. et al and khonsari, S. et al studies)

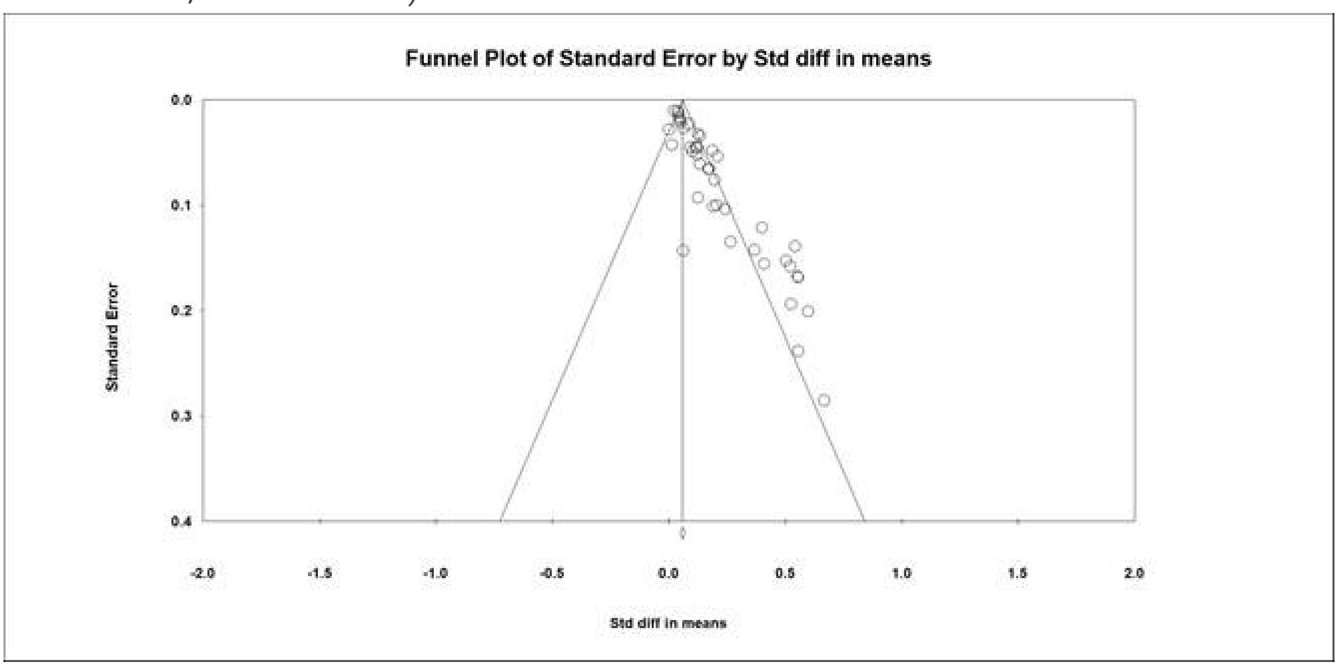

Figure 6

Funnel plot of standard error by std diff in means

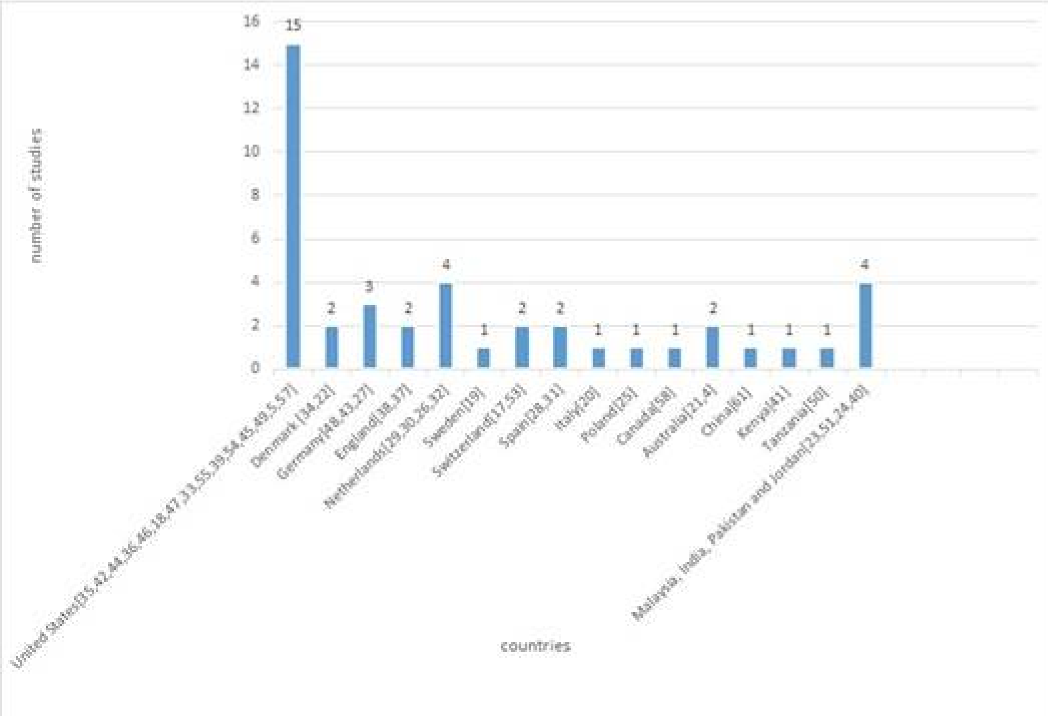

Figure 7

The number of studies associated with each country

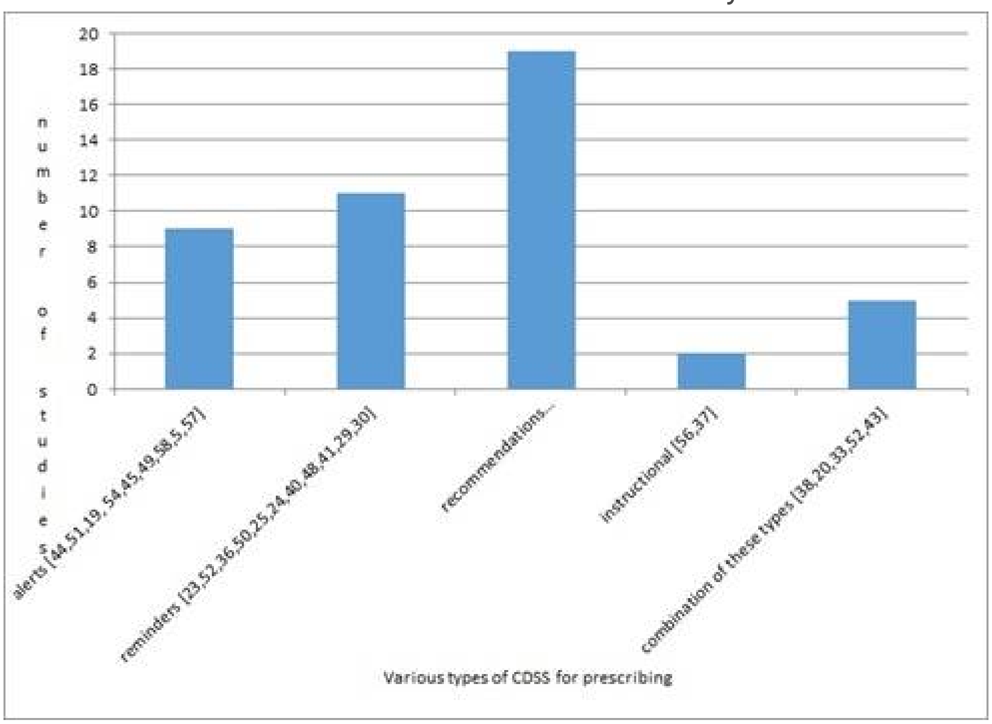

Figure 8

The number of studies associated with each CDSS type

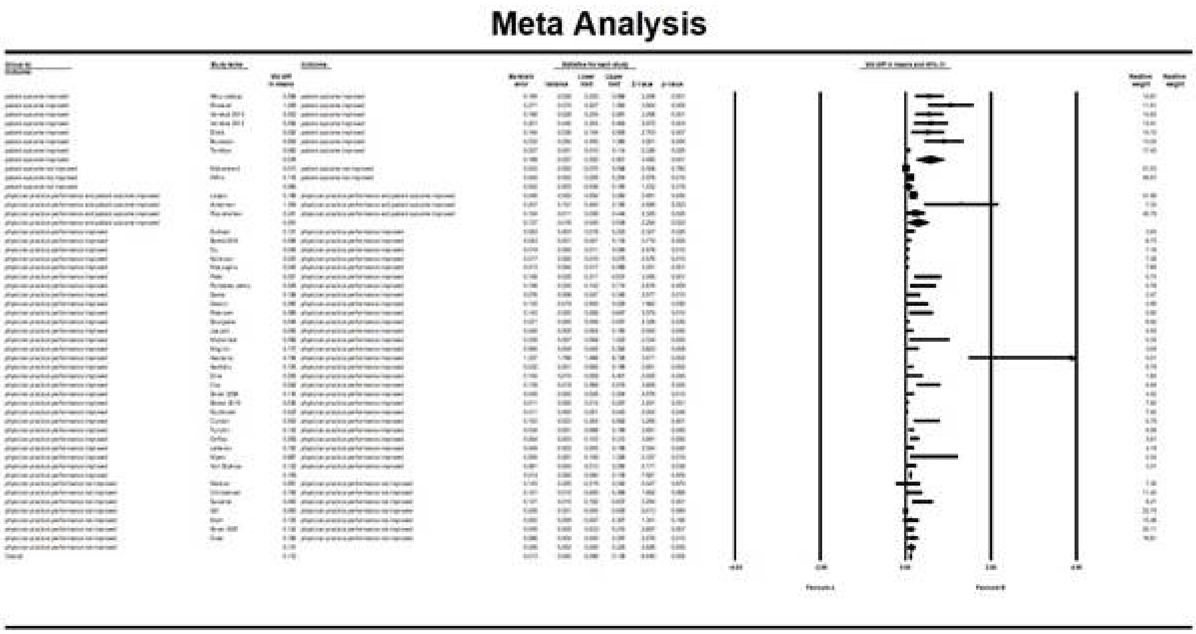

Figure 9

Forest plot of the overall effect of CDSS for prescribing on physician practice performance and patient outcome based on outcome categorization

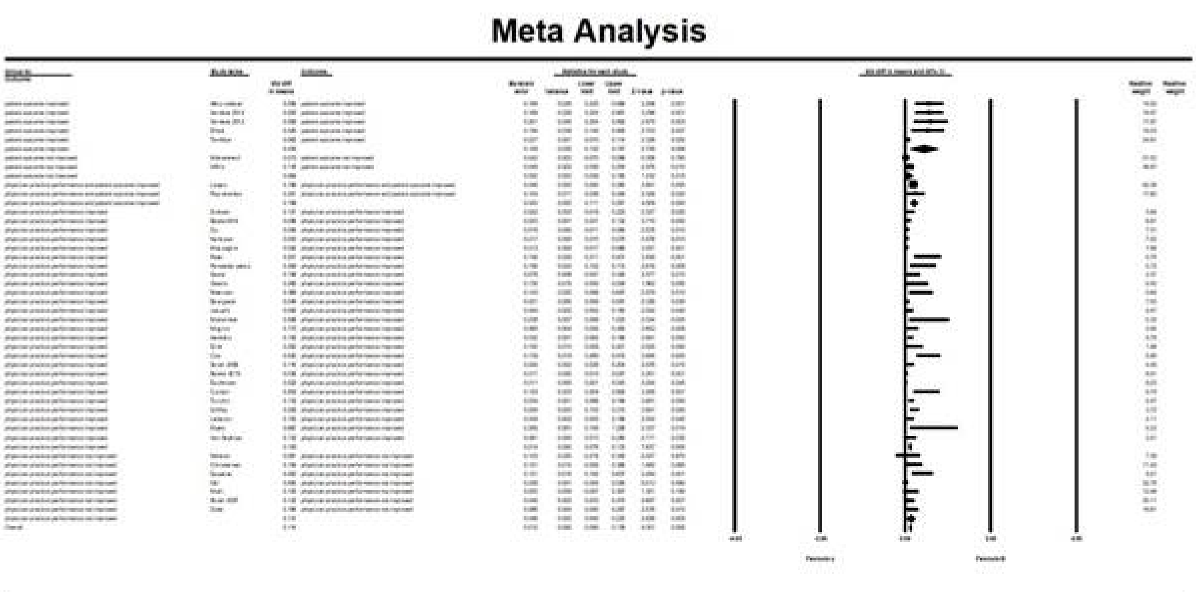

Figure 10

Forest plot of the overall effect of CDSS for prescribing on physician practice performance and patient outcome based on outcome categorization. (excluded Bruxvoort, K. et al; Ackerman, S. et al; Avansino, J. et al and khonsari, S. et al studies)