

Cramer JA, Spilker B, eds. *Patient Compliance in Medical Practice and Clinical Trials*. Raven Press, New York, 1991, 414 pages, ISBN 0-88167-735-3.

This book contains five sections. The first deals with the question as to what patient compliance is, and how it affects the physician's recommendations for dosage, as well as the performance of clinical trials. In subsequent chapters on compliance in children, adolescents and older people, various authors seek to determine whether the degree of compliance differs among special populations. Thereafter a section of the book discusses the effect of missing doses on patients, and provides an elaborate overview of monitoring techniques in some specific fields of therapy: epilepsy, asthma, glaucoma, hyperlipoproteinemia, depression, diabetes and oral contraception. Next the book tackles the question as to how the issue of incomplete compliance in clinical trials can be handled. The book ends with a review of the impact of partial compliance on health care and research.

Most of the research carried out into patient compliance in the past was concerned with identifying factors which either promote or impair compliance. Compliance has been found to be unrelated to a patient's age, sex, personality traits, income, social class, or educational background. In this book there is a consensus among authors that instead of this correlational research there is a clear need for prospective and controlled experimental manipulation of variables to improve compliance. Such strategies to improve compliance can be broadly classified as educational, organizational, and behavioral. In children, for instance, educational strategies have been proven to be helpful components of compliance intervention where short-term treatment is concerned, but not in the treatment of chronic disease. Successful behavioral strategies relate to monitoring, prompting, contingent performance feedback and reinforcement strategies implemented by health care providers or parents. Research on the improvement of compliance might nevertheless best be described as still being in the technique-building phase.

Many reviews in the book show that too many compliance studies in the past have relied on insufficiently objective methods to assess compliance. The techniques traditionally used comprise patient interviews or observation, the periodic counting of tablets, chemical monitoring of drug levels or of markers in body fluids, radioactive tracer studies or the review of pharmacy records. A new method of assessment, however, has undermined many traditional beliefs about compliance; this newer method uses a tablet container which incorporates a microprocessor to record the date and time of every opening, thus providing data in real time. The resulting electronic monitoring data confirm that standard compliance measures provide little insight into medication-taking patterns. Any clinical test or measure that reflects the last 24 h of medication use will substantially overestimate compliance, because medication compliance increases before a return appointment. The level of treatment efficacy attained will be overstated and the physician is likely to have an overly optimistic view of the patient's prognosis. There is thus little correlation between the physician's estimate of compliance and what is measured by the electronic monitor. Research shows that physicians, regardless of their training or experience, have no better than a chance probability of identifying those patients who will or will not comply with an intervention. Many authors in this book acknowledge that it is difficult to draw firm conclusions from a review of the literature, due to lack of reliable methodologies in the past. Or as one reviewer puts it: "The conclusions (i.e. of this study) mimic the weak methodologies employed in the studies reviewed".

In the section on patient compliance in clinical trials some very convincing arguments are given to justify including medication compliance as a co-variable of the outcome data of clinical trials. Many clinical trials of medication given at frequent intervals (e.g., four times a

day) may be of questionable validity because of partial compliance. In fact, potentially valuable medications may be discarded because of unrecognized under-use which has led investigators to conclude incorrectly that they are not effective. Conversely, if a new form of medication is overused, adverse reactions may in fact be related to this overuse rather than be a true characteristic of the medication when taken as prescribed. The opposite situation is also likely to be encountered: various effective medicines have been removed from the market (e.g. zomepirac, benoxaprofen, nomifensine) because of an unacceptable rate of adverse reactions; it is conceivable that, if specific compliance information (in this case under-use during clinical trials, resulting in a misleading impression of safety) had been available at the time of marketing, some of those medicines would never have come to the market at all. In this section of the book there is a very interesting contribution on patient compliance as an explanatory variable in four selected cardiovascular studies; in those studies, data on compliance played an important role in the analysis and interpretation of the results. An example is the interpretation of the outcome of the Coronary Drug Project trial on clofibrate. On the whole no difference in mortality was found between the clofibrate and the placebo group, but a subgroup analysis showed that in the clofibrate group there was a statistically significant decrease in mortality in the good compliers as compared with the poor compliers. However, a similar analysis of patients in the placebo group revealed a similar statistically significant decrease in mortality in the good compliers as compared with the poor compliers. Some authors use this as an argument for not excluding non-compliers in the analysis of data from clinical trials. Others see it as an obligation to gain as much useful information as possible from a trial by applying subgroup analysis by including data on compliance. In this specific case it was concluded that probably the most likely basis for the association of decreased mortality with good placebo compliance was a linkage between compliance with placebo and compliance with important non-trial medications.

This book is, as pointed out in the text, written for practising physicians and health care personnel who recognize the possibility and occurrence of noncompliance by their patients but remain unable to make any reliable guess as to 'who, when and how much'. The book contains contributions from about fifty different authors. The editors should have edited the book a little more rigorously. As it is, there is a considerable overlap in the oft-repeated descriptions of the monitoring techniques used in compliance research. The chapters on specific therapies, such as epilepsy and asthma, are valuable for specialists in these fields. The section on clinical trials is of great interest to drug researchers and registration officers. The greatest virtue of the book however is the insight it gives into the shortcomings of compliance research in the past and the direction it sets for the future. With the recent introduction of new and more reliable techniques for assessment of compliance, work in real compliance research is in fact only just beginning. For practising physicians, pharmacists and other health care workers many useful findings may be anticipated which will have repercussions for their daily work. Further editions of this book will therefore be awaited with great interest.

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