

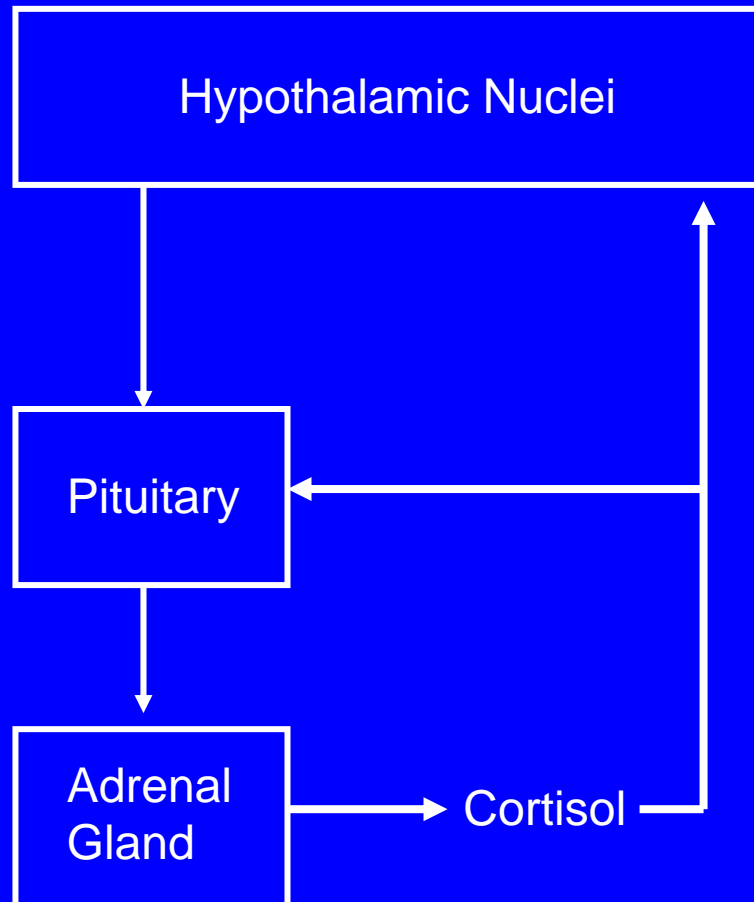




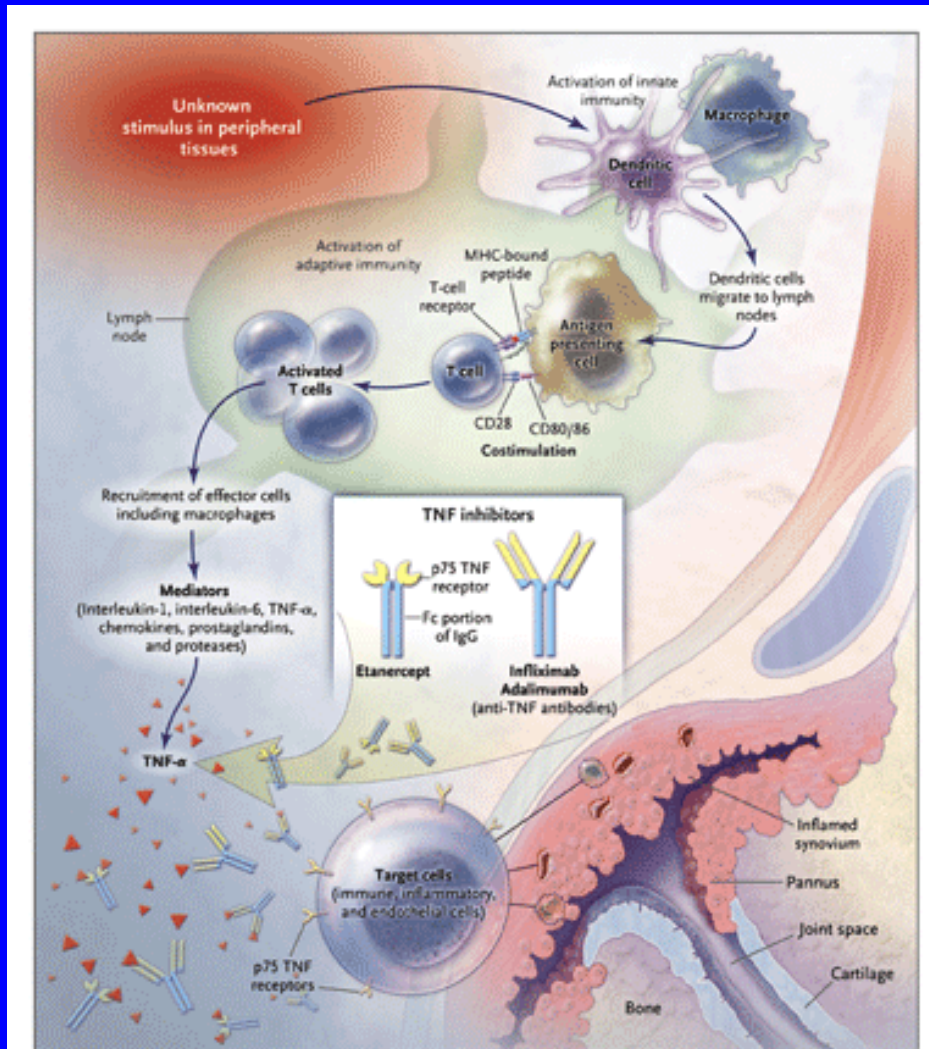
Some Reasons Why Clinical Medicine and Public Health Went Separate Ways

- **The biomedical model**
- **Specialization**
- **Politics**

Example of a Biologic Mechanism: Regulation of Cortisol Secretion



Modern Biologic Mechanism: Pathophysiologic Role of Cytokines and Other Mediators and their Inhibition of Rheumatoid Arthritis



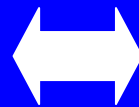
New Engl J Med 2006;
355:704-12

Two Perspectives on Health

Individual

Population

**Clinical Medicine
Cure
Biology of Disease**



**Public Health
Prevention
Epidemiology**

Two Separate Careers

	Clinical Medicine	Epidemiology
Schools/ degree	Medicine (M.D.)	Public Health (Ph.D.)
Departments	Medicine, Surgery, Pediatrics, ...	Epidemiology, Community Medicine
Journals	N Engl J Med, Lancet, Science, Nature, Gastroenterology, ...	Int J Epidemiol, Am J Public Health, ...
Societies	Am. College of Physicians, Clinical Oncology	Am. College of Epidemiology, Statistical Association
Meetings	“Heart”, “Digestive Disease” meetings, ACP	APHA, German Society of Informatics, Biometry and Epidemiology

Frontiers of Primary care

Kerr L. White

**Healing
The Schism
Epidemiology,
Medicine, and
the Public's Health**

Springer-Verlag

Treatments should be given not
because they ought to work but
because they do work

Opie on the Heart. Lancet 1980;1:692

BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 30 1948

STREPTOMYCIN TREATMENT OF PULMONARY TUBERCULOSIS

A MEDICAL RESEARCH COUNCIL INVESTIGATION

The following gives the short-term results of a controlled investigation into the effects of streptomycin on one type of pulmonary tuberculosis. The inquiry was planned and directed by the Streptomycin in Tuberculosis Trials Committee, composed of the following members: Dr. Geoffrey Marshall (chairman), Professor J. W. S. Blacklock, Professor C. Cameron, Professor N. B. Capon, Dr. R. Cruickshank, Professor J. H. Gaddum, Dr. F. R. G. Heaf, Professor A. Bradford Hill, Dr. L. E. Houghton, Dr. J. Clifford Hoyle, Professor H. Raistrick, Dr. J. G. Scadding, Professor W. H. Tytler, Professor G. S. Wilson, and Dr. P. D'Arcy Hart (secretary). The centres at which the work was carried out and the specialists in charge of patients and pathological work were as follows:

Brompton Hospital, London.—Clinician: Dr. J. W. Crofton, Streptomycin Registrar (working under the direction of the honorary staff of Brompton Hospital); Pathologists: Dr. J. W. Clegg, Dr. D. A. Mitchison.

Colindale Hospital (L.C.C.), London.—Clinicians: Dr. J. V. Hurford, Dr. B. J. Douglas Smith, Dr. W. E. Snell; Pathologists (Central Public Health Laboratory): Dr. G. B. Forbes, Dr. H. D. Holt.

Harefield Hospital (M.C.C.), Harefield, Middlesex.—Clinicians: Dr. R. H. Brent, Dr. L. E. Houghton; Pathologist: Dr. E. Nassau.

Bangour Hospital, Bangour, West Lothian.—Clinician: Dr. I. D. Ross; Pathologist: Dr. Isabella Purdie.

Killingbeck Hospital and Sanatorium, Leeds.—Clinicians: Dr. W. Santon Gilmour, Dr. A. M. Reeve; Pathologist: Professor J. W. McLeod.

Northern Hospital (L.C.C.), Winchmore Hill, London.—Clinicians: Dr. F. A. Nash, Dr. R. Shoulman; Pathologists: Dr. J. M. Alston, Dr. A. Mohun.

Sully Hospital, Sully, Glam.—Clinicians: Dr. D. M. E. Thomas, Dr. L. R. West; Pathologist: Professor W. H. Tytler.

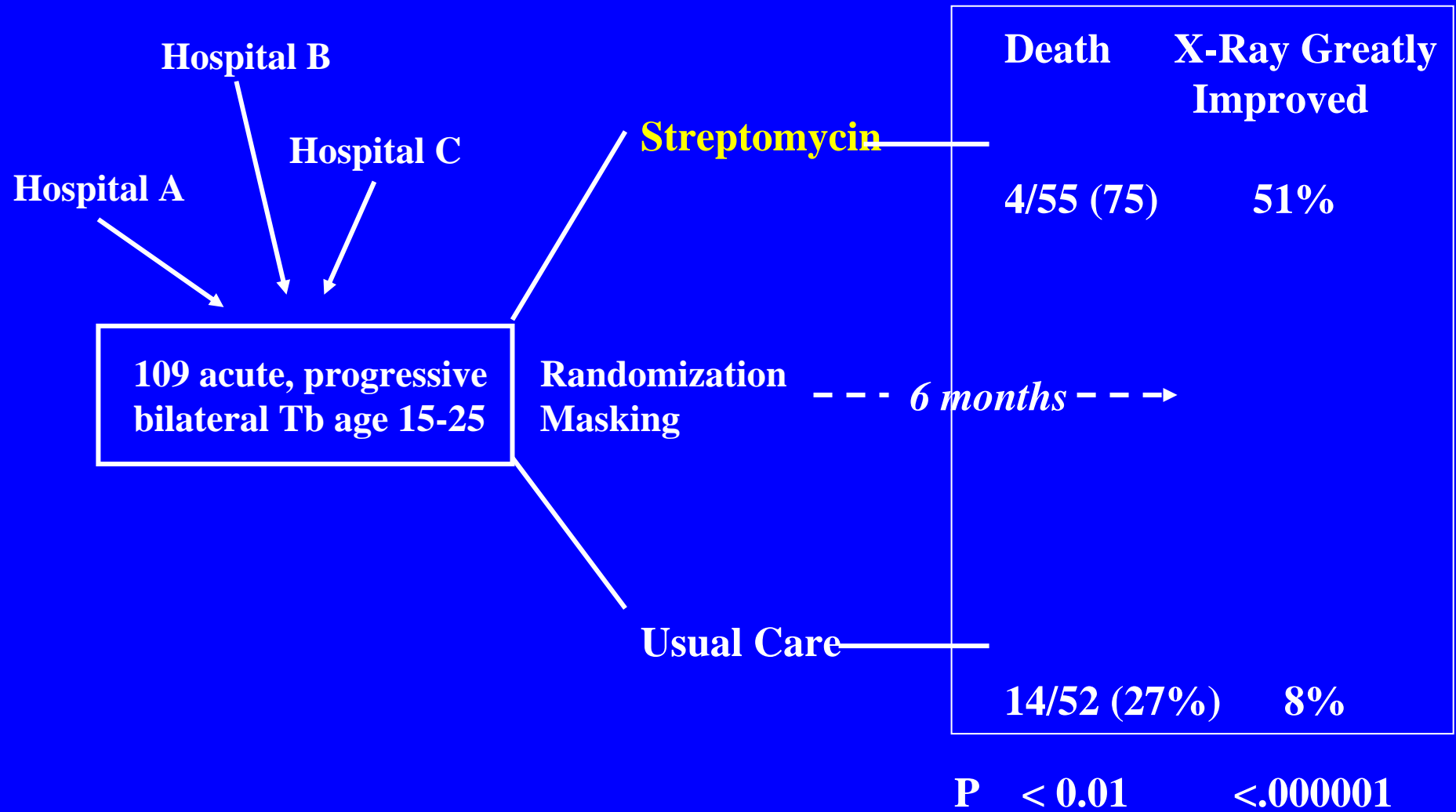
The clinicians of the centres met periodically as a working subcommittee under the chairmanship of Dr. Geoffrey Marshall; so also did the pathologists under the chairmanship of Dr. R. Cruickshank. Dr. Marc Daniels, of the Council's scientific staff, was responsible for the clinical co-ordination of the trials, and he also prepared the report for the Committee, with assistance from Dr. D. A. Mitchison on the analysis of laboratory results. For the purpose of final analysis the radiological findings were assessed by a panel composed of Dr. L. G. Blair, Dr. Peter Kerley, and Dr. Geoffrey S. Todd.

Introduction

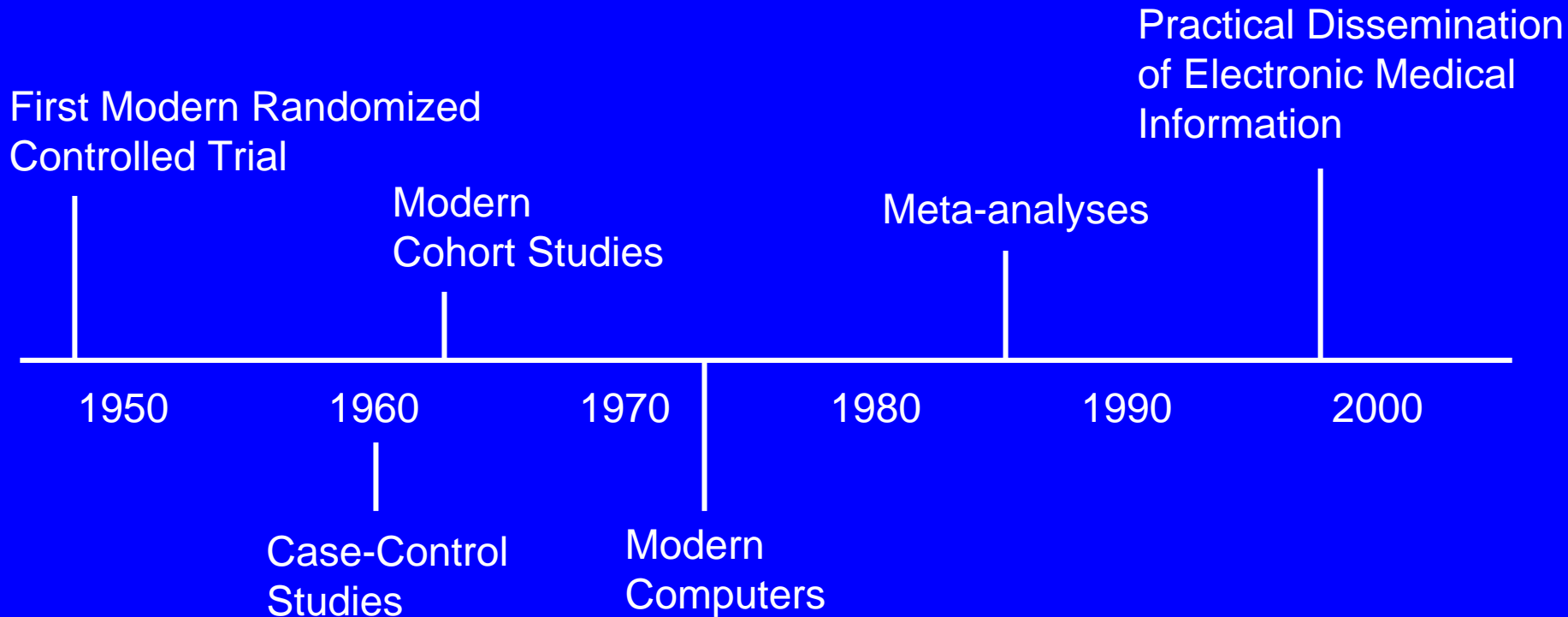
When a special committee of the Medical Research Council undertook in September, 1946, to plan clinical trials of streptomycin in tuberculosis the main problem faced was that of investigating the effect of the drug in pulmonary tuberculosis. This antibiotic had been discovered two years previously by Waksman (Schatz, Bugie, and Waksman, 1944); in the intervening period its power of inhibiting tubercle bacilli *in vitro*, and the results of treatment in experimental tuberculous infection in guinea-pigs, had been

if based on adequately controlled clinical trials (Hinshaw and Feldman, 1944). The one controlled trial of gold treatment (and the only report of an adequately controlled trial in tuberculosis we have been able to find in the literature) reported negative therapeutic results (Amberson, McMahon, and Pinner, 1931). In 1946 no controlled trial of streptomycin in pulmonary tuberculosis had been undertaken in the U.S.A. The Committee of the Medical Research Council decided then that a part of the small supply of streptomycin allocated to it for research purposes would be best employed

The MRC Trial of Streptomycin for Tuberculosis



This Development of Strong Clinical Research Methods



Some Names for Translating Strong Research Results into Clinical Medicine

- Clinical Epidemiology
- Evidence Based Medicine*
 - Answerable questions
 - Finding the best available evidence
 - Critique the evidence for validity
 - Integrate into practice
- Knowledge Management

* David Sackett and colleagues

Some Founders

- **Kerr White.** “the effects of medical interventions in relation to their hazards and costs.”
- **Archie Cochrane: Effectiveness and Efficiency**
- **Alvan Feinstein: Clinical Judgment, Clinimetrics**
- **David Sackett: “A basic science for clinical medicine”**
- **Brian Haynes: “scientifically strong and clinically applicable”**
- **Ian Chalmers: The Cochrane Collaboration**

Clinical Questions

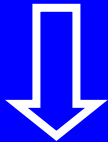
- Frequency
- Risk factors
- Accuracy of diagnosis
- Prognosis
- Effects of Treatment
- Effects of preventive interventions

Clinical Questions and Epidemiologic Methods to Answer Them

Frequency	Survey (Cross-sectional)
Risk factors	Cohort and case-control
Accuracy of diagnosis	Bayesian logic
Prognosis	Cohort studies
Effects of treatment	Randomized trials
Effects of prevention	(Observational studies)

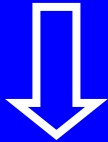
Points of Influence on the Natural History of Research

Research Ideas



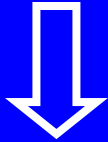
..... Review Committees

Grant Funding



..... Multidisciplinary Teams

Conduct of Study



..... Editors and Peer Reviewers

Publication



..... Modern "Journal Clubs"

Read and Use

Electronic textbooks, etc

Membership on a Typical U.S. Review Panel for Clinical Research Grants

- Clinical medicine
- Health services research
- Epidemiology
- Biostatistics
- Social and behavioral sciences
- Clinical Economics
- Quantitative decision-making

Original Articles in The Lancet with Design. 26 August 2006 Issue

- Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood. Multi-country survey
- Effect of budesonide in combination with formoterol for reliever therapy in asthma exacerbations. Randomized controlled trial
- Secondary prevention of asthma by the use of inhaled Fluticasone propionate in wheezy infants. Randomized controlled trial
- Perennial allergen sensitization early in life and chronic asthma in children. Cohort study
- Beta-adrenoceptor polymorphisms and asthma from childhood to middle age the British 1958 birth cohort Cohort study

A Meta-Analysis of Antioxidants and Gastrointestinal Cancers

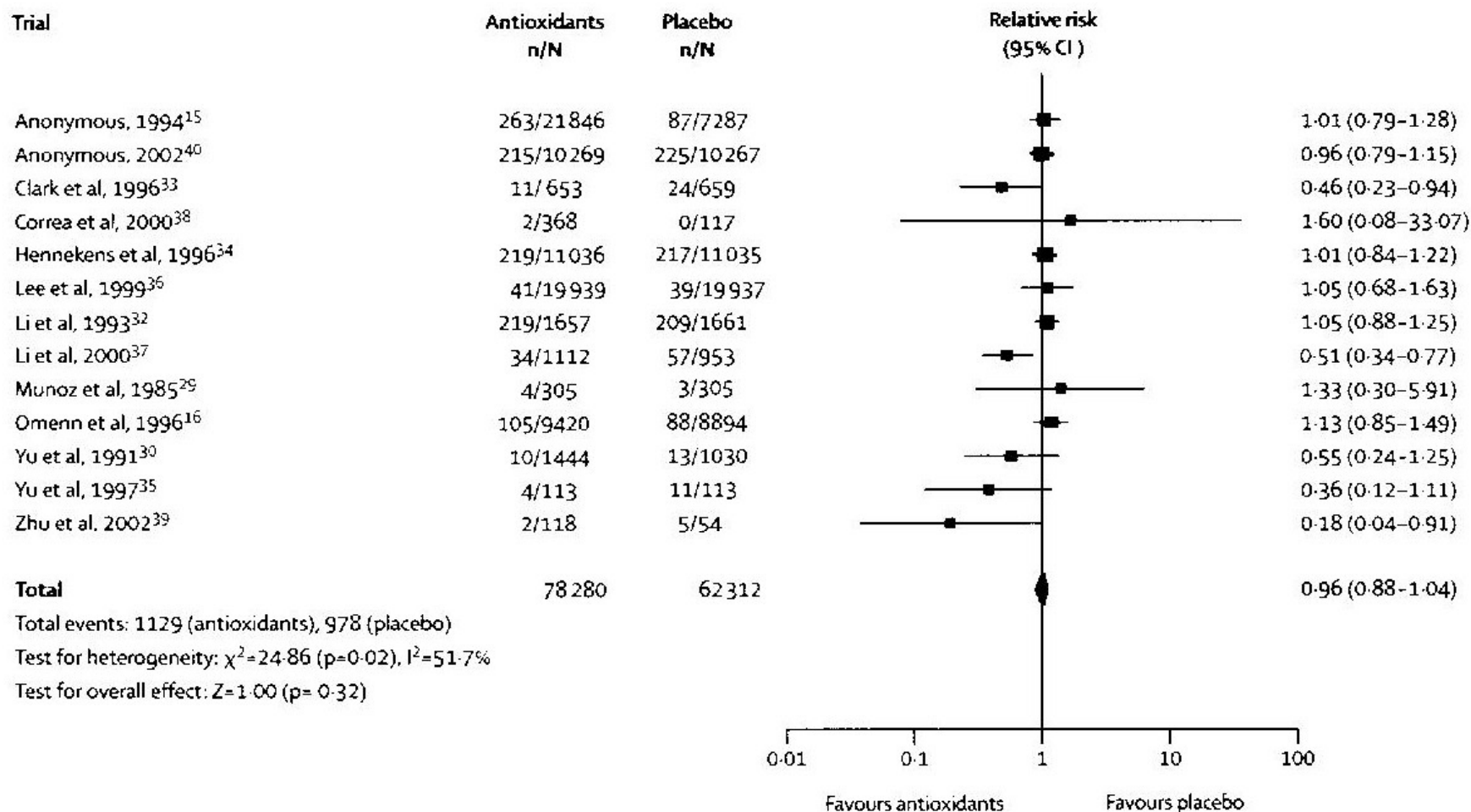
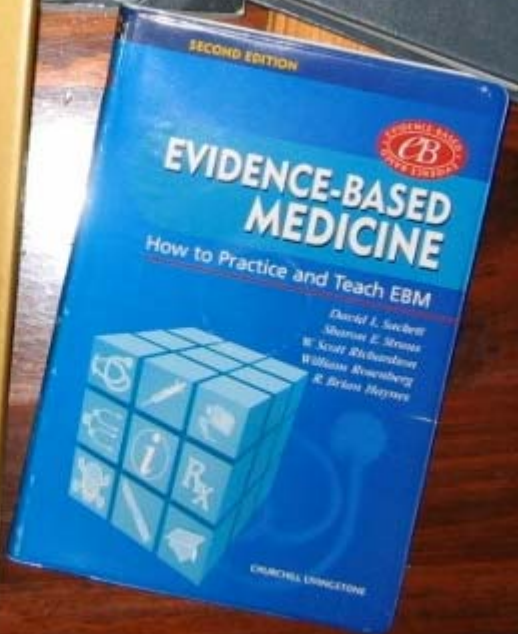
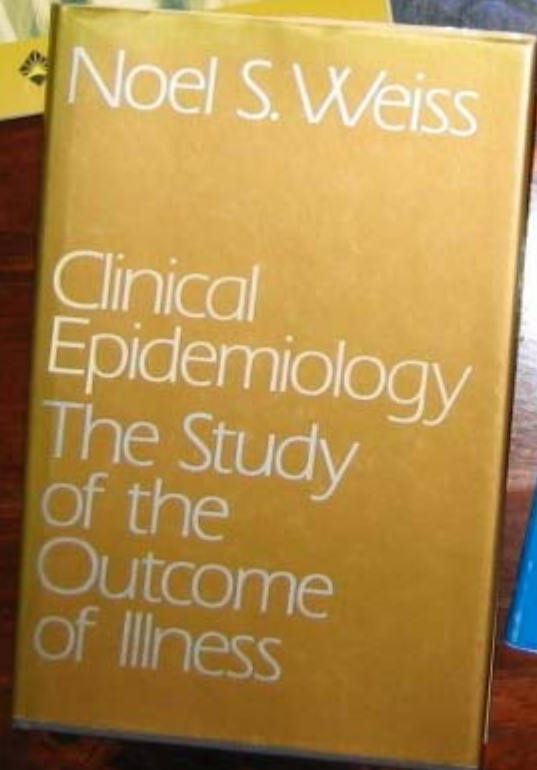
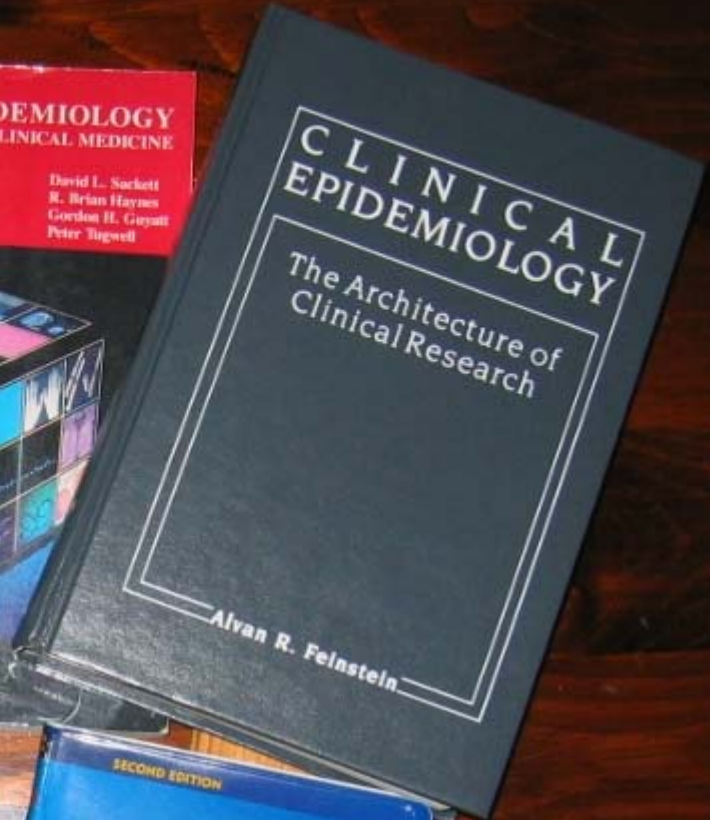
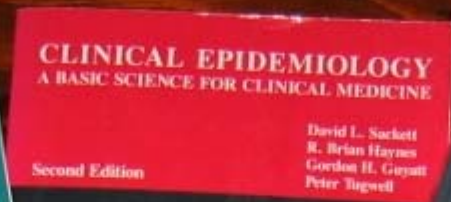
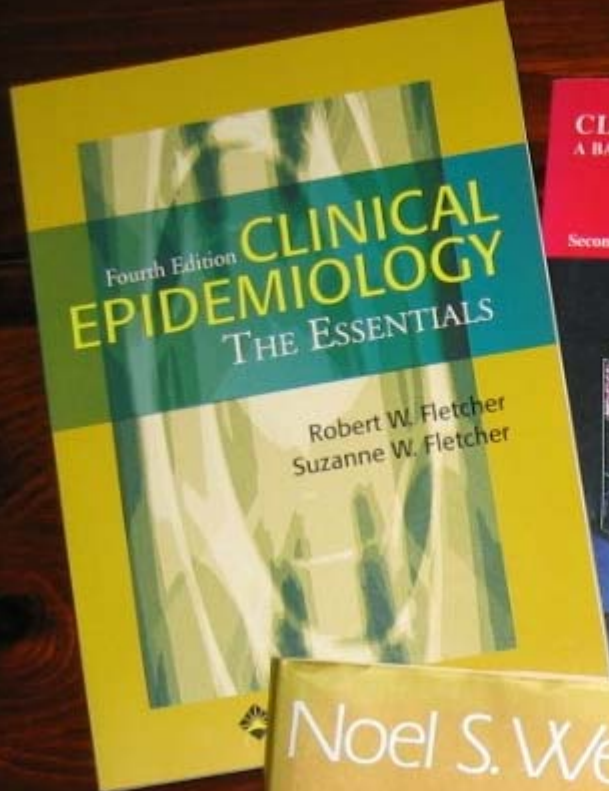


Figure 2: Intervention effect of all antioxidant supplements versus placebo on incidence of all gastrointestinal cancers combined
 Relative risks analysed with fixed-effect model.

Methodologic Questions in Clinical Medicine

- Why do RCTs disagree with each other?
- Why do RCTs sometimes disagree with consistent results from observational studies?
- How generalizable is clinical research to the community?
- When can we trust the results of observational studies?



Students in the Clinical Trials Course at the University of North Carolina

- 16 with clinical careers
 - 9 medical students earning masters degree in Epidemiology
 - 7 academic physicians or dentists getting an MPH or PhD in Epidemiology
- 11 non-physicians getting MSc or PhD in Biostatistics
- 1 PhD student in the Department of Health Policy

*Offered by the Department of Epidemiology,
School of Public Health

Training Programs for Fellows and Junior Faculty. A Typical Curriculum

Major

- Epidemiology + Biostatistics.
 - Design
 - Measurement
 - Analysis
- Population perspective
- Cost-effectiveness
- Social Science Methods

Minor

- Research Ethics
- Leadership
- Teaching Methods
- Research Management
- Qualitative Research

About 1 year leading to a Master's degree in Epidemiology

INCLIN GLOBAL MEETING XIX 2003, Kunming, china



International Standards for Reporting Clinical Research

- **CONSORT**: Consolidated Standards for Reporting Trials
- **QUOROM**: Quality of Reporting of Meta-analyses
- **MOOSE**: Meta-analysis of Observational Studies
- **STARD**: Standards for Reporting of Diagnostic Accuracy
- **TREND**: Transparent Reporting of Evaluations with Non-randomized Designs



THE COCHRANE
COLLABORATION®

International, Interdisciplinary Collaboration to Summarize and Disseminate the Best Available Research Evidence

- Gather evidence on effectiveness of interventions
- Voluntary teams throughout the world
- Many disciplines participate
- Search the world's research literature
- Prepare structured reviews
- Central synthesis and dissemination (Oxford, UK)
- Summaries available anywhere in the world

Evidence Based Medicine in Textbooks. *Example: UpToDate*

- Electronic-only “textbook” (library of medicine, pediatrics, OB/GYN, etc.)
- Over 70,000 pages (if it were printed)
- Abstracts of Original Research embedded
- Updated continually
- Widely used – in practice, academic medical centers, and throughout the world

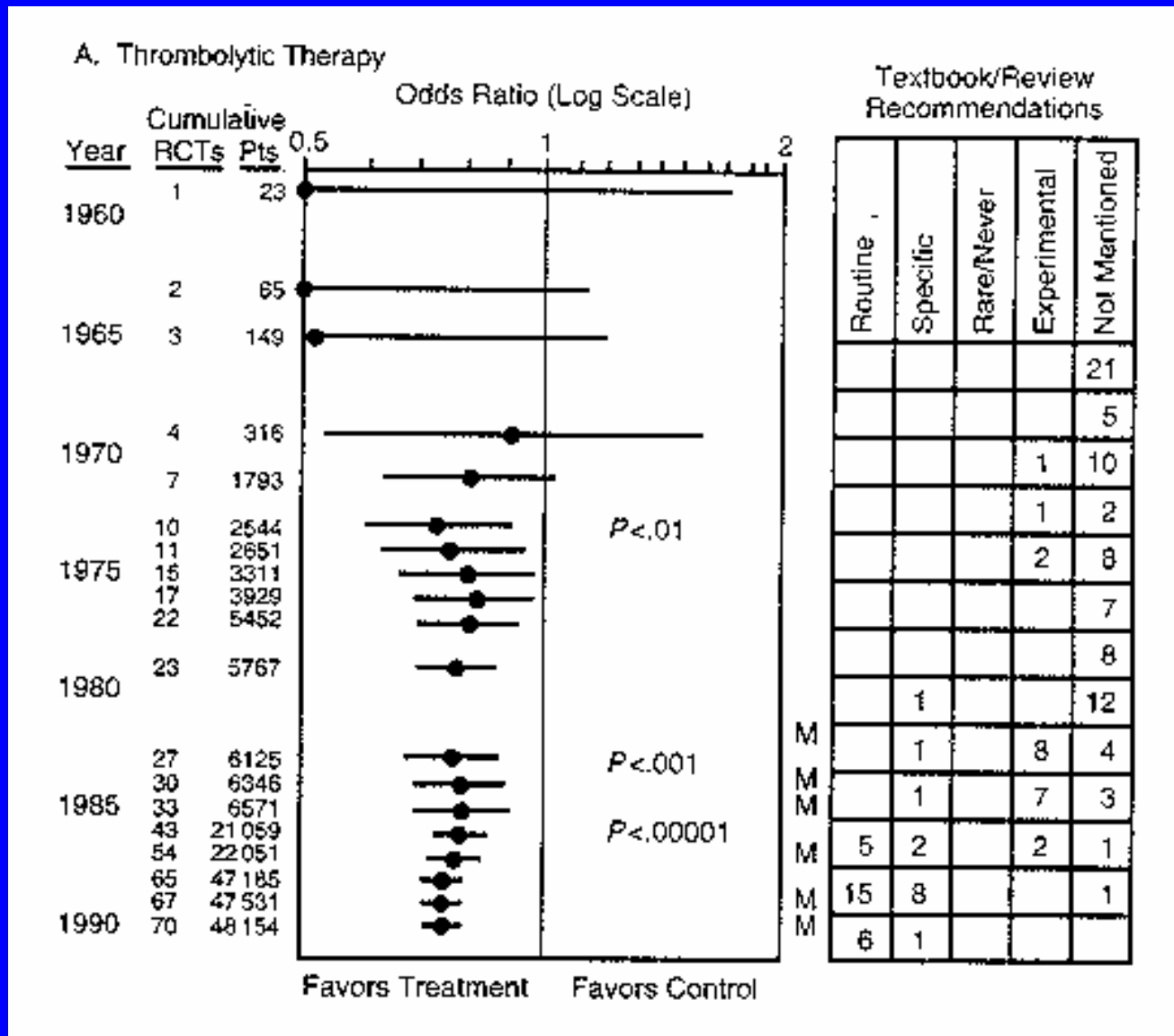
Programs to Strengthen Evidence Based Medicine Content of *UpToDate*

- Linking research abstracts to text
- Grading evidence
- Seminars for editors
- Use of the Cochrane Database
- Reviews by medical societies, methodologists
- Clinical epidemiologists on the editorial team
- Readers' feedback

Remaining Challenge: Narrowing the Gap Between Evidence and Practice

- Improve how clinical “opinion leaders” understand evidence
- Help clinicians understand how validity and generalizability are established
- Learn how to communicate risk effectively
- Compete successfully with alternatives to EBM

Cumulative Meta-analysis of Clinical Trials of Thrombolytic Therapy For Acute Myocardial Infarction and Experts' Recommendations



How accurate are estimates of probability that a positive screening test means that a baby actually had Down's syndrome?

Respondents	Number	Percent Correct
Obstetricians	41	43
Midwives	42	0
Pregnant Women	43	9

Alternatives to EBM

- **Eminence** based medicine
- **Vehemence** based medicine
- **Eloquence** (or elegance) based medicine
- **Providence** based medicine
- **Diffidence** based medicine
- **Nervousness** based medicine
- **Confidence** based medicine

How can clinical medicine benefit?

- Understand populations and prior probabilities for diagnostic tests
- Wiser judgments about the generalizability of research results
- Understand variation in disease rates, presentation (“Completing the clinical picture”)
- Understand expressions of risk

How can Epidemiology benefit?

- Expand research paradigm
- Make common cause with clinicians who are experts in biology of disease, relevant variables (exposure, disease, confounding, effect modifying)
- Encourage more “action” epidemiology, public health orientation
- Challenge conventional practice

Expanding Epidemiology's Domain

