Features predicting the success of computerized decision support for prescribing: a systematic review of randomized controlled trials

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Abstract

Background: Computerized decision support systems (CDSS) are believed to have the potential to improve the quality of health care delivery, although results from high quality studies have been mixed. We conducted a systematic review to evaluate whether certain features of prescribing decision support systems (RxCDSS) predict successful implementation, change in provider behaviour, and change in patient outcomes.

Methods: A literature search of Medline, EMBASE, CINAHL and INSPEC databases (earliest entry to June 2008) was conducted to identify randomized controlled trials involving RxCDSS. Each citation was independently assessed by two reviewers for outcomes and 28 predefined system features. Statistical analysis of associations between system features and success of outcomes was planned.

Results: Of 4534 citations returned by the search, 41 met the inclusion criteria. Of these, 37 reported successful system implementations, 25 reported success at changing health care provider behaviour, and 5 noted improvements in patient outcomes. A mean of 17 features per study were mentioned. The statistical analysis could not be completed due primarily to the small number of studies and lack of diversity of outcomes. Descriptive analysis did not confirm any feature to be more prevalent in successful trials relative to unsuccessful ones for implementation, provider behaviour or patient outcomes.

Conclusion: While RxCDSSs have the potential to change health care provider behaviour, very few high quality studies show improvement in patient outcomes. Furthermore, the features of the RxCDSS associated with success (or failure) are poorly described, thus making it difficult for system design and implementation to improve.
Background
Prescribing skills are core to the practice of medicine. As in most developed countries, prescription drugs are currently the fastest growing cost category in Canadian healthcare, exceeding $22 billion annually and increasing at 10.5% yearly [1]. With this increase in medication prescribing follows the potential for adverse drug events, including prescribing errors. It is estimated that medication errors occur in 57 per 1000 orders, with 18.7 - 57.7% of these errors having the potential for harm [2]. The suggestion that detection of preventable errors by healthcare professionals could improve patient safety and reduce the cost of adverse drug events [3], has been sufficient to spawn a multitude of medication safety initiatives with limited rigorous evaluation of their benefits and harms. Although they have several uses, the main interest in electronic health records (EHR) and computerized decision support systems (CDSS) is to improve patient outcomes by influencing the decision making process of providers [4-6]. CDSS provide patient-specific advice by using algorithms to compare patient characteristics against a knowledge base [7-9]. Prescribing CDSS (RxCDSS) specifically deal with medications and can support basic (e.g. checking for drug-drug interactions) to complex (e.g. integrating patient-specific diagnoses, risk factors, and prior treatments to make a drug recommendation) functions [10]. These systems may include, but do not require, a formal e-prescribing link with pharmacies.

Reviews evaluating the literature surrounding decision support have noted that technologies have the potential to improve practitioner performance, but effects on patient outcomes are still unclear [11-15]. Several features have been linked with successful clinical decision support. These include use of a computer to generate the decision support based on automated EHR data analysis, including provision of recommendations instead of just assessments, and provision of the decision support at the time and location of decision-making and in synchrony with usual clinician workflow [11,12,14,15].

However, only one of these reviews [14] limited their analysis to high quality evidence (randomized controlled trials). None of the reviews systematically separated outcomes by their natural hierarchy of difficulty – system implementation, provider behaviour change and patient outcomes, and focused on features predicting success versus failure for each outcome domain. Finally, while one review was limited to drug order entry systems [14], no study to date has examined all RxCDSS irrespective of the presence of this system feature.

Our objective was to conduct a systematic review of randomized trials, to evaluate the effectiveness of RxCDSS using a hierarchical approach to defining success, and to determine which features of system design or implementation were associated with the success or failure of RxCDSS implementation, change in provider behaviour, and change in patient outcomes.

Methods
The two primary research questions of this review were: (1) When evaluated rigorously in randomized controlled trials, have current RxCDSS successfully been implemented and altered physician prescribing or patient outcomes? Furthermore, (2) what features of these RxCDSS are associated with success versus failure? Based on the literature and our own experience, we hypothesized that: a) high quality studies of RxCDSS may report successful implementation, but fewer have changed prescriber behaviour and fewer still have demonstrated improved patient outcomes and b) a number of RxCDSS features will be associated with successful versus unsuccessful outcomes as defined above.

RxCDSS Features
Potentially important features were identified primarily from our own e-health research program and clinical experience [16] as well as reviews of the literature [11,12,17-19]. A list of 40 features was generated, 12 features were ultimately removed during the review process due to lack of reporting or inability to assess. The remaining 28 features were grouped into 4 categories: Pure technical features, Technical/user interactions, Logic of decision support, and Developmental and Administrative environment (see Figure 1; Additional File 2).

Study Inclusion/Exclusion
We included reports of RCTs of RxCDSS published in English. We considered a RxCDSS to be an intervention which utilized a computer to analyze patient-specific information to advise a prescriber (primarily a physician) or pharmacist when they were writing or filling a prescription, respectively. Although the decision support itself had to be generated electronically, the support could be delivered by any means (e.g. computer terminal, fax, mail, patient record insert). We only considered systems which intervened before a drug therapy had been chosen by a physician, or had the ability to suggest alternate therapies (i.e. a drug different then that initially prescribed) to be a RxCDSS. These are the more challenging decisions for which to intervene and change. Systems whose sole purpose was to offer ‘fine-tuning’ advice on a pre-defined therapy – usually dose modification – were not included in this review. Systems primarily focused on diagnosis, vaccination, or nutrition, were also excluded.

Search Strategy
We searched the databases Medline, EMBASE, CINAHL, and INSPEC for articles published since the earliest entry
to June 2008. The detailed search strategy is shown in Additional File 3. The search terms were individually tailored for each database, with search terms from domains of study methodology, general CDSS terms and RxCDSS identifiers. These included: randomized controlled trial, artificial intelligence, decision support systems, computer-assisted therapy, computerized medical records system, reminder systems, hospital information systems, computer systems, decision support techniques, ambulatory care information systems, computer assisted decision making, medical errors, therapeutic uses, drug therapy, drug information services, drug interactions, drug monitoring, guideline adherence, medication systems, drug administration schedule, drug costs, drug dose-response relationship, and computer assisted drug therapy. A pilot test was completed to ensure that known relevant studies were identified. All citations obtained were downloaded into Reference Manager, version 11.0.

Study Selection
The titles of all returned studies were reviewed, and those potentially matching our definition of a RxCDSS were kept. Next, the abstracts were assessed independently by two reviewers to determine whether the studies met the inclusion criteria. Disagreements between reviewers were resolved by consensus and, if necessary, by arbitration of a third reviewer. If uncertain whether a study met the inclusion criteria, it moved to the next stage of assessment in order to decrease the likelihood that a relevant study was overlooked.

During full-text review, articles were once again reviewed independently using detailed data extraction forms which extracted details on methods, study validity, study outcomes and features. Before use, the data extraction forms were critiqued for face validity by a panel of methodologists experienced in systematic reviews and CDSS. The forms were also piloted to improve usability.

Analysis
Methodological quality of each RCT was assessed using a modified scale adapted from Garg et al [11]. Our rating system assessed studies on four potential sources of bias: unit of allocation, presence of baseline differences between groups potentially linked to study outcomes, objectiveness of outcome, and completeness of follow-up. Each source of bias was rated on a scale of 0 to 2, with 2 indicating the highest methodological quality. The results of this evaluation were summed with a maximum total possible score of 8.

Study outcomes were assessed for success in each of our three domains of focus: 'Implementation', 'Change in Health Care Provider Behaviour', and 'Change in Patient Outcomes'. Implementation was considered successful if the RxCDSS was successfully introduced and utilized by the clinical staff. A successful change in provider behaviours required reporting of changes such as a decrease in inappropriate prescribing or a change to a more cost-effective therapy. Lastly, impact on patient outcomes was considered successful if the study reported improvements in
patients' health (e.g. decreases in morbidity or mortality). These domains of outcomes were hypothesized to be conditional and hierarchical, with success required in implementation before changes in provider behaviour would be noted, and so on. Since the concept of minimal clinically important difference in this area of research remains undefined, outcomes were assessed for statistical significance as reported by the original study [20].

Each RCT report was reviewed several times independently to ensure complete abstraction of features of interest. Each feature on our list was rated for each study as present, absent, or could not assess. ‘Could not assess’ was used when, even after extensive discussion, reviewers could not agree that a feature was present or absent. For the purposes of analysis, features that could not be assessed were considered absent.

Consensus was obtained as described above for methodological quality scores, RxCDSS success and presence/absence of features. Descriptive statistics were used to characterize the studies included, their degree of success, and the number of features reported. Inter-rater reliability for selected methodological quality score, success and features present or not, was calculated and reported as a kappa statistic. We planned to measure the association between our three-tier definition of success of the individual studies and the feature list using univariate binary logistic regression. This method requires roughly equivalent numbers of successful and unsuccessful studies per outcome. Statistical analyses were conducted using SAS 9.1 (Cary, North Carolina).

Results
Our search protocol returned 4534 unique citations (1179 from Medline, 1072 from EMBASE, 1053 from CINAHL, and 1204 from INSPEC plus an additional 26 from the reference lists). Of these, 332 abstracts were evaluated, and 110 were chosen for full text review (see study flow diagram in Figure 2). At this stage, 33 (30%) were removed for not meeting initial inclusion criteria (18 did not deal with prescribing, 7 were not randomized controlled trials, 3 were not drug-related, 3 were extension studies or interim analysis, 1 was a foreign language study, and 1 did not use a computer to offer the decision support). In addition, 36 (32.7%) were deemed to be a drug dosing CDSS and were excluded. The final review sample consisted of 41 studies (see Additional File 4) [9,21-60].

Figure 2
Study flow diagram. This diagram details the flow of citations through each stage of this systematic review.
Key ratings, such as study quality and successful implementation showed good agreement, with kappa estimates of 0.62 (95% CI 0.50–0.73; weighted) and 0.77 (0.48 – 1.00) respectively. However, the features in the individual studies were more difficult to rate (see Additional File 5). Although the proportion of agreement for the presence of a feature was substantial, varying from 58.1% to 93%, the nature of the kappa statistic resulted in scores such as for ‘CDSS supports the user’s task at hand’ at 0.14 (95% CI -0.18 to 0.46). Ultimately, the consensus rating for each variable was used for final data analysis.

Description of Studies
The 41 RCTs involved a total of 612,556 patients (range 169–407,460 per study) and 2963 providers (range 17–334 per study). The mean methodological score was 5.9 with a range of 2–8, indicating generally good quality studies. Twenty-three studies (56.1%) used a RxCDSS in an outpatient general practice or internal medicine setting. 10 (24.4%) in inpatient hospital wards or emergency rooms, 5 (12.2%) in pharmacies and 3 (7.3%) in specialty clinics (2 for pediatrics and 1 for diabetes). The systems addressed a variety of problems – cardiovascular care (36.6%), general/internal medicine (29.3%), diabetes (9.8%), respiratory disease (9.8%), otitis media (7.3%), depression, osteoporosis and infectious disease (2.4% each). Nineteen (46.3%) of the RxCDSS were integrated with drug order entry, 16 (39.0%) with management/electronic health record (EHR) software and 9 (22.0%) also printed the suggestions. While 20 (48.8%) of these systems appeared to be developed by independent vendors, 21 (51.2%) were developed within an (experienced) home EHR environment such as the Regenstreif Medical System [61] and the Veterans Health Information System [62].

The studies most often employed a traditional 2-arm parallel design (31, or 75.6%), although 6 studies (14.6%) used a 3-arm design and 4 (9.8%) used a 2 x 2 factorial design. The nature of the control arm of studies was also mixed but most often was labelled as usual care (35 or 85.4%). The remaining 6 studies employed a control group intervention that was felt to be much less effective such as distribution of general treatment guidelines or education, reminders regarding an unrelated condition or such as distribution of general treatment guidelines or education, reminders regarding an unrelated condition or reminders. Another study [42] randomized two groups to guideline-based suggestions for treating congestive heart failure versus these suggestions plus others based on symptoms gleaned from the linked EHR, and found that the intervention group fared worse in terms of more hospitalizations. As this study did not have a control arm without a RxCDSS, it was not considered further in the analysis of features.

Because of the small number of studies, the lack of rigorous attention to features descriptions by the trials and, especially, the lack of diversity of outcomes across the 3 domains, we were unable to statistically evaluate whether there are features more associated with success than failure using logistic regression as originally planned. In general, the features most prevalent across the 40 remaining studies included: support of the user’s task at hand (95%), provision of decision support at the time and place of decision-making (85%), provision of a recommendation rather than just an assessment (85%), automatic provision of decision support as part of clinician workflow (78%), integration with charting or order entry (75%), and convenient locations for the computers (68%). However, with few exceptions, the prevalence of these features was similar between successful and unsuccessful studies when examining implementation, provider behaviour
Discussion

We have systematically reviewed the literature surrounding RxCDSS. The distribution of success in these 41 studies – the majority successfully implemented, more than half reporting changes in provider process but only five were able to successfully impact patient-related outcomes, appears to validate our hierarchal definition of success. The primary finding of the review is the continued poor reporting of and, by implication, the poor attention to system design and implementation features [12]. The lack of rigorous attention to and reporting of intervention features severely hampers progress in this field. All CDSS are by definition, complex interventions meaning multifactorial, multidisciplinary and usually multi-staged [20,63].

If the ideal set of features was known, these could be highlighted and those more likely to be wasteful of time and resources could be dropped. For example, an activity with enormous cost in time and effort such as training and support of users, would rapidly change if high quality evidence suggested that only selected components and timing were the key to success.

The small number of trials and the lack of consistent reporting of features in the individual studies prevented statistical analysis of associations of features with outcomes. The descriptive examination of feature prevalence and their association with success versus failure returned no clear message.

The strengths of this review include a detailed search protocol tailored to four individual databases, the explicit use of a comprehensive features list, and a multi-level evaluation of system success. However, our study was limited, as mentioned, by the small sample size of included studies and the lack of systematic reporting of system features. Publication bias is always a possibility and is difficult to refute – in this case there may be an under-representation of negative studies. Many studies were excluded because the interventions dealt only with drug dosing suggestions. This group of studies should be systematically reviewed separately; it may well be that the simplicity of dosing decision support is an easier area to build success than complex processes of connecting diagnosis with therapy in light of contraindications, allergies and co-medications.

Despite the substantial interest and investment in developing electronic decision aids [64-68], our review supports the results of others who have noted a lack of demonstrated impact on clinically important patient outcomes [11-13]. Only 23 studies reported on patient outcomes; of these, 5 were successful. In the limited literature that evaluated such endpoints, patient outcomes were frequently secondary outcomes, with resultant lack of power to detect a difference between the intervention and control groups. This speaks to the lack of mature research programs in this field as well as the difficulties organizing and completing these difficult, complex intervention trials.

Conclusion

This systematic review suggests that electronic prescribing decision support systems can be implemented and have the potential to change clinician behaviours, but there is no consistent translation into improved patient outcomes. We have demonstrated that trials do not adequately report and may not give sufficient attention to features of their system design and implementation. We believe that the lack of attention to evidence-based optimization of RxCDSS interventions continues to hamper the development and implantation of these essential systems.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

BM and JJRC were involved in all aspects of study design, literature search, data extraction, descriptive statistical analysis, and manuscript preparation. AMH was responsible for the study’s conception and funding, participated in its design and execution, helped to draft the manuscript and revisions. MS was involved in review and renovation of the manuscript and led the latest update of results. LT was involved in the design of the statistical analysis and aided in the interpretation of the results. GF was responsible for conducting the statistical analysis and aided in the interpretation of the results.

Additional material

Additional file 1
Table 1 – Prevalence of 28 features in 40 successful and unsuccessful randomized trials. This table provides a detailed look at the prevalence of 28 RxCDSS features in 40 randomized controlled trials
Click here for file
[http://www.biomedcentral.com/content-supplementary/1472-6947-9-11-S1.xls]
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References

1. Canadian Institute for Health Information: Drug Expenditure in Canada 1985 to 2004. 2005 [http://dsp-psd.pwgsc.gc.ca/Collection/H115-27-2004E.pdf].
2. Von Laue NC, Schwappach DLB, Koecck CM: The epidemiology of preventable adverse drug events: A review of the literature. Wien Klin Wochenschr 2003, 115:407-415.
3. Benten PM van den, Postma MJ, van Rozen EN, Chow MC, Fijn R, Brouwers JR: Cost-benefit analysis of the detection of prescribing errors by hospital pharmacy staff. Drug Saf 2002, 25:135-143.
4. Bates DW, Gawande AA: Improving safety with information technology. N Engl J Med 2003, 348:2526-2534.
5. Bates DW, Evans RS, Murff H, Stetson PD, Pizziiferri L, Hripczas G: Detecting adverse events using information technology. J Am Med Inform Assoc 2003, 10:115-128.
6. Delaney BC, Fitzmaurice DA, Riaz A, Hobbs FD: Computerised decision support systems deliver improved quality in primary care? Interview by Abi Berger. BMJ 1999, 319:1281-1284.
7. Friedman C, Wyatt E: Evaluation methods in medical informatics New York: Springer-Verlag; 1997.
8. Grimshaw J, Freemantle N, Wallace S, Russell I, Hurwitz B, Wact I, et al.: Developing and implementing clinical practice guidelines. Qual Health Care 1995, 4:55-64.
9. Eccles M, McColl E, Steen N, Rousseau N, Grimshaw J, Parkin D, et al.: Effect of computerised evidence based guidelines on management of asthma and angina in adults in primary care: cluster randomised controlled trials. BMJ 2002, 325:941-944.
10. Coiera E: Clinical Decision Support Systems. In Guide to Health Informatics Australia: Arnold Publishers; 2003.
11. Garg AX, Adhikari NKJ, McDonald H, Rosas-Arellano MP, Devereaux PJ, Beyene J, et al.: Effects of computerized clinical decision support systems on practitioner performance and patient outcomes: a systematic review. JAMA 2005, 293:1245-1258.
12. Kawamoto K, Houlihan CA, Balas EA, Lobach DF: Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. BMJ 2005, 330:765.
13. 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.
14. Kawamoto K, Lobach DF: Computer 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.
15. Niës J, Colombet I, Dugouot P, Durieux P: Determinants of success for computerized clinical decision support systems integrated into CPOE systems: A systematic review. AMIA Annu Symp Proc 2006:594-598.
16. COMPETE: Computerization of medical practice for the enhancement of therapeutic effectiveness [http://www.compete-study.com/]
17. Wears RL, Berg M: Computer technology and clinical work: still waiting for Godot. JAMA 2005, 293:1261-1263.
18. Koppel R, Metlay JP, Cohen A, Abaluck B, Localio AR, Kimmel SE, et al.: Role of computerized physician order entry systems in facilitating medication errors. JAMA 2005, 293:1297-1303.
19. Holbrook AM, Xu S, Banning J: What factors determine the success of clinical decision support systems? AMIA Annu Symp Proc 2003:862.
20. Holbrook AM, Thabane L, Scherbatskyt JY, O'Reilly D: E-Health interventions as complex interventions: improving the quality of methods of assessment. AMIA Annu Symp Proc 2006:952.
21. Hershey CO, Porter DK, Breslau D, Cohen D: Influence of simple computerized feedback on prescription charges in an ambulatory clinic. A randomized clinical trial. Med Care 1986, 24:472-481.
22. Tierney WM, Miller ME, Overhage JM, McDonald CJ: Physician inpatient order writing on microcomputer workstations. Effects on resource utilization. JAMA 1992, 269:379-383.
23. Rotman BL, Sullivan AN, McDonald TW, Brown BW, DeSmedt P, Goodnature D, 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.
24. 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.
25. Dextner 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.
26. Tamblyn R, Huang A, Perreault R, Jacques A, Roy D, Hanley J, et al.: The medical office of the 21st century (MOXXI): effective-
ness of computerized decision-making support in reducing inappropriate prescribing in primary care. CMAJ 2003, 168:549-556.

20. Jovits JC, Steinberg G, Locke T, Couch JB, Jacques J, Juster I, et al.: Using a claims data-based sentinel system to improve compliance with clinical guidelines: results of a randomized prospective study. Am J Manag Care 2005, 11:93-102.

21. Linnser ES, Houston TK, Ray MN, Allison JJ, Heudebert GR, Chatham WW, et al.: Improving ambulatory prescribing safety with a handheld decision support system: a randomized controlled trial. J Am Med Inform Assoc 2006, 13:171-179.

22. Judge J, Field TS, DeFlorio M, Laprino J, Auger J, Rochon P, et al.: Prescribers’ Responses to Alerts During Medication Ordering in the Long Term Care Setting. J Am Med Inform Assoc 2006, 13:385-390.

23. Martens J, Weijden T van der, Severens J, de Clerq P, de Brujin D, Kester A, et al.: The effect of computer reminders on GPs’ prescribing. BMJ 2007, 335:S141-S141.

24. Rabel MA, Carroll NM, Kelleher JA, Chester EA, Berga S, Magid D, et al.: Randomized trial to improve prescribing safety during pregnancy. J Am Med Inform Assoc 2007, 14:440-450.

25. Culous MH, Coveny BH, Torrance E, Lee A, Wichtig FE. Randomised controlled trial of computer assisted management of hypertension in primary care. Br Med J (Clin Res Ed) 1986, 293:670-674.

26. Hobbs FD, Delaney BC, Carson K, Kenkre JE: A prospective controlled trial of computerized decision support for lipid management in primary care. Fam Pract 1996, 13:133-137.

27. Rossi RA, Every NR: Improvement of blood pressure control through provider education. J Am Med Inform Assoc 2003, 10:479-1500.

28. Sequist TD, Gandhi TK, Karson AS, Fiskio JM, Bugbee D, Sperling M, et al.: Implementing computerized decision support to improve the antplatelet drug-prescribing behavior among Italian general practitioners in diabetic patients: an intervention trial. Diabetes Care 2003, 26:175-180.

29. Sequist TD, Gandhi TK, Karson AS, Fiskio JM, Bugbee D, Sperling M, et al.: A randomized trial of electronic clinical reminders to improve quality of care for diabetes and coronary artery disease. J Am Med Inform Assoc 2005, 12:431-437.

30. McCowan C, Neville KG, Ricketts IW, Warner FC, Hoskins G, Thomas JE: 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.

31. Samore MH, Bateman K, Alder SC, Hannah E, Donnelly S, Stoddard G, et al.: Clinical decision support and appropriateness of anticoagulant prescribing: a randomized trial. JAMA 2005, 294:2303-2314.

32. Tierney WM, Overhage JM, Murray MD, Zhou XH, Eckert GJ, et al.: Can computer-generated evidence-based care suggestions enhance evidence-based management of asthma and chronic obstructive pulmonary disease? A randomized, controlled trial. Health Serv Res 2003, 40:477-497.

33. Kullboer MM, van Wijk MA, Moseveld M, van der DE, de Jongste JC, Overbeek B, et al.: Computer critiquing integrated into daily clinical practice affects physicians’ behavior – a randomized clinical trial with AsthmaCritic. Methods Inf Med 2006, 45:447-454.

34. David RL, Wright J, Chalmers F, Levenson L, Brown JC, Lozano P, et al.: Clinical cluster randomized clinical trial to improve prescribing patterns in ambulatory pediatrics. PLoS Clinical Trials 2007, 2:e25.

35. Subramanian U, Fihn SD, Weinerberger M, Plue L, Smith FE, Udris EM, et al.: A controlled trial of including symptom data in computer-based care suggestions for managing patients with chronic heart failure. Am J Med 2004, 116:375-384.

36. Cobos A, Vilaseca J, Asero C, Pedro-Botet J, Sanchez E, Val A, et al.: Computer decision support system based on the recommendations of the European Society of Cardiology and other societies for the management of hypercholesterolemia: Report of a cluster-randomized trial. Dis Manag Outcomes Res 2005, 13.

37. Kucher N, Koo S, Quiroz R, Cooper JM, Paterno MD, Soukannikov B, et al.: Electronic alerts to prevent venous thromboembolism among hospitalized patients. N Engl J Med 2005, 352:969-977.

38. Lester WT, Grant RW, Barnett GO, Chueh HC, Lester WT, Grant RW, et al.: Randomized controlled trial of an informatics-based intervention to increase statin prescription for secondary prevention of coronary disease. J Gen Intern Med 2006, 21:22-29.

39. Roumie CL, Elasy TA, Greer V, Griffin MR, Liu X, Stone WJ, et al.: Improving blood pressure control through provider education, provider and patient education: a cluster randomized trial. Ann Intern Med 2006, 145:165-175.

40. Hicks LS, Sequist TD, Ayasun JZ, Shayevevik S, Fairchild DG, Orav EJ, et al.: Impact of computerized decision support on blood pressure management and control: a randomized controlled trial. Am J Med 2007, 123:429-441.

41. McDonald GJ: Use of a computer to detect and respond to clinical events: its effect on clinician behavior. Ann Intern Med 1976, 84:162-167.

42. Ledevik I, Holmen J, Kruger O, Kristensen P, Iversen H, Furumek S: 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.

43. D’Alessio V, Sabatini A, Soldi L, Samani F, Mazzaglia G, Catapano A, et al.: Effects of an automated electronic reminder in changing the antplatelet drug-prescribing behavior among Italian general practitioners in diabetic patients: an intervention trial. Diabetes Care 2003, 26:1-7.

44. Brown SH, Lincoln MJ, Groen PJ, Kolodner RM: A prospective controlled trial of including symptom data in computer-based decision support for managing patients with acute ischaemic stroke. QJM 2003, 96:171-179.

45. Brown SH, Lincoln MJ, Groen PJ, Kolodner RM: A prospective controlled trial of including symptom data in computer-based decision support for managing patients with acute ischaemic stroke. QJM 2003, 96:171-179.

46. Brown SH, Lincoln MJ, Groen PJ, Kolodner RM: A prospective controlled trial of including symptom data in computer-based decision support for managing patients with acute ischaemic stroke. QJM 2003, 96:171-179.
64. Bates DW: Computerized physician order entry and medication errors: finding a balance. *J Biomed Inform* 2003, 38:259-261.

65. Teich JM, Osheroff JA, Pifer EA, Sittig DF, Jenders RA. The CDS Expert Review Panel: Clinical decision support in electronic prescribing: recommendations and an action plan: report of the joint clinical decision support workgroup. *JAMIA* 2005, 12:365-376.

66. Canada Health Infoway: 2003–2004 annual report and corporate plan summary 2004–2005. [http://www.infoway-inforoute.ca](http://www.infoway-inforoute.ca).

67. Health Canada: A 10-year plan to strengthen health care. [http://www.hc-sc.gc.ca/hcs-sss/delivery-prestation/fptcollab/2004-fmm-rpm/index-eng.php](http://www.hc-sc.gc.ca/hcs-sss/delivery-prestation/fptcollab/2004-fmm-rpm/index-eng.php).

68. Baker M, Robson B, Shears J: Clinical decision support in the NHS – the clinical element. *The Journal of Clinical Governance* 2002, 10:77-82.

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