EDITOR’S CHOICE

Randomization, trials and tribulations

The decision of who to treat—the issue of allocation of scarce resources—was the doctor’s dilemma that formed the substance of George Bernard Shaw’s play first performed in 1906. The excerpts reproduced here come from the Preface on Doctors which Shaw added as a commentary to the play in 1911. Shaw develops a number of themes—of particular note is his championing of a socialized system of medicine to avoid the perverse incentives to investigate and treat patients needlessly that were (and probably still are) rampant in a largely private health care system. Shaw also notes the inconsistencies in clinical practice in which different doctors will consider their own treatments superior to those of other doctors, even when not a shred of evidence exists to choose between them. Systematic reviews of randomized controlled trials conducted by the Cochrane Collaboration are now improving this situation and hopefully contributing to reducing the humbug and paternalism in medicine lamented by Shaw.

Randomization is the theme of the series of papers on Ronald Aylmer Fisher and Austin Bradford Hill. Both appreciated the importance of randomization in experimental design, although in Bradford Hill’s case he emphasized its value as a means of concealing allocation, and thereby avoiding selection bias. Fisher’s emphasis was different. He saw randomization as a means of ensuring that valid tests of significance of differences between comparison groups could be conducted. The commentaries published here give intriguing insights into the personalities, relationships and, importantly, the immense contributions both men made to medical science.

This issue’s theme is mental health. Are ‘psychological factors’, such as vital exhaustion, causally linked to increased risk of cardiovascular disease?1 Does smoking cause suicide?2 The implications for health promotion of the answers to these questions are profoundly important. Our commentators note that non-causal associations arise through mechanisms of reporting bias, are profoundly important. Our commentators note that non-causal associations arise through mechanisms of reporting bias, and through psychological factors acting as causal associations.3 Few studies are capable of excluding this range of explanations and ultimately the answer lies—where possible—in conducting randomized controlled trials. The ENRICHD trials4 of psychological interventions after myocardial infarction failed to show any benefit in terms of recurrence of cardiovascular events suggesting that the psychological factors are not causally related to disease. However, the accompanying commentary in the Journal of the American Medical Association5 called for further trials of more powerful treatments and large enough to detect smaller effect sizes—despite the confidence intervals of the estimate from ENRICHD excluding an effect as small as a 14% reduction in events. It is understandably hard for some investigators to let such hypotheses die.

The smoking and suicide relationship was originally used to illustrate that even strong associations can be seriously confounded6 but many investigators believe the association is causal. In this issue we publish Hemmingsson and colleagues paper7 showing that the association is attenuated by adjustment for heavy alcohol consumption and mental problems among smokers which they interpret as providing evidence against the causal hypothesis. Our commentator thinks the relationship is indeed causal and that Hemmingsson’s analysis is spurious as it has ‘overadjusted’ for factors on the causal pathway between smoking and suicide.7 This debate will doubtless continue.

SHAH EBRAHIM
Co-Editor

References