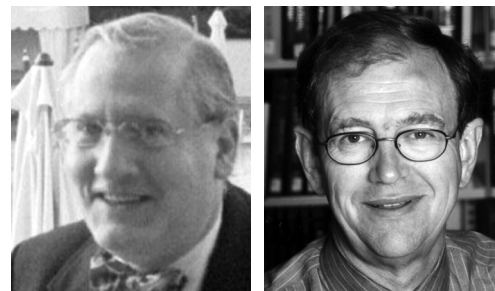


Shouldn't Standard Rheumatology Clinical Care Be Evidence-Based Rather Than Eminence-Based, Eloquence-Based, or Elegance-Based?



Evidence-based medicine is increasingly accepted as the gold standard for medical care¹, advocated to replace traditional approaches, including eminence-based medicine, characterized by making the same mistakes with increasing confidence over an impressive number of years, eloquence-based medicine, in which brilliant oratory and a year-round suntan may overcome absence of any supporting data, and elegance-based medicine, in which the sartorial splendor of a silk-suited sycophant substitutes for substance (Table 1, adapted²).

Many health professionals, including students, trainees, and senior physicians, often use the term “evidence-based medicine” almost as a synonym for data from randomized controlled clinical trials^{3,4}. A widely-used hierarchy concerning levels of evidence for patient care lists randomized clinical trials and metaanalyses as the highest forms of evidence, while observational studies and case reports are regarded as poorer forms of evidence⁵ (Table 2). However, much evidence to guide the clinician must be derived from sources beyond randomized controlled clinical trials^{1,6,7}.

The clinical trial remains the gold standard to assess the efficacy of an active treatment versus a control treatment over defined periods. However, evidence-based medicine is not restricted to randomized clinical trials and metaanalyses of these trials^{1,6}. Simple categorization of research designs is not adequate to grade the quality of evidence, as criteria other than randomization must be considered in evaluation of clinical research studies (Table 3)⁸⁻¹¹.

Table 1. Evidence-based medicine and its alternatives. Adapted with permission from Isaacs and Fitzgerald. *BMJ* 1999;319:1618².

Evidence Based Medicine — The best approach to clinical knowledge. Requires both clinical trials and clinical observations outside of clinical trials

Traditional approaches to clinical expertise:

Eminence Based Medicine — Making the same mistakes with increasing confidence over an impressive number of years

Eloquence Based Medicine — Brilliant oratory and a year-round suntan may overcome absence of any supporting data

Elegance Based Medicine — Where the sartorial splendor of a silk-suited sycophant substitutes for substance

A need for breadth in the approach to evidence based medicine is especially important in chronic diseases^{3,4,12-44}. For example, the therapeutic pyramid was developed as a framework for rheumatologists to care for patients with rheumatoid arthritis (RA)⁴⁵, based on short term clinical trial results indicating efficacy of nonsteroidal antiinflammatory drugs (NSAID) and disease modifying antirheumatic drugs (DMARD). However, the rheumatology community had to reassess this approach when longterm longitudinal observational analyses of patients, treated according to the recommended therapeutic pyramid, indicated that the longterm out-

Table 2. Grades of evidence for the purported quality of study design. Adapted with permission from Guide to Clinical Prevention Services. Williams and Wilkins; 1996⁵.

- I Evidence obtained from at least one properly randomized, controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

Table 3. A comprehensive view of evidence-based medicine. Adapted with permission from Glasziou and Vandembroucke. *BMJ* 2004;328:39-41⁹.

- 1. Different types of research are needed to answer different types of clinical questions.
- 2. Irrespective of the type of research, systematic reviews are necessary.
- 3. Adequate grading of quality of evidence goes beyond the categorization of research design.
- 4. Risk-benefit assessments should draw on a variety of types of research.
- 5. Clinicians need efficient search strategies for identifying reliable clinical research.

comes were disappointingly poor⁴⁶⁻⁴⁸. This approach was flawed in part due to absence of longterm clinical trials that were (and remain) unavailable for many logistical and ethical reasons⁴⁹.

Short term efficacy of NSAID⁴⁶ and disease modifying antirheumatic drugs⁴⁷ (DMARD) in clinical trials was not seen over long periods. Remission was generally seen only over 3–12 months⁵⁰. Although short term clinical trials and even a large metaanalysis [regarded as the highest form of medical evidence (Table 2)] indicated that the DMARD methotrexate (MTX), sulfasalazine, gold injections, and penicillamine were not distinguishable in efficacy for people with RA⁵¹, substantive differences were seen over 5 years, as about 70% of courses of MTX were continued, compared to about 20% of the other DMARD^{47,52}.

Results from clinical care over one year were quite similar to those of clinical trials in indicating comparable efficacies of all DMARD over one year, although MTX was much more effective over 5 years⁴⁷. Such studies indicated that most patients with RA experienced radiographic progression⁵³ and premature mortality^{54,55} over 5–10 years. Therefore, short term efficacy of many therapies cannot be assumed to persist⁴⁸, and longterm observational studies are required in addition to clinical trials to provide accurate evidence concerning results of therapies and outcomes of chronic diseases.

Three types of research studies contribute evidence concerning therapies and disease outcomes: randomized controlled clinical trials, prospective multi-center longitudinal observational studies, and reports from usual clinical care, generally by individual or a small group of practitioners. Each design has advantages and limitations: (1) Randomized controlled clinical trials, conducted according to the highest standards of quantitative measurement using established indices⁵⁶⁻⁶⁰, provide the most rigorous data to compare efficacy of active versus control treatments. However, clinical trials include pragmatic and intrinsic limitations, particularly in chronic diseases, that are important not to ignore^{3,4,12-44}. (2) Large scale prospective longitudinal observational studies have provided many important observations concerning RA that were initially hypothesis generating, including high levels of work disability⁶¹ and premature mortality in RA⁶², and gastropathy associated with the use of NSAID^{63,64}. Given the challenges, including co-interventions, contamination of the control over time by new interventions, compliance, in addition to expense, and ethical issues involved in longterm clinical trials, few trials in rheumatology are conducted over much longer than 12–24 months. Nonetheless, the longitudinal observational study design is the only practical design for assessing the degree of benefit and toxicities of therapies over time⁶⁵. (3) Observations in usual clinical care by individual or a small group of practitioners in RA initiated reports of the efficacy of weekly low dose MTX^{66,67}, frequent early radiographic damage^{53,68}, severe functional declines, work disability and premature mortality⁵⁴, absence of longterm remis-

sion⁵⁰, and better patient status at this time compared to previous decades⁶⁹. Such reports may lead to clinical trials and prospective longitudinal observational studies, as well as composite analytical reviews (as needed for individual clinical trials and longitudinal observational studies as well) to confirm and extend the findings.

Reports from standard clinical care are greatly enhanced by quantitative data, collected prospectively and for later analyses to provide evidence. However, most rheumatologists do not perform formal quantitative joint counts⁷⁰ or collect patient questionnaires⁷¹ at most visits of most patients with RA. Therefore, most clinical rheumatology practice continues to be based largely on “gestalt” qualitative impressions — eminence, eloquence, and elegance — rather than evidence.

The most pragmatic approach to introduce quantitative assessment into standard rheumatology care is to ask each patient to complete a simple patient questionnaire at each visit. Patient questionnaires designed for standard care differ from research questionnaires in that they may provide medical history and review of systems data and be amenable to review and scoring in 15 seconds or less to guide clinical care, while saving time for the clinician and improving the quality and documentation of a patient visit⁷²⁻⁷⁴. Patient questionnaire data provide the best evidence to predict severe longterm outcomes in patients with RA, including functional status^{54,75}, work disability⁷⁶⁻⁷⁸, costs⁷⁹, joint replacement surgery⁸⁰, and premature death^{54,81-87}, as effectively as any clinical measure, including joint counts, radiographs, and laboratory tests.

Any rheumatologist can practice evidence-based clinical care by recording quantitative data at each patient visit. If no data are recorded at the time of the visit, the data can never be replaced. More evidence, and less eminence, eloquence, and elegance will enhance rheumatology care for patients and their rheumatologists.

THEODORE PINCUS, MD,

Division of Rheumatology and Immunology,
Department of Medicine,
Vanderbilt University Medical Center,
Nashville, Tennessee, USA;

PETER TUGWELL, MD,

Center for Global Health,
University of Ottawa, Ontario, Canada.

Address reprint requests to Dr. T. Pincus, Division of Rheumatology and Immunology, Vanderbilt University School of Medicine, 203 Oxford House, Box 5, Nashville, TN 37232-4500, USA. E-mail: t.pincus@vanderbilt.edu

REFERENCES

1. Sackett DL, Rosenberg WM, Gray JM, Haynes RB, Richardson WS. Evidence based medicine: what it is and what isn't. It's about integrating individual clinical expertise and the best external evidence. *BMJ* 1996;312:71-2.
2. Isaacs D, Fitzgerald D. Seven alternatives to evidence based medicine. *BMJ* 1999;319:1618.
3. Buchanan WW, Kean WF. Evidence based medicine: the median is not the message. *J Rheumatol* 2001;28:2371-2.

4. Urowitz MB. How do I know thee...? Let me count the ways. The varieties of medical evidence. *J Rheumatol* 2001;28:2373-4.
5. Preventive Services Task Force. Guide to clinical preventive services: report of the U.S. Preventive Services Task Force 2nd edition. Baltimore: Williams & Wilkins; 1996.
6. Ray JG. Evidence in upheaval: incorporating observational data into clinical practice. *Arch Intern Med* 2002;162:249-54.
7. Vandembroucke J. When are observational studies as credible as randomised trials? *Lancet* 2004;363:1728-31.
8. Atkins D, Best D, Briss PA, et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004;328:1490-7.
9. Glasziou P, Vandembroucke J, Chalmers I. Assessing the quality of research. *BMJ* 2004;328:39-41.
10. Tugwell P, Shea B, Boers M, et al. Evidence-based rheumatology. 1st ed. London: BMJ Publishing Group; 2004.
11. Sackett D, Haynes RB, Guyatt G, Tugwell P. Clinical epidemiology: a basic science for clinical medicine. 3rd edition. Little, Brown and Company; 2006.
12. Freiman JA, Chalmers TC, Smith H, Jr., Kuebler RR. The importance of beta, the type II error and sample size in the design and interpretation of the randomized control trial: survey of 71 "negative" trials. *N Engl J Med* 1978;299:690-4.
13. Sackett DL, Gent M. Controversy in counting and attributing events in clinical trials. *N Engl J Med* 1979;301:1410-2.
14. Sackett DL. The competing objectives of randomized trials. *N Engl J Med* 1980;303:1059-60.
15. Huskisson EC. Important factors in the success and failure of clinical trials (closing remarks). *Agents Actions* 1980;7 Suppl:323-4.
16. Freireich EJ. The randomized clinical trial as an obstacle to clinical research. In: Varco RL, Delaney JP, editors. Controversy in surgery. Philadelphia: WB Saunders; 1983:5-12.
17. Feinstein AR. An additional basic science for clinical medicine: II. The limitations of randomized trials. *Ann Intern Med* 1983;99:544-50.
18. Diamond GA, Forrester JS. Clinical trials and statistical verdicts: probable grounds for appeal. *Ann Intern Med* 1983;98:385-94.
19. Chalmers TC, Celano P, Sacks HS, Smith H, Jr. Bias in treatment assignment in controlled clinical trials. *N Engl J Med* 1983;309:1358-61.
20. Bombardier C, Tugwell P. Controversies in the analysis of long-term clinical trials of slow acting drugs [editorial]. *J Rheumatol* 1985;12:403-5.
21. Guyatt G, Sackett D, Taylor DW, Chong J, Roberts R, Pugsley S. Determining optimal therapy - randomized trials in individual patients. *N Engl J Med* 1986;314:889-92.
22. Pincus T. Rheumatoid arthritis: disappointing long-term outcomes despite successful short-term clinical trials. *J Clin Epidemiol* 1988;41:1037-41.
23. Gotzsche PC. Methodology and overt and hidden bias in reports of 196 double-blind trials of nonsteroidal antiinflammatory drugs in rheumatoid arthritis. *Control Clin Trials* 1989;10:31-56.
24. Sanz I, Dang H, Takei M, Talal N, Capra JD. VH sequence of a human anti-Sm autoantibody. Evidence that autoantibodies can be un-mutated copies of germline genes. *J Immunol* 1989;142:883-7.
25. Felson DT, Anderson JJ, Meenan RF. Time for changes in the design, analysis, and reporting of rheumatoid arthritis clinical trials. *Arthritis Rheum* 1990;33:140-9.
26. Klippel JH. Comment: Winning the battle, losing the war? Another editorial about RA. *J Rheumatol* 1990;17:1118-22.
27. Hawley DJ, Wolfe F. Are the results of controlled clinical trials and observational studies of second line therapy in rheumatoid arthritis valid and generalizable as measures of rheumatoid arthritis outcome: analysis of 122 studies. *J Rheumatol* 1991;18:1008-14.
28. Pincus T, Wolfe F. Response to letter: Gold therapy for rheumatoid arthritis: Challenges to traditional paradigms. *Ann Intern Med* 1992;117:169-70.
29. Pincus T. Limitations of randomized controlled clinical trials to recognize possible advantages of combination therapies in rheumatic diseases. *Semin Arthritis Rheum* 1993;23 Suppl 1:2-10.
30. Pincus T, Stein M. What is the best source of useful data on the treatment of rheumatoid arthritis: Clinical trials, clinical observations, or clinical protocols? *J Rheumatol* 1995;22:1611-7.
31. Rothwell PM. Can overall results of clinical trials be applied to all patients? *Lancet* 1995;345:1616-9.
32. Egger M, Smith GD. Misleading meta-analysis: lessons from "an effective, safe, simple" intervention that wasn't. *BMJ* 1995;310:752-4.
33. Shahar E. Re: Evidence based medicine/letter to the editor. *Lancet* 1995;346:1172.
34. Grahame-Smith D. Evidence based medicine: Socratic dissent. *BMJ* 1995;310:1126-7.
35. Poulter NR, Farley TMM, Chang CL, Marmot MG, Meirik O. Authors' reply: Safety of combined oral contraceptive pills. *Lancet* 1996;347:547.
36. McPherson K, Britton AR, Wennberg JE. Are randomized controlled trials controlled? Patient preferences and unblind trials. *J Roy Soc Med* 1997;90:652-6.
37. Feinstein AR, Horwitz RI. Problems in the "evidence" of "evidence-based medicine". *Am J Med* 1997;103:529-35.
38. Pincus T. Analyzing long-term outcomes of clinical care without randomized controlled clinical trials: The consecutive patient questionnaire database. *Advances* 1997;13:3-32.
39. Pincus T, Stein CM. Why randomized controlled clinical trials do not depict accurately long-term outcomes in rheumatoid arthritis: Some explanations and suggestions for future studies. *Clin Exp Rheumatol* 1997;15 Suppl 17:S27-S38.
40. Vandembroucke JP. Observational research and evidence-based medicine: what should we teach young physicians? *J Clin Epidemiol* 1998;51:467-72.
41. Dieppe P. Evidence-based medicine or medicines-based evidence? *Ann Rheum Dis* 1998;57:385-6.
42. Horwitz RI. Clinical versus statistical considerations in the design and analysis of clinical research. *J Clin Epidemiol* 1998;51:305-7.
43. Dieppe P, Szebenyi S. Evidence based rheumatology. *J Rheumatol* 2000;27:4-7.
44. Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. *N Engl J Med* 2000;342:1887-92.
45. Kantor TG. Order out of chaos — the primary mission of the pyramid. *J Rheumatol* 1990;17:1580-1.
46. Pincus T, Marcum SB, Callahan LF, et al. Long-term drug therapy for rheumatoid arthritis in seven rheumatology private practices: I. Nonsteroidal antiinflammatory drugs. *J Rheumatol* 1992;19:1874-84.
47. Pincus T, Marcum SB, Callahan LF. Long-term drug therapy for rheumatoid arthritis in seven rheumatology private practices: II. Second-line drugs and prednisone. *J Rheumatol* 1992;19:1885-94.
48. Wolfe F, Lassere M, van der Heijde D, et al. Preliminary core set of domains and reporting requirements for longitudinal observational studies in rheumatology. Omeract IV: Outcome measures in rheumatology. Cancun, Mexico, April 16-20, 1998. *J Rheumatol* 1999;26:484-9.
49. Stein CM, Pincus T. Placebo-controlled studies in rheumatoid arthritis: Ethical issues. *Lancet* 1999;353:400-3.
50. Wolfe F, Hawley DJ. Remission in rheumatoid arthritis. *J Rheumatol* 1985;12:245-52.
51. Felson DT, Anderson JJ, Meenan RF. The comparative efficacy and toxicity of second-line drugs in rheumatoid arthritis: results of two meta-analyses. *Arthritis Rheum* 1990;33:1449-61.

52. Wolfe F, Hawley DJ, Cathey MA. Termination of slow acting anti-rheumatic therapy in rheumatoid arthritis: A 14-year prospective evaluation of 1017 consecutive starts. *J Rheumatol* 1990;17:994-1002.
53. Scott DL, Grindulis KA, Struthers GR, Coulton BL, Popert AJ, Bacon PA. Progression of radiological changes in rheumatoid arthritis. *Ann Rheum Dis* 1984;43:8-17.
54. Pincus T, Callahan LF, Sale WG, Brooks AL, Payne LE, Vaughn WK. Severe functional declines, work disability, and increased mortality in seventy-five rheumatoid arthritis patients studied over nine years. *Arthritis Rheum* 1984;27:864-72.
55. Rasker JJ, Cosh JA. The natural history of rheumatoid arthritis: a fifteen year follow-up study. The prognostic significance of features noted in the first year. *Clin Rheumatol* 1984;3:11-20.
56. Felson DT, Anderson JJ, Boers M, et al. American College of Rheumatology preliminary definition of improvement in rheumatoid arthritis. *Arthritis Rheum* 1995;38:727-35.
57. Felson DT, Anderson JJ, Boers M, et al. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. *Arthritis Rheum* 1993;36:729-40.
58. Tugwell P, Boers M. OMERACT Committee. Proceedings of the OMERACT Conferences on outcome measures in rheumatoid arthritis clinical trials, Maastricht, Netherlands. *J Rheumatol* 1993;20:527-91.
59. van der Heijde DMFM, van't Hof M, van Riel PLCM, van de Putte LBA. Development of a disease activity score based on judgment in clinical practice by rheumatologists. *J Rheumatol* 1993;20:579-81.
60. Pincus T, Sokka T. Clinical trials in rheumatic diseases: designs and limitations. *Rheum Dis Clin North Am* 2004;30:701-4.
61. Yelin E, Meenan R, Nevitt M, Epstein W. Work disability in rheumatoid arthritis: effects of disease, social, and work factors. *Ann Intern Med* 1980;93:551-6.
62. Wolfe F, Mitchell DM, Sibley JT, et al. The mortality of rheumatoid arthritis. *Arthritis Rheum* 1994;37:481-94.
63. Griffin MR, Ray WA, Schaffner W. Nonsteroidal anti-inflammatory drug use and death from peptic ulcer in elderly persons. *Ann Intern Med* 1988;109:359-63.
64. Fries JF, Miller SR, Spitz PW, Williams CA, Hubert HB, Bloch DA. Identification of patients at risk for gastropathy associated with NSAID use. *J Rheumatol* 1990;17 Suppl 20:12-9.
65. Wolfe F, Michaud K. A brief introduction to the National Data Bank for rheumatic diseases. *Clin Exp Rheumatol* 2005;23:S168-71.
66. Willkens RF, Watson MA, Paxson CS. Low dose pulse methotrexate therapy in rheumatoid arthritis. *J Rheumatol* 1980;7:501-5.
67. Hoffmeister RT. Methotrexate therapy in rheumatoid arthritis: 15 years experience. *Am J Med* 1983; 75 Suppl 6A:69-73.
68. Fuchs HA, Kaye JJ, Callahan LF, Nance EP, Pincus T. Evidence of significant radiographic damage in rheumatoid arthritis within the first 2 years of disease. *J Rheumatol* 1989;16:585-91.
69. Pincus T, Sokka T, Kautiainen H. Patients seen for standard rheumatoid arthritis care have significantly better articular, radiographic, laboratory, and functional status in 2000 than in 1985. *Arthritis Rheum* 2005;52:1009-19.
70. Pincus T, Segurado OG. Most visits of most patients with rheumatoid arthritis to most rheumatologists do not include a formal quantitative joint count. *Ann Rheum Dis* 2006;65:820-2.
71. Wolfe F, Pincus T, Thompson AK, Doyle J. The assessment of rheumatoid arthritis and the acceptability of self-report questionnaires in clinical practice. *Arthritis Care Res* 2003;49:59-63.
72. Pincus T, Wolfe F. An infrastructure of patient questionnaires at each rheumatology visit: Improving efficiency and documenting care. *J Rheumatol* 2000;27:2727-30.
73. Wolfe F, Pincus T. Listening to the patient: A practical guide to self-report questionnaires in clinical care. *Arthritis Rheum* 1999;42:1797-808.
74. Pincus T, Wolfe F. Patient questionnaires for clinical research and improved standard patient care: is it better to have 80% of the information in 100% of patients or 100% of the information in 5% of patients? *J Rheumatol* 2005;32:575-7.
75. Wolfe F, Cathey MA. The assessment and prediction of functional disability in rheumatoid arthritis. *J Rheumatol* 1991;18:1298-306.
76. Callahan LF, Bloch DA, Pincus T. Identification of work disability in rheumatoid arthritis: Physical, radiographic and laboratory variables do not add explanatory power to demographic and functional variables. *J Clin Epidemiol* 1992;45:127-38.
77. Wolfe F, Hawley DJ. The longterm outcomes of rheumatoid arthritis: Work disability: A prospective 18 year study of 823 patients. *J Rheumatol* 1998;25:2108-17.
78. Sokka T, Kautiainen H, Möttönen T, Hannonen P. Work disability in rheumatoid arthritis 10 years after the diagnosis. *J Rheumatol* 1999;26:1681-5.
79. Lubeck DP, Spitz PW, Fries JF, Wolfe F, Mitchell DM, Roth SH. A multicenter study of annual health service utilization and costs in rheumatoid arthritis. *Arthritis Rheum* 1986;29:488-93.
80. Wolfe F, Zwillich SH. The long-term outcomes of rheumatoid arthritis: A 23-year prospective, longitudinal study of total joint replacement and its predictors in 1,600 patients with rheumatoid arthritis. *Arthritis Rheum* 1998;41:1072-82.
81. Wolfe F, Kleinheksel SM, Cathey MA, Hawley DJ, Spitz PW, Fries JF. The clinical value of the Stanford health assessment questionnaire functional disability index in patients with rheumatoid arthritis. *J Rheumatol* 1988;15:1480-8.
82. Leigh JP, Fries JF. Mortality predictors among 263 patients with rheumatoid arthritis. *J Rheumatol* 1991;18:1307-12.
83. Pincus T, Brooks RH, Callahan LF. Prediction of long-term mortality in patients with rheumatoid arthritis according to simple questionnaire and joint count measures. *Ann Intern Med* 1994;120:26-34.
84. Callahan LF, Cordray DS, Wells G, Pincus T. Formal education and five-year mortality in rheumatoid arthritis: Mediation by helplessness scale scores. *Arthritis Care Res* 1996;9:463-72.
85. Callahan LF, Pincus T, Huston JW, III, Brooks RH, Nance EP, Jr., Kaye JJ. Measures of activity and damage in rheumatoid arthritis: Depiction of changes and prediction of mortality over five years. *Arthritis Care Res* 1997;10:381-94.
86. Söderlin MK, Nieminen P, Hakala M. Functional status predicts mortality in a community based rheumatoid arthritis population. *J Rheumatol* 1998;25:1895-9.
87. Sokka T, Hakkinen A, Krishnan E, Hannonen P. Similar prediction of mortality by the health assessment questionnaire in patients with rheumatoid arthritis and the general population. *Ann Rheum Dis* 2004;63:494-7.