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

Sharare Taheri Moghadam
Iranshahr University of Medical Sciences
Farnia Velayati
Iran University of Medical Sciences
Farahnaz Sadoughi (sadoughi.f@iums.ac.ir)
Iran University of Medical Sciences https://orcid.org/0000-0002-7452-0864
S.J. Ehsanzadeh
Tehran University of Medical Sciences
Shayan Poursharif
Shaheed Beheshti University of Medical Sciences

Research article

Keywords: computerized Clinical Decision Support Systems, Drug prescription, systematic review

Posted Date: March 23rd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-18677/v1

Version of Record: A version of this preprint was published on March 10th, 2021. See the published version at https://doi.org/10.1186/s12911-020-01376-8.

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 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 January 2005 to November 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, data were extracted from the articles; however, we could not able to conduct meta-analysis due to the heterogeneity of the studies and the narrative form of the findings.

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, namely cardiovascular diseases, hypertension, diabetes, gastrointestinal and respiratory diseases, AIDS, appendicitis, kidney disease, malaria, high blood potassium, mental disease. Meanwhile, other cases such as the concurrent prescription of multiple drugs for the patient 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. 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 type of CDSS requirements that influence the comparison.

Conclusions Our findings suggest that the 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.

Registration number on PROSPERO CRD42018079936.

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 and mortality, extended hospital stay, and other common medical errors 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, the 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 with the ability to overcome these deficiencies and provide 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, among other types of CDSS [6]. The advantages of CDSS may include reducing and prevention of prescription errors through using alerts and immediate reminders, automatic dosage error checking, drug interaction and drug interaction. Meanwhile, these advantages will help save the physicians' time which consequently leads to improving the overall efficiency of healthcare system [7].

Most studies have shown an upward trend with respect to the use and effectiveness of CDSSs, compared to usual clinical practices. Accordingly, CDSSs are known to be effective tools for reducing prescription errors. To this end and given the significance of CDSSs, we in the present study examine the effects of CDSSs on physicians' prescription performance and patient outcomes as well.

Methods

The method used in this study was a systematic review. The method section is divided into some subsections, namely Search strategy, Inclusion/exclusion criteria, Screening and data extraction, Quality assessment and data synthesis and presentation. 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) 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. The search was conducted in 2018 using 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 for PubMed is given below:

(("Clinical decision support system" OR "Clinical Decision Support" OR "Information System" OR "hospital information system" OR "Computerized Medical Record system" OR "computer-assisted decision making" OR "reminder system" OR "computer-assisted diagnosis" OR "Clinical Informatics")) AND ("Medical Mistake" OR "medical error" OR "therapeutic error" OR "diagnostic error" OR "drug interaction" OR "drug dose-response relationship" OR "drug administration schedule").

Registration number on PROSPERO was CRD42018079936 available at:" https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=79936" [8].

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 have 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 experts in this field (F.S).

Quality assessment

quality of studies was assessed by the Jadad scale, the Oxford research methods scoring system for bias in clinical trials [9, 10]. We finally reached the conclusion that the results of the quality assessment were acceptable.

Data synthesis and presentation

The data were extracted from eligible articles using a structured data extraction process. Meta-analysis was not possible due to the heterogeneity of the studies; therefore, the results of studies were presented in a descriptive-narrative form. We used PRISMA checklist as a reporting guideline in our study. PRISMA checklist is a known standard checklist for systematic review reports [11].

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 respectively in Figures 2 and 3.

The effect of CDSS on cardiovascular diseases

For patients admitted to hospital, the level of venous thromboembolism prophylaxis and the proportion of prescribed prophylaxis increased from six to 24 hours after admission for clinicians allocated to venous thromboembolism reminder CDSS [12]. In another study, differences among physicians over the thromboprophylaxis treatment effect decreased with the help of CDSS providing treatment recommendation (p-value=0.02) [13]. 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 [14-16]. 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 [17].

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) [18, 19]. Table 1 shows the result briefly.

The effect of CDSS on hypertension

For one study, the electronic monitoring and recall program had no effect on blood pressure reduction and the admission of patients [21]. However, in the other study, the patient outcome improved after the implementation of the CDSS [22]. Table 2 shows the result briefly.

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 [23-26]. In another study, HbA1c and group differences were greater in the intervention group using recommendation CDSS than in the control group [27]. 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 using CDSS [24]. Table 3 shows the result briefly.

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 [28-30]. The alert based CDSS was able to improve the quality of patient care to some degree in the other study [29]. Table 4 shows the result briefly.

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 minimizing inappropriate use of antibiotics (p-value=0.0005), decreasing resistance to antibiotics (p-value=0.04), and enhancing primary care [31-35]. The patients had adhered to the reminder message of using their medication in another study; however, the messages did not affect therapy success [36]. Table 5 shows the result briefly.

The effect of CDSS on AIDS

In the 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) [37]. Table 6 shows the result briefly.

The Effect of CDSS on appendicitis

The study showed that the system's systematically developed order set using 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 method resulted in the Computerized Provider Order Entry (CPOE) improving efficiency, quality and safety [38]. Table 7 shows the result briefly.

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 [39]. In the other study, the appropriate prescription rate for kidney problems was rather low, contrary to the results of the study by the former. Furthermore, the effectiveness of the CDSS equipped with physician guidelines has been increased, especially for new versions [40]. Table 8 shows the result briefly.

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 [41]. 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 [42]. 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 [43]. 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 intervention group using alert or reminder CDSS with control group [44, 45]. Table 9 shows the result briefly.

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 in continuing to use the medication. In addition, text messages had an effect on the physicians' knowledge in using medication with fatty foods (p-value<0.0001) [46]. Table 10 shows the result briefly.

The effect of CDSS on increasing blood potassium

In one study, in following alerts and patient compliance rate, there is no statistical difference between 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) [47]. 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 [48]. 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 use of three different kind of reminder and alert based CDSSs [49]. Table 11 shows the result briefly.

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, 50]. 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, 51]. There was no difference in drug prescription between 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 [52]. In another study, alert based CDSSs have been effective in identifying evidence-based pharmacotherapies (EBP) and the compliance with treatment by health care managers and have had no effect on the outcome of patients [53]. Table 12 shows the result briefly.

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 start of the study up to a year. Therefore, the CDSS reduced the risk of injury (p-value=0.02) [55]. Table 13 shows the result briefly.

Discussion

The aim of this systematic review is to establish the effect of CDSS on patient outcomes and physicians' performance. Figures 4 and 5 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 physicians' performance and patient outcomes was positive and in others was ineffective.

The results show that the use of CDSSs in cardiovascular patients has positive effects on physicians' 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 [12, 14, 15, 20]. 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 [47, 56]. The system's user-friendliness and low running CDSS cost resulted in system efficiency in the care delivery process [12, 14, 15, 20].

However, the study results showed that using CDSSs for cardiac patients did not affect the physicians' performance in a number of outcomes such as physician conduct in prescribing drugs, the warfarin treatment system, and minimizing dissatisfaction with guidelines for antithrombotic diagnosis and job satisfaction [13, 15–17]. The results of this study are consistent with studies by Byrnes and Lazaro who discussed that clinical factors and treatment issues were the reasons for physicians' disagreement with system recommendations [57, 58]. 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 [13, 15–17].

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 [18, 19]. Similarly, according to clinical guidelines and reminders, the study by Schedlbauer et al. evaluated the effect of CDSS on cardiovascular patient outcome as positive [59]. 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 [18, 19].

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 [18, 19]. Similarly, Simpson et al.'s study findings indicate that accurate compliance with the Short Message System (SMS) reduces mortality risk and has improved health outcomes in close relationship with patients [60]. 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 [18, 19]. 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 [22].

Zwart et al.'s study was consistent with the results of this study and assessed the impact of CDSS on adherence to clinical guidelines to be effective in improving treatment for pregnant women with hypertensive disorders [61]. In addition, physicians' awareness about special care during pregnancy for hypertension results in more patient care and adherence to CDSS [22].

Based on the results of this research, use of CDSS in diabetic patients has a positive effect on physicians' performance in a number of outcomes such as adjusting the form of insulin, improving the quality of decision-making about statin prescription [23, 24, 27]. The findings of Den Ouden et al. and Mann et al. studies are consistent with the results of our research, which suggest physicians' strong adherence to CDSS, enhanced statin prescribing, and improved quality of care [62, 63]. 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 [23, 24, 27].

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 [25, 26]. The results of this study are consistent with Vervloet et al. and Krishna et al.'s systematic review of the positive effect of CDSS fitted with alerts on patients with diabetes, assessed and published [64, 65]. The main reason for the effect of CDSS on improving patient adherence was that it caused awareness and greater precision of patients in taking medication. [25, 26].

The results of this study show that the use of CDSS in digestive disorders has a positive effect on the physicians' performance in a number 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 [28–30]. The results of this study are 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 [66]. The reason for the positive effect of CDSS on the prescribing 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 [28–30].

The results of this study also showed that use of CDSS in respiratory patients in some cases such as physician self-efficacy in the management of chronic respiratory patients has a positive effect on physicians' performance and reduced antibiotic prescription [31–35]. The results of this study are consistent with the findings of Mcdermott et al. and Butler et al., noticing with the help of clinical guidelines the positive effect of CDSS on the self-efficacy of physicians in managing chronic respiratory patients and reducing prescription of antibiotics [67, 68]. The reason for the system's positive effect on the self-efficacy of physicians was their tendency to cooperate in decision-making and not to receive mandatory CDSS recommendations [31–35].

The results of this study show that the use of CDSS in respiratory patients has a positive effect on some patient outcomes such as reduced antibiotic resistance and a reduction in antibiotic prescription [31, 36]. Similarly, Steinman and Hebert studies show reduced antibiotic resistance [69, 70]. The explanation for the effect of CDSS in reducing irrational prescription of antibiotics and reducing resistance was the patient-physicist collaboration with the aid of CDSS guidance which played a significant role in the prescription of drugs [31, 36].

The study results indicate that the use of CDSS for appendicitis has a positive effect on the physicians' performance in certain outcomes such as performance, quality and safety with the aid of the physician's computerized order entry [38]. The results of this study are in line with Holden's report, which explores how doctors who use the order entry system get more easily up-to-date information and boost the system's ability to use it [71]. Although prescriptions are not strong in terms of content, errors are reduced as they cause doctors to think about the cases and the data are not selected automatically [38].

The results also show that use of CDSS in kidney patients has a positive effect on the behavior of the physician in some outcomes such as reduced dosage of inadequately prescribed drug and improved rate of adequate prescription [39, 40]. Such findings are consistent with Bates et al. and Chertow et al. studies, showing the positive effect of CDSS alerts in modifying insufficient prescriptions and increasing the recommended level of inadequate dosage [72, 73]. Timeliness of the CDSS alerts was among reasons for the success of CDSS in prescribing adequate drugs and correct dosage [39, 40].

Based on the results of our study, use of CDSS in patients with high blood potassium has a positive effect on the behavior of doctors in some outcomes such as the faster response of doctors in the intervention group to system alerts and reminders [48]. The research results are consistent with Paterno et al. and Helmous et al. reports which show that doctor adherence to alerts improved by 19 percent insulin [74, 75]. Among reasons for the success of CDSS on the positive effect of physician behavior were uninterrupted alerts and reminders [48].

Results of the study showed that use of CDSS in prescribing drugs for patients has a positive effect on physicians' 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, 50–52]. The results of this study are consistent with the results of Curtis and Shah et al. which indicated that relevant CDSS, while providing users with performance-related information, reduces patients' harms and errors, and increases the physician's enhanced knowledge and skills [76, 77]. One of the main reasons for the proton pump's enhanced medication performance was the monitoring of the physician's prescribed drug dose, as well as equipping pharmacies with CDSS with hard alerts which reduced costs and improved usability [4, 5, 50–52].

Results show that 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, determination and supervision of the amount of drugs including the initial dose [42, 43]. 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 [78, 79]. The reason for CDSS ' positive effect on the number of re-hospitalizations, emergency ward visits, and reduced morbidity rate was that CDSS had knowledge base in pharmacogenetics and was equipped with drug interaction alerts [42, 43].

Analysis of the results of the reviewed studies shows that use of CDSS in prescribing a number of drugs has no effect on the physicians' performance in outcomes such as drug prescription rates with drug suitability index and average functional status outcome and drug complexity index [41, 44, 45]. Our study results are consistent with Olsson, suggesting that CDSS for elderly people who use multiple types of medicines has no effect on important outcomes when prescribing medicines [80]. The explanation for the incidence of unexpected findings in this research was the lack of information for patients with serious infections requiring immediate care and the lack of relevance of the checklist given for the drug problems of the patient [41, 44, 45].

Conclusion

This systematic review study was conducted with the aim of identifying the effect of CDSS on patient outcomes and physicians' performance. The results show that use of CDSS in some diseases has positive effects on the outcomes of patients and the physicians' performance as well, while it has no significant effect on others. In addition, the type of outcomes and the effects of CDSS on the disease are different. Using this technique in some cases yields positive results in patients and doctors, while in others 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, useful short messages, the existence of algorithms with dynamic functioning based on patient data, existence of patient medical records, 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 and the identification of important alerts, equipping pharmacies with CDSS and system applicability, considering the opinions of doctors when assessing the value of alerts and notifications for drug interaction.

Limitation

The selected papers in this study were about different diseases; therefore, we had to have different process design, results and evaluation criteria which made it impossible for us to conduct a meta-analysis. The results are therefore presented in a narrative form.

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.

- **Funding**

There was no funding resource for this study.

- **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. SE assisted in the writing process and language editing. SP helped analyze the clinical outcomes. All authors read and approved the final manuscript.

- **Acknowledgment**

This article is a research project entitled "The effects of clinical decision support system for prescribing medication on patient outcomes and physician practice performance: A systematic review", approved by

Iran University of Medical Science (IUMS), in March 2018 with the ethical code "IR.IUMS.REC 1396.32465". Also, we thank Professor Brian Haynes for his valuable comments.

References

1. Leape L, Berwick D, Clancy C, Conway J, Gluck P, Guest J, et al. Transforming healthcare: a safety imperative. BMJ Quality & Safety. 2009;18(6):424-8.
2. Hemens BJ, Holbrook A, Tonkin M, Mackay JA, Weise-Kelly L, Navarro T, et al. Computerized clinical decision support systems for drug prescribing and management: a decision-maker-researcher partnership systematic review. Implementation Science. 2011;6(1):89.
3. Moghadasi H, SHEYKH TA, HASHEMI N. Reducing medication errors: Role of computerized physician order entry system. 2007.
4. Curtain C, Peterson GM, Tenni P, Bindoff IK, Williams M. Outcomes of a decision support prompt in community pharmacy-dispensing software to promote step-down of proton pump inhibitor therapy. Br J Clin Pharmacol. 2011;71(5):780-4.
5. Turchin A, James OD, Godlewski ED, Shubina M, Coley CM, Gandhi TK, et al. Effectiveness of interruptive alerts in increasing application functionality utilization: A controlled trial. J Biomed Inform. 2011;44(3):463-8.
6. Moore M, Loper KA. An introduction to clinical decision support systems. Journal of Electronic Resources in Medical Libraries. 2011;8(4):348-66.
7. Scott GPT, Shah P, Wyatt JC, Makubate B, Cross FW. Making electronic prescribing alerts more effective: Scenario-based experimental study in junior doctors. Journal of the American Medical Informatics Association. 2011;18(6):789-98.
8. Sharare Taheri Moghadam FS, Brian Haynes. PROSPERO, International prospective register of systematic reviews.
9. Chalmers TC, Smith Jr H, Blackburn B, Silverman B, Schroeder B, Reitman D, et al. A method for assessing the quality of a randomized control trial. Controlled clinical trials. 1981;2(1):31-49.
10. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled clinical trials. 1996;17(1):1-12.
11. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Annals of internal medicine. 2009;151(4):264-9.
12. Beeler P, Eschmann E, Schumacher A, Studt J, Amann-Vesti B, Blaser J. Impact of electronic reminders on venous thromboprophylaxis after admissions and transfers. Journal of the American Medical Informatics Association : JAMIA. 2014;21(e2):e297-e303.
13. Eckman MH, Lip GY, Wise RE, Speer B, Sullivan M, Walker N, et al. Impact of an atrial fibrillation decision support tool on thromboprophylaxis for atrial fibrillation. Am Heart J. 2016;176:17-27.

14. Karlsson LO, Nilsson S, Bång M, Nilsson L, Charitakis E, Janzon M. A clinical decision support tool for improving adherence to guidelines on anticoagulant therapy in patients with atrial fibrillation at risk of stroke: A cluster-randomized trial in a Swedish primary care setting (the CDS-AF study). PloS Med. 2018;15(3).
15. Mazzaglia G, Piccinni C, Filippi A, Sini G, Lapi F, Sessa E, et al. Effects of a computerized decision support system in improving pharmacological management in high-risk cardiovascular patients: A cluster-randomized open-label controlled trial. Health Inform J. 2016;22(2):232-47.
16. Patel B, Usherwood T, Harris M, Patel A, Panaretto K, Zwar N, et al. What drives adoption of a computerised, multifaceted quality improvement intervention for cardiovascular disease management in primary healthcare settings? A mixed methods analysis using normalisation process theory. Implementation Science. 2018;13(1):140.
17. Nielsen PB, Lundbye-Christensen S, van der Male M, Larsen TB. Using a personalized decision support algorithm for dosing in warfarin treatment: A randomised controlled trial. Clin Trials Regul Sci Cardiol. 2017;25:1-6.
18. Akhu-Zaheya LM, Shiyab WY. The effect of short message system (SMS) reminder on adherence to a healthy diet, medication, and cessation of smoking among adult patients with cardiovascular diseases. Int J Med Inform. 2017;98:65-75.
19. Khonsari S, Subramanian P, Chinna K, Latif LA, Ling LW, Gholami O. Effect of a reminder system using an automated short message service on medication adherence following acute coronary syndrome. Eur J Cardiovasc Nurs. 2015;14(2):170-9.
20. Du J, Rao C, Zheng Z, Group MC. P1701 Randomized cluster trial to improve guideline-adherence of secondary preventive drugs prescription after coronary artery bypass grafting in China. European Heart Journal. 2018;39(suppl_1):ehy565. P1701.
21. Christensen A, Christrup LL, Fabricius PE, Chrostowska M, Wronka M, Narkiewicz K, et al. The impact of an electronic monitoring and reminder device on patient compliance with antihypertensive therapy: a randomized controlled trial. J Hypertens. 2010;28(1):194-200.
22. Luitjes SHE, Hermens R, de Wit L, Heymans MW, van Tulder MW, Wouters M. An innovative implementation strategy to improve the use of Dutch guidelines on hypertensive disorders in pregnancy: A randomized controlled trial. Pregnancy hypertension. 2018;14:131-8.
23. Buhse S, Kuniss N, Liethmann K, Müller UA, Lehmann T, Mühlhauser I. Informed shared decision-making programme for patients with type 2 diabetes in primary care: cluster randomised controlled trial. BMJ open. 2018;8(12):e024004.
24. Perestelo-Pérez L, Rivero-Santana A, Boronat M, Sánchez-Afonso J, Pérez-Ramos J, Montori V, et al. Effect of the statin choice encounter decision aid in Spanish patients with type 2 diabetes: a randomized trial. Patient Educ Couns [Internet]. 2016; 99(2):[295-9 pp.].
25. Vervloet M, van Dijk L, de Bakker DH, Souverein PC, Santen-Reestman J, van Vlijmen B, et al. Short- and long-term effects of real-time medication monitoring with short message service (SMS)

reminders for missed doses on the refill adherence of people with Type 2 diabetes: Evidence from a randomized controlled trial. Diabet Med. 2014;31(7):821-8.

26. Vervloet M, van Dijk L, Santen-Reestman J, van Vlijmen B, van Wingerden P, Bouvy ML, et al. SMS reminders improve adherence to oral medication in type 2 diabetes patients who are real time electronically monitored. Int J Med Inform. 2012;81(9):594-604.
27. Sáenz A, Brito M, Morón I, Torralba A, García-Sanz E, Redondo J. Development and validation of a computer application to aid the physician's decision-making process at the start of and during treatment with insulin in type 2 diabetes: a randomized and controlled trial. J Diabetes Sci Technol. 2012;6(3):581-8.
28. Geurts D, de Vos-Kerkhof E, Polinder S, Steyerberg E, van der Lei J, Moll H, et al. Implementation of clinical decision support in young children with acute gastroenteritis: a randomized controlled trial at the emergency department. Eur J Pediatr. 2017;176(2):173-81.
29. Gill JM, Mainous AG, Koopman RJ, Player MS, Everett CJ, Chen YX, et al. Impact of EHR-based clinical decision support on adherence to guidelines for patients on NSAIDs: a randomized controlled trial. Ann Fam Med. 2011;9(1):22-30.
30. Petersen J, Jarbol D, Hallas J, Munch M, Schaffalitzky DMO, Hansen J. Can the use of a computer decision support system prevent complicated ulcer among patients treated with NSAID or aspirin? a randomised controlled cluster trial in general practice. UNITED EUR GASTROENT Conference: 25th united european gastroenterology week, UEG 2017 Spain [Internet]. 2017; 5(5 Supplement 1):[A806 p.].
31. Ackerman S, Gonzales R, Stahl M, Metlay J. One size does not fit all: evaluating an intervention to reduce antibiotic prescribing for acute bronchitis. BMC Health Serv Res [Internet]. 2013; 13:[462 p.].
32. Bourgeois FC, Linder J, Johnson SA, Co JP, Fiskio J, Ferris TG. Impact of a computerized template on antibiotic prescribing for acute respiratory infections in children and adolescents. Clin Pediatr (Phila). 2010;49(10):976-83.
33. Juszczyk D, Charlton J, Gulliford M. Incorporating electronic health records data into efficient trial interventions-cluster randomised trial to reduce antibiotic prescribing in primary care. Trials Conference: 4th international clinical trials methodology conference , ICTMC and the 38th annual meeting of the society for clinical trials United kingdom [Internet]. 2017; 18(Supplement 1) (no pagination).
34. McDermott L, Yardley L, Little P, Van Staa T, Dregan A, McCann G, et al. Process evaluation of a point-of-care cluster randomised trial using a computer-delivered intervention to reduce antibiotic prescribing in primary care. BMC Health Serv Res. 2014;14(1).
35. McGinn TG, McCullagh L, Kannry J, Knaus M, Sofianou A, Wisnivesky JP, et al. Efficacy of an evidence-based clinical decision support in primary care practices: a randomized clinical trial. JAMA Intern Med. 2013;173(17):1584-91.
36. Mohammed S, Glennerster R, Khan AJ. Impact of a daily SMS medication reminder system on tuberculosis treatment outcomes: A randomized controlled trial. PLoS ONE. 2016;11(11).

37. Pop-Eleches C, Thirumurthy H, Habyarimana JP, Zivin JG, Goldstein MP, De Walque D, et al. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. AIDS (London, England). 2011;25(6):825.
38. Avansino J, Leu MG. Effects of CPOE on provider cognitive workload: A randomized crossover trial. Pediatrics. 2012;130(3):e547-e52.
39. Erler A, Beyer M, Petersen JJ, Saal K, Rath T, Rochon J, et al. How to improve drug dosing for patients with renal impairment in primary care - A cluster-randomized controlled trial. BMC Fam Pract. 2012;13.
40. Awdishu L, Coates CR, Lyddane A, Tran K, Daniels CE, Lee J, et al. The impact of real-time alerting on appropriate prescribing in kidney disease: A cluster randomized controlled trial. Journal of the American Medical Informatics Association : JAMIA. 2016;23(3):609-16.
41. Strom BL, Schinnar R, Aberra F, Bilker W, Hennessy S, Leonard CE, et al. Unintended effects of a computerized physician order entry nearly hard-stop alert to prevent a drug interaction: A randomized controlled trial. Arch Intern Med. 2010;170(17):1578-83.
42. Cox ZL, Nelsen CL, Waitman LR, McCoy JA, Peterson JF. Effects of clinical decision support on initial dosing and monitoring of tobramycin and amikacin. American Journal of Health-System Pharmacy. 2011;68(7):624-32.
43. Elliott LS, Henderson JC, Neradilek MB, Moyer NA, Ashcraft KC, Thirumaran RK. Clinical impact of pharmacogenetic profiling with a clinical decision support tool in polypharmacy home health patients: A prospective pilot randomized controlled trial. PLoS One. 2017;12(2):e0170905.
44. Muth C, Uhlmann L, Haefeli WE, Rochon J, van den Akker M, Perera R, et al. Effectiveness of a complex intervention on Prioritising Multimedication in Multimorbidity (PRIMUM) in primary care: results of a pragmatic cluster randomised controlled trial. BMJ open. 2018;8(2):e017740.
45. Strom BL, Schinnar R, Bilker W, Hennessy S, Leonard CE, Pifer E. Randomized clinical trial of a customized electronic alert requiring an affirmative response compared to a control group receiving a commercial passive CPOE alert: NSAIDe-warfarin co-prescribing as a test case. Journal of the American Medical Informatics Association : JAMIA. 2010;17(4):411-5.
46. Bruxvoort K, Festo C, Kalolella A, Cairns M, Lyaruu P, Kenani M, et al. Cluster randomized trial of text message reminders to retail staff in tanzanian drug shops dispensing artemether-lumefantrine: Effect on dispenser knowledge and patient adherence. Am J Trop Med Hyg. 2014;91(4):844-53.
47. Duke JD, Li X, Dexter P. Adherence to drug-drug interaction alerts in high-risk patients: a trial of context-enhanced alerting. Journal of the American Medical Informatics Association : JAMIA. 2013;20(3):494-8.
48. Eschmann E, Beeler P, Blaser J. Impact of Specific Alerts in Potassium-Increasing Drug-Drug Interactions. Stud Health Technol Inform [Internet]. 2015; 216:[949 p.].
49. Beeler PE, Eschmann E, Schneemann M, Blaser J. Negligible impact of highly patient-specific decision support for potassium-increasing drug-drug interactions–a cluster-randomised controlled trial. Swiss Med Wkly. 2019;149(1516).

50. Myers JS, Gojraty S, Yang W, Linsky A, Airan-Javia S, Polomano RC. A randomized-controlled trial of computerized alerts to reduce unapproved medication abbreviation use. Journal of the American Medical Informatics Association. 2011;18(1):17-23.
51. Griffey RT, Lo HG, Burdick E, Keohane C, Bates DW. Guided medication dosing for elderly emergency patients using real-time, computerized decision support. Journal of the American Medical Informatics Association : JAMIA. 2012;19(1):86-93.
52. van Stiphout F, Zwart-van Rijkom J, Versmissen J, Koffijberg H, Aarts J, van der Sijs I, et al. Effects of training physicians in electronic prescribing in the outpatient setting on clinical, learning and behavioral outcomes: a cluster randomized trial. British journal of clinical pharmacology. 2018;84(6):1187-97.
53. Willis JM, Edwards R, Anstrom KJ, Johnson FS, Del Fiol G, Kawamoto K, et al. Decision support for evidence-based pharmacotherapy detects adherence problems but does not impact medication use. Stud Health Technol Inform. 2013;183:116-25.
54. Leibovici L, Kariv G, Paul M. Long-term survival in patients included in a randomized controlled trial of TREAT, a decision support system for antibiotic treatment. Journal of antimicrobial chemotherapy [Internet]. 2013; 68(11):[2664-6 pp.].
55. Tamblyn R, Eguale T, Buckeridge DL, Huang A, Hanley J, Reidel K, et al. The effectiveness of a new generation of computerized drug alerts in reducing the risk of injury from drug side effects: A cluster randomized trial. Journal of the American Medical Informatics Association : JAMIA. 2012;19(4):635-43.
56. Brokel J. Randomised controlled trial: evidence-based clinical decision support improves the appropriate use of antibiotics and rapid strep testing. Evid Based Med [Internet]. 2014; 19(3):[118 p.].
57. Byrnes PD. Why Haven't I Changed That?: Therapeutic Inertia in General Practice. Australian family physician. 2011;40(1/2):24.
58. Lázaro P, Murga N, Aguilar D, Hernández-Presa MA, Investigators IS. Therapeutic inertia in the outpatient management of dyslipidemia in patients with ischemic heart disease. The inertia study. Revista Española de Cardiología (English Edition). 2010;63(12):1428-37.
59. Schedlbauer A, Schroeder K, Peters T, Fahey T. Interventions to improve adherence to lipid lowering medication. Cochrane database of systematic reviews. 2004(4).
60. Simpson SH, Eurich DT, Majumdar SR, Padwal RS, Tsuyuki RT, Varney J, et al. A meta-analysis of the association between adherence to drug therapy and mortality. Bmj. 2006;333(7557):15.
61. Zwart JJ, Richters A, Öry F, de Vries JI, Bloemenkamp KW, van Roosmalen J. Eclampsia in the Netherlands. Obstetrics & Gynecology. 2008;112(4):820-7.
62. Den Ouden H, Vos RC, Rutten GE. Effectiveness of shared goal setting and decision making to achieve treatment targets in type 2 diabetes patients: A cluster-randomized trial (OPTIMAL). Health Expectations. 2017;20(5):1172-80.
63. Mann DM, Ponieman D, Montori VM, Arciniega J, McGinn T. The Statin Choice decision aid in primary care: a randomized trial. Patient education and counseling. 2010;80(1):138-40.

64. Krishna S, Boren SA. Diabetes self-management care via cell phone: a systematic review. Journal of diabetes science and technology. 2008;2(3):509-17.
65. Vervloet M, Linn AJ, van Weert JC, De Bakker DH, Bouvy ML, Van Dijk L. The effectiveness of interventions using electronic reminders to improve adherence to chronic medication: a systematic review of the literature. Journal of the American Medical Informatics Association. 2012;19(5):696-704.
66. Nicastro E, Vecchio AL, Liguoro I, Chmielewska A, De Bruyn C, Dolinsek J, et al. The impact of e-learning on adherence to guidelines for acute gastroenteritis: a single-arm intervention study. PloS one. 2015;10(7):e0132213.
67. Butler CC, Kinnersley P, Prout H, Rollnick S, Edwards A, Elwyn G. Antibiotics and shared decision-making in primary care. Journal of Antimicrobial Chemotherapy. 2001;48(3):435-40.
68. McDermott L, Yardley L, Little P, Ashworth M, Gulliford M. Developing a computer delivered, theory based intervention for guideline implementation in general practice. BMC family practice. 2010;11(1):90.
69. Hebert C, Beaumont J, Schwartz G, Robicsek A. The influence of context on antimicrobial prescribing for febrile respiratory illness. A cohort study Ann Intern Med. 2012;157:160-9.
70. Steinman MA, Landefeld CS, Gonzales R. Predictors of broad-spectrum antibiotic prescribing for acute respiratory tract infections in adult primary care. Jama. 2003;289(6):719-25.
71. Holden RJ. Physicians' beliefs about using EMR and CPOE: in pursuit of a contextualized understanding of health IT use behavior. International journal of medical informatics. 2010;79(2):71-80.
72. Bates DW, Kuperman GJ, Wang S, Gandhi T, Kittler A, Volk L, et al. Ten commandments for effective clinical decision support: making the practice of evidence-based medicine a reality. Journal of the American Medical Informatics Association. 2003;10(6):523-30.
73. Chertow GM, Lee J, Kuperman GJ, Burdick E, Horsky J, Seger DL, et al. Guided medication dosing for inpatients with renal insufficiency. Jama. 2001;286(22):2839-44.
74. Helmons PJ, Suijkerbuijk BO, Nannan Panday PV, Kosterink JG. Drug-drug interaction checking assisted by clinical decision support: a return on investment analysis. Journal of the American Medical Informatics Association. 2015;22(4):764-72.
75. Paterno MD, Maviglia SM, Gorman PN, Seger DL, Yoshida E, Seger AC, et al. Tiering drug–drug interaction alerts by severity increases compliance rates. Journal of the American Medical Informatics Association. 2009;16(1):40-6.
76. Curtis JR, Back AL, Ford DW, Downey L, Shannon SE, Doorenbos AZ, et al. Effect of communication skills training for residents and nurse practitioners on quality of communication with patients with serious illness: a randomized trial. Jama. 2013;310(21):2271-81.
77. Shah NR, Seger AC, Seger DL, Fiskio JM, Kuperman GJ, Blumenfeld B, et al. Improving acceptance of computerized prescribing alerts in ambulatory care. Journal of the American Medical Informatics Association. 2006;13(1):5-11.

78. Cordero L, Kuehn L, Kumar RR, Mekhjian HS. Impact of computerized physician order entry on clinical practice in a newborn intensive care unit. Journal of perinatology. 2004;24(2):88.
79. Vincent WR, Martin CA, Winstead PS, Smith KM, Gatz J, Lewis DA. Effects of a pharmacist-to-dose computerized request on promptness of antimicrobial therapy. Journal of the American Medical Informatics Association. 2009;16(1):47-53.
80. Olsson IN, Runnamo R, Engfeldt P. Drug treatment in the elderly: an intervention in primary care to enhance prescription quality and quality of life. Scandinavian journal of primary health care. 2012;30(1):3-9.

Tables

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 [23] 2014	15 /-/1493	CDSS providing treatment recommendation	Reducing disagreement among physicians	*0/02
Beeler [12] 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 [20] 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 [14] 2016	43 /-/14134	CDSS equipped with alerts for patients with atrial fibrillation	Increasing the prescription of anticoagulation after 12 months	*0/01
Mazzaglia [15] 2014	-/197 /-	Alert-based CDSS for patients using cardiovascular drugs	Increasing prescription of anti-blocking drugs	*P-value<0/001
Nielsen [17] 2014	-/-/191	CDSS to regulate the rate of warfarin use	Increasing the time outcome in the scope of treatment	0/67 Percent
Patel [16] 2011	23 /178/-	Framework for the UK Medical Research Council (MRC)	Increasing the number of anti-inflammatory/lipid-lowering drugs	*P-value <0/001
Akhu-zaheya[18] 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 [19] 2014	-/-/62	Web-based software equipped with text reminders for patients with chronic coronary syndrome	Increasing adherence to drug usage	*P-value<0/01

able 2. Data extracted for CDSS trials on hypertension

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P-value
Christensen [19] 2009	-/-/398	Reminder in patient admission and blood pressure control	Reducing blood pressure after 12 months	0/06
Luitjes [22] 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

Table 3. Data extracted for CDSS trials on diabetes

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P-value
Susanne [23] 2019	22/-/363	ISDM-P program composed of CDSS and sessions	Reduction in faulty knowledge causing risk	*P-value <0/001
Perestelo-pérez[24] 2015	14/29/168	The CDSS selects statin with an estimate of cardiovascular disease risk	Increasing satisfaction of decision making	*0/009
Sáenz [27] 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 [25] 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 [26] 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

Table 4. Data extracted for CDSS trials on digestive diseases

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P-value
Geurts [28] 2010	-/-/222	Recommendation decision support system	Increasing the standard use of oral rehydration solution	*P-value <0/05
Gill [29] 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 [30] 2013	General physicians	CDSS equipped with risk notification service	Increasing the drug prescription in patients with risk above 5 percent	*0/01

Table 5. Data extracted for CDSS trials on pulmonary diseases

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P-value
Bourgeois [32] 2010	-/112/-	Chronic obstructive pulmonary disease pattern in electronic health records	Reduced antibiotic prescriptions in visits by using templates	*0/02
Jusuzik [33] 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 [34] 2014	-/103/-	DSS and electronic learning	Increasing physicians self-efficacy	*0/02
Mcginn [36] 2010	-/-/984	A real time and unified CDSS during care combined with integrated clinical prediction rules	Reduced antibiotic prescription	*0/008
Mohammed [36] 2011	-/-/2207	Short message as a two-way reminder	Inability to be effective in treatment success rate	0/76
Ackerman [31] 2010	-/29/33	CDSS in Electronic Health Records	Reducing excess prescription of antibiotics	*0/003

Table 6. Data extracted for CDSS trials on AIDS

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P-value
Pop-eleches [37] 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

Table 7. Data extracted for CDSS trials on appendicitis

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P-value
Avansino [38] 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

Table 8. Data extracted for CDSS trials on kidney diseases

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P-value
Awdishu [40] 2012	-/514/1278	DSS Warning	An increase in not taking medication or changing dose of inadequate drugs	*P-value<0/0001
Erler [39] 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

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

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

Cox [42] 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 [44] 2017	-/71/465	Reminder-based CDSS	Ineffectiveness of drug prescriptions after 6 and 9 months	0/31, 0/18
Strom [41] 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 [45] 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 [43] 2016	-/-/110	Prescribing CDSS for creating drug treatment recommendations such as drug-drug and drug-gene interaction	Reducing the average number of days re-hospitalized 60 days after discharge	*0/007
			Reducing the combination of re-hospitalizations, emergency ward visits and morbidity 60 days after discharge	*0/005

Table 10. Data extracted for CDSS trials on Malar

Author/year	Population	Type of computer system	Outcome	P-value
Bruxvoort [46] 2012	82/-/-	Text message reminders for Malaria treatment	Physicians' knowledge in using Lumefantrine orthometer	*P-value <0/0001

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

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P-value
Beeler [49] 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 [47] 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 [48] 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

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 [51] 2006	-/-/1407	CDSS for recommending drug dosage	Increasing the number of prescriptions by recommending the determined system dose	*P-value <0/0001
Leibovici [54] 2012	-/-/1683	CDSS for antibiotics treatment	Increasing the survival percentage difference in protocol-based analysis	*0/04
Myers [50] 2006	-/59/-	Computerized alerts for manual or automatic correction of medical abbreviation	Reducing the significant number of inappropriate abbreviations	*0/02
Van Stiphout [52] 2014	2/115/1094	CDSS integrated with training session	More efficient medical summary	*0/03
Willis [53] 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	

Table 13: Data extracted for CDSS trials on mental disorders

Author/year	Hospitals/physicians/patients	Type of computer system	Outcome	P-value
Tamblyn [55] 2008 to 2010	-/81/5628	DSS equipped with three types of alerts	Reduction in dose of drugs after one year for antipsychotics	*0/02

Figures

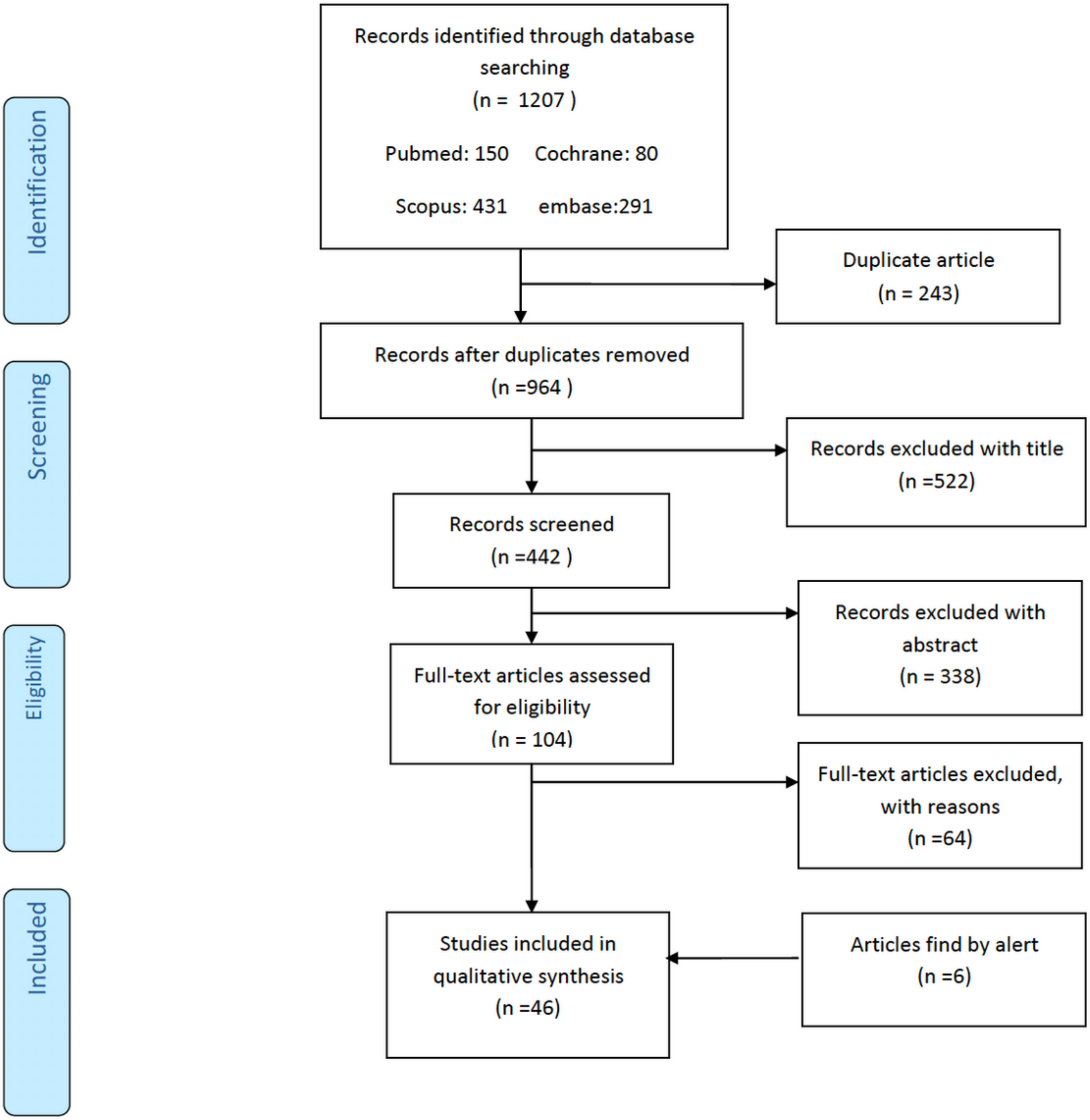

Figure 1

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

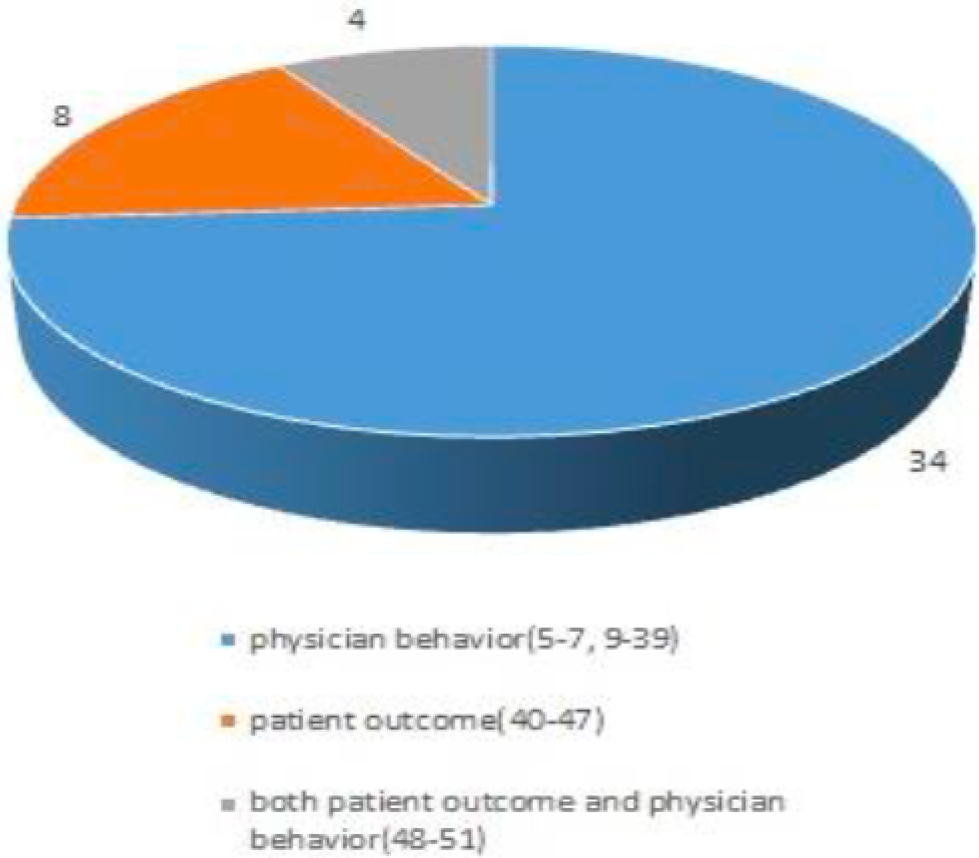

Figure 2

The number of studies based on several evaluating outcomes

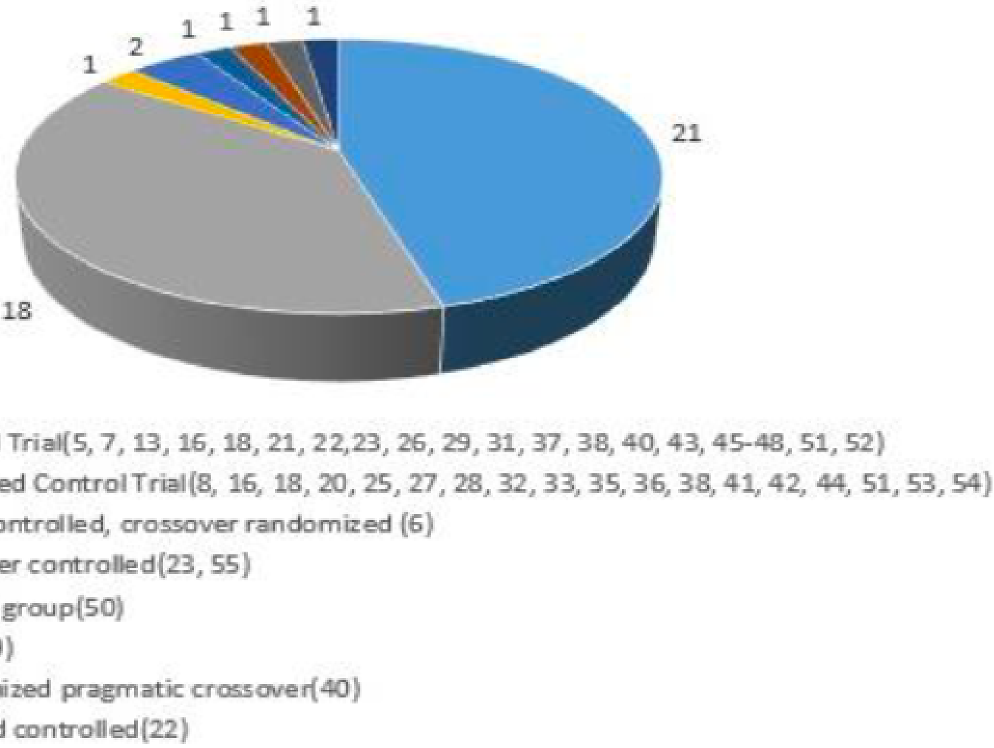

Figure 3

Type of included studies

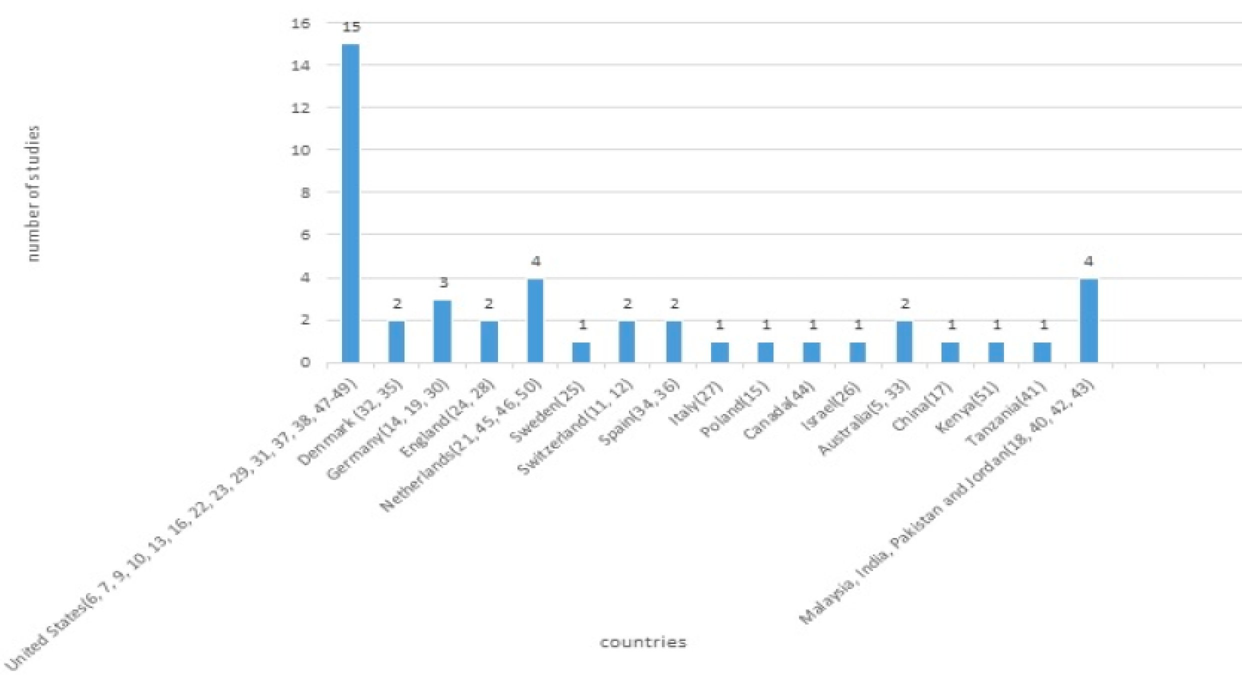

Figure 4

The number of studies associated with each country

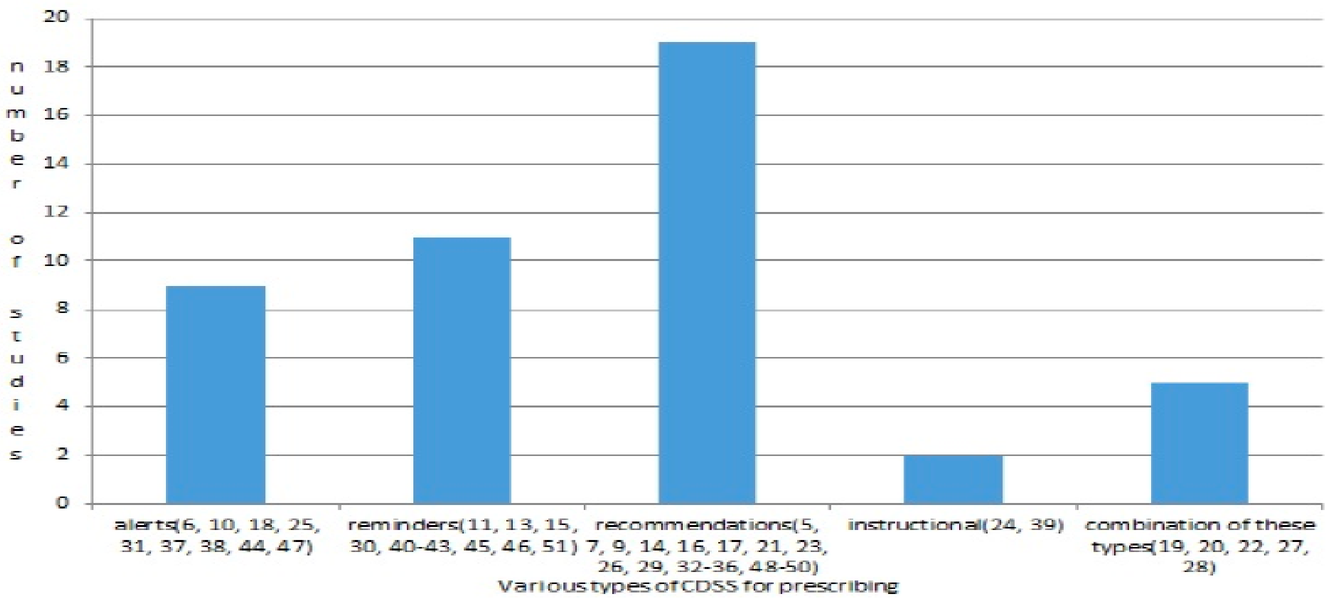

Figure 5

The number of studies associated with each CDSS type