Healthcare Improvement Scotland | SHTG Advice on health technologies

SHTG Assessment
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Knowledge-based clinical decision support systems

What were we asked to look at?

The Scottish Government asked us to review the evidence on the impact of knowledge-based clinical decision support systems on service delivery, patient, and clinical outcomes. They also asked that we review the evidence on barriers and enablers for successful implementation of these systems in clinical practice.

Why is this important?

Healthcare professionals are required to make decisions relating to patient care on a daily basis. With the increasing volume of evidence available, and improvements in technology, there is an opportunity to introduce tools to aid healthcare professionals in making decisions relating to patient care. Clinical decision support systems (CDSS) are one such tool, generating evidence-based, patient-specific advice at the point-of-care.

What was our approach?

We produced an SHTG Assessment based on a rapid review of published evidence on the effectiveness, safety, and implementation of knowledge-based CDSS in healthcare. Information on our SHTG Assessment product can be found here.

What next?

The SHTG Assessment will be presented to the NHSScotland CDSS steering group and integrated into a business case being prepared for the Scottish Government in relation to funding the next three years of the National Decision Support Programme.

Key points

Effectiveness and safety

- The evidence base for the effectiveness and safety of CDSS consisted of three overviews of systematic reviews and 10 systematic reviews that were not included in the overviews.
- There is a greater volume of evidence focusing on the impact of clinical decision support systems (CDSS) on care processes, than on impact on patient outcomes.
- CDSS had a positive impact on guideline adherence, process efficiency, safe prescribing, prescriber behaviour, and appropriate test ordering.
- An overview of systematic reviews reported two potentially negative responses to CDSS: use of risky workarounds and old paper forms. One systematic review found a negative impact of CDSS on prescriber behaviour (increased errors and overrides) in 6% of primary studies.
- The impact of CDSS on patient outcomes is less clear, with effects varying between indications, outcomes, and studies. Individual studies have shown a positive effect of CDSS on mortality, diagnostic yield from medical imaging, diabetes management, and inappropriate prescribing in older adults.
- None of the systematic reviews reporting patient outcomes described a negative impact of CDSS.
- Limitations of the secondary evidence on CDSS included: a lack of meta-analyses to quantify the effects of CDSS (due to heterogeneity of included studies); the challenge of determining how much change in an outcome is attributable to the CDSS; and the potential lack of generalisability of study results to Scotland.

Implementation barriers and facilitators

- The evidence base on barriers and facilitators to implementation of CDSS consisted of 11 systematic reviews.
- The most commonly identified barriers to implementation of CDSS were user mistrust of the system, lack of efficiency due to disruption of workflow, and poor system design.
- Factors most frequently cited as facilitating CDSS implementation included: encouraging positive user expectations; designing the system for ease of use; involving stakeholders in the design process; and generating trust in the quality of recommendations produced by the system, through transparency about the underpinning evidence sources.

Costs and cost effectiveness

- The economic evidence on CDSS was limited, tended to be specific to an indication or clinical setting, and was unlikely to be generalisable to Scotland.
- One economic evaluation reported that printed decision support for reducing antibiotic prescribing in patients with acute bronchitis dominated (lower costs and fewer prescriptions) usual care and computerised decision support systems.
- Three primary studies in a systematic review on CDSS for cardiovascular disease prevention reported cost per quality adjusted life-year (QALY). Two of these studies found CDSS to be cost-effective at the US willingness-to-pay-threshold (<$50,000) but only in conjunction with additional interventions. There was uncertainty about the cost effectiveness of CDSS alone.

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Literature search

A systematic search of the secondary literature was carried out between 20 December 2019 and 7 January 2020 to identify systematic reviews, meta-analyses, health technology assessments, and other evidence-based reports relating to the clinical effectiveness, safety and implementation of clinical decision support systems. Multiple databases, including Medline, Embase, Web of Science, Health Business Fulltext and ASSIA, were searched.

All search results were limited to studies published in English between January 2015 and January 2020 on the basis that a Scottish Government report summarising evidence on clinical decision support systems was published in 2015.

Concepts used in all searches included: clinical decision support, decision support programme, knowledge-based decision support, expert-led support, and expert decision support. Further details of the literature search methods are available in appendix 2.

Studies were selected for inclusion if they met all the following criteria, based on the PICOS framework.

- Population: health or social care patients or clients; professionals working in health or social care.
- Intervention: computerised knowledge-based clinical decision support systems that used algorithms and inference models to generate evidence-based, patient-specific recommendations.
- Intervention: a) addressed one of six key areas encompassed by the Scottish National Decision Support Programme – prescribing practice, polypharmacy or medication safety; pain management; referral management; palliative or end of life care; unscheduled care; mental health

  OR

  b) assessed the use of knowledge-based clinical decision support systems across multiple health or social care settings.
- Comparator: usual care; no clinical decision support system; pre-implementation period; no comparator.
- Outcomes: effectiveness; safety; self-management; person-centred care; implementation barriers or facilitators.
- Setting: health or social care.

Three reviewers applied the inclusion criteria to abstracts identified in the literature search. Disagreements were resolved by consensus.

Economics literature search

A systematic search of selected bibliographic databases was carried out between 8 and 22 January 2020 to identify studies relating to the cost effectiveness of clinical decision support systems. The Medline, Embase, HMIC, and the Centre for Reviews and Dissemination Economic Evaluations Database (CRD EED) were searched.

The publication date range, language limits, and search concepts, used in the main literature search (outlined above) were also applied to the economics literature.

Due to the low volume of economic evidence identified, cost effectiveness literature was selected using a broader set of inclusion criteria.

- Population: health or social care patients or clients.
- Intervention: a computerised clinical decision support system; any setting or topic area.
- Comparator: any comparator or no comparator.
- Outcomes: costs; cost effectiveness.
- Setting: health or social care.

Two reviewers applied the inclusion criteria to abstracts identified in the literature search.

Introduction

Healthcare professionals are required to make decisions relating to patient care on a daily basis. These decisions involve acquiring patient information, and applying personal experience and knowledge of relevant clinical evidence. With the increasing volume of clinical evidence available and developments in information technology, there is an opportunity to support healthcare professionals in making evidence-based decisions relating to patient care. Computer technology, in the form of clinical decision support systems (CDSS), can provide this assistance by generating evidence-based, patient-specific advice at the point-of-care.

Research questions

1. What effects do knowledge-based CDSS have on decision-making, and the delivery of safe and effective health and social care?
2. What are the enablers and barriers for effective implementation of knowledge-based CDSS?
3. Are knowledge-based CDSS cost-effective in health and social care?

Health technology description

There are multiple definitions of CDSS. For example, a CDSS has been described as "any electronic system designed to aid directly in clinical decision making, in which characteristics of individual patients are used to generate patient-specific assessments or recommendations that are then presented to clinicians for consideration"[1]. Another definition of CDSS is "a computerised system that uses case-based reasoning to assist clinicians in assessing disease status, in making a diagnosis, in selecting appropriate therapy or in making other clinical decisions. Characteristics of individual patients are matched to a computerised knowledge base, and software algorithms generate patient-specific information in the form of assessments or recommendations"[2]. Across all definitions identified, key features of a CDSS appear to be: a computer program that applies algorithms or rules and inference modelling to data; the generation of patient-specific advice or recommendations; and the integration of a knowledge or evidence base.

CDSS have increasingly been integrated with other electronic systems in healthcare[3]. Computerised physician / prescriber order entry (CPOE) refers to systems that automate the medication prescribing process, ensuring legible, standardised ordering of drugs. These CPOE systems can interface with the CDSS, or there may be a CDSS integrated into the CPOE. Increasingly CDSS are also being integrated with electronic health records (EHR) to streamline workflow and provide individual patient data for the CDSS to use when generating advice.

As indicated in the inclusion criteria for this assessment, the CDSS described in the following sections were considered to be 'knowledge-based', since they used a repository of knowledge, for example clinical guidelines, and a set of rules or algorithms to generate evidence-based, patient-specific recommendations for health and social care professionals.

Effectiveness and safety

The evidence base for the effectiveness and safety of CDSS consisted of three overviews of systematic reviews[2, 4, 5] and 10 systematic reviews that were not included in the overviews[6-15]. Due to heterogeneity in patient populations, interventions, comparators, outcomes, and study settings, none of the identified literature reported a meta-analysis. Summary information for each of the overviews and systematic reviews is presented in appendix 3.

General CDSS

Two overviews of systematic reviews[4, 5] and one systematic review[15] assessed the use of CDSS across multiple healthcare settings, patient populations, and indications.

Both overviews used the same methodology and study selection criteria, with one incorporating 21 systematic reviews published 2010-2015[5] and the other updating these results with data from seven reviews published from 2015 to 2017[4]. Since the individual systematic reviews varied in quality, only the findings from moderate or high quality reviews are captured here.

The most recent overview found evidence from four systematic reviews that CDSS had a positive impact on guideline adherence, indicated care, organisational efficiency, safe prescribing, and patient outcomes[4]. Two potential negative effects were reported, with CDSS implementation leading to the use of risky workarounds or persistent use of paper forms. The earlier overview reached similar conclusions, reporting that CDSS led to improvements in care processes (such as number of glucose measurements in the recommended range), an increase in appropriateness of test ordering, an increase in preventive care services, an increase in ordering or completion of recommended clinical investigations, and an increase in adherence to treatment guidelines. The effect of CDSS on patient outcomes was described in this overview as inconsistent. For example, one systematic review reported no impact on mortality but another found a 17% reduction in this outcome.

In the systematic review, clinicians assigned the outcomes reported in each primary study a 'medical effect score' to represent the perceived impact of the CDSS on individual patient outcomes and the connection to mortality risk[15]. Twenty studies out of 70 (29%) included in the review found no significant effects of CDSS on patient outcomes. Five studies out of 25 (20%) reporting mortality as an outcome found a significant reduction after implementation of CDSS. There was a reduction in life-threatening events in 16 studies, and 20 studies showed a moderate positive effect of CDSS in reducing non-life-threatening events that required medical attention. Based on the evidence from primary studies, the review authors identified six disease areas where CDSS may have the maximum impact: blood glucose management; blood transfusion management; prevention of physiologic deterioration / physiologic surveillance; pressure ulcer prevention; acute kidney injury prevention; and venous thromboembolism (VTE) prophylaxis.

Medication safety

One overview of systematic reviews[2] and two systematic reviews that were not included in the overview[11, 13], assessed CDSS in the context of medication safety.

The overview of 20 systematic reviews evaluated the impact of CDSS on processes of care and patient outcomes relating to medication safety[2]. Twelve reviews (63%) found strong evidence* that CDSS improved process of care outcomes relating to medication safety in

* Strong evidence = evidence from RCTs with >50% of studies showing effect.

acute care. Seven systematic reviews reported limited evidence[†] of an impact on prescribing errors, dosage errors, and medication or drug-related intermediate outcomes. Thirteen systematic reviews reported CDSS impact on patient outcomes relating to medication safety. Two of these reviews reported strong evidence that CDSS affected patient outcomes, three found limited evidence of an effect, and eight found insufficient evidence[‡] of an effect on patient outcomes relating to medication safety.

As part of the development of a NICE guideline on medicines optimisation, a systematic review was conducted that included 20 randomised controlled trials (RCTs) evaluating the use of CDSS to reduce suboptimal prescribing and improve patient outcomes[13]. In the final guideline, NICE recommended consideration of CDSS to support clinical decision making and prescribing, but stated that CDSS should not replace clinical judgement. Evidence was not consistent for impact of CDSS on suboptimal prescribing and potential medicine-related problems. For both of these outcomes one or more RCT reported a significant effect and one or more found no significant effect.

The final systematic review[11] on CDSS for medication safety did not provide a narrative synthesis of the seven included studies, instead reporting results from each primary study separately. Overall, five studies described improvements in medication safety following the introduction of CDSS, and two studies found no effect of CDSS on medication safety. The greatest impact on medication safety was reportedly in patients who had the highest baseline risk of medication injury ($p<0.03$). For more detail on the findings of individual studies in this review refer to appendix 3.

Polypharmacy and prescribing

Four systematic reviews were identified that assessed CDSS in relation to prescribing: prescribing in older adults[12]; insulin and glycaemic control[9]; generating interruptive alerts in CPOE systems[14]; and decision support tools in the form of standardised order sets[8].

The first systematic review explored the impact of CDSS on potentially inappropriate prescribing (over-, under- and miss-prescribing) in older adults, who are more vulnerable to polypharmacy[12]. This review incorporated 10 RCTs and six observational studies. The review authors concluded that CDSS were associated with reductions in the number of new potentially inappropriate prescriptions and the mean number of potentially inappropriate prescriptions per elderly patient. The review also found an improvement in appropriateness of drugs prescribed and an increase in the number of discontinued potentially inappropriate

[†] Limited evidence = evidence from RCTs showing an effect in 40-50% of studies, or a mixture of RCTs and non-randomised studies with an effect in >50% of studies.

[‡] Insufficient evidence = results from non-randomised studies only or an effect in <40% of studies.

medications. Changes in these measures were not statistically significant in all the primary studies considered.

A systematic review of 24 RCTs assessed the use of CDSS to improve insulin use and glycaemic control in patients with insulin-dependent diabetes mellitus, and critically ill patients with hyperglycaemia[9]. The included RCTs reported that CDSS had a significant positive effect on mean glucose levels (7/10 studies), HbA1c levels (6/11 studies), and number of hypoglycaemic events (3 studies). The review authors concluded that CDSS that match insulin dose to individual patients may be an effective intervention for improving glycaemic control in patients with diabetes mellitus and critically ill patients with hyperglycaemia.

The third systematic review assessed the impact of a CPOE with an integrated CDSS and interruptive prescribing alerts in 23 primary studies[14]. Two primary studies that reported patient outcomes found no significant effects of the CDSS. In 53% of primary studies a significant positive impact on prescriber behaviour was reported. Thirty-four percent of studies found no significant impact of the intervention on prescriber behaviour, and in 6% of studies interruptive alerts from the CDSS had a significant negative impact on prescriber behaviour (increase in errors and override rates).

The final systematic review explored the use of standardised order sets (SOS) as decision support tools for medication prescribing[8]. The nine studies in this review related to patients with respiratory conditions, patients with diabetes, antibiotic prescribing, and end-of-life care. In patients with respiratory conditions, prescribing errors, length of hospital stay and odds of returning to hospital within 30-days, were reduced with use of SOS. Mortality was lower in patients hospitalised with ischaemic stroke or coronary heart failure with the use of SOS. Studies on antibiotic prescribing reported an increase in appropriate antibiotic dose (1 study) and a reduction in prescribing errors. Use of SOS in end-of-life care reduced the mean number of adjustments for symptom management in these patients.

Unscheduled care

A single systematic review of 23 studies discussed the use of CDSS in unscheduled care, specifically hospital emergency departments[6]. Results reported in primary studies in this review were mixed, with 13 studies demonstrating a positive impact of CDSS on aspects of clinical care, two finding no benefits of CDSS, and eight showing small improvements that mainly related to documentation. Based on analysis of only the high quality studies, the review authors concluded that CDSS are likely to have most impact on care processes, rather than patient outcomes.

Referral management

One systematic review of 14 observational studies explored the use of CDSS for ordering diagnostic medical imaging[7]. High quality evidence in this review demonstrated that CDSS were associated with a decrease in patient radiation exposure, an increase in adherence to guidelines, an increase in diagnostic yield, and no significant increase in missed diagnoses. None of the included primary studies reported a decrease in diagnostic yield, an increase in inappropriate imaging, or an increase in adverse events, following implementation of CDSS. Evidence of varying quality indicated there was no increase in safety risk to patients following introduction of CDSS.

Mental health

One low quality systematic review explored the use of CDSS in child and adolescent psychiatry and mental health care[10]. The authors of this review included 'evidence' from journal articles, books and websites, and made no assessment of the quality of any included materials. The results of the review were reported per 'study' (n=10), each of which had described the effect of a specific CDSS. The results for these CDSS were generally positive, with indications of an improvement in guideline adherence, rate of misclassification and diagnostic accuracy for schizophrenia, use of structured diagnostic assessments, documentation, and risk.

Implementation barriers and facilitators

In this section, systematic reviews reporting barriers and/or facilitators for implementation of CDSS in any health or social care setting were selected. Since the evidence on implementation barriers and facilitators did not relate to individual indications or settings, a thematic analysis was conducted. The barriers and facilitators identified from the literature were themed under three headings: usefulness, credibility, and usability. These headings were originally proposed in the systematic review by Kennedy *et al* (2019)[16] and reiterated in other reviews in the thematic analysis.

The evidence base on barriers and facilitators for implementation of CDSS consisted of eleven systematic reviews with narrative syntheses[15-25]. One review described itself as a meta-synthesis of qualitative literature[21]. Summary information for each systematic review is presented in appendix 4.

Usefulness

A useful CDSS had to be visibly beneficial and valued in different settings, for example, general practice, hospital wards, emergency care, and pharmacies[24]. The CDSS also had to be suitable for use in multiple situations by people with varying levels of understanding and

knowledge[16]. The systems had to be seen to be adding value, and the recommendations generated by the CDSS had to be actionable but not time-consuming, invasive or costly. If the recommendations produced by a CDSS were not clearly actionable, the perceived usefulness of the CDSS decreased considerably[24].

The following barriers were identified within the theme of usefulness:

- Efficiency

  Successful implementation of CDSS in practice decreased when there was evidence of poor efficiency, such as extensive scrolling or clicking, and frequent interruptions to workflow, either through manual input processes or alerts (3 reviews)[19, 22, 24]. Mistrust of CDSS due to perceived conflicts with professional autonomy or personal preferences also resulted in reduced CDSS usage (3 reviews)[16, 19, 24]. In some cases CDSS were considered to be primarily learning tools for less experienced clinicians (1 review)[24] or as good educational tools that were too difficult to implement in routine clinical practice (1 review)[17].

- Alerts

  High levels of users overriding alerts in CDSS have been reported in the literature[15]. CDSS that produced interruptive alerts which disrupted workflow, were irrelevant or intrusive, resulted in users ignoring or overriding the alerts (4 reviews)[15, 18, 21, 24]. Alerts could be viewed as patronising by some people using the CDSS (1 review)[18]. Excessive workload and time constraints also led to people disabling or ignoring alerts (1 review)[22]. Careful consideration of the content, timing and usability of alerts would potentially address these issues.

- Design

  Poor system design and lack of consideration of human factors• in the design process led to lower usage of CDSS because the systems were not intuitive (1 review)[21]. The issues relating to system alerts that were described above, could also be considered system design flaws (1 review)[22]. In particular, alerts could become a design fault when the CDSS had high sensitivity (ability to detect potential errors) but low specificity, as this could result in a large volumes of potentially inappropriate alerts (1 review)[22].

- Staff support and training

  When staff were not supported with training, and not given time to learn how to use a new CDSS, this led to increased resistance to using the CDSS (3 reviews)[17, 19, 25].

• Human factors are defined as the inter-relationships between humans, the tools they use, and the environment they live and work in[22].

- System complexity

  The complexity of a CDSS could act as a barrier to use in practice (2 reviews)[17, 21]. For effective implementation, systems needed to be designed with the end user in mind and be easy to use, with clear, easily understood guidance on how to use the system. Greater usage levels and user acceptance of a CDSS required transparency about the evidence underpinning the system, and open, understandable validity of the CDSS.

The following facilitators were identified within the theme of usefulness:

- System standardisation

  Standardisation within and between CDSS, including standardising the terminology used, was beneficial to user acceptance of CDSS, as familiarity facilitated greater system usage (1 review)[22]. As noted earlier, human factors should be taken into account when designing a CDSS. External system developers, with little knowledge of clinical settings or environments, may find it challenging to account for human factors in CDSS design, so standardisation can lead to consistency of design and development processes[22].

- Integration with existing systems

  The integration of CDSS into existing healthcare systems, such as an existing and familiar EHR, led to improved acceptance of the CDSS and improved system usefulness by presenting patient-specific recommendations (1 review)[15].

- Regulatory environment

  Adherence of CDSS content and systems to local regulatory arrangements must be considered. There was evidence in the literature that UK clinicians believed the use of CDSS protected them from legal claims made against them, by providing documentation of the rationale behind decisions they had made or treatments they had recommended (1 review)[16].

Credibility

To be credible, a CDSS had to have clear validity and the rules which underpinned recommendations had to be transparent[17, 24]. Health and social care practitioners needed to have confidence in the validity of the CDSS and in the knowledge-base that supported it[19].

The following barriers were identified within the theme of credibility:

- Professional autonomy / conflict with personal preferences

  Mistrust of CDSS arose from identity conflict based on the perceptions of system users (1 review)[24]. These perceptions were sometimes driven by an individual's perceived need to defend their professional autonomy and clinical practice preferences.

- System validity

  Mistrust of information within the CDSS, and concerns about the reliability of the knowledge-base, were a barrier to system acceptance and credibility (2 reviews)[19, 24]. To mitigate these barriers the CDSS should be kept up-to-date with reliable and relevant evidence-based knowledge.

The following facilitators were identified within the theme of credibility:

- Patient-specific advice

  Alerts which were patient-specific and tailored to clinical requirements were viewed more positively, and were less likely to be disabled or overridden, than irrelevant or general alerts (3 reviews)[19, 22-24].

- User involvement in CDSS design

  System end users and their perspectives needed to be incorporated into both the development and implementation phases of a CDSS (2 reviews)[22, 24]. A particularly important group to involve in CDSS development were junior doctors, since they were most frequently exposed to CDSS in practice[24]. Involving system users, including prescribers and clinicians, in the design and development of a CDSS resulted in a greater likelihood that the system would align with clinical requirements and workflow patterns[24].

- User expectations and acceptance

  Increased acceptance of CDSS in clinical practice required a change in culture (1 review)[24]. One way to achieve this culture change was to highlight evidence on patient benefits derived from adherence to CDSS. Patient benefits and patient safety, especially in relation to pharmacotherapy and medication alerts, were strong drivers of increased uptake of a CDSS (1 review)[24]. Publishing evidence of benefits experienced in practice following CDSS implementation could also increase user expectations[24].

Usability

When implementing CDSS in practice, high value was placed on ease of system use, simplicity of user interfaces, and understandability of recommendations and alerts generated by the system[24, 26].

The following barriers were identified within the theme of usability:

- Workflow

  The importance of considering workflows in the clinical setting, and how CDSS design impacts on this, has been discussed under the usefulness theme. Workflow also needed

to be considered in relation to system usability, in terms of not creating artificial barriers to CDSS implementation (2 reviews)[19, 24].

- Human factors not considered

  If human factors (discussed under the usefulness theme) were not taken into account during the design of a CDSS, this led to ineffective system design and formed a considerable barrier to system usage and acceptance (1 review)[22]. Poor system design in turn, reduced usability of the CDSS due to users ignoring, disabling or overriding alerts (1 review)[21].

- Complexity of guidelines

  Complex guidance on how to use a CDSS, and the subsequent impact on time needed to learn and operate the system, resulted in reduced system usability and decreased staff awareness of the capabilities of the system (1 review)[17].

The following facilitators were identified within the theme of usability:

- User receptiveness

  User receptiveness to CDSS – positive beliefs about the benefits of CDSS – led to increased system usage (4 reviews)[17, 21, 24]. Successful implementation strategies needed to foster these positive beliefs, and reduce any negative assumptions about workflow disruption or poor patient experiences associated with CDSS[19]. Successful strategies involved clinicians in both the design and implementation phases of CDSS development, as noted under the credibility theme[20].

- User expectations

  CDSS usage increased when clinical staff expected the system to result in improved patient safety and greater efficiency in the workplace (1 review)[24]. Positive expectations could be created by dedicating time to user education and training about the CDSS and its potential benefits (1 review)[15]. It was postulated in the literature that on-site awareness raising about the CDSS, and increased visibility of the CDSS to system users, would lead to increased positive expectations among clinical staff and higher levels of system use[24].

- Ease of system use

  As described earlier, the ease of use of a CDSS can be improved by involving end users in the design and implementation of systems (1 review)[24] and by understanding and integrating human factors into system design (1 review)[22].

Limitations of the secondary evidence

There were a number of limitations to the evidence on CDSS that should be considered alongside the findings of the published systematic reviews described above.

The literature searches for this evidence synthesis deliberately sought to identify systematic reviews that addressed CDSS in six priority areas for Scotland or evaluated CDSS across multiple settings. Topic-specific systematic reviews on the effectiveness and safety of CDSS were only found for unscheduled care, medication safety and prescribing, mental health, and referral management. There are a number of potential explanations for these apparent gaps in the evidence. Other priority topic areas may have been addressed in primary studies or within the systematic reviews that assessed CDSS across multiple settings. Publication bias is another potential explanation which was commented on in several systematic reviews. Since many CDSS are developed in-house, it is possible that studies evaluating systems that failed to demonstrate a positive impact, or that had a negative effect, may not have been submitted for publication.

All the systematic reviews and overviews identified in the literature search were narrative syntheses rather than meta-analyses. The explanation for the lack of meta-analyses is the high levels of heterogeneity in definitions of CDSS, populations, comparators (if any), and outcomes. Consequently quantitative results reported in the systematic reviews were derived from individual primary studies and consequently lack the power of a meta-analysis. The lack of meta-analyses means that the impact of CDSS on processes of care and patient outcomes cannot be easily quantified.

CDSS are commonly implemented in clinical settings where a raft of other interventions, including active treatments, are simultaneously being used to improve outcomes. Since CDSS are not interventions applied directly to patients, it is therefore unclear how much any effect on patient outcomes can be directly attributed to the CDSS in these circumstances.

The generalisability of findings from the secondary literature on the impact of CDSS may be limited. Many of the primary studies within the systematic reviews involved in-house or bespoke CDSS developed specifically for a particular hospital or setting, which may not produce the same results in other hospitals or settings. CDSS were often evaluated in academic or teaching hospitals where implementation of new interventions may be more readily accepted by staff. Almost all of the primary studies were conducted in the US, Canada or Europe, which has implications not only for generalisability of results to Scotland of the CDSS, but for the generalisability of the usual care comparator.

Finally, the consideration of only secondary evidence raises the risk that the same primary study could be included within several systematic reviews. Checking the included studies in systematic reviews on the impact of CDSS suggests little, if any, overlap in primary studies.

However, the same primary study may have been included in several reviews within an overview. If this is the case, it is possible that the effects of CDSS could have been over-emphasised. The potential for overlap of included studies within systematic reviews on facilitators and barriers to implementation of CDSS is even greater, due to the lack of clear reporting of studies included in these reviews. This may result in some barriers/facilitators appearing more common than they are in practice.

Primary studies in the UK

Following peer review comments on the potential lack of generalisability of international evidence to the Scottish context, a brief literature search was performed (2 March 2020) using the Medline database and Google Scholar to identify primary studies that reported impact or implementation of CDSS within the NHS (UK). Study inclusion was not limited by publication date, indication, or clinical setting.

Effectiveness and safety

Three primary studies were identified that described the impact of a CDSS in the UK[27-29].

Conway *et al* (2018)[27] integrated an alert-based CDSS into the SCI-Diabetes network in two health boards in Scotland – Tayside and Lothian – as part of two improvement cycles running over an 18-month period. To assess the impact of the CDSS on clinical processes and patient outcomes, a large case-control study was performed. In total, 5,692 patients with diabetes (cases) for whom their healthcare provider received a CDSS alert were matched 2:1 with patients with diabetes (10,667 controls) who resided in regions of Scotland where the CDSS was not available. More 'cases' received appropriate guideline-mandated screening for foot disease, kidney disease, and hypercholesterolaemia, compared with 'controls'. Patients in both the case and control groups showed improvements in HbA1c levels, but these were significantly greater for patients in the case group. There were no significant differences between groups for changes in cholesterol or diastolic blood pressure. Systolic blood pressure improved significantly more in the control group compared with the case group. Urinary albumin/creatinine ratio increased in both groups, but increased significantly more in the control group. The greater improvement in HbA1c levels in the case group compared with controls was in keeping with evidence from the secondary literature.

The second study used a pragmatic cluster RCT design, involving 45 general practices in England, to evaluate the effect of patient assessment using GRAIDS software (Genetic Risk Assessment on the Internet with Decision Support) on the management of familial colorectal or breast cancer risk in primary care compared with current best practice[28]. The GRAIDS software indicated to general practitioners (GP) when patients should be referred to secondary care based on the relevant UK best practice guidance. Twenty-three practices

were randomised to the GRAIDS group, and 22 practices to the comparator group who received an education session and guidelines on familial cancer risk. The study results indicated that using GRAIDS software increased the likelihood of patient referrals consistent with best practice guidelines (OR 5.2, 95% CI 1.7 to 15.8, p=0.006), and provided reassurance to the majority of patients who were unlikely to benefit from a referral.

The third study used a mixed-methods approach to assess how GPs interacted with a computerised decision support system for prescribing, in order to better understand how to improve prescribing decisions in primary care[29]. The decision support system provided information, safety alerts and process warnings to GPs in relation to prescribing. The study included 112 patient consultations with eight GPs from three practices. Quantitative and qualitative analyses were used to explore the interactions between GPs, patients and the decision support software. Of the 117 alerts generated during GP consultations, only three resulted in the GP checking the prescription, and none resulted in the prescription being changed. The study authors concluded that the alerts were being generated too late in the consultation, at a point when the GP had already decided on a course of action and discussed it with the patient.

Implementation barriers and facilitators

Three primary studies – two qualitative and one quantitative - described barriers and facilitators for implementation of CDSS in the NHS[30-32].

One qualitative study assessed a pilot version of the Decision Support Platform in Scotland using 30 semi-structured interviews and observation of eight stakeholder workshops[30]. The majority of the facilitators and barriers identified in this study aligned with those described in the secondary literature: managing user expectations; engaging with staff during system development and implementation; raising awareness of the CDSS; interoperability and integration with existing systems; alert fatigue; increased workloads; and conflict with professional autonomy. New barriers and facilitators discussed by participants in this study included the need for strong leadership and direction for national implementation of CDSS, and avoiding over-reliance on CDSS by clinicians with limited experience in practice.

The second qualitative study facilitated six focus groups (n=29) in Glasgow to evaluate barriers and facilitators to implementation of a differential diagnosis decision support system (DDDSS) for out-of-hours and primary care[31]. Clinicians described currently using passive sources of information on their computer or mobile devices during consultations. Several barriers and facilitators outlined in the secondary literature were identified by focus group participants: conflict with professional autonomy; the need for user education; interoperability with current systems; time constraints; credibility and transparency around the source of evidence; and the need for integration into current workflows. Additional factors reported by study participants included:

- Increased diagnostic uncertainty
- Overriding alerts may leave clinicians open to litigation
- Improved clinician confidence in a diagnosis
- Could prevent new clinicians from developing essential diagnostic decision-making skills if they rely too heavily on the DDDSS
- Reduced eye-contact and communication with patients during consultations
- Reduced clinician workload

The quantitative study used a multiple case study design to explore what nurses and healthcare managers at four sites in NHS England perceived to be the organisational features that facilitated successful implementation of a computerised decision support system[32]. The study involved 124 observations of nurse/patient consultations, 36 patient interviews, 55 nurse interviews and 18 interviews with clinical unit or NHS managers. Many of the facilitators outlined by study participants were similar to those described in the secondary literature: clinical engagement; adequate training and resources; a supportive environment; and staff dedication to improving the quality of patient services. Additionally, the study authors noted the need for the decision support system to 'fit' with the local working environment and processes, and for the system to be adaptable to the needs of the local setting.

Cost effectiveness

Cost effectiveness studies were not required to meet the same inclusion criteria as the evidence on clinical effectiveness, safety and implementation. Due to the low volume of economic evidence, included studies related to any patient population, indication, type of CDSS, and setting.

The economic evidence consisted of two systematic reviews[33, 34], a cost effectiveness analysis[35], a cluster RCT[36], and an observational before-and-after study[37]. In one of the systematic reviews[33] and the cluster RCT[36], economic aspects were secondary considerations.

The systematic review by Jacob *et al* (2018) assessed the economic value of CDSS in cardiovascular disease (CVD) prevention[34]. The review authors described CDSS as "computer-based information systems designed to assist healthcare providers [.....] to implement guidelines and evidence-based practices by providing tailored reminders [.....] and alerts [.....] at the point of care, based on individual patient data [.....]." All included studies were conducted in high-income countries (67% the US) and were performed in clinics (97%) rather than hospitals.

Among the five studies in the systematic review that reported the intervention cost[§] for EHR-embedded CDSS, mean annual costs were $102 (£78) per patient and $6,056 (£4,653) per practice with 1-4 physicians, and $49 (£38) per patient and $35,201 (£27,045) per practice with 5-24 physicians. The cost of collecting and populating a database with patient information was not considered to be part of the CDSS intervention cost. Fifteen studies assessed change in healthcare costs with CDSS implementation. Several of these studies combined CDSS with other interventions, thus any effects on healthcare costs cannot be attributed to CDSS alone. Based on six studies with reasonably complete assessments of costs and no intervention other than CDSS, the median change in healthcare cost per patient per year was -$35 (-£27), inter-quartile range (IQR) -$114 to +$93 (-£88 to +£71).

Three studies in the systematic review reported cost-benefit ratios for EHR-based CDSS (table 1). Each study quantified the economic benefits using different measures, such as averted cost of medication or averted cost of inpatient stays, and therefore the results are not directly comparable. A further three studies presented cost-utility analyses with reasonably complete accounting of costs (table 1). Both studies which found CDSS to be cost-effective (<$50,000 per QALY) included interventions in addition to CDSS, and therefore cost-effectiveness of CDSS alone cannot be assumed.

Table 1: cost-benefit ratios and cost per QALY data for EHR-based CDSS derived from primary studies in the systematic review by Jacob *et al* (2017)[34]

Study	Cost:benefit ratio	Study	Cost per QALY saved
Fretheim (2006)	1:2.03	Cleveringa[+] (2010)	$49,500 (£38,032)
Khan (2010)	1:3.8	Gilmer[+] (2012)	$16,500 (£12,677)
Bu (2007)	1:0.55	O'Reilly (2012)	$143,000 (£109,869)

[+]Study included interventions alongside CDSS and therefore results represent cost-effectiveness of a combined intervention.

The second systematic review reported cost of antibiotics as a secondary outcome in their evaluation of computerised decision support (CDS) for antibiotic prescribing in a hospital inpatient setting[33]. A CDS was defined as a "computer-based system [.....] in which characteristics of individual patients are utilised to generate recommendations [.....] as

[§] The annualised implementation cost was estimated by distributing the one-time development and implementation (capital) cost equally over an assumed 5-year life span of the CDSS, and adding this annual amortised cost, discounted at 3%, to the annual cost of CDSS operation (maintenance and operation).

alerts, reminders and guidelines". Fifteen low quality studies reported impact of CDS on antibiotic costs. Units of cost were left in the currency they were originally reported in and not adjusted to account for inflation. Costs were not reported as a standardised measure, for example per patient. Nine primary studies showed a decrease in cost of antibiotics after implementation of CDS and four reported an increase. One study found that antibiotic costs decreased when CDS recommendations were adopted, but increased when recommendations were overridden. The final study found that antibiotic costs after CDS implementation were superior to baseline costs but inferior to academic detailing. No study reported overall intervention costs for CDS.

The cost-effectiveness analysis, based on a cluster RCT, compared three strategies for reducing antibiotic prescribing: printed decision support, computer decision support, and usual care[35]. The study cohort consisted of US patients, aged 13 to 63, who were diagnosed with acute bronchitis in ambulatory care. The analysis took a societal perspective, assumed the intervention lasted 5 years, had a time horizon of 30 days, and compared interventions in terms of cost per antibiotic prescription safely avoided. In the model, patients underwent clinical assessment, then had a chest x-ray (or not), received antibiotics (or not), and benefited from reduced loss of work days (or not) if prescribed antibiotics. Probabilities for prescribing an antibiotic were 76.7% for usual care, 63.1% for printed decision support, and 65.7% for computer decision support, in each of the 5 years. There were assumed to be no incremental changes in odds of antibiotic prescribing over the 5 years, which may bias the analysis results. A societal willingness-to-pay threshold of $43 (£33) per antibiotic prescription safely avoided was assumed, based on estimates of downstream societal costs of antibiotic resistance.

In the base-case, printed decision support dominated (lower costs and fewer prescriptions) usual care and computer decision support (table 2)[35]. These results were sensitive to variations in the probability of hospitalisation within 30 days and the adjusted odds of antibiotic prescribing. Printed decision support still dominated computer decision support across all tested parameters, except when the adjusted odds of antibiotic use relative to baseline was ≥0.64 in the printed strategy or ≤0.57 in the computer strategy, and when the probability of hospitalisation within 30 days was ≥0.9% in the printed decision support group or ≤0.4% in the computer decision support group. The printed decision support strategy was preferred across all societal willingness-to-pay thresholds from $0 to $100 (£77). The printed decision support strategy remained below the threshold of $43 (£33) per antibiotic safely avoided, except when the probability of hospitalisation within 30 days was reduced in the usual care or computer decision support strategies, or increased in the printed decision support group. It should be noted that the printed decision support strategy only reduced antibiotic prescribing by 11.7%, therefore antibiotics continued to be prescribed to >70% of patients presenting with acute bronchitis despite minimal clinical benefit.

Table 2: base case results in a cost effectiveness analysis of three strategies for reducing inappropriate antibiotic prescribing in patients presenting with acute bronchitis[35]

Strategy	Cost	Incremental cost	Effectiveness*	Incremental effectiveness	ICER
Printed decision support	$2,574 (£2,011)	-	3.78	-	-
Usual care	$2,768 (£2,163)	$194 (£152)	4.60	-0.82	Dominated
Computer decision support	$2,802 (£2,190)	$34 (£27)	3.95	-0.16	Dominated

*Effectiveness was measured in terms of antibiotic prescriptions per patient over 5 years; lower prescriptions imply greater effectiveness.

Another cluster RCT explored clinical and cost effectiveness of CDSS compared with chart-based support in managing hypertension in primary care in rural India[36]. The study calculated cost-effectiveness ratios of $96.01 (£74) per mm reduction in systolic blood pressure for the chart-based support group, and $36.57 (£28) per mm reduction in systolic blood pressure in the CDSS group. The details of this study are not considered further as the findings are unlikely to be generalisable to the Scottish context.

Finally, the observational before-and-after study explored the economic impact of introducing a CDSS for requesting eight common laboratory tests as part of an existing CPOE system in Italy[37]. The CDSS was implemented on a voluntary basis in five wards across three hospitals, and compared with test ordering without CDSS in seven other wards in the same hospitals. Test ordering was compared for the same three-month period in two consecutive years (2014 and 2015) within each ward. The economic impact was measured as cost reduction, from a healthcare system perspective, of not performing unnecessary duplicate laboratory tests, based on the cost of each test as per regional funding arrangements. Indirect costs relating to patients and other costs relating to testing, such as staff time and reagent use, were not considered. Overall, there was a reduction in the number of tests requested by the intervention wards after CDSS implementation (7,646 fewer tests, 16.44% reduction) leading to a 16.53% reduction in the cost of laboratory testing (€34,000/£28,782 saving). In the control wards, test ordering increased by 3.75% and total costs increased by 1.78%. There was a greater volume of test ordering in both years for the intervention wards (46,506 and 38,860) compared with control wards (16,282 and 16,893), and variation in the change in costs between wards post-intervention, which may indicate underlying differences between the wards.

Conclusion

Evidence from systematic reviews indicates that CDSS could have significant positive effects on clinical decision making and delivery of healthcare. A larger proportion of the evidence demonstrated an impact of CDSS on processes of care, rather than effects on patient outcomes. Few negative effects of CDSS were reported for any outcome. Unfortunately, the lack of meta-analysis due to high heterogeneity makes quantification of any effects of CDSS impractical. It is unclear if the results of primary studies in these systematic reviews, many of which were conducted in the US or Europe, are generalisable to NHSScotland.

A range of potential barriers and facilitators for implementation of CDSS in healthcare were identified from systematic reviews. These can be summarised as system design factors and the need to develop user trust in the system, through education, transparency, and involvement in system design/implementation. The presence or absence of these barriers and facilitators in a particular healthcare setting appear likely to have an impact on the effectiveness of CDSS.

Three primary studies reported on the impact of CDSS on diabetes care, cancer referrals, and primary care prescribing, in Scotland or England. The diabetes and cancers referral studies reported positive effects of CDSS on patient care. In another three primary studies discussing facilitators and barriers to CDSS implementation in the UK, the factors described were very similar to those identified in the secondary literature.

The evidence on cost effectiveness of CDSS was limited and specific to an indication or clinical setting. The generalisability of the published evidence to the Scottish context is low, as all identified studies were from the US, Europe or India. The only primary cost effectiveness analysis identified, concluded that computer decision support was dominated by printed decision support for antibiotic prescribing for acute bronchitis. The cost effectiveness results from three primary studies in a systematic review on CVD prevention could not be attributed to CDSS alone due to the way studies were designed, and observational evidence on changes in healthcare costs following CDSS implementation was conflicting.

Equality and diversity

Healthcare Improvement Scotland is committed to equality and diversity in respect of the nine equality groups defined by age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion, sex, and sexual orientation.

The process for producing evidence syntheses has been assessed and no adverse impact across any of these groups is expected. The completed equality and diversity checklist is available on www.healthcareimprovementscotland.org

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Appendix 1: Abbreviations

AMSTAR	assessing the methodological quality of systematic reviews
CDS	computerised decision support
CDSS	clinical decision support systems
CI	confidence interval
CPOE	computerised physician / prescriber order entry
CPR	clinical prediction rules
CRD EED	Centre for Reviews and Dissemination Economic Evaluations Database
DDDSS	differential diagnosis decision support system
CVD	cardiovascular disease
ECG	electrocardiogram
EHR	electronic health record
GRAIDS	Genetic Risk Assessment on the Internet with Decision Support
GP	general practitioner
ICER	incremental cost effectiveness ratio
IQR	inter-quartile range
NICE	National Institute for Health and Care Excellence
PICOS	population, intervention, comparator, outcome, setting
QALY	quality adjusted life-years
RCT	randomised controlled trial
RR	relative risk
SOS	standardised order sets
US	United States
VTE	venous thromboembolism

Appendix 2: Supplementary Literature Search Methods

All literature searches were undertaken by an experienced information professional (Juliet Brown, Health Information Scientist).

Search dates

All systematic searches relating to effectiveness, safety and implementation were conducted between 20 December 2019 and 7 January 2020. These searches were limited to secondary literature, published in English, between January 2015 and January 2020, on the basis that a Scottish Government report summarising evidence on clinical decision support systems was published in 2015.

Grey literature sources

The following grey literature sources were searched:

- Agency for Healthcare Research and Quality (AHRQ) https://www.ahrq.gov/
- Canadian Agency for Drugs and Technologies in Health (CADTH) https://www.cadth.ca/
- Commonwealth Scientific and Industrial Research Organisation (CSIRO) https://www.publish.csiro.au/
- Department of Health (UK) https://www.gov.uk
- eHealth.scot https://www.ehealth.scot/
- Health Economics Research Unit (HERU) https://www.abdn.ac.uk/heru/outputs/publications/reports/
- Healthcare Improvement Scotland http://www.healthcareimprovementscotland.org/
- Institute for Healthcare Improvement (IHI) http://www.ihi.org/resources/Pages/default.aspx
- Kings Fund https://www.kingsfund.org.uk/
- NHS Education for Scotland https://www.nes.scot.nhs.uk/publications-and-resources/publications-search.aspx
- NICE Medtech Innovation Briefings https://www.nice.org.uk/about/what-we-do/our-programmes/nice-advice/medtech-innovation-briefings
- NICE https://www.nice.org.uk/
- National Institute for Health Research (NIHR) https://www.nihr.ac.uk/explore-nihr/support/dissemination-centre.htm

- Publications Office of the European Union https://op.europa.eu/en/web/general-publications/publications
- Scottish Government https://www.gov.scot/publications/
- SHOW https://www.publications.scot.nhs.uk/
- The Health Foundation https://www.health.org.uk/
- US National Academy of Medicine https://nam.edu/publications/
- WHO https://www.who.int/publications/en

Bibliographic databases

The following bibliographic databases were searched to identify relevant systematic reviews and meta-analyses:

- ASSIA / Public Health / Sociological Abstracts (PROQUEST)
- Cinahl (EBSCOhost)
- ClinicalKey (ELSEVIER)
- Cochrane Database of Systematic Reviews (WILEY)
- Centre for Reviews and Dissemination NHS Economic Evaluation Database (EED)
- Centre for Reviews and Dissemination NHS Health Technology Assessment (HTA) database
- Centre for Reviews and Dissemination NHS Database of Abstracts of Reviews of Effects (DARE)
- DynaMed Plus
- Embase (OVID)
- Emerald Insight
- Epistemonikos https://www.epistemonikos.org/
- Health Business Full text (EBSCOhost)
- HMIC (OVID)
- Library, Information Science and Technology Abstracts: LISTA (PROQUEST)
- Medline (OVID)
- PsycINFO (OVID)
- SCIE: Social Care Online
- Web of Science (CLARIVATE)

Database-provided search filters for systematic reviews and meta-analyses were applied in each database. In Medline and Embase the SIGN search filters for systematic reviews and meta-analyses were used.

Database search strategy

The search strategy in the table below was translated for each database searched.

#	Searches
1	knowledge based expert system.mp.
2	*Expert Systems/
3	decision support program$.mp.
4	*Decision Support Systems, Clinical/
5	*Decision Making, Computer-Assisted/
6	knowledge based clinical support.mp.
7	knowledge based decision support.mp.
8	or/1-7
9	limit 8 to yr="2015 -Current"

Additional search techniques

The first five pages of results from Google Scholar were scanned for relevant papers.

The PubMed 'similar articles' and 'cited by' functions were used to identify additional references based on relevant articles found during the bibliographic database and grey literature searching.

Study selection

Studies were selected for inclusion in the evidence synthesis on effectiveness, safety and implementation of CDSS if they met the following criteria based on the PICOS framework:

- Population: health or social care patients or clients; professionals working in health or social care.
- Intervention: computerised expert knowledge-based clinical decision support systems that use algorithms and inference models to generate evidence-based, patient-specific recommendations.
- Intervention: a) addressed one of six key areas encompassed by the Scottish National Decision Support Programme – prescribing practice, polypharmacy or medication safety; pain management; referral management; palliative or end of life care; unscheduled care; mental health

  OR

  b) assessed the use of knowledge-based clinical decision support systems across multiple health or social care settings.

- Comparator: usual care, no clinical decision support system, pre-implementation period, no comparator.
- Outcomes: effectiveness, safety, self-management, person-centred care, implementation barriers or enablers.
- Setting: health or social care.

Three reviewers applied the inclusion criteria to abstracts identified by the literature searches. Disagreements were resolved by consensus.

PRISMA diagram

The PRISMA diagram below shows the process of identification and selection of secondary evidence reported in this synthesis.

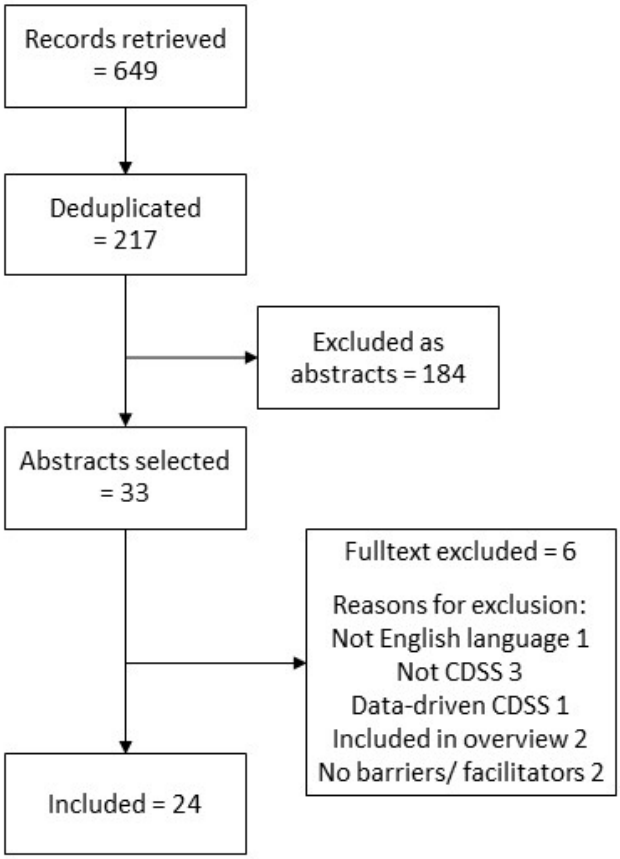

Figure 1: PRISMA diagram showing secondary evidence selection for the current review

Appendix 3: Systematic Reviews on Effectiveness and Safety

Study	Population/ clinical setting	Intervention & comparator	Findings	Comments
Clinical decision support across multiple indications and/or settings				
Eden (2018)[4]	Any secondary care setting.	CDSS (no definition provided). Comparator: traditional paper-based systems.	Intervention effects were categorised using a typology of outcome measures. Effects were then coded as positive or negative for each outcome if more than 50% of primary studies in a systematic review reported positive / negative results for that outcome. Results below are those reported in moderate or high quality systematic reviews. Two moderate and two high quality systematic reviews demonstrated positive effects of CDSS on guideline adherence, indicated care, organisational efficiency, safe prescribing, and patient outcomes. Other positive impacts included improvements in data integrity and clinical judgement in one high quality systematic review. Two potential negative effects of CDSS were identified: changes in practice leading to risky workarounds (one low quality review) and	Overview* of seven systematic reviews published 2015-2017. Updates Keasberry *et al* (2017)[5]. Six out of seven reviews related to CDSS. Quality of reviews was assessed using the AMSTAR checklist (score ≥8 high quality; <4 low quality). For CDSS there were two systematic reviews in each category: low, moderate, and high. Some systematic reviews assessed eHealth as a whole and did not distinguish between components. Bias could have been introduced when the overview authors subjectively extracted the effects of CDSS from these studies.

			persisting use of paper formats (one high quality review).	
Keasberry (2017)[5]	Any secondary care setting.	CDSS (no definition provided). Comparator: traditional paper-based systems.	The systematic reviews in this overview described CDSS with varying degrees of sophistication. <u>From high quality systematic reviews</u>: More than 50% of primary studies demonstrated improvements in care processes and appropriateness of test ordering. In one systematic review there was moderate quality evidence that CDSS were associated with a 42% increase in preventive care services and a 72% increase in ordering or completion of recommended clinical investigations. High quality evidence from one systematic review showed a 57% increase in adherence to treatment guidelines. Evidence on the effects of CDSS on patient outcomes was less consistent. One systematic review reported no effects on mortality, adverse drug reactions, length of hospital stay or clinical confidence in patient care. Another found that morbid events were reduced by 18% and a third review reported a 17% reduction in mortality. <u>From a high quality review of reviews</u>:	Overview* of 19 systematic reviews and two reviews of reviews, all published 2010-2015. Eighteen out of 21 included reviews related to CDSS. Quality of included studies was assessed using the AMSTAR checklist (score ≥8 high quality). Nine out of 21 reviews were rated high quality. The results from primary studies that were included in several systematic reviews may be over-emphasised in the overview.

			In one high quality review of reviews there was evidence of improved delivery of indicated care and guideline adherence using CDSS.	
Varghese (2018)[15]	Inpatient care setting.	CDSS defined as "any electronic system designed to aid directly in clinical decision making, in which characteristics of individual patients are used to generate patient-specific assessments or recommendations that are then presented to clinicians for consideration". Comparator: usual care, with no clinical decision support component.	Rule-based algorithms were the basis of 72% of CDSS described in primary studies. Twenty-five studies reported mortality as an outcome; five found a significant reduction in mortality. Sixteen studies were considered to show a strong positive effect of CDSS as there was a reduction in life-threatening events. Twenty studies showed a moderate positive effect by reducing non-life-threatening events that required medical attention. Eight studies were assessed as showing a slight positive effect in reducing non-life-threatening events that did not necessarily require treatment. Twenty studies showed no or non-significant effects on clinical outcomes. One study reported a negative impact of CDSS where a blood glucose management system led to an increase in hypoglycaemic events.	Systematic review of 70 studies published 2005-2016: 33 before-and-after or prospective cohort studies; 20 RCTs; 18 retrospective studies. The Agency for Healthcare Research and Quality tool was used to assign a low, medium, or high risk of bias rating to each primary study. Four studies had high, 22 medium, and 16 low risk of bias. Clinicians assigned each study a 'medical effect score' that represented the perceived impact on patient outcomes and the relatedness of outcomes to mortality risk.

			From the primary studies, clinicians identified six disease areas that had high clinical impact scores and low risk of bias scores (where CDSS may have maximal effect): blood glucose management, blood transfusion management, prevention of physiologic deterioration / physiologic surveillance, pressure ulcer prevention, acute kidney injury prevention and venous thromboembolism prophylaxis.	
Medication safety				
Jia (2016)[2]	Any healthcare setting.	CDSS defined as a computerised system using case-based reasoning and software algorithms to match individual patient data with a knowledge base to generate patient-specific recommendations. Comparator: not specified.	Nineteen systematic reviews assessed the impact of CDSS on medication process of care outcomes: prescribing errors, dose errors, adherence, and medication or drug-related intermediate outcomes. Within these systematic reviews CDSS significantly affected the process of care in 108 out of 143 primary studies (75%). <u>Of these nineteen systematic reviews</u>: Twelve found strong evidence that CDSS improved process of care outcomes. Seven reviews reported limited evidence that CDSS improved prescribing errors, dose errors, and medication or drug-related intermediate outcomes. Six reviews found insufficient evidence that CDSS improved dose errors, adherence, and medication or drug related intermediate outcomes.	Overview* of 20 systematic reviews published prior to August 2015. Systematic review quality was assessed using the AMSTAR checklist. Four reviews were rated high quality and 16 moderate quality (score range 7.5 to 10.5 out of 11). The strength of evidence provided by the systematic reviews was determined by the design of included studies and the proportion of studies showing an effect. Strong evidence = RCTs and >50% showing effect. Limited evidence

			Thirteen systematic reviews explored the impact of CDSS on patient outcomes. Eighteen out of 90 primary studies (20%) in these reviews reported an impact on patient outcomes. <u>Of these thirteen systematic reviews</u>: Two reported strong evidence that CDSS impacted on patient outcomes. Three found limited evidence of an effect on patient outcomes and eight reviews reported finding insufficient evidence of an effect of CDSS on patient outcomes.	= RCTs and effect in 40-50% or mixed RCTs and non-randomised studies with effect in >50%. Insufficient evidence = results from non-randomised studies or effect in <40%.
NICE (2015)[13]	Primary or secondary care.	CDSS defined as an "active, computerised intervention that occurs at the time and location of prescribing, to support prescribers with decision making". Systems should generate interruptive alerts, match individual	*References to quality of evidence are derived from the GRADE assessment for each outcome. High and moderate quality evidence from two RCTs showed no significant effect of CDSS on patient mortality. Moderate and high quality evidence from two RCTs indicated that CDSS significantly reduced HbA1c levels in patients with type 2 diabetes. Moderate quality evidence from one RCT in patients with type 2 diabetes found significant improvements in systolic blood pressure with use of clinical decision support.	Systematic review of 20 RCTs published 2009-2015. The quality of RCTs was assessed using the NICE checklist. Quality of included RCTs ranged from low to high, with only two studies rated high quality. Quality of evidence for specific outcomes was assessed using the GRADE criteria. GRADE quality ranged from very low, to high, for outcomes reported in the systematic review.

		patient data with a knowledge base, and be integrated within electronic health records. Comparator: usual care or another intervention that does not include a CDSS.	High quality evidence from one RCT reported no significant difference in change in blood pressure with CDSS compared with controls. High and moderate quality evidence from five RCTs, reporting a range of outcomes measures for healthcare utilisation, found no significant differences between the CDSS and usual care groups. High quality evidence from one RCT, moderate quality evidence from four RCTs, low quality evidence from two RCTs, and very low quality evidence from one RCT, demonstrated significant reductions in suboptimal prescribing with CDSS compared with usual care. Moderate quality evidence from four RCTs and low quality evidence from one RCT found no significant difference between groups for this outcome. High and moderate quality evidence from two RCTs indicated that CDSS significantly reduced potential medicines-related problems. High and low quality evidence from two RCTs found no significant difference between groups for this outcome. Based on the evidence outlined above, NICE recommended consideration of CDSS for clinical	No relevant RCTs conducted in the UK were identified.

			decision making and prescribing, but these systems should not replace clinical judgement.	
Marasinghe (2015)[11]	Long-term care settings.	Computerised CDSS, defined as systems that apply algorithms to a knowledge base and individual patient data to generate and present recommendations on the initiation, administration, modification, monitoring or discontinuation of medications. Comparator: not specified.	Five studies reported improved medication safety with the use of computerised CDSS and two found no improvements. The impact on medication safety was greatest in patients with the highest baseline risk of injury ($p<0.03$). One study described a positive effect on number of alerts generated, but a negative effect on physician response to these alerts. Individual primary studies reported: • CDSS influenced prescribing decisions but did not improve prescribing quality. • Higher proportion of appropriate drug orders with CDSS: relative risk (RR) 1.2, 95% confidence interval (CI) 1.0 to 1.4. • CPOE systems with built-in clinical decision support did not reduce adverse or preventable drug event rates. • Adverse drug reactions can be detected with a high degree of accuracy using a clinical event monitor (positive predictive value 81%). • Prescribers receiving alerts from a CPOE system with integrated computerised decision support were slightly more likely to take appropriate action: RR 1.11, 95% CI 1.00 to 1.22.	Systematic review of seven studies (published prior to 2014), five of which were RCTs. Quality of included studies was assessed using the Downs and Black tool. Studies scored 14 to 21 out of 26. Three studies were rated good quality, three were moderate quality and one was poor quality.

			• Physicians responded to 70% of alerts by changing a drug dose or discontinuing a medication. • Computerised CDSS reduced the risk of medication-related injury by 1.7 per 1,000 patients (95% CI 0.2 to 3.2 per 1,000, p=0.02).	
Prescribing and polypharmacy				
Monteiro (2019)[12]	Patients aged 65 or older.	Computerised decision support tools, defined as "systems providing passive and active referential information as well as reminders, alerts and guidelines" and "computer applications designed to aid clinicians in making diagnostic and therapeutic decisions in patient care". 11 studies used standard of care as the comparator.	Computerised decision support tools consistently reduced the number of potentially inappropriate prescriptions started and the mean number of inappropriate prescriptions per elderly patient. These tools also increased the number of discontinued potentially inappropriate medications and improved drug appropriateness. Statistically significant differences were not reported in all primary studies for the latter outcomes. One RCT found no significant difference in the mean number of prescriptions in the intervention group. Another RCT demonstrated that patients in the intervention group were prescribed significantly fewer drugs. There was no effect on the proportion of patients prescribed more than five drugs at once. A cross-over study reported no significant differences in median number of medications prescribed per patient.	Systematic review of 16 studies: 10 RCTs, one cross-over study, and five before-and-after studies, all published prior to February 2018. RCT quality was assessed using the Cochrane risk of bias tool. Studies scored 1 to 5 out of 7. Before-and-after studies were considered to have a high risk of bias due to the presence of confounding factors. Seven studies were conducted in teaching hospitals where staff may be more likely to accept new interventions.

			One RCT reported a significant reduction in adverse drug reactions in the intervention group. One RCT reported a decrease in initiation of potentially inappropriate prescriptions, but no similar impact on stopping prescriptions. One before-and-after study observed that the proportion of patients exposed to potential drug-drug interactions increased after implementing a computerised decision support system, although the mean number of potential drug-drug interactions per patient at discharge was reduced.	
Jia (2019)[9]	Patients with diabetes mellitus type 1 or 2. Critically ill surgical or burn patients with hyperglycaemia.	CDSS that interact with users to generate tailored content aimed at improving insulin therapy. Comparator: no CDSS.	Conclusion from the systematic review: use of CDSS that match insulin dose to individual patients may be an effective intervention for improving glycaemic control. Thirteen RCTs (n=1,331) used computerised algorithms or computer-assisted insulin protocols for insulin dose and therapy adjustment. Four studies reported significant changes in insulin dose in the intervention group compared with the control group. In seven out of 10 trials measuring mean glucose levels, computerised insulin dose adjustment resulted in significantly lower mean glucose levels among patients in the intervention group.	Systematic review of 24 RCTs published prior to October 2018. Six trials were conducted in the UK. RCT quality was assessed using the Cochrane risk of bias tool. The majority of trials were considered to be of moderate quality. None of the trials were blinded.

			Four out of six RCTs reported beneficial effects of CDSS on HbA1c levels. Three trials showed significant reductions in the number of hypoglycaemic events. It is not clear how many studies measured this outcome.	
CADTH (2019)[8]	Adult and paediatric patients in acute care.	Standardised order sets (SOS) defined as clinical decision support tools for prescribing, that use a predefined set of drugs and doses based on guidelines for specific diseases. Comparator: ordering without SOS, including no order sets, usual care and pre-implementation of SOS.	Standardised order sets appear to reduce length of stay in hospital, mortality, and medication errors in acute care. Seven studies were conducted in patients with respiratory conditions, two related to diabetes, and one included patients receiving end of life care. Four studies were in a paediatric population. In adults with respiratory conditions, the number of hospitalisations with no prescribing errors was higher, hospital length of stay was shorter, and the odds of returning to hospital within 30 days were significantly improved, with SOS. Paediatric patients with respiratory conditions had a reduced length of hospital stay with SOS. In paediatric patients <1 year old with respiratory distress, who required enteral nutrition, initiation of therapy within 48 hours was significantly higher (81% vs. 63%, p<0.01) and time to	Systematic review of 14 non-randomised studies published 2014-2019. Nine studies were retrospective. Quality of included studies was assessed using the Downs and Black checklist. Before-and-after studies were at risk from time-related confounding and retrospective studies were at risk of selection bias. Adjustment for confounding factors was reported in three studies. It is unclear if all the studies in this review used an intervention that would be considered a knowledge-based clinical decision support tool. Two studies only used paper-based or pre-printed SOS.

			initiation significantly shorter (1.3 vs. 1.7 days, p<0.0001) when SOS was integrated with EHR. In adult patients with type 2 diabetes, blood glucose levels decreased significantly with SOS compared with no SOS (p=0.02). Errors in antibiotic ordering in adult patients undergoing laryngectomy were significantly lower with SOS (38.2% vs. 80.6%, p<0.0001). A higher percentage of patients receiving vancomycin as an antibiotic for any indication received an appropriate dose following implementation of CPOE with an integrated SOS (p<0.0001). Adult patients received significantly fewer mean adjustments to end of life symptom management with SOS (1.7 vs. 3.3, p=0.00014). In patients hospitalised for ischaemic stroke, SOS significantly reduced 30-day, 60-day and 90-day mortality, and rates of pneumonia. Patients with coronary heart failure had significantly lower mortality (1.8% vs. 3.2%, p=0.04) and significantly shorter length of hospital stay (p=0.004) with SOS.	Most studies were conducted at single centres and the order sets were developed for specific indications. Study results may therefore not generalise to other settings or indications.
Page (2017)[14]	Acute care inpatients.	CPOE systems with a clinical decision support element	There was limited evidence what type of interruptive prescribing alert was most effective.	Systematic review of 23 studies (19 in adults) published 2000-2016. Three were RCTs, three

		that generates immediate interruptive alerts on potential medication errors or safety risks. Comparators: pre-intervention, control groups (handwritten orders or systems without alerts).	Two studies assessed the effect of interruptive alerts on patient outcomes and found no significant effects. Fifty-three percent (53%) of primary studies reported a significant positive impact of CPOE with decision support on prescriber behavior. Thirty-four percent (34%) of studies reported no significant impact and 6% a significant negative impact (increased errors and overrides) on prescriber behavior. The greatest volume of published evidence related to three alert types: drug-condition, drug-drug, and corollary order alerts. Five out of six studies assessing drug-condition alerts showed significant positive effects on prescriber behaviour. Two out of six studies reported positive benefits of drug-drug interaction alerts on prescriber behaviour. One study out of six on corollary alerts reported positive effects on prescriber behaviour. The remaining studies on each alert type reported no significant impact on prescriber behaviour. Three studies reported significant positive effects of dose range checking alerts on prescriber behaviour. Three studies found that formulary alerts increased prescriber adherence to preferred medicines. Two studies assessed drug-	interrupted time series, 15 before-and-after studies, and two were 'other' designs. No assessment of risk of bias for included studies was reported.

			allergy alerts: one found a significant reduction in errors, while the other reported an increase in alert overrides. One study on duplicate order alerts reported no impact, while another reported a significant increase in duplicate orders.	
Unscheduled care				
Bennett (2017)[6]	Emergency department patients.	Computerised CDSS (no definition provided). Comparator: usual care.	Overall, 13 studies demonstrated a positive impact of computerised CDSS on aspects of clinical care. Two studies found no benefit of introducing computerised clinical decision support and eight showed small improvements, mainly relating to documentation. Analysis of high quality studies suggested computerised CDSS had the most impact on care processes. <u>RCTs (n=3)</u> One RCT demonstrated a significant increase in the appropriateness of diagnostic workup compared with usual practice (19.3%, p=0.023). The other two RCTs did not demonstrate any benefits. <u>Before-and-after studies (n=13)</u> The majority of these studies (n=10) reported positive results supporting the use of computerised decision support in the emergency department; none included a control group. One study reported an increase in appropriate	Systematic review of 23 studies published 1994-2015. One study was conducted in the UK. Three RCTs, 13 before-and-after studies, five interrupted time series, one prospective observational study and one comparative cohort study were included. Quality of included studies was assessed using pragmatic tools to determine risk of bias for each study design. Seventeen studies had a high risk of bias. Only one RCT addressed performance and detection bias. One interrupted time series addressed the underlying trend over time. Less than one-third of before-and-after studies adjusted for confounding factors.

			documentation of pain in children but no associated change in use of analgesia. <u>Interrupted time series (n=5)</u> These studies demonstrated significant improvements in appropriate antibiotic prescribing and in the documentation and discharge advice for back pain (but no change in x-rays ordered or medication use). <u>Prospective observational study (n=1)</u> This study assessed triage decisions using the Canadian Acuity and Triage Scale integrated into a computerised CDSS. Study results indicated the intervention led to better triage decisions compared with usual practice. However, this study introduced confounding by having the same patients assessed using both interventions at different times. <u>Comparative cohort study (n=1)</u> This retrospective cohort study explored the impact of an electronic guideline on management of neutropenic sepsis. Although use of the guideline was low (37.8%), when used there was a significant increase in ECG recording and blood culture collection, as well as reductions in time from triage to doctor assessment and first antibiotic.	Most studies were conducted in academic emergency departments (n=21) and may not generalise to non-academic emergency settings.

Referral management				
CADTH (2019)[7]	Patients presenting with symptoms that may require diagnostic / medical imaging.	CDSS for ordering diagnostic / medical imaging based on guidelines. Comparator: usual care, control (no support system), pre-intervention.	High quality evidence reported a decrease in radiation exposure, an increase in guideline adherence, an increase in diagnostic yield, and no increase in missed diagnoses, with CDSS. A systematic review, an RCT and three before-and-after studies reported diagnostic yield as an outcome. The highest quality evidence for this outcome came from the RCT, which indicated a statistically significant increase in foot and total diagnostic yield. No study reported a decrease in diagnostic yield, an increase in inappropriate imaging, or an increase in adverse events following implementation of CDSS. Varying quality evidence indicated no additional safety risk to patients. There were no statistically significant changes in missed diagnoses, perforated appendicitis, negative appendectomy, length of stay in the emergency department, mortality, complications of thromboembolic or bleeding events, or other adverse events following implementation of a CDSS. Two RCTs and three before-and-after studies reported both a significant increase in diagnostic	Systematic review of nine studies published 2013-2018. Studies included one systematic review, one RCT, three prospective and four retrospective before-and-after studies. Two studies were in a paediatric population. The systematic review included was assessed using the AMSTAR checklist and rated high quality. The quality of other included studies was assessed using the Downs and Black checklist. The RCT was limited by unclear success of randomisation and high attrition bias. The before-and-after studies did not adjust for time bias and in some cases used multifaceted interventions. None of the studies assessed a commercially available system, which may limit generalisability of study results.

			yield and no increase in adverse events with implementation of CDSS for medical imaging. One before-and-after study reported no significant improvement in appropriate imaging.	
Mental health				
Koposov (2017)[10]	Child and adolescent psychiatry and mental health services.	Computerised CDSS. Usually based on ICD and/or DSM criteria to allow the system to help with diagnosis based on patient data, a knowledge base, treatment guidelines, and knowledge-sharing between local practitioners. Comparator: not specified.	Eight computerised CDSS were identified that focused on child and adolescent mental disorders. Most systems were developed in the US and therefore used DSM criteria. Six studies described systems that were integrated with EHR. Positive results were reported in a single study for almost all of the identified computerised CDSS: • CDSS-D improved adherence to guidelines. • SADDESQ had a low rate of misclassification (18% to 34%) and diagnostic accuracy of 66% to 82% for schizophrenia. • An RCT assessing the CHICA system found that use of structured diagnostic assessments increased from 60% to 81% in the intervention group, and decreased from 50% to 38% in the control group. • The GRiST system and its' self-assessment version myGRaCE helped service users assess and self-manage their mental health. • The CompTMAP system was reported to be easy to use, demonstrated potential for	Systematic review of 10 'studies' published prior to December 2016. This review included evidence from journal articles, books and websites. Results from each included 'study' were presented separately. No assessment of study quality was reported. Studies in which participants were a mix of adults and children were eligible for inclusion.

			simplifying and improving record keeping, and highlighted current research to physicians. • Routine use of the NetDSS system led to identification of unanticipated clinical issues. • More frequent use of the EDSS system led to a significant reduction in risks. However, only 36% of clinicians felt this system provided the information they needed and 64% reported rarely using the information. • No evaluation was identified for the InterQual system.	

*Primary studies within the systematic reviews included in overviews may be incorporated into other systematic reviews in this table.

Appendix 4: Systematic Reviews Describing Implementation Facilitators and Barriers

Study	Population / clinical setting	Aim / intervention	Findings	Comments
Hussain (2019)[18]	Pharmacists and prescribers. Inpatient and outpatient settings.	Medication safety alerts.	Interrupting prescribers with pop-up alerts has become the least acceptable, but most common, design of medication safety alert. Barriers to implementing prescriber interruptive alert models include etiquette – alerts need to be polite, without being patronising. Alerts should be relevant to the situation. Division of expert labour: more detailed and frequent alerts presented to pharmacists, allows prescribers to focus on patients and rely on the pharmacist for interpretation of alerts. Recommendations: • Avoid prescriber interruptive models. • Use event analysis to measure acceptance rates rather than in-dialog analysis. Some barriers were noted to be due to methodological inconsistencies in individual primary studies.	Systematic review of 39 studies published 2007-2017. No assessment of study quality was reported. Primary studies used event analysis and in-dialog action analysis. Included studies concentrated on reporting acceptance rates or patient outcomes, not both. The majority of studies (61%) were conducted in the US. One study was conducted in the UK.
Kennedy (2019)[16]	Healthcare providers.	Clinical prediction rules (CPR).	The systematic review generated three themes:	Systematic review of 52 qualitative studies: 28 surveys,

		Aim: to inform the design and implementation of future CPR systems by describing provider opinions and preferences with respect to the use of CPR.	Utility: decreases if the predicted outcome doesn't have a significant impact on the patient or if the outcome is numerical and not clearly actionable. CPR systems should include directive outcomes and causal pathways. Credibility: the roll-out phase of a system should include steps to educate professional organisations and to comply with their requirements for validation and user training. Usability: the system needs to be a smooth fit within the clinician-patient interaction and not require a lot of data entry.	14 interviews, nine focus groups and four formal usability testing. Studies were all published prior to August 2017. No assessment of study quality was reported. Low number of usability testing in studies so there is little evidence of how CPR systems are used in practice.
Van Dort (2019)[24]	Hospital prescribers.	Aim: to identify factors that prevent and promote uptake of medication-related CDSS based on the perceptions of prescribers.	User's perceptions were divided into the domains of organisation, human, and technology. A high number of perceptions were categorised into the human domain, in particular into the subset of system use. Facilitators of use: • Expectation that CDSS improves patient safety and efficiency. • Ease of use (clear screen layout and appropriate placement of information), usefulness and efficiency. • User involvement with implementation and support.	Systematic review of 13 qualitative studies published prior to March 2018. Study quality was assessed using the Joanna Briggs Institute Checklist for Qualitative Research. The HOT-fit framework was used to collate available evidence on prescriber perceptions of medication-related CDSS via in-depth qualitative interviews. The HOT-fit framework is a

			Barriers to use: • Mistrust of information • Conflict between CDSS recommendations and prescribers' professional autonomy or personal prescribing preferences. • Lack of perceived usefulness. • Senior practitioners viewing CDSS as a tool for junior prescribers rather than themselves. • Systems perceived to reduce efficiency via excessive clicking, scrolling and interruptions to workflow. Recommendations: 1. Seek user perspectives on usability and integration prior to implementation. 2. Provide local evidence to users that CDSS improves patient safety. 3. Keep CDSS information up-to-date to increase the likelihood of trust from users. 4. For alerts, ensure they are minimal and relevant to users. 5. For order sets, minimise the options available and avoid excessive clicking and scrolling.	combination of an Information Software success model and the IT Organisational Fit Model – it integrates the factors and concept of fit between human, organisation and technology.
Borum (2018)[25]	Nurse practitioners in inpatient facilities.	Aim: to assess barriers to nurse practitioner use of CDSS.	Primary studies identified the following barriers: • System issues, including alerts (n=5) • Hardware issues (n=1) • Software flaws / data issues (n=9)	Systematic review of nine studies: four qualitative, four quantitative, one qualitative meta-synthesis.

			• Training / knowledge / usability (n=5) • Time to use (n=2) • Patient safety (n=1) Facilitators identified in primary studies can be summarised as: • Right information • Right people • Right format • Right channel • Right time	Two studies were considered weak due to the sampling technique used.
Khairat (2018)[19]	CDSS system users.	Aim: to develop a new framework for CDSS design in order to achieve greater user acceptance.	Users with better computer skills had higher acceptance rates. Barriers: • Related to interruption of workflow. • Questionable validity of CDSS systems. • Excessive disturbance caused by systems. • Lack of efficiency. Facilitators: More likely to use the system if it matches the user's own decision making process. Proposed two models of system design: 1. User acceptance and system adaptation design model: includes physicians in the CDSS design process.	Systematic review of 14 studies: 11 qualitative, three quantitative. It is unclear when the literature search was conducted. No assessment of study quality was reported.

			2. Input-process-output-engage model: displays the CDSS process to the physician, allowing them to maintain professional autonomy.	
Tolley (2018)[22]	Prescribers in primary, secondary or ambulatory care.	Aim: to review current uses of medication-related clinical decision support that were linked with CPOE systems, and make recommendations for improving clinical decision support systems.	Facilitators identified included: • Standardisation of systems. • Patient-specific parameters used in decision making algorithms. • Consideration of human factors design principles. Recommendations: • Incorporate patient-specific information into decision-making algorithms. • Employ human factors design principles during development and implementation. • Drug-drug interaction alerts should have a severity level attached. • Maximise system interoperability. • Consider the usual clinical practice and workflow when configuring systems. • Ensure records that integrate with medication related system are kept up-to-date.	Systematic review of 184 articles published 2007-2014. No detail is given about study designs. No assessment of study quality was reported.
Van de Velde (2018)[23]	Healthcare professionals or professionals and patients.	Computer-generated decision support presented either on screen (62% of studies) or	Facilitators: • Provide advice automatically on screen. • Make the recommendations patient-specific.	Systematic review of 68 studies published prior to December 2016. RCTs, non-randomised controlled trails, and controlled before-and-after studies were included.

	88% of studies were in outpatient settings, 9% in inpatients, and 3% both.	on paper (30% of studies). Aim: examine the factors which make CDSS more effective.	When CDSS interventions are combined with professional-orientated, patient-orientated, or staff-orientated strategies, adherence improves slightly.	Reported risk difference analysis. Assessed studies for risk of bias using the EPOC criteria. Sixty-five percent of included studies were considered to be at high risk of bias, 27% unclear risk of bias, and 8% low risk of bias. Certainty of evidence was rated as low-to-moderate using the GRADE system.
Varghese (2018)[15]	Inpatient care setting.	Classify the clinical impact of CDSS on inpatient care.	The higher the specificity of CDSS system alerts or recommendations, the less likely there is to be alert fatigue. Integration with all relevant hospital stakeholders: some sites may already have high adherence to officially recommended guidelines, in this case implementation should be carefully considered in collaboration with clinical stakeholders. System testing and validation should involve all potential system users.	Systematic review of 70 studies published 2005-2016: 33 before-and-after or prospective cohort studies; 20 RCTs; 18 retrospective studies. The Agency for Healthcare Research and Quality tool was used to assign a low, medium, or high risk of bias rating to each primary study. Four studies had high, 22 medium, and 16 low risk of bias. Clinicians assigned each study a 'medical effect score' that

			Risk analysis should be considered (what could potentially go wrong with system) and risk mitigating measures created.	represented the perceived impact on patient outcomes and the relatedness of outcomes to mortality risk.
Kilsdonk (2017)[20]	Physicians in mixed settings.	Aim: to evaluate implementation success factors for guideline-based CDSS.	List of barrier and facilitators very similar to Van Dort (2019)[24]. Implementation strategies need to create positive beliefs about the usefulness and benefits of CDSS, while reducing negative assumptions about disrupting work and damaging patient experience. Successful implementation requires physician involvement from the beginning.	Systematic review of 35 articles published prior to December 2015: 20 qualitative, 12 mixed-methods, three quantitative. Success factors were mapped against the HOT-fit framework to better understand the barrier and facilitators to successful implementation. (HOT-fit = human, organisational and technology-fit framework) 32 unique were CDSS identified: 16 standalone CDSS (desktop or web-based), nine embedded in EHR, seven standalone systems with some links into an EHR.
Blum (2015)[17]	Healthcare professionals.	Aim: to assess the effects of CDSS on patient reported outcomes.	Primary studies that found an impact on patient reported outcomes all implemented a CDSS at the point-of-care. Barriers to implementation identified included: • Complex guidelines on how to use the system.	Systematic review of 15 studies published 1996-2014. Ten RCTs, three controlled trials, two cohort studies. No assessment of study quality was reported.

			• Low user awareness of content. • Limited staff support for the system. • Time constraints. • Physicians not trusting instructions and overriding them (especially if alerts occurred to often – alert fatigue). • Difficult to implement in clinical practice.	
Miller (2015)[21]	Clinicians in inpatient or outpatient settings.	Aim: to identify possible reasons and causes for difficulties in integrating CDSS into clinical practice.	Five themes emerged from the primary literature: • Clinician-patient-system integration. • User interface usability. • Need for better algorithms. • System immaturity leading to issues with integration, system crashes, etc. • Patient safety alerts. Lack of consideration of interactions between human decision makers and the CDSS was identified as a barrier to implementation. CDSS implementation appears to be undermined by poor information and poor design affecting the usability of alerts and reminders.	Meta synthesis of nine qualitative studies published 2000-2013 (after 47 studies were excluded for not meeting quality criteria). Study quality was assessed using an adaptation of the JBI's Qualitative Assessment and Review Instrument. Most included studies related to CDSS involving alerts and reminders associated with medication prescription and administration.