American Journal of Preventive Cardiology 20 (2024) 100855

Contents lists available at ScienceDirect

American Journal of Preventive Cardiology

journal homepage: www.journals.elsevier.com/american-journal-of-preventive-cardiology

Do clinical decision support tools improve quality of care outcomes in the primary prevention of cardiovascular disease: A systematic review and meta-analysis

Iva Buzancic [a,b], Harvey Jia Wei Koh [c], Caroline Trin [c], Caitlin Nash [c], Maja Ortner Hadziabdic [a], Dora Belec [a], Sophia Zoungas [c], Ella Zomer [c], Lachlan Dalli [d], Zanfina Ademi [c,e,f,g], Bryan Chua [c], Stella Talic [c,*]

[a] Faculty of Pharmacy and Biochemistry, University of Zagreb, A. Kovacica 1, Zagreb, Croatia
[b] City Pharmacies Zagreb, Ulica kralja Drzislava 6, Zagreb, Croatia
[c] School of Public Health and Preventive Medicine, Monash University, 553 St Kilda Road, Alfred Precinct, Melbourne, VIC. 3004, Australia
[d] Stroke and Ageing Research, School of Clinical Sciences at Monash Health, Monash University, Level 2, 631 Blackburn Road, Clayton, VIC, 3168, Australia
[e] Health Economics and Policy Evaluation Research Group, Centre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Level 1, 407 Royal Parade, Parkville, VIC, 3052, Australia
[f] Department of Neuroscience, Central Clinical School, Monash University, Melbourne VIC 3004, Australia
[g] School of Pharmacy, Faculty of Health Sciences, Kuopio Campus, University of Eastern Finland, Kuopio, Finland

ARTICLE INFO

Key words:
Clinical decision support tool
Primary prevention
Cardiovascular disease
Meta-analysis
Blood pressure
Lipid levels
Blood glucose

ABSTRACT

Aim: To assess the effectiveness of Clinical Decision Support Tools (CDSTs) in enhancing the quality of care outcomes in primary cardiovascular disease (CVD) prevention.
Methods: A systematic review was undertaken in accordance with PRISMA guidelines, and included searches in Ovid Medline, Ovid Embase, CINAHL, and Scopus. Eligible studies were randomized controlled trials of CDSTs comprising digital notifications in electronic health systems (EHS/EHR) in various primary healthcare settings, published post-2013, in patients with CVD risks and without established CVD. Two reviewers independently assessed risk of bias using the Cochrane RoB-2 tool. Attainment of clinical targets was analysed using a Restricted Maximum Likelihood random effects meta-analysis. Other relevant outcomes were narratively synthesised due to heterogeneity of studies and outcome metrics.
Results: Meta-analysis revealed CDSTs showed improvement in systolic (Mean Standardised Difference (MSD)= 0.39, 95 %CI=-0.31, -1.10) and diastolic blood pressure target achievement (MSD=0.34, 95 %CI=-0.24, -0.92), but had no significant impact on lipid (MSD=0.01; 95 %CI=-0.10, 0.11) or glucose target attainment (MSD=-0.19, 95 %CI=-0.66, 0.28). The CDSTs with active prompts increased statin initiation and improved patients' adherence to clinical appointments but had minimal effect on other medications and on enhancing adherence to medication.
Conclusion: CDSTs were found to be effective in improving blood pressure clinical target attainments. However, the presence of multi-layered barriers affecting the uptake, longer-term use and active engagement from both clinicians and patients may hinder the full potential for achieving other quality of care outcomes.
Lay Summary: The study aimed to evaluate how Clinical Decision Support Tools (CDSTs) impact the quality of care for primary cardiovascular disease (CVD) management. CDSTs are tools designed to support healthcare professionals in delivering the best possible care to patients by providing timely and relevant information at the point of care (ie. digital notifications in electronic health systems). Although CDST are designed to improve the quality of healthcare outcomes, the current evidence of their effectiveness is inconsistent. Therefore, we conducted a systematic review with meta-analysis, to quantify the effectiveness of CDSTs. The eligibility criteria targeted patients with CVD risk factors, but without diagnosed CVD. The meta-analysis found that CDSTs showed improvement in systolic and diastolic blood pressure target achievement but did not significantly impact lipid or

* Corresponding author at: School of Public Health and Preventive Medicine, Monash University, 553 St Kilda Road, Alfred Precinct, Melbourne, VIC. 3004, Australia.
E-mail address: Stella.Talic@monash.edu (S. Talic).

https://doi.org/10.1016/j.ajpc.2024.100855
Received 12 May 2024; Received in revised form 20 August 2024; Accepted 5 September 2024
Available online 20 September 2024

glucose target attainment. Specifically, CDSTs showed effectiveness in increasing statin prescribing but not antihypertensives or antidiabetics prescribing. Interventions with CDSTs aimed at increasing screening programmes were effective for patients with kidney diseases and high-risk patients, but not for patients with diabetes or teenage patients with hypertension. Alerts were effective in improving patients' adherence to clinical appointments but not in medication adherence. This study suggests CDSTs are effective in enhancing a limited number of quality of care outcomes in primary CVD prevention, but there is need for future research to explore the mechanisms and context of multiple barriers that may hinder the full potential for cardiovascular health outcomes to be achieved.

1. Introduction

Cardiovascular disease (CVD) is the largest contributor to global mortality and a substantial factor in the prevalence of disability [1]. According to the World Health Organization (WHO), an estimated 17.9 million people died from CVD in 2019, representing 32 % of all global deaths [2]. The impact of CVD on public health is particularly evident in Australia [3], where >1.2 million individuals were affected by CVD in 2018, constituting the underlying cause of 15 % of all deaths in the country in 2021 [4]. A similar trend is observed globally, with CVD being the leading cause of death in the European Union (EU), accounting for one-third (32.7 %) of all deaths in 2020, and resulting in 1.7 million deaths in the EU [5].

Management of patients at high risk of CVD predominantly occurs within primary care practices, with a major focus on appropriate lifestyle changes and pharmaceutical interventions (i.e. medications). In 2021, CVD medications comprised 37 % of all prescriptions under the Pharmaceutical Benefits Scheme (PBS) in Australia and is also continuously rising in Europe and North America as well, as reported by national annual reports on medicine consumption [6,7]. Despite this, medication adherence in CVD prevention remains suboptimal, with 49 % of patients exhibiting non-adherence within five years following their lipid prescription [8,9]. Poor adherence to CVD medications, such as lipid and blood pressure lowering therapies is linked with significantly worse risk factor control and increased incidence of cardiovascular events and death [10,11]. A meta-analysis of 161 studies found that the global prevalence of antihypertensive medication nonadherence ranged between 27 % and 40 % and no significant change in trend was detected between 2010 and 2020 [12]. The impact of non-adherence to CVD medications directly leads to lost therapeutic benefit and wastage of resources [13].

Clinical Decision Support Tools (CDSTs) have been explored as a potential method of addressing medication non-adherence and ensuring best-practice quality of primary care. CDSTs are typically integrated with electronic health records (EHRs) to prompt clinicians or health practitioners to administer evidence-based and patient-specific care [14]. These tools encompass various features such as digital alerts, pop-ups, and notifications, either active or passive, offering recommendations related to clinical management, diagnostics, or patient safety [15]. While some studies have explored the potential of CDSTs in addressing medication adherence, follow-up and screening practices in CVD care, there is a pressing need to quantitatively assess and evaluate their effectiveness in the context of primary care [16].

Current evidence on CDSTs is inconclusive for several important CVD outcomes. While CDSTs have demonstrated success in facilitating referrals for screening and prompting clinical tests and treatments, [14, 17] their effectiveness in supporting medication adherence and risk factor attainment is unclear [14]. Furthermore, the most recent systematic review of CDSTs in CVD care was published in 2015, but with development of new tools and inclusion of new patient subgroups, a new analysis on effectiveness is needed. Past research has emphasised the necessity to quantify the magnitude of improvements in medication adherence and risk factor attainment resulting from CDSTs rather than highlighting their features [14]. Therefore, the primary objective of this review is to systematically examine and assess the effectiveness of CDSTs in enhancing the quality of care outcomes associated with primary CVD prevention.

2. Methods

A systematic review was undertaken in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocols [18], with the study prospectively registered with PROSPERO (CRD42023449368) on 14th of August 2023.

2.1. Eligibility criteria

Studies of patients with one or more risk factors for CVD, such as hypertension, hyperlipidaemia, diabetes, high Body Mass Index (BMI), and chronic kidney disease (CKD), were considered eligible for inclusion and studies focusing on patients with an existing CVD diagnosis (i.e. atrial fibrillation, myocardial infarction, heart failure, angina pectoris etc.) were excluded. For this review CDST comprised digital notifications or alerts delivered through the Electronic Health Record (EHR) prompted to healthcare providers. Studies employing tools unrelated to patient care, utilising simulated patients, designed for diagnostic decisions or directed to patients were excluded. Additionally, studies comparing different types of CDSTs were excluded from this scope of research.

Studies were included if they reported on at least one of the primary outcomes and were not published before 2013 to reflect technological advancements in CDSTs and time since the last systematic review on this topic was published [17]. Only randomised controlled trials were considered for inclusion.

Primary outcomes included measures related to the quality of care and/or patient-related outcomes. Quality of care included: changes in prescribing or prescription adjustments, changes in ordered screening tests (i.e. clinical biomarkers) for monitoring of clinical targets attainment and completion of preventive care services. Patient outcomes encompassed follow-up on medication or appointment adherence, and attainment of clinical biomarkers (i.e. low-density lipoprotein cholesterol (LDL-C), blood pressure, glucose levels)

2.2. Search strategy and study selection

A comprehensive search was conducted across Ovid Medline, Ovid Embase, CINAHL, and Scopus, limited to English literature. The search strategy underwent validation by a medical librarian (LR) and is documented in Appendix 1. Covidence was employed for the management of study selection and quality assessment [19]. Protocols were checked for updated, published results to identify additional relevant studies. Six independent reviewers (CN, IB, DB, CT, ST, MOH) screened titles and abstracts for inclusion, with conflicts resolved by team supervisors (ST, MOH). Studies passing the initial screening were then assessed for full-text inclusion by at least two independent investigators (CN, IB, DB, CT), resolving conflicts through team discussion with senior authors (ST, MOH).

2.3. Data extraction

Data extraction was performed by two reviewers (CN, IB) using an Excel-based form following Cochrane guidelines [20], capturing information on the intervention, effect measures, outcomes, and results. Extracted data were verified by another investigator (either BC, ST or JK) to ensure accuracy and relevance.

2.4. Risk of Bias assessment

At least two reviewers (CN, IB, DB, CT) independently assessed the Risk of Bias (RoB) for each study using a quality assessment form adapted from the Cochrane RoB-2 tool [21] within Covidence [19]. Each domain of overall risk was rated as low, unclear, or high. Consensus for the overall risk of bias in each domain was reached through a senior third reviewer's judgement (ST, MOH), and the results were condensed into an Excel spreadsheet for visualisation. In addition, 3 reviewers (ST, CT, JK) applied GRADE to independently assess the level of evidence based on the study's outcomes as referred to in the supplementary material.

2.5. Data synthesis

The subsequent phase involved data analysis, where the synthesised data were examined and interpreted to draw meaningful conclusions regarding the impact of CDSTs on quality of care and/or patient-related outcomes in primary CVD prevention**.** Due to the differences in the effect outcomes reported by the included studies, we were limited to performing quantitative data synthesis for studies reporting on the attainment of clinical biomarkers (LDL-C, blood pressure, and glucose levels). Remaining outcomes were synthesised narratively Means and standard deviations (SDs) associated with baseline and post-intervention outcomes were included in the meta-analysis. The mean difference (MD) was the effect size. A random-effects model was employed to account for potential heterogeneity among included studies. The restricted maximum likelihood (REML) method was used to estimate the between-study variance [22]. Forest plots were generated to visually assess individual study effects, along with the overall pooled effect estimate and 95 % confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic, where values of 25 %, 50 %, and 75 % represented low, moderate, and high heterogeneity, respectively. Subgroup analyses were conducted to explore potential sources of heterogeneity based on study characteristics (Appendix 2). In addition, sensitivity analyses were performed to assess the robustness of the results by excluding studies with a high risk of bias or those with specific characteristics that may influence the overall effect estimate. R programming language, version 4.3.2., was used for statistical computing.

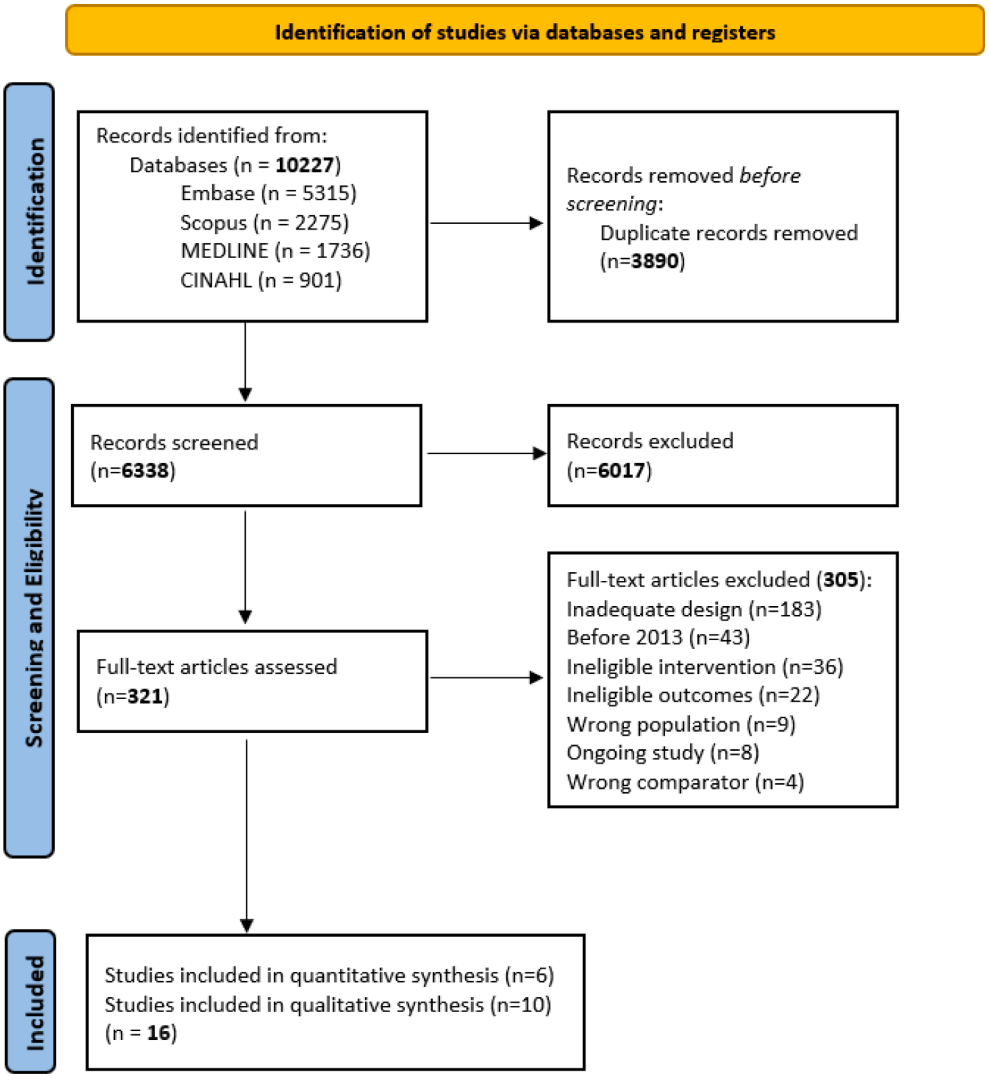


Fig. 1. PRISMA flow diagram.

3. Results

3.1. Study selection and exclusion

A comprehensive search initially identified 6337 potential studies. After screening, 6017 studies were deemed irrelevant based on title and abstract, and 321 studies proceeded to full-text review. Following rigorous scrutiny, 183 studies were excluded during full-text review due to updated criteria (inclusion of randomized controlled trials only), and a further 43 studies were excluded due to pre-2013 publication. Various other reasons for exclusion are shown in Fig. 1.

3.2. Characteristics of included studies

Of the 16 studies meeting inclusion criteria, the majority were conducted in high-income countries. Specifically, seven studies originated from the USA [23–29], three from European countries, one each from Belgium [30], Italy [31], and Spain [32], two from the UK [33,34], two from Asian countries [35,36], and one each from Australia [37] and Ghana [38]. All studies adopted a randomized controlled trial design, with eight utilising a cluster-randomized control trial design [23–25,27,30,32,34,35]. The primary settings for these studies were predominantly within primary care facilities, encompassing primary care departments and general practitioner practices, with two studies reporting hospital setting [32,36], and one each an integrated multispecialty group practice [28] and an academic medical centre [23].

Variability was observed in follow-up durations, ranging from 3 months to 24 months, with a median of 12 months. Although studies generally maintained a balanced distribution of sex, participant ethnicities were predominantly reflective of the most prominent ethnicity within the respective country. All studies included adults (mean age ranging 50–73 years), apart from one conducted in adolescents 10–17 years old [26].

The primary prevention cohorts comprised patients with type 2 diabetes mellitus [30,34,36,38], hypertension [26,27,31,35] and chronic kidney disease [28,29]. Sample sizes ranged from 77 to 74,608, with larger sample sizes in studies with a greater number of randomized practices. The most commonly measured outcome was change in clinical targets such as blood pressure (BP), LDL-C, or glycated haemoglobin (HbA1c) levels [27,29–32,34–38], followed by changes in adherence to clinical guidelines such as guideline directed prescribing [23–25,28,34,37], changes in patients' adherence [27,29,31,38], and changes in number of ordered or completed healthcare procedures (i.e. referrals, tests, follow-ups) [26,28,33,37].

CDSTs were mostly intended to be used by primary care or specialist physicians [23,24,38,25,28,30,32,34–37], but several were designed for nursing personnel [26,31,36] and wider clinical staff including pharmacists, physician assistants, therapists, and healthcare students [27,29,33].

Diversity was evident in the reporting of CDST descriptions. Only six studies reported how CDST alerts could be responded to, with three studies reporting the alerts required an action (accepting or dismissing the alert) [23,24,27], and three reporting the alert could be ignored [26,33,35]. Two CDST tools used multiple colour schemes (red, yellow, green) to draw attention to the clinical reminder [30,38]. The tools could be grouped into three categories: risk assessment, guideline-based recommendation, and combination CDST. Risk assessment tools used clinical data to stratify patients into risk categories [29,33,36,38], guideline-based CDST employed available clinical guidelines to form alerts for healthcare providers [23–25,30,31], and combination CDST employed both methods to inform decisions regarding primary prevention [26–28,32,34,35,37].

Overall, seven studies [23,26,27,29,30,34,37] demonstrated no effectiveness for either quality of care or patient-related outcomes. Four studies demonstrated partial effectiveness [25,28,31,32], meaning effectiveness of the CDST was evident for a portion of reported outcomes. In those instances, effectiveness was shown for the quality of care outcomes of specialist referral and adherence to screening and treatment guidelines, and for the patient-related outcomes of attainment of risk factor targets. Five studies demonstrated effectiveness of CDST in improving quality of care and patient-related outcomes [24,33,35,36,38]. Table 1 provides additional information on study characteristics, while Appendix 3 contains a comprehensive table with detailed information on selected studies.

3.3. Risk of bias

Owing to the inherent characteristics of the intervention, a considerable number of studies had indeterminate risk of bias concerning the blinding of both practitioners and participants. This primarily emanated from practitioners being cognisant of their utilisation of the intervention tool, and in five instances, patients also being aware. Conversely, a majority of the studies demonstrated a low risk of bias concerning the generation of randomization sequences and the reporting of comprehensive outcome data. The blinding and concealment processes, however, were frequently inadequately detailed across studies, posing challenges in rendering a definitive assessment of paper quality. A graphical representation of the evaluation of each paper is presented in Fig. 2, and details on risk of bias assessment for each domain can be found in Appendix 4.

3.4. Effects of interventions - Quantitative synthesis attainment of clinical targets (i.e. biomarkers)

A total of ten studies [27,29–32,34–38] reported on attainment of risk factor targets as a measure for monitoring risk factor improvement, of which nine focused on blood pressure changes [30–32,35–38], five on LDL-C levels [30–32,36,37], and three on HbA1c levels [30,32,36] (Table 1). Based on reported results, six studies were included in the meta-analysis [30–32,34,36,38] presented in Figs. 3-6. Of the four studies which could not be included in the meta-analysis, due to differences in reported outcome measures, one was assessed as effective in achieving lower blood pressure levels [35], with the mean difference in systolic blood pressure between intervention and control group of −7.11 mmHg (95 %CI −13.11 to −2.23 mmHg; $p = 0.008$), and the mean difference in diastolic blood pressure of −3.29 mmHg (95 % CI −6.32 to −0.87 mmHg; $p = 0.041$) while three were assessed as ineffective in achieving changes in blood pressure [27,29,37]. Kressin et al. report a non-significant 0.10 mmHg decrease in systolic blood pressure ($p = 0.88$) and a 0.70 mmHg decrease in diastolic blood pressure ($p = 0.06$) in the reminder group [27]. Similarly, Tuot at al. indicated a non-statistically different change in systolic blood pressure in the intervention group (−0.5 mmHg (95 % CI −5.5–4.5)) compared to usual care (0.5 mmHg (95 % CI −5.2–6.3)) [29]. Webster et al. stated similar percentages of patients in both groups achieved treatment targets of blood pressure and LDL cholesterol (19.6 % in the intervention versus 20.1 % in control, RR= 1.06 (95 % CI 0.85–1.32)) [37].

3.5. Attainment of LDL-C

Three studies [30,31,36] with a total of 5705 people involved/randomised and followed up for 6 months were included in the analysis of the effect of CDST and attainment of LDL-C recommended targets. Overall pooled analysis suggested an estimated Mean Standardised Difference (MSD) = 0.01, 95 %CI = −0.10 - 0.11, as represented in Fig. 3. Risk of bias across these three studies ranged from low/unclear [30,31] to high [36] (Table 1).

3.6. Attainment of SBP/DBP

Three studies [30,31,38] with a total of 4213 people involved/randomised and followed up for 6 months were included in the

Table 1
Characteristics of included studies.

Author, year of publication, country	Total study duration	Setting	Intervention description	Outcome assessed	Sample Size	Effect Size/Standard Error (95 %CI)	Effectiveness of the assessed intervention	Risk of Bias
Attainment of clinical targets (i.e. biomarkers)								
Adjei et al.[38], 2015, Ghana	6 months	national diabetes management and research centre	newly developed clinical reminder - generated pop-ups	compliance with appointment dates and changes in blood pressure	200	SBP IG −4.3 vs UC −2.8 (p = 0.002), DBP IG −5.3 vs UC −3.1 (p = 0.001)	Effective	High
Anchala et al.[35], 2015, India	12 months	primary health care centres	CDSS with guidelines and alerts - could be ignored	SBP and DBP differences	1634	SBP: IG vs UC −7.11 (−13.11 to −2.23), DBP: IG vs UC −3.29 (−6.32 - −0.87)	Effective	High
Chan et al.[36], 2022, Multinational - Asia	4 years and 7 months	Hospital-based diabetes centres	JADE portal - automated decision support for patients and physicians	change in HbA1c, LDL-C and blood pressure levels	2393	HbA1c: IG vs UC −0.39 % (p = 0.004), LDL-C: IG vs UC −0.14 (p = 0.001)	Effective	High
Cicolini et al.[31], 2013, Italy	8 months	primary care practices	NRP-e - email and phone call alerts	changes in fasting blood glucose, LDL-C, blood pressure levels and lifestyle parameters	203	SBP change: IG −14.9 vs UC −10, (p < 0.001), DBP change: IG 11 vs UC −7.6, (p < 0.001), LDL-C change: IG −36.9 vs UC −26.8, p < 0.001)	Effective	Low/ Unclear
Heselmans et al.[30], 2020, Belgium	12 months	primary care practices	EBMeDS - patient-specific reminders, therapeutic suggestions and diagnoses specific guidelines to practitioners	change in HbA1c, LDL-C and blood pressure levels	3815	HbA1c 12 month change mean difference −0.40 (−0.70, −0.09), LDL-C 12 month change mean difference 0.14 (−4.84, 5.11), SBP 12 months change mean difference 0.06 (−2.39, 2.27), DBP 12 month change mean difference 0.87 (−0.69, 2.44)	Not effective	Low/ Unclear
Kressin et al.[27], 2016, USA	8 months	primary care clinics	EMR reminder for hypertension care	changes in blood pressure and antihypertensive medication adherence	11,528	DBP: IG vs UC −0.70 (p = 0.06), SBP: IG vs UC −0.10 (p = 0.88)	Not effective	High
Tuot et al.[29], 2019, USA	18 months	primary care clinics	EHR enabled CKD registry tool	changes in systolic blood pressure	137	IG −0.5 (05.5 to 4.5), UC 0.5 (−5.2 - 6.3)	Not effective	High
Webster et al.[37], 2021, Australia	33 months	general practices	INTEGRATE - recommendations based on individual CV risk	achievement of optimal blood pressure and LDL-cholesterol levels	4477	IG 19.6% vs UC 20.1 %, - RR 1.06 (0.85–1.32)	Not effective	High
Willis et al.[34], 2020, United Kingdom	24 months	health care practices	IT software prompt appeared at consultation time	achievement of target blood pressure and total cholesterol levels	2721	OR 7 % increased rate of achievement of targets (p = 0.647)	Not effective	High
Zamora et al.[32], 2013, Spain	3 months	hospitals and primary care centres	HTE-DLP - creates recommendations based on treatment efficiency, safety and cost	changes in LDL-C and HbA1c	77	mean change HbA1c: IG 0.2 vs UC 0.3 (p=NS); mean decreased LDL-C: IG 63.3 vs UC 33.8, (p = 0.05)	Effective for LDL Not effective for HbA1c	Unclear
Adherence to clinical guidelines (treatment choices, prescribing)								
Adusumalli et al.[23], 2021, USA	12 months	Penn Medicine, University of Pennsylvania	passive and active choice EHR alerts to cardiologists	change in guideline directed prescribing of statins	11,693	active choice 0.2 % change (−2.9 - 2.8), passive choice 2.4 % change (−0.6 - 5.0	Not effective	Low
Adusumalli et al.[24], 2023, USA	18 months	primary care practices	active prompts including guidelines for prescribing	initiation of statin prescription at visit	4131	IG vs UC 5.5 % (3.4 - 7.8) increase in prescribing	Effective	Low
Carter et al.[25], 2018, USA	12 months	family medicine officers	real time guideline based recommendations placed into the EHR	changes in adherence to screening and treatment guidelines	302	IG 63.3 % to 67.8 % (p = 0.02); UC 64.7 % to 63.1 % (p = 0.21)	Partially effective*	High
Sequist et al.[28], 2018, USA	18 months	Harvard Vanguard Medical Associates	referral and prescription recommendations from EHR alerts	proportion of patients prescribed ACEi or ARB	7691	high risk population-intervention 76% vs control 79 %; p = 0.17 low risk population-intervention 64% vs 65 %; p = 0.57	Not effective	Low/ Unclear
Willis et al.[34], 2020, United Kingdom	24 months	health care Practices	IT software prompt appeared at consultation time	changes in T2DM, BP, and cholesterol-lowering medication prescribing	2721	antihypertensives: mean difference IG vs UC −3.5; OR= 0.84 (0.66–106), p = 0.143 lipid-lowering: mean difference IG vs UC 3.62; OR= 0.99 (0.76–1.29), p = 0.955 antidiabetics: mean	Not effective	High

(*continued on next page*)

Table 1 (*continued*)

Author, year of publication, country	Total study duration	Setting	Intervention description	Outcome assessed	Sample Size	Effect Size/Standard Error (95 %CI)	Effectiveness of the assessed intervention	Risk of Bias
						difference IG vs UC 2.41; OR=1.04 (0.66–1.65), p = 0.862		
Webster et al.[37], 2021, Australia	33 months	general practices	INTEGRATE - recommendations based on individual CV risk	proportion of patients with intensified treatment (newly prescribed or added medication)	4477	not significant: IG 24.4% vs UC 26.8 %, RR=0.94 (0.76–1.16)	Not effective	High
Screening/Clinical Tests Completed/Ordered:								
Gold et al.[33], 2021, UK	4 months	primary care practices	clinical staff prompted with referral for check	attendance at the NHS Health Check	7564	4.58 % increase attendance, OR = 2.62 (1.46 to 3.55), p < 0.001	Effective	Low/ Unclear
Kharbanda et al.[26], 2017, USA	24 months	primary care practices	EHR alerts and best-practice advisories that appear	return for follow up BP measurement	1824	IG 14.3 %, UC 10.6 % (p = 0.07) return for follow up	Not effective	Unclear
Sequist et al.[28], 2018, USA	18 months	Harvard Vanguard Medical Associates	referral and prescription recommendations from EHR alerts	return for follow up nephrologist visit/ urine test	7691	IG 45 %, UC 34 % likely to follow up with nephrologist (p < 0.001) IG 45% vs UC21 % likely to receive urine test (p < 0.001)	Effective	Low/ Unclear
Webster et al.[37], 2021, Australia	33 months	general practices	INTEGRATE - recommendations based on individual CV risk	proportion of patients with appropriate CVD risk screening (smoking status, SBP and cholesterol levels)	4477	not significant: IG 58.6% vs UC 62.2 %, RR=0.99 (0.82–1.20), p = 0.11	Not effective	High
Patients' adherence:								
Adjei et al.[38], 2015, Ghana	6 months	national diabetes management and research centre	newly developed clinical reminder - generated pop-ups	adherence to appointments	200	IG 97.8% vs UC 89.4 % (p = 0.01)	Effective	High
Cicolini et al.[31], 2013, Italy	8 months	primary care practices	NRP-e - email and phone call alerts	antihypertensive medication adherence	203	IG 100% vs UC 100 % (p = 0.9)	Not effective	Low/ Unclear
Kressin et al.[27], 2016, USA	8 months	primary care clinics	EMR reminder for hypertension care	antihypertensive medication adherence	11,528	IG 85.7% vs UC 84.3 %; p=not significant	Not effective	High
Tuot et al.[29], 2019, USA	18 months	primary care clinics	EHR enabled CKD registry tool	adherence to CKD medications	137	not significant: mean difference IG −0.1 vs UC −0.2, p = 0.09	Not effective	High

ACEi- angiotensin-converting enzyme inhibitor, ARB- angiotensin receptor blocker; BP- blood pressure; CDSS- clinical decision support system; CI- confidence interval; CKD- chronic kidney disease; CV- cardiovascular; DBP- diastolic blood pressure; EBMeDS- Evidence-Based Medicine electronic Decision Support; EHR/EMR- electronic health/medical records; HbA1c - glycated haemoglobin; HTE-DLP- clinical decision support system for dyslipidaemia treatment in high vascular risk patients; IG- intervention group; INTEGRATE- Integrated combination Therapy, Electronic General practice support tool, pharmacy-led intervention and combination Therapy Evaluation; IT- information technology; JADE- Joint Asia Diabetes Evaluation web portal; LDL-C- low-density lipoprotein cholesterol; NHS- National Health Service; NRP-e - nurse-led reminder program through email; NS- not significant; OR- odds ratio, RR- risk ratio; SBP- systolic blood pressure; T2DM- type 2 diabetes mellitus; UC- usual care * intervention was effective for a portion of reported outcome.

analysis of the effect of CDST and attainment of recommended systolic blood pressure (SBP) targets. Fig. 4 depicts, overall pooled analysis suggested an estimated MSD = 0.39, 95 %CI = −0.31 - 1.10. Risk of bias across these three studies ranged from low/unclear [30,31] to high [38] (Table 1).

Three studies [30,31,38] with a total of 4213 people involved/randomised and followed up for 6 months were included in the analysis of the effect of CDST and attainment of recommended diastolic blood pressure (DBP) targets. Overall pooled analysis suggested an estimated MSD of 0.34 (95 % CI: −0.24, 0.92; depicted in Fig. 5). Risk of bias across these three studies ranged from low/unclear [30,31] to high [38] (Table 1).

3.7. Attainment of HBA1C

Four studies [30,32,34,36] with a total of 8229 people involved/randomised and followed up for 6 months were included in the analysis of the effect of CDST and attainment of recommended glucose level targets. Overall pooled analysis suggested an estimated MSD of −0.19 (95 %CI −0.66, 0.28) The meta-analysis results are presented in Fig. 6. Risk of bias across these four studies ranged from low/unclear [30] to unclear [32] and high [34,36].

3.8. Effects of intervention - qualitative synthesis adherence to clinical guidelines (treatment choices, prescribing of medications)

In total, six studies [23–25,28,34,37] addressed adherence to clinical guidelines. Five studies explored changes in statin prescribing [23–25,34,37], four changes in antihypertensives prescribing, such as angiotensin-converting enzyme inhibitors or angiotensin receptor blockers [25,28,34,37], and two changes in prescribing of glucose lowering therapies [34,37]. While the meta-analysis shows CDST did not significantly impact lipid levels attainment, two studies reported effectiveness of active prompt CDST in increasing initiation of statin prescribing. Adusumalli et al. in 2023. described a 5.5 % (95 % CI 3.4, 7.8) difference in prescribing between intervention and usual care [24], while Carter et al. reported an increase in the intervention group from 33.3 % to 67.5 % (p < 0.001) and insignificant change in the control group (32.9 % to 33.1 %, p= NA) [25]. CDST were not effective in increasing or changing guideline directed prescribing of antihypertensives (neither for treatment intensification nor for different patient groups such as high or low risk patients or patients with uncontrolled hypertension), or glucose lowering therapies.

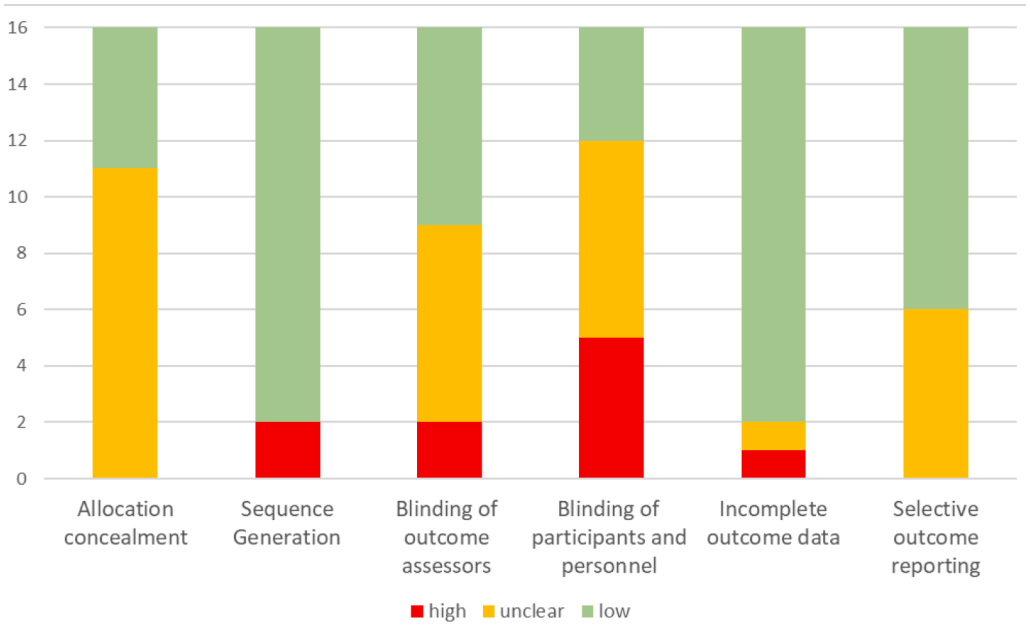


Fig. 2. Risk of bias.

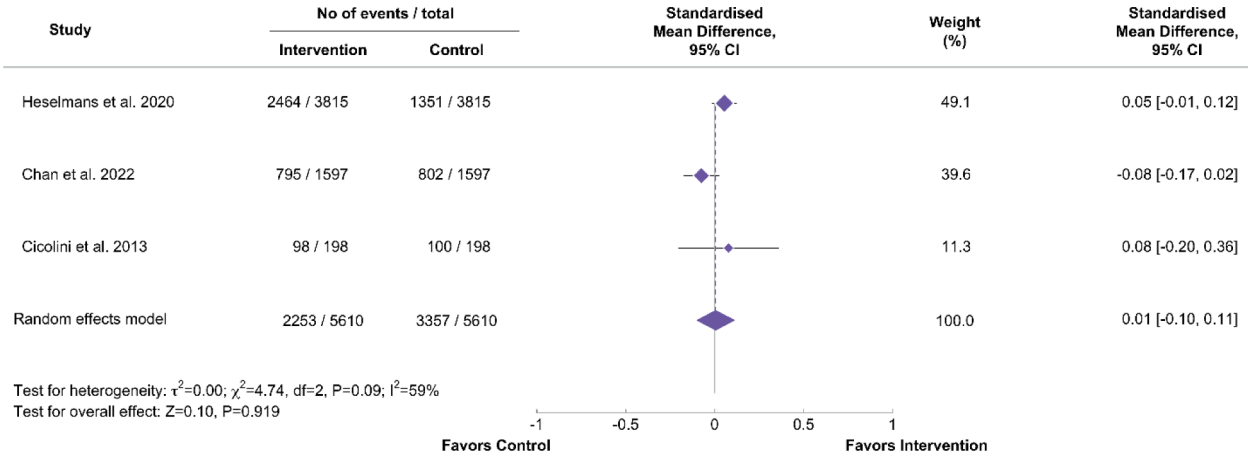


Fig. 3. Meta-analysis results for LDL cholesterol attainment.

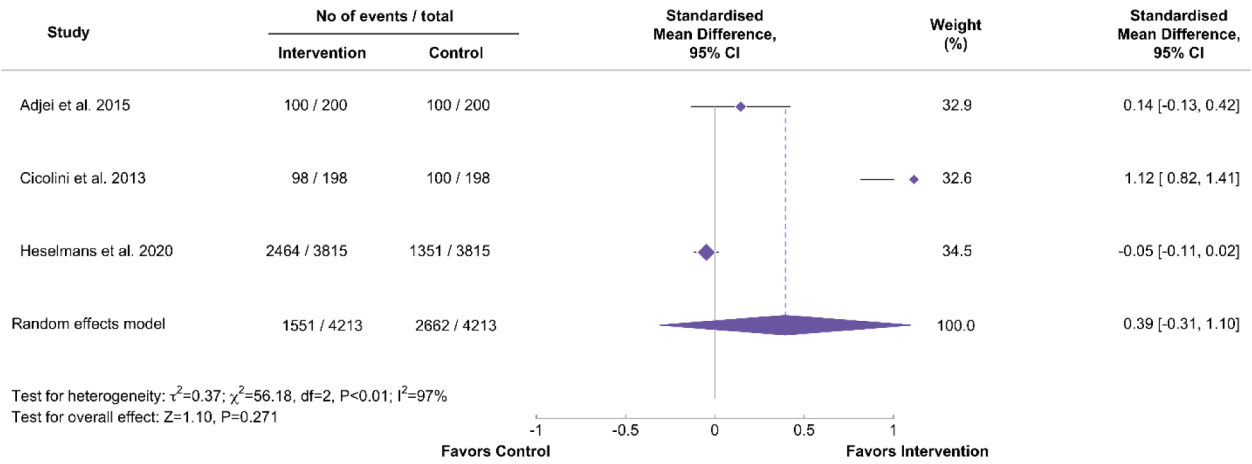


Fig. 4. Meta-analysis results for systolic blood pressure attainment.

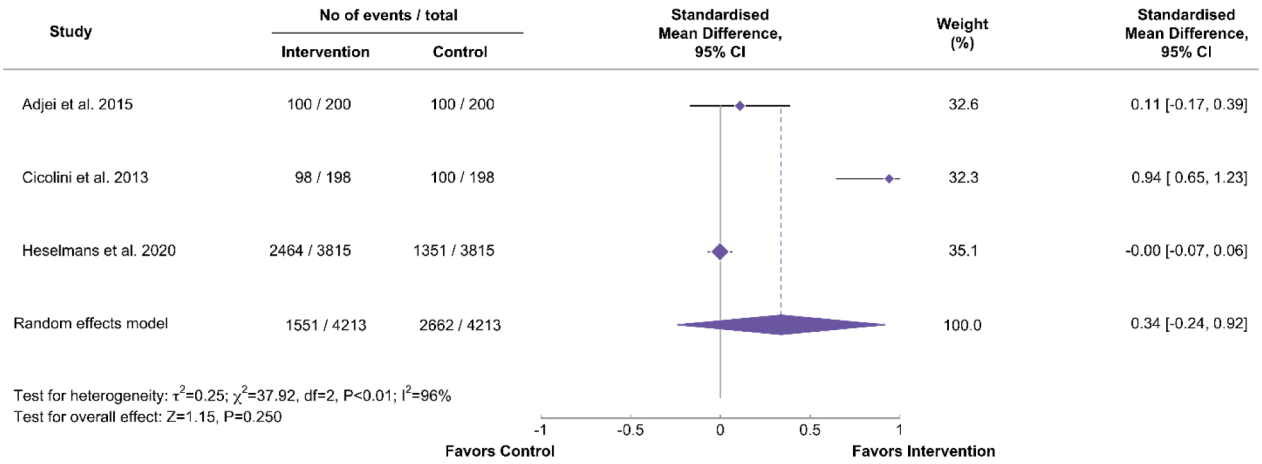


Fig. 5. Meta-analysis results for diastolic blood pressure attainment.

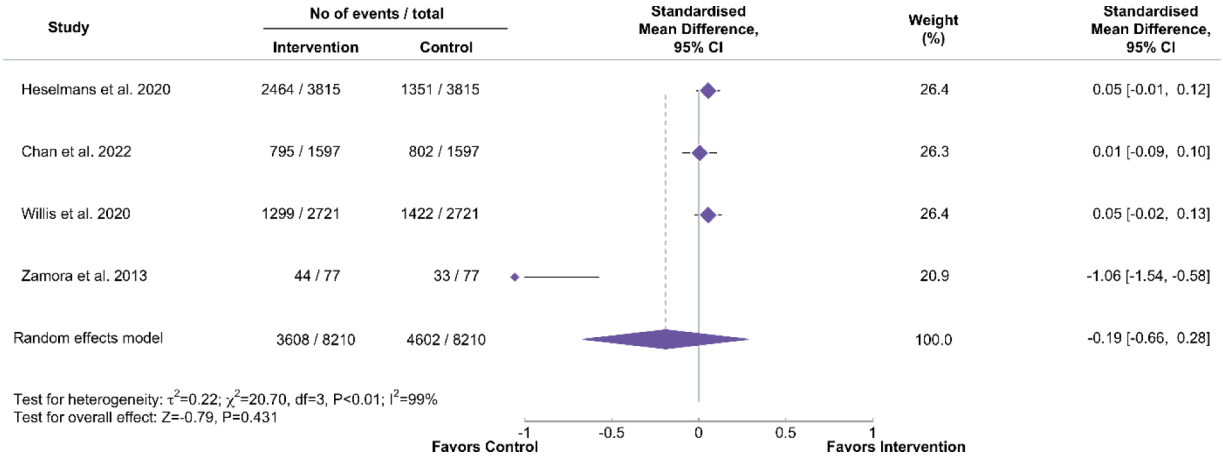


Fig. 6. Meta-analysis results for HbA1c attainment.

3.9. Screening/Clinical tests completed/ordered

Besides reporting on results of clinical tests used for biomarker control, such as blood glucose levels, HbA1c, or cholesterol levels, four studies reported referrals, follow up visits, or screenings as outcomes [26,28,33,37] with presence of conflicting results. Kharbanda et al. found no significant difference between groups in return to follow-up blood pressure screening (14.3 % in intervention versus 10.6 % in control group, $p = 0.07$) and Webster et al. reported no significant difference between groups in cardiovascular disease risk screening, for the composite outcome which included recorded smoking status, total and high-density lipoprotein cholesterol level, and systolic blood pressure screening (58.6 % in intervention versus 62.2 % in control group; RR=0.99 (95 % CI 0.82–1.20), $p = 0.11$) [26,37]. Whereas Gold et al. reported a significant increase (4.58 % absolute increase and a 61.81 % relative increase) in follow-up screening attendance in the intervention group (OR=2.62 [95 % CI 1.46,3.55]; $p < 0.001$), and Sequist et al. found CDST was effective in increasing nephrologist referrals and visits, and urine microalbumin testing (both $p < 0.001$) [28,33].

3.10. Patients' adherence

In total, four studies provided insights into patients' adherence, three focusing on medication adherence [27,29,31], and one focusing on adherence to appointments [38]. Due to high heterogeneity in follow-up periods and measurement/reporting methods, meta-analysis was deemed unfeasible for this outcome. Kressin et al., Tuot et al., and Cicolini et al. collectively indicated no significant difference in medication adherence between intervention and control groups, while Adjei et al. reported a statistically significant difference between groups in clinical appointments adherence (97.8 % in intervention versus 89.4 % in control group, $p = 0.010$) [27,29,31,38].

4. Discussion

Our systematic review investigated diverse clinical decision support interventions aimed at improving risk of developing CVD across various primary healthcare settings and regions. Our findings offer a nuanced understanding of the effectiveness of these complex health interventions, shedding light on both successful and less impactful interventions. Overall, we found evidence on the effectiveness of CDST on a limited number of quality of care outcomes, which demonstrates their potential provided there is a successful implementation, uptake and duration of use of such tools in clinical settings. These results remained largely unchanged from the last review performed on this topic [17] and an earlier review of CDSTs on clinical and economic outcomes in the general population [39].

Pooled meta-analysis for blood pressure target attainment (i.e. systolic and diastolic) shows a trend towards improvement with the integration of CDST in primary care practices, whereas attainment of lipid and glucose clinical targets (LDL-C and Hba1c) did not seem to improve with the implementation of CDSTs. It is important to note that these trends were not statistically significant, but suggest potential benefit. A systematic review and meta-analysis on the effect of CDSS on

cardiovascular risk factors in both primary and secondary prevention, by Groenhof et al., confirms heterogeneity of findings and results tending towards a beneficial effect of CDST but only for LDL-C attainment in diabetes patients [40]. A cluster randomized trial exploring the effect of clinical decision support on the risk of cardiovascular disease reports CDST failed to improve CVD risk, but could be beneficial for patients with high baseline risk. [41] In regard to adherence to clinical guidelines for treatment choices and prescribing of medication, the study by Adusumalli et al. in the US revealed that CDST with a choice of dismissible (passive choice) and undismissible (active choice) alert EHR alerts targeted at academic specialist practices had limited effectiveness in influencing guideline-directed prescribing of statins [23]. Conversely, the follow-up study [24] in primary care practices demonstrated that active choice prompts, including guidelines for prescribing, were successful in increasing the initiation of statin prescriptions during patient visits [24]. This may be due to the nature of active prompts in forcing clinicians to address these alerts. In a family medicine setting, real-time guideline-based recommendations placed into the EHR showed partial effectiveness in changing adherence to screening and treatment guidelines [25]. In contrast, a large-scale study in the United Kingdom by Willis et al. using CDSTs alerts in the form of information technology (IT) software prompts did not demonstrate significant improvements in the prescribing of medications for blood pressure, blood glucose and cholesterol management[34]. Additionally, the INTEGRATE intervention in general practices in Australia did not significantly impact the proportion of patients with intensified treatment, indicating challenges in achieving treatment optimisation based on individual cardiovascular risk [37].

In terms of screening and provision of clinical tests completed or ordered, a study involving staff prompts for a health check in the UK was successful in increasing attendance, illustrating the positive impact of targeted reminders on patient engagement [33]. In contrast, EHR alerts in the US did not significantly influence the return for follow-up blood pressure measurement [26]. The study by Sequist et al. demonstrated the effectiveness of EHR alerts in increasing patient follow-up with nephrologists and adherence to urine tests, suggesting the potential role of targeted interventions in promoting screening and clinical test completion [28]. However, in Australia, the INTEGRATE recommendations did not significantly impact the proportion of patients undergoing appropriate cardiovascular disease risk screening, emphasising the challenges in achieving optimal screening rates [37].

In relation to patients' adherence, a study conducted in Ghana reported that newly developed clinical reminders significantly improved patient adherence to appointments [38]. However, in an Italian primary care setting, the NRP-e intervention, involving email and phone call alerts to patients, significant improvements in antihypertensive medication adherence within six months were not reported [31]. Similarly in the US, Kressin et al. found EMR reminders for hypertension care were not effective in improving patient adherence to antihypertensive medications [27]. Another US study focusing on chronic kidney disease (CKD) medications also found the EHR-enabled CKD registry tool did not significantly impact medication adherence, indicating challenges in addressing adherence issues in this patient population [29]. Alasiri et al., in their five-study- systematic review on the role of clinical decision support systems in preventing stroke in primary care, confirm that CDST can facilitate decision-making process in the primary care setting, but there are various barriers in designing, implementing and using such support systems and tools [42].

It is evident that the effectiveness of CDSTs is context-dependent, influenced by the nature of the intervention, the population under study, and the healthcare setting and workforce. These findings contribute to the ongoing dialogue on the optimisation of CDSTs for enhanced patient care and management of cardiovascular conditions. The results obtained in our study align with and contribute to the broader literature on the effectiveness of CDST in healthcare settings. Comparisons with existing studies highlight both consistencies and divergences, offering valuable insights into the complexities of implementing such interventions.

Adusumalli et al.'s research echoes the challenges of achieving significant changes in prescribing behaviour solely through passive EHR alerts, a sentiment supported by studies such as O'Connor et al. and Olakotan et al. [43,44]. Active prompts, as demonstrated by Adusumalli et al. (2022), are consistent with the success reported in interventions by Bright et al. [39] and Persell et al. (2013) [39,45], showcasing the impact of proactive strategies. It is believed that active alerts are associated with higher compliance rates compared with passive alerts. This is because active presentation causes disruption to the clinical workflow, increasing urgency for the alert to be actioned. Comparatively, a study explored the psychological notion that passive alerts provided clinicians the option to cancel or defer the CDS alert, which is formally conceptualised as a 'workaround', resulting in poorer compliance.

Similarly, Carter et al.'s [25] findings of partial effectiveness in guideline adherence resonate with studies like Cabana et al. [46], emphasising that comprehensive changes often require multifaceted interventions. Willis et al.'s [34] challenges in achieving significant changes in medication prescribing align with observations in studies like Garg et al. [47] and Bates et al. [48], illustrating the intricacies of IT software prompts [47,48].

The positive impact of clinical staff prompts on patient appointment attendance aligns with the success reported in studies such as Sequist et al. [49] and Anhoj and Hellesøe (2004). However, challenges in influencing follow-up behaviours through EHR alerts, as observed by Kharbanda et al.[26], are consistent with findings from studies like Sequist et al. (2011) and Dexter et al. (2018) [26,50].

Patient adherence findings in our study align with broader literature trends. The positive impact of clinical reminders on appointments concords with findings reported by Stockwell et al. (2007) and Szilagyi et al. (2002) [51]. Challenges in achieving significant improvements in medication adherence, as observed by Cicolini et al. (2013)' are consistent with findings in studies by Rasmussen et al. (2007) and Haynes et al. (2008) [31,52,53].

4.1. Barriers to successful implementation of CDST

Despite the potential for CDST to improve the delivery of patient care and cardiovascular health outcomes, various barriers hinder its successful implementation, thereby limiting its effectiveness in achieving health targets. A systematic review revealed that 31 out of 58 RCTs encountered barriers during the implementation of CDS interventions. The prevalent barriers identified were time and resource constraints, lack of compatibility with workflow, alert fatigue, technical difficulties with the CDS system, lack of trust in CDS recommendations and complexity of real world clinical management of CVD. In relation to time and resource constraints, clinicians reported that CDS was not well integrated into daily practice routines where busy practitioners manage patients with complex conditions. In addition, it was reported that alert fatigue was a significant contributor to the low uptake of CDS. More specifically, clinicians would ignore the recommendation made by the alerts as it did not provide actionable and appropriate recommendations that are of relevance to their current diagnosis.

Given the complexity of real world clinical situations, the implementation of CDSTs and its ability to reach cardiovascular health outcomes may be difficult. A study in the UK with 1493 patients assessed the effect of a CDS tool for atrial fibrillation. Post-survey results reveal that more than half of clinicians discussed anticoagulation treatment with their patients, however only 6 % followed through with the change. Reasons associated with failure to be receptive to treatment include; patient preferences, treatment being managed by another specialist, and concerns associated with adverse risks such as being more susceptible to falls in elderly patients. Thus, it is important to acknowledge that barriers to implementation of CDS tools exist on multiple levels which can affect its ability to achieve clinical outcomes. The presence of these

barriers may contribute to the heterogeneity of our study's findings.

In summary, our study contributes to a growing body of evidence emphasising the context-dependent and multifaceted nature of CDSTs in healthcare. This is significant given the ongoing usage of CDSTs to enhance primary health care practices in the management and prevention of CVD. Importantly, we highlight that the effectiveness of CDSTs is context-dependent and that results are largely specific to healthcare settings and patient populations. Health care systems and providers should consider the unique characteristics of their environment when implementing CDSTs.

Secondly, our findings underscore the need for multifaceted approaches to improve guideline adherence, screening rates, and patient adherence. Combining interventions, such as active prompts and real-time recommendations, may enhance overall effectiveness. This aligns with the evolving consensus in healthcare that no single strategy fits all scenarios. The success observed with proactive interventions, such as active prompts, suggests that a more engaged and targeted approach with both patients and health professionals may be crucial. Healthcare practices may benefit from incorporating interactive decision support tools that actively guide practitioners, fostering a more responsive and patient-centred care environment.

Thirdly, acknowledging the challenges in achieving significant changes for certain outcomes highlights the complexities faced in real-world healthcare settings. Practitioners should recognise that the impact of interventions may vary, and continuous evaluation and adaptation are essential for sustained improvements.

Lastly, all the interventions reported in this review focused on clinicians, but given the growing literature supporting patient-centred care, providers should explore this interface or combination of approaches to reinforce the need to prioritise patient-centred care. The positive impact of clinical reminders on patient adherence to appointments highlights the potential for patient engagement strategies. Healthcare providers should explore ways to involve patients actively in their care plans, fostering a collaborative and supportive relationship. In addition, our findings emphasise the dynamic nature of healthcare practices, and the importance of continuous evaluation and research. Practitioners and policymakers should stay abreast of evolving evidence and regularly reassess the impact of interventions to ensure they align with current best practices and guidelines [54].

The present study lays the groundwork for future research by revealing the context-dependent nature of CDSTs. Future studies should delve into comparative effectiveness, exploring variations in design and interactivity across diverse healthcare settings. Longitudinal investigations are essential to assess the sustainability of improvements over time. Integrating patient perspectives, optimising user experiences, and tailoring interventions to specific organisational structures and cultural contexts will enhance the relevance and impact of decision support tools. Future research should explore the global applicability of these interventions, their potential to address health disparities, and the economic considerations associated with their implementation. Implementing these research directions will contribute to the ongoing refinement and optimisation of decision support systems in healthcare practices.

It is important to note that the duration of follow-up periods in the reviewed studies may not have been sufficiently long to fully comprehend the genuine effectiveness of the intervention. Notably, studies addressing medication adherence, a process that typically spans five years, lacked extended follow-up periods, hindering a comprehensive exploration of medication adherence dynamics[9]. The inherent challenge in quantifying and monitoring medication adherence is evident in the limited reporting on this aspect across the reviewed studies. Subsequent research dedicated to investigating medication adherence is imperative for elucidating the potential role of CDSTs in monitoring and enhancing outcomes in this domain. However, in the present review, studies with extended follow-up times or intervention durations did not show significant improvements for quality of care or patient-related outcomes. This trend may suggest the existence of alert fatigue, or a diminishing intended usage of the intervention over time. Future investigations should delve into understanding the underlying reasons for this phenomenon and explore strategies for optimising the sustained effectiveness of these tools, particularly in the context of primary care. The nature of the intervention introduced subtle variations in its delivery across diverse studies. Studies featuring passive choice alerts or alerts that could be disregarded demonstrated notably lower effectiveness. This observation underscores the significance of considering alert design when shaping the development of future CDSTs. However, this must be balanced with the imperative of aligning future CDSTs with the user-demands and preferences of healthcare practitioners.

5. Strengths and limitations

Our search was restricted to English literature, potentially excluding relevant studies conducted in other languages. It is conceivable that pertinent research may exist in non-English publications, but their exclusion is a limitation of our study due to language constraints.

This study's findings are constrained by the geographic and socio-economic focus on high-income developed countries, with 14 out of 16 studies conducted in such settings, which limits the generalizability of the review and meta-analysis. Results may affect the applicability of the findings to low- or middle-income settings. Additional research is needed to further evaluate the effectiveness and impact of clinical decision support tools in care for cardiovascular patients in developing and lower-income settings.

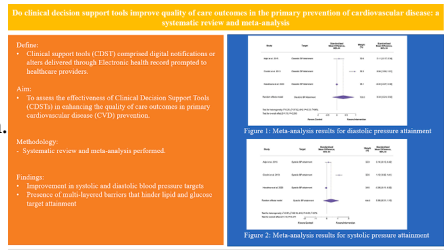
Results of this review should be viewed within a wider context of cardiovascular risk management as well. While this review and meta-analysis mainly focused on the effectiveness of CDST in enhancing the quality of care outcomes in primary cardiovascular disease management, contributions of healthcare professionals, directly or indirectly involved in patient care, should not be overlooked. Research shows that nursing staff, pharmacists, and other allied health professionals can positively impact and lower cardiovascular risk factors [55–57]. For complex interventions involving the use of clinical decision support tools and contribution of various members of the multidisciplinary team, it could be hard to discern the level of impact each aspect of the intervention had in risk factor management. The absence of blinding among practitioners and personnel likely introduced a degree of bias into the studies, acknowledging the inherent challenges in blinding practitioners when dealing with interventions such as CDSTs. It is plausible that practitioners, being cognisant of their CDST usage being monitored, might have exhibited heightened adherence to guidelines and best practices.

Significant heterogeneity was observed in both outcome measures and reporting across the studies. Variations in follow-up durations posed challenges in drawing meaningful comparisons and aggregating data for meta-analysis. Additionally, discrepancies in the implementation and design of CDSTs further complicated efforts to pinpoint the specific components of the intervention that contribute most effectively to outcomes. This heterogeneity warrants cautious interpretation of the overall findings.

6. Conclusion

CDSTs exhibit potential in enhancing quality of care outcomes within primary CVD prevention. However, the presence of barriers that result in slow uptake of CDS may hinder the ability for cardiovascular health outcomes to be achieved. This underscores the imperative for further research to comprehensively explore the mechanisms and contexts surrounding the use of these tools, aiming to address these barriers that prevent uptake of CDS and optimise their efficient use in clinical practice. Such investigations should encompass an in-depth analysis of the specific features of the tools that can be modified to enhance user engagement and effectiveness. With the growing interest and use of

artificial intelligence (AI) in patient care and health risk management, future development and research of clinical decision support tools should include the aspect of AI application. Additionally, there is a pressing need for extended research into the sustained implementation of these tools over an extended temporal horizon.



CRediT authorship contribution statement

Iva Buzancic: Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Formal analysis, Data curation, Conceptualization. **Harvey Jia Wei Koh:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation. **Caroline Trin:** Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Methodology. **Caitlin Nash:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Conceptualization. **Maja Ortner Hadziabdic:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Formal analysis. **Dora Belec:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Formal analysis, Data curation. **Sophia Zoungas:** Writing – review & editing, Validation. **Ella Zomer:** Writing – review & editing, Validation. **Lachlan Dalli:** Writing – review & editing, Validation. **Zanfina Ademi:** Writing – review & editing. **Bryan Chua:** Writing – review & editing. **Stella Talic:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2024.100855.

References

[1] Roth GA, Mensah GA, CO Johnson, Addolorato G, Ammirati E, Baddour LM, et al. Global burden of cardiovascular diseases and risk factors, 1990-2019: update from the GBD 2019 study. J Am Coll Cardiol 2020;76:2982–3021.
[2] World Health Organization. Cardiovascular diseases (CVDs). Fact Sheets 2021. https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds. Accessed 20 Nov 2023.
[3] Marquina C, Talic S, Vargas-Torres S, Petrova M, Abushanab D, Owen A, et al. Future burden of cardiovascular disease in Australia: impact on health and economic outcomes between 2020 and 2029. Eur J Prev Cardiol 2022;29:1212–9.
[4] Australian Institute of Health and Welfare. Heart, stroke and vascular disease: australian facts. 2023. https://www.aihw.gov.au/reports/heart-stroke-vascular-disease/hsvd-facts/contents/about. Accessed 27 Jan 2024.
[5] Eurostat EU. Cardiovascular diseases statistics. Cardiovasc Dis 2021. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Cardiovascular_diseases_statistics#Deaths_from_cardiovascular_diseases. Accessed 27 Jan 2024.
[6] Organisation for Economic Cooperation and Development iLibrary. Pharmaceutical consumption | Health at a Glance 2021 : OECD Indicators | OECD iLibrary. OECD Health Statistics. 2021. https://www.oecd-ilibrary.org/sites/5689c05c-en/index.html?itemId=%2Fcontent%2Fcomponent%2F5689c05c-en. Accessed 21 Feb 2024.
[7] Canadian Institute for Health Information. Prescribed drug spending in Canada, 2022. Prescribed drug spending 2022. https://www.cihi.ca/en/prescribed-drug-spending-in-canada-2022. Accessed 21 Feb 2024.
[8] Talic S, Marquina C, Zomer E, Ofori-Asenso R, Petrova M, Vargas-Torres S, et al. Attainment of low-density lipoprotein cholesterol goals in statin treated patients: real-world evidence from Australia. Curr Probl Cardiol 2022;47:101068.
[9] Talic S, Marquina C, Ofori-Asenso R, Petrova M, Liew D, Owen AJ, et al. Switching, persistence and adherence to statin therapy: a retrospective cohort study using the australian national pharmacy data. Cardiovasc Drugs Ther 2022;36:867–77.
[10] Hero C, Karlsson SA, Franzén S, Svensson AM, Miftaraj M, Gudbjörnsdottir S, et al. Adherence to lipid-lowering therapy and risk for cardiovascular disease and death in type 1 diabetes mellitus: a population-based study from the Swedish National Diabetes Register. BMJ open diabetes Res care 2020;8.
[11] Dalli LL, Kim J, Cadilhac DA, Greenland M, Sanfilippo FM, Andrew NE, et al. Greater adherence to secondary prevention medications improves survival after stroke or transient ischemic attack: a linked registry study. Stroke. 2021;52:3569–77.
[12] Lee EKP, Poon P, Yip BHK, Bo Y, Zhu M, Yu C, et al. Global burden, regional differences, trends, and health consequences of medication nonadherence for hypertension during 2010 to 2020: a meta-analysis involving 27 million patients. J Am Heart Assoc 2022:11.
[13] Marquina C, Morton J, Zomer E, Talic S, Lybrand S, Thomson D, et al. Lost therapeutic benefit of delayed low-density lipoprotein cholesterol control in statin-treated patients and cost-effectiveness analysis of lipid-lowering intensification. Value Heal 2023;26:498–507.
[14] Kwan JL, Lo L, Ferguson J, Goldberg H, Diaz-Martinez JP, Tomlinson G, et al. Computerised clinical decision support systems and absolute improvements in care: meta-analysis of controlled clinical trials. BMJ 2020;370:3216.
[15] Sutton RT, Pincock D, Baumgart DC, Sadowski DC, Fedorak RN, Kroeker KI. An overview of clinical decision support systems: benefits, risks, and strategies for success. npj Digit Med 2020;3:17.
[16] Bhat S, Derington CG, Derington CG, Trinkley KE, Trinkley KE. Clinicians' values and preferences for medication adherence and cost clinical decision support in primary care: a qualitative study. Appl Clin Inform 2020;11:405–14.
[17] Njie GJ, Proia KK, Thota AB, Finnie RKC, Hopkins DP, Banks SM, et al. Clinical decision support systems and prevention: a community guide cardiovascular disease systematic review. Am J Prev Med 2015;49:784.
[18] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Syst Rev 2021;10.
[19] Veritas Health Innovation. Covidence systematic review software. 2023. www.covidence.org. Accessed 27 Jan 2024.
[20] Li T., Higgins J., Deeks J. Collecting data | Cochrane Training. In: Cochrane Handbook for Systematic Reviews of Interventions version 6.4. 2023.
[21] Higgins JP, Savović J, Page MJ, Elbers RG, Sterne JA, et al. Assessing risk of bias in a randomized trial. In: Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al., editors. Cochrane handbook for systematic reviews of interventions. Cochrane; 2023.
[22] Tanriver-Ayder E, Faes C, Van De Casteele T, McCann SK, Macleod MR. Comparison of commonly used methods in random effects meta-analysis: application to preclinical data in drug discovery research. BMJ Open Sci 2021;5.
[23] Adusumalli S, Westover JE, Jacoby DS, Small DS, Vanzandbergen C, Chen J, et al. Effect of passive choice and active choice interventions in the electronic health record to cardiologists on statin prescribing: a cluster randomized clinical trial. JAMA Cardiol 2021;6:40–8.
[24] Adusumalli S, Kanter GP, Small DS, Asch DA, Volpp KG, Park SH, et al. Effect of nudges to clinicians, patients, or both to increase statin prescribing: a cluster randomized clinical trial. JAMA Cardiol 2023;8:23–30.
[25] Carter BL, Levy B, Gryzlak B, Xu Y, Chrischilles E, Dawson J, et al. Cluster-randomized trial to evaluate a centralized clinical pharmacy service in private family medicine offices. Circ Cardiovasc Qual Outcomes 2018:11.
[26] Kharbanda EO, Asche SE, Sinaiko A, Nordin JD, Ekstrom HL, Fontaine P, et al. Evaluation of an electronic clinical decision support tool for incident elevated BP in adolescents. Acad Pediatr 2018;18:43–50.
[27] Kressin NR, Long JA, Glickman ME, Bokhour BG, Orner MB, Clark C, et al. A brief, multifaceted, generic intervention to improve blood pressure control and reduce disparities had little effect. Ethn Dis 2016;26:27–36.
[28] Sequist T, Holliday A, Orav EJ, Bates D, Denker B. Physician and patient tools to improve chronic kidney disease care. Am J Manag Care 2018;24:107–14.
[29] Tuot DS, Rubinsky AD, Velasquez A, McCulloch CE, Schillinger D, Handley MA, et al. Interventions to improve blood pressure control among socioeconomically disadvantaged patients With CKD: kidney awareness registry and education pilot randomized controlled trial. Kidney Med 2019;1:242–52.
[30] Heselmans A, Delvaux N, Laenen A, Van De Velde S, Ramaekers D, Kunnamo I, et al. Computerized clinical decision support system for diabetes in primary care does not improve quality of care: a cluster-randomized controlled trial. Implement Sci 2020;15:1–14.
[31] Cicolini G, Simonetti V, Comparcini D, Celiberti I, Di Nicola M, Capasso LM, et al. Efficacy of a nurse-led email reminder program for cardiovascular prevention risk reduction in hypertensive patients: a randomized controlled trial. Int J Nurs Stud 2014;51:833–43.
[32] Zamora A, Fernández De Bobadilla F, Carrion C, Vázquez G, Paluzie G, Elosua R, et al. Pilot study to validate a computer-based clinical decision support system for dyslipidemia treatment (HTE-DLP). Atherosclerosis 2013;231:401–4.

[33] Gold N, Tan K, Sherlock J, Watson R, Chadborn T. Increasing uptake of NHS Health Checks: a randomised controlled trial using GP computer prompts. Br J Gen Pract 2021;71:e693–700.
[34] Willis A, Crasto W, Gray LJ, Dallosso H, Waheed G, Davies M, et al. Effects of an electronic software "Prompt" with health care professional training on cardiovascular and renal complications in a multiethnic population with type 2 diabetes and microalbuminuria (the GP-Prompt Study): results of a pragmatic cluster-randomized trial. Diabetes Care 2020;43:1893–901.
[35] Anchala R, Kaptoge S, Pant H, Di Angelantonio E, Franco OH, Prabhakaran D. Evaluation of effectiveness and cost-effectiveness of a clinical decision support system in managing hypertension in resource constrained primary health care settings: results from a cluster randomized trial. J Am Heart Assoc 2015;5.
[36] Chan JCN, Thewjitcharoen Y, Nguyen TK, Tan A, Chia YC, Hwu CM, et al. Effect of a web-based management guide on risk factors in patients with type 2 diabetes and diabetic kidney disease: a JADE randomized clinical trial. JAMA Netw Open 2022;5:e223862.
[37] Webster R, Usherwood T, Joshi R, Saini B, Armour C, Critchley S, et al. An electronic decision support-based complex intervention to improve management of cardiovascular risk in primary health care: a cluster randomised trial (INTEGRATE). Med J Aust 2021;214:420–7.
[38] Adjei DN, Agyemang C, Dasah JB, Kuranchie P, Amoah AGB. The effect of electronic reminders on risk management among diabetic patients in low resourced settings. J Diabetes Complications 2015;29:818–21.
[39] Bright TJ, Wong A, Dhurjati R, Bristow E, Bastian L, Coeytaux RR, et al. Effect of clinical decision-support systems: a systematic review. Ann Intern Med 2012;157:29–43.
[40] Groenhof TKJ, Asselbergs FW, Groenwold RHH, Grobbee DE, Visseren FLJ, Bots ML. The effect of computerized decision support systems on cardiovascular risk factors: a systematic review and meta-analysis. BMC Med Inform Decis Mak 2019:19.
[41] Gold R, Larson AE, Sperl-Hillen JM, Boston D, Sheppler CR, Heintzman J, et al. Effect of clinical decision support at community health centers on the risk of cardiovascular disease: a cluster randomized clinical trial. JAMA Netw Open 2022;5:e2146519.
[42] Alasiri SF, Douiri A, Altukistani S, Porat T, Mousa O. The role of clinical decision support systems in preventing stroke in primary care: a systematic review. Perspect Heal Inf Manag 2023;20:1d.
[43] O'Connor SD, Dalal AK, Anik Sahni V, Lacson R, Khorasani R. Does integrating nonurgent, clinically significant radiology alerts within the electronic health record impact closed-loop communication and follow-up? J Am Med Informatics Assoc 2015;23:333–8.
[44] Olakotan OO, Mohd Yusof M. The appropriateness of clinical decision support systems alerts in supporting clinical workflows: a systematic review. Health Informatics J 2021:27.
[45] Persell SD, Karmali KN, Lazar D, Friesema EM, Lee JY, Rademaker A, et al. Effect of electronic health record–based medication support and nurse-led medication therapy management on hypertension and medication self-management: a randomized clinical trial. JAMA Intern Med 2018;178:1069–77.
[46] Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PAC, et al. Why Don't physicians follow clinical practice guidelines?: a framework for improvement. JAMA 1999;282:1458–65.
[47] Garg AX, Adhikari NKJ, McDonald H, Rosas-Arellano MP, Devereaux PJ, Beyene J, et al. Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. JAMA 2005;293:1223–38.
[48] Bates DW, Teich JM, Lee J, Seger D, Kuperman GJ, Ma'Luf N, et al. The impact of computerized physician order entry on medication error prevention. J Am Med Informatics Assoc 1999;6:313–21.
[49] Sequist TD, Zaslavsky AM, Marshall R, Fletcher RH, Ayanian JZ. Patient and physician reminders to promote colorectal cancer screening: a randomized controlled trial. Arch Intern Med 2009;169:364–71.
[50] Sequist TD. Health information technology and disparities in quality of care. J Gen Intern Med 2011;26:1084–5.
[51] Szilagyi PG, Bordley C, Vann JC, Chelminski A, Kraus RM, Margolis PA, et al. Effect of patient Reminder/Recall interventions on immunization rates: a review. JAMA 2000;284:1820–7.
[52] Rasmussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. JAMA 2007;297:177–86.
[53] Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. Cochrane database Syst Rev 2008. https://doi.org/10.1002/14651858.CD000011.PUB3.
[54] Kawamoto K, McDonald CJ. Designing, conducting, and reporting clinical decision support studies: recommendations and call to action. Ann Intern Med 2020;172. 11 Suppl:S101–9.
[55] Su JJ, fung Yu DS. Effects of a nurse-led eHealth cardiac rehabilitation programme on health outcomes of patients with coronary heart disease: a randomised controlled trial. Int J Nurs Stud 2021;122:104040.
[56] Alshehri AA, Jalal Z, Cheema E, Haque MS, Jenkins D, Yahyouche A. Impact of the pharmacist-led intervention on the control of medical cardiovascular risk factors for the primary prevention of cardiovascular disease in general practice: a systematic review and meta-analysis of randomised controlled trials. Br J Clin Pharmacol 2020;86:29–38.
[57] Kappes M, Espinoza P, Jara V, Hall A. Nurse-led telehealth intervention effectiveness on reducing hypertension: a systematic review. BMC Nurs 2023;22:1–13.