

Human Experimentation: a Guided Step into the Unknown

William A Silverman, Oxford, 204 pages, £20.00, Oxford University Press, 1985.

Silverman, formerly professor of paediatrics at Columbia University, New York, argues eloquently for the wider use of randomised trials when introducing new treatment, not least because therapies have become increasingly powerful ('medical weapons in a popular war') and so the potential for harm has increased enormously. The author's poignant main example – competing risks of perinatal mortality, blindness from retrolental fibroplasia, cerebral palsy, associated with different modifications of oxygen therapy for premature infants – is devastatingly well chosen to illustrate the fireworks factory thesis: 'It is better to curse the darkness than to light the wrong candle'.

The text is generously gilded with pithy parables, apt aphorisms and quaint quotations, such as 'God is the answer! But what is the question?' to introduce the chapter on framing the question. 'Knowing' in medicine is traced from a heritage of authoritarianism through the growth of scepticism and the spirit of Galilean experimentation to the randomised clinical trial. The third chapter on representative patients distinguishes between random and haphazard selection and lists some biases described by Sackett in specifying and selecting the study sample. The Sackett list appears as a boxed textual digression on a single page, but elsewhere in the book similar blocks of boxed illustrative text have been split between pages to tax the reader! Controlled comparison is introduced by an attributed, joyously exasperated expostulation on the pitfalls of interpreting retrospective experience: 'Looking backward: is it worth the crick in the neck?' A good chapter on intervention follows, the problems of flexible dosage, timing of intervention, monitoring of on-going effects and multiple end points being superbly illustrated in the retrolental fibroplasia (RLF) trial example. Moreover, an appendix on the RLF story makes fascinating, challenging reading – how could the research effort have been better directed? Chapters follow on accurate observation (chapter

6), with cunning illustrations, for example of measurement scales – a begging man's summary of his plight:

wars	2
legs	1
wives	2
children	4
bankruptcies	2

11

on the event of interest (chapter 7) and avoiding entrapment (chapter 8), (for example, in multicentre trials; the need to ensure external relevance and vigilance to thwart misguided sabotage – as when night nurses turned up the oxygen of premature babies randomised to curtailed oxygen therapy).

Silverman discourses divertingly, a generalist who has dabbled in philosophy, decision analysis (chapter 11), and experimental design but who readily invokes the authority of others by generous quotation from their writings when those contributions are well put. Silverman's own love of language and clever use of it attest to the sincerity of these references.

It is in respect of statistics that language occasionally becomes licence or illustrations are alarmingly simplistic, as in the illustration of a three-patient three-period cross-over design unbalanced for carryover. When the number of periods is odd, the smallest design which gives balance for first order carryover requires twice as many patients as periods. In discussing a chance difference in mortality the author notes that: 'Variations of this magnitude can be expected as the result of chance allocation of patients at relatively high risk to one treatment group'. Silverman's scenario is a sufficient, but not a necessary explanation. The vagary of statistical terminology, more than the author, is responsible for any misunderstanding that may derive from the statement: 'a 95 per cent confidence interval, for example, is the 2 standard deviation range surrounding the observed value'. Paradoxically, statisticians use the term standard error to denote the standard deviation of a statistic.

The chapter on stopping rules (chapter 9) suggests that the magnitude of an 'important' difference should reflect a view of public gain or loss, yet the power functions which are illustrated on page 117 relate only to large target differences such as an increase from 30 per cent to 60 per cent response and could seem to promote trials with low power to detect more modest target differences. *Human Experimentation: a Guided Step into the*

Unknown is not a book on statistics (but see chapter 10) and so it is churlish of me to overemphasise these remarks except insofar as the final chapter, on the ethics of human experimentation, notes correctly that there is no point in obtaining informed consent to a useless study. Human experimentation must first reach the beach* between statistics and ethics before a direct trial assault can proceed.

Silverman advocates informal surveillance via the patient's personal and disinterested physician and notes that general ethical propositions do not decide concrete cases. Is complete candour warranted or should the patient decide the extent of disclosure? Attitude surveys are referenced. The public character of scientific method is its best advocate and Silverman supports the principle of rationality and notes that: 'Science teaches us to doubt and, in ignorance, to refrain'.

This non-technical, well written, exemplified text should appeal to public and professional readership alike and develops the sound ethical case for reasoned human experimentation.

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Mental Health and Human Conscience – the True and the False Self

E K Ledermann, Aldershot, Hants/Brookfield, Vermont USA, 228 pages, £7.95 paperback, £20 hardback US \$14.50 paperback US \$36 cloth, Gower Publishing Co Ltd, 1984.

Existentialism will be familiar to few psychiatrists and fewer doctors whose empirical training has eschewed the study of philosophy. To others it will be indelibly associated with radical 40s and 50s intellectualism, the ideas of J P Sartre and a rather asocial, individualistic ethic. In this country R D Laing is the only major psychiatrist to have systematically applied existentialism to the concepts and treatment of mental illness and it is fashionable to decry his ideas as invalid and antitherapeutic.

Ledermann attempts a new and valuable exploration of such concepts and thereon develops a non-dogmatic existential therapy. His book is timely:

* Gaelic for a high pass or watershed [Editor].