

Standards for reporting randomized controlled trials in medical informatics: a systematic review of CONSORT adherence in RCTs on clinical decision support

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ABSTRACT

Introduction The Consolidated Standards for Reporting Trials (CONSORT) were published to standardize reporting and improve the quality of clinical trials. The objective of this study is to assess CONSORT adherence in randomized clinical trials (RCT) of disease specific clinical decision support (CDS).

Methods A systematic search was conducted of the Medline, EMBASE, and Cochrane databases. RCTs on CDS were assessed against CONSORT guidelines and the Jadad score.

Result 32 of 3784 papers identified in the primary search were included in the final review. 181 702 patients and 7315 physicians participated in the selected trials. Most trials were performed in primary care (22), including 897 general practitioner offices. RCTs assessing CDS for asthma (4), diabetes (4), and hyperlipidemia (3) were the most common. Thirteen CDS systems (40%) were implemented in electronic medical records, and 14 (43%) provided automatic alerts. CONSORT and Jadad scores were generally low; the mean CONSORT score was 30.75 (95% CI 27.0 to 34.5), median score 32, range 21–38. Fourteen trials (43%) did not clearly define the study objective, and 11 studies (34%) did not include a sample size calculation. Outcome measures were adequately identified and defined in 23 (71%) trials; adverse events or side effects were not reported in 20 trials (62%). Thirteen trials (40%) were of superior quality according to the Jadad score (≥ 3 points). Six trials (18%) reported on long-term implementation of CDS.

Conclusion The overall quality of reporting RCTs was low. There is a need to develop standards for reporting RCTs in medical informatics.

INTRODUCTION

Randomized controlled trials (RCTs) are considered the gold standard for investigating the results of clinical research because they inherently correct for unknown confounders and minimize investigator bias.^{1–3} The results of these trials can have profound and immediate effects on patient care. When RCTs are reported, it is recommended that the Consolidated Standards of Reporting Trials (CONSORT)⁴ are followed. CONSORT was first published in 1996 and has been revised several times since.⁵ The CONSORT statement is widely supported and has been translated into several

languages to facilitate awareness and dissemination. An extension of the CONSORT statement was published in 2008, focusing on randomized trials in non-pharmacologic treatment.⁶ CONSORT consists of a checklist of information to include when reporting on an RCT; however, inadequate reporting remains common among clinicians.^{6–12} Higher quality reports are likely to improve RCT interpretation, minimize biased conclusions, and facilitate decision making in light of treatment effectiveness.¹ Furthermore, there is evidence that studies of lower methodological quality tend to report larger treatment effects than high quality studies.^{13–15}

Research on clinical decision support (CDS) tools has rapidly evolved in the last decade. CDS provides clinicians with patient specific assessment or guidelines to aid clinical decision making¹⁶ and improve quality of care and patient outcome.^{17–18} CDS has been shown to improve prescribing practices,¹⁹ reduce serious medication errors,^{20–21} enhance delivery of preventive care services,²² and improve guidelines adherence,²³ and likely results in lasting improvements in clinical practice.²⁴ However, clinical research on CDS tools faces various methodological problems^{25–28} and is challenging to implement in the field of health informatics.²⁹ Guidelines for reporting studies in health informatics have been published,²⁶ but there is no universal consensus.

Numerous RCTs examining (disease specific) CDS tools aimed at improving patient treatment have been performed. It is unclear whether these studies provided CONSORT statements when the trials were reported. Although several studies have evaluated the quality of RCTs in medical journals,^{3–7,8} to date none have been directed at medical informatics literature published in dedicated journals. The objective of this paper is to perform a systematic review of RCTs to assess the quality of clinical CDS research focusing on disease specific interventions. We aimed to score the identified RCTs according to the CONSORT⁶ checklist and Jadad score.³ Finally, we discuss the implications of these results in the context of evidence-based medicine.

MATERIALS AND METHODS

The review followed the PRISMA statements (Preferred Reporting Items for Systematic Reviews



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and Meta-Analyses)³⁰ and was divided into two work phases: (a) identification of RCT trials assessing disease specific CDS and (b) data extraction and assessment of RCT quality.

The Study Group of Research Quality in Medical Informatics and Decision Support (SQUID) is a multidisciplinary study group. Members have expertise in hospital medicine (KL, ROL, KMA), RCTs in medicine (surgery) (KL),³¹ RCTs in telemedicine (RW),³² trials of medical informatics (JGB, KMA),^{33–37} and epidemiological research (GB).^{38–41} The group's objective is to assess and improve the quality of clinical informatics research with special focus on randomized controlled trials aimed at enhancing physician performance.

We defined CDS as 'any electronic or non-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 subsequently presented to clinicians for consideration.'⁴² We defined disease specific CDS as 'a clinical decision support aimed at a specific disease, describing symptoms, diagnosis, treatment, and follow-up.'

Search strategy

This systematic review is based on a PubMed, EMBASE, and Cochrane Controlled Trials Register search using EndNote X3 (EndNote, San Francisco, California, USA) for relevant publications published through November 2010. We piloted search strategies and modified them to ensure they identified known eligible articles. We combined keywords and/or subject headings to identify CDS (*clinical decision support system, computer-assisted decision making, computer-assisted diagnosis, hospital information systems*) in the area of RCTs (ie, *randomized controlled trial*). We searched publications accessible from the web pages of the *International Journal of Medical Informatics, Journal of the American Medical Informatics Association, and BMC Medical Informatics and Decision Making*. We systematically searched the reference lists of included studies. Reviews addressing CDS were investigated and papers fulfilling the inclusion criteria were included.^{17 42–44} The searches were individually tailored for each database or journal. Experienced clinicians reviewed all search hits and decided whether a CDS was aimed at a specific disease and fulfilled inclusion criteria. The titles, index terms, and abstracts of the identified references were studied and each paper was rated as 'potentially relevant' or 'not relevant.' Disagreements regarding inclusion were resolved by discussion. Only trials performed the last 10 years were included.

Inclusion criteria were:

- ▶ Randomized controlled trial
- ▶ CDS describing specific diseases and treatment guidelines
- ▶ CDS aimed at physicians.

Exclusion criteria were:

- ▶ Papers published before the year 2000
- ▶ Not published in English
- ▶ Proceedings, symposium, and protocol papers.

The search strategy yielded 3784 papers. We retrieved and reviewed the full text of 364 papers; 32 papers^{45–76} were included in the final review (figure 1).

Assessing RCT quality

Scoring according to CONSORT

A checklist of 22 items from the revised 2001 CONSORT guidelines was analyzed.^{4–6} The score for each item ranged from 0 to 2 (0=no description, 1=inadequate description, 2=adequate description). The maximum score a paper could obtain was 44 points.

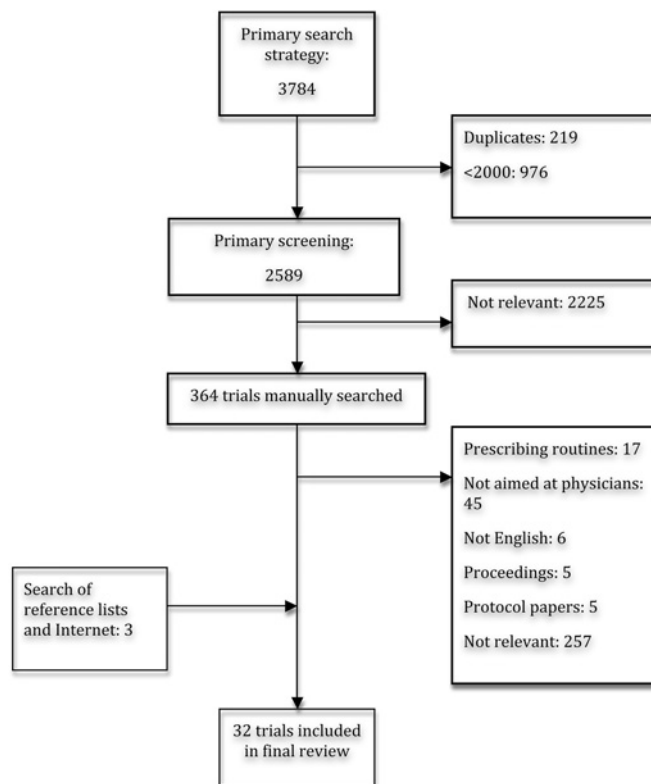


Figure 1 Selection process of randomized controlled trials of disease specific clinical decision support.

Each article was then assessed for every item on the checklist and scored independently by two observers (KMA and GB). The scores for the 22 items were added together and a percentage score for each trial was calculated.

Scoring according to Jadad

The Jadad scale is a 5-point scale for evaluating the quality of randomized trials in which three points or more indicates superior quality.³ The Jadad scale is commonly used to evaluate RCT quality.^{7 8} The scale contains two questions each for randomization and masking, and one question evaluating reporting of withdrawals and dropouts.

Scoring according to the sequential phases of a complex intervention

An RCT evaluating a CDS tool is defined as a complex intervention, that is an intervention consisting of various inter-connecting parts.^{29 77–79} Campbell *et al*⁷⁷ suggested four sequential phases for developing RCTs for complex interventions: *theory, modeling, exploratory trial, definitive randomized controlled trial, and long-term implementation*. Included trials were scored according to these sequential phases, that is one point was given for each phase.

Scoring according to CDS features critical for success

Kawamoto *et al* identified certain CDS factors associated with clinical improvement.⁴² These factors are: *automatic provision of CDS, CDS at the time and location of decision making, provision of a recommendation rather than just an assessment, computer based assessment, and automatic provision of decision as part of clinician workflow*. The identified CDS tools were scored according to these factors, giving one point for each feature.

All appraised papers were discussed by the two reviewers and, if necessary, by a third independent reviewer to verify the

appraisal process and resolve disagreement; when consensus could not be reached, the third reviewer assessed the items and provided the tiebreaker score.

Statistics

Trial characteristics and CONSORT adherence were analyzed and interpreted with the trial as unit of analysis. Descriptive statistics were analyzed using percentages, standard deviation, confidence intervals, 2×2 contingency tables, χ^2 test, and Fisher's exact test when appropriate. We used proportions for categorical variables and mean for continuous variables. For reasons of comparison, trials were divided into groups according to whether or not their outcome was positive. A positive outcome was defined as either a primary or secondary outcome with $p < 0.05$. All tests were two-sided and a probability (p) value of < 0.05 was considered statistically significant. Microsoft Excel and SPSS PASW Statistics v 18.0 were used for the statistical analyses.

RESULTS

Clinical features

Of 3784 potentially relevant articles screened, 32 papers met all our inclusion criteria (table 1).

Fourteen (43%) of the trials were performed in the US, seven (21%) in the Netherlands, and four (12%) in the UK. Four of the trials were published in medical informatics journals, and the rest in medical journals. The trials included 181 702 patients and 7315 physicians. The majority (22 trials) were performed in primary care, including 897 general practitioner (GP) offices. Of the 11 trials performed at hospital level, two were performed in an outpatient department, three in internal medicine departments, one in a surgical department, one in an intensive care unit, two in emergency departments, one in a trauma unit, and one in various different departments. Asthma ($n=4$), diabetes ($n=4$), and hyperlipidemia ($n=3$) were the most common diseases addressed (table 1).

General trial features

Twenty-six trials (81%) did not provide an RCT registration number (ie, <http://Clinicaltrials.gov> and others), while only seven trials (21%) offered web access to the full trial protocol. One trial did not state funding sources (table 2). In nine trials (28%), more than half of the authors were medical doctors; in 10 trials, information on the background and education of the author(s) was not provided. Twenty-two (68%) trials chose a cluster-randomized design, which was the most common design among trials in primary care (21 of 22). Of the nine trials performed in a hospital setting, four had a cluster-randomized design and in these cases the department was chosen as the clustering unit. Two trials provided information on changes to the trial protocol, and one trial addressed CONSORT guidelines.

CDS features

Less than half of the CDS tools were implemented in an electronic medical record, and 14 (43%) of the CDS tools provided automatic alerts (table 2). Twenty-four (75%) of the developed CDS tools provided decision support at the time and location of the decision need. Eighteen (56%) of the CDS tools did not disrupt the natural workflow of the physician. None of these CDS features had a significant influence upon the primary endpoint or overall conclusions.

Addressing sequential phases of a complex intervention

None of the trials defined the intervention as complex or discussed the definition of a complex intervention.^{77 78 80} Four

trials defined all phases of a complex intervention and these phases were described in detail (table 2).

Trials reporting on long-term CDS implementation

Six trials reported on the long-term implementation of the CDS tool used in the RCT (table 1).

Four of these trials addressed all phases of a complex intervention and had a statistically higher CONSORT score compared to trials not reporting long-term implementation (OR 1.64, $p=0.04$). Three of these trials were performed at a hospital level, with the largest trial including 87 000 patients.

Inter-rater reliability and CONSORT score

The intraclass correlation coefficient used to establish inter-rater reliability was 0.69 for the 22-item CONSORT scale. The mean CONSORT score was 30.75 (95% CI 27.0 to 34.5), median score 32, range 21–38.

CONSORT: title, abstract, and background

Five trials did not identify a randomized design in their title. All trials had a structured abstract and gave a solid background and rationale for the trial (table 3).

CONSORT: materials and methods

One trial addressed the CONSORT guidelines in their Material and Methods section. Twenty-seven trials (84%) clearly defined their participants, eligibility, and ethics approval. Fourteen trials (43%) did not clearly define the study objective or hypothesis. Twenty-three trials (72%) had an adequate definition of outcome measures. Fourteen studies (37%) did not perform or had an inadequate sample size calculation (table 3).

CONSORT: randomization

Most trials described mechanisms to generate random allocation (59%) and the method of implementing the random sequence (47%). In contrast, only five trials (15%) gave adequate information regarding blinding (whether or not blinding was necessary and if necessary, how it was performed) (table 3).

CONSORT: results

Most trials (87%) provided a detailed description of statistical methods (table 3). Five trials had no figure showing participant flow and four trials did not include a table showing demographics. Nine trials did not address exclusions during the trial, and 10 trials did not define the date of trial initiation and termination. Only two trials performed an interim analysis, and only one trial addressed the 'harms or unintended effects' of the intervention.

CONSORT: discussion

The interpretation of results was justified in 28 trials (87%). Four trials did not discuss limitations and six trials did not address generalizability or provide recommendations for the future (table 3).

Jadad score

Thirteen trials (40%) were classified as superior quality trials (≥ 3 points). Nineteen (59%) described the study as randomized, and the sequence of randomization was explained and was appropriate. Twenty-seven (85%) did not describe blinding. Ten (32%) did not describe dropouts (table 4).

DISCUSSION

Summary of findings

This is the first review assessing the quality of RCTs of disease specific CDS as a primary intervention. We have analyzed their

Table 1 Summary of 32 RCTs on disease specific clinical decision support systems

Author	Author MD/total	Setting	Disease	Country	Sample	Primary outcome (PO)	Effect of PO (CI, p value)	Overall conclusion	Journal
Apkon <i>et al</i> (2005) ⁴⁶	5/11	Hospt	Multiple diseases	USA	1902 pts, 4639 consul	% of 24 healthcare quality process measures	NE	NE	Clinical
Bell <i>et al</i> (2010) ⁴⁷	6/9	GP	Asthma	USA	12 offices, 19450 pts	Updated asthma care plan	14% (0.03)	CDS improved adherence to guidelines	Clinical
Bertoni <i>et al</i> (2009) ⁴⁵	4/9	GP	Hyperlipidemia	USA	61 offices, 5057 pts	Proportion of patients screened with appropriate decision making	10% (2.8% to 16.6%, 0.01)	Improved adherence to guidelines	Clinical
Bosworth <i>et al</i> (2008) ⁴⁸	3/10	GP	Blood pressure	USA	32 GPs, 588 pts	% <140/90 mm Hg, 2-year follow up	NE	NE	Clinical
Cleveringa <i>et al</i> (2008) ⁴⁹	3/4	GP	Diabetes	Netherl.	55 offices, 3391 pts	A1C levels	NE	NE on A1C levels, but reduced cardiovascular risk	Clinical
Dexter <i>et al</i> (2001) ⁵⁰	4/6	Hospt	Pneumococcal influenza vaccination, thrombo-embolism	USA	202 phys, 10065 pts	Rates of preventive therapies ordered	35% (0.001)	Increased preventive treatment	Clinical
Emery <i>et al</i> (2007) ⁵¹	NA/10	GP	Genetic risk assessment	Australia	45 offices	% of referrals consistent with guidelines	OR 5.2 (1.7 to 15.8, 0.006)	Increased number and quality of referrals	Clinical
Feldstein <i>et al</i> (2006) ⁵²	3/8	GP	Osteoporosis	USA	159 GPs, 311 pts	% BMD measurement	45% (0.001)	Increased BMD measurement	Clinical
Flottorp <i>et al</i> (2002) ⁵³	NA/5	GP	UVI sore throat	Norway	142 offices, >20000 consul	Rate of AB use	-6% (0.032)	Little overall effect on changing practice	Clinical
Frijling <i>et al</i> (2002) ⁵⁴	NA/8	GP	Diabetes	Netherl.	185 GPs, 2800 consul	Rate of foot and eye examination	OR 1.68 (1.19 to 2.39)	Increase rates of foot and eye examination	Clinical
Gilutz <i>et al</i> (2009) ⁵⁵	13/15	GP	Hyperlipidemia	Israel	112 offices, 448 pts	Appropriate lipoprotein monitoring	6% (<0.001)	Facilitated adherence to guidelines	Clinical
Hicks <i>et al</i> (2008) ⁵⁶	5/7	GP	Blood pressure	USA	14 GP offices, 2027 pts	Blood pressure	NE	No reduction in BP but better prescribing routines	Clinical
Holbrook <i>et al</i> (2009) ⁵⁷	4/9	GP	Diabetes	Canada	46 GPs, 511 pts	Process composite score (PCS)	PCS 1.27 (0.79 to 1.75, 0.001)	Improved process of care and some clinical markers	Clinical
Kuilboer <i>et al</i> (2006) ⁵⁸	NA	GP	Asthma	Netherl.	32 offices, 40 GPs, 10863 pts	Contact frequency	10% (0.034)	Improved adherence to guideline	Clinical
McGovern <i>et al</i> (2008) ⁶⁰	NA/4	GP	Multiple diseases	Canada	88 GPs	Impact assessment scores	48% (no p value)	CDS positive impact on decision making	Clinical
McKinley <i>et al</i> (2000) ⁶¹	4/10	Hospt	Acute respiratory distress syndrome	USA	67 pts	Survival and ICU stay	No negative impact on survival	Effectively standardized ventilator management	Clinical
Maclean <i>et al</i> (2009) ⁵⁹	1/4	GP	Diabetes	USA	132 GPs, 64 GP offices, 7412 pts	Glycemic control mean A1C and A1C <7%	NE	CDS feasible for patients and providers but no physiologic effect	Clinical
Mulvaney <i>et al</i> (2008) ⁶²	1/7	Hospt	Several diseases	USA	226 phys	Action index, CDS induced different or new treatment	OR 8.19 (1.04 to 64.0)	Treatment issues were significantly impacted by CDS	Informa
Poels <i>et al</i> (2007) ⁶³	NA/8	GP	Asthma	Netherl.	78 GPs	GP diagnosis was compared with an expert panel judgment	OR 1.08 (0.70 to 1.8)	NE	Clinical
Rollman <i>et al</i> (2002) ⁶⁴	3/6	GP	Depression	USA	200 pts	Hamilton rating scale for depression	NE	Little effect on patients and providers' achievement	Clinical
Rosenbloom <i>et al</i> (2005) ⁶⁵	5/9	Hospt	Several diseases	USA	202 phys	Rates of opportunity, access, and utilization of CDS	NE	Increased CDS utilization	Informa
Roukema <i>et al</i> (2008) ⁶⁶	3/4	Hospt	High fever in children	Netherl.	164 pts	Total ED time	NE	Increased guideline adherence, increased ED stay	Informa
Roy <i>et al</i> (2009) ⁶⁷	11/13	Hospt	Pulmonary embolism	France	20 hospt, 1015 pts	% sequence of tests that yielded a post-test probability <5%	19% (2.9% to 35%, 0.023)	Improved diagnostic decision making	Clinical
Thomas <i>et al</i> (2003) ⁶⁸	NA/7	GP	Urology	UK	66 offices, 959 pts	Guideline compliance	Increase 0.5 points (0.2 to 0.8, 0.001)	Improved process of out-patient referral	Clinical

Continued

Table 1 Continued

Author	Author MD/total	Setting	Disease	Country	Sample	Primary outcome (PO)	Effect of PO (CI, p value)	Overall conclusion	Journal
Tierney <i>et al</i> (2005) ⁶⁹	4/10	Hospit	Asthma	USA	246 phys, 706 pts	Adherence to guideline based care suggestions	NE	NE	Clinical
Unrod <i>et al</i> (2006) ⁷⁰	0/6	GP	Addiction	USA	70 GPs, 518 pts	Physician adherence guidelines	OR 5.0 (3.22 to 7.95, 0.001)	Improve physician guidance and increased patient quit rates	Clinical
van Steenkiste <i>et al</i> (2007) ⁷¹	NA/6	GP	Cardiovascular disease	Netherl.	34 GPs, 490 pts	Five performance indicators	NE	NE	Clinical
van Wyk <i>et al</i> (2007) ⁷²	4/7	GP	Hyperlipidemia	Netherl.	38 offices, 77 GPs, 87886 pts	% pts screened and treated in 12 months	40%, RR 1.76 (1.41 to 2.20)	Reduced lipid levels effectively	Clinical
Watson <i>et al</i> (2001) ⁷³	1/8	GP	Cancer	UK	170 offices, 426 GPs	% GPs making correct referral decision	40% (30% to 50%, 0.001)	CDS improved referral quality	Clinical
Weir <i>et al</i> (2002) ⁷⁴	NA	Hospit	Ischemic stroke	UK	16 hospit, 1952 pts	% pts with optimal therapy	OR 1.32 (0.8 to 1.8)	NE	Clinical
Whelan <i>et al</i> (2004) ⁷⁵	4/10	Hospit	Breast cancer	Canada	20 surgeons, 208 pts	Pts knowledge of surgical treatment	8% (0.001)	Patients using CDS were more likely to choose BCT	Clinical
Wilson <i>et al</i> (2006) ⁷⁶	NA/11	GP	Genetics/breast cancer	UK	86 offices, 346 GPs	GP self-reported confidence level	NE	NE	Clinical

The trials included 181 702 patients and 7315 physicians. The majority (22 trials) were performed in primary care including 897 GP offices. Of the 11 trials performed at hospital level, two were performed in an outpatient department, three in internal medicine departments, one in a surgical department, one in an intensive care unit, two in emergency departments, one in a trauma unit and one in various different departments.

AB, antibiotics; BCT, breast conserving therapy; BMD, bone mineral density; BP, blood pressure; consul, consultation; ED, emergency department; GP, general practitioner; hospit, hospital; MD, medical doctor; NA, no information available; NE, no effect; Netherl, the Netherlands; phys, physicians; PO, primary outcome; pts, patients; RCT, randomized controlled trial; UVI, urinary tract infection; UK, United Kingdom.

outcome, CONSORT adherence and Jadad score. Methodologically, research quality varies and adherence to CONSORT guidelines is low for certain checklist items. Thirteen trials (40%) were classified as superior quality trials according to their Jadad score (≥ 3 points). According to our analysis, there is considerable room for improving methodology in areas such as the description of specific research objectives, randomization methods, sample size calculations, reporting of adverse events, and a general focus on CONSORT. Similarly, the Jadad score was low on several checklist items. Surprisingly few studies defined their CDS intervention as a complex intervention; only four studies described all phases of a complex intervention including long-term implementation.

Research challenges of complex interventions

A complex intervention was defined by Cambell *et al*^{77 81} as an intervention that is 'built up from a number of components, which may act both independently and interdependently.' Similarly, Campbell defined an intervention with a decision support system as a complex intervention.⁷⁷ In 2000, the Medical Research Council in the UK proposed a framework for the development and evaluation of RCTs for complex interventions (theory, modeling, exploratory trial, definitive RCT, long-term implementation),⁷⁷ which was further improved in 2007.⁸¹ The methodological challenges of complex interventions have been thoroughly discussed in the field of medical informatics,^{25 29} as well in the area of health service research.^{79 82–85} There have been arguments against over-standardization of complex interventions. Complex and large health organizations are characterized by flux, contextual variation, and adaptive learning rather than stability, and a standardized approach will not fit such organizations.⁸⁶ However, our review shows that most trials do not address the term 'complex intervention' and as many as 23 trials (71%) did not perform an exploratory trial before the definitive RCT. This problem is well discussed by Friedman, who introduces the 'tower of achievements'.⁸⁷ According to Friedman, integration across research phases is of utmost importance to success in the field.

Quality of RCTs in medical informatics versus clinical trials

Our survey shows generally low CONSORT adherence and only 13 trials were defined as superior quality trials according to their Jadad score. However, the research quality of RCTs has been of varying quality in medical research as well. In a review from 2006⁸ assessing 69 RCTs of surgery, only 37% of trials were classified as of superior quality. CONSORT scores were generally low but significantly higher in trials with higher author numbers, multi-centre trials, and trials with a declared funding source.⁸ It has been concluded that there is a need to improve awareness of the CONSORT statement among authors, reviewers, and editors.⁸ Similar concerns were recently reported in several medical journals, which concluded that there was low adherence to key methodological items.^{88–90} These conclusions from the medical literature are in accordance with our review findings.

Strength and limitations of our study

This study has several important strengths. First, our literature search was thorough and we screened more than 3700 articles. Second, this is the first review to evaluate the general trial quality and CONSORT adherence of RCTs evaluating CDS tools as a clinical intervention. Research on CDS tools is methodologically challenging.²⁸ Thus, a focus on research methods in medical informatics is important, and adherence to CONSORT

Table 2 Characteristics of RCTs of clinical decision support and impact on outcome and implementation

	Outcome +, n=24 (%)	Outcome −, n=8 (%)	Total, n=32 (%)
General trial features			
Protocol access	7 (29)	0	7 (21)
Identification of RCT number	6 (25)	0	6 (18)
Funding sources identified	23 (95)	8 (100)	31 (96)
>50% MD authors	8 (33)	1 (12)	9 (28)
Primary care	17 (70)	5 (62)	22 (68)
Clustered design	18 (75)	4 (50)	22 (68)
Patients	158 240	23 462	181 702
Participating MDs	2270	846	3116
CDS feature			
CDS time/location of decision	17 (70)	7 (87)	24 (75)
Automatic alert	11 (45)	3 (37)	14 (43)
Implemented in EMR	10 (41)	3 (37)	13 (40)
No disruption to workflow	15 (62)	3 (37)	18 (56)
All features present	8 (33)	0	8 (25)
Phases of complex interventions			
Theory	24 (100)	8 (100)	32 (100)
Modeling	8 (33)	5 (62)	13 (40)
Exploratory trial	7 (29)	2 (25)	9 (28)
Definitive RCT	24 (100)	8 (100)	32 (100)
Long-term implementation	4 (16)	2 (25)	6 (18)
All phases present	3 (12)	1 (12)	4 (12)
RCT assessment tool			
CONSORT score mean (SD)	29.9 (4.7)	33.1 (3.9)	30.7 (4.7)
Jadad score mean (SD)	2.0 (1.5)	2.75 (1.6)	2.2 (1.5)

Outcome + is defined as either a positive primary or positive secondary endpoint ($p < 0.05$). There were no significant differences between Outcome + and Outcome −. CDS, clinical decision support; EMR, electronic medical record; MDs, medical doctors, including hospital physicians and general practitioners; RCT, randomized controlled trial.

has never been assessed. Third, we are currently recruiting patients into an RCT addressing the use of disease specific CDS tools³⁷ and thus have experienced the inherent methodological challenges. In addition to technological problems, these trials also face the challenges of a complex intervention. These research questions have been addressed in this review.

One limitation of our study might be that only RCTs assessing CDS systems aimed at physicians were included. However, when planning this review, the research group wanted to identify CDS trials to improve patient treatment as these trials should ideally adhere to research conventions in general medical society. In this context the research group felt it natural to exclude CDS not addressing physicians.

Another limitation might be the reporting of the various phases in a complex intervention. Our review shows that only six trials (18%) report on long-term implementation. However, all studies were RCTs and thus were in the stage prior to implementation. It may be that implementation did occur after the RCT was published but was not part of the publication. It might also be that some providers implemented their long-term intervention, but as the RCT did not support this, they were reluctant to report on it. Similarly, it is possible that theoretical and preliminary work might have been carried out but was not fully described in an RCT paper.

Finally, it is unclear whether or not 'complex intervention' is a term widely accepted in medical informatics circles. We identified the term 'complex intervention' in one *JAMIA* article from 2008, with the other mentions of this concept all being in *BMJ*. Since *JAMIA* readership is largely within the US, it is unclear whether it is mandatory for CDS and their evaluation to be declared as complex interventions and thus follow the required phases.

Table 3 The CONSORT checklist: scoring of 32 RCT trials of disease specific clinical decision support systems

Item*	Description	No description, n (%)	Inadequate, n (%)	Adequate, n (%)
1	Allocation (eg, 'random allocation,' 'randomly assigned,' or 'randomized')	0	5 (15.6)	27 (84.4)
2	Justification	0	3 (9.4)	29 (90.6)
3	Eligibility criteria for participants and location of data collection	2 (6.3)	3 (9.4)	27 (84.4)
4	Details and timing of interventions	8 (25.0)	2 (6.3)	22 (68.8)
5	Specific objectives and hypotheses	3 (9.4)	11 (34.4)	18 (56.3)
6	Identification and definition of outcome measures	4 (12.5)	5 (15.6)	23 (71.9)
7	Prestudy sample size calculation	11 (34.4)	3 (9.4)	18 (56.3)
8	Method of generation of the random sequence	5 (15.6)	8 (25.0)	19 (59.4)
9	Method of implementation of the random sequence	10 (31.3)	7 (21.9)	15 (46.9)
10	Details of personnel involved in recruitment, allocation, and outcome measurement	14 (43.8)	7 (21.9)	11 (34.4)
11	Whether subjects, treatment providers, or assessors/analysts were blinded	24 (75.0)	3 (9.4)	5 (15.6)
12	Statistical methods	0	4 (12.5)	28 (87.5)
13	Flow of participants through each stage	5 (15.6)	2 (6.3)	25 (78.1)
14	Dates defining the periods of recruitment and follow-up	9 (28.1)	1 (3.1)	22 (68.8)
15	Baseline demographic and clinical characteristics of each group	4 (12.5)	0	28 (87.5)
16	Number of participants in each group analysis; whether the analysis was by 'intention to treat'	1 (3.1)	16 (50.0)	15 (46.9)
17	Complete reporting of results with CIs	2 (6.3)	12 (37.5)	18 (56.3)
18	Multiple testing and corrections	0	0	0
19	All important adverse events or side effects	20 (62.5)	11 (34.4)	1 (3.1)
20	Interpretation of the results, including trial limitations and weaknesses	1 (3.1)	3 (9.4)	28 (87.5)
21	Generalizability (external validity) of the trial findings	1 (3.1)	5 (15.6)	26 (81.3)
22	General interpretation of the results in the context of current evidence	0	1 (3.1)	31 (96.9)

The mean CONSORT score for the 32 included trials was 30.75 (95% CI 27.0 to 34.5), median score 32, range 21–38. The intraclass correlation coefficient used to establish inter-rater reliability was 0.69. All appraised papers were discussed by the two reviewers and, if necessary, by a third independent reviewer to verify the appraisal process and resolve disagreement; when consensus could not be reached, the third reviewer assessed the items and provided the tiebreaker score.

*Score for each item: 0=no description, 1=inadequate description, 2=adequate description; maximum score=44. RCT, randomized controlled trial.

Table 4 The Jadad instrument: scoring of 32 RCT trials of disease specific clinical decision support systems

Item*	Description	% max score (n)	% 0 points (n)
1	Was the study described as randomized? Additional point if the method for generating the sequence of randomization was described and it was appropriate Deduct 1 point if the method for generating the sequence of randomization was described and it was inappropriate	59 (19)	41(13)
2	Was the study described as double blind? Additional point if the method of double-blinding was described and it was appropriate Deduct 1 point if the method of double-blinding was described and it was inappropriate	15 (5)	85 (27)
3	Was there a description of withdrawals and dropouts?	68 (22)	32 (10)

Results: 5 points: 5 trials (15%); ≥ 3 points: 13 trials (40%).

*Yes=1, for a total of 5 possible points; ≥ 3 points indicates a superior quality trial.
RCT, randomized controlled trial.

Challenges of RCTs in medical informatics

Recently, Liu²⁸ discussed the pros and cons of RCTs in medical informatics. We agree with their view that RCTs are not the only method for evaluation. Medical informatics interventions are usually performed in a complex organizational environment. In this context, there is a need for different research methods, and often a mixture of qualitative and quantitative methods, depending on the research subject. However, when an RCT is deemed the proper design, standards of reporting must be followed. In addition, RCTs in medical informatics face several methodological challenges, some of which have been clarified in this review.

Choice of outcome measures

In principal, outcomes can either be patient orientated, process orientated, or system orientated. The choice of outcome measures should be clearly related to the research question. Our review shows a large mixture of primary outcomes, which makes meta-analyses of effects impossible. Thus, a clear conclusion regarding the effects of CDS (in the form of a meta-analyses) cannot be reached.

Sample size calculations

The planning of an RCT should begin with sample size calculation. This assessment is closely related to the choice of primary outcome, as different primary outcomes can result in different sample size estimates. The sample estimate is crucial to determine the resources and time needed to conduct a properly designed RCT with enough power to reject or accept the null hypothesis. Kiehan *et al*⁷ address concerns about the poor standards of reporting sample size calculations. They conclude that many of these trials are flawed from the start due to inadequate power to assess any real difference between interventions. In this review, approximately 50% of the trials had an inadequate estimate of sample size, a surprisingly low number.

Randomization

Should randomization be performed at an individual or an organizational level? In this review, 68% preferred a clustered design, clustered at the level of hospitals, departments, or GP offices. There are obvious advantages to a cluster design in complex health organizations, as problems of blinding and random sequence implementation will be avoided. In addition, clustering randomization is usually less demanding of resources, as randomization can be performed before the actual trial period with fewer personnel involved.

Conclusion

The research methodology in the identified trials is of low quality, suggesting a need for increased focus on the methods of

conducting and reporting RCT trials. Study designs that adhere to CONSORT are not always appropriate in medical informatics research.²⁶ However, RCTs evaluating CDS tools in a clinical setting should adjust to the accepted consensus. Thus, CONSORT guidelines for conducting RCT trials should be addressed and subsequently implemented in the trial. CONSORT guidelines for non-pharmacological treatment⁶ provide a solid basis for reporting RCTs evaluating CDS systems, but an adjustment for medical informatics is needed. The societies for medical informatics should aim for a consensus statement to improve the quality of reporting RCTs, trials of informatics applications, and CDS.

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Competing interests None

Ethics approval No patients were involved in the survey and thus approval by the hospital IRB board was not required.

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