

Effects of Computerized Clinical Decision Support Systems on Practitioner Performance and Patient Outcomes

A Systematic Review

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COMPUTERIZED CLINICAL DECISION support systems (CDSSs) are information systems designed to improve clinical decision making. Characteristics of individual patients are matched to a computerized knowledge base, and software algorithms generate patient-specific recommendations. Practitioners, health care staff, or patients can manually enter patient characteristics into the computer system; alternatively, electronic medical records can be queried for retrieval of patient characteristics. Computer-generated recommendations are delivered to the clinician through the electronic medical record, by pager, or through printouts placed in a patient's paper chart. Such systems have been developed for a myriad of clinical issues, including diagnosis of chest pain, treatment of infertility, and timely administration of immunizations. These systems provide several modes of decision support, including alerts of critical val-

Context Developers of health care software have attributed improvements in patient care to these applications. As with any health care intervention, such claims require confirmation in clinical trials.

Objectives To review controlled trials assessing the effects of computerized clinical decision support systems (CDSSs) and to identify study characteristics predicting benefit.

Data Sources We updated our earlier reviews by searching the MEDLINE, EMBASE, Cochrane Library, Inspec, and ISI databases and consulting reference lists through September 2004. Authors of 64 primary studies confirmed data or provided additional information.

Study Selection We included randomized and nonrandomized controlled trials that evaluated the effect of a CDSS compared with care provided without a CDSS on practitioner performance or patient outcomes.

Data Extraction Teams of 2 reviewers independently abstracted data on methods, setting, CDSS and patient characteristics, and outcomes.

Data Synthesis One hundred studies met our inclusion criteria. The number and methodologic quality of studies improved over time. The CDSS improved practitioner performance in 62 (64%) of the 97 studies assessing this outcome, including 4 (40%) of 10 diagnostic systems, 16 (76%) of 21 reminder systems, 23 (62%) of 37 disease management systems, and 19 (66%) of 29 drug-dosing or prescribing systems. Fifty-two trials assessed 1 or more patient outcomes, of which 7 trials (13%) reported improvements. Improved practitioner performance was associated with CDSSs that automatically prompted users compared with requiring users to activate the system (success in 73% of trials vs 47%; $P=.02$) and studies in which the authors also developed the CDSS software compared with studies in which the authors were not the developers (74% success vs 28%; respectively, $P=.001$).

Conclusions Many CDSSs improve practitioner performance. To date, the effects on patient outcomes remain understudied and, when studied, inconsistent.

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See also pp 1197 and 1261.

ues, reminders of overdue preventive health tasks, advice for drug prescribing, critiques of existing health care orders, and suggestions for various active care issues.

As with any health care innovation, CDSSs should be rigorously evaluated before widespread dissemination into clinical practice. Various stages in this assessment process have been previously described. Iterative qualitative and quantitative assessment begin early in the software development cycle.^{1,2} When preliminary testing suggests that a CDSS improves clinical care or patient outcomes, confirmatory controlled trials are warranted. We previously reviewed controlled trials of computer-aided quality assurance³ and CDSSs published up to 1992⁴ and 1998.⁵ This field is rapidly evolving because of technological advances, increasing access to computer systems in clinical practice, and growing concern about the process and quality of medical care. We therefore updated previous reviews to provide a cumulative summary of controlled trials evaluating the effectiveness of CDSSs on practitioner performance and patient outcomes.

METHODS

Research Questions

The primary questions of this review were (1) Do CDSSs improve practitioner performance or patient outcomes? and (2) Which CDSS and study-level factors are associated with effective CDSSs? A priori, we hypothesized that studies reporting better outcomes would assess CDSSs that automatically prompted users (vs requiring the user to actively initiate the system), were built into an electronic medical record or computer order entry system (vs a stand-alone system), provided reminders (vs information on disease management, drug dosing, or diagnosis), were tested using less rigorous study methods, were studied by their software developers (vs by evaluators not involved in the CDSS design), described pilot testing, and described user training.

Studies Eligible for Review

We included English-language randomized and nonrandomized trials with a contemporaneous control group that compared patient care with a CDSS to routine care without a CDSS and evaluated clinical performance (ie, a measure of process of care) or a patient outcome. We stipulated that the CDSS had to provide patient-specific advice that was reviewed by a health care practitioner before any clinical action. Studies were excluded if the system (1) was used solely by medical students, (2) only provided summaries of patient information, (3) provided feedback on groups of patients without individual assessment, (4) only provided computer-aided instruction, or (5) was used for image analysis. Studies assessing CDSS diagnostic performance against a defined gold standard were not included in this review unless clinical use of the diagnostic CDSS was also compared with routine care. Based on these criteria, we reevaluated all studies from our previous reviews for inclusion.

Finding Relevant Studies

We have previously described our methods for finding relevant studies until March 1998.⁵ For this update, we examined citations from MEDLINE, EMBASE, Evidence-Based Reviews databases (Cochrane Database of Systematic Reviews, ACP Journal Club, Database of Abstracts of Reviews of Effects, and Cochrane Central Register of Controlled Trials), and Inspec bibliographic databases from 1998 through September 2004. All citations were downloaded into Reference Manager, version 10.0 (Thomson ISI ResearchSoft, Philadelphia, Pa). An experienced librarian developed the search strategies using sensitive terms for identifying clinical studies of CDSSs. We pilot-tested search strategies and modified them to ensure that they identified known eligible articles. The final strategies used the terms *computer-assisted decision making*, *computer-assisted diagnosis*, *computer-assisted therapy*, *decision support systems*, *reminder systems*, *hospital information systems*, *random-*

ized controlled trial, and *cohort studies* (complete strategies available from the authors). Pairs of reviewers independently evaluated the eligibility of all studies identified in our search. Disagreements were resolved by a third reviewer or by consensus. Full-text articles were retrieved if any reviewer considered a citation potentially relevant. Supplementary methods of finding studies included a review of article reference lists, articles citing included studies as listed in the Science Citation Index, PubMed related articles feature, informatics conference proceedings, information provided by primary study authors, and other recent reviews.⁶⁻¹¹ Where data from a trial were distributed in more than 1 publication, we cited the principal publication.

Data Abstraction

Pairs of reviewers independently abstracted the following data from all studies meeting eligibility criteria: study setting, study methods, CDSS characteristics, patient characteristics, and outcomes. Disagreements were resolved by a third reviewer or by consensus. We attempted to contact primary authors of all included studies to confirm data and provide missing data.

All studies were scored for methodological quality on a 10-point scale consisting of 5 potential sources of bias, which we have described elsewhere.⁵ In brief, we considered the method of allocation to study groups (random, 2, vs quasi-random, 1, vs selected concurrent controls, 0), the unit of the allocation (a cluster such as a practice, 2, vs physician, 1, vs patient, 0), the presence of baseline differences between the groups that were potentially linked to study outcomes (of particular importance for observational studies; no baseline differences present or appropriate statistical adjustments made for differences, 2, vs baseline differences present and no statistical adjustments made, 1, vs baseline characteristics not reported, 0), the objectivity of the outcome (objective outcomes or subjective outcomes with blinded assessment, 2, vs subjective outcomes with no blinding but

clearly defined assessment criteria, 1, vs subjective outcomes with no blinding and poorly defined, 0), and the completeness of follow-up for the appropriate unit of analysis (>90%, 2, vs 80 to 90%, 1, vs <80% or not described, 0). The unit of allocation was included because of the possibility of group contamination in trials in which interventions were applied to clinicians even though individual patients were allocated to the intervention and control groups.¹² Contamination bias would lead to underestimating the effect of a CDSS.

The studies substantially differed in the type and number of outcomes assessed. In addition, the majority of studies did not define a single outcome for statistical testing. We aimed to efficiently summarize the benefits of CDSSs and to identify CDSS and study characteristics that predicted success. For a given study we abstracted all reported practitioner performance and patient health outcomes. Situations where the CDSS worsened outcomes were rare. Thus, for each study we defined the effects of CDSSs in terms of success, defined as an improvement in at least 50% of outcomes measured, each at a 2-sided significance level less than .05.

Statistical Analysis

Reviewer agreement on study eligibility was quantified using the Cohen κ .¹³ Study and CDSS characteristics predicting success were analyzed and interpreted with the study as the unit of analysis. Data were summarized using descriptive summary measures, including proportions for categorical variables and mean (standard deviation) for continuous variables. Univariable and multivariable logistic regression models, adjusted for study methodological quality, were used to investigate associations between the outcomes of interest and study-specific covariates defined in our a priori hypotheses. All analyses were carried out using the SAS statistical package, version 8.2 (SAS Institute Inc, Cary, NC). We interpreted $P \leq .05$ as indicating statistical significance; all P values are 2-sided. When reporting results from individual studies,

we cited the measures of association and P values reported in the studies.

RESULTS

Finding and Selecting Studies

From 3997 screened citations, we retrieved 226 full-text articles, and 100 trials met our criteria for review. The chance-corrected agreement between 2 independent reviewers for article inclusion was good ($\kappa=0.81$; 95% confidence interval [CI], 0.73-0.88).

Description of Studies

The 100 trials examined more than 3826 practitioners or practices (median, 42; range, 2-300 [when reported]) caring for more than 92895 patients (median, 488; range, 19-12989 [when reported]) from 1973 to 2004.¹⁴⁻¹¹³ The number of eligible trials increased with time: 1 in 1970-1974, 4 in 1975-1979, 10 in 1980-1984, 13 in 1985-1989, 20 in 1990-1994, 26 in 1995-1999, and 26 in 2000–September 2004. Of these 100 trials, most were conducted in the United States (69%), followed by the United Kingdom (14%), Canada (5%), Australia (4%), Italy (2%), and Austria, France, Germany, Israel, Norway, and Switzerland (1% each). Sixty-nine percent of trials described funding from the public sector and 16% from the private sector. Developers of CDSS software were also study authors in 72% of trials. Ninety-seven trials described the effect of CDSS on at least 1 measure of health care practitioner performance. Fifty-two trials assessed at least 1 patient outcome. We successfully contacted authors of 91 trials, and authors of 64 trials provided additional information or confirmed the accuracy of abstracted data.*

Methodological Quality Assessment

Trial methodological rigor increased with time—36% of trials before the year 2000 were cluster randomized, compared with 67% after this time ($P=.01$).

*References 15-18, 20, 21, 24-33, 35-40, 42, 43, 46, 47, 49, 51, 52, 56, 60-64, 67, 68, 71, 73-75, 80, 81, 83-98, 101, 106, 113-115.

Of all trials, 88% were randomized. Of the randomized trials, 49% were cluster randomized and 40% used a cluster as the unit of analysis or adjusted for clustering in the analysis. Twenty-four randomized trials and 1 cohort study reported a power calculation for a pre-specified difference between groups on a specific outcome. Fifteen of these trials (60%) calculated sample size based on a practitioner performance outcome, 9 (36%) based on a patient outcome, and 1 (4%) based on the cost of prescribed medications. Only 2 studies examined patient outcomes without measuring practitioner performance. Of the 88 randomized trials, 52% described an appropriate method of generating random numbers and 28% reported allocation concealment. On the 10-point methods scale, the mean score was 7 (SD, 1.7) and the range was 2 to 10.

Description of Users and CDSSs

The 100 trials had the following characteristics: 92% of trials enrolled physicians as primary users, 48% enrolled training health care practitioners (interns and residents) as users, 34% described pilot testing with users prior to implementation, 42% described user instructional training at the time of implementation, 76% took place in academic centers, and 33% were inpatient-based. In 47% of studies, the CDSS was part of an electronic medical record or computer order entry system. Most of these were early generation systems lacking the full functionality of current systems. In 15% of studies, the CDSS had a graphical user interface. Feedback from the CDSS occurred at the time of patient care in 88% of studies; in 60% the user was automatically prompted to use the system (vs the user actively initiating the system), and in 91% the CDSS suggested new orders (vs critiquing existing orders). Expert physician opinion or clinical practice guidelines usually formed the knowledge base for the CDSS.

The process of data entry into the CDSS was clear in 80% of trials, some of which used more than 1 method. Existing personnel most often entered data (attending or training physician, 38%;

other health care staff [eg, nurses, clerks], 29%), although many trials used staff paid by research funds (21%) or automated data capture from an electronic medical record (30%). The method of delivering computer recommendations to the clinician was clear in 81% of trials. Most CDSSs directly provided the recommendation on a computer screen viewed by the practitioner (41% of all trials) or generated printed reports that were placed in medical charts by health care staff (29%) or by staff paid by research funds (16%). Only 13% of trials evaluated the impact of the CDSS on clinician workflow, with more than half of these CDSSs requiring more time and effort from the user compared with paper-based methods.

Systems for Diagnosis

There were 10 trials evaluating diagnostic systems (TABLE 1). All studies measured practitioner performance, and the CDSS was beneficial in 4 studies (40%). Two of the 4 successful CDSSs were diagnostic systems for cardiac ischemia in the emergency department, and these decreased the rate of unnecessary hospital or coronary care admissions by 15% ($P<.05$).^{18,20} The third increased mood disorder screening in a posttraumatic stress disorder clinic by 25% ($P=.008$).¹⁵ The fourth improved the time to diagnosis of acute bowel obstruction (1 hour when computer was used vs 16 hours when diagnosis was made with contrast radiography; $P<.001$).²³ Of the 5 trials assessing patient outcomes, none reported an improvement.

Reminder Systems for Prevention

There were 21 trials evaluating reminder systems for prevention (TABLE 2). All trials measured practitioner performance, and the CDSS was beneficial in 16 studies (76%). Performance outcomes were usually rates of screening, counseling, vaccination, testing, medication use, or the identification of at-risk behaviors. Successful use of CDSSs was typically demonstrated in ambulatory care, although 1 system was successful in hospitalized patients.⁴⁴ The single trial measuring pa-

tient outcomes failed to demonstrate an improvement in the primary analysis.³⁴ Post hoc subgroup analyses, however, demonstrated a significant reduction in winter hospitalization and emergency department visits in patients eligible for pneumococcal or influenza vaccination. One trial examined the effect of adding a cervical cancer screening reminder to an existing mammography reminder system.³⁰ This trial suggested no interaction between the 2 reminders on screening efficacy.

Systems for Disease Management

There were 40 studies of CDSSs for active health conditions. These CDSSs improved practitioner performance in 23 (62%) of 37 studies evaluating this outcome. Of the 27 trials measuring patient outcomes, 5 (18%) demonstrated improvements.

For diabetes care, practitioner performance was usually judged by rates of retinal, foot, urine protein, blood pressure, and cholesterol examinations, with 5 (71%) of 7 trials reporting improvements (TABLE 3). Similarly, in studies of cardiovascular prevention, performance was judged by blood pressure and cholesterol assessment, identification of smoking, and use of cardioprotective medications, with 5 (38%) of 13 trials reporting improvements (TABLE 4). One CDSS provided electrocardiogram recommendations to improve thrombolytic prescribing in emergency departments.⁶¹ Other CDSSs varied in purpose, providing recommendations for urinary incontinence, human immunodeficiency virus infection management, functional assessment, and acute respiratory distress syndrome, with 6 of 9 reporting improvements (TABLE 5). Clinical decision support system corollary orders were used to monitor the effects of other prescribed treatments, such as the need for renal biochemistry measurements in patients receiving amphotericin B,⁷⁹ with all 4 trials reporting improvements (TABLE 6). Trials testing CDSS performance to reduce unnecessary health care utilization measured the fre-

quency of redundant testing and unnecessary hospital admissions and hospital length of stay, with 3 of 4 trials reporting improvements (Table 6).

Five CDSSs (18%) examining patient outcomes described improvements. One CDSS improved blood pressure control (70% of patients had controlled blood pressure with CDSS use vs 52% with routine care; $P<.05$).⁵⁴ A second CDSS reduced urinary incontinence in nursing home residents over a 10-week period (23% incontinent with CDSS vs 69% with routine care; $P<.01$).⁶⁶ A third CDSS improved scores of barotrauma ($P<.001$) and organ dysfunction ($P=.04$) in mechanically ventilated patients with acute respiratory distress syndrome.⁷⁰ One participating center in this trial provided data demonstrating lower tidal volumes ($P\leq.03$) and a reduction in exposure to high plateau pressures in the group receiving CDSS-guided mechanical ventilation ($P<.001$).¹¹⁴ A fourth CDSS reduced patient-reported asthma exacerbations (8% vs 17%; odds ratio, [OR], 0.43; 95% CI, 0.21-0.85), emergency nebulizer use (1% vs 5%; OR, 0.13; 95% CI, 0.01-0.91), and the need for additional consultations for asthma management (22% vs 34%; OR, 0.59; 95% CI, 0.37-0.95) over 6 months.⁷³ A fifth CDSS reduced hospital length of stay ($P=.02$) for patients with a variety of general medical diagnoses.⁸³

In post hoc secondary or subgroup analyses, some trials described statistically significant improvements in thrombolytic prescribing with the CDSS,⁶¹ as well as patient outcomes of disease-specific emergency department visits,⁶⁵ hospital length of stay,^{45,54,116,117} body weight,^{54,116,117} diastolic blood pressure,^{59,115,118} serum lipids,^{51,58} and a reduced estimated risk of future cardiovascular events.⁵⁸

Systems for Drug Dosing and Drug Prescribing

There were 29 trials of drug dosing and prescribing (TABLE 7 and TABLE 8). Single-drug dosing improved practitioner performance in 15 (62%) of 24 studies, and 2 of the 18 systems assessing patient outcomes reported an im-

provement (Table 7 and Table 8). Another 5 systems used computer order entry for multidrug prescribing (Table 8). Four of these systems improved practitioner performance, but none improved patient outcomes.

The 24 single-drug dosing systems ranged from a simple calculator for parenteral nutrition to more complex algorithms that considered the pharmacokinetics of warfarin, aminoglycosides, or theophylline. Most studies evalu-

ated the serum drug level in medications with a high risk of toxicity. In a study of heparin dosing for patients receiving thrombolysis for myocardial infarction, the proportion of individuals with an adverse thrombotic or cardiac

Table 1. Trials of Computer-Assisted Diagnosis*

Source	Methods Score	No. of Sites	Indication	Performance Outcomes	Patient Outcomes	Improvement in Practitioner Performance†	Improvement in Patient Outcomes†
Diagnostic systems for mental health							
Lewis et al, ¹⁴ 1996	5	1	Common mental disorders for outpatients	Rate of patient referral to mental health, psychotropic medications, psychological consultations	Symptom score after 6 wk	No	No
Cannon et al, ¹⁵ 2000	7	1	Mental health diagnosis for outpatients	Screening for mood disorder, complete documentation for major depressive disorder	...	Yes	...
Schriger et al, ¹⁶ 2001	6	1	Psychiatric interview and diagnosis in emergency department	Psychiatric diagnosis and referrals, documentation of complete psychiatric history	...	No	...
Rollman et al, 2002 ¹⁷	9	17	Major depression diagnosis for outpatients	Use of antidepressants, discussion about depression with patients	Depression score after 6 mo	No	No
Diagnostic systems for acute cardiac ischemia							
Pozen et al, ¹⁸ 1984	3	1	Acute cardiac ischemia in emergency department	Inappropriate coronary care unit admission for patients without ischemic heart disease	...	Yes	...
Wyatt, ¹⁹ 1989	6	1	Chest pain in emergency department	Time to transfer to coronary care unit, time to see physician, total time in emergency department	...	No	...
Selker et al, ²⁰ 1998	4	10	Electrocardiogram interpretation for cardiac ischemia in emergency department	Inappropriate hospital or coronary care unit admission for patients without acute ischemic heart disease	Mortality in first 30 d, in-hospital complications, need for rehospitalization	Yes	No
Diagnostic systems for other conditions							
Wexler et al, ²¹ 1975	2	1	Admitted pediatric inpatients without clear diagnosis	No. of consultations requested, time to diagnosis, orders for unnecessary laboratory tests	...	No	...
Wellwood et al, ²² 1992	6	1	Acute abdominal pain in emergency department	Appropriate diagnosis for appendicitis, unnecessary hospital admissions	Unnecessary surgery with negative findings	No	No
Bogusevicius et al, ²³ 2002	7	1	Acute small bowel obstruction in surgical inpatients	Time to diagnosis, correct diagnosis	Bowel necrosis, morbidity, mortality, hospital length of stay	Yes	No

*Ellipses indicate outcome was not assessed. Methods score based on 10-point scale (see the "Methods" section).

†Improvement was defined as a statistically significant positive effect on at least 50% of outcomes measured. Most studies had inadequate statistical power to detect a clinically important improvement in patient outcomes.

Table 2. Trials of Computer-Assisted Reminders for Cancer Screening, Vaccination, and Other Types of Preventive Care

Source	Methods Score	No. of Sites	Indication	Improvement in Practitioner Performance*
Reminders primarily for cancer screening				
Turner et al, ²⁴ 1989	8	1	Outpatient screening (stool occult blood, digital rectal examination, Papanicolaou test, breast examination, mammography)	No
McPhee et al, ²⁵ 1989	9	1	Outpatient screening (stool occult blood, digital rectal examination, sigmoidoscopy, pelvic examination, Papanicolaou test, breast examination, mammography)	Yes
McPhee et al, ²⁶ 1991	10	Multiple	Outpatient screening (digital rectal examination, stool occult blood, sigmoidoscopy, pelvic examination, Papanicolaou test, breast examination, mammography) and preventive counseling (smoking assessment and counseling, dietary assessment and counseling)	Yes
Burack et al, ²⁷ 1994	7.5	5	Mammography for outpatients	Yes
Burack et al, ²⁸ 1996	7.5	2	Mammography for outpatients	Yes
Burack and Gimotty, ²⁹ 1997	7.5	4	Mammography for outpatients	Yes
Burack et al, ³⁰ 2003	7.5	3	Papanicolaou test for outpatients; in addition to physician prompt, a patient reminder (personal letter) was generated by the system and was part of the intervention	Yes
Reminders primarily for vaccination				
Chambers et al, ³¹ 1991	9	1	Influenza vaccination for outpatients	Yes
Flanagan et al, ³² 1999	7.5	1	Tetanus, hepatitis, pneumococcal, measles, and influenza vaccination for outpatients	No
Tang et al, ³³ 1999	5	1	Influenza vaccination for outpatients	Yes
Reminders for preventive care†				
McDonald et al, ³⁴ 1984	8	1	Cancer screening (stool occult blood, mammogram), counseling (weight reduction), immunization (influenza, pneumococcal) in addition to >1000 physician behavior rules for outpatients	Yes
Tierney et al, ³⁵ 1986	5	1	Cancer screening (stool occult blood, Papanicolaou test, mammogram), pneumococcal vaccination, tuberculosis skin test, use of antidepressants, metronidazole for trichomonas, cardiovascular medications (β -blockers, long-acting nitrates, aspirin), prophylactic antacids, and calcium supplements for outpatients	Yes
Ornstein et al, ³⁶ 1991	9	1	Cancer screening (stool occult blood, mammography, Papanicolaou test), cholesterol measurement, and tetanus vaccination for outpatients	No
Rosser et al, ³⁷ 1991	7.5	1	Cancer screening (Papanicolaou test), blood pressure measurement, assessment of smoking status, and vaccination (influenza, tetanus toxoid) in outpatients	Yes
Tape and Campbell, ³⁸ 1993	7.5	1	Cancer screening (stool occult blood, Papanicolaou test, mammogram, proctosigmoidoscopy), thyroid function screening, vaccination (tetanus, pneumococcal, influenza) for outpatients	Yes
Turner et al, ³⁹ 1994	6	44	Cancer screening (stool occult blood, Papanicolaou test, breast examination, mammogram) and influenza vaccination for outpatients	No
Frame et al, ⁴⁰ 1994	6	5	Cancer screening (stool occult blood, Papanicolaou test, breast examination, mammogram), cardiovascular disease preventive screening (blood pressure, cholesterol, body weight), identification of at-risk behavior (smoking), patient education (self-examination, recognition of postmenopausal bleeding), and vaccination (tetanus) in outpatients	Yes
Overhage et al, ⁴¹ 1996	10	1	Cancer screening (Papanicolaou test, mammogram), cardiovascular disease preventive screening and medications (cholesterol, β -blockers, aspirin), diabetes care reminders (retinal examination, urinalysis), vaccination (pneumococcal, rubella, hepatitis B), and an additional 11 reminders for hospital inpatients	No
Bonevski et al, ⁴² 1999	7	Multiple	Cancer screening (Papanicolaou test), cardiovascular disease preventive screening (blood pressure, cholesterol), and identification of 3 risk behaviors (smoking, excessive alcohol use, benzodiazepine use) in outpatients	Yes
Demakis et al, ⁴³ 2000	10	12	Screening (urinalysis, retinal examination, foot examination), monitoring (glycated hemoglobin), and counseling (dietary advice) to prevent diabetic complications in outpatients; reminders for other conditions including vaccination, smoking cessation, appropriate β -blocker and nonsteroidal anti-inflammatory use; cholesterol screening	Yes
Dexter et al, ⁴⁴ 2001	10	1	Vaccination (pneumococcal, influenza), prophylactic heparin and aspirin use for hospital inpatients	Yes

*Improvement was defined as a statistically significant positive effect on at least 50% of outcomes measured. Practitioner performance outcomes were the rate of screening, medication use, and/or identification of at-risk behaviors. Improvement in patient outcomes was not assessed except in McDonald et al,³⁴ in which there was no improvement in body weight, blood pressure, hospitalizations, or emergency department visits.

†These systems were designed for more than 1 type of condition, including cancer screening, vaccination, and cardiovascular disease prevention.

event was significantly lowered with the CDSS (0/25 with the CDSS vs 6/26 in usual care; $P=.02$).⁹⁷ One warfarin-dosing CDSS reduced hospital length of stay from 20 to 13 days ($P=.01$).⁸⁷ Two systems reduced hospital length of stay in patients receiving theophylline (from 8.7 to 6.3 days; $P=.03$)⁹⁸ and aminoglycosides (20.3 to 16.0 days; $P=.03$).¹⁰⁴ although the majority of patient outcomes measured were not improved in these trials.

Study Factors Associated With CDSS Success

Given sparse data for patient outcomes, we only assessed study-level predictors of improved practitioner performance.

Studies in which users were automatically prompted to use the system described better performance compared with studies in which users had to actively initiate the system (success in 44/60 studies [73%] vs 17/36 studies [47%]; $P=.02$; unadjusted OR, 2.8; 95% CI, 1.2-6.6; OR adjusted for methodological quality, 3.0; 95% CI, 1.2-7.1). Similarly, studies in which the authors also created the CDSS reported better performance compared with those in which the trialists were independent of the CDSS development process (success in 51/69 studies [74%] vs 5/18 studies [28%]; $P=.001$; unadjusted OR, 6.7; 95% CI, 1.7-25.3; OR adjusted for methodological quality, 6.6; 95% CI, 1.7-26.7).

No other predefined study-level covariate was associated with CDSS success. In a post hoc analysis of the 85 studies that measured practitioner performance and enrolled physicians, we did not find an association ($P=.40$) between performance and physician experience (trainee vs attending physician).

COMMENT

We identified 100 randomized and non-randomized trials testing a wide variety of CDSSs, with the number of trials and their methodological quality increasing over time. Of the 97 controlled trials assessing practitioner performance, the majority (64%) improved diagnosis, preventive care, disease

Table 3. Trials of Computer-Assisted Diabetes Management*

Source	Methods Score	No. of Sites	Indication	Patient Outcomes	Improvement in Practitioner Performance†‡	Improvement in Patient Outcomes†
Thomas et al, ⁴⁵ 1983	4	1	Computer-generated reminders for outpatients	Change in blood pressure, obesity, glucose, hospitalization, emergency department visits	Yes	No
Mazzuca et al, ⁴⁶ 1990	8	1	Counseling (exercise and dietary advice), glucose control monitoring, medication use, education for outpatients	...	No	...
Nilasena and Lincoln, ⁴⁷ 1995	8	2	Screening (foot examination, retinal examination, renal tests), cardiovascular disease prevention, neurological assessment, and glycemic control in outpatients	...	No	...
Lobach and Hammond, ⁴⁸ 1997	9	1	Screening (foot examination, complete physical, retinal examination, cholesterol, urine protein), vaccination (influenza and pneumococcal), as well as glycated hemoglobin monitoring for outpatients	...	Yes	...
Montori et al, ⁴⁹ 2002	5	2	Screening (microalbuminuria, retinal examination, cholesterol, foot examination) and counseling (exercise and dietary advice, smoking cessation) to prevent complications in outpatients; system also identified drug contraindications	Glycated hemoglobin, total cholesterol, blood pressure, calculated 10-y Framingham risk score	Yes	No
Filippi et al, ⁵⁰ 2003	9	Multiple	Aspirin use in outpatients	...	Yes	...
Meigs et al, ⁵¹ 2003	7	1	Screening (retinal examination, foot examination, glycated hemoglobin, blood pressure, cholesterol), use of cholesterol-reducing and blood pressure medications in outpatients	Change in glycated hemoglobin, low-density lipoprotein cholesterol, blood pressure	Yes	No

*Ellipses indicate outcome was not assessed.

†Improvement was defined as a statistically significant positive effect on at least 50% of outcomes measured. Most studies had inadequate statistical power to detect a clinically important improvement in patient outcomes.

‡Practitioner performance outcomes were the rate of screening (such as retinal examination or urine protein measurement), medication use, and/or identification of at-risk behaviors.

Table 4. Trials of Computer-Assisted Cardiovascular Disease Management and Prevention*

Source	Methods Score	No. of Sites	Indication	Patient Outcomes	Improvement in Practitioner Performance†‡	Improvement in Patient Outcomes†
Coe et al, ⁵² 1977	6	2	Blood pressure management in outpatients	Diastolic blood pressure, drug adverse effects	...	No
Barnett et al, ⁵⁴ 1983	4	1	Follow-up for patients with elevated blood pressure	Diastolic blood pressure <100 mm Hg or receiving treatment	Yes	Yes
Rogers et al, ⁵³ 1984	6	1	Management of hypertension, obesity, and renal disease in outpatients	Systolic and diastolic blood pressure, hospitalization, weight (improved), hospital length of stay (improved)	Yes	No
Brownbridge et al, ⁵⁵ 1986	4	3	Hypertension management in outpatients; prompts for hypertension care (such as urine protein measurement, pulse assessment and retinal examination)	...	Yes	...
McAlister et al, ⁵⁶ 1986	7	50	Recommendations for antihypertensive use	Diastolic blood pressure <90 mm Hg	No	No
Rossi and Every, ⁵⁷ 1997	8	1	Alerts to substitute calcium channel blocker antihypertensives to those recommended in practice guidelines in outpatient hypertensives	...	Yes	...
Lowensteyn et al, ⁵⁸ 1998	7	Multiple	Calculating coronary risk factor profile for outpatients	Blood pressure, body mass index, smoking cessation, cholesterol (total, LDL, total/ HDL ratio) (improved) Predicted 8-y coronary risk factor score (improved)	Yes	No
Hetlevik et al, ⁵⁹ 1999	9	29	Diagnosis, treatment, and follow-up recommendations for hypertension, diabetes mellitus, and hypercholesterolemia in outpatients; identification of smokers	Glycated hemoglobin, smoking status, body mass index, cholesterol, risk score for future myocardial infarction, diastolic blood pressure (improved)	No	No
Montgomery et al, ⁶⁰ 2000	8	27	Calculation of risk of new cardiovascular event in outpatients	Predicted 5-y cardiovascular risk score	No	No
Selker et al, ⁶¹ 2002	6	28	Thrombolytic prescribing in emergency department, with recommendations printed on electrocardiograms	Mortality, stroke, bleeding	No	No
Ansari et al, ⁶² 2003	9	1	β-Blocker use in outpatients with congestive heart failure	Emergency department visit or hospitalization, mortality	No	No
Tierney et al, ⁶³ 2003	8	1	Appropriate medications for patients with ischemic heart disease and congestive heart failure; exercise promotion, weight loss, and smoking cessation; treatment of hypertension and hypercholesterolemia	Quality of life (SF-36), emergency department visits for heart disease, hospitalizations, chronic heart disease questionnaire	No	No
Weir et al, ⁶⁴ 2003	9	16	Antiplatelets and anticoagulant prescribing in patients with an acute ischemic stroke or transient ischemic attack; included both inpatients and outpatients	Predicted relative risk reduction of future ischemic vascular events, hemorrhagic vascular events	No	No
Murray et al, ⁶⁵ 2004	9	1	Hypertension management and drug prescriptions for outpatients (2 × 2 factorial trial; randomization for physician to receive CDSS, and randomization for pharmacist to receive CDSS)	Health-related quality of life, emergency department visits and hospitalizations, systolic and diastolic blood pressure	No	No

Abbreviations: CDSS, clinical decision support system; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SF-36, Short Form 36.

*Ellipses indicate outcome was not assessed.

†Improvement was defined as a statistically significant positive effect on at least 50% of outcomes measured. Most studies had inadequate statistical power to detect a clinically important improvement in patient outcomes.

‡Practitioner performance outcomes were adherence to recommended guidelines that usually included assessment of cardiac risk factors (blood pressure, cholesterol, smoking) and the use of cardioprotective medications. The exception was Selker et al⁶¹ in which practitioner performance outcomes were proportion receiving thrombolytics, use of thrombolytics within 1 hour of initial electrocardiogram, and achievement of cardiac reperfusion.

management, drug dosing, or drug prescribing. However, the effects of these systems on patient health remain understudied—and inconsistent

when studied. Fifty-two trials assessed patient outcomes, often in a limited capacity without adequate statistical power to detect clinically im-

portant differences. Only 7 trials reported improved patient outcomes with the CDSS, and no study reported benefits for major outcomes such as mor-

Table 5. Trials of Computer-Assisted Management for Other Active Health Conditions*

Source	Methods Score	No. of Sites	Indication	Performance Outcomes	Patient Outcomes	Improvement in Practitioner Performance†	Improvement in Patient Outcomes†
Petrucchi et al, ⁶⁶ 1991	7	2	Recommendations for nurse management of urinary incontinence in nursing homes	Nurse knowledge of incontinence	Rate of urinary incontinence	Yes	Yes
Rubenstein et al, ⁶⁷ 1995	8	1	Detection and management of functional status impairments in outpatients; patient self-reported information was collected for computer-assisted system	Physician recognition of functional status problems, recommended interventions undertaken to improve patient functioning	Functional status (physical, psychological, and social) at 6 mo as measured by questionnaire	Yes	No
Safran et al, ⁶⁸ 1995	6	1	Screening, treatment, and management recommendations for outpatients with human immunodeficiency virus infection	Vaccination, ophthalmologic referral, CD4 cell count and blood cell count, <i>Pneumocystis jiroveci</i> prophylaxis	Need for physician visits; emergency and hospital admission; mortality	Yes	No
Dexter et al, ⁶⁹ 1998	10	1	Reminders to discuss and complete advanced directives in outpatients	Rates of discussions and documentation	...	Yes	...
East et al, ⁷⁰ 1999	8	10	Mechanical ventilation management (respiratory evaluation, oxygenation, ventilation, weaning, and extubation) in critically ill patients with acute respiratory distress syndrome	...	Survival to hospital discharge, intensive care unit length of stay, barotrauma score (improved), multiorgan dysfunction score (improved)	...	Yes
Kuperman et al, ⁷¹ 1999	6	1	Automated physician alerts via pager for critical laboratory results for hospital inpatients	Time to ordering of treatment for critical laboratory value, time to resolution of alerting condition	Adverse events (death, cardiac arrest, transfer to intensive care unit, stroke, renal impairment) within 48 h of alerting event	Yes	No
Christakis et al, ⁷² 2001	8	1	Recommendations for antibiotic use in outpatient children with otitis media	Unnecessary antibiotic prescriptions, prescriptions of excessive duration	...	Yes	...
McCowan et al, ⁷³ 2001	6	17	Recommended guidelines for treatment of asthma in outpatients	Review of self-management plan, inhaler technique, and treatment adherence with patient; issuance of peak flow meter	Symptoms, need for oral steroid, need for hospital services, patient-initiated consultation to manage asthma (improved), exacerbation of asthma (self-report; improved), emergency nebulizer use (improved)	No	Yes
Eccles et al, ⁷⁴ 2002	9	62	Recommendations for angina and asthma management in outpatients	Adherence to guidelines including medication prescribing, screening, and assessment of at-risk behaviors	Self-reported quality of life (generic and disease-specific measures), symptoms	No	No
Lesourd et al, ⁷⁵ 2002	7	3	Hormonal ovarian stimulation for infertile women	No. of missed menstrual cycles	Pregnancy	No	No

*Ellipses indicate outcome was not assessed.

†Improvement was defined as a statistically significant positive effect on at least 50% of outcomes measured. Most studies had inadequate statistical power to detect a clinically important improvement in patient outcomes.

tality. Surrogate patient outcomes such as blood pressure and glycated hemoglobin were not meaningfully improved in most studies.

Determinants of CDSS Success

Recent literature has called for a better understanding of factors that predict CDSS success.¹¹⁹ Barriers to implemen-

tation include failure of practitioners to use the CDSS, poor usability or integration into practitioner workflow, or practitioner nonacceptance of computer

Table 6. Trials of Computer Use to Monitor the Effects of Other Prescribed Treatments (Corollary Orders) or to Reduce Unnecessary Health Care Utilization*

Source	Methods Score	No. of Sites	Indication	Practitioner Outcomes	Patient Outcomes	Improvement in Practitioner Performance†	Improvement in Patient Outcomes†
Systems to monitor the effects of corollary orders							
McDonald, ⁷⁶ 1976	5	1	Laboratory tests to monitor potential medication adverse effects (such as measurement of serum creatinine, potassium or hemoglobin) in a diabetes clinic	Adherence to recommended care	...	Yes	...
Young, ⁷⁷ 1981	4	1	Recommended investigations for 79 medical problems in hospital inpatients	Adherence to recommended ordering	...	Yes	...
Fihn et al, ⁷⁸ 1994	8	6	Frequency of anticoagulant monitoring in outpatients	Ability to increase intervals between visits, proximity to target international normalized ratio value	Hemorrhagic and thromboembolic complications	Yes	No
Overhage et al, ⁷⁹ 1997	10	1	Recommended tests or treatments to monitor or ameliorate the effects of other tests or treatments for hospital inpatients	Compliance with orders	Hospital length of stay, maximum creatinine level during hospitalization	Yes	No
Systems to reduce unnecessary health care utilization							
Tierney et al, ⁸⁰ 1988	5	1	Prompts to dissuade ordering of routine unnecessary diagnostic tests, such as electrolyte levels, blood counts, chest radiographs, and electrocardiograms in outpatients	Frequency of unnecessary testing	...	Yes	...
Tierney et al, ⁸¹ 1993	9	1	Alerts for drug allergies and drug interactions, choices for cost-effective testing as part of inpatient computerized order entry for medications, tests, and nursing orders	Cost per patient admission	Hospital length of stay, need for hospital readmission	Yes	No
Hales et al, ⁸² 1995	6	1	Computer system for hospital admission screening	Rate of unnecessary admissions	...	No	...
Shea et al, ⁸³ 1995	7	1	Messages for hospital inpatients on diagnosis, expected length of stay	...	Hospital length of stay	...	Yes
Bates et al, ⁸⁴ 1999	8	1	Reminders for redundant clinical laboratory tests in hospital inpatients	Rate of redundant test ordering	...	Yes	...

*Ellipses indicate outcome was not assessed.

†Improvement was defined as a statistically significant positive effect on at least 50% of outcomes measured. Most studies had inadequate statistical power to detect a clinically important improvement in patient outcomes.

Table 7. Trials of Computer-Assisted Anticoagulant Dosing*

Source	Methods Score	No. of Sites	Indication	Practitioner Performance Outcomes	Patient Outcomes	Improvement in Practitioner Performance†	Improvement in Patient Outcomes†
Warfarin							
Abbrecht et al, ⁸⁵ 1982	6	1	Warfarin initiation in postoperative cardiac surgery inpatients	Proportion of days in therapeutic range, average number of days to achieve therapeutic INR	...	Yes	...
Carter et al, ⁸⁶ 1987	6	1	Warfarin initiation for hospital inpatients	Time to achieve therapeutic stable INR	Time to hospital discharge after first dose	No	No
White et al, ⁸⁷ 1987	8	2	Warfarin initiation for hospital inpatients	Time to achieve therapeutic INR, time to reach stable warfarin dose, time above therapeutic INR	Bleeding complications, hospital length of stay (improved)	Yes	Yes
White and Mungall, ⁸⁸ 1991	8	1	Warfarin maintenance for outpatients	Proportion of time with therapeutic INR, need for follow-up appointments for anticoagulation adjustment	...	No	...
Poller et al, ⁸⁹ 1993	8	1	Warfarin maintenance for outpatients	Proportion achieving target INR, average follow-up time for appointments needed for anticoagulation	Bleeding complications, mortality	No	No
Fitzmaurice et al, ⁹⁰ 1996	6	2	Warfarin maintenance for outpatients	Proportion of time with therapeutic INR, number of follow-up appointments needed to adjust anticoagulation	Mortality, bleeding, and thrombotic complications	Yes	No
Vadher et al, ⁹¹ 1997	6	1	Warfarin initiation and maintenance for inpatients	Time to achieve therapeutic INR, time with therapeutic INR, number of supratherapeutic and subtherapeutic INR levels	Bleeding and thrombotic complications	No	No
Vadher et al, ⁹² 1997	6	1	Warfarin maintenance for outpatients; system used by nurse practitioner compared with training physicians in routine care	Proportion of time with therapeutic INR, number of days between INR testing, number of test measurements	Thrombotic episodes, bleeding complications	Yes	No
Ageno and Turpie, ⁹³ 1998	7	1	Warfarin maintenance for outpatients with mechanical heart valves	Proportion of time with therapeutic INR, proportion of INRs within therapeutic range, number of required dose adjustments; number of INR measurements	...	No	...
Poller et al, ⁹⁴ 1998	8	5	Warfarin initiation and maintenance for outpatients	Time to achieve therapeutic INR, proportion of time with therapeutic INR	...	Yes	...
Fitzmaurice et al, ⁹⁵ 2000	8	12	Warfarin maintenance for outpatients; nurse-led clinic with point-of-care testing	Proportion of time with therapeutic INR, proportion of patients with therapeutic INR	Mortality, adverse events (bleeding or thrombosis)	Yes	No
Manotti et al, ⁹⁶ 2001	5	5	Warfarin maintenance for outpatients	Proportion of time with therapeutic INR over 1 y, proportion of patients achieving therapeutic stable INR at 1 mo, number of physician follow-up appointments for anticoagulation control	...	Yes	...
Heparin							
Mungall et al, ⁹⁷ 1994	8	2	Heparin dosing used with acute myocardial infarction treated with thrombolytic	Therapeutic anticoagulation after 24 h	Composite of cardiovascular events (ie, recurrent chest pain, need for additional thrombolytics, stroke, cardiac arrest) (improved)	Yes	Yes

Abbreviation: INR, international normalized ratio.

*Ellipses indicate outcome was not assessed.

†Improvement was defined as a statistically significant positive effect on at least 50% of outcomes measured. Most studies had inadequate statistical power to detect a clinically important improvement in patient outcomes.

Table 8. Trials of Computer-Assisted Drug Dosing and Prescribing*

Source	Methods Score	No. of Sites	Indication	Practitioner Performance Outcomes	Patient Outcomes	Improvement in Practitioner Performance†	Improvement in Patient Outcomes†
Drug-dosing systems							
Theophylline/aminophylline Hurley et al, ⁹⁸ 1986	6	1	Theophylline dosing for inpatients	Proportion of patients within therapeutic range	Theophylline toxicity, peak expiratory flow rate, asthma symptom questionnaire, mortality, duration of hospitalization (shorter with CDSS)	Yes	No
Gonzalez et al, ⁹⁹ 1989	7	1	Aminophylline dosing in emergency department	Proportion of patients within therapeutic range	Aminophylline toxicity, emergency department discharge, peak expiratory flow rate	No	No
Verner et al, ¹⁰⁰ 1992	6	1	Theophylline dosing in emergency department	Proportion of patients within therapeutic range	Clinical score of respiratory status, peak expiratory flow rate	Yes	No
Casner et al, ¹⁰¹ 1993	6	1	Theophylline dosing for inpatients	Proportion of time within therapeutic range	Theophylline toxicity, number of hospital days	No	No
Aminoglycosides							
Begg et al, ¹⁰² 1989	6	1	Aminoglycoside dosing for inpatients	Proportion of patients within therapeutic range	Mortality, decrease in creatinine clearance	Yes	No
Hickling et al, ¹⁰³ 1989	5	1	Aminoglycoside dosing in intensive care unit	Proportion of patients within therapeutic range	Estimated creatinine clearance	Yes	No
Burton et al, ¹⁰⁴ 1991	7	1	Aminoglycoside dosing for inpatients	Peak concentration of aminoglycoside within therapeutic range	Mortality due to infection, response to therapy, increase in serum creatinine level, hospital length of stay (shorter with CDSS)	Yes	No
Other medications							
Peck et al, ¹⁰⁵ 1973	7	1	Digoxin dosing for outpatients with congestive heart failure	Achievement of actual digoxin concentration relative to target concentration	Digoxin toxicity, change in heart failure medications	No	No
Rodman et al, ¹⁰⁶ 1984	8	1	Lidocaine dosing for hospital inpatients	Proportion needing additional lidocaine dose, achievement of therapeutic dose within 30 min	Lidocaine toxicity	Yes	No
Ryff-de Leche et al, ¹⁰⁷ 1992	4	1	Insulin dosing for outpatients	Blood glucose within therapeutic range, glucose level <4.0 mmol/L (72 mg/dL)	Hypoglycemic events, glycosylated hemoglobin level	Yes	No
Horn et al, ¹⁰⁸ 2002	5	1	Parenteral nutrition dosing for hospital inpatients	Time required to calculate nutrition composition and amount, inappropriate ordering	...	No	...

(continued)

recommendations.¹²⁰ In our review, studies in which users were automatically prompted to use the system described better performance compared with studies in which users were required to actively initiate the system. A similar finding was also reported in a meta-

regression of 11 studies of computer order entry.¹²¹ Compared with manual initiation, automatic prompting may improve integration into practitioner workflow as well as provide better opportunities to correct inadvertent deficiencies in care. In this review, we also

identified better performance in studies in which the trial authors also developed the CDSS software. Potential explanations of this finding include the motivational effect of a developer's enthusiasm, creation of more usable and integrated software, better access to tech-

Table 8. Trials of Computer-Assisted Drug Dosing and Prescribing (cont)

Source	Methods Score	No. of Sites	Indication	Practitioner Performance Outcomes	Patient Outcomes*	Improvement in Practitioner Performance†	Improvement in Patient Outcomes*†
Drug-prescribing systems McDonald, ¹⁰⁹ 1976	7	1	390 Recommended management protocols guiding drug use, recognition of adverse drug reactions, and laboratory tests in outpatients	Adherence to recommendations	...	Yes	...
McDonald et al, ¹¹⁰ 1980	8	1	410 Computerized management rules dealing primarily with use and follow-up of medications in outpatients	Adherence to recommendations	...	Yes	...
White et al, ¹¹¹ 1984	7.5	1	Alerts of potential drug interactions and toxicity with digoxin in inpatients	Adherence to recommendations	...	Yes	...
Rotman et al, ¹¹² 1996	7	1	Recommendation for less expensive drug substitute when available, alerts for drug interactions in outpatients	Adherence to recommendations	Adverse drug interactions	No	No
Tamblyn et al, ¹¹³ 2003	8	Multiple	Alerts for prescribing errors, including drug contraindications in outpatients	Inappropriate prescriptions per 1000 visits, discontinuation of potentially inappropriate prescriptions	...	Yes	...

Abbreviation: CDSS, computerized clinical decision support system.

*Ellipses indicate outcome was not assessed.

†Improvement was defined as a statistically significant positive effect on at least 50% of outcomes measured. Most studies had inadequate statistical power to detect a clinically important improvement in patient outcomes.

nical support and training, improved on-site promotion and tailoring, biases in assessing outcomes, and selective publication of successful trials. Most of the CDSSs in this review were “home grown,” and the importance of local champions to facilitate implementation cannot be underestimated.

Strengths and Weaknesses of This Review

We identified relevant controlled trials through a comprehensive search of the literature. We extended our previous review from 1998 in a number of important ways.³ Using better-defined inclusion criteria, we reconsidered all prior articles and identified 37 new articles. To identify CDSS and study characteristics that predicted positive effects, we abstracted relevant data from all articles in duplicate, confirmed our abstractions with a majority of primary au-

thors, and conducted a multivariable analysis of study-level covariates.

However, limitations of this review should be appreciated. We included only English-language studies. The CDSSs were grouped into categories based on clinical applications rather than on other aspects of CDSS design.¹²² Although trial methods are improving with time, this summary is limited by the methods used in the primary studies. We were unable to use meta-analysis to pool effect sizes, given substantial differences among primary studies in the types of CDSSs and outcomes evaluated. In addition, we defined improvement as a positive effect on at least 50% of outcomes measured. This approach, along with the strict inclusion criteria of this review, may have underestimated the influence of some system and study methodological factors on CDSS success. The wide confidence intervals for the statistically significant de-

terminants of CDSS success imply substantial imprecision in the strength of these associations, which may be non-causal. Furthermore, it is possible that CDSSs for disease management promoted the implementation of ineffective therapies, or that CDSSs of drug dosing used incorrect pharmacokinetic models. Although this appears to be an unlikely explanation for the lack of effect on patient outcomes, we did not evaluate the appropriateness of CDSS algorithms or recommendations. Finally, we summarized controlled trials of CDSSs and did not consider less rigorous but more common designs, such as before-after studies.

When to Adopt a CDSS for Practice

The decision to adopt a CDSS for local patient care is complex and is influenced by many considerations. Those

responsible for CDSS implementation are typically administrators, information technology managers, and clinicians, all of whom are increasingly pushed by technology and guided by government regulations.¹²³ Important issues include CDSS user acceptance, workflow integration, compatibility with legacy applications, system maturity, and upgrade availability. Some are concerned about increased practitioner dependence on CDSSs, with eroded capacity for independent decision making.³¹ Finally, cheaper, non-computerized alternatives may be equally or more effective in improving care and reducing medical errors.¹²⁴⁻¹²⁷

One of the primary considerations in adopting a CDSS is its clinical effectiveness: To what extent should it be proven beneficial before mass deployment? Clearly, some testing is required, as a CDSS can have unanticipated effects when used in patient care.⁸⁵ Some highlight the need for multicenter cluster-randomized controlled trials demonstrating improvements in important patient outcomes.¹² Using such a standard, this review suggests that the majority of available systems are not yet ready for mainstream use. Most trials were unable to enroll enough clusters or patients for adequate statistical power to detect improvements in patient outcomes. Unfortunately, this situation is unlikely to change soon, given the substantial time and resources needed to conduct such trials, particularly in the area of preventive health. Furthermore, CDSSs are limited by the cumulative knowledge used to program their recommendations. It would be unrealistic to require repeat CDSS testing every time advances in the knowledge base become available. Thus, for initial consideration, it may be reasonable to require proof of CDSS effectiveness only on practitioner performance, particularly if such outcomes represent current accepted standards in care. In our review, many systems met this requirement. However, this does not preclude the need for subsequent trials or in-practice assessment to confirm system performance in improving patient health. Institutions

need to measure effects on local outcomes and be prepared to iteratively modify their system in response to practice-based knowledge.²

While some perceive that CDSSs improve efficiency and reduce costs, the current supporting evidence is limited. Although some studies have assessed the costs when outcomes were improved,^{40,45,79-81,84,128} the cost-effectiveness of these systems remains unknown. Many studies suggested the CDSS was inefficient, requiring more time and effort from the user compared with paper-based methods.^{14,15,38,64,81,95,112} Finally, most CDSSs used research funding to facilitate implementation. As highlighted in this review, up to 21% of trials used staff paid by research funds for data entry or CDSS recommendation delivery. When investing in a commercially available system, funding for support personnel is an additional cost to be considered.

There is currently widespread enthusiasm for introducing electronic medical records, computerized physician order entry systems, and CDSSs into hospitals and outpatient settings. In other commercial, industrial, and scientific spheres of activity, computers have become ubiquitous and have improved safety, productivity, and timeliness. Given this progress, computerization of the health care environment should offer tremendous benefits. However, uptake has been slow, and multiple challenges have arisen at every phase of software development, testing, and implementation. The progress of CDSSs has mirrored these trends. Systems are proliferating, their technical performance and usability are improving, and the number and quality of evaluations is increasing. These evaluations have shown that many CDSSs improve practitioner performance. However, further research is needed to elucidate the effects of such systems on patient health.

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REFERENCES

- Wyatt J, Spiegelhalter D. Evaluating medical expert systems: what to test and how? *Med Inform (Lond)*. 1990;15:205-217.
- Sim I, Gorman P, Greenes RA, et al. Clinical decision support systems for the practice of evidence-based medicine. *J Am Med Inform Assoc*. 2001;8:527-534.
- Haynes RB, Walker CJ. Computer-aided quality assurance. *Arch Intern Med*. 1987;147:1297-1301.
- Johnston ME, Langton KB, Haynes RB, Mathieu A. Effects of computer-based clinical decision support systems on clinician performance and patient outcome. *Ann Intern Med*. 1994;120:135-142.
- Hunt DL, Haynes RB, Hanna SE, Smith K. Effects of computer-based clinical decision support systems on physician performance and patient outcomes: a systematic review. *JAMA*. 1998;280:1339-1346.
- Kaushal R, Shojania KG, Bates DW. Effects of computerized physician order entry and clinical decision support systems on medication safety: a systematic review. *Arch Intern Med*. 2003;163:1409-1416.
- Payne TH. Computer decision support systems. *Chest*. 2000;118:475-525.
- Shiffman RN, Liaw Y, Brandt CA, Corb GJ. Computer-based guideline implementation systems: a systematic review of functionality and effectiveness. *J Am Med Inform Assoc*. 1999;6:104-114.
- Kaplan B. Evaluating informatics applications—clinical decision support systems literature review. *Int J Med Inform*. 2001;64:15-37.
- Gordon RB, Grimshaw JM, Eccles M, Rowe RE, Wyatt JC. On-screen computer reminders: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev*. 1998;2:CD001096.
- Mitchell E, Sullivan F. A descriptive feast but an evaluative famine: systematic review of published articles on primary care computing during 1980-97. *BMJ*. 2001;322:279-282.
- Chuang JH, Hripcsak G, Heitjan DF. Design and analysis of controlled trials in naturally clustered environments: implications for medical informatics. *J Am Med Inform Assoc*. 2002;9:230-238.
- Fleiss JL, Cohen J. The equivalence of weighted kappa and the intraclass correlation coefficient as measures of reliability. *Educ Psychol Meas*. 1973;33:613-619.
- Lewis G, Sharp D, Bartholomew J, Pelosi AJ. Computerized assessment of common mental disorders in

- primary care: effect on clinical outcome. *Fam Pract*. 1996;13:120-126.
15. Cannon DS, Allen SN. A comparison of the effects of computer and manual reminders on compliance with a mental health clinical practice guideline. *J Am Med Inform Assoc*. 2000;7:196-203.
 16. Schriger DL, Gibbons PS, Langone CA, Lee S, Altschuler LL. Enabling the diagnosis of occult psychiatric illness in the emergency department: a randomized, controlled trial of the computerized, self-administered PRIME-MD diagnostic system. *Ann Emerg Med*. 2001;37:132-140.
 17. Rollman BL, Hanusa BH, Lowe HJ, et al. A randomized trial using computerized decision support to improve treatment of major depression in primary care. *J Gen Intern Med*. 2002;17:493-503.
 18. Pozen MW, D'Agostino RB, Selker HP, Sytkowski PA, Hood WB. A predictive instrument to improve coronary-care-unit admission practices in acute ischemic heart disease: a prospective multicenter clinical trial. *N Engl J Med*. 1984;310:1273-1278.
 19. Wyatt JR. Lessons learnt from the field trial of ACORN, an expert system to advise on chest pain. In: Barber B, Cao D, Quin D, Wagner G, eds. *Proceedings of the 6th World Conference on Medical Informatics*; Singapore; 1989:111-115.
 20. Selker HP, Beshansky JR, Griffith JL, et al. Use of the acute cardiac ischemia time-insensitive predictive instrument (ACI-TIPI) to assist with triage of patients with chest pain or other symptoms suggestive of acute cardiac ischemia: a multicenter, controlled clinical trial. *Ann Intern Med*. 1998;129:845-855.
 21. Wexler JR, Swender PT, Tunnessen WWJ, Oski FA. Impact of a system of computer-assisted diagnosis. *AJDC*. 1975;129:203-205.
 22. Wellwood J, Johannessen S, Spiegelhalter DJ. How does computer-aided diagnosis improve the management of acute abdominal pain? *Ann R Coll Surg Engl*. 1992;74:40-46.
 23. Bogusevicius A, Maleckas A, Pundzius J, Skaudickas D. Prospective randomised trial of computer-aided diagnosis and contrast radiography in acute small bowel obstruction. *Eur J Surg*. 2002;168:78-83.
 24. Turner BJ, Day SC, Borenstein B. A controlled trial to improve delivery of preventive care: physician or patient reminders? *J Gen Intern Med*. 1989;4:403-409.
 25. McPhee SJ, Bird JA, Jenkins CN, Fordham D. Promoting cancer screening: a randomized, controlled trial of three interventions. *Arch Intern Med*. 1989;149:1866-1872.
 26. McPhee SJ, Bird JA, Fordham D, Rodnick JE, Osborn EH. Promoting cancer prevention activities by primary care physicians: results of a randomized, controlled trial. *JAMA*. 1991;266:538-544.
 27. Burack RC, Gimotty PA, George J, et al. Promoting screening mammography in inner-city settings: a randomized controlled trial of computerized reminders as a component of a program to facilitate mammography. *Med Care*. 1994;32:609-624.
 28. Burack RC, Gimotty PA, George J, Simon MS, Dews P, Moncrease A. The effect of patient and physician reminders on use of screening mammography in a health maintenance organization: results of a randomized controlled trial. *Cancer*. 1996;78:1708-1721.
 29. Burack RC, Gimotty PA. Promoting screening mammography in inner-city settings: the sustained effectiveness of computerized reminders in a randomized controlled trial. *Med Care*. 1997;35:921-931.
 30. Burack RC, Gimotty PA, Simon M, et al. The effect of adding Pap smear information to a mammography reminder system in an HMO: results of randomized controlled trial. *Prev Med*. 2003;36:547-554.
 31. Chambers CV, Balaban DJ, Carlson BL, Grasseberger DM. The effect of microcomputer-generated reminders on influenza vaccination rates in a university-based family practice center. *J Am Board Fam Pract*. 1991;4:19-26.
 32. Flanagan JR, Doebbeling BN, Dawson J, Beekmann S. Randomized study of online vaccine reminders in adult primary care. *Proc AMIA Symp*. 1999:755-759.
 33. Tang PC, LaRosa MP, Newcomb C, Gorden SM. Measuring the effects of reminders for outpatient influenza immunizations at the point of clinical opportunity. *J Am Med Inform Assoc*. 1999;6:115-121.
 34. McDonald CJ, Hui SL, Smith DM, et al. Reminders to physicians from an introspective computer medical record: a two-year randomized trial. *Ann Intern Med*. 1984;100:130-138.
 35. Tierney WM, Hui SL, McDonald CJ. Delayed feedback of physician performance versus immediate reminders to perform preventive care: effects on physician compliance. *Med Care*. 1986;24:659-666.
 36. Ornstein SM, Garr DR, Jenkins RG, Rust PF, Arnon A. Computer-generated physician and patient reminders: tools to improve population adherence to selected preventive services. *J Fam Pract*. 1991;32:82-90.
 37. Rosser WW, McDowell I, Newell C. Use of reminders for preventive procedures in family medicine. *CMAJ*. 1991;145:807-814.
 38. Tape TG, Campbell JR. Computerized medical records and preventive health care: success depends on many factors. *Am J Med*. 1993;94:619-625.
 39. Turner RC, Peden JGJ, O'Brien K. Patient-carried card prompts vs computer-generated prompts to remind private practice physicians to perform health maintenance measures. *Arch Intern Med*. 1994;154:1957-1960.
 40. Frame PS, Zimmer JG, Werth PL, et al. Computer-based vs manual health maintenance tracking: a controlled trial. *Arch Fam Med*. 1994;3:581-588.
 41. Overhage JM, Tierney WM, McDonald CJ. Computer reminders to implement preventive care guidelines for hospitalized patients. *Arch Intern Med*. 1996;156:1551-1556.
 42. Bonevski B, Sanson-Fisher RW, Campbell E, Caruthers A, Reid AL, Ireland M. Randomized controlled trial of a computer strategy to increase general practitioner preventive care. *Prev Med*. 1999;29:478-486.
 43. Demakis JG, Beauchamp C, Cull WL, et al. Improving residents' compliance with standards of ambulatory care: results from the VA Cooperative Study on Computerized Reminders. *JAMA*. 2000;284:1411-1416.
 44. Dexter PR, Perkins S, Overhage JM, Maharry K, Kohler RB, McDonald CJ. A computerized reminder system to increase the use of preventive care for hospitalized patients. *N Engl J Med*. 2001;345:965-970.
 45. Thomas JC, Moore A, Qualls PE. The effect on cost of medical care for patients treated with an automated clinical audit system. *J Med Syst*. 1983;7:307-313.
 46. Mazza SA, Vinicor F, Einterz RM, Norton JA, Kalasinski LA. Effects of the clinical environment on physicians' response to postgraduate medical education. *Am Educ Res J*. 1990;27:473-488.
 47. Nilasena DS, Lincoln MJ. A computer-generated reminder system improves physician compliance with diabetes preventive care guidelines. *Proc Annu Symp Comput Appl Med Care*. 1995:640-645.
 48. Lobach DF, Hammond WE. Computerized decision support based on a clinical practice guideline improves compliance with care standards. *Am J Med*. 1997;102:89-98.
 49. Montori VM, Dinneen SF, Gorman CA, et al. The impact of planned care and a diabetes electronic management system on community-based diabetes care. *Diabetes Care*. 2002;25:1952-1957.
 50. Filippi A, Sabatini A, Badioli L, et al. Effects of an automated electronic reminder in changing the antiplatelet drug-prescribing behavior among Italian general practitioners in diabetic patients: an intervention trial. *Diabetes Care*. 2003;26:1497-1500.
 51. Meigs JB, Cagliero E, Dubey A, et al. A controlled trial of Web-based diabetes disease management: the MGH Diabetes Primary Care Improvement Project. *Diabetes Care*. 2003;26:750-757.
 52. Coe FL, Norton E, Oparil S, et al. Treatment of hypertension by computer and physician: a prospective controlled study. *J Chronic Dis*. 1977;30:81-92.
 53. Rogers JL, Haring OM, Goetz JP. Changes in patient attitudes following the implementation of a medical information system. *QRB Qual Rev Bull*. 1984;10:65-74.
 54. Barnett GO, Winickoff RN, Morgan MM, Zielstorff RD. A computer-based monitoring system for follow-up of elevated blood pressure. *Med Care*. 1983;21:400-409.
 55. Brownbridge G, Evans A, Fitter M, Platts M. An interactive computerized protocol for the management of hypertension: effects on the general practitioner's clinical behaviour. *J R Coll Gen Pract*. 1986;36:198-202.
 56. McAlister NH, Covvey HD, Tong C, Lee A, Wigle ED. Randomised controlled trial of computer assisted management of hypertension in primary care. *Br Med J (Clin Res Ed)*. 1986;293:670-674.
 57. Rossi RA, Every NR. A computerized intervention to decrease the use of calcium channel blockers in hypertension. *J Gen Intern Med*. 1997;12:672-678.
 58. Lowenstein I, Joseph L, Levinton C, Abrahamowicz M, Steinert Y, Grover S. Can computerized risk profiles help patients improve their coronary risk? the results of the Coronary Health Assessment Study (CHAS). *Prev Med*. 1998;27:730-737.
 59. Hetlevik I, Holmen J, Kruger O. Implementing clinical guidelines in the treatment of hypertension in general practice: evaluation of patient outcome related to implementation of a computer-based clinical decision support system. *Scand J Prim Health Care*. 1999;17:35-40.
 60. Montgomery AA, Fahey T, Peters TJ, MacIntosh C, Sharp DJ. Evaluation of computer based clinical decision support system and risk chart for management of hypertension in primary care: randomised controlled trial. *BMJ*. 2000;320:686-690.
 61. Selker HP, Beshansky JR, Griffith JL. Use of the electrocardiograph-based thrombolytic predictive instrument to assist thrombolytic and reperfusion therapy for acute myocardial infarction: a multicenter, randomized, controlled, clinical effectiveness trial. *Ann Intern Med*. 2002;137:87-95.
 62. Ansari M, Shlipak MG, Heidenreich PA, et al. Improving guideline adherence: a randomized trial evaluating strategies to increase beta-blocker use in heart failure. *Circulation*. 2003;107:2799-2804.
 63. Tierney WM, Overhage JM, Murray MD, et al. Effects of computerized guidelines for managing heart disease in primary care. *J Gen Intern Med*. 2003;18:967-976.
 64. Weir CJ, Lees KR, MacWalter RS, et al. Cluster-randomized, controlled trial of computer-based decision support for selecting long-term anti-thrombotic therapy after acute ischaemic stroke. *QJM*. 2003;96:143-153.
 65. Murray MD, Harris LE, Overhage JM, et al. Failure of computerized treatment suggestions to improve health outcomes of outpatients with uncomplicated hypertension: results of a randomized controlled trial. *Pharmacotherapy*. 2004;24:324-337.
 66. Petrucci K, Petrucci P, Canfield K, et al. Evaluation of UNIS: urological nursing information systems. *Proc Annu Symp Comput Appl Med Care*. 1991:43-47.
 67. Rubenstein LV, McCoy JM, Cope DW, et al. Improving patient quality of life with feedback to physicians about functional status. *J Gen Intern Med*. 1995;10:607-614.
 68. Safran C, Rind DM, Davis RB, et al. Guidelines for management of HIV infection with computer-based patient's record. *Lancet*. 1995;346:341-346.
 69. Dexter PR, Wolinsky FD, Gramelspacher GP, et al. Effectiveness of computer-generated reminders for increasing discussions about advance directives and completion of advance directive forms: a randomized, controlled trial. *Ann Intern Med*. 1998;128:102-110.
 70. East TD, Heermann LK, Bradshaw RL, et al. Efficacy of computerized decision support for mechanical

cal ventilation: results of a prospective multi-center randomized trial. *Proc AMIA Symp*. 1999;251-255.

71. Kuperman GJ, Teich JM, Tanasijevic MJ, et al. Improving response to critical laboratory results with automation: results of a randomized controlled trial. *J Am Med Inform Assoc*. 1999;6:512-522.

72. Christakis DA, Zimmerman FJ, Wright JA, et al. A randomized controlled trial of point-of-care evidence to improve the antibiotic prescribing practices for otitis media in children. *Pediatrics*. 2001;107:E15.

73. McCowan C, Neville RG, Ricketts IW, Warner FC, Hoskins G, Thomas GE. Lessons from a randomized controlled trial designed to evaluate computer decision support software to improve the management of asthma. *Med Inform Internet Med*. 2001;26:191-201.

74. Eccles M, McColl E, Steen N, et al. Effect of computerised evidence based guidelines on management of asthma and angina in adults in primary care: cluster randomised controlled trial. *BMJ*. 2002;325:941.

75. Lesourd F, Avril C, Boujennah A, Parinaud J. A computerized decision support system for ovarian stimulation by gonadotropins. *Fertil Steril*. 2002;77:456-460.

76. McDonald CJ. Use of a computer to detect and respond to clinical events: its effect on clinician behavior. *Ann Intern Med*. 1976;84:162-167.

77. Young DW. Improving the consistency with which investigations are requested. *Med Inform (Lond)*. 1981;6:13-17.

78. Fihn SD, McDonnell MB, Vermees D, et al. A computerized intervention to improve timing of outpatient follow-up: a multicenter randomized trial in patients treated with warfarin. *J Gen Intern Med*. 1994;9:131-139.

79. Overhage JM, Tierney WM, Zhou XH, McDonald CJ. A randomized trial of "corollary orders" to prevent errors of omission. *J Am Med Inform Assoc*. 1997;4:364-375.

80. Tierney WM, McDonald CJ, Hui SL, Martin DK. Computer predictions of abnormal test results: effects on outpatient testing. *JAMA*. 1988;259:1194-1198.

81. Tierney WM, Miller ME, Overhage JM, McDonald CJ. Physician inpatient order writing on microcomputer workstations: effects on resource utilization. *JAMA*. 1993;269:379-383.

82. Hales JW, Gardner RM, Jacobson JT. Factors impacting the success of computerized preadmission screening. *Proc Annu Symp Comput Appl Med Care*. 1995:728-732.

83. Shea S, Sideli RV, DuMouchel W, Pulver G, Arons RR, Clayton PD. Computer-generated informational messages directed to physicians: effect on length of hospital stay. *J Am Med Inform Assoc*. 1995;2:58-64.

84. Bates DW, Kuperman GJ, Rittenberg E, et al. A randomized trial of a computer-based intervention to reduce utilization of redundant laboratory tests. *Am J Med*. 1999;106:144-150.

85. Abbrecht PH, O'Leary TJ, Behrendt DM. Evaluation of a computer-assisted method for individualized anticoagulation: retrospective and prospective studies with a pharmacodynamic model. *Clin Pharmacol Ther*. 1982;32:129-136.

86. Carter BL, Taylor JW, Becker A. Evaluation of three dosage-prediction methods for initial in-hospital stabilization of warfarin therapy. *Clin Pharm*. 1987;6:37-45.

87. White RH, Hong R, Venook AP, et al. Initiation of warfarin therapy: comparison of physician dosing with computer-assisted dosing. *J Gen Intern Med*. 1987;2:141-148.

88. White RH, Mungall D. Outpatient management of warfarin therapy: comparison of computer-predicted dosage adjustment to skilled professional care. *Ther Drug Monit*. 1991;13:46-50.

89. Poller L, Wright D, Rowlands M. Prospective comparative study of computer programs used for management of warfarin. *J Clin Pathol*. 1993;46:299-303.

90. Fitzmaurice DA, Hobbs FD, Murray ET, Bradley CP, Holder R. Evaluation of computerized decision support for oral anticoagulation management based in primary care. *Br J Gen Pract*. 1996;46:533-535.

91. Vadher B, Patterson DL, Leaning M. Evaluation of a decision support system for initiation and control of oral anticoagulation in a randomised trial. *BMJ*. 1997;314:1252-1256.

92. Vadher BD, Patterson DL, Leaning M. Comparison of oral anticoagulant control by a nurse-practitioner using a computer decision-support system with that by clinicians. *Clin Lab Haematol*. 1997;19:203-207.

93. Ageno W, Turpie AG. A randomized comparison of a computer-based dosing program with a manual system to monitor oral anticoagulant therapy. *Thromb Res*. 1998;91:237-240.

94. Poller L, Shiach CR, MacCallum PK, et al. Multicentre randomised study of computerised anticoagulant dosage. *Lancet*. 1998;352:1505-1509.

95. Fitzmaurice DA, Hobbs FD, Murray ET, Holder RL, Allan TF, Rose PE. Oral anticoagulation management in primary care with the use of computerized decision support and near-patient testing: a randomized, controlled trial. *Arch Intern Med*. 2000;160:2343-2348.

96. Manotti C, Moia M, Palareti G, Pengo V, Ria L, Dettori AG. Effect of computer-aided management on the quality of treatment in anticoagulated patients: a prospective, randomized, multicenter trial of AP-ROAT (Automated PProgram for Oral Anticoagulant Treatment). *Haematologica*. 2001;86:1060-1070.

97. Mungall DR, Anbe D, Forrester PL, et al. A prospective randomized comparison of the accuracy of computer-assisted versus GUSTO nomogram-directed heparin therapy. *Clin Pharmacol Ther*. 1994;55:591-596.

98. Hurley SF, Dziukas LJ, McNeil JJ, Brignell MJ. A randomized controlled clinical trial of pharmacokinetic theophylline dosing. *Am Rev Respir Dis*. 1986;134:1219-1224.

99. Gonzalez ER, Vanderheyden BA, Ornato JP, Comstock TG. Computer-assisted optimization of aminophylline therapy in the emergency department. *Am J Emerg Med*. 1989;7:395-401.

100. Verner D, Seligmann H, Platt S, et al. Computer assisted design of a theophylline dosing regimen in acute bronchospasm: serum concentrations and clinical outcome. *Eur J Clin Pharmacol*. 1992;43:29-33.

101. Casner PR, Reilly R, Ho H. A randomized controlled trial of computerized pharmacokinetic theophylline dosing versus empiric physician dosing. *Clin Pharmacol Ther*. 1993;53:684-690.

102. Begg EJ, Atkinson HC, Jeffery GM, Taylor NW. Individualised aminoglycoside dosage based on pharmacokinetic analysis is superior to dosage based on physician intuition at achieving target plasma drug concentrations. *Br J Clin Pharmacol*. 1989;28:137-141.

103. Hickling K, Begg E, Moore ML. A prospective randomised trial comparing individualised pharmacokinetic dosage prediction for aminoglycosides with prediction based on estimated creatinine clearance in critically ill patients. *Intensive Care Med*. 1989;15:233-237.

104. Burton ME, Ash CL, Hill DP Jr, Handy T, Shepherd MD, Vasko MR. A controlled trial of the cost benefit of computerized Bayesian aminoglycoside administration. *Clin Pharmacol Ther*. 1991;49:685-694.

105. Peck CC, Sheiner LB, Martin CM, et al. Computer-assisted digoxin therapy. *N Engl J Med*. 1973;289:441-446.

106. Rodman JH, Jelliffe RW, Kolb E, et al. Clinical studies with computer-assisted initial lidocaine therapy. *Arch Intern Med*. 1984;144:703-709.

107. Ryff-de Leche A, Engler H, Nutzi E, Berger M, Berger W. Clinical application of two computerized diabetes management systems: comparison with the log-book method. *Diabetes Res*. 1992;19:97-105.

108. Horn W, Popow C, Miksch S, et al. Development and evaluation of VIE-PNN, a knowledge-based system for calculating the parenteral nutrition of newborn infants. *Artif Intell Med*. 2002;24:217-228.

109. McDonald CJ. Protocol-based computer reminders, the quality of care and the non-perfectability of man. *N Engl J Med*. 1976;295:1351-1355.

110. McDonald CJ, Wilson GA, McCabe GP Jr. Physician response to computer reminders. *JAMA*. 1980;244:1579-1581.

111. White KS, Lindsay A, Pryor TA, Brown WF, Walsh K. Application of a computerized medical decision-making process to the problem of digoxin intoxication. *J Am Coll Cardiol*. 1984;4:571-576.

112. Rotman BL, Sullivan AN, McDonald TW, et al. A randomized controlled trial of a computer-based physician workstation in an outpatient setting: implementation barriers to outcome evaluation. *J Am Med Inform Assoc*. 1996;3:340-348.

113. Tamblyn R, Huang A, Perreault R, et al. The medical office of the 21st century (MOXXI): effectiveness of computerized decision-making process in reducing inappropriate prescribing in primary care. *CMAJ*. 2003;169:549-556.

114. McKinley BA, Moore FA, Sailors RM, et al. Computerized decision support for mechanical ventilation of trauma induced ARDS: results of a randomized clinical trial. *J Trauma*. 2001;50:415-424.

115. Hetlevik I, Holmen J, Kruger O, Kristensen P, Iversen H, Furuseth K. Implementing clinical guidelines in the treatment of diabetes mellitus in general practice: evaluation of effort, process, and patient outcome related to implementation of a computer-based decision support system. *Int J Technol Assess Health Care*. 2000;16:210-227.

116. Rogers JL, Haring OM, Wortman PM, Watson RA, Goetz JP. Medical information systems: assessing impact in the areas of hypertension, obesity and renal disease. *Med Care*. 1982;20:63-74.

117. Rogers JL, Haring OM. The impact of a computerized medical record summary system on incidence and length of hospitalization. *Med Care*. 1979;17:618-630.

118. Hetlevik I, Holmen J, Kruger O, et al. Implementing clinical guidelines in the treatment of hypertension in general practice. *Blood Press*. 1998;7:270-276.

119. Holbrook A, Xu S, Banting J. What factors determine the success of clinical decision support systems? *AMIA Annu Symp Proc*. 2003:862.

120. Reisman Y. Computer-based clinical decision aids: a review of methods and assessment of systems. *Med Inform (Lond)*. 1996;21:179-197.

121. Kawamoto K, Lobach DF. Clinical decision support provided within physician order entry systems: a systematic review of features effective for changing clinician behavior. *AMIA Annu Symp Proc*. 2003:361-365.

122. Berlin A, Sorani M, Sim I. Characteristics of outpatient clinical decision support systems: a taxonomic description. *Medinfo*. 2004;2004:578-581.

123. Fox J, Thomson R. Clinical decision support systems: a discussion of quality, safety and legal liability issues. *Proc AMIA Symp*. 2002:265-269.

124. Ofman JJ, Badamgarav E, Henning JM, et al. Does disease management improve clinical and economic outcomes in patients with chronic diseases? a systematic review. *Am J Med*. 2004;117:182-192.

125. Warsi A, Wang PS, LaValley MP, Avorn J, Solomon DH. Self-management education programs in chronic disease: a systematic review and methodological critique of the literature. *Arch Intern Med*. 2004;164:1641-1649.

126. Grimshaw JM, Thomas RE, MacLennan G, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. *Health Technol Assess*. 2004;8:iii-iv, 1-72.

127. Stone EG, Morton SC, Hulscher ME, et al. Interventions that increase use of adult immunization and cancer screening services: a meta-analysis. *Ann Intern Med*. 2002;136:641-651.

128. McDonald CJ, Hui SL, Tierney WM. Effects of computer reminders for influenza vaccination on morbidity during influenza epidemics. *MD Comput*. 1992;9:304-312.