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## Review Paper

# Managing Clinical Knowledge for Health Care Improvement

Quality health care rests fundamentally on the achievements of biomedical research. All *health outcomes* are improved by sound science: *health status* can be turned around by transplantation when someone's life is in jeopardy due to a diseased organ; *social functioning* can be improved by shock wave lithotripsy that leads to faster recovery; and *satisfaction* can be enhanced when children with moderate or severe asthma receive appropriate anti-inflammatory treatment. To improve the quality of health care that patients actually receive, both biomedical research production and especially its introduction into clinical practice need to be examined.

### Growth of Clinical Research Production

Over the past 20 years, the number of articles indexed annually in the Medline database of the National Li-

brary of Medicine has nearly doubled (Table I). Certainly, the achievements of the Human Genome Project, innovative medical technologies, and scientific discoveries make further investment in biomedical research appealing.

The growth in publications is particularly spectacular in the category of the most rigorous clinical evaluations, randomized controlled clinical trials. Such trials have long been considered sources of the highest quality evidence on the value of a new clinical intervention. Over the past two decades, the number of clinical trials in cardiology has increased five-fold. Similar growth has occurred in many other clinical specialty areas (Table I). Improvement in the quality and efficiency of health care also depends on progress in the science of organizational, reimbursement, workforce, and information system issues. Correspondingly, 10 times more clinical trials are published today than 20 years ago in health

services research (e.g., comparisons of inpatient care with outpatient care, physician profiling, and other information interventions). Yet, health care practices appear to be ill prepared to absorb and efficiently introduce this constantly growing amount of information.

### Slow Transfer of Research to Practice

In 1843 before the Boston Society for Medical Improvement, Oliver Wendell Holmes read the first of his famous papers on the "Contagiousness of Puerperal Fever" [3]. It advocated hand washing before examining a pregnant woman — a revolutionary idea at the time. Yet, it took decades for his recommendation to become a universally accepted practice and change did not come without resistance. Today, more scientific discoveries are being achieved than ever

Table I. Surge in Biomedical Research Production

Published Reports	1966-70	1971-75	1976-80	1980-81	1986-90	1991-95
All articles indexed in MEDLINE <sup>a</sup>	986,567	1,131,779	1,279,584	1,433,460	1,758,217	1,921,938
Family medicine articles <sup>a</sup>	2279	3455	3526	3353	4363	7778
Clinical trials in family medicine <sup>b</sup>	13	45	39	69	203	433
Cardiology articles <sup>a</sup>	319	472	523	460	702	1060
Clinical trials in cardiology <sup>b</sup>	75	141	268	776	2850	4557
Clinical trials in care management <sup>c</sup>	10	23	78	163	427	868

<sup>a</sup> MEDLINE database of the National Library of Medicine. <sup>b</sup> Cochrane Controlled Trials Register [1].

<sup>c</sup> Columbia Registry of Medical Management Trials [2].

before, but practical introduction of new scientific discoveries does not seem to be much faster today than it was more than 100 years ago.

Apparently, the practical application of scientifically sound diabetic eye care recommendations does not fare much better today than hand washing in the last century. The landmark study by the Diabetic Retinopathy Study Research Group, a randomized controlled clinical trial published in 1981, linked early treatment to improved outcomes in diabetes care [4]. The American Diabetes Association published its eye care guidelines for patients with diabetes mellitus in 1988 [5]. Today, according to the HEDIS (Health Employer Data and Information Set) report [6] of the National Committee on Quality Assurance, the national rate for annual diabetic eye exam is still significantly below the recommended level. The rate of compliance for many procedures remains low after several decades of the original application in a landmark trial (Table II).

Studies suggest that it takes an average of 17 years for research evidence to reach clinical practice (Figure I) [20-26]. In one study, the interval between acceptance and publication of a research project has been found to be around 316 ( $\pm 21$ ) days in 1982, and 206 ( $\pm 89$ ) days in 1992 [27]. Using citation analysis, Altman and

Goodman [28] found that newer technical innovations still take 4 to 6 years before they achieve 25 citations in the medical literature. In their meta-analysis, Antman et al [26] noticed that it took 13 years for experts to recommend thrombolytic drugs in the treatment of acute myocardial infarction after the publication of randomized controlled trials that indicated therapeutic efficacy. Treatment recommendations for new therapies appearing in medical textbooks showed a delay of more than 10 years [26].

To calculate the time needed to implement evidence from reviews, papers and textbooks, we looked at nine clinical procedures listed in Table II. The annual increase in use was calculated by dividing the current rate of use by the number of years between the publication of the landmark trial and the reported current use. An average annual increase of 3.2 percent was calculated using all nine clinical procedures. Correspondingly, it would take 15.6 years to reach a rate of use of 50 percent from a rate of zero assumed at the time of publication of the landmark study. It takes a minimum of 6.3 years for evidence to reach reviews, papers and textbooks [24] [26]. By subtracting 6.3 years from 15.6 years, an estimated 9.3 years transition period is needed to implement evidence from reviews, papers and textbooks (Figure I).

Is 50 percent utilization rate an acceptable threshold for declaring success in the practical implementation of clinical recommendations? The problem of translating clinical research into clinical practice is not a new one. In 1989, an article in the *New England Journal of Medicine* asked the following question: "Do Practice Guidelines Guide Practice?" [29] The answer in the article was "no" and, obviously, more needs to be done to put well-substantiated recommendations into clinical practice.

## Malfunction of Passive Diffusion and Mediation

Relying on the passive diffusion of information to keep health professionals' knowledge up to date is doomed to failure in a global environment in which about 2 million articles on medical issues are published annually [30]. While amazed by new scientific achievements, few realize the implications of abundant and growing production in biomedical research. If a physician were to read just two articles daily, within one year that physician would still fall centuries behind. To read everything of potential biomedical importance, physicians would have to peruse about 6000 articles per day [31]. Unfortunately, in spite of all scientific achievements, biomedical research production cannot be developed for the next millennium if dissemination of pertinent findings to practitioners remains on a nineteenth century level. General physicians who want to keep up with relevant journals face the task of examining 19 articles a day 365 days a year [32].

Textbooks, classic mediators of research results, can provide inadequate and inaccurate information. In a study, fourteen common symptoms and nine diseases representing 20% to 40% of primary care patient visits were identified. In seven of the most

Table II. Landmark Clinical Trials and Current Rate of Use for Selected Procedures

Clinical Procedure	Landmark Trial	Current Rate of Use
Flu vaccination	1968 [7]	55% [8]
Thrombolytic therapy	1971 [9]	20% [10]
Pneumococcal vaccination	1977 [11]	35.6% [8]
Diabetic eye exam	1981 [4]	38.4% [6]
Beta blockers after MI	1982 [12]	61.9% [6]
Mammography	1982 [13]	70.4% [6]
Cholesterol screening	1984 [14]	65% [15]
Fecal occult blood test	1986 [16]	17% [17]
Diabetic foot care	1993 [18]	20% [19]

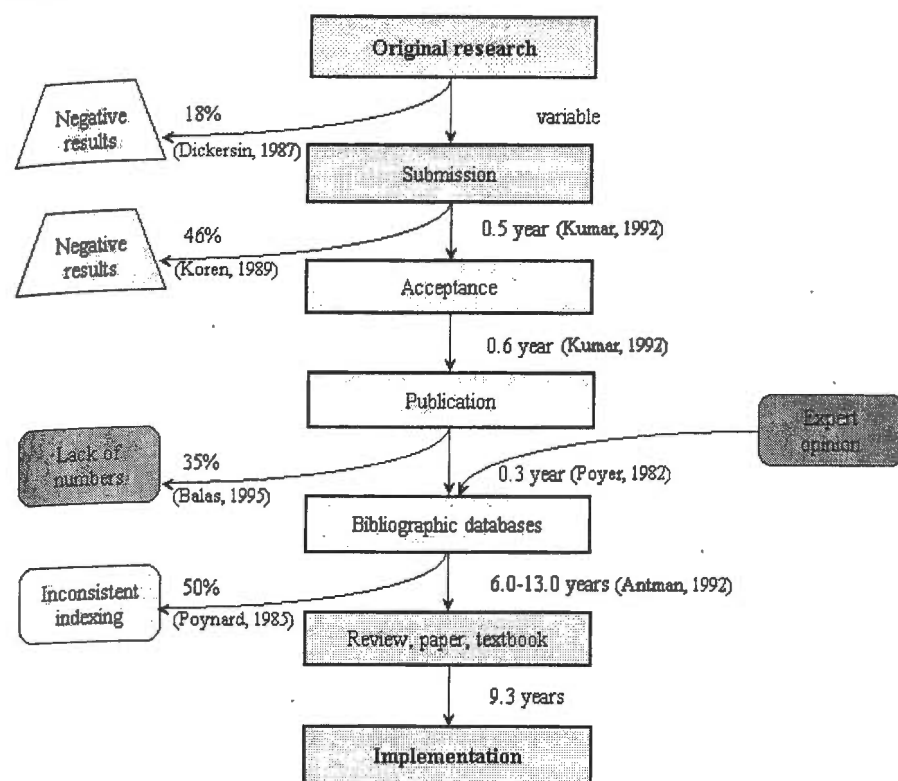


Figure I. Transfer of Research

frequently used textbooks of internal medicine, the average number of pages devoted to all 14 symptoms was 30 (1.5%) and the number of pages devoted to the nine diseases was 40 (2%) [33]. A survey of 13 popular current surgical textbooks and review journals found a high level of inaccuracy for staging of gastric adenocarcinoma. Two texts (15%) did not mention any staging systems, 8% described a non-standard system, three (23%) described staging systems that were out of date and six descriptions (46%) were inaccurate [34]. An analysis of content of 14 nursing textbooks revealed that only one textbook stated correctly the definition of opioid addiction and its likelihood following use of opioid analgesics for pain control. Almost all texts used confusing terminology and some erroneously promoted the fear of addiction when opioids are used for pain relief [35].

Medicine lacks an information infrastructure to efficiently connect those who produce and archive medical

knowledge to those who must apply that knowledge [36]. Clinical trial evidence may be difficult to understand and apply in practice. Seventy-five percent of physicians admitted having problems understanding statistics commonly found in medical journals [37]. Only 4 to 13 percent of the patients who now undergo coronary bypass surgery would meet the eligibility criteria for the randomized controlled trials that established its efficacy [38]. A general medicine service at a university affiliated hospital found that only 53 percent of patients admitted to the service received primary treatments that had been validated in randomized controlled trials or systematic reviews of randomized controlled trials [39]. Medical education and the acquisition of professional credentials do not guarantee that medical knowledge will be coupled rigorously to the decision making process of everyday clinical practice [40]. Innovative techniques are needed to deliver credible and sub-

stantial clinical evidence to the point of care where patient care decisions are made.

## Seeking Conclusive Knowledge

In recent years, several evidence-rating systems have been developed to identify substantial medical knowledge. The U.S. Preventive Services Task Force recommended a scale to evaluate the strength of the recommendation and quality of evidence of research studies. Studies supporting the intervention are placed into one of the following categories according to study design: I: randomized, controlled trials; II-1: controlled trials without randomization; II-2: cohort or case-control analytic studies; II-3: multiple time series, uncontrolled experiments with dramatic results; III: respected opinions, descriptive epidemiology [41].

The Agency for Health Care Policy and Research also has a similar system to evaluate the type of evidence and the strength and consistency of evidence. A numeral is assigned based on the type of evidence: I: meta-analysis of multiple, well-designed controlled studies; II: at least one well-designed experimental study; III: well-designed, quasi-experimental studies such as non-randomized controlled, single group, pre-post, cohort, time series, or matched case-controlled studies; IV: well-designed non-experimental studies, such as comparative and correlational descriptive and case studies; V: case reports and clinical examples. The strength and consistency of evidence are measured by: A: evidence from type I or consistent findings from multiple studies of types II, III, or IV; B: evidence of types II, III, or IV, and findings are generally consistent; C: evidence of types II, III, or IV, but findings are inconsistent; D: little or no evidence, or there is type V evidence only.

Once a source of substantial research results has been located, the credibility of medical evidence has to be examined. Many strategies for critically reviewing clinical trials have been developed and reviewed [42-44]. These methods, presented in more than 26 scales and 11 checklists, are designed to help the reader understand and interpret clinical trials. However, there are disadvantages to some of the existing trial evaluation methods (e.g., no evaluation of patient assignment; no items about masking; patient follow-up not addressed; statistical analysis not assessed). Many currently available evidence rating and quality scoring system lack granularity in recognizing credible and substantial clinical evidence. For example, current techniques are unable to distinguish clinical trials that yielded results with major outcome implications from those trials that led to accurate but negligible results.

Actionable knowledge representation is needed to make a difference in the process and outcome of patient care [45]. Unfortunately, the current publication standards often do not provide information in the necessary structure and cannot be converted into it. The Arden Syntax is a language for representing vast medical knowledge in a standardized format that can be shared by system developers, individual practitioners, and health care administrators across many institutions at different locations. The Arden Syntax is comprised of rule-based independent modules known as Medical Logic Modules (MLMs), each of which contains sufficient logic to make a single medical decision (task-specific knowledge) [46]. However, Arden Syntax is not generally adequate for encoding complex decision logic involving coordination among multiple MLMs [47]. GuideLine Interchange Format (GLIF), has been developed to address the problems of encoding complex clinical guidelines and guideline sharing. The

GLIF guideline specifications consist of action steps, conditional steps, branch steps, and synchronization steps [48].

At the University of Missouri, the Columbia Registry of Medical Management Trials provides a unique source of randomized clinical trials for meta-analyses, traditional reviews, and executive summaries for quality improvement of health services. A study concluded that with the emergence of computerized electronic networks, clinicians and physician executives gaining direct access to bibliographic databases could be better served by structured indexing of critical aspects of randomized controlled clinical trials: design, sample, intervention, and effects [2]. Based on a large sample of randomized controlled clinical trials of organizational interventions, a study analyzed the various methods of such trials and identified the special requirements of applying randomized trials in health services research [23]. In this study, a validated trial quality scoring method was also developed for health services research. An analysis of clinical trial information needs explored the loss that occurs in transferring information from researchers to practitioners. A streamlined abstraction process could better generate helpful information for practitioners, system developers, and researchers simultaneously.

### Computerized Delivery of Clinical Evidence

Several systematic reviews and meta-analyses indicate differences in physician decisions after adding literature. To enhance clinical decision support, presented messages can be supplemented with information from the medical literature. One study evaluated the effect of clinical direct reports (practice data with pertinent evidence from the literature) on dialysis modality selection for patients with end-

stage renal disease [49]. A randomized controlled clinical trial was conducted at five dialysis centers. The number of patients allocated to peritoneal dialysis was significantly higher in the intervention group than in the control group (15.3% versus 2.4%,  $p = 0.044$ ). Another study demonstrated that physicians believe clinical trial evidence to be the most valuable in changing clinical practices [50]. The goal of this study was to identify types of evidence that can lead to the biggest difference. Family practice physicians and internists across the United States were asked about the perceived values of evidence from randomized controlled trials, locally developed recommendations, no evidence, cost-effectiveness studies, expert opinion, epidemiologic studies, and clinical studies. On a Likert scale from one to six, randomized controlled clinical trial was the highest rated evidence (mean 5.07,  $SD \pm 1.14$ ).

Information interventions have been used widely to improve health care. The provider reminder intervention has been used to improve the provision of preventive care procedures such as mammography [51-53], sigmoidoscopy [52,54], influenza vaccinations [53,55,56], and tetanus immunizations [57,58]. A cumulative meta-analysis of physician prompting indicated that prompting can significantly increase preventive care performance by 13.1% (CI: 10.5% to 15.6%) [59]. The statistical analysis included 33 eligible studies involving 1,547 clinicians and 54,693 patients. The effect ranged from 5.8% (CI: 1.5% to 10.1%) for Pap smear to 18.3% (CI: 11.6% to 25.1%) for influenza vaccination. The effect is not cumulative and the length of intervention period did not show correlation with effect size  $R = -.015$ , N.S.). Vigorous application of this simple and effective information intervention could save thousands of lives annually. Health care organizations could effectively use prompting to provide information



to clinicians at the time when patient care decisions are made.

Computerized education programs have helped patients improve their health as well as the process through which they receive care. Some examples include computerized health promotion [60,61] and educational information in the management of medical condition [62,63]. A recent systematic review of 39 eligible randomized clinical trials found that patient participation in and outcomes of diabetes care can be improved by computerized knowledge management interventions. HgbA1c and blood glucose levels were significantly improved in seven and six trials respectively. Significant impact on guideline compliance was reported in six out of eight studies that tested computerized prompting. Three out of four insulin dosage programs of small pocket-size computers reduced hypoglycemic events while reducing insulin doses. Several computerized educational programs improved diet and metabolic indicators. Only two out of eight studies have been successful in linking computerized data reporting to improved outcomes. Insulin dosage programs, computerized prompting, electronic data recording and analysis, computerized patient education, and various distance technologies can make a significant difference in the quality of diabetes care.

### Connecting Those Who Produce Knowledge with Those Who Apply It

Clinicians and biomedical investigators should probably pay more attention to Hamlet's admonition: "Suit the action to the word, the word to the action." Many troubling reports highlight the unrealized practical benefits of significant scientific achievements. Clinical practices often fail to change in response to recommendations sub-

stantiated by controlled evidence. Numerous studies have documented the existence of major unexplained variations in clinical practice patterns. It is equally disappointing that the standards of research publications have not changed for decades while clinicians are inundated with hard-to-read research reports. The words of scientists should be presented in ways that are more helpful to those who must translate them into action. Certainly, computerized information systems hold the promise of better connecting clinical research and patient care practices.

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### References

1. Cochrane Library. The Cochrane Controlled Trials Register. Oxford, England: Cochrane Collaboration, 1996.
2. Balas EA, Stockham MG, Mitchell JA, Austin SM, West DA, Ewigman BG. The Columbia Registry of Information and Utilization Management Trials. *J Am Med Inform Assoc* 1996;2:307-15.
3. Bordley J, McGehee Harvey A. *Two centuries of American Medicine*. Philadelphia: W.B. Saunders, 1976.
4. Diabetic Retinopathy Study Research Group. Photocoagulation treatment of proliferative diabetic retinopathy. Clinical application of Diabetic Retinopathy study (DRS) findings. *Ophthalmology* 1981;88:583-600.
5. American Diabetes Association. Eye care guidelines for patients with diabetes mellitus. *Diabetes Care* 1988;11:745-6.
6. National Committee for Quality Assurance. *Quality Compass 1997*. Annapolis Junction: NCQA Publications Center, 1997.
7. Beare AS, Hobson D, Reed SE, Tyrrell DA. A comparison of live and killed influenza-virus vaccines. Report to the Medical Research Council's Committee on Influenza and other Respiratory Virus Vaccines. *Lancet* 1968;2:418-22.
8. Centers for Disease Control Prevention Guidelines. *MMWR* 1997;46:913-9.
9. European working party. Streptokinase in recent myocardial infarction: a controlled multicentre trial. *Br Med J* 1971;3:325-31.
10. Sullivan HL. *Eminase approval*. Food and Drug Administration press release, 1989: 89-51.
11. Riley ID, Tarr PI, Andrews M, Pfeifer M, Howard R, Challands P, Jennison G. Immunisation with a polyvalent pneumococcal vaccine. Reduction of adult respiratory mortality in a New Guinea Highlands community. *Lancet* 1977;1:1338-41.
12. A randomized trial of propranolol in patients with acute myocardial infarction. I. Mortality results. *JAMA* 1982;247:1707-14.
13. Shapiro S, Venet W, Strax P, Venet L, Roser R. Ten-to fourteen-year effect of screening on breast cancer mortality. *J Natl Cancer Inst*. 1982;69:349-55.
14. Lipid Research Clinics Program. The Lipid Research Clinics Coronary Primary Prevention Trial results. I. Reduction in incidence of coronary heart disease. *JAMA* 1984;251:351-64.
15. Recommendations regarding public screening for measuring blood cholesterol. National Heart, Lung, and Blood Institute, NIH Publication No. 95-3045, September 1995.
16. Hardcastle JD, Armitage NC, Chamberlain J, Amar SS, James PD, Balfour TW. Fecal occult blood screening for colorectal cancer in the general population. Results of a controlled trial. *Cancer* 1986;58:397-403.
17. National Health Interview Survey, 1992. <http://www.cdc.gov/nccdphp/dpcp/colorctl/colorect.htm>
18. Malone JM, Snyder M, Anderson G, Bernhard VM, Holloway GA Jr, Bunt TJ. Prevention of amputation by diabetic education. *Am J Surg* 1989;158:520-3.
19. Ziegler JE. ADA offers revised guidelines for treating diabetes patients. *Drug Topics* 1998;142:44.
20. Dickersin K, Chan S, Chalmers TC, Sacks HS, Smith H. Publication bias and clinical trials. *Contr Clin Trials* 1987;8:343-59.
21. Koren G, Graham K, Shear H, Einarsen T. Bias against the null hypothesis: the reproductive hazards of cocaine. *Lancet* 1989;50:1440-2.
22. Kumar PD. Publication lag intervals - a reason for authors' apathy? *J Assoc Physicians India* 1992;40:623-4.
23. Balas EA, Austin SM, Ewigman BG, Brown GD, Mitchell JA. Methods of randomized controlled clinical trials in health services research. *Med Care* 1995;33:687-99.
24. Poyer RK. Time lag in four indexing services. *Special Libraries* 1982;73:142-6.
25. Poynard T, Conn HO. The retrieval of randomized clinical trials in liver disease from the medical literature: a comparison of MEDLARS and manual methods. *Contr Clin Trials* 1985;6:271-9.
26. Antman EM, Lau J, Kupelnick B, Mosteller

- F, Chalmers TC. A comparison of results of meta-analyses of randomized control trials and recommendations of clinical experts: treatments for myocardial infarction. *JAMA* 1992;268:240-8.
27. Pulido M, Gonzalez JC, Sanz F. Original articles published in *Medicina Clinica* during 30 years (1962-1992): number of authors, interval between acceptance and publication and bibliographic references. *Med Clin (Barc)* 1994;103:770-5.
  28. Altman DG, Goodman SN. Transfer of technology from statistical journals to the biomedical literature: past trends and future predictions. *JAMA* 1994;272:129-32.
  29. Lomas J, Anderson GM, Domnick-Pierre K, Vayda E, Enkin MW, Hannah WJ. Do practice guidelines guide practice? The effect of a consensus statement on the practice of physicians. *N Engl J Med* 1989;321:1306-11.
  30. Mulrow CD. Rationale for systematic reviews. *Br Med J* 1994;309:597-9.
  31. Lundberg GD. Perspective from the editor of *JAMA*, the Journal of the American Medical Association. *Bull Med Libs Assoc* 1992;80:110-4.
  32. Davidoff F, Haynes RB, Sackett DL, Smith R. Evidence-based medicine: a new journal to help doctors identify the information they need. *Br Med J* 1995;310:1085-6.
  33. Elks ML. Malaise in medicine: we don't teach what we do. *South Med J* 1994;87:70-3.
  34. Fung AS. Accuracy of current educational literature on the staging of gastric carcinoma. *World J Surg* 1997;21:237-9.
  35. Ferrell BR, McCaffery M, Rhiner M. Pain and addiction: an urgent need for change in nursing education. *J Pain Symptom Manage* 1992;7:117-24.
  36. Weed LL. New connections between medical knowledge and patient care. *Br Med J* 1997;315:231-5.
  37. Cranney M, Walley T. Same information, different decisions: the influence of evidence on the management of hypertension in the elderly. *Br J Gen Pract* 1996;46:661-3.
  38. Gelijns AC, Rosenberg N, Moskowitz AJ. Capturing the unexpected benefits of medical research. *N Engl J Med* 1998;339:693-8.
  39. Ellis J, Mulligan I, Rower J, Sackett DL. Inpatient general medicine is evidence based. *Lancet* 1995;346:407-10.
  40. Weed LL. Knowledge coupling, medical education and patient care. *Crit Rev Med Inform* 1986;1:55-79.
  41. U.S. Preventive Services Task Force. *Guide to Clinical Preventive Services*. U.S. Department of Health and Human Services, 1996. Second Edition.
  42. Spilker B. *Guide to Clinical Trials*. New York: Raven Press, 1991.
  43. Moher D, Jadad AR, Nichol G, Penman M, Tugwell P, Walsh S. Assessing the quality of randomized controlled trials: an annotated bibliography of scales and checklists. *Contr Clin Trials* 1995;16:62-73.
  44. Bigby M, Gadenne AS. Understanding and evaluating clinical trials. *J Am Acad Dermatol* 1996;34:555-90.
  45. McDonald CJ, Overhage JM. Guidelines you can follow and can trust: an ideal and an example. *JAMA* 1994;271:872-3.
  46. Gao X, Johansson B, Shahsavari N, Arkad K, Ahlfeldt H, Wigertz O. Pre-compiling medical logic modules into C++ in building medical decision support systems. *Computed Methods Programs Biomed* 1993;41:107-19.
  47. Patel VL, Allen VG, Arocha JF, Shortliffe EH. Representing clinical guidelines in GLIF: Individual and collaborative expertise. *J Am Med Inform Assoc* 1998;5:467-83.
  48. Ohno-Machado L, Gennari JH, Murphy SN, Jain NL, Tu SW, Oliver DE, Pattison-Gordon E, Greenes RA, Shortliffe EH, Barnett GO. The GuideLine interchange format: A model for representing guidelines. *J Am Med Inform Assoc* 1998;5:357-72.
  49. Balas EA, Boren SA, Hicks LL, Chonko AM, Stephenson K. Effects of linking practice data to published evidence: a randomized controlled trial of clinical direct reports. *Med Care* 1998;36:79-87.
  50. Balas EA, Su KC, Solem JF, Li RZ, Brown GD. Upgrading clinical decision-support with published evidence: What can make the biggest difference? In: Cesnik B, McCray AT, Scherrer J-R. *Proceedings MEDINFO 1998*. Amsterdam: IOS Press, 1998:845-8.
  51. Chambers CV, Balaban DJ, Carlson BL, Ungemack JA, Grasberger DM. Micro-computer-generated reminders: Improving the compliance of primary care physicians with mammography screening guidelines. *J Fam Pract* 1989;3:273-80.
  52. Fordham D, McPhee SJ, Bird JA, Rodnick JE, Detmer WM. The cancer prevention reminder system. *MD Comp* 1990;7:289-95.
  53. McDonald CJ, Hui SL, Smith DM, Tierney WM, Cohen SJ, Weinberger M, McCabe GP. Reminders to physicians from an introspective computer medical record: A two-year randomized trial. *Ann Int Med* 1984;100:130-38.
  54. McPhee SJ, Bird JA, Jenkins C, Fordham D. Promoting cancer screening: A randomized controlled trial of three interventions. *Arch Intern Med* 1989;149:1866-72.
  55. Chambers CV, Balaban DJ, Carlson BL, Grasberger DM. The effect of microcomputer-generated reminders on influenza vaccination rates in a university-based family practice center. *J Am Board Fam Pract* 1991;4:19-26.
  56. McDowell I, Newell C, Rosser W. A follow-up study of patients advised to obtain influenza immunizations. *Fam Med* 1990;22:303-6.
  57. Ornstein SM, Garr DR, Jenkins RG, Rust PF, Arnon A. Computer-generated physician and patient reminders: Tools to improve population adherence to selected preventive services. *J Fam Pract* 1991;32:82-90.
  58. Turner BJ, Day SC, Borenstein B. A controlled trial to improve delivery of preventive care: physician or patient reminders? *J Gen Intern Med* 1989;4:403-9.
  59. Balas EA, Weingarten S, Garb CT, Blumenthal D, Boren SA, Brown GD. Improving preventive care by prompting physicians. *Arch Int Med* (in press).
  60. Chan CW, Witherspoon JM. Health risk appraisal modifies cigarette smoking behavior among college students. *J Gen Intern Med* 1988;3:555-9.
  61. Robinson TN. Community health behavior change through computer network health promotion: Preliminary findings from Stanford Health-Net. *Comp Meth Prog Biomed* 1989;30:137-44.
  62. Rubin DH, Leventhal JM, Sadock RT, Letovsky E, Schottland P, Clemente I, McCarthy P. Educational intervention by computer in childhood asthma: A randomized clinical trial testing the use of a new teaching intervention in childhood asthma. *Pediatrics* 1986;77:1-10.
  63. Wetstone SL, Sheehan TJ, Votaw RG, Peterson MG, Rothfield N. Evaluation of a computer based education lesson for patients with rheumatoid arthritis. *J Rheumatol* 1985;12:907-12.

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