JAMES LIND SYMPOSIUM

From scurvy to systematic reviews and clinical guidelines: how can clinical research lead to better patient care?

31 October 2003

SESSION 1

250 YEARS AGO

Chairman: Dr NDC Finlayson, President, Royal College of Physicians of Edinburgh

AN ANCIENT DEBATE: HOW RELEVANT ARE STATISTICAL DATA IN CLINICAL PRACTICE?

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ABSTRACT

Background: The relationship between numbers and clinical medicine has been a (minority) interest since the eighteenth century. It first gained momentum around 1780 in Britain,[1] and later in France and the USA, when the pros and cons were debated.[2] This paper focuses on the little-known British (Scottish) contributions, the underlying motives, the arguments for and against, and their later history, as well as the proposed ways out of the 'maze'. It sets James Lind's contributions in context.

Methods: Searching for, analysis and interpretation of published primary sources. Use of secondary literature.

Results: Clinical statistics were a means to lute the century-old schism between the rationalistic and empirical approaches to medical knowledge by the new means of 'rational (i.e. guided) empiricism.' It was meant to put medicine on a par epistemically with the natural sciences and thereby raise the social status of empirically minded doctors, particularly surgeons.

Opposition came from two sources: (i) those who defended medicine as an 'art' rather than a science, and who maintained that medical inference was a form of tacit knowledge rather than something explicit and quantitative, and (ii) those who stressed the clinical and ethical inappropriateness of statistics, particularly in therapeutics.[3,4]

Conclusions: Without denying the changed social and political circumstances, there are some striking parallels between aspects of the developments in Britain around 1800 and those 200 years later.

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KEY WORDS
Clinical statistics, motives, arguments pro and con, eighteenth century Britain, nineteenth century France, lessons from history

SPONSORS
Swiss National Science Foundation, Swiss Academy of Medical Sciences, University of Freiburg, Germany.

DECLARATION
No conflicts of interest declared

THE JAMES LIND LIBRARY: DOCUMENTING THE DEVELOPMENT OF METHODS TO EVALUATE THE EFFECTS OF MEDICAL TREATMENTS

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ABSTRACT
Background: An examination of the Bibliotheca Scorbutica section of James Lind's 1753 treatise suggests that the author both had a library and used libraries. Lind, in the Bibliotheca's 'critical and chronological view' of what had been published on scurvy, brought together almost all the then-available writings before critically appraising his predecessors' results and conclusions.

Two hundred and fifty years later the James Lind Library brings together examples illustrating the evolution of fair tests of medical treatments and contemporary expert commentaries. As in James Lind's day, many uncertainties exist today about the effects of medical treatments. Treatment effects – good and bad – are only very rarely so obvious that carefully designed, fair tests are not needed to identify them reliably. The James Lind Library has been created to introduce people to the characteristics of fair tests, and to illustrate how these tests have evolved. The Library contains examples from nearly 100 books and journal articles, illustrated by images of the key passages of text. New records are being added continuously, as well as biographical material, portraits, translations and other relevant material.

Methods: http://www.jameslindlibrary.org

Results: Not applicable

Conclusions: Not applicable

REFERENCES
1 http://www.jameslindlibrary.org
2 Lind J. *A treatise of the scurvy. In three parts. Containing an inquiry into the nature, causes and cure, of that disease. Together with a critical and chronological view of what has been published on the subject.* Edinburgh: Printed by Sands, Murray and Cochran for A Kincaid and A Donaldson; 1753.

KEY WORDS
James Lind, controlled trials, fair tests, bias, critical appraisal.

SPONSORS
Not submitted

DECLARATION
No conflict of interest declared.

SESSION 2

250 YEARS LATER

Chairman: Professor J Cash, Past President, Royal College of Physicians of Edinburgh

ASSESSING THE HOPED-FOR AND UNWANTED EFFECTS OF CLINICAL INTERVENTIONS TODAY

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ABSTRACT
Background: The randomised controlled trial is the key instrument to assess 'hoped for' effects of treatment. However, other causal effects, like adverse effects of treatment or disease aetiologies (e.g. genetic), are equally important in medical science. The latter are usually assessed by observational studies. The question arises whether observational studies can be as credible as randomised studies.

Methods: Review of achievements of randomisation and of assumptions that underlie observational comparisons, taking adverse effects research and genetic research as examples.

Results: Under specific conditions, observational comparisons can be as credible as randomised studies.

Conclusions: By way of generalisation, a three-pronged restriction is proposed (of research questions, of study design and of analysis) to give the best guarantee for the credibility of observational clinical and epidemiologic research.

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KEY WORDS
Randomisation, observational research, adverse drug reactions, genetic epidemiology, history of epidemiology.

SPONSORS
I am a full time employee of Leiden University Medical School.

DECLARATION
No financial conflict of interest. Several of the topics in the lecture were discussed during a sabbatical at Oxford in 2002–3.

DOES CLINICAL RESEARCH TO INFORM DECISIONS IN HEALTHCARE HAVE ANY FUTURE?

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ABSTRACT
Background: Two hundred and fifty years after Lind's work on scurvy, this question sadly remains relevant. At a time when patients, the profession and politicians all profess to seek improvements in clinical practice, it is instructive to reflect on some reasons why the question continues to be asked.

Methods: Not applicable

Results: Clinical research depends on admitting and understanding areas of uncertainty. Paradoxically, although the evidence base for much of clinical practice is weak, patients seek certainty and doctors generally feel comfortable discussing the options with which they have become familiar in the course of their clinical practice. 'In my experience' is an expression still commonly heard. Not many practising doctors are interested in health services research and few have an understanding of advances in research methodology. The biomedical model, based on the advances of the nineteenth century, continues to be predominant. Many doctors focus on clinical work, inevitably providing treatments for which the evidence base is weak or absent. The funding agencies contribute to the problem; research councils favour the basic sciences,[1] NHS Research and Development funds are not focussed only on research quality,[2] and the Research Assessment Exercise assesses clinical departments (Units of Assessment), not clinical research.[3]

Conclusions: Whatever the prevailing views on medical regulation, professional standards alone are no longer sufficient.[4] The information explosion, increasing evidence on clinical outcomes, introduction of guidelines, audit and the impact of the *Bristol Report*[5] in the UK all indicate the need for coordinated and high-quality clinical research. Improvements in patient care are dependent upon such an approach. Patients and the profession must together ensure that medical education, both undergraduate and postgraduate, motivates medical practitioners and other health professionals to seek answers to clinically relevant questions throughout their careers.

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4 General Medical Council. Good medical practice. September, 2003 http://www.gmc-uk.org/standards.
5 Bristol Inquiry. September, 2003. http://www.bristol-inquiry.org.uk/final_report/rpt_print.htm.

KEY WORDS
Clinical research, standards, clinical practice, clinical guidelines

SPONSORS
Graeme Catto is the President, General Medical Council, Vice-Principal, King's College London, and was formerly Chief Scientist, Scottish Executive Health Department

DECLARATION
No conflict of interest declared.

SESSION 3

INFORMATION TO SUPPORT TREATMENT DECISIONS
Chairman: Professor GDO Lowe, Chairman, Scottish Intercollegiate Guidelines Network

THE INTUITIVE PRACTITIONER: INTEGRATING CLINICAL EXPERIENCE AND JUDGEMENT WITH EVIDENCE-BASED MEDICINE

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ABSTRACT
Background: Evidence-based medicine offers exciting opportunities for improving outcomes, but the inexperienced, protocol-driven practitioner may provide evidence-burdened rather than evidence-informed care.

Old-fashioned, 'touchy-feely' medicine has a lot going for it, but it's hard to put a science to the intuitive knowledge and embodied wisdom of the experienced practitioner. By drawing on both real-life case examples and contemporary theories of knowledge creation and utlisation, this lecture offered some inroads to such science, and argued that it is time to move the evidence-intuition debate from either-or to both-and.*

The lecture was based on a previously published literature review and hypothesis (see below).

Methods: Not applicable

Results: Not applicable

Conclusions: Not applicable

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Greenhalgh T. Intuition and evidence – uneasy bedfellows? *Br J Gen Pract* 2002; **52:**395–400.

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* © Reproduced with the permission of the Royal College of General Practitioners. Greenhalgh T. Intuition and evidence – uneasy bedfellows? *Br J Gen Pract* 2002; **52:**395–400.

KEY WORDS

Evidence, intuition

SPONSORS

No sponsors

DECLARATION

No conflict of interest declared.

THE INFORMED PATIENT

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ABSTRACT

Background: 'Your patient has no more right to all the truth you know than he has to all the medicine in your saddlebags … He should get only just so much as is good for him.'

Oliver Wendell Holmes, 1871

Healthcare 'delivery', relationships and attitudes have changed since 1871, but not uniformly. Attitudes to the 'informed patient' today are perhaps as variable as clinicians' perceptions of the 'truth you know'. Whilst encouragement was given in June 2003 to UK National Health Service delegates by John Reid, Secretary of State for Health, 'to help every patient to be an informed patient',[1] the informed patient's rôle requires closer definition to achieve wider appreciation, acceptance and influence. Policy and practice must converge.

The author's 'Damascus Road' experience in 1991[2] of being invited (and refusing) to join a clinical trial that failed to accommodate or address her experience of the condition, or provide adequate information,[3] following receipt of even worse-quality information as a healthy citizen invited to attend for mammographic screening, compelled her to advocate for better-quality information for citizens and patients,[4] and for public involvement in the whole research process through a working collaboration of profession and public.[5] Today's patient may be passive or involved:[6] it is necessary for the involved patient to be an informed one. (Involved either individually in terms of their own health management and decision-making (to a degree according to their own preference),[7] or involved societally or more widely on behalf of others.)

Methods:

- dialogues and debates with (mostly) helpful health professionals: by correspondence, face-to-face, in medical journals, at conferences and meetings;
- forming an advisory working group of health professionals and patients to improve quality of research and education of the public;[5]
- writing;
- presenting papers;
- engaging in debates;
- addressing (educating?) medical students;
- initiating, through the Consumers' Advisory Group for Clinical Trials, a collaborative research project;[8]
- working in various research teams (advisory; as steering committee member; as Data Monitoring and Ethics Committee member);
- reviewing, commenting and advising from the 'consumer' perspective on papers for publication, research reviews and research proposals; and
- media interviews.

Results: Collaborations and involvements have led to increasing and ongoing improvement in both the appreciation of the need for good quality, accessible information in all aspects of healthcare, for citizens and patients, within and without research. It is becoming more widely accepted that there is a rôle for the 'informed patient' and that it can be a valuable one.

Conclusions: Great advances have been made. Much

remains to be done.

The public should also take the initiative: it should not necessarily wait to be asked.[9] The benefits that can accrue to the public and health service delivery from well-informed patients and health professionals working together might even have converted Oliver Wendell Homes, were he with us today.

We need to cultivate and nurture a new culture of collective responsibility.[10]

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KEY WORDS

Informed patient, public involvement, policy, good quality information, public professional collaboration, collective responsibility.

SPONSORS

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DECLARATION

No competing interests.

TRIBUTE TO PROFESSOR JAMES C PETRIE CBE

Chairman: Professor GDO Lowe, Chairman, Scottish Intercollegiate Guidelines Network

GUIDELINES CAN IMPROVE PROCESS AND OUTCOMES OF HEALTHCARE

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ABSTRACT

Background: Clinical practice guidelines are an increasingly common element of clinical care throughout the world.[1] Such guidelines have the potential to improve the care received by patients by promoting interventions of proven benefit and discouraging ineffective interventions. However, the development and introduction of guidelines are not themselves without costs. In some circumstances, the costs of development and introduction are likely to outweigh their potential benefits.[2] In other circumstances, it may be more efficient to adopt less costly but less effective dissemination and implementation strategies. Local healthcare organisations have relatively few resources for clinical effectiveness activities and policy-makers need to consider how best to use these to maximise benefits.

Methods: Systematic review of the effectiveness and resources of different guideline development, dissemination and implementation strategies.[3]

Results: Two hundred and thirty-five studies reporting 309 comparisons met the inclusion criteria. The overall quality of the studies was poor; 95% of studies reported data on process of care. The majority of interventions observed modest to moderate improvements in the process of care. For example, the median absolute improvement in performance across interventions ranged from 14·1% in 14 cluster-randomised comparisons of reminders, 8·1% in four cluster-randomised comparisons of dissemination of educational materials, 7·0% in five cluster-randomised comparisons of audit and feedback and 6·0% in 13 cluster-randomised comparisons of multifaceted interventions involving educational outreach. We found no relationship between the number of component

interventions and the effects of multifaceted interventions. Only 22% of studies reported data on outcome of care; approximately two-thirds of these reported improvements. Few studies provided reliable data on the resources required for the different dissemination and implementation strategies.

Conclusions: There is an imperfect evidence base to support decisions about which guideline dissemination and implementation strategies are likely to be efficient under different circumstances. Nevertheless guidelines do appear to be able to improve process and outcome of care.

Decision-makers need to use considerable judgement about how best to use the limited resources they have for clinical governance and related activities to maximise population benefits, based upon consideration of the potential clinical areas for clinical effectiveness activities, the likely benefits and costs required to introduce guidelines, and the likely benefits and costs as a result of any changes in provider behaviour.

Further research is required to: develop and validate a coherent theoretical framework of health professional and organisational behaviour and behaviour change to inform better the choice of interventions in research and service settings; and to estimate the efficiency of dissemination and implementation strategies in the presence of different barriers and effect modifiers.

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KEY WORDS

Clinical practice guidelines, dissemination and implementation strategies, behaviour change, systematic review

SPONSORS

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DECLARATION

No conflict of interest declared.

GUIDELINES, ALGORITHMS, SCIENCE AND AUTOMATA

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ABSTRACT

Background: 'There are three great branches of science: theory, experiment, and computation.'

Nick Trefethen

Advance in the mid-third of the twentieth century, the golden age of medical research, was predicated on earlier discoveries in the nineteenth century in both physiology and medicinal chemistry.[1] Genetics dominated biology in the latter third of the twentieth century and many believe changes in medical practice will owe much to genetics over the next third-century.[1] I disagree, and I will give an alternative view more credence: in 30 years' time we will look back more to Neumann and Morgenstern than we will to Watson and Crick. What the Nobel laureate Herbert Simon referred to as *The Sciences of the Artificial*,[2] subjects which have largely been peripheral to medicine, will become central.

Over the last 20 years we have seen the first (largely inadequate, I would add) attempts to explicitly demarcate methods of obtaining and promulgating knowledge about clinical practice.[3, 4] This has usually taken the form of proselytising a particular set of terms – systematic reviews, evidence-based practice, guidelines and the like, terms that have little to commend them – or rigour. What is interesting, however, is that they reflect a long overdue renaissance of interest with the practice of medicine and medical epistemology.

The change of emphasis from the natural to the artificial[2] is being driven by a number of forces, mostly extraneous to biomedicine: the increasing instrumental role of science in medicine and society; the increase in corporatisation of knowledge, whether by private corporations or monopsonistic institutions like the NHS;[5] the rising costs of healthcare; and a remaining inability to frame questions with broad support about how to chose between alternative disease states at the level of society.[6, 7]

I will try to illustrate some of these issues by the use of three examples. First, the widespread use of a mode of statistical inference largely ill-suited to medicine, namely Neyman–Pearson hypothesis testing (decision-making), and the way in which this paradigm has been used to undermine expert opinion.[8] Second, I will argue that we need to think much harder about clinical practice and fashion a more appropriate theoretical underpinning for clinical behaviour. Third, I will suggest how UK medical schools, in so far as they remain interested in clinical practice, should look to alternative models, perhaps business and law schools, for ideas of how they should operate.[2]

Methods: Not submitted

Results: Not submitted

Conclusions: Not submitted

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KEY WORDS
Epistemology, statistics, hypothesis testing, dermatology

SPONSORS
I am an employee of The University of Edinburgh.

DECLARATION
The University receives funding from The Wellcome Trust, Industry and the NHS (CSO) on my behalf. I occasionally consult for pharmaceutical and cosmetics companies

EDITOR'S FOOTNOTE

Von Neumann (1903–57)[1] is considered to have been a mathematical genius of similar status to Albert Einstein and is often referred to as the father of the modern computer. His algorithms allowed reliable answers to be obtained from the first large computers in spite of their unreliable components. He is best known to mathematicians for the development of the methods that revolutionised quantum mechanics, the theory of operator algebra and the invention of game theory. His mathematical approach contributed to Edward Teller's development of the implosion nuclear bomb dropped on Nagasaki and to the theoretical basis of the deterrent defence strategy of the US.

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EDITORIAL NOTE

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