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Clinical Decision Support Systems to Identify Drug-Related Problems in Diabetes Mellitus Patients: A Systematic Review

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ABSTRACT

Clinical decision support systems (CDSSs) have been developed based on individual conditions to provide rational therapy by offering recommendations for therapeutic as well as dosage selection and preventing drug interactions. This study aims to summarize the available evidence on CDSSs intervention, key outputs, and impact of the user in DM patients. The study was conducted using a systematic review which search strategy in Pubmed, and Scopus was used to find relevant records and the initial search was conducted on November 6-7, 2021, reviewing all records in the last 10 years. This study evaluated CDSSs to improve the use of technology in medication for DM patients. The scope of the study included prescription, medication errors, and medication safety. Furthermore, other studies that met the inclusion criteria evaluated CDSSs electronic prescriptions, and computerized physician order entry/CPOE systems in medication prescription, emphasizing the reduction of medication errors, adverse drug events, drug-allergy checking, and dosing support. Total records identified were 855, consisting of 786 articles from Pubmed, 64 from Scopus, and 5 from manually searching the bibliographies of articles that have been found. The result of this study showed the significant roles of CDSSs in improving prescribing, reducing side effects, and drug interactions, as well as increasing patient safety. Despite the significant improvement in practitioners and process performance facilitated by CDSSs, minimal information was found regarding the impact of these systems on outcomes of patients. CDSSs are used in hospitals and primary care settings to identify potential drug interactions, correct therapy regimens, monitor therapy, blood glucose documentation, ensure patients receive medication according to the guideline, provide nutritional advice, and schedule physical activity. The usage of CDSSs improves blood glucose levels, detects possible drug interactions, reduces face-to-face consultations, improves documentation, assists in identifying dose, and promotes prescribing in line with the guideline. The use of CDSSs can help to reduce the risk of errors in management therapy.

Keywords: clinical decision support systems, drug-related problems, diabetes mellitus

INTRODUCTION

Diabetes Mellitus (DM) is a long-term chronic disease, influencing lives, families, and societies worldwide (International Diabetes Federation, 2017). The prevalence of DM among individuals aged 20-79 years old in 2021 was 537 million, which was predicted to increase by 643 million in 2030 and 785 million in 2045. This

disease is among the top ten causes of death in adults, with a projected 6.7 million mortalities globally in 2021 (International Diabetes Federation, 2021). A recent study has shown that approximately 10.5% (34.2 million) of the population in the US had DM in 2018, with an increasing prevalence as the age rises (Centers for Disease Health and Human Services, 2020). Moreover, the causes of this increasing trend include the high incidence of T1DM in children, the occurrence of T2DM in young adults due to lifestyles, high-energy diets, and other unknown factors (Saeedi *et al*., 2019).

Drug-related problems (DRPs) in DM patients are events associated with drug use, which can affect therapeutic goals. Bekele *et al*. (2021) showed that the most common DRPs categories in inpatients were unnecessary prescription of drug (27.79%), non-adherence (17.22%), and excessively high doses (16.92%), with hospital stays of more than 7 days, and polypharmacy serving as a trigger factor. Another study showed that the majority of DRPs category occurring in DM patients are the effect of suboptimal drug treatment (49.2%), untreated indications and symptoms (21.1%), unnecessary drug treatment (10.7%), and adverse drug reactions (19%) (Ayele *et al*., 2018). To address DRPs, clinical decision support systems (CDSSs) have been developed based on individual conditions to provide rational therapy by offering recommendations for therapeutic as well as dosage selection and preventing drug interactions (Robertson *et al*., 2020). CDSSs are integrated with Electronic Health Records (EHR), which are often found in modern healthcare, as part of the electronic prescribing function. The implementation of CDSSs is part of efforts to improve patients safety and quality of service (Chin *et al*., 2020).

Several systematic reviews related to the use of CDSSs for DRPs identification have been carried out to observe the impact, results, evaluate the quality of methods, and reports (Jia *et al*., 2016; Shahmoradi *et al*., 2021). Therefore, this study aims to summarize the available evidence on CDSSs intervention, key outputs, and impact of the user in DM patients.

METHODS

The study was conducted using a systematic review, which consisted of two primary questions. These included (1) how CDSSs intervention design was used to identify DRPs in DM patients and (2) the outcomes after implementing CDSSs for identified DRPs in DM patients. The methods section included the search strategy, study selection, data extraction, and quality assessment

Search strategy

The protocol was constructed using PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analysis) guidelines. Search strategy in Pubmed, and Scopus was used to find relevant records and the initial search was conducted on November 6-7, 2021, reviewing all records in the last 10 years. The Boolean Operator was used to combine them (AND, OR, NOT) and the search in Pubmed was conducted using medical subject headings (MeSH) terms. The query used to perform the Pubmed search included "Decision Support Systems, Clinical"[Mesh]) AND "Drug-Related Side Effects and Adverse Reactions"[Mesh]) OR "Medication Errors" [Mesh]) OR "Drug Hypersensitivity"[Mesh]) OR "Drug Interactions"[Mesh]) AND "Diabetes Mellitus"[Mesh]. Due to different systems and technical limitations, this list of search phrases was modified when searching in other databases. The final terms used in Scopus were “Decision Support System” AND “Side Effect” OR “Adverse Reaction” OR “Medication Error” OR “Drug Hypersensitivity” OR “Drug Interaction” AND “Diabetes Mellitus”.

Study selection and data extraction

This study evaluated CDSSs to improve the use of technology in medication for DM patients. The scope of the study included prescription, medication errors, and medication safety. Furthermore, other studies that met the inclusion criteria evaluated CDSSs electronic prescriptions, and computerized physician order entry/CPOE systems in medication prescription, emphasizing the reduction of medication errors, adverse drug events, drug-allergy checking, and dosing support. The exclusion criteria were studies written in a language other than English, systematic review studies, commentaries, opinion papers, editorials, conference proceedings, summaries, and theses. The selection process comprised three, firstly, screening of all titles and abstracts. Secondly, possible studies that were included in the first phase were evaluated for relevance by evaluating the full-text version against inclusion criteria. Thirdly, the reference lists of the publications that were selected were carefully observed. The result of the records was entered into the Mendeley software, and the duplicate was removed and rechecked manually.

Table I. Quality assessment for studies (Jadad *et a*l., 1996)

Reference	Q_1	Q_2	Q_3	Q_4	Q_5	Q_6	Q_7	Q_8	Total
Berger *et al*. (2020)	1	1	0	0	1	1	1	1	6
Pérez-Gandía *et al*. (2018)	1	0	0	0	0	1	1	1	4
Spat *et al*. (Spat et al., 2017)	0	0	0	0	0	1	1	1	3
Caballero-Ruiz *et al*.(2017)	1	0	0	0	1	1	1	1	5
Donsa *et al*. (Donsa et al., 2016)	0	0	0	0	1	1	1	1	4
Mazzaglia *et al*.(2016)	1	1	0	0	1	1	1	1	6
Neubauer *et al*.(2015)	0	0	0	0	0	1	1	1	3
Charpentier *et al*.(2011)	1	1	0	0	1	1	1	1	6

NOTE: *Q = Question.*

(Q_1) Was the study referred to as randomized? (Q_2) Was the randomization strategy appropriate? (Q_3) Was the study described as blinding? (Q_4) Was the blinding strategy appropriate? (Q_5) Was there a presentation on dropouts and withdrawal? (Q_6) Was there a presentation of the criteria inclusion and exclusion? (Q_7) Was a method employed to evaluate the outcome? (Q_8) Was the statistical analysis method described?

Following the initial screening, full-text studies were obtained and examined to ensure eligibility for the development of the data extraction table. Data were collected from all papers that matched the review's eligibility and inclusion criteria. Subsequently, the required information was collected and analyzed, namely first author, publication date, location, study design, CDSSs type, major study results, and CDSSs impact.

Methodological quality assessment

The Jadad scale, an Oxford study for bias in clinical trials, was used to assess study quality (Jadad *et al*., 1996). The quality score was calculated by adding the total score for each sample, as shown in Table I. In this context, scoring systems of 0 and 1 was used to exclude or include randomization, blindness, removal, dropouts, inclusion criteria, results assessment, and statistical analysis explanation (Moghadam *et al*., 2021). Each article's score should vary from 0 to 1, showing the lowest and best quality, respectively. A score of 4-8 shows good to great quality, while value ranging from 0-3 suggests poor to low quality (Wang *et al*., 2014).

RESULTS AND DISCUSSION

Search results

The search for studies was conducted through a database on November 6-7, 2021. PRISMA flow diagram showed total records identified were 855, consisting of 786 articles from Pubmed, 64 from Scopus, and 5 from manually searching the bibliographies of articles that have been found (Figure 1). The studies were evaluated by Jadad's scale for inclusion in the full text by two members of the study team (NL and SAK). All studies were entered into the Mendeley software, except 1 duplicate, resulting in the inclusion of 8 studies. A total of 45 studies were reviewed but did not meet the criteria, namely, 33 non-specific studies describing CDSSs, 7 were unrelated to diabetes, and 5 used another type of study.

Characteristics of the included studies

Based on the review, the application of CDSSs in DM patients was carried out in the Netherlands (Berger *et al*., 2020), Spain (Caballero-Ruiz *et al*., 2017; Pérez-Gandía *et al*., 2018), Austria (Donsa *et al*., 2016; Neubauer *et al*., 2015; Spat *et al*., 2017), Italy (Mazzaglia *et al*., 2016), and France (Charpentier *et al*., 2011). The majority of specialists in the Netherlands were open to using CDSSs but mentioned several obstacles, including a lack of time, validation studies, and trust (Ankolekar *et al*., 2022). Decentralization of healthcare assignments to lower governmental and administrative levels in Spain contributed to regional variations in systems, inefficiencies, as well as decreased productivity in resource and technology development (Perestelo-Perez dkk., 2022).

Geographical factors were found to impact health services, as persistent geographic disparities presented a vulnerability to the French health systems (Or & Gandré, 2022). In central Austria, the proportion of general practitioners and specialists was relatively high, but low in certain rural districts.

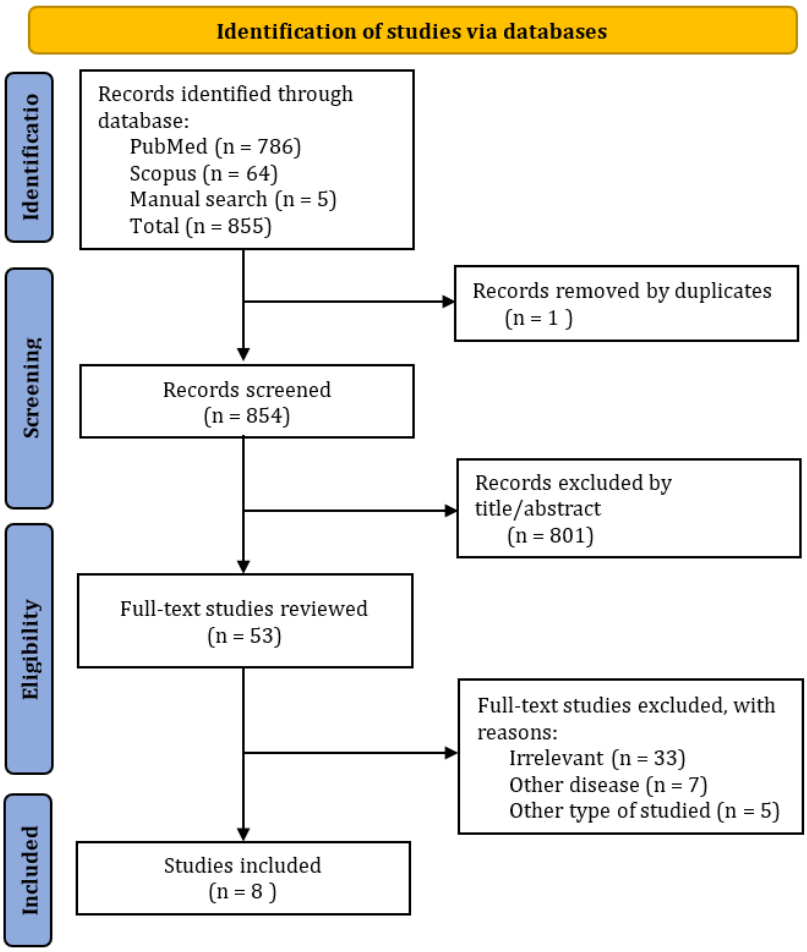

Table IQuality assessment for studies (Jadad *et al*., 1996)

Due to the aging physician workforce, rural areas experienced difficulty in filling available positions, thereby increasing already problematic regional disparities (Bachner *et al*., 2022). Variations in Italy influenced the geographic accessibility of health services, with financial constraints leading to more than half of individuals in the South avoiding visiting a doctor. In the northern region, the underuse of medical services is attributed to work and family obligations (Cavalieri, 2013).

Table II shows 4 studies presenting specific CDSSs implementations in T2DM patients (Donsa *et al*., 2016; Mazzaglia *et al*., 2016; Neubauer *et al*., 2015; Spat *et al*., 2017), 2 studies on T1DM (Charpentier *et al*., 2011; Pérez-Gandía *et al*., 2018), 1 on gestational diabetes (Caballero-Ruiz *et al*., 2017), and 1 on diabetes without classification (Berger *et al*., 2020). Berger *et al* (2020) conducted a study focusing on specific DM patients and other accompanying diseases such as hypertension and heart diseases. Meanwhile, (Mazzaglia *et al*., 2016) included patients and general practitioners with comorbid acute myocardial infarction (AMI) and stroke. The analysis data used were IBM SPSS Statistics (Berger *et al*., 2020; Caballero-Ruiz *et al*., 2017), R-statistics (Donsa *et al*., 2016; Neubauer *et al*., 2015; Spat *et al*., 2017), Stata 10.1 (Charpentier *et al*., 2011; Mazzaglia *et al*., 2016), while only a study specified the software (Pérez-Gandía *et al*., 2018). The differences in tools used for data analysis have the potential to impact the results due to varied algorithms, features, and capabilities. Therefore, the selection of data analysis tools can be based on several considerations such as suitability for specific types or having more advanced statistical methods compared to others. The user interface and ease of use could also affect the accuracy and reliability of the results when the software is not used correctly or there are differences in interpretation.

Table II. Characteristics of included studies

Authors	Year	Country	Respondents	Sample size	Method	Data analysis tools
Berger *et al*. (2020)	2020	Netherland	Patients admitted to the hospital who are taking ≥ 2 QTc-prolonging medications	107	Randomized controlled trial	IBM SPSS Statistics 21.0
Pérez-Gandía *et al*. (2018)	2018	Spain	People with T1DM	12	Randomized crossover	N/A
Spat *et al*. (Spat et al., 2017)	2017	Austria	Adult patients (≥ 18 years) with T2DM who were admitted to the general ward and treated with di*et al*one and/or with any oral or injectable antihyperglycemic	30	Noncontrolled intervention study	R-statistics version 3.0.1
Caballero-Ruiz *et al*. (2017)	2017	Spain	Patient with gestational diabetes	90	Randomized controlled trial	IBM SPSS Statistics 23
Donsa *et al*. (Donsa et al., 2016)	2016	Austria	Adults' patients with T2DM who were admitted to a general ward and treated with di*et al*one and/or with any oral or injectable antihyperglycemic	79	A posthoc analysis of a before and after study	R-statistics version 3.0.1
Mazzaglia *et al*. (2016)	2016	Italy	Patient with T2DM, AMI, or ischemic stroke (≥ 45 years) who had been registered with a general practitioner for at least a year previous to the index date.	25.491	Cluster-randomized open-label controlled trial	Stata 10.1
Neubauer *et al*. (2015)	2015	Austria	Patient with T2DM (≥ 18 years), managed with diet, oral antihyperglycemic, non-insulin injectable antidiabetic drugs, insulin therapy, or any combination therapy. In the event of hyperglycemia, patients were shifted to insulin therapy based on evidence-based recommendations to use insulin therapy as the optimal strategy for glycemic management in hospitalized patients.	99	Non controlled intervention	R-statistics version 2.13.1
Charpentier *et al.* (2011)	2011	France	Patient with T1DM (≥ 18 years) and have been on a basal-bolus insulin regimen for at least 6 months.	180	Randomized control trial	Stata 10.1

Table III. Studies of Clinical Decision Support Systems (CDSSs)

Authors	Year	Objectives	System description	Outcome measure study
Berger *et al.*(2020)	2020	To design and implement QT-DDIs support system to assess the risk of QTc prolongation by drug interactions in clinical practice	This system would detect an elevated risk of QTc-prolongation, requiring therapeutic adjustments and/or further ECG monitoring in patient with ≥ 2 QTc-prolonging medicines	This study measured the risk of QTc-prolongation, which was defined as a QTc interval > 450 ms for males and > 470 ms for females
Pérez-Gandía *et al.*(2018)	2018	To describe glucose predictor-based CDSS for patients with T1DM and evaluate its impact on their decision making	The system is aimed to aid patients in real-time while conducting therapeutics necessary actions such as insulin bolus injection to correct hyperglycemia or carbohydrate consumption to correct hypoglycemia. The CDSS is linked to a telemedicine platform, allowing endocrinologists to monitor remotely	This study measured changes in Kovatchev's risk index, a measure of the risk of hypoglycemia and hyperglycemia, was assessed during the post-prediction (PP) time window
Spat *et al.*(Spat et al., 2017)	2017	To provide the outcomes of a clinical feasibility study evaluating the system and to discuss its implication for hypoglycemia prevention	The system's primary function is to provide insulin dose recommendations for T2DM patients. On a basal-bolus insulin regimen. The system has three main features for user input: blood glucose (BG) documentation, meal insulin dose calculation, and daily insulin dose modification.	This study measured the occurance of medication errors, hypoglycemic episodes, and glycemic control in patients with T2DM using insulin treatment in the hospital
Caballero-Ruiz *et al.*(2017)	2017	To assess a clinical decision support system for managing the treatment of a patient with gestational diabetes	This system is a web-based CDSS to offer a secure and efficient platform for managing GDM (Gestational Diabetes Mellitus) patient care. The system's major components include remote patient monitoring, automatic data analysis, and therapeutic planning recommendations.	This study calculated the percentage of coincidence between the recommendatios generated by CDSS and the therapy adjusments performed by physicians. It also monitored the interactions between patients and physicians through the web-based CDSS
Donsa *et al.*(Donsa et al., 2016)	2016	To see how a paper-based protocol compares to a computerized prescription management system with clinical workflow and decision support	It assists in organizing the treatment workflow by providing automated process assistance, such as task presentation, documentation, and visualization of BG values, nutrition, and insulin dosage. The systems' primary function is to provide insulin dose recommendations for T2DM patients on basal-bolus regimens.	This study used a post-hoc analysis of a before and after study design to measure the impact errors in paper-based and computerized diabetes management with CDSS

Table III. Studies of Clinical Decision Support Systems (CDSSs)

Authors	Year	Objectives	System description	Outcome measure study
Mazzaglia *et al.*(2016)	2016	To see how computerized decision support systems impacted the prescription of medications for cardiovascular prophylaxis	A reminder message will be sent to general practitioners twice. First, if a patient has not received the medicine according to the rules, a reminder will display. If there is a drug interaction, the second warning will show.	The outcomes evaluated were the proportion of patients prescribed with cardiovascular drugs and the days of drug-drug interaction exposure
Neubauer *et al.*(2015)	2015	To see whether standardized glycemic management with the system was effective, safe, and easy, to use for a non-critically ill patient with T2DM.	This system is for subcutaneous insulin administration that assists nurses and physicians in two key activities. To initiate, this system provides automated workflow support, such as a display for open tasks, facilitating documentation, and providing visualization of blood glucose levels, nutrition, and insulin doses. Second, it provides two standardized recommendations for total daily insulin dose and insulin dose suggestions.	This study measured the adherence to insulin dosing suggestions. It also assessed the usability and acceptance of system by healthcare professionals
Charpentier *et al.*(2011)	2011	To assess the system's effectiveness in reducing HbA1C levels in T1DM patients.	This system is a checked bolus calculator which analyzes SMPG (Self-Monitoring Plasma Glucose) level, carbohydrate counts, and planned physical activity. Adjustment to carbohydrate ratio, long-acting insulin analog dose, or pump basal rates may be suggested by the system if fasting or postprandial SMPG levels fall short of the target.	This study measured the HbA1c levels at the end of the six-month study period for each group

This phenomenon shows the need for careful consideration regarding the selection of tools and discussion of potential implications on the results.

Studies of CDSSs

The majority of studies aimed to evaluate the implementation of CDSSs applied to DM patients (Table III) shows that. Study conducted by (Donsa *et al*., 2016) compared the use of systems with a manual, while Neubauer *et al* (2015) and Charpentier *et al* (2011) observed the efficacy and efficiency of CDSSs systems. Moreover, CDSSs are used in hospitals and primary care settings to identify potential drug interaction (Berger *et al*., 2020; Mazzaglia *et al*., 2016), correct therapy regimens (Charpentier *et al*., 2011; Donsa *et al*.,

2016; Mazzaglia *et al*., 2016; Neubauer *et al*., 2015; Pérez-Gandía *et al*., 2018; Spat *et al*., 2017), monitoring therapy (Caballero-Ruiz *et al*., 2017; Pérez-Gandía *et al*., 2018), blood glucose documentation (Donsa *et al*., 2016; Neubauer *et al*., 2015; Spat *et al*., 2017). These systems are also used to ensure patients receive medication according to guidelines (Caballero-Ruiz *et al*., 2017), provide nutritional advice (Charpentier *et al*., 2011; Neubauer *et al*., 2015; Pérez-Gandía *et al*., 2018; Spat *et al*., 2017), and schedule of physical activity (Charpentier *et al*., 2011).

Impact of CDSSs

The usage of CDSSs (Table IV), improves blood glucose levels (Charpentier *et al*., 2011; Neubauer *et al*., 2015; Pérez-Gandía *et al*., 2018; Spat *et al*., 2017), detect possible drug interactions (Berger *et al*., 2020), reduce face-to-face consultations (Caballero-Ruiz *et al*., 2017), enhance documentation (Spat *et al*., 2017), assist in identifying dose (Donsa *et al*., 2016), and promote prescription in line with the guideline (Mazzaglia *et al*., 2016). Another study observed that the use of CDSSs could reduce the risk of errors in management therapy (Donsa *et al*., 2016). Although HbA1C levels decreased, the majority of CDSSs users perceived benefits and potential in aiding healthcare services (Charpentier *et al*., 2011).

Some studies did not directly address the consistency of outcome measures (Berger *et al*., 2020; Caballero-Ruiz *et al*., 2017; Charpentier *et al*., 2011; Mazzaglia *et al*., 2016; Pérez-Gandía *et al*., 2018; Spat *et al*., 2017). Therefore, future systematic reviews should provide a more comprehensive understanding of the consistency of outcome measures in this study. The measures used the impact of errors in paper-based and computerized diabetes management were consistent across the two previously published clinical studies (Mader *et al*., 2013; Neubauer *et al*., 2015). The measurement of adherence to insulin dosing suggestions was consistent across studies, with high rates of adherence reported in multiple studies. The usability and acceptance of the GlucoTab systems by healthcare professionals were also consistent across studies, with high levels of confidence, practicality, and belief in the ability to prevent medication errors reported (Neubauer *et al*., 2015).

Blood glucose changes and other CDSS-related outcomes are not specifically investigated in certain studies (Berger *et al*., 2020; Mazzaglia *et al*., 2016). Although these changes were directly attributed to CDSSs, there could be confounding factors that influence the outcomes. These factors included individual patients characteristics, lifestyle factors, adherence to treatment, variations in response to therapy, type of hospital admission, pre-existing home insulin therapy, and the specific ward where patients are admitted (Caballero-Ruiz *et al*., 2017; Charpentier *et al*., 2011; Donsa *et al*., 2016; Neubauer *et al*., 2015; Pérez-Gandía *et al*., 2018; Spat *et al*., 2017)

Main Results

The objective of this systematic review is to synthesize all of the existing information on CDSSs intervention in DM patients, important outputs, and user impact. Other characteristics include identification of drug interactions, regimen dose recommendations, therapeutic recommendations by guideline, documentation of blood glucose, monitoring therapy, suggestions for physical activity, and nutrition and food consumption. In the studies included, all key outputs and impacts of CDSSs users have been measured using various methods, with the majority showing beneficial effects on patients outcomes, physician performance, and user acceptance.

The methods used in this review are randomized control trial (Caballero-Ruiz *et al*., 2017; Charpentier *et al*., 2011; Mazzaglia *et al*., 2016; Pérez-Gandía *et al*., 2018), noncontrolled intervention study (Neubauer *et al*., 2015; Spat *et al*., 2017), a post-hoc analysis of a before and after study (Donsa *et al*., 2016), and prospective design (Berger *et al*., 2020). However, not all studies directly contain information about potential bias in the use of CDSSs in DM patients. Pérez-Gandía *et al*. (2018) reported a small sample size of 12 participants and did not show benefits in glucose control, but no hypoglycemic events were observed. These results suggested that CDSSs have a positive impact on patients' decision-making and confidence, although there are limitations or confounding factors influencing the outcomes. Another study reported that the presence of potential biases from non-randomized groups, limited observations, differences in insulin distribution, improper documentation, and confounding factors should be considered when interpreting the results (Donsa *et al*., 2016).

Table IV. Impact of Clinical Decision Support Systems (CDSSs)

Authors	Year	CDSSs	Key outputs	User acceptance
Berger *et al*.(2020)	2020	QT-DDIs	Risk factors in the system included renal function, age, gender, cardiac comorbidities, hypertension, diabetes mellitus, potassium levels, loop diuretics, and QTc-prolonging drugs. This system can detect QTc-prolongation risk with a sensitivity of 83.9%.	N/A
Pérez-Gandía *et al*.(2018)	2018	GlucoP®	Average subcutaneous glucose during a postprandial period (142.35 ± 59.28 in the experimental phase vs –142.02 ± 46.03 in the control phase) indicated no significant differences.	Patients rated the systems positively across the whole, with an average score of more than 7 in the questionnaire of usability.
Spat *et al*.(Spat et al., 2017)	2017	GlucoTab®	Only 1.3% of BG levels were below 70 mg/dl and only 2.6% above 300 mg/dl. The system's availability (97.3%) and the rate of therapeutic activities documented with the system (>93.5%) both were high. Only a few of the system's recommendations were ignored by the users (>95.7% adherence).	The three questionnaires for evaluating user acceptance indicated respondents' belief in the system increased. Users thought the system was appropriate for daily use.
Caballero-Ruiz *et al*.(2017)	2017	Sinedie®	Clinician's time spent assessing patients was decreased by 27.389%, and the number of face-to-face visits per patient was lowered by 88.556%. As directed by their physician, patients measured their blood sugar 3.890 times a day and uploaded their monitoring data every 3.477 days. Patients are only required to attend consultations when their doctor requests them in order to assess a therapy modification.	Patients followed their physician's advised self-monitoring regimen. Regarding the system, patients expressed great satisfaction, believing it to be well-managed and useful.
Donsa *et al*.(Donsa et al., 2016)	2016	Glucotab®	PaperG and CompG both have similar mistake rates. In the PaperG group, 11% of manual insulin dose estimates were incorrect, and the odds of a hypoglycemic episode after insulin administration were 3.1 (95% CI: 1.4-6.8). Workflow deviations occurred in 5.0% of the tasks in the CompG group, resulting in an elevated risk of odds of hyperglycemia was 2.2 (95% CI: 1.1-4.6)	User calculation mistakes of insulin dose were detected in 11.1% of the PaperG group. No user input mistakes were found in the CompG group.

Table IV. Impact of Clinical Decision Support Systems (CDSSs)

Authors	Year	CDSSs	Key outputs	User acceptance
Mazzaglia *et al*.(2016)	2016	CDSS	The use of CDSS resulted in a significant increase in antiplatelet and lipid-lowering medication prescriptions among patients with AMI and stroke. Due to drug-drug interaction, CDSS means reducing the mean number of days of concurrent administration of cardiovascular medicines and non-recommended therapy	All participating general practitioners agreed to use the CDSS
Neubauer *et al*.(2015)	2015	GlucoTab®	Percentage of blood glucose measurements in the 70-140 mg/dl range occurs in 50.2±-22.2% of all measures, according to the key outcomes measures. The average blood glucose level was 154±-35 mg/dl. BG values in the ranges of 60-70 mg/dL (1.4%), 40-60 mg/dL (0.5%), and 40 mg/dL (0.0%) were found in all measurement.	In 97.5% of cases, practitioners followed the recommended total daily insulin doses. This system was referred to as reliable by 91% of healthcare experts, with 89% believing in its practical and 80% believing in its potential to reduce prescription.
Charpentier *et al*.(2011)	2011	Diabeo®	The endpoint is the primary outcome. G1 had a higher HbA1C level (9.10%±1.16%) than G2 (8.63%±1.07%) or G3 (8.41%-1.04%). The proportion of patients attaining the HbA1C objective of 7.5% at the endpoint was 17 percent (n=10) in G3, 6.7% (n=4) in G2, and 1.6% (n=1) in G1. There were no differences in quality of life (QOL) across groups at baseline and endpoint, as measured by satisfaction in the Diabetes QOL and Diabetes Health Profile questionnaires.	Upon agreement with their doctor, 67% of G2 participants and 75% of G3 participants reported that they prefer to remain with the system for routine follow-up.

The Diabeo systems combined with telemedicine showed significant results in improving HbA1c levels in DM patients (Charpentier *et al*., 2011). Additionally, CDSSs significantly increased the proportion of DM patients prescribed antiplatelet and lipid-lowering drugs compared to the control group (Mazzaglia *et al*., 2016). The GlucoTab system significantly improved glycemic management in hospitalized T2DM patients, with high adherence to insulin-dosing recommendations and positive feedback from healthcare professionals (Neubauer *et al*., 2015). CDSSs showed a significant reduction in hypoglycemia by implementing a computerized system for diabetes management in T2DM patients compared to a paper-based process (Spat *et al*., 2017). Furthermore, CDSSs can reduce errors and improve clinical outcomes in hospitalized T2DM patients (Donsa *et al*., 2016).

Despite these advancements, several limitations have been observed in CDSSs. For example, the usefulness of CDSSs depends on the availability of automatic and continuous glucose monitoring readings, which are not integrated into systems (Pérez-Gandía *et al*., 2018). CDSSs also used manual data entry which could potentially

lead to errors (Caballero-Ruiz *et al*., 2017). Patients' willingness to use smartphones and continue with system after the study, particularly considering cost-effectiveness can impact the long-term adoption and success of the Diabeo systems (Charpentier *et al*., 2011). Computerized systems can have limitations, such as technical issues, user interface challenges, and potential errors in data entry or interpretation, hindering universal applicability across all healthcare settings (Donsa *et al*., 2016; Mazzaglia *et al*., 2016). To address these limitations, further optimization and validation in larger settings could be considered to make systems more applicable (Berger *et al*., 2020).

Use of CDSSs

CDSSs in healthcare

The majority of DM patients struggle to improve their glycemic control, often requiring treatment support to enhance the effectiveness of existing therapies, prevent complications, self-management education, and increase adherence. Therefore, patients and healthcare professionals can use digital technologies for progress tracking and management. In this context, pharmacological therapies, medical equipment, and patients lifestyles can benefit from technological advancements (Fleming *et al*., 2020; Kesavadev *et al*., 2021).

CDSSs use a predetermined algorithm to process patients-specific data and provide clinicians with data-driven recommendations for assistance in making decision. Moreover, for CDSSs to succeed in clinical context, three principles are required, namely a strong evidence and knowledge basis, clinician adoption, and consistently updated information (Beauchemin *et al*., 2020).

CDSSs for identification of adverse drug reaction

Several studies have been carried out on the use of technology in the detection of drug interaction. These include the identification of individuals with chronic and comorbid diseases in Canada's aging population experiencing polypharmacy. Furthermore, the mHealth app showed the capacity to check for potential drug interactions to improve patients safety. The Mobile App Rating Scale reported an average score of 3.23 out of 5 for the quality apps (Kim *et al*., 2018). Several applications have also been examined, showing high quality, and providing accurate, comprehensive drug interaction information (Shen *et al*., 2021).

CDSSs for adjustment dosage

CDSSs can be used to calculate therapeutic doses to minimize calculation errors through medication dosing calculators. Previous studies have shown that medication dosage support is associated with a reduced number of adverse events (Stultz & Nahata, 2012). The level of renal function impacts the medications that are usually prescribed. However, prescribers can experience difficulty in explaining the complex relationship between levels of renal insufficiency and dose guidelines. To address this challenge, CDSSs offer a solution by facilitating the individualized estimation of the optimal dose for patients with variable levels of renal function. The integration of CDSSs for renal dosing enhances several aspects of prescribing, including frequency of administration, lower rates of orders for medications that should be avoided, and greater rates of orders for blood creatinine testing when results were unavailable (Stultz & Nahata, 2012).

CDSSs for recommendation therapy

Mazzaglia (2016) has shown that automatically prompted CDSSs can improve the pharmacological management of specific categories of high-risk cardiovascular patients in primary care. Systems assist general practitioners in detecting therapy for patients with chronic diseases, T2DM, acute myocardial infarction, and stroke. By analyzing patient's diagnosis and treatment history, CDSSs identify gaps in therapy, particularly regarding antithrombotic, antihypertensive, and LLD drug, to provide warnings and therapeutic recommendations. Other CDSSs have been developed using concepts from evidence-based guidelines. These web-based systems provide screening, diagnosis, and treatment recommendations, thereby assisting healthcare professionals in delivering optimal services.

CDSSs for managing diabetes mellitus

Integrating CDSSs into an EHR can assist healthcare professionals in managing diabetes and documentation. Moreover, an additional method for improving adherence to hyperglycemia treatment procedures should be investigated (Gibbs *et al*., 2019). This includes the use of a comprehensive diabetes management program that integrates with HER systems and facilitates data uploading from memory glucose meters. This software provides results for the overall quality of glycemic management and shows issues such as hypoglycemia, hyperglycemia, glycemic fluctuation, and lack of data. Furthermore, it can advise on

whether to continue with the present therapy, adjust current medication dosages, or change the regimen, along with the required recommendations. When the user rejects the suggestions, the application provides another different option. This tool offers access to FDA-approved prescribing information, professional organization guidelines, and a selection of studies from the medical literature (Rodbard & Vigersky, 2011). Furthermore, diabetes decision support systems play a crucial role in blood glucose control by offering reminders for lifestyle adjustments (diet and physical activities), physician alerts for drug administration (insulin dose adjustment), and warnings for problematic laboratory results (Kiyani *et al.*, 2020). A mobile health application will be built for telemonitoring systems providing a promising method of collecting patients measurements both manually and through sensors (Kart *et al*., 2017).

The effects of CDSSs on patients outcomes

The use of CDSSs in diabetic patients resulted in a significant improvement in laboratory parameters (James *et al*., 2019). Moreover, hospital-based CDSSs have shown significant effect in reducing recurrent hyperglycemic episodes in hospitalized patients with dysglycemia and diabetes, as well as incorrect insulin use in T1DM (A. Pichardo-Lowden *et al*., 2021). Improvements in patients outcomes were reported, confirming the potential efficacy of CDSSs. One of the trials, observing three outcomes (HbA1C, LDL-C, and blood pressure) at the 6-month follow-up, found that CDSSs decreased HbA1C and some elements of blood pressure significantly (Ota *et al*., 2018). Physicians agree on the use of decision support systems, particularly in navigating increasingly complex pharmacological algorithms. Other studies found no differences in glycemic control or secondary outcomes such as blood pressure, total cholesterol, medication intensification, or service use between intervention and control groups (Murphy *et al*., 2020). Zhao *et al*. (2021) showed that CDSSs intervention was insignificantly associated with a decreased probability of acute kidney injury (AKI) progression. However, the result showed significant outcomes after AKI progressed to stage 3 or started renal replacement therapy. Another study showed that customized CDSSs tools did not improve patient outcomes but significantly enhanced the contextualization of patient care (Weiner *et al*., 2022)

The effects of CDSSs on user acceptance

Memorability, learnability, flexibility, shortcuts, and consistency are elements of CDSSs that require specific consideration (Hardenbol & Knols, 2020). Furthermore, factors such as user-friendliness, adherence to clinical guidelines, patients and physician cooperation, as well as integration of EHR with CDSSs contribute to outcomes effectiveness (Moghadam *et al*., 2021). A previous study has shown that well-designed and precisely implemented diabetes CDSSs improve test ordering and preventive treatment to provide important care outcomes. Some of these systems are cost-effective, have high adoption rates, and are correlated by both physicians as well as patients (O'Connor *et al*., 2016; Sim *et al*., 2017). The implementation of CDSSs can be successful when there is adequate program validation, evidence, and knowledge-based assimilation, user feedback, widespread partnership with stakeholders, and consistent evaluation of program impact (A. R. Pichardo-Lowden, 2021). Based on the results, this study suggests that healthcare facilities should learn to adjust to digitalization and leverage technology to support healthcare practitioners in delivering patients care effectively. Existing technology can also be a good investment for businesses when the design systems that are simple to use and provided with proper guidelines. Moreover, there is a need to explore the economic impacts of CDSSs implementation and identification of key elements for successful integration with existing systems such as CPOE, EHR, e-prescribing, and others important aspects.

Khairat *et al*. (2018) showed some of the poor responses from CDSSs users, which were often related to workflow disruptions, questionable validity, excessive distractions, and lack of efficiency. Specifically, workflow constraints related to CDSSs cause excessive alerts, increased computer handling time, and reduced face-to-face time with patients. CDSSs design that is minimally complex with poor visibility, multiple steps per task, or a confusing layout, can prevent barriers to use. This is because users are facilitated when there is easy and quick access to extract all the information on the screen (Jones *et al*., 2022).

Interoperability of CDSSs in healthcare systems

The growth of CDSSs provides an extensive pattern of advancement and technological integration, from conception to the existing sophisticated modern systems. This shows the

close relationship between artificial intelligence and data analytics to digital transformation (Choi *et al*., 2020). In the expanding field of personalized medicine, clinicians can find the best treatments for patients by integrating genomic, proteomic, and other -omics data into CDSSs, thereby reducing side effects and enhancing treatment results. CDSSs offer clinicians timely and useful insights by integrating real-time patients data from multiple sources, including wearable technology and remote monitoring systems. These data can improve patients outcomes by enhancing the monitoring process and providing information on treatment decision (Chen *et al*., 2023).

The integration and implementation of CDSSs within current healthcare systems is a challenging process that requires careful planning and performance (Shah *et al*., 2022). This challenge includes the process of migrating relevant patients data and integrating CDSSs with the existing EHR systems. Therefore, providers must ensure that data exchange can run smoothly through collaboration between CDSSs vendor and EHR providers to ensure proper data integration and security (Wulff *et al*., 2018).

Technical, organizational, and human factors can be used as broad categories to group challenges related to CDSSs implementation (Shah *et al*., 2022). A supportive environment that includes capable leadership, an innovative culture, and the accessibility of resources for education and training is necessary for the successful implementation of CDSSs (Chen *et al*., 2023).

Limitations of the review

The limitations included the use of specific search terms, which might have eliminated relevant studies. In categories of the search, a range of internationally applicable keywords and mesh titles were used, but some relevant publications were missed. Several solutions can be considered to overcome these limitations, including the use of synonyms, related terms, or more general keywords to ensure that no publications are missed. Since literature sources are continuously developing, there is a need to regularly update and expand searches to ensure the inclusion of relevant studies. The relevance of the publication year of the studies included in the literature review needs to be considered. This is advisable considering the rapidly developing digital health technologies. Furthermore, there is a need to ensure the use of relevant and current studies to make for accurate and informative analysis.

CONCLUSION

In conclusion, this study showed the use of digitalization strategies to improve the quality and safety of diabetes clinical care. The results showed the significant roles of CDSSs in improving prescribing, reducing side effects, and drug interactions, as well as increasing patients safety. Despite the significant improvement in practitioners and process performance facilitated by CDSSs, minimal information was found regarding the impact of these systems on patients outcomes. However, the use of CDSSs has proven to be beneficial for DM patients, showing potential for improving healthcare delivery.

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CONFLICT OF INTEREST

The authors declare no conflict of interest for this review.

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683

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