Inpatient general medicine is evidence based

*Jonathan Ellis, Ian Mulligan, James Rowe, David L Sackett, on behalf of the A-Team, Nuffield Department of Clinical Medicine**

Summary

For many years clinicians have had to cope with the accusation that only 10–20% of the treatments they provide have any scientific foundation. Their interventions, in other words, are seldom "evidence based". Is the profession guilty as charged?

In April, 1995, a general medical team at a university-affiliated district hospital in Oxford, UK, studied the treatments given to all 109 patients managed during that month on whom a diagnosis had been reached. Medical sources (including databases) were then searched for randomised controlled trial (RCT) evidence that the treatments were effective. The 109 primary treatments were then classified: 82% were evidence based (ie, there was RCT support [53%] or unanimity on the team about the existence of convincing non-experimental evidence [29%]).

This study, which needs to be repeated in other clinical settings and for other disciplines, suggests that earlier pessimism over the extent to which evidence-based medicine is already practised is misplaced.

Lancet 1995; **346:** 407–10

Introduction

Commentators on the scientific basis for medical care lament the paucity of solid evidence for most medical interventions.[1] Summarising the state of affairs in 1991 the editor of the *British Medical Journal* noted that a health care conference in Manchester, UK, had been told that "only about 15% of medical interventions are supported by solid scientific evidence".[2] Such laments are not new. In 1861, Oliver Wendell Holmes wrote: "I firmly believe that if the whole materia medica, as used now, could be sunk to the bottom of the sea, it would be all the better for mankind—and all the worse for the fishes".[3] Despite advances in knowledge of human biology and health care these gloomy characterisations have continued to the present day. In 1992, in a personal communication to Iain Chalmers (a leading light in the Cochrane Collaboration) the distinguished epidemiologist Kerr White reported having suggested in 1976 that "only about 15–20% of physicians' interventions were supported by objective evidence that they did more good than harm". White had been speaking in Wellington, New Zealand, and was interrupted in mid-sentence by Archie Cochrane, who called out: "Kerr, you're a damned liar, you know it isn't more than 10%". Two years later, an estimate that "only 10 to 20% of all procedures currently used in medical practice have been shown to be efficacious by controlled trial" was published by the Office of Technology Assessment of the US Congress,[4] a charge OTA repeated in 1983.[5] In between these two reports, Williamson examined common medical practices for three subspecialties of internal medicine and concluded that fewer than 10% had any foundation in published research.[6] More recently Dubinsky and Ferguson reviewed 126 therapeutic and diagnostic technologies assessed by the US National Institutes of Health and concluded that only 21% were firmly based on research-generated scientific evidence.[7] The accusation was embellished in the United States in 1993, when one radio chat-show host opined that since only 10–20% of medical procedures had been shown to be effective in controlled trials, that "would put 80 to 90% of accepted medical procedures in this country under the heading of quackery".

As both a general physician and an advocate of evidence-based medicine one of us (DLS) was sceptical about the validity of these gloomy verdicts. First, because they tended to focus on high-profile, and expensive, procedures, the pronouncements risked ignoring low-profile, low-technology interventions. Second, because these pessimistic assessments used clinical manoeuvres rather than patients as the denominator for their rates, treatments that were rarely used received the same weight as common ones. Third, access to evidence from randomised trials is hampered by the fact that up to half such trials are not indexed as such in databases like MEDLINE.[8]

DLS' own clinical experience suggsted that the situation at the bedside was not as depressing as described in the literature so, for all these reasons, when he started on the general medicine service at the John Radcliffe Hospital, Oxford, UK (a university-affiliated tertiary care and district general hospital) in April, 1995, he suggested to the other members of his clinical team that they determine the extent to which the patients they cared for during that month received evidence-based therapy. They agreed.

Methods

In the first 2 days of April a protocol was generated and initiated by the 17-strong clinical team (1 professor, 1 senior registrar, 2 registrars, 1 senior house-officer, 2 house-officers, 10 students). We included every inpatient diagnosed and treated by the team in April. At the time of the patient's discharge or death or at the end of the month if the patient was still in hospital the team met to seek consensus on two items, the primary diagnosis and the primary intervention.

Type of evidence	No of patients
(I) Evidence from randomised controlled trials	58 (53%)
(II) Convincing non-experimental evidence	32 (29%)
(III) Interventions without substantial evidence	19 (18%)

Table 1: **Summary of results**

Centre for Evidence-Based Medicine, Nuffield Department of Clinical Medicine, Oxford-Radcliffe NHS Trust, Headley Way, Headington, Oxford OX3 9DU, UK (Prof D L Sackett FRCP); **and General Medicine Service, John Radcliffe Hospital, Oxford** (J Ellis BM, I Mulligan MRCP, J Rowe BM)

Correspondence to: Prof David L Sackett

Primary diagnosis	Primary therapy	No	Citation for RCT
Cardiac			
Unstable angina pectoris	Aspirin, heparin	10	10,11
Stable angina pectoris	Beta-blockers	1	12
Impending myocardial infarction	Thrombolytics	3	13
	Immediate angioplasty	1	14
Completed myocardial infarction	Aspirin+beta-blocker	1	15,16
	Aspirin+ACE inhibitor	3	17
Congestive heart failure	ACE inhibitor*	6	18
Congestive heart failure with sinus rhythm	Digoxin	1	20
Recent onset of atrial fibrillation	Flecainide	1	21
	Amiodarone	1	22
Thromboembolism			
Deep vein thrombosis	Heparin and warfarin	2	23
Multiple pulmonary emboli after hip replacement	Heparin and warfarin	1	23
Cerebrovascular			
Transient ischaemic attack	Aspirin	2	24
Stroke with atrial fibrillation	Warfarin	3	25
Severe stroke	Referral to stroke unit	2	26
Completed stroke	Aspirin	1	24
Other CNS			
Epilepsy	Carbamazepine	1	27
Respiratory			
Chronic obstructive airways disease	Corticosteroid	1	28
Exacerbation of asthma	Corticosteroid	1	29
Poisonings			
Combination of paracetamol and propranolol	Lavage and charcoal	6	30
Carbon monoxide	100% oxygen†	1	31
Gastrointestinal			
Oesophagitis (endoscopically confirmed)	Omeprazole	2	32
Crohn's disease exacerbation	Corticosteroid	1	33
Infections			
Presumed herpes encephalitis	Acyclovir	1	34
Cancer			
Lung	Referral for chemotherapy	1	35
Breast	Tamoxifen	1	36
Advanced metastatic	Pain control with morphine	3	37

*Plus cromoglycate for ACE inhibitor cough in 1.[19] †Pending transport to hyperbaric chamber.

Table 2: **Evidence from randomised controlled trials (group I, n=58)**

Primary diagnosis	Primary therapy	No of Pts
Infections		
Pneumonitis	Antibiotics	10
Sepsis from infected pacemaker	Antibiotics	1
Symptomatic urinary tract infection	Antibiotics	3
Extensive cellulitis	Antibiotics	2
Poisoning		
Paracetamol	Acetylcysteine	1
Cardiac		
Cardiac arrest	Cardiopulmonary resuscitation	1
Heart failure	Diuretics	3
Symptomatic complete heart block	Implanted pace-makers	2
Angina from non-compliance with anti-anginal therapy	Re-establish compliance	1
Miscellany		
Hyperglycaemia from non-compliance with insulin	Re-establish compliance	1
Large haemorrhage from excessive warfarin	Transfusion and warfarin adjustment	1
Gastrointestinal haemorrhage; refused endocopy	Transfusion and ranitidine	1
Vomiting and dehydration	Parenteral rehydration	1
Symptomatic hyponatraemia on on thiazide diuretic	Stop diuretic; oral fluid restriction	1
Micturition syncope when standing	Advised to sit	1
Complete small bowel obstruction from caecal cancer	Hemicolectomy	1
Complete urinary obstruction and hypodronephrosis from prostatism	Indwelling urinary catheter	1

Table 3: **Convincing non-experimental evidence (group II, n=32)**

The primary diagnosis was defined as the disease, syndrome, or condition entirely or, if there were several diagnoses, most responsible for the patient's admission to hospital. Characteristic symptoms, signs, and laboratory investigations were used to establish these. In the special case of pneumonitis, we required cough and sputum plus either definitive chest radiographic changes or signs of inflammation (fever, raised peripheral blood white cell count, or raised C-reactive protein). The primary intervention was the treatment or other manoeuvre that represented our most important attempt to cure, alleviate, or care for the patient in respect of his or her primary diagnosis. The primary intervention was then discussed and traced into an "instant resource book of evidence-based medicine" (maintained by DLS) or medical textbooks or published journal articles, for which purpose we used the bibliographic databases SilverPlatter (SilverPlatter Information Inc) or Knowledge Finder (ARIES Systems Corp). On the basis of the evidence unearthed in this way every primary intervention was classified as:

(I) Intervention with evidence from RCTs—Interventions whose value (or non-value) had been established in one or more RCTs or overviews of RCTs;

(II) Intervention with convincing non-experimental evidence—Interventions whose face validity is so great that randomised trials were unanimously judged by the team to be both unnecessary and, if a placebo would have been involved, unethical. Examples are starting the stopped hearts of victims of heart attacks and transfusing otherwise healthy individuals in haemorrhagic shock. A self-evident intervention was judged effective for the individual patient when we concluded that its omission would have done more harm than good.

(III) Intervention without substantial evidence—An intervention in common use but meeting neither the above two criteria.

Primary interventions were classified "evidence based" if they were categories I or II. Interventions that had not been validated in randomised trails were classified as "convincing non-experimental evidence" (group II) only when the team was unanimous; even if there was only one dissenting voice, that intervention was relegated to category III.

Results

During April, 1995, the team cared for 121 patients. No primary diagnosis was made for 12 (9 admitted on April 30), leaving a study sample of 109. The evidentiary basis for the interventions we offered them is summarised in table 1.

82% of patients (90/109) were judged on our criteria to have received evidence-based interventions. Table 2 shows that our selection of the primary interventions for 53% of patients was based on our interpretations of one or more RCTs. Of the 28 trials or overviews we consulted, 21 had already been summarised in the instant resource book carried by DLS (often in the form of critically appraised topics[9]) and were examined when that treatment decision was being made. The other 7 were identified a few hours later through literature-searching by a team member—ie, they only confirmed a clinical decision already taken.

Table 3 summarises the 32 patients (29%) who received interventions unanimously judged to be based on convincing non-experimental evidence after literature searches had uncovered no randomised trials or systematic reviews. Despite this absence of experimental evidence, in none of these cases would any team member have been willing to have the patient entered into a randomised trial in which the patient might have received

Primary diagnosis	Primary therapy	No of Pts
Central nervous system		
Severe cerebral haemorrhage	Specific sumptomatic and supportive care	1
Inoperable cervical myelopathy		1
Terminal motor neurone disease		1
Late, mild Guillain-Barré syndrome		1
Mild or late poisonings		
Benzodiazepines, flupenthixol, ibuprofen, paracetamol, or procyclidine		7
Miscellaneous		
Non-cardiac chest pain	Antacids and reassurance	3
Viral (non-herpetic) meningitis	Specific symptomatic and supportive care	2
Inoperable acute cholecystitis		1
Presumed food poisoning		1
Confusion and protruding rectal adenoma		1

Table 4: **Interventions without substantial evidence (group III, n=19)**

a placebo or other major deviation from the intervention we had offered them. Many of these patients had major infections and were treated with antibiotics.

19 patients (18%) received specific symptomatic and supportive care without substantial evidence that it was superior to some other intervention, including nothing at all (table 4).

Discussion

In this monitoring of the day-to-day operation of a busy general medicine inpatient service at a university-affiliated district general hospital, the overwhelming majority of patients were offered (and accepted) evidence-based interventions. More than half received interventions previously shown to do more good than harm in one or more randomised controlled trials, and another one-third received interventions judged to be self-evidently effective to the extent that the team members considered it unethical to conduct a trial in which the intervention would be withheld. These results support the view that learning how to practise evidence-based medicine is not just an academic exercise but can influence clinical decisions.

Other clinicians may disagree with our classification system and/or they way we applied it to the interventions offered to our patients. Moreover, some "convincing non-experimental" interventions (table 3) may have been subjected to randomised trials that our search missed and deserve to be promoted to table 2 (if proved effective) or banished from our armamentarium if proven worthless or harmful. We would welcome learning about our errors here. Given the repeated demonstration that other "self-evidently" effective treatments (such as encainide for post-myocardial infarction ventricular ectopy) are harmful, it could be argued that some of the interventions in table 3 are so uncertain that randomised trials might reveal them to be useless or even harmful. We will keep the entries in table 3 under careful scrutiny and hope that opportunities to test them in randomised clinical trials will be seized so that they can either gain a place in table 2 or be abandoned. Finally, some of our primary diagnoses may have been wrong, and many of our patients might have recovered without the interventions we offered them (eg, pneumonitis, which is often a difficult diagnosis to establish in its milder forms).

On the other hand, it could be argued that we have penalised ourselves by omitting deserving patients from table 2. For example, non-compliant patients in whom we re-established adherence with interventions previously validated in randomised trials could have been upgraded to table 2 rather than relegated, as we did, to table 3 (non-experimental). Similarly, we did not enter the patients into table 2 when validated diagnostic tests (such as lung scans for pulmonary embolism) demonstrated that they did not need specific interventions previously validated in randomised trials.

However, even in a "worst-case scenario", in which none of the interventions in table 3 proved to be effective, we still provided interventions validated by controlled trials to over 50% of patients admitted to our general medical service, a figure far higher than the 10–20% so often cited. Why this disparity? We suggest two reasons. First and more important, we selected patients, not procedures, as the focus of our attention and as the denominator for our rates and proportions. This clinical perspective provides the more appropriate measure of the extent to which we are providing patients with up-to-date, evidence-based medicine. Second, only one of the earlier, pessimistic estimates found in our literature search was backed up by real evidence; the rest were armchair conjecture.

We do not know how far our experience in one month on a general medical service is generalisable. It may not be shared by other clinical teams with other therapeutic or educational philosophies, or in hospitals with different referral patterns or mixes of patients. And certainly it may not be observed in other branches of medicine. We encourage our colleagues in these other settings to improve on our methods and expand our limited knowledge of the practice of evidence-based medicine.

Other members of the A-Team, Nuffield Department of Clinical Medicine—Ben Box, Laura Burgoyne, Camille Caroll, Jo Chikwe, Gerry Christofi, Derralynn Hughes, Katie Jeffery, Rowena Jones, Sharon Peacock, Moyra Reid, Kopal Tandon, Clare Wood-Allum, and Sebastian Walter.

Special thanks to e-mail colleagues, notably Hellen Gelband, for helping us complete our search for the references cited in the introduction.

References

1 Smith R. The ethics of ignorance. *J Med Ethics* 1992; **18:** 117–18.
2 Smith R. Where is the wisdom . . .? the poverty of medical evidence. *BMJ* 1991; **303:** 798–99.
3 Holmes OW. In: Strauss MB, ed. Familiar medical quotations. Boston: Little, Brown, 1968: 124.
4 Office of Technology Assessment of the Congress of the United States. Assessing the efficacy and safety of medical technologies. Washington, DC: US Government Printing Office, 1978.
5 Office of Technology Assessment of the Congress of the United States. The impact of randomised clinical trials on health policy and medical practice. Washgton, DC: US Government Printing Office, 1983.
6 Williamson JW, Goldschmidt PG, Jillson IA. Medical Practice Information Demonstration Project: final report. Baltimore, Maryland: Policy Research, 1979.
7 Dubinsky M, Ferguson JH. Analysis of the National Institutes of Health Medicare Coverage Assessment. *Int J Technol Assess Health Care* 1990; **6:** 480–88.
8 Dickersin K, Scherer R, Lefebvre C. Identifying relevant studies for systematic reviews. *BMJ* 1994; **309:** 1286–91.
9 Lee HM, Sauve JS, Farkouh ME, Sackett DL. The critically appraised topic: a standardized aid for the presentation and storage of evidence-based medicine. *Clin Res* 1993; **41:** 543A.
10 Cairns JA, Gent M, Singer J, et al. Aspirin, sulfinpyrazone, or both in unstable angina. *N Engl J Med* 1985; **313:** 1369–75.
11 RISC Group. Risk of myocardial infarction and death during treatment with low dose aspirin and intravenous heparin in men with unstable coronary artery disease. *Lancet* 1990; **336:** 827–30.
12 McLenachan JM. Wilson JT, Dargie HJ. Importance of ancillary properties of beta blockers in angina: a study of selirolol and atenolol. *Br Heart J* 1988; **59:** 685–89.
13 Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction. *Lancet* 1994; **343:** 311–12.
14 Zijlstra F, de Boer MJ, Hoorntje JC, Reiffers S, Reiber JH,

Suryapranata H. A comparison of immediate angioplasty with intravenous streptokinase in acute myocardial infarction. *N Engl J Med* 1993; **328:** 726–28.

15 Antiplatelet Trialists' Collaboration. Collaborative overview of randomised trials of antiplatelet therapy: prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories. *BMJ* 1994; **308:** 81–106.

16 Yusuf S, Peto R, Lewis J, Collins R, Sleight P. Beta blockade during and after myocardial infarction: an overview of the randomised trials. *Prog Cardiovas Dis* 1985; **27:** 335–71.

17 Gruppo Italiano per lo Studio Della Sopravvivenza nell' Infarto Miocardico. GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after myocardial infarction. *Lancet* 1994; **343:** 1115–22.

18 The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *N Engl J Med* 1991; **325:** 294–302.

19 Hargreaves MR, Benson MK. Inhaled sodium cromoglycate in angiotensin-converting enzyme inhibitor cough. *Lancet* 1995; **345:** 13–18.

20 Jaeschke R, Oxman AD, Guyatt GH. To what extent do congestive heart failure patients in sinus rhythm benefit from digoxin therapy? *Am J Med* 1990; **88:** 279–86.

21 Hohnloser SH, Zabel M. Short- and long-term efficacy and safety of flecainaide acetate for supraventricular arrhythmias. *Am J Cardiol* 1992; **70:** 3A–9A.

22 Cochrane AD, Siddins M, Rosenfeldt FL, et al. A comparison of amiodarone and digoxin for treatment of supraventricular arrhythmias after cardiac surgery. *Eur J Cardiothorac Surg* 1994; **8:** 194–98.

23 Barritt DW, Jordan SC. Anticoagulant drugs in the treatment of pulmonary embolism: a controlled trial. *Lancet* 1960; i: 1309–12.

24 The Canadian Cooperative Study Group. A randomised trial of aspirin and sulfinpyrazone in threatened stroke. *N Engl J Med* 1978; **299:** 53–59.

25 Atrial Fibrillation Investigators. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation: analysis of pooled data from five randomised controlled trials. *Arch Intern Med* 1994; **154:** 1449–57.

26 Stroke Unit Trialists' Collaboration. A systematic review of specialist multidisciplinary team (stroke unit) care for stroke patients. In: Stroke module of the Cochrane database of systematic reviews. Oxford: Cochrane Centre, 1995.

27 Mattson RH, Cramer JA, Collins JF. A comparison of valproate with carbamazepine for the treatment of complex partial seizures and secondarily generalized tonic-clonic seizures in adults. *N Engl J Med* 1992; **327:** 765.

28 Callahan CM, Dittus RS, Katz BP. Oral corticosteroid therapy for patients with stable chronic obstructive pulmonary disease: a meta-analysis. *Ann Intern Med* 1991; **114:** 216–23.

29 Chapman KR, Verbeek PR, White JG, Rebuck AS. Effect of a short course of prednisone in the prevention of early relapse after the emergency room treatment of acute asthma. *N Engl J Med* 1991; **325:** 585–88.

30 Vale JA, Proudfoot AT. How useful is activated charcoal? *BMJ* 1993; **306:** 78–79.

31 Raphael JC, Jekharrat D, Jars-Guincestre MC, et al. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. *Lancet* 1989; ii: 414–19.

32 Sontag SJ, Hirschowitz BI, Holt S, et al. Two doses of omeprazole versus placebo in symptomatic erosive esophagitis: the US Multicentre Study. *Gastroenterology* 1992; **102:** 109–18.

33 Summers RW, Switz DM, Sessions JT Jr, et al. National Cooperative Crohn's Disease Study: results of drug treatment. *Gastroenterology* 1979; **77:** 847.

34 Whitley RJ, Alford CA, Hirsch MS, et al. Vidarabine versus acyclovir therapy in herpes simplex encephalitis. *N Engl J Med* 1986; **314:** 144.

35 Le Chevalier T, Arrigada R, Yubiana M. Combined chemotherapy and radiotherapy in small-cell lung cancer. *Cancer Treat Res* 1991; **58:** 139–53.

36 Early Breast Cancer Trialists' Collaborative Group. Systemic treatment of early breast cancer by hormonal, cytotoxic, or immune therapy: 133 randomised trials involving 31, 000 recurrences and 24,000 deaths among 75,000 women. *Lancet* 1992; **339:** 71.

37 Levine MN, Sackett DL, Bush H. Heroin versus morphine for cancer pain? *Arch Intern Med* 1986; **146:** 353–56.

Eosinophilic colitis associated with larvae of the pinworm *Enterobius vermicularis*

Leo X Liu, Jonathan Chi, Melissa P Upton, Lawrence R Ash

Various helmintic parasites, most of which are uncommon in economically developed countries, can cause abdominal pain and eosinophilic inflammation of the bowel. A homosexual man presented with severe abdominal pain and haemorrhagic colitis, eosinophilic inflammation of the ileum and colon, and numerous unidentifiable larval nematodes in diarrhoeal stool. His symptoms resolved with anthelmintic treatment alone. Using comparative morphology and molecular cloning of nematode ribosomal RNA genes, we identified the parasites as larvae of the pinworm *Enterobius vermicularis*, which are rarely observed or associated with disease. Occult enterobiasis is widely prevalent and may be a cause of unexplained eosinophilic enterocolitis.

Lancet 1995; **346:** 410–12

Various intestinal nematodes can cause abdominal pain and enteritis, including hookworm, and species of strongyloides, anisakis, and intestinal trichinella.[1] These infections primarily involve the small intestine and usually cause peripheral eosinophilia due to parasitic penetration of mucosa. The dog hookworm *Ancylostoma caninum* is recognised as a cause of human eosinophilic enteritis.[2] Heavy infections with the colonic whipworm *Trichuris trichiura* can result in a dysentery-like syndrome.[3] Infections with the common pinworm, *Enterobius vermicularis*, are usually asymptomatic or cause only anal pruritis, except for occasional ectopic migration into the appendix or the female genital tract by adult pinworms.[4] We describe a patient with haemorrhagic eosinophilic enterocolitis associated with numerous nematode larvae, which were identified by morphological and molecular criteria as *E vermicularis*.

An 18-year-old man was admitted with a 3 day history of abdominal pain and melena, without vomiting or fever. He had no relevant medical history, including atopy and food allergy, did not drink alcohol excessively, and had not recently taken aspirin or other drugs. He was born and lived in Boston, did not own a dog, had never travelled abroad, and was homosexual with a single partner. He had normal vital signs, severe abdominal tenderness in the right lower quadrant, and melenic stool. His white cell count was $12{\cdot}6\times10^9$/L with 77% neutrophils, 15% lymphocytes, 5% monocytes, and 3% eosinophils. Other routine haematological and blood chemistry test results were normal. HIV antibody was negative. Upper endocopy findings were normal. Colonoscopy showed purulent discharge from the rectum to the terminal ileum, erythematous and friable mucosa, and numerous small stellate ulcerations. Six biopsy specimens, from rectum to ileum, revealed intense infiltration of the surface enterocyte layer by eosinophils, and patchy ulceration with overlying pseudomembranes composed of fibrin, neutrophils, and, especially in the lamina propria, crypts, and capillaries, many eosinophils. No biopsy sample revealed granulomas, invasive microorganisms, viral inclusions, dysplasia, or extension of inflammation below the muscularis mucosae.