Effectiveness of Computerized Decision Support Systems Linked to Electronic Health Records: A Systematic Review and Meta-Analysis

We systematically reviewed randomized controlled trials (RCTs) assessing the effectiveness of computerized decision support systems (CDSSs) featuring rule- or algorithm-based software integrated with electronic health records (EHRs) and evidence-based knowledge. We searched MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, and Cochrane Database of Abstracts of Reviews of Effects. Information on system design, capabilities, acquisition, implementation context, and effects on mortality, morbidity, and economic outcomes were extracted.

Twenty-eight RCTs were included. CDSS use did not affect mortality (16 trials, 37395 patients; 2282 deaths; risk ratio [RR] = 0.96; 95% confidence interval [CI] = 0.85, 1.08; I^2 = 41%). A statistically significant effect was evident in the prevention of morbidity, any disease (9 RCTs; 13868 patients; RR = 0.82; 95% CI = 0.68, 0.99; I^2 = 64%), but selective outcome reporting or publication bias cannot be excluded. We observed differences for costs and health service utilization, although these were often small in magnitude.

Across clinical settings, new generation CDSSs integrated with EHRs do not affect mortality and might moderately improve morbidity outcomes. (*Am J Public Health.* 2014;104:e12–e22. doi: 10.2105/AJPH.2014.302164)

Lorenzo Moja, MD, MSc, PhD, Koren H. Kwag, BSc, MSc, Theodore Lytras, MD, MPH, Lorenzo Bertizzolo, MD, Linn Brandt, MD, Valentina Pecoraro, BSc, Giulio Rigon, MD, MSc, Alberto Vaona, MD, MSc, Francesca Ruggiero, BA, MA, Massimo Mangia, Alfonso Iorio, MD, PhD, Ilkka Kunnamo, MD, PhD, and Stefanos Bonovas, MD, MSc, PhD

THE QUALITY OF MEDICAL care is variable and often suboptimal across health care systems.[1] Despite the growing availability of knowledge from randomized controlled trials (RCTs) and systematic reviews to guide clinical practice, there remains a discrepancy in the application of evidence into health care services.[2] Current research demonstrates the potential of computerized decision support systems (CDSSs) to assist with problems raised in clinical practice, increase clinician adherence to guideline- or protocol-based care, and, ultimately, improve the overall efficiency and quality of health care delivery systems.[1,3,4] CDSSs have been additionally shown to increase the use of preventive care in hospitalized patients, facilitate communication between providers and patients, enable faster and more accurate access to medical record data, improve the quality and safety of medication prescribing, and decrease the rate of prescription errors.[5–9] A recent study estimated that the adoption of Computerized Physician Order Entry and Clinical Decision Support could prevent 100 000 inpatient adverse drug events (ADEs) per year, resulting in increased inpatient bed availability by more than 700 000 bed-days and opportunity savings approaching €300 million in the studied European Union member states (i.e., the Czech Republic, France, the Netherlands, Sweden, Spain, and the United Kingdom).[10]

Electronic Health Records (EHRs) represent another innovation that is gaining momentum in health care systems. In the United States, the use of EHRs is encouraged by the $27 billion allocated in reimbursement incentives by the 2009 Health Information Technology for Economic and Clinical Health (HITECH) Act. Under the Act, clinicians and hospitals must demonstrate "meaningful use" of EHRs by adhering to a set of criteria, which includes the implementation of clinical decision support rules relevant to a specialty or high priority hospital condition such as diagnostic test ordering.[11] The integration of CDSSs with EHRs through the delivery of guidance messages to health care professionals at the point of care may maximize the impact of both innovations.

A primary barrier to successful CDSS evaluation is its broad definition adopted by the research community, which encompasses a diverse range of interventions and functions (see the box on page e2). The inclusion of studies with variable interventions across diverse health care settings precluded systematic reviews from reaching a decisive understanding of the impact of CDSSs.[9,12–14] To address this issue, we conducted a systematic review to rigorously evaluate the impact of CDSSs linked to EHRs on critical outcomes—mortality, morbidity, and costs—and adopted a narrow definition of the intervention to facilitate its coherent and accurate evaluation.

METHODS

Our study protocol[18] is registered on PROSPERO: the international prospective register of systematic reviews (ID: 2014: CRD42014007177). This work was performed in accordance with the PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions.[19]

Eligibility Criteria

Population. Postgraduate health professionals (medical, nursing, and allied health) in primary, secondary, and tertiary care settings. Only interventions that were implemented in real, nonsimulated, clinical settings were considered.

Types of interventions. We adapted the definition of a CDSS by Haynes et al.[20] and Eberhardt et al.[21] We defined a CDSS as an information system aimed to support clinical decision-making, linking patient-specific information in EHRs with evidence-based knowledge to generate case-specific guidance messages through a rule- or algorithm-based software. Our inclusion criteria emphasize the implementation of evidence-based medicine, meaning that computer-generated guidance messages had to be based on

Definitions of Computerized Decision Support Systems (CDSSs) Adopted by Authors of Other Systematic Reviews

Bates et al.[15(p524)] (and later adopted by Ash et al.[4(p980)]) defined a CDSS as a computer-based system providing "passive and active referential information as well as reminders, alerts, and guidelines."

Kawamoto et al.[16(p1)] (and later adopted by Bright et al.[9(p29)]) identified a CDSS 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."

Payne[17(p47S)] classified CDSSs as "computer applications designed to aid clinicians in making diagnostic and therapeutic decisions in patient care."

literature or a priori evidence (e.g., guidelines or point-of-care services) and not on expert opinions. This knowledge had to then be delivered to medical doctors or allied health care professionals through electronic media (e.g., computer, smartphone, or tablet). We did not exclude a CDSS, however, based on the degree of literature it covered in the literature surveillance system. In other words, we included a CDSS if it integrated a single evidence-based guideline or incorporated multiple evidence-based guidelines. We also included CDSSs irrespective of the level of patient information archived in the EHR.

Systems that alter the guidance based on previous experience or average behaviors were excluded.

We included software guidance messages, irrespective of the form (e.g., recommendations, alerts, prompts, or reminders), as well as guidance messages, regardless of the target assistance (e.g., diagnostic test ordering and interpretation, treatment planning, therapy recommendations, primary preventive care, therapeutic drug monitoring and dosing, drug prescribing, or chronic disease management). Patient-specific information had to derive from EHRs. Our operational definitions for considering a study "compliant" with the EHR were inclusive: from clinical data repository and health data repository (CDHR), to electronic medical–patient record (EMR and EPR), and EHR.[22]

Our inclusion criteria match the "6S" Haynes' model for evidence-based literature products[23] and the evolution of online point-of-care services.[24] The box below describes, in detail, the characteristics of the CDSSs we evaluated.

Types of comparison groups. To address our objectives, we considered the following comparisons: access to CDSSs according to our definition compared with (1)

Characteristics of Computerized Decision Support Systems (CDSSs)

Implementation strategy	
Channel	Electronic-based
Sharing	Local application, networked, or Web applications
Type of device	Local personal computer or handheld device
Computational architecture	CDSS built into local EHR, knowledge available from central repository, entire system housed outside local site, clouding system
Information	
Nature	Knowledge-based
Provider	Contents provided by national/international publisher, professional society, health care organization, or governmental agency
EBM methodology	General references, specific guidelines for a given clinical condition, suggestions considering a patient's unique clinical data, list of possible diagnoses, drug interaction alerts, or preventive care reminders
Format: delivery form	Messages reminders, prompts, alerts, algorithms, recommendations, rules, order sets, warnings, data reports, and dashboards
Target	
Targeted setting	Primary, secondary, or tertiary
Target expertise	Preventive care (e.g., immunization, screening, or disease management guidelines for secondary prevention)
	Diagnosis (e.g., suggestions for possible diagnoses that match a patient's signs and symptoms)
	Planning or implementing treatment (e.g., guidelines for specific diagnoses, drug dosage recommendations, or warnings for drug interactions).
	Follow-up management (e.g., corollary orders, reminders for ADE monitoring)
	Hospital, provider efficiency (e.g., care plans to minimize length of stay)
	Cost reductions and improved patient convenience (e.g., duplicate testing alerts or drug formulary guidelines)
Overall goals	Improved overall efficiency, early disease identification, accurate diagnosis, adherence of treatment to protocols, or prevention of ADEs
Time	
Timing	Immediately at the point of care, before the patient encounter, after the patient encounter, or at any time
Type of presentation	"Automatic" (key issues: timing, autonomy and user control over response)
	"On demand" (key issues: speed, ease of access, autonomy and user control over response)
Person: health professional	Physicians, nurses, or allied health professionals

Note. ADE = adverse drug event; EBM = evidence-based medicine; EHR = electronic health record.

standard care with no access to CDSSs, (2) CDSSs that do not generate advice, or (3) CDSSs that are not based on evidence. Trials comparing arms accessing the same CDSS at different intensities (e.g., one arm having guidance messages pushed to the health professional vs another arm having guidance message statically available in a folder) were not pooled together with the other trials in the quantitative analyses.

Types of outcomes and assessment measures. We identified a priori the following (primary) outcome measures for included studies:

1. Mortality: We selected mortality as it is the most relevant and objective outcome, although there may exist variability across studies with regards to the time frame during which mortality is captured.
2. Morbidity: We selected and grouped objective patient outcomes such as occurrence of illness (e.g., pneumonia, myocardial infarction, stroke), progression of diseases and hospitalizations.
3. Economic outcomes: Information about health care utilization (e.g., length of stay, emergency department visits, and primary care consultations), and costs.

We did not consider the following outcomes: patient satisfaction, measures of process, and health care professional activity or performance (e.g., adherence to guidelines, rates of screening and other preventive measures, provision of counseling, rates of appropriate drug administration, and identification of at-risk behaviors).

Types of studies. To be eligible, studies had to be randomized controlled trials (RCTs). Randomization was allowed to be either at the individual- or at the cluster-level.

Data Sources

We systematically searched the English-language literature indexed in MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, and Cochrane Database of Abstracts of Reviews of Effects. Studies found in the bibliographies of Systematic Reviews on CDSSs, as well as those identified by experts, were also considered. The full search strategies for MEDLINE and EMBASE are included in the Appendix.

Study Selection and Data Extraction

We identified RCTs of the CDSSs fulfilling the aforementioned eligibility criteria. We combined the results into a reference management software program (EndNote X5 for Windows, Thomson Reuters, Philadelphia, PA). The database was filtered for duplications to derive a unique set of records. Investigators (K. H. K., T. L., L. B., L. B., V. P., G. R., A. V., and S. B.) independently examined the search results and screened the titles and abstracts; the full text reports of all potentially relevant trials were subsequently screened. Investigators (K. H. K., T. L., L. B., L. B., V. P., G. R., A. V., and S. B.) independently abstracted information on CDSS characteristics and effect estimates from all included trials using a modified version of The Cochrane Effective Practice and Organisation of Care Review Group (EPOC) data collection checklist: study setting and methods (design), comparators, computerized CDSS characteristics, patient or provider characteristics, and outcomes. We performed all steps in the study selection and data extraction processes in duplicate. When necessary, we attempted to contact the study authors to clarify uncertainties in the study design or results.

Risk of Bias Assessment

Two investigators (K. H. K., L. M.) assessed the potential risk for bias in included studies using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions.[25] The assessment involved the following key domains: sequence generation, allocation concealment, blinding of outcome assessors, incomplete outcome data, selective outcome reporting, and other sources of bias (e.g., extreme baseline imbalance or failure to disclose source of funding for the study). We did not assess the blinding of personnel and participants given the nature of the intervention. In fact, the use of masking procedures to prevent personnel and participants from knowing the allocation to the intervention or control arms was impractical. Furthermore, blinding does not affect mortality, an outcome of this review. Our assessment referred only to studies reporting mortality or morbidity outcomes. Any disagreement was resolved by discussion or by the involvement of a third investigator (S. B.).

Data Synthesis

Risk ratios and 95% confidence intervals (CIs) were calculated for each trial by reconstructing contingency tables based on the number of patients randomly assigned and the number of patients with the outcome of interest (analysis in accordance with the intention-to-treat principle). For the cluster-randomized trials, to calculate adjusted (inflated) CIs that account for the clustering, we performed an approximate analysis as recommended in the Cochrane Handbook.[25] Our approach was to multiply the standard error of the effect estimate (from the analysis ignoring the clustering) by the square root of the design effect.[25] For this, we used an intracluster correlation coefficient (ICC = 0.027) borrowed from an external source.[26] Then, each meta-analysis was performed twice, assuming either a fixed-effects[27] or a random-effects model.[28] In the absence of heterogeneity, the fixed-effects and the random-effects models provide similar results. When heterogeneity is found, the random-effects model is considered to be more appropriate, although both models may be biased.[29]

For all statistical analyses we used the R software environment,[30] version 3.0.1, and the "meta" package for R,[31] version 2.3–0. Selective outcome reporting or publication bias was assessed using the Begg and Mazumdar adjusted rank correlation test[32] and the Egger regression asymmetry test.[33] To evaluate whether the results of the studies were homogeneous, we used the Cochran Q test with a 0.10 level of significance.[34] We also calculated the I^2 statistic[35] that describes the percentage variation across studies that is attributed to heterogeneity rather than chance. We regarded an I^2 value less than 40% as indicative of "not important heterogeneity" and a value higher than 75% as indicative of "considerable heterogeneity."[25] To evaluate the stability of the results, we also performed a "leave-one-out" sensitivity analysis. The scope of this approach was to evaluate the influence of individual studies by estimating the summary relative risk in the absence of each study.[36] All *P* values are 2-tailed. For all tests (except for heterogeneity), a probability

level less than .05 was considered statistically significant.

RESULTS

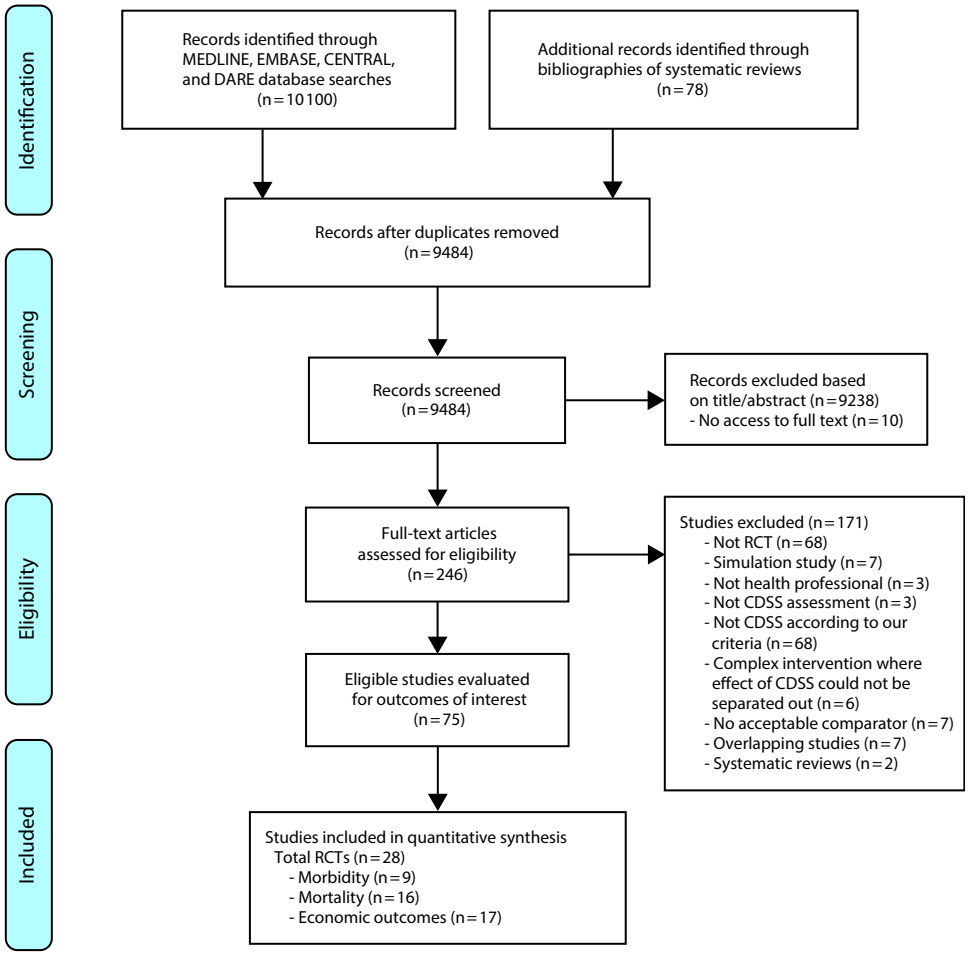
The results of our search and selection process are presented in Figure 1. We identified 28 RCTs, which met the predefined inclusion criteria.[37–64] Eighteen studies reported mortality or morbidity data[37–54] and were included in the meta-analyses, while 10 more studies reported only economic outcomes.[55–64] A description of the RCTs is provided in the Appendix (available as a supplement to this article at http://www.ajph.org).

Risk of Bias in Studies Included in the Meta-Analyses

Overall, the assessment of the 18 studies incorporated in the meta-analyses indicated high risk of bias across 7 (39%) and unclear risk for 10 studies (56%). Only 1 study[44] (5%) was judged to be at low risk for bias. We noticed that the majority of trials did not measure mortality as an outcome, but reported it as additional information, often as a reason for loss to follow-up. Readers should be aware that our risk of bias assessment did not evaluate studies based on their intended outcomes, but according to 2 outcomes of our systematic review: mortality and morbidity. Quality assessment items are summarized in Figure 2.

Meta-Analysis of Mortality Outcomes

Sixteen RCTs contributed to this analysis.[37–52] A total of 37 395 individuals participated in these trials: 18 848 in the intervention groups and 18 547 in the control groups. Seven trials[37,41,42,44,47,48,50] reported a lower mortality in the intervention group, while 8 trials[38–40,42,46,49,51,52] reported a higher mortality. Only 3 were statistically significant.[44,46,47] The overall mortality rate on all 16 RCTs was 6.2% in the intervention groups (1171 deaths) and 6.0% in the control groups (1111 deaths). The pooled effect estimate was not statistically significant assuming either a fixed effects model (RR = 1.00; 95% CI = 0.92, 1.08), or a random effects model (RR = 0.96; 95% CI = 0.85, 1.08). Figure 3 shows the forest plot of the RR estimates and 95% CIs from the individual trials and the pooled results. The Cochran Q test had a P value of .047 and the corresponding I^2 statistic was 41%, both indicating moderate variability between studies. Visual inspection of the funnel plot (Figure 4a) indicated that pooled data did not appear to be heavily influenced by publication bias, although it is also possible that few studies are "missing" from the area of nonsignificance. The P values for the tests of Begg and Egger were $P = .96$ and $P = .29$, respectively, also suggesting a low probability of publication bias. The "leave-one-out" sensitivity analysis, removing a study at a time (Figure 5), confirmed the stability of our results.

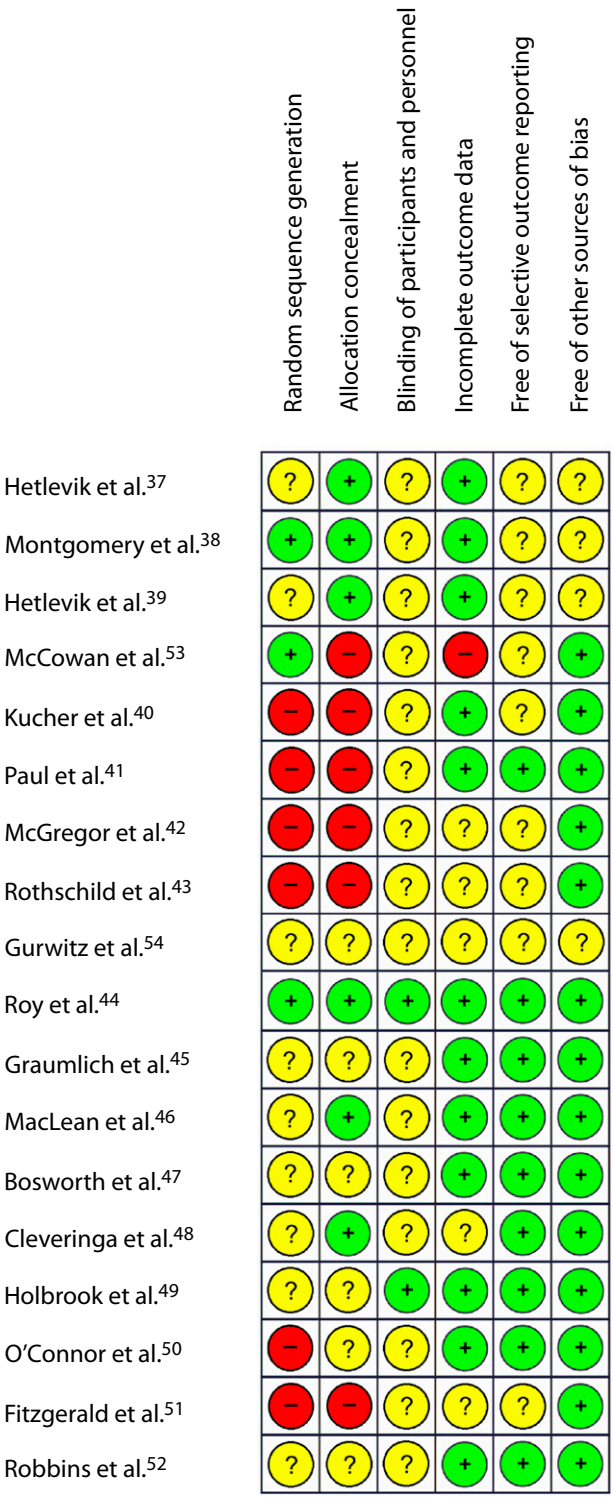


Note. CDSS = computerized decision support systems; RCT = randomized controlled trial

FIGURE 1—Summary of evidence search and selection.

Meta-Analysis of Morbidity Outcomes

Nine RCTs contributed to this analysis.[40,42,44,45,49,51–54] A total of 13 868 individuals participated in these trials. The analysis revealed a weak inverse association between CDSS use and morbidity from any disease. The difference between the CDSS and control groups in the occurrence of morbidity outcomes was marginally significant assuming a random-effects model (RR = 0.82; 95% CI = 0.68, 0.99), but not significant assuming a fixed-effects model (RR = 0.91; 95% CI = 0.83, 1.00). Figure 3 shows the forest plot of the RR estimates and 95%



Note. Green (+) = low risk of bias; Yellow (?) = unclear risk of bias; Red (–) = high risk of bias.

FIGURE 2—Summary of risk-of-bias assessments of the randomized controlled trials included in the meta-analyses.

CIs from the individual trials and the pooled results. The Cochran's Q test had a P value of .005 and the corresponding I^2 statistic was 64%, both indicating substantial variability between studies. Visual inspection of the funnel plot (Figure 4b) indicated slight asymmetry, with relatively few studies existing midway in the area of nonsignificance. The P values for the Begg and the Egger's tests were $P = .18$ and $P = .07$, respectively, suggesting the possible existence of selective outcome reporting bias or small study effects. The sensitivity analysis confirmed that the pooled estimates were fairly unstable (Figure 5).

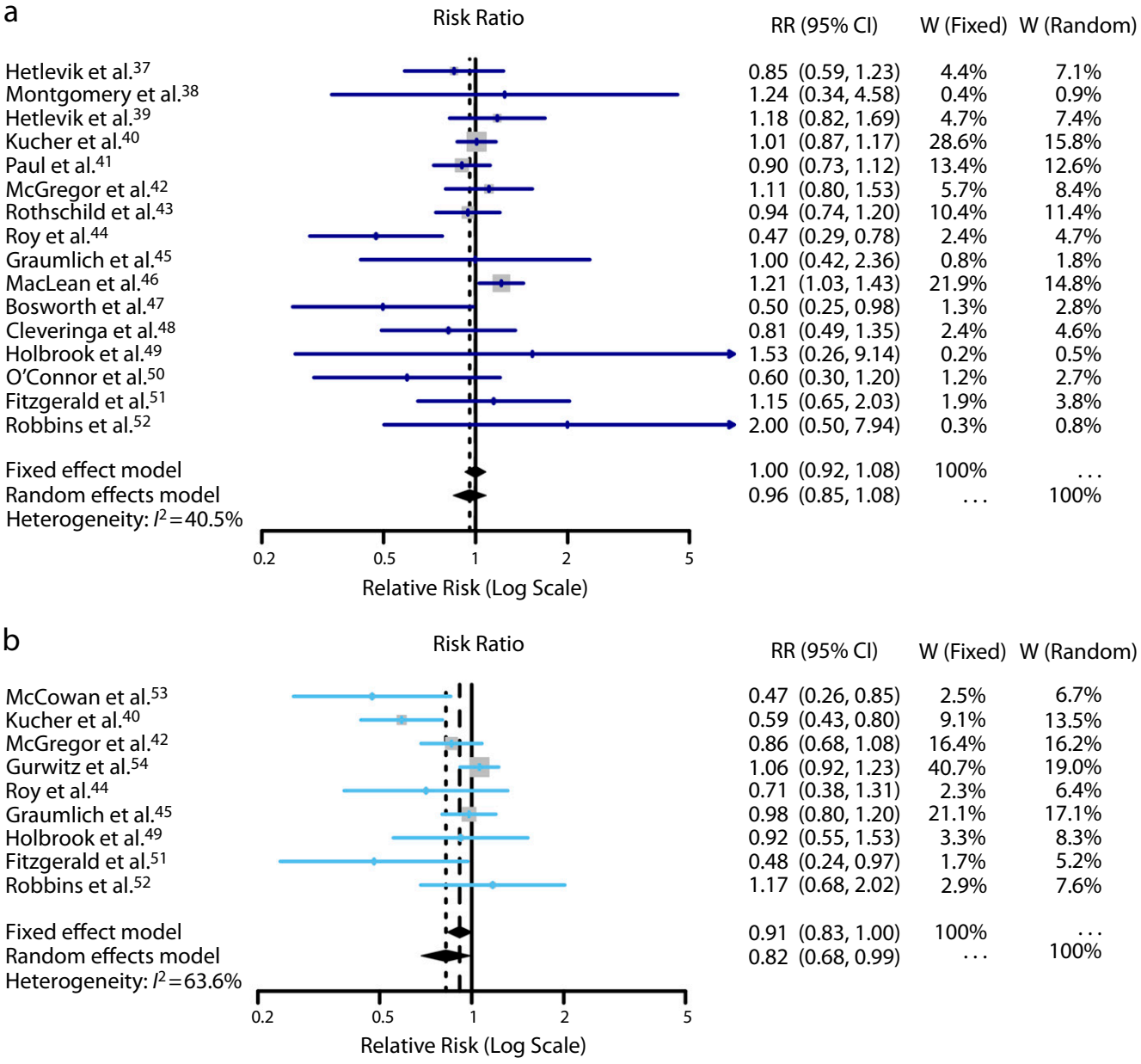
Qualitative Assessment of Economic Outcomes

Seventeen RCTs reported economic outcomes.[41–43,45,46,50,53,55–64] Three of these[46,50,59] presented the economic data in separate publications.[65–67] Differences were seen for costs and health service utilization (e.g., drug or test orders), but these were often small in magnitude. Across economic outcomes, interventions equipped with CDSSs did not consistently perform better than nonequipped ones. Data regarding the impact of CDSSs on cost and health services utilization are given in Table 1.

DISCUSSION

This systematic review of 28 RCTs revealed little evidence for a difference in mortality when pooling results from comparisons of adoption of a CDSS integrated with an EHR versus health care settings without a CDSS. Our review indicates that differences in mortality outcomes, if they exist, appear small across studies and health care services, and may exist only in particular settings with specific diseases and circumstances. However, most of the studies were underpowered and too short to prove or exclude an effect on mortality, and effects as large as a 25% increase or reduction could still be possible. We found weak evidence that an active CDSS is associated with a lower risk for morbidity. All morbidity outcomes selected were relevant from a clinical and health services perspective. Again, results on morbidity outcomes were very diverse, limiting quantitative inferences; however, the summary RR morbidity decrease of 10% to 18% places CDSSs linked to EHRs at the top of the spectrum of quality improvement interventions for their potential impact on health outcomes. The beneficial effects of CDSSs might still be greater than that suggested by the current analysis given the limited number of actual studies providing results on hard outcomes. Finally, we observed differences for costs and health service utilization, but these were often small in magnitude.

Several other systematic reviews provided pooled estimates of the RRs for CDSSs. All reviews observed large between-study heterogeneity. This is expected given the variability in intervention, settings, diseases, and study designs. Despite this limitation, they concluded in favor of CDSSs. Our review exhibits several differences. We adopted stricter inclusion criteria, selecting only CDSSs featuring a rule- or algorithm-based software integrated with EHRs and evidence-based knowledge. The CDSSs we included can be viewed as a second generation in terms of their technology, information management, and linkage to EHRs. Furthermore, we did not include process and laboratory outcomes such as adherence to guideline recommendations or change in blood values. Analyzing



Note. CI = confidence interval; RR = risk ratio; W = weight. The RR and 95% CI for each study are displayed on a logarithmic scale.

FIGURE 3—Forest plots from individual studies and meta-analysis for (a) mortality, all follow-up, and (b) morbidity, any disease.

estimates from process outcomes is problematic. Their relevance is questionable and the quality of the data may have been less than optimal, particularly when the data sources were administrative rather than clinical. The overlap between our review and others is limited, as there exists approximately 50% in terms of the studies and less in terms of the rough data. The results of our review complement previous analyses showing that CDSSs are best oriented to directly affect process outcomes (recommendation adherence) and, with decreasing impact, morbidity and mortality.

Several included studies were cluster-RCTs that did not report if they accounted for clustering effects. Trials randomizing at the group level should not be analyzed at the individual participant level. If the clustering is ignored, *P* values will be artificially small. This problem might result in false positive conclusions that the CDSS has an effect when it does not. Thus, we adjusted estimates of the RRs for our data synthesis using a method that inflates variances.

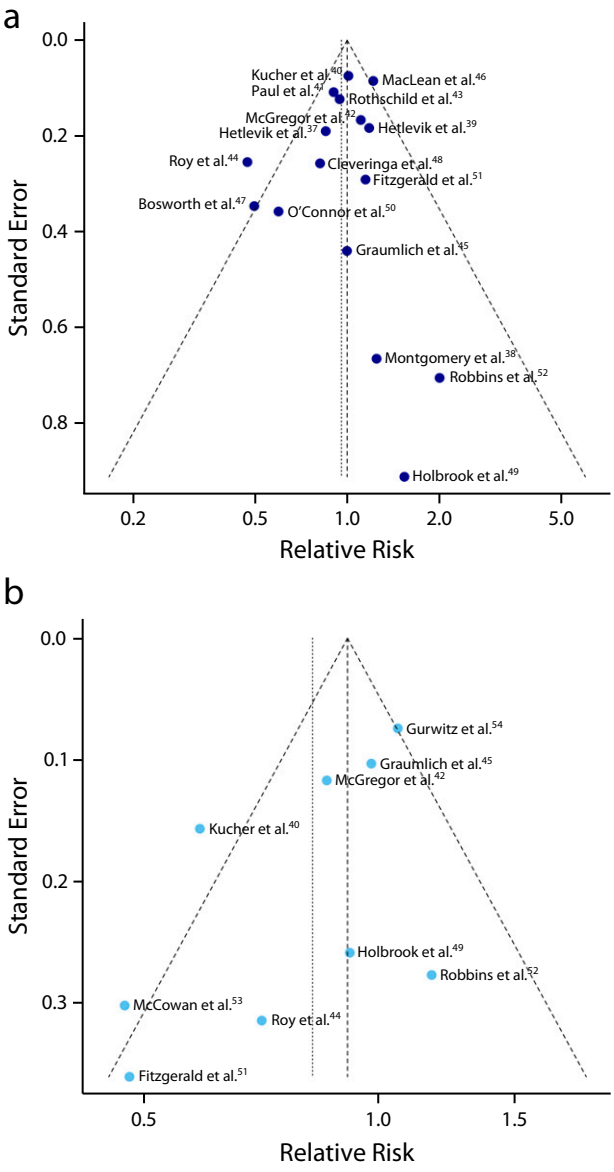


FIGURE 4—Funnel plots of observed relative risk against standard error for (a) mortality and (b) morbidity.

However, such adjusted results should be interpreted cautiously; if the clustering effect is limited across studies, the analysis may be too conservative.

Our meta-analysis has additional limitations. We did not evaluate the quality of the evidence-based information supporting the CDSS recommendations. We accepted study authors' description of a CDSS as evidence-based at face value, even if the authors did not explain the source of evidence or knowledge in detail. Furthermore, the limited number of trials, especially regarding the meta-analysis for the morbidity outcomes, increases the uncertainty of the findings and conclusions. The trials included were conceptually heterogeneous in terms of their design, setting, participants, and interventions, as well as the definition and measurement of outcomes. In addition, although our literature search was as inclusive as possible without the exclusion of studies based on methodological characteristics, the search was restricted to studies published in indexed journals. We did not search for unpublished studies or for source data. Moreover, the trials included in this meta-analysis were not designed to specifically analyze the relationship between mortality and CDSS use. In fact, mortality was additional information provided often as a reason behind loss to follow-up. Additionally, the follow-up was too short to detect a sufficient number of deaths to show potentially relevant differences. Finally, we cannot exclude that pooling the mortality outcome across different settings (e.g., intensive care units versus primary care) could have influenced the overall result toward a null effect with primary care studies bearing larger weight in the meta-analysis.

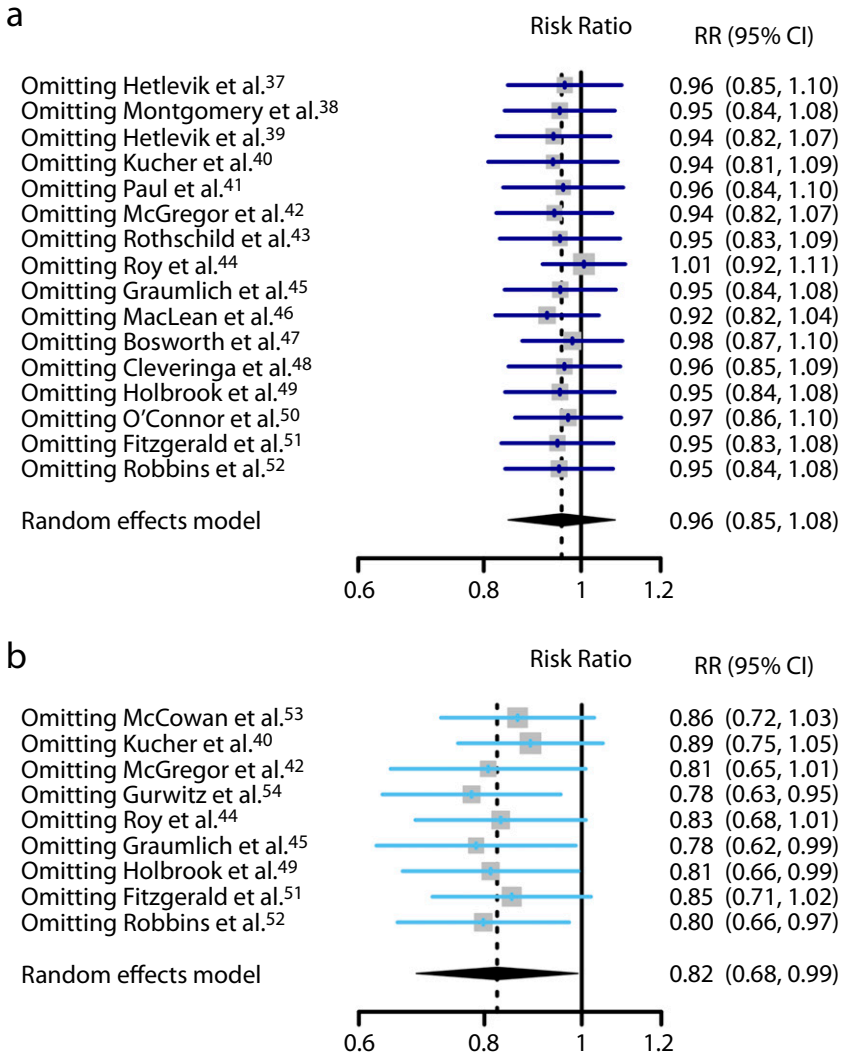
The results of this review may provide sufficient evidence to fuel the debate on the prospects of CDSSs linked to EHRs. For those perceiving CDSSs as an autocratic command to doctors, our systematic review may be interpreted as evidence that they do not affect patient mortality, on average, and should be abandoned. For those interested in CDSS dissemination, our results, which show a decrease in morbidity across all settings by one fifth, may be used as an argument to increase CDSS adoption within health care services. Both interpretations might be exaggerated as the evidence is still in its infancy along with the technology and implementation. Many of the trials adopted locally developed CDSS interventions, which may have compromised their level of integration into clinicians' workflow. The next generation of CDSS trials should focus on systems with a more global outlook featuring authoritative point-of-care services[68] and full integration with EHRs. The conclusion of a landmark article by Sim et al.,[69] published almost 15 years ago, still reflects the current scenario:

> Although the promise of clinical decision support system-facilitated evidence-based medicine is strong, substantial work remains to be done to realize the potential benefits.[69(p527)]

In conclusion, our results on health care services equipped with versus health care not equipped with CDSSs suggest, in broad terms, that this technology does not result in substantial benefits or risks for patients in terms of mortality. This effect, when it occurs, is largely dependent on the disease and setting characteristics. Focusing on subgroup analyses, however, can lead to misleading claims when the overall data are limited and unavoidably weak because of inherent design problems. Effects on morbidity might exist and the magnitude of the effect, in the order of 10% to 20%, could be large enough to impact mortality if appropriate follow-up is ensured. The results of this study may provide enough evidence to advance the debate on the prospects of CDSSs. ■

About the Authors

Lorenzo Moja is with the Department of Biomedical Sciences for Health, University of Milan, and the Unit of Clinical Epidemiology, IRCCS Orthopedic Institute Galeazzi, Milan, Italy. Koren H. Kwag is with the Unit of Clinical Epidemiology, IRCCS Orthopedic Institute Galeazzi, Milan. Theodore Lytras is with the



Note. CI = confidence interval; RR = risk ratio. Pooled estimates are from random-effects models with 1 study omitted at a time.

FIGURE 5—"Leave-one-out" sensitivity analyses for studies with (a) mortality outcomes and (b) morbidity outcomes.

Department of Epidemiological Surveillance and Intervention, Hellenic Centre for Disease Control and Prevention, Athens, Greece, the Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain, and the Department of Experimental and Health Sciences, Universitat Pompeu Fabra, Barcelona. Lorenzo Bertizzolo and Francesca Ruggiero are with the Department of Biomedical Sciences for Health, University of Milan. Linn Brandt is with the Department of Internal Medicine, Inland Hospital Trust, Oslo, Norway, the Department of Internal Medicine, Diakonhjemmet Hospital, Oslo, and HELSAM, University of Oslo. Valentina Pecoraro is with the University of Milan. Giulio Rigon and Alberto Vaona are with Azienda ULSS 20, Verona, Italy. Massimo Mangia is with Medilogy SRL, Milan. Alfonso Iorio is with the Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario. Ilkka Kunnamo is with Duodecim Medical Publications Ltd, Helsinki, Finland. Stefanos Bonovas is with the Laboratory of Drug Regulatory Policies, IRCCS Mario Negri Institute for Pharmacological Research, Milan, and the Department of Pharmacology, School of Medicine, University of Athens, Athens.

Correspondence should be sent to Lorenzo Moja, MD, MSc, PhD, Dr Public Health, IRCCS Orthopedic Institute Galeazzi, Via R. Galeazzi 4, 20161 Milan, Italy (e-mail: lorenzo.moja@unimi.it). Reprints can be ordered at http://www.ajph.org by clicking the "Reprints" link.

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Contributors

All authors participated in conceptualization and design of the study, and critical revision and final approval of the article. L. Moja obtained funding. L. Moja, K. H. Kwag, T. Lytras, L. Bertizzolo, L. Brandt, V. Pecoraro, G. Rigon, A. Vaona, and S. Bonovas collected and assembled the data. L. Moja, K. H. Kwag, T. Lytras, and S. Bonovas analyzed and interpreted the data. L. Moja, K. H. Kwag, and S. Bonovas drafted the article. L. Moja, T. Lytras, and S. Bonovas provided statistical expertise.

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Human Participant Protection

An institutional review board approval was not needed for this systematic review because data were obtained from secondary sources.

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TABLE 1—Impact of Computerized Decision Support Systems (CDSSs) on Costs and Health Services Utilization

Study	Impact Dimension	Outcomes Reported	Reference Time, Months	CDSS Costs[a]	Cost Difference[b]	Variable[c]	Impact[d]
O'Connor et al.[50,e]	Cost-effectiveness	Outpatient and pharmacy costs	12	Year 1: 120; following years: 76	21 690	$/QALY	↑
		Pharmacy costs	12		Dominant	$/QALY	↓
		Pharmacy costs	12		3017	$/QALY	↑
Holbrook et al.[59,f]	Cost-effectiveness	Disease management costs	12	1821	153 169	$/QALY	↑
Subramanian et al.[56]	Cost allocation	Drug order costs	12	. . .	−7.31	Cost/resident-y	↔
		Drug order and laboratory test costs	12	. . .	−4.71	Cost/resident-y	↔
Paul et al.[41]	Cost allocation	Antibiotic costs	6	. . .	−68	Cost per patient	↔
	Health services utilization	Length of hospital stay	6	. . .	−0.62	Days/patient	↓
McGregor et al.[42]	Cost allocation	Antimicrobial costs	3	. . .	−37.64	Cost/patient	↔
	Health services utilization	Length of hospital stay	3	. . .	−1.0	Days/patient	↓
		Time spent to perform interventions		. . .	−0.9	Person-hours/d	↓
Abdel-Kader et al.[57]	Health services utilization	Renal referrals	12	. . .	−6.8%	Absolute change in referrals	↓
		Renal test orders	12	. . .	9.2%	Absolute change in referrals	↑
		Renal drug orders	12	. . .	No difference		↔
Tamblyn et al.[60]	Health services utilization	Psychotropic drug orders	22	. . .	−0.05	Drug unit/patient	↔
Bell et al.[58]	Health services utilization	Hospital visits	24	. . .	0.15	No./patient	↑
		Drug order and laboratory/diagnostic tests	24	. . .	Mixed results	. . .	↑↓
MacLean et al.[46,g]	Cost allocation	Hospital and emergency room costs	1	4	−10.94	Cost/patient/mo	↔
MacLean et al.[46]	Cost allocation	Cost of hospital days and primary/secondary care visits	12	. . .	−2426	Cost for all patients/y	↔
Javitt et al.[61]	Cost allocation	Cost of visits and drug orders	1	. . .	−24.8	Cost per patient/mo	↔
Apkon et al.[62]	Cost allocation	Cost of visits, drug orders, and tests	2	. . .	91	Cost/patient	↑
Tierney et al.[63]	Cost allocation	Outpatient and inpatient charges	12	. . .	Mixed results	Cost/patient	↑↓
Graumlich et al.[45]	Health services utilization	Emergency room visits	6	. . .	−5.2%	Absolute change in visits	↓
McCowan et al.[53]	Health services utilization	Hospital visits	6	. . .	−3%	Absolute change in no. patients	↓
		Primary care visits	6	. . .	−19%	Absolute change in no. patients	↓
		Drug orders	6	. . .	−19%	Absolute change in no. patients	↓
Rothschild et al.[43]	Health services utilization	Length of stay	5-6	. . .	−1.4 (total), −1.8 (ICU)	Days/patient	↓
Cobos et al.[64]	Cost allocation	Costs for disease management	12	. . .	−82	Cost/patient	↓
		Drug order costs	12	. . .	−80	Cost/patient	↓
Gonzales et al.[55]	Health services utilization	Antibiotic drug order	6	. . .	−15.1%	% of patients prescribed antibiotics	↓

Note. ICU = intensive care unit; QALY = quality-adjusted life year.
[a]Costs are reported in US$, per patient. For costs not originally reported in US$, they were converted to US$ at the rate of January 1 of the study's publication year.
[b]When the cost to implement the CDSS was not reported, it was not accounted for in the cost difference between the intervention and control.
[c]If the time period corresponding to the variable was not reported, it was assumed it to be the duration of the follow-up (provided in time horizon).
[d]↑, increase; ↓, decrease; ↔, no change; ↑↓, mixed impacts for this outcome.
[e]Economic analysis in Gilmer et al.[65]
[f]Economic analysis in O'Reilly et al.[66]
[g]Economic analysis in Khan et al.[67]

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