JOURNAL OF THE ROYAL SOCIETY OF MEDICINE

December 2003 Volume 96 Number 12 ISSN 0141-0768

The James Lind Initiative

Just 250 years ago James Lind, a Scottish naval surgeon, published his *Treatise of the Scurvy*.[1] The disease in question was killing thousands of people every year and had caused many more deaths in the Royal Navy than enemy action. In Lind's opinion, one reason for the prevailing confusion about the diagnosis, prevention and cure of scurvy was that 'no physician conversant with this disease at sea had undertaken to throw light upon the subject'. He set about filling this gap, with a clear commitment to base his work on 'observable facts' rather than the theories of medical decision-making at that time. Lind's *Treatise* consists largely of what we would now call a systematic review of the published work. He specified his search strategy for relevant material, and observed bluntly that 'before the subject could be set in clear and proper light, it was necessary to remove a great deal of rubbish'.

Famously, the book also contains one of the earliest accounts of a prospective controlled trial, in which Lind compared six of the many different treatments for scurvy then in use. He selected for the experiment twelve sailors who were all at a clinically similar stage of the disease, and arranged for them to receive the same basic diet and to be accommodated in the same part of the ship. Lind's systematic review and experiment suggested that oranges and lemons were more effective than other treatments for scurvy; but almost half a century was to pass before British sailors began to benefit from the results of this research and other evidence. It was not until 1795 that the Admiralty issued a general order sanctioning the provision of lemon juice on a far more generous scale than previously. Within two years scurvy had almost disappeared from the Royal Navy.[2]

James Lind's systematic review of existing evidence and his concurrently controlled experiment are not above criticism; for example, we are not told how he allocated his twelve patients to each of the six treatments he compared. Even so, his methodical approach to generating empirical evidence to test therapeutic theories and inform policy and practice remains exemplary.

250 years after publication of the *Treatise* there is wide acceptance of the principle that decisions in healthcare and health policy should be informed by up-to-date systematic reviews of reliable relevant research. However, attempts to apply this principle in practice often fail because reviews reveal that the information needed is simply not available. The effects of many healthcare interventions remain uncertain. Furthermore, controlled trials are still too often done without first assessing what is known already; they are frequently designed and conducted in ways that yield little information relevant to patients, health professionals, and policy-makers;[3] and it is usually impossible to assess the significance of individual controlled trials because the reports seldom indicate what difference the new results make in an updated systematic review of all the other relevant evidence.[4]

The James Lind Initiative has been established to lobby for better randomized controlled trials because these studies can provide some of the most important information needed to improve healthcare. Various strategies will be needed. One involves promoting greater public demand for better, more relevant, controlled trials. Because of the perverse incentives that distort the research agenda,[3] patients and their representatives should be encouraged to discriminate between controlled trials that deserve their support and those that do not.[5] Involvement of people using the health services in all phases of controlled trials should help to ensure that these studies address issues of real importance, and that the results are made public. In particular, patients and the public need to press for funding of trials addressing questions that are important to patients but of no interest to industry.[6–8]

The James Lind Initiative will also press for controlled trials to become a more usual element within routine healthcare. When systematic reviews have shown that the effects of healthcare interventions are unclear, participation in controlled trials should be seen as a professional responsibility.[9] This principle is already reflected in the *NHS Plan*,[10] which calls for a doubling of the number of people enrolled in controlled trials to address uncertainties about cancer treatments.

Engaging the public, patients and the professions in these matter implies provision of readily accessible information about the rationale for controlled trials; about what is and is not known about the effects of treatments on offer; and about planned and ongoing trials that are addressing important uncertainties. The National electronic Library for Health is an increasingly rich source of this information [www.nelh.nhs.uk]. In collaboration with the

Royal College of Physicians of Edinburgh (where James Lind was Treasurer), the James Lind Initiative has contributed by developing *The James Lind Library* [www.jameslindlibrary.org]. This digital library is helping to increase general knowledge about how, in assessing the effects of medical treatments, the effects of biases and chance can be reduced. *The James Lind Library* contains images of key passages of text from books and journal articles illustrating the evolution of fair tests of medical treatments. New records are being added continuously, as well as biographical material, portraits, translations, commentaries, and other material. Encouragingly, the *Library* received one of only five awards issued by *Scientific American* for medical websites in 2003.

In summary, the James Lind Initiative will promote better controlled trials for better healthcare by emphasizing certain key principles. All controlled trials should be designed in the light of systematic reviews of what is known already, and all reports of new results from controlled trials should make clear what impact they have on updated systematic reviews of all the evidence relevant to the questions addressed. Involvement of patients and the public in all phases of controlled trials should increase the relevance of these studies to their principal intended beneficiaries. Finally, when systematic reviews have revealed important uncertainties about the effects of healthcare interventions, patients and professionals should come to regard participation in controlled trials as the norm. In other words, therapeutic uncertainties should be confronted as an integral element of responsible healthcare—just as James Lind did a quarter of a millennium ago.

Acknowledgments I am grateful to Jan Chalmers, Carolan Davidge, Paul Glasziou, Muir Gray and Iain Milne for comments on earlier drafts.

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In an article on page 605, Dr Graham Sutton reports large discrepancies between the ship's papers and Lind's account of sickness aboard the Salisbury. *In Dr Sutton's opinion, Lind's version is the more credible.—Editor, JRSM*