Review

Design, effectiveness, and economic outcomes of contemporary chronic disease clinical decision support systems: a systematic review and meta-analysis

Winnie Chen¹, Kirsten Howard², Gillian Gorham¹, Claire Maree O’Bryan¹, Patrick Coffey¹, Bhavya Balasubramanya¹, Asanga Abeyaratne¹, and Alan Cass¹

¹Menzies School of Health Research, Charles Darwin University, Casuarina, Northern Territory, Australia, and ²School of Public Health, Faculty of Medicine and Health, University of Sydney, Sydney, New South Wales, Australia

Corresponding Author: Dr Winnie Chen, Menzies School of Health Research, Charles Darwin University, PO Box 41096, Casuarina, NT 0811, Australia; winnie.chen@menzies.edu.au

Received 1 April 2022; Revised 21 June 2022; Editorial Decision 23 June 2022; Accepted 25 June 2022

ABSTRACT

Objectives: Electronic health record-based clinical decision support (CDS) has the potential to improve health outcomes. This systematic review investigates the design, effectiveness, and economic outcomes of CDS targeting several common chronic diseases.

Material and Methods: We conducted a search in PubMed (Medline), EBSCOHOST (CINAHL, APA PsychInfo, EconLit), and Web of Science. We limited the search to studies from 2011 to 2021. Studies were included if the CDS was electronic health record-based and targeted one or more of the following chronic diseases: cardiovascular disease, diabetes, chronic kidney disease, hypertension, and hypercholesterolemia. Studies with effectiveness or economic outcomes were considered for inclusion, and a meta-analysis was conducted.

Results: The review included 76 studies with effectiveness outcomes and 9 with economic outcomes. Of the effectiveness studies, 63% described a positive outcome that favored the CDS intervention group. However, meta-analysis demonstrated that effect sizes were heterogenous and small, with limited clinical and statistical significance. Of the economic studies, most full economic evaluations (n = 5) used a modeled analysis approach. Cost-effectiveness of CDS varied widely between studies, with an estimated incremental cost-effectiveness ratio ranging between USD$2192 to USD$151,955 per QALY.

Conclusion: We summarize contemporary chronic disease CDS designs and evaluation results. The effectiveness and cost-effectiveness results for CDS interventions are highly heterogeneous, likely due to differences in implementation context and evaluation methodology. Improved quality of reporting, particularly from modeled economic evaluations, would assist decision makers to better interpret and utilize results from these primary research studies.

Registration: PROSPERO (CRD42020203716)

Key words: chronic disease clinical decision support system economic evaluation meta-analysis systematic review
INTRODUCTION

Background and significance
Clinical decision support (CDS) is a process of using relevant clinical knowledge, or intelligently filtered patient information, to enhance health-related decisions. A broad definition of CDS includes both manual and computerized interventions. However, with the wide adoption of electronic health record (EHR) use in recent decades, contemporary CDS systems are increasingly computerized and data-driven. CDS builds upon existing EHR functionality, whereby algorithms are used to process EHR data, and individual-specific decision support is presented to clinician or patient end-users. CDS functions may be embedded into EHRs or exist as standalone applications.

Chronic diseases are the leading cause of death worldwide. Chronic disease CDS systems can target the whole continuum of care from screening to diagnosis, to treatment, and follow-up. For example, CDS for diabetes can screen for the presence of disease based on laboratory results, improve diagnosis documentation, recommend appropriate medications or nonpharmacological management, and prompt adherence to guideline-based cycle of care. CDS holds great potential for improving chronic disease health care and outcomes, but what evidence exists to demonstrate CDS effectiveness?

The first systematic reviews of CDS interventions emerged in the late 1990s and a number of earlier reviews (including articles up to 2011) were conducted with a broad chronic disease or all-disease focus. Among these is a landmark systematic review by Bright et al., commissioned by the US Agency of Health Research and Quality; this review included 148 full texts of randomized controlled trials (RCTs), and examined the effectiveness of CDS systems across all medical fields, spanning primary research articles from 1976 to 2011. With the expansion of CDS literature over the past decade, recent CDS systematic reviews (including articles from 2011 onwards) have grown increasingly specialized. In particular, a large number of recent reviews have exclusively focused on medication-related CDS interventions. Other examples of recent CDS systematic reviews with a specific scope include: reviews that focus on specific CDS type—such as laboratory test-related CDS, or diagnostic image-related CDS. In contrast to these systematic reviews, few recent reviews have had a broad chronic disease or all-disease focus—significantly, of these recent reviews, only 2 have explicitly excluded outdated computerized CDS systems that are not EHR-integrated. Thus our review sought to investigate the effectiveness of contemporary, EHR-based CDS interventions, with a broad chronic disease focus. Our review scope is most similar to El Asmar et al.’s 2021 review with a focus on EHR-based CDS for chronic diseases—however, the authors of this review had a limited number of outcomes of interest, and only included a small number of studies (n = 8).

Even where CDS interventions are effective, investment into such interventions is likely to depend on economic considerations. The cost of new health technologies and unsustainable rise in healthcare expenditure is a concern for economies worldwide. Additionally, since the 2020 COVID-19 pandemic, OECD countries have seen a sharp rise in the ratio of healthcare expenditure to gross domestic product. CDS interventions require substantial upfront investment and in the face of competing healthcare priorities, weak financial business cases have been highlighted as a major rolevel barrier for widespread CDS adoption. On the other hand, CDS interventions can also result in cost savings—for example, from averting adverse events, reducing unnecessary treatment, or reducing cost of downstream disease complications. While several systematic reviews of CDS effectiveness have reported costs alongside other health outcomes, there are few examples of comprehensive economic systematic reviews. Given the high importance of financial considerations to policy makers, we included a detailed economic review alongside the effectiveness review.

Study objectives
CDS technology is continuously evolving and there remains a need to summarize up-to-date evidence of clinical and economic outcomes. To address this need, we conducted a systematic review to summarize the effectiveness and economic outcomes of contemporary EHR-based CDS interventions in cardiovascular disease, diabetes, chronic kidney disease, hypertension, and hypercholesterolemia. We selected these chronic diseases as they are common, share modifiable risk factors, and often exist as comorbid conditions. Our specific research questions are outlined below:

1. CDS design characteristics:
   a. What are the design characteristics of contemporary EHR-based chronic disease CDS systems?
   b. What clinical task do the CDS systems address, what EHR data types are used, and how does the CDS interact with users?

2. Effectiveness:
   a. Are CDS interventions effective compared to control groups in improving chronic disease care?
   b. Is there evidence for longer-term sustained effectiveness (beyond 12 months)?
   c. Are certain CDS features more likely to result in positive effectiveness outcomes?

3. Economic:
   a. What are the costs and cost-effectiveness of CDS systems compared to usual care?
   b. What economic evaluation methods are used in the analyses?

MATERIALS AND METHODS
This systematic review was registered on PROSPERO (CRD42020203716). The overall approach to the review was a mixed methods study summarizing the effectiveness, economic, and qualitative outcomes of CDS for use in chronic disease management. Effectiveness and economic reviews are included in this paper and the qualitative component will be reported separately. JBI methods for review of effectiveness and economic evidence informed our methods. The review adhered to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.
guideline adherence). The outcomes of interest for the economic component of the study were costs and cost-effectiveness. Relevant study designs included RCTs, quasi-experimental studies, partial economic evaluations (cost analysis), and full economic evaluations. The landmark systematic review by Bright et al and at least a dozen other broad systematic reviews adequately covered the period up to January 2011, thus, we restricted our search to a 10-year window between January 2011 and January 2021.

Exclusions consisted of CDS targeting populations with acute conditions (eg, acute heart failure) or targeting chronic disease management in acute settings (eg, perioperative diabetes blood sugar management). Computerized CDS interventions not linked to an individual’s EHR (eg, web-based cardiovascular risk calculator), or those that performed basic EHR functions (eg, simple recall functions) were excluded. In terms of article type, we excluded EHR-based CDS prototypes if they were not implemented in a clinical setting. Nonprimary research studies and non-English language studies were also excluded. For our full inclusion and exclusion criteria, see Supplementary Appendix SI.

Search strategy
We searched PubMed (Medline), EBSCOHOST (CINAHL, APA PsychInfo, EconLit), and Web of Science databases. PubMed MeSH terms and title/abstract search terms included concepts of “clinical decision support systems,” “cardiovascular disease,” “diabetes,” “chronic kidney disease,” “hypertension,” “hypercholesterolemia,” and were translated into the other included databases. A research librarian provided input into the search strategy. See Supplementary Appendix SII for the full PubMed search strategy.

Study selection and data extraction
Abstracts and titles were screened in duplicate by 2 independent reviewers (WC, and BB or PC) using the Covidence software (Veritas Health Innovation, Melbourne, Victoria, Australia). Full texts were verified against the inclusion and exclusion criteria, and classified into effectiveness, economic, or qualitative outcome categories by a single reviewer (WC). Reasons for exclusion at full text stage were recorded. Citations were then imported into JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) (JBI, Adelaide, Australia) for critical appraisal, data extraction, and meta-analysis.

Data extraction was conducted in duplicate by 2 reviewers (WC, and CO or PC). Study characteristics were extracted using the JBI SUMARI forms for effectiveness and economic studies. Additional standardized data forms were created to extract details of CDS characteristics and economic evaluation methods. Several dimensions of CDS design features were recorded: (1) clinical task addressed by the CDS (eg, CDS for screening); (2) EHR data types used in generating the decision support; and (3) CDS user interface features using a modified classification from Osheroff et al. We classified CDS types in effectiveness studies only—this is because CDS descriptions in economic studies are limited and typically reference a previously published effectiveness study. The Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Checklist informed our economic evaluation data extraction form. Details extracted included vehicle of analysis (trial or modeled), and methods for estimating costs and outcomes. Authors were contacted for further information where economic evaluation methods were limited in the primary research article.

Methodological quality assessment
Quality assessment was conducted by 2 reviewers (WC, and CO, KH, or GG) using the JBI critical appraisal tool for randomized control studies, quasi-experimental studies, and economic evaluations. To ensure consistency, a random sample of 25% of studies was independently assessed in duplicate by 2 reviewers. Discrepancies at all stages of the review (screening, data extraction, and methodological quality assessment) were resolved by consensus and where necessary, by a third team member. Our review aimed to summarize all relevant CDS studies in the field; therefore, studies were not excluded from data extraction or synthesis based on quality assessment scores.

Analysis
Descriptive statistics were reported for study characteristics and CDS design characteristics. A meta-analysis was conducted to summarize similar effectiveness outcomes. The meta-analysis included results from RCTs only due to inconsistent study design, lack of similar effectiveness outcomes, and variable reporting methods in quasi-experimental studies. The meta-analysis was conducted with the primary objective of providing a visual (forest plot) and quantitative summary of existing literature, rather than providing an estimate of effect size for CDS interventions. We used a random effects model; examined effect sizes in terms of relative risks (RR) for categorical variables and mean difference for continuous variables; and reported the $I^2$ statistic to describe study heterogeneity. Heterogeneity of effectiveness results was investigated with an exploratory meta-regression analysis using R (R Core Team 2021)—univariate and multivariate logistic regression (using a full-model approach) were conducted to examine the presence of associations between CDS features and a primary positive outcome.

A narrative review was conducted for economic studies. Key economic evaluation methods and results are outlined in a summary table and costs are converted to USD 2021 prices to enable comparison. Costs in the original currency were inflated to 2021 values, then converted to USD using 2021 purchasing power parity conversion factors.

RESULTS
Study selection
The search of databases yielded 14,422 citations and 6,423 duplicate records were removed (Figure 1). Of the 7,999 articles undergoing abstract and title screening, 625 were eligible for full text screen. Articles were excluded from full text screening primarily due to absence of a relevant chronic disease CDS systems mentioned in the title or abstract. Of the full text articles screened, 377 were excluded based on article type (eg, protocol or other nonprimary research articles) and 148 were excluded based on article content. Common reasons for exclusion based on article content included CDS intervention lacking an EHR component, or EHR interventions lacking a CDS component. A total of 76 studies met the criteria for inclusion in the effectiveness review, and 9 studies met the criteria for inclusion in the economic review. Five studies had both effectiveness and economic outcomes, and were therefore included in the article count for both reviews. Qualitative outcomes studies (n=33) of the systematic review are reported separately. Of the effectiveness studies, 32 were RCTs and 44 were quasi-experimental studies. Thirty-one of the 32 RCTs had a suitable outcome for inclusion in the meta-analysis of effectiveness outcomes.
The number of articles in the field has increased substantially since 2011. Figure 2 reveals a doubling of articles identified using our PubMed search strategy from the past decade (January 2011 to January 2021), compared to the number of articles present prior to 2011.

Methodological quality
Methodsological quality was moderate for RCT and quasi-experimental studies. The main source of bias in RCTs arose from the inability to blind healthcare providers or assessors (JBI checklist for RCTs Q5 and Q6). For quasi-experimental studies, the main methodology quality issues were that less than half of all studies demonstrated a similar comparison group (JBI checklist for quasi-experimental studies Q2), and that few studies had multiple measurements of outcomes pre- and postintervention (Q5). Economic evaluation studies were of limited methodological quality. Most studies had unclear descriptions of the “usual care” comparison group (JBI checklist for economic evaluations Q2), and limited descriptions of how identification and valuation of costs and outcomes were conducted (Q3, Q5, Q6). See Supplementary Appendix SIII for the methodological quality of included studies.

Characteristics of included studies
Study design of effectiveness studies included 32 RCTs and 44 quasi-experimental studies. RCTs were predominantly clustered RCTs randomized at a practice or practitioner level (n = 26), with few RCTs being randomized at an individual level. For quasi-experimental studies 32 were before-after studies and 12 included a nonrandomized control group. Nonrandomized control groups include self-selection into a control group (natural experiment), or allocation without randomization into a control group. See Supplementary Appendix SIV for characteristics of included studies and full reference list of included studies.

Table 1 presents an overview of study characteristics and settings. Most studies (88%) were conducted in high income countries, with half of all studies (50%) conducted in the United States. Several studies from low- and middle-income countries were also included (12%). The top 3 diseases addressed by CDS interventions were multiple cardiovascular risk factors (25%), diabetes (18%), and...
chronic kidney disease (13%). Included studies were predominantly conducted in primary care settings (70%). In the United States, “primary care” referred to primary care practices staffed by family physicians, internal medicine physicians, and supporting clinicians; in other countries, primary care referred to general practice or community health clinics. Forty-one percent of studies had additional interventions bundled alongside the CDS intervention—these interventions included additional education, audit, or other quality-improvement initiatives, individualized feedback, and financial incentives. Start dates for CDS studies included in this analysis ranged from 2001 to 2017 with a median study duration of 12 months. There was a median lag-time of 4 years between study commencement and year of publication (Supplementary Appendix SVI and Figure S2).

Characteristics of CDS systems
A summary of CDS design characteristics is displayed in Figure 3. Definitions and examples of our CDS classification are outlined in Table 2. The majority of CDS systems were computer-based, with several studies reporting mobile- or tablet-based systems (n = 6). The most common clinical task addressed was pharmacological management (71%). Few individual CDS system (9%) addressed all aspects of chronic disease care (screening/diagnosis, pathway, pharmacological, and nonpharmacological management). A variety of EHR data types were used to generate decision support recommendations, with a median of 4 EHR data types used per individual CDS system. Alerts and pop-ups were the most common CDS user interface feature (89%), but most CDS interventions used 2 or more different user interface features (83%). See Supplementary Appendix SV for CDS design characteristics classification. See also Supplementary Appendix SVI for other additional figures and tables.

Findings of effectiveness studies
Studies reported a mix of health process (78%), clinical (70%), and/or user outcomes (5%). Overall, 63% of studies described a positive primary trial outcome that favored the CDS group compared to controls; the remaining studies reported equivocal primary outcomes. Results from 31 RCTs were included in the meta-analysis. One RCT was excluded from the meta-analysis because it did not include a similar effectiveness outcome for synthesis.

Figure 4 is a forest plot showing relative risk (RR) of the proportion of patients meeting study-determined clinical targets for CDS versus control groups (HbA1c, SBP, LDLc). Figure 5 shows the absolute mean differences in clinical outcomes. Meta-analysis of other clinical and process outcomes (eg, proportion of patients meeting guideline adherence) is reported in Supplementary Appendix SVI. Results of our meta-analysis demonstrated small improvements in outcomes in CDS versus control, but these were generally of limited clinical and statistical significance. High levels of heterogeneity existed among the studies, particularly in relative risks (RR) of outcomes between the studies with I² ranging between 78 and 85 (Figure 4). Effectiveness outcomes were commonly reported up to a 12-month timeframe (66%) and none of the RCTs were conducted beyond this 12-month timeframe. Thus, the sustained longer-term effects of chronic disease CDS interventions remain unclear. An exploratory meta-regression did not reveal CDS design features that were clear and statistically significant predictors of a positive primary outcome (Supplementary Appendix SVI and Figures S2 and S3).

Findings of economic evaluation studies
Study methodology
Table 3 provides an overview of economic evaluation methodology and findings. Detailed economic evaluation methods for each included study are outlined in Supplementary Appendix SVII. Full economic evaluation was conducted in 6 studies and cost analysis was conducted in 3 studies. Most studies used a healthcare system or healthcare funder perspective (n = 7). Five out of 6 economic evaluations used modeled approaches—Markov models were the most common approach and model type was unclear in the remaining 2 modeled studies. Time horizon ranged from 1 year in the trial-based study, up to 40 years in modeled studies. Discount rate per annum ranged from 3% to 5%.

Costs and outcomes
Resource utilization was measured with a combination of micro-costing and aggregate costing approaches. Valuation of unit costs
For modeled studies, short-term trial-based outcomes were extrapolated to long-term outcomes. Short-term outcomes in all studies consisted of clinical differences in SBP, HbA1c, or LDLc at 12 months. The effect sizes of these short-term outcomes were small—of note, short-term changes were included in modeled analyses, regardless of whether clinical improvements were statistically significant. Modeled long-term outcomes included morbidity and mortality outcomes (eg, cardiovascular event and cardiovascular death). Method for valuation of health states, that is, sources of utility weights used to calculate QALYs, was not described in any of the included studies.

Cost-effectiveness and sensitivity analysis
The reported incremental cost-effectiveness ratios (ICERs) ranged widely from a minimum of USD$2192 per QALY, to USD$151 955 per QALY. One-way sensitivity analysis was conducted in all 6 full economic evaluations but probabilistic sensitivity analysis was conducted in only 2 out of the 5 modeled studies.

### DISCUSSION

#### Main findings
The volume of literature on CDS interventions for chronic diseases has risen substantially over the past decade. This review contributes to our understanding of CDS systems in several ways. Firstly, we provide an up-to-date summary of CDS effectiveness, across a broad range of chronic disease CDS interventions. Secondly, we provide insight into the design characteristics of contemporary, EHR-based chronic disease CDS systems. Many authors have attributed heterogeneity in meta-analysis results to differences within individual CDS systems—yet, surprisingly little has been published alongside reviews to systematically categorize CDS design features. For example, Kwan et al recently conducted a recent meta-analysis of CDS effectiveness studies; while comprehensive in terms of EHR-based CDS types included, the authors’ description of individual CDS type was mostly limited to user interface features (eg, interruptive vs non-interruptive). Taxonomies of CDS systems have been published but are rarely used in full. We simplified a previous review’s approach to extracting CDS design characteristics and provide a clinically relevant insight into what each CDS does, how they work (EHR data types used in CDS algorithms), and how decisions are communicated to users. Thirdly, our economic review not only summarizes economic outcomes, but also critiques evaluation methods and economic models used—this body of work is increasingly relevant as the number of modeled studies in the field exceeds that of trial-based studies.

It is encouraging that many CDS interventions sought to tackle several related cardiometabolic comorbid conditions. However, as with a previous systematic review, we found that CDS systems mainly addressed an index condition of concern and poorly accounted for multimorbidity. Our analysis of CDS design features found that a narrow scope of EHR data types contributes to a lack of wide clinical applicability. For example, a CDS targeting abdominal aortic aneurysm screening may only use coded diagnosis for aortic aneurysm but requires additional manual data entry for existing comorbidity (eg, hypertension); or, a CDS that targets hypertension management may only extract EHR medication data for first line medication classes but not account for presence of related cardiac medications. Kawamoto and McDonald have called out this “mismatch” between information needed for decision rules and the

---

### Table 1. Characteristics and settings of included studies

| Study characteristic | Effectiveness articles (n) | Economic articles (n) | Study setting | Country |
|----------------------|-----------------------------|-----------------------|---------------|---------|
|                      | (total n = 76)              | (total n = 9)          |               |         |
| Country              |                             |                       |               |         |
| USA                  | 38                          | 50                    | 2             | 22      |
| Australia            | 6                           | 8                     | 2             | 22      |
| India                | 5                           | 7                     | 1             | 11      |
| UK                   | 5                           | 7                     | 1             | 11      |
| Canada               | 3                           | 4                     | 2             | 22      |
| South Korea          | 2                           | 3                     | 0             | 0       |
| Sweden               | 2                           | 3                     | 0             | 0       |
| Italy                | 2                           | 3                     | 0             | 0       |
| Belgium              | 2                           | 3                     | 0             | 0       |
| Netherlands          | 2                           | 3                     | 0             | 0       |
| Multiple countries   | 2                           | 3                     | 0             | 0       |
| Other                | 5                           | 7                     | 1             | 11      |
| CDS disease focus    |                             |                       |               |         |
| Cardiovascular risks | 19                          | 25                    | 3             | 33      |
| Diabetes             | 14                          | 18                    | 2             | 22      |
| Chronic kidney disease | 10                         | 13                    | 1             | 11      |
| Multiple other       | 8                           | 11                    | 0             | 0       |
| Atrial fibrillation  | 8                           | 11                    | 1             | 11      |
| Hypertension         | 7                           | 9                     | 0             | 0       |
| Vascular conditions  | 4                           | 5                     | 0             | 0       |
| Other                | 6                           | 8                     | 2             | 22      |
| Study duration       |                             |                       |               |         |
| ≤6 months            | 17                          | 22                    | N/A           | N/A     |
| 6–12 months          | 33                          | 43                    | N/A           | N/A     |
| >12 months           | 24                          | 32                    | N/A           | N/A     |
| Study setting        |                             |                       |               |         |
| Primary care—other   | 31                          | 41                    | 3             | 33      |
| Primary care—general | 22                          | 29                    | 4             | 44      |
| practice             |                             |                       |               |         |
| Multiple settings    | 13                          | 17                    | 1             | 11      |
| Specialist outpatients | 8                          | 11                    | 0             | 0       |
| Other                | 2                           | 3                     | 1             | 11      |
| Clinics/practices    |                             |                       |               |         |
| ≤25                  | 47                          | 62                    | 5             | 56      |
| 25–50                | 6                           | 8                     | 1             | 11      |
| 50–100               | 10                          | 13                    | 2             | 22      |
| >100                 | 5                           | 7                     | 1             | 11      |

Note: Studies with missing data (eg, no study duration reported) are not included in this table.

Five of the 9 economic studies had both effectiveness and economic outcomes and were included in both reviews.

See Table 3 for time horizon of economic studies.

came from both trial-based data and published country-specific data. Implementation cost was the most common type of CDS intervention cost included (67%) and medication costs was the most common type of healthcare cost included (89%).

CDS intervention costs were the main driver of the overall incremental cost differences between CDS versus control groups. The highest CDS intervention cost reported was by Willis et al at USD$3934 per patient per year. In contrast, the relative contribution of healthcare costs to overall incremental cost differences was minor—healthcare costs in the CDS groups ranged from a maximum of an additional USD$11 per patient per year, to cost savings of up to USD$25 per patient per year. Increased healthcare cost in the CDS group was primarily attributable to increased medication costs. Conversely, cost savings in the CDS group arose from decreased downstream disease management and hospitalization costs.
lack of EHR data availability as a critical reason for CDS failure. An assortment of user interface features was described, with most CDS systems utilizing more than one user interface feature. However, many contemporary CDS designs are still centered around alerts and reminders. Alerts and reminders have been the main CDS type described since the late 1990s, and progress in CDS user interface design is slow. This is problematic as alert fatigue is a well described issue—furthermore, poor usability can be a barrier to CDS uptake, and contribute to clinician burnout.

Several reviews to date have shown that CDS systems have a modest effect on improving health processes or morbidity, but not mortality. Results for CDS specifically targeting primary care or chronic disease settings has been less clear. Our meta-analysis found that CDS generally resulted in a favorable effectiveness outcome, but with small effect sizes of limited clinical and statistical significance. In our review, heterogeneity likely occurred due to differences in study design and diverse real-world contexts for CDS implementation. Meta-analyses of complex interventions, such as CDS interventions, is notoriously difficult to interpret. In CDS studies, varying effect sizes can be due to inconsistent CDS uptake despite availability of the intervention.

Previous meta-regressions have identified automated provision of decision support, CDS systems requiring reasons for override, and other CDS success factors. Our meta-regression did not highlight CDS features associated with a primary positive outcome. The difference is unsurprising, as meta-regression results are highly dependent on study selection, as well as reviewer-defined abstraction of CDS factors. It is also possible that factors not considered in our meta-regression (eg, user factors, clinical champions) were more influential in determining CDS success than the CDS features extracted. Qualitative evaluation have an important role in explaining quantitative results—as such, a qualitative review has been conducted alongside this systematic review to further explore human and technological factors to CDS success.

Full economic evaluations are notoriously scarce in the CDS literature. Our economic review results are consistent with previous publications that describe inconclusive evidence for cost-effectiveness of CDS interventions. In a 2015 review, Jacob et al described ICERs of cardiovascular CDS interventions ranging widely from USD$16 500 to USD$162 000 per QALY. We found a similarly large variation in estimated cost-effectiveness, which was largely dependent on parameters selected for modeled analyses. As with previous reviews, we found that reporting quality was poor and hindered interpretation of economic results. For example, some authors reported an aggregate figure for incremental cost without specifying whether these...
Table 2. Definitions and examples of clinical decision support classifications

| CDS clinical task addressed | Definition and/or examples                                                                                                                                 |
|-----------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Prevention/ Diagnosis       | Screening for disease or likelihood of disease (eg, cardiovascular risk screening), and diagnosis (eg, documentation of hypertension diagnosis)             |
| Pharmacological             | Referral for investigations (eg, bloods), referral to specialist, and other care pathway tasks                                                             |
| Nonpharmaceutical management| Patient education (eg, via patient dashboard), diet and exercise recommendations, and other non-pharmaceutical management (eg, smoking cessation)        |

EHR data types used

| EHR data types used | Definition and/or examples                                                                                   |
|---------------------|--------------------------------------------------------------------------------------------------------------|
| Demographics        | Age, sex, and other demographic data                                                                          |
| Diagnosis           | Checks for existing coded diagnosis within EHR (eg, displays alert based on existing diagnosis of atrial fibrillation) |
| Medication          | Medications within EHR (eg, uses presence or absence of ACE-inhibitors to generate a decision support in chronic kidney disease prescribing) |
| Observation         | Structured EHR data for observations (eg, systolic blood pressure readings, body mass index)                 |
| Laboratory          | Structured EHR data for laboratory results (eg, HbA1c, urine albumin–creatinine ratio)                      |
| Manual entry        | Use of additional manual data entry for CDS to generate decision (eg, family history, depression scale)      |

CDS user interface features

| CDS user interface features | Definition and/or examples                                                                 |
|-----------------------------|-------------------------------------------------------------------------------------------|
| Form/template               | Provides auto-fill pathology (order set), imaging templates, automated specialist referrals |
| Data presentation—written summary | Displays written patient summaries, primarily text-based (eg, one-page patient summary with recent results) |
| Data presentation—visual summary | Displays visual patient summaries, primarily graphics-based (eg, dashboard with dial, traffic light systems) |
| Data presentation—risk scoring | Provides risk scores displayed in numerical, color, or other format (eg, risk scoring for atrial fibrillation to aid with prescribing decisions) |
| Prescribing/dosing          | Provides recommendations or tools for prescribing, dosing, and other medication changes     |
| Pathway support             | Provides cycle of care pathways, checklists for periodic visits, and other follow-up support |
| Reference info              | Provides general or patient-specific knowledge resources (eg, Info Buttons, links to relevant guidelines) |
| Alerts/reminder             | Displays alerts and reminders (eg, pop-up to identify at risk patients, red alert for incorrect drug dosing) |
| Service/population-level summary | Provides overview of patients and assists with quality improvement at a service or population level (eg, disease registry, service-level tools) |

ACE-inhibitor: Angiotensin Converting Enzyme Inhibitor; EHR: Electronic Health Record; HbA1c: Hemoglobin A1c.

There are several limitations to our review. We considered common chronic diseases but did not include noncardiometabolic chronic diseases such as chronic obstructive pulmonary disease. Two reviewers conducted title and abstract screening, but full text screening was performed by a single reviewer. We did not exclude effectiveness and economic studies of lower methodological quality because our review aimed for breadth and generalizability. We used a comprehensive search query across several large databases, but did not include non-English articles and gray literature. Due to limited CDS descriptions within the text, data extraction for some CDS features were based on implicit information rather than explicit information found in the primary research articles. Over a third of CDS interventions were bundled together as part of an overall quality improvement initiative; furthermore, chronic disease interventions are implemented in the context of multimorbidity and health systems changes. Thus, effectiveness outcomes could not be attributed to the EHR-based CDS alone. Similarly, cost-effectiveness of the CDS was often unable to be separated from the cost-effectiveness of the overall intervention within the primary research (eg, overall screening initiative). The meta-analysis results need to be interpreted with caution given varied methodological quality in primary research studies and heterogeneity in the CDS interventions. Finally, we focused on contemporary EHR-based CDS studies published over the past decade but recognize that limiting our search from 2011 onwards does not guarantee that the most up-to-date CDS technology are included. We found that some of the included interventions (eg, alert-based CDS) are similar in nature to computerized CDS described in previous reviews of studies prior to 2011. Furthermore, a considerable lag-time exists between year of study commencement and year of publication, which limits our ability to capture the most up-to-date tools in our review.

Future directions

Learning from the collective experience of CDS design, development, implementation, and evaluation is key to achieving the full benefits of CDS technology.166 We provide 2 key recommendations for future CDS design and research. Firstly, despite decades of CDS research, many recent CDS interventions remained limited in scope—for exam-
A CDS may concentrate on hypertension screening without relevant tools to aid hypertension prescribing. Instead of building multiple CDS systems of narrow clinical scope, an ideal CDS system would target screening, diagnosis, and management of multiple chronic diseases. A generalized chronic disease CDS would also require innovative user-interfaces that evolve beyond simple alerts to communicate decision support to users. Several authors have proposed problem orientated summaries—displaying relevant EHR information and decision support for each disease—as a promising solution for reducing cognitive load, and improving CDS usability in chronic disease settings. Nevertheless, such approaches depend on integration of a much wider variety of EHR data types than what is currently used; requires ongoing work toward technological standards, and needs greater subject matter expertise collaboration across clinical specialties. Secondly, we echo previous authors in recommending that CDS evaluations include sufficient details of the CDS technology itself. "Clinical decision support" is a broad term. During data extraction, we found that descriptions of CDS systems were limited. Authors should clearly describe CDS features—ideally through graphical representations (e.g., screenshots of the live

### Figure 4. Meta-analysis of clinical outcomes (relative risks).

| Study     | CDS Events | Control Events | Relative Risk |
|-----------|------------|----------------|---------------|
| All 2016  | 52         | 247            | 15.42%        |
| All 2020  | 96         | 184            | 21.47%        |
| Lim 2011  | 17         | 49             | 10.23%        |
| Lim 2016  | 15         | 43             | 8.37%         |
| Shah 2020 | 134        | 571            | 26.04%        |
| Willis 2020 | 69728    | 288130         | 24.47%        |

| Total (95% CI) | 289224 | 291310 |
|----------------|--------|--------|

| Study     | CDS Events | Control Events | Relative Risk |
|-----------|------------|----------------|---------------|
| All 2016  | 116        | 247            | 6.71%         |
| All 2020  | 101        | 185            | 6.97%         |
| Peris 2019| 1792       | 4348           | 22.95%        |
| Shah 2020 | 324        | 571            | 13.35%        |
| Willis 2020 | 133770  | 249571         | 28.36%        |
| Dregan 2014 | 1631    | 5875           | 21.66%        |

| Total (95% CI) | 260797 | 250115 |
|----------------|--------|--------|

| Study     | CDS Events | Control Events | Relative Risk |
|-----------|------------|----------------|---------------|
| All 2016  | 156        | 247            | 33.49%        |
| All 2020  | 74         | 182            | 29.69%        |
| Shah 2020 | 330        | 571            | 37.42%        |

| Total (95% CI) | 1000 | 3032 |
|----------------|------|------|

| HbA1c | CDS Events | Control Events | Relative Risk |
|-------|------------|----------------|---------------|
|       | 289224     | 291310         |               |
|       | 6.71%      | 116            |               |
|       | 6.97%      | 101            |               |
|       | 22.95%     | 1792           |               |
|       | 13.35%     | 324            |               |
|       | 28.36%     | 133770         |               |
|       | 21.66%     | 1631           |               |
|       | 33.49%     | 156            |               |
|       | 29.69%     | 74             |               |
|       | 37.42%     | 330            |               |
|       | 1000%      | 1000           |               |

| SBP    | CDS Events | Control Events | Relative Risk |
|--------|------------|----------------|---------------|
|        | 260797     | 250115         |               |
|        | 6.71%      | 116            |               |
|        | 6.97%      | 101            |               |
|        | 22.95%     | 1792           |               |
|        | 13.35%     | 324            |               |
|        | 28.36%     | 133770         |               |
|        | 21.66%     | 1631           |               |
|        | 33.49%     | 156            |               |
|        | 29.69%     | 74             |               |
|        | 37.42%     | 330            |               |
|        | 1000%      | 1000           |               |

| LDLc   | CDS Events | Control Events | Relative Risk |
|--------|------------|----------------|---------------|
|        | 1000       | 3032           |               |
|        | 6.71%      | 116            |               |
|        | 6.97%      | 101            |               |
|        | 22.95%     | 1792           |               |
|        | 13.35%     | 324            |               |
|        | 28.36%     | 133770         |               |
|        | 21.66%     | 1631           |               |
|        | 33.49%     | 156            |               |
|        | 29.69%     | 74             |               |
|        | 37.42%     | 330            |               |
|        | 1000%      | 1000           |               |

---

**Figure 4. Meta-analysis of clinical outcomes (relative risks).**
CDS interface), and make full use of Supplementary Materials to describe what their CDS systems entailed, and the degree to which it was EHR-enabled.44

Our findings also have implications for CDS evaluation research. Chronic diseases impact individuals and health systems over time but evidence for CDS effectiveness beyond 12 months is unclear. Funding for CDS interventions tends to be small in comparison to drug and device trials and there remains a need to fund high quality, longer-term studies with meaningful evaluation measures.44,158 Modeled studies are increasingly used to project longer-term CDS costs and outcomes. While useful in enabling complexity in economic evaluations,49 to be credible and replicable, future economic modeling needs to move beyond a “black box” approach—that is, there needs to be greater transparency in the reporting of model types, key parameter differences between intervention and control groups, and description of parameter sources (eg, trial-based, expert opinion). Finally, both effectiveness and economic studies should better account for “e-iatrogenesis” in terms of unintended consequences associated with CDS use.49,172 In our review, the main adverse health outcome considered was bleeding events secondary to CDS interventions for anticoagulation. The clinical and economic impact of e-iatrogenesis, for example, from false positive CDS screening results and increased healthcare utilization, needs to be further considered in future evaluations.49,172

Figure 5. Meta-analysis of clinical outcomes (mean differences).
| Study type | Study vehicle | Model type | Perspective | Time horizon (years) | Discount rate (%) | Cost—CDS intervention | Cost—healthcare costs | Sensitivity analysis | ICER CDS vs control in original currency | ICER CDS vs control in USD (2021 prices) |
|------------|---------------|------------|-------------|---------------------|------------------|-----------------------|----------------------|-------------------|-------------------------------|--------------------------------------|
| Anchala 2015 | CEA | Trial-based | NA | Healthcare system | 1 | 3 | + | + | Unclear | + | − | + | + | + | N/A | Not reported |
| Gilmer 2012 | CUA | Modeled | Markov micro-simulation | Healthcare system | 40 | 3 | − | + | + | + | + | + | + | + | + | USD $3017 per QALY |
| Orchard 2020 | CUA | Modeled | Not-specified | Healthcare funder | 10 | 5 | − | + | − | Unclear | + | − | + | + | − | USD $3811 per QALY |
| O’Reilly 2012 | CUA | Modeled | Markov micro-simulation | Healthcare funder | 40 | 5 | + | + | − | + | + | + | + | − | AUD $16,578 per QALY, AUD $84,383 per stroke |
| Oxendine 2014 | Cost analysis | N/A | N/A | Local facility | 40 | 5 | − | + | − | + | + | + | + | − | CAD $160,845 per QALY |
| Patel 2020 | CEA | Modeled | Not-specified | Healthcare system | 53 | 3 | − | + | + | − | + | + | + | − | AUD $7406 per primary CVD event prevented, AUD $17,988 per secondary CVD event prevented |
| Ranta 2015 | Cost analysis | N/A | N/A | Healthcare system | N/A | N/A | − | − | + | + | − | + | + | N/A | N/A | N/A | N/A | N/A | N/A |
| Subramanian 2012 | Cost analysis | N/A | N/A | Local facility | N/A | N/A | − | − | − | − | − | − | + | − | N/A | N/A | N/A | N/A | N/A | N/A |
| Willis 2020 | CUA | Modeled | Markov cohort | Healthcare funder | Lifetime horizon | 3.5 | + | + | − | + | + | + | + | + | GBP £1359 per risky prescribing module |
| Total (Yes—n) | | | | | | | | | | | | | | | 3 | 6 | 3 | 5 | 7 | 8 | 6 | 2 |
| Total (Yes—%) | | | | | | | | | | | | | | | 33 | 67 | 33 | 56 | 78 | 89 | 67 | 22 |

CEA: Cost Effectiveness Analysis; CUA: Cost Utility Analysis; CVD: Cardiovascular Disease; QALY: Quality-Adjusted Life Years; PSA: Probabilistic Sensitivity Analysis.
CONCLUSION

Our systematic review summarizes contemporary CDS systems used in chronic diseases and provides recommendations for future CDS designs. CDS interventions demonstrated small improvements to health or process outcomes, but the effect sizes tended to be of limited clinical and statistical significance. Evidence for cost-effectiveness was inconclusive with large variations in ICERs between studies. The diverse nature of CDS technologies, real-world implementation contexts, and evaluation methodologies all contributed to highly heterogeneous results. Future CDS evaluations should aim for higher quality reporting of CDS design characteristics and evaluation methods. Improved reporting would ensure that results from CDS evaluations are interpretable and useful for decision makers.

FUNDING

This research was supported by the Royal Australian College of General Practitioners (RACGP), the Australian Government Research Training Program (RTP) Scholarship, and Menzies School of Health Research scholarship.

AUTHOR CONTRIBUTIONS

WC, KH, AC, GG, and AA contributed to the conception and design of the study. WC conducted the search strategy. WC, BB, and PC screened titles and abstracts for eligibility. WC screened full texts for inclusion. WC, CO, KH, and GG conducted critical appraisal. WC, CO, and PC conducted data extraction. WC and PC analyzed the data. WC prepared the original draft. All authors reviewed the final manuscript.

SUPPLEMENTARY MATERIAL

Supplementary material is available at Journal of the American Medical Informatics Association online.

ACKNOWLEDGMENTS

The researchers gratefully acknowledge the Royal Australian College of General Practitioners (RACGP) Foundation for their support of this project. We thank Ms Lisa Ban (Charles Darwin University academic research librarian) for her review of the search strategy.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY

The data supporting the findings of this study are available within the article and Supplementary Files.

REFERENCES

1. Osheroff JA, Teich JM, Levick D, et al. Improving Outcomes with Clinical Decision Support: An Implementer’s Guide. 3rd ed. Milton, United Kingdom: Healthcare Information & Management Systems Society; 2012.

2. Waylenwick A, Scheeps-Hoeks A. Clinical decision support systems. In: Kupper P, Dumontier M, Dekker A, eds. Fundamentals of Clinical Data Science. Switzerland: Springer; 2018: 153–69.

3. Sutton RT, Pincove D, Baumgart DC, Sadowski DC, Fedorak RN, Kroeker KL. An overview of clinical decision support systems: benefits, risks, and strategies for success. NPJ Digit Med 2020; 3: 17.

4. Tov S, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020; 396 (10258): 1204–22.

5. Souza-Pereira L, Pombo N, Oubbi S, Felizardo V, Garcia N. Clinical decision support systems for chronic diseases: a systematic literature review. Comput Methods Programs Biomed 2020; 195: 105565.

6. Hunt DL, Haynes RB, Hanna SE, Smith K. Effects of computer-based clinical decision support systems on physician performance and patient outcomes: a systematic review. JAMA 1998; 280 (15): 1339–46.

7. Kawamoto K, Lobach DF. Clinical decision support provided within physician order entry systems: a systematic review of features effective for changing clinician behavior. AMIA Annu Symp Proc 2003; 2003: 361–5.

8. Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. BMJ 2003; 330 (7494): 765.

9. Garg AX, Adhikari NK, McDonald H, et al. Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. JAMA 2005; 293 (10): 1223–38.

10. Bryan C, Boren SA. The use and effectiveness of electronic clinical decision support tools in the ambulatory/primary care setting: a systematic review of the literature. Inform Prim Care 2008; 16 (2): 79–91.

11. Heselmans A, Van de Velde S, Donceel P, Aertgeerts B, Ramaekers D. Effectiveness of electronic guideline-based implementation systems in ambulatory care settings – a systematic review. Implement Sci 2009; 4 (82): 82.

12. Damiani G, Pinnarelli L, Colosimo SC, et al. The effectiveness of computerized clinical guidelines in the processes of care: a systematic review. BMC Health Serv Res 2010; 10: 2.

13. Rosanov PS, You JJ, Dhaliwal J, et al.; CCDSS Systematic Review Team. Can computerized clinical decision support systems improve practitioners’ diagnostic test ordering behavior? A decision-maker-researcher partnership systematic review. Implement Sci 2011; 6: 88.

14. Souza NM, Sebaldt RJ, Mackay JA, et al.; CCDSS Systematic Review Team. Computerized clinical decision support systems for primary preventive care: a decision-maker-researcher partnership systematic review of effects on process of care and patient outcomes. Implement Sci 2011; 6: 87.

15. Rosanov PS, Misra S, Gerstein HC, et al.; CCDSS Systematic Review Team. Computerized clinical decision support systems for chronic disease management: a decision-maker-researcher partnership systematic review.Implement Sci 2011; 6: 92.

16. Bright TJ, Wong A, Dhurjati R, et al. Effect of clinical decision-support systems: a systematic review. Ann Intern Med 2012; 157 (1): 29–43.

17. Rosanov PS, Fernandez N, Wilczynski JM, et al. Features of effective computerised clinical decision support systems: meta-regression of 162 randomised trials. BMJ 2013; 346:f657.

18. Taheri Moghadam S, Sadooghi F, Velayati F, Ehsanzadeh SJ, Poursharif S. The effects of clinical decision support system for prescribing medication on patient outcomes and physician practice performance: a systematic review and meta-analysis. BMC Med Inform Decis Mak 2021; 21 (1): 98.

19. Whitehead NS, Williams L, Meleth S, et al. The effect of laboratory test-based clinical decision support tools on medication errors and adverse drug events: a laboratory medicine best practices systematic review. J Appl Lab Med 2019; 3 (6): 1035–48.

20. Bayoumi I, Al Balas M, Handler SM, Dolovich L, Hutchison B, Holbrook A. The effectiveness of computerized drug-lab alerts: a systematic review and meta-analysis. Int J Med Inform 2014; 83 (6): 406–15.
21. Rawson TM, Moore ISP, Hernandez B, et al. A systematic review of clinical decision support systems for antimicrobial management: are we failing to investigate these interventions appropriately? Clin Microbiol Infect 2017; 23 (8): 524–32.
22. Holstiege J, Mathes T, Pieper D. Effects of computer-aided clinical decision support systems in improving antibiotic prescribing by primary care providers: a systematic review. J Am Med Inform Assoc 2015; 22 (1): 236–42.
23. Carracedo-Martinez E, Gonzalez-Gonzalez C, Texeira-Rodrigues A, et al.; Galician Pharmacoepidemiology Research Group. Computerized clinical decision support systems and antibiotic prescribing: a systematic review and meta-analysis. Clin Ther 2019; 41 (3): 552–81.
24. Nuckols TK, Smith-Spangler C, Morton SC, et al. Computerized clinical decision support systems on laboratory test ordering: a systematic review. Clin Pharmacol Ther 2015; 97 (5): 557–65.
25. Frazer A, Rowland J, Mudge A, Barras M, Martin J, Donovan P. Systematic review of interventions to improve safety and quality of anticoagulant prescribing for therapeutic indications for hospital inpatients. Eur J Clin Pharmacol 2019; 75 (12): 1645–57.
26. Jia P, Zhang L, Chen J, Zhao P, Zhang M. The effects of clinical decision support systems on medication safety: an overview. PLoS One 2016; 11 (12): e0167683-e.
27. Kaplan B. Evaluating informatics applications – clinical decision support systems literature review. Int J Med Inform 2001; 64 (1): 15–37.
28. Sakurai R, Ohe K. Effects of computerized guideline-oriented clinical decision support system on glycemic control in diabetic patients: a systematic review and meta-analysis. Stud Health Technol Inform 2017; 245: 1376.
29. Jeffery R, Herman E, Haynes RB; CDSS Systematic Review Team. Can computerized clinical decision support systems improve diabetes management? A systematic review and meta-analysis. Diabet Med 2013; 30 (6): 739–45.
30. Jia P, Zhao P, Chen J, Zhang M. Evaluation of clinical decision support systems for diabetes care: an overview of current evidence. J Eval Clin Pract 2019; 25 (1): 66–77.
31. Akbar S, Lyell D, Magrabi F. Automation in nursing decision support systems: a systematic review of effects on decision making, care delivery, and patient outcomes. J Am Med Inform Assoc. 2021; 28 (11): 2502–13.
32. van Balveren JA, Verhoek-van de Venne W, Erdem-Eraslan L, et al. Galician Pharmacoepidemiology Research Group. Computerized clinical decision support systems and antibiotic prescribing: a systematic review and meta-analysis. Clin Ther 2019; 41 (3): 552–81.
33. El Asmar ML, Dharmayat KI, Vallejo-Vaz AJ, Irwin R, Mastellon N. Effect of computerised, knowledge-based, clinical decision support systems on patient-reported and clinical outcomes of patients with chronic disease managed in primary care settings: a systematic review. BMJ Open 2021; 11 (12): e054659-e.
34. Njie GJ, Proia KK, Thota AB, et al.; Community Preventive Services Task Force. Clinical decision support systems and prevention: a community guide cardiovascular disease systematic review. Am J Prev Med 2015; 49 (5): 784–95.
35. Harada T, Miyagami T, Kunitomo K, Shimizu T. Clinical decision support systems for diagnosis in primary care: a scoping review. Int J Environ Res Public Health 2021; 18 (16): 8435.
36. Kwan JL, Lo L, Ferguson J, et al. Computerised clinical decision support systems and absolute improvements in care: meta-analysis of controlled clinical trials. BMJ 2020; 370: m3216.
37. Neame MT, Chacko J, Surace AE, Sinha IP, Hawcutt DB. A systematic review of the effects of implementing clinical pathways supported by health information technologies. J Am Med Inform Assoc 2019; 26 (4): 356–63.
38. Van de Velde S, Helsemans A, Delvaux N, et al. A systematic review of trials evaluating success factors of interventions with computerised clinical decision support. Implement Sci 2018; 13 (1): 114.
39. Blum D, Raj SX, Oberholzer R, Riphagen II, Strasser F, Kaasa S; EURO IMPACT, European Intersectoral Multidisciplinary Palliative Care Research Training. Computer-based clinical decision support systems and patient-reported outcomes: a systematic review. Patient 2015; 8 (5): 397–409.
40. Jacob V, Thota AB, Chatropadhay SK, et al. Cost and economic benefit of clinical decision support systems for cardiovascular disease prevention: a community guide systematic review. J Am Med Inform Assoc 2017; 24 (3): 669–76.
41. 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.
42. World Health Organization, Bertram M, Dhaene G, Tan-Torres Edejer T. Institutionalizing Health Technology Assessment Mechanisms: A How to Guide. Geneva: World Health Organization; 2021.
43. OECD. Health at a Glance. Paris, France: OECD publishing; 2021.
44. Tcheng JE, Bakken S, Bates DW III, Gandhi, TK, Josephs, M, et al. Optimizing Strategies for Clinical Decision Support (Meeting). Washington, DC: National Academy of Sciences; 2017.
45. Filimore CL, Bray BE, Kawamoto K. Systematic review of clinical decision support interventions with potential for inpatient cost reduction. BMC Med Inform Decis Mak 2013; 13: 135.
46. Lewkowicz D, Woolbrandt A, Boettinger E. Economic impact of clinical decision support interventions based on electronic health records. BMC Health Serv Res 2020; 20 (1): 871.
47. Thompson G, O’Horo JC, Pickering BW, Herascevich V. Impact of the electronic medical record on mortality, length of stay, and cost in the hospital and ICU: a systematic review and metaanalysis. Crit Care Med 2015; 43 (6): 1276–82.
48. Moja L, Kwag KH, Lytras T, et al. Effectiveness of computerized decision support systems linked to electronic health records: a systematic review and meta-analysis. Am J Public Health 2014; 104 (12): e12–22.
49. O’Reilly D, Tarride J-E, Goerre R, Lokker C, McKibben KA. The economics of health information technology in medication management: a systematic review of economic evaluations. J Am Med Inform Assoc 2012; 19 (3): 423–38.
50. Australian Institute of Health and Welfare (AIHW). Chronic Conditions and Multimorbidity. Canberra: Australian Institute of Health and Welfare; 2020. https://www.aihw.gov.au/reports/australias-health/chronic-conditions-and-multimorbidity Accessed March 2022.
51. Australian Institute of Health and Welfare (AIHW). Cardiovascular Disease, Diabetes and Chronic Kidney Disease: Australian Facts: Prevalence and Multimorbidity Accessed March 2022. https://www.aihw.gov.au/reports/heart-stroke-vascular-disease/cardiovascular-disease-chronic-kidney-prevalence/contents/summary Accessed July 2020.
52. Aromataris E, Munn Z. JBI Manual for Evidence Synthesis. Adelaide, Australia: JBI; 2020. https://synthesismanual.jbi.global Accessed November 2021.
53. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372: n71.
57. Covidence. Covidence Systematic Review Software. Melbourne, Australia: Veritas Health Innovation; 2021. https://www.covidence.org/ Accessed November 2021.

58. JBI, JBI SUMARI Software. Adelaide, Australia: The University of Adelaide; 2021.

59. Sirajuddin AM, Osheroff JA, Sittig DF, Chuo J, Velasco F, Collins DA. Implementation pears from a new guidebook on improving medication use and outcomes with clinical decision support. Effective CDS is essential for addressing healthcare performance improvement imperatives. *J Healthc Inf Manag* 2009; 23 (4): 38–45.

60. Husereau D, Drummond M, Petrou S, et al.; ISPOR Health Economic Evaluation Publication Guidelines-CHEERS Good Reporting Practices Task Force. Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—explanation and elaboration: a report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force. *Value Health* 2013; 16 (2): 231–50.

61. Sculpher MJ, Claxton K, Drummond M, McCabe C. Whither trial-based economic evaluation for health care decision making? *Health Econ* 2006; 15 (7): 677–87.

62. R Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2021.

63. Chowdhury MZI, Turin TC. Variable selection strategies and its importance in clinical prediction modelling. *Fam Med Community Health* 2020; 8 (1): e000622.

64. Turner HC, Lauer JA, Tran BX, Teerawattananon Y, Jit M. Adjusting for inflation and currency changes within health economic studies. *Value Health* 2019; 22 (9): 1026–32.

65. World Bank. *World Bank Open Data*. Washington, DC: The World Bank Group; 2022, https://data.worldbank.org/ Accessed June 2022.

66. Abdel-Kader K, Fischer GS, Li J, Moore CG, Hess R, Urrut ML. Automated clinical reminders for primary care providers in the care of CKD: a small cluster-randomized controlled trial. *Am J Kidney Dis* 2011; 58 (6): 894–902.

67. Ali MK, Chwastiak L, Poongothai S, et al.; for the INDEPENDENT Study Group. Effect of a collaborative care model on depressive symptoms and glycated hemoglobin, blood pressure, and serum cholesterol among patients with depression and diabetes in India: the INDEPENDENT randomized clinical trial. *JAMA* 2020; 324 (7): 651–62.

68. Ali MK, Singh K, Kondal D, et al.; CARRS Trial Group. Effectiveness of a multicomponent quality improvement strategy to improve achievement of diabetes care goals: a randomized, controlled trial. *Ann Intern Med* 2016; 165 (6): 399–408.

69. Anchala R, Kaptoge S, Pant H, Angelantonio D, Franco E, Prabhakaran OH. 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; 4 (1): e001213.

70. Arts DL, Abu-Hanna A, Medlock SK, van Weert HC. Effectiveness and usage of a decision support system to improve stroke prevention in general practice: a cluster randomized controlled trial. *PLoS One* 2017; 12 (2): e0170974.

71. Awdisu L, Coates CR, Lyddane A, et al. The impact of real-time alerting on appropriate prescribing in kidney disease: a cluster randomized controlled trial. *J Am Med Inform Assoc* 2016; 23 (3): 609–16.

72. Bhardwaja B, Carroll NM, Rachel MA, et al. Improving prescribing safety in patients with renal insufficiency in the ambulatory setting: the Drug Renal Alert Pharmacy (DRAP) program. *Pharmacotherapy* 2011; 31 (4): 346–56.

73. Chalasani S, Peiris DP, Usherwood T, et al. Reducing cardiovascular disease risk in diabetes: a randomised controlled trial of a quality improvement initiative. *Med J Aust* 2017; 206 (10): 436–41.

74. Cox JL, Parkash R, Foster GA, et al.; IMPACT-AF Investigators. Integrated Management Program Advancing Community Treatment of Atrial Fibrillation (IMPACT-AF): a cluster randomized trial of a computerized clinical decision support tool. *Am Heart J* 2020; 224: 35–46.

75. Delvaux N, Pessens V, Burghgraefe TD, et al. Clinical decision support improves the appropriateness of laboratory test ordering in primary care without increasing diagnostic error: the ELMO cluster randomized trial. *Implant Sci* 2020; 15 (1): 1–10.

76. Dropen A, van Staa TP, McDermott L, et al.; Data Monitoring Committee. Point-of-care cluster randomized trial in stroke secondary prevention using electronic health records. *Stroke* 2014; 45 (7): 2066–71.

77. Gill J, Kucharski K, Turk B, Pan C, Wei W. Using electronic clinical decision support in patient-centered medical homes to improve management of diabetes in primary care: the DECIDE study. *J Ambul Care Manage* 2019; 42 (2): 105–15.

78. Heselmann A, Delvaux N, Laenen A, 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): 5–14.

79. Holbrook A, Pullenayagum E, Thabane L, et al. Shared electronic vascular risk decision support in primary care: Computerization of Medical Practices for the Enhancement of Therapeutic Effectiveness (COMPETE III) randomized trial. *Arch Intern Med* 2011; 171 (19): 1736–44.

80. Holt TA, Dalton A, Marshall T, et al. Automated software system to promote anticoagulation and reduce stroke risk: cluster-randomized controlled trial. *Stroke* 2017; 48 (3): 787–90.

81. Karlsson LO, Nilsson S, Bång M, Nilsson L, Charitakis E, Janzon M. A clinical decision support tool for improving adherence to guidelines on anticoagulant therapy in patients with atrial fibrillation at risk of stroke: a cluster-randomized trial in a Swedish primary care setting (the CDS-AF study). *PLoS Med* 2018; 15 (3): e0012528.

82. Lim S, Kang SM, Kim KM, et al. Multifactorial intervention in diabetes care using real-time monitoring and tailored feedback in type 2 diabetes. *Acta Diabetol* 2016; 53 (2): 189–98.

83. Lim S, Kang SM, Shin H, et al. Improved glycemic control without hypoglycemia in elderly diabetic patients using the ubiquitous healthcare service, a new medical information system. *Diabetes Care* 2011; 34 (2): 308–13.

84. Mazzaglia G, Piccinni C, Filippi A, et al. Effects of a computerized decision support system in improving pharmacological management in high-risk cardiovascular patients: a cluster-randomized open-label controlled trial. *Health Informatics J* 2016; 22 (2): 323–47.

85. McKay PM, Kor DJ, Cook DA, et al. Computerized advisory decision support for cardiovascular diseases in primary care: a cluster randomized trial. *Am J Med* 2020; 133 (6): 750–6.e2.

86. O’Connor PJ, Sperl-Hillen JM, Rush WA, et al. Impact of electronic health record clinical decision support on diabetes care: a randomized controlled trial. *Am Fam Med* 2011; 9 (1): 12–21.

87. Peiris D, Praveen D, Mogulluru K, et al. SMARTHealth India: a stepped-wedge, cluster randomised controlled trial of a community health worker managed mobile health intervention for people assessed at high cardiovascular disease risk in rural India. *PLoS One* 2019; 14 (3): e0213708.

88. Peiris D, Usherwood T, Panaretto K, et al. Effect of a computer-guided, quality improvement program for cardiovascular disease risk management in primary health care: the treatment of cardiovascular risk using electronic decision support cluster-randomized trial. *Circ Cardiovasc Qual Outcomes* 2015; 8 (1): 87–95.

89. Ranta A, Dovey S, Weatherall M, O’Dea D, Gommans J, Tilyard M. Cluster randomized controlled trial of TIA electronic decision support in primary care. *Neurology* 2015; 84 (15): 1545–51.

90. Rondola MCM, Dijkstra-Oei LT, Vos RC, Westers P, Rutten G. Cluster randomised trial on the effectiveness of a computerised prompt to refer (back) patients with type 2 diabetes. *PLoS One* 2018; 13 (12): e0207653.

91. Sequet TD, Hollliday AM, Orav EJ, Bates DW, Denker BM. Physician and patient tools to improve chronic kidney disease care. *Am J Manag Care* 2018; 24 (4): e107–14.

92. Sequet TD, Morong SM, Marston A, et al. Electronic risk alerts to improve primary care management of chest pain: a randomized, controlled trial. *J Gen Intern Med* 2012; 27 (4): 438–44.

93. Singh K, Kondal D, Patel V, et al.; Members of the Research Steering Committee, Investigators, Members of the Data Safety and Monitoring Board. Effectiveness of an mHealth-based electronic decision support
system for integrated management of chronic conditions in primary care: the mWellCare cluster-randomized controlled trial. Circulation 2019; 139 (3): 380–91.
94. Sperl-Hillen JM, Crain AL, Margolis KL, et al. Clinical decision support directed to primary care patients and providers reduces cardiovascular risk: a randomized trial. J Am Med Inform Assoc 2018; 25 (9): 1137–46.
95. Weiner M, Cunnings J, Raji A, et al. A randomized study on the usefulness of an electronic outpatient hypoglycemia risk calculator for clinicians of patients with diabetes in a safety-net institution. Curr Med Res Opin 2020; 36 (4): 583–93.
96. Willis TA, Collinson M, Glidewell L, et al. ASPIRE Programme Team. An adaptable implementation package targeting evidence-based indicators in primary care: a pragmatic cluster-randomised evaluation. PLoS Med 2020; 17 (2): e1003045.
97. Ayaj VS, Jindal D, Roy A, et al. Development of a smartphone-enabled hypertension and diabetes mellitus management package to facilitate evidence-based care delivery in primary healthcare facilities in India: the mPower Heart Project. J Am Heart Assoc 2016; 5 (12): 1–10.
98. Akenroye AT, Kumthekar AA, Alevizos MK, Mowrey WB, Broder A. Implementing an electronic medical record-based reminder for cardiovascular risk screening in rheumatoid arthritis. Arthritis Care Res (Hoboken) 2017; 69 (5): 625–32.
99. Albu JB, Sohler N, Li R, et al. An interrupted time series analysis to determine the effect of an electronic health record-based intervention on appropriate screening for type 2 diabetes in urban primary care clinics in New York City. Diabetes Care 2017; 40 (8): 1058–64.
100. Barbieri C, Molina M, Ponce P, et al. An international observational study suggests that artificial intelligence for clinical decision support optimizes anemia management in hemodialysis patients. Kidney Int 2016; 90 (2): 422–9.
101. Bellows J, Patel S, Young SS. Use of IndiGO individualized clinical guidelines in primary care. J Am Med Inform Assoc 2014; 21 (3): 432–7.
102. Bronner JP, Fontanesi J, Goel A. Improving prompt effectiveness in diabetes care: an intervention study. Am J Med Qual 2012; 27 (5): 406–10.
103. Brunstrom M, Ng N, Dahlstrom J, et al. Association of physician education and feedback on hypertension management with patient blood pressure and hypertension control. JAMA Netw Open 2020; 3 (1): e1918625.
104. Chaudhry B, Tuileadge-Scheitel SM, Parks DA, Angstman KB, Decker RA. An adaptable implementation package targeting evidence-based indicators in primary care: a pragmatic cluster-randomised evaluation. J Card Fail 2017; 23 (10): 719–26.
105. Gold R, Bunce A, Cowburn S, et al. Does increased implementation support improve community clinics’ guideline-concordant care? Results of a mixed methods, pragmatic comparative effectiveness trial. Implement Sci 2019; 14 (1): 100.
106. Graven M, Allen P, Smith I, MacDonald NE. Decline in mortality with the Belize Integrated Patient-Centred Country Wide Health Information System (BHIS) with embedded program management. Int J Med Inform 2013; 82 (10): 954–63.
107. Grunathlak W, Gunawardena S, Fernando R, Thomson G, Fernando D. The impact of a decision support tool linked to an electronic medical record on glycemic control in people with type 2 diabetes. J Diabetes Sci Technol 2013; 7 (3): 653–9.
108. Kawamoto K, Anstrom KJ, Anderson JB, et al. Long-term impact of an electronic health record-enabled, team-based, and scalable population health strategy based on the chronic care model. AMIA Annu Symp Proc 2016; 2016: 686–95.
109. Kelly E, Wasser T, Fraga JD, Scheier JJ, Alweiss RL. Impact of an EMR clinical decision support tool on lipid management. J Clin Outcomes Manag 2011; 18 (12): 551–5.
110. Keohane DM, Dennehy T, Keohane KP, Shanahan E. Reducing inappropriate non-steroidal anti-inflammatory prescription in primary care patients with chronic kidney disease. Int J Health Care Qual Assur 2017; 30 (7): 638–44.
111. Kirby AM, Kruger B, Jain R, O’Hair DP, Granger BB. Using clinical decision support to improve referral rates in severe symptomatic aortic stenosis: a quality improvement initiative. Comput Inform Nurs 2018; 36 (11): 525–9.
112. Kumar S, Woodward-Kron R, Frank O, Krieneriem A, Lau P. Patient-directed reminders to improve preventive care in general practice for patients with type 2 diabetes: a proof of concept. Aust J Gen Pract 2018; 47 (6): 383–8.
113. Lau B, Overby CL, Wirtz HS, Devine EB. The association between use of a clinical decision support tool and adherence to monitoring for medication-laboratory guidelines in the ambulatory setting. App Clin Inform 2013; 4 (4): 476–98.
114. Litvin CB, Hyer JM, Ornstein SM. Use of clinical decision support to improve primary care identification and management of chronic kidney disease (CKD). J Am Board Fam Med 2016; 29 (5): 604–12.
115. Lopez PM, Divney A, Goldfeld K, et al. Feasibility and outcomes of an electronic health record intervention to improve hypertension management in immigrant-serving primary care practices. Med Care 2019; 57 (Suppl 2): S164–71.
116. Majka DS, Lee JY, Peprah YA, et al. Changes in care after implementing a multifaceted intervention to improve preventive cardiology practice in rheumatoid arthritis. Am J Med Qual 2019; 34 (3): 276–83.
117. Meador M, Osheroff JA, Reisler B. Improving identification and diagnosis of hypertensive patients hiding in plain sight (HIPS) in health centers. Jr Conn J Qual Patient Saf 2018; 44 (3): 117–29.
118. Orchard J, Neubeck L, Freedman B, et al. eHealth tools to provide structured assistance for atrial fibrillation screening, management, and guideline-recommended therapy in metropolitan general practice: the AF-SMART study. J Am Heart Assoc 2019; 8 (1): e010959.
119. Orchard J, Jinlin L, Freedman B, et al. Atrial fibrillation screen, management, and guideline-recommended therapy in the rural primary care setting: a cross-sectional study and cost-effectiveness analysis of eHealth tools to support all stages of screening. J Am Heart Assoc 2020; 9 (18): 1–15.
120. O’Reilly DJ, Bowen JM, Sebaldt RJ, et al. Evaluation of a chronic disease management system for the treatment and management of diabetes in primary health care practices in Ontario: an observational study. Ont Health Technol Assess Ser 2014; 14 (3): 1–37.
121. Oxendine V, Meyer A, Reid PV, Adams A, Sadoh V. Evaluating diabetes outcomes and costs within an ambulatory setting: a strategic approach utilizing a clinical decision support system. Clin Diabetes 2014; 32 (3): 113–20.
122. Patel A, Praveen D, Maharani A, et al. Association of multifaceted mobile technology-enabled primary care intervention with cardiovascular disease risk management in rural Indonesia. JAMA Cardiol 2019; 4 (10): 978–86.
123. Pefanis A, Bottero R, Langham RG, Nelson CL. eMAP:CKD: electronic diagnosis and management assistance to primary care in chronic kidney disease. Nephril Dial Transplant 2018; 33 (1): 121–8.
130. Persell SD, Kaiser D, Dolan NC, et al. Changes in performance after implementation of a multifaceted electronic-health-record-based quality improvement system. Med Care 2011; 49 (2): 117–25.

131. Ramírez M, Chen K, Follett RW, Mangione CM, Moreno G, Bell DS. Impact of a “chart closure” hard stop alert on prescribing for elevated blood pressures among patients with diabetes: quasi-experimental study. JMIR Med Inform 2020; 8 (4): e16421.

132. Ranta A, Yang CF, Funnell M, Cariga P, Murphy-Rahal C, Cogger N. Utility of a primary care based transient ischaemic attack electronic decision support tool: a prospective sequential comparison. BMC Fam Pract 2014; 15: 86.

133. Robson J, Dostal I, Mathur R, et al. Improving anticoagulation in atrial fibrillation: observational study in three primary care trusts. Br J Gen Pract 2014; 64 (622): e275–81.

134. Shelley D, Tseng TY, Matthews AG, et al. Technology-driven intervention to improve hypertension outcomes in community health centers. Am J Manag Care 2011; 17 (12 Spec No): Sp103–10.

135. Shih SC, McCullough CM, Wang JJ, Singer J, Parsons AS. Health information systems in small practices. Improving the delivery of clinical preventive services. Am J Prev Med 2011; 41 (6): 603–9.

136. Swedlund M, Norton D, Birsteller J, Chen G, Cruz L, Hanzathan L. Effectiveness of a best practice alerts at improving hypertension control. Am J Hypertens 2019; 32 (1): 70–6.

137. Syper D, Van Dyke K, Dhillon N, Elliott JO, Jordan K. Improved resident adherence to AAA screening guidelines via an electronic reminder. J Healthc Qual 2017; 39 (1): e1–9.

138. Thomas B. Improving blood pressure control among adults with CKD and diabetes: provider-focused quality improvement using electronic health records. Adv Chronic Kidney Dis 2011; 18 (6): 406–11.

139. Tolli J, Flanagan E, McCorkindale S, et al. Improved management of acute kidney injury in primary care using e-alerts and an educational outreach programme. Fam Pract 2018; 35 (6): 684–9.

140. Trinadha P, Gaurav J, Edgard AC, Andrew JV. Impact of an electronic medical record based clinical decision support system. J Am Med Inform Assoc 2012; 19 (3): 341–5.

141. Patel B, Peiris DP, Patel A, et al. Improving anticoagulation in atrial fibrillation: observational study in three primary care trusts. Br J Gen Pract 2014; 64 (622): e275–81.

142. Gilmer TP, O’Connor PJ, Sperl-Hillen JM, et al. Cost-effectiveness of an electronic medical record based clinical decision support system. Health Serv Res 2012; 47 (6): 2117–58.

143. O’Reilly D, Holbrook A, Blackhouse G, Troyan S, Goeree R. Cost-effectiveness of a shared computerized decision support system for diabetes linked to electronic medical records. J Am Med Inform Assoc 2012; 19 (3): 341–5.

144. Patel B, Peiris DP, Patel A, et al. A computer-guided quality improvement tool for primary health care: cost-effectiveness analysis based on TORDPEDO trial data. Med J Aust 2020; 213 (2): 73–8.

145. Subramanian S, Hoover S, Wagner JL, et al. Immediate financial impact of computerized clinical decision support for long-term care residents with renal insufficiency: a case study. J Am Med Inform Assoc 2012; 19 (3): 439–42.

146. Sim I, Berlin A. A framework for classifying decision support systems. AMIA Annu Symp Proc 2003; 2003: 599–603.

147. Berlin A, Sorani M, Sim I. A taxonomic description of computer-based clinical decision support systems. J Biomed Inform 2006; 39 (6): 656–67.

148. Wright A, Sittig DF, Ash JS, et al. Development and evaluation of a comprehensive clinical decision support taxonomy: comparison of front-end tools in commercial and internally developed electronic health record systems. J Am Med Inform Assoc 2013; 18 (3): 232–42.

149. Fraccaro P, Arguello Castelero M, Ainsworth J, Buchan I. Adoption of clinical decision support in multimorbidity: a systematic review. JMIR Med Inform 2015; 3 (1): e4.

150. Jankovic I, Chen JH. Clinical decision support and implications for the clinician burnout crisis. Yearb Med Inform 2020; 29 (1): 145–54.

151. Hussain MI, Reynolds TL, Zheng K. Medication safety alert fatigue may be reduced via interaction design and clinical role tailoring: a systematic review. J Am Med Inform Assoc 2019; 26 (10): 1141–9.

152. McCoy AB, Thomas EJ, Krousel-Wood M, Sittig DF. Clinical decision support alert appropriateness: a review and proposal for improvement. Ochsner J 2014; 14 (2): 195–202.

153. Miller A, Moon B, Anders S, Walden R, Brown S, Montella D. Integrating computerized clinical decision support systems into clinical work: a meta-synthesis of qualitative research. Int J Med Inform 2015; 84 (12): 1009–18.

154. Westerbeek L, Ploegmakers KJ, de Bruijn GJ, et al. Barriers and facilitators influencing medication-related CDSS acceptance according to clinicians: a systematic review. Int J Med Inform 2021; 152: 104506.

155. Moxey A, Robertson J, Newby D, Hains I, Williamson M, Pearson S-A. Computerized clinical decision support for prescribing: provision does not guarantee uptake. J Am Med Inform Assoc 2010; 17 (1): 25–33.

156. 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 (2): 14604582211073536.

157. Poon EG, Trent Rosenbloom S, Zheng K. Health information technology and clinician burnout: current understanding, emerging solutions, and future directions. J Am Med Inform Assoc 2021; 28 (5): 895–8.

158. Groenhof TKJ, Asselbergs FW; Groenwold RHH, Grobbee DE, Visseren FLJ, Bots ML, on behalf of the UCC-SMART Study Group. The effect of computerized decision support systems on cardiovascular risk factors: a systematic review and meta-analysis. BMC Med Inform Decis Mak 2019; 19 (1): 108.

159. Campbell NC, Murray E, Darbyshire J, et al. Designing and evaluating complex interventions to improve health care. BMJ 2007; 334 (7591): 455–9.

160. Tanner-Smith EE, Grant S. Meta-analysis of complex interventions. Annu Rev Public Health 2018; 39 (1): 135–51.

161. Kouri A, Yamada J, Lam Shin Cheung J, Van de Velde S, Gupta S. Do providers use computerized clinical decision support systems? A systematic review and meta-regression of clinical decision support uptake. Implement Sci 2022; 17 (1): 21.

162. Lobach D. Enabling Health Care Decision Making Through Clinical Decision Support and Knowledge Management. Rockville, MD: Rockville, MD Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services; 2012. https://www.ncbi.nlm.nih.gov/books/NBK97318/Accesed June 2022.

163. Liu S, Reese TJ, Kawamoto K, Del Fiol G, Weir C. A systematic review of theoretical constructs in CDS literature. BMC Med Inform Decis Mak 2021; 21 (1): 102.

164. Fillmore CL, Rommel CA, Welch BM, Zhang M, Kawamoto K. The perils of meta-regression to identify clinical decision support system success factors. J Biomed Inform 2015; 56: 65–8.

165. Sim I, Gorman P, Greenea RA, et al. Clinical decision support systems for the practice of evidence-based medicine. J Am Med Inform Assoc 2001; 8 (6): 527–34.

166. Sittig DF, Wright A, Osheroff JA, et al. Grand challenges in clinical decision support. J Biomed Inform 2008; 41 (2): 387–92.

167. Semanik MG, Kleinschmidt PC, Wright A, et al. Impact of a problem-oriented view on clinical data retrieval. J Am Med Inform Assoc 2021; 28 (5): 895–906.

168. Curran RL, Kukhareva PV, Taft T, et al. Integrated displays to improve chronic disease management in ambulatory care: a SMART on FHIR application informed by mixed-methods user testing. J Am Med Inform Assoc 2020; 27 (8): 1225–34.

169. Kawamoto K, Del Fiol G, Lobach DF, Jenders RA. Standards for scalable clinical decision support: need, current and emerging standards, gaps, and proposal for progress. Open Med Inform J 2010; 4: 235–44.

170. Kawamoto K, Kukhareva PV, Weir C, et al. Establishing a multidisciplinary initiative for interoperable electronic health record innovations at an academic medical center. JAMIA Open 2021; 4 (3): ooab041.

171. Sarkar U, Samal L. How effective are clinical decision support systems? BMJ 2020; 370: m3499.

172. Stone EG. Unintended adverse consequences of a clinical decision support system: two cases. J Am Med Inform Assoc 2018; 25 (5): 564–7.