



Statistics Notes: Time to event (survival) data

Douglas G Altman and J Martin Bland

BMJ 1998;317:468-469

Updated information and services can be found at:
<http://bmj.com/cgi/content/full/317/7156/468>

These include:

References

This article cites 7 articles, 4 of which can be accessed free at:
<http://bmj.com/cgi/content/full/317/7156/468#BIBL>

8 online articles that cite this article can be accessed at:
<http://bmj.com/cgi/content/full/317/7156/468#otherarticles>

Rapid responses

You can respond to this article at:
<http://bmj.com/cgi/eletter-submit/317/7156/468>

Email alerting service

Receive free email alerts when new articles cite this article - sign up in the box at the top left of the article

Topic collections

Articles on similar topics can be found in the following collections
[Other Statistics and Research Methods: descriptions](#) (604 articles)

Notes

To order reprints follow the "Request Permissions" link in the navigation box

To subscribe to *BMJ* go to:
<http://resources.bmj.com/bmj/subscribers>

The results of primary research should be systematically reviewed to identify promising implementation techniques and areas where more research is required.³ Undertaking reviews in this area is difficult because of the complexity inherent in the interventions, the variability in the methods used, and the difficulty of generalising study findings across healthcare settings. The Cochrane Effective Practices and Organisation of Care Review Group is helping to meet the need for systematic reviews of current best evidence on the effects of continuing medical education, quality assurance, and other interventions that affect professional practice. A growing number of these reviews are being published and updated in the *Cochrane Database of Systematic Reviews*.^{4 31}

This paper is based on a briefing paper prepared by the authors for the Advisory Group on the NHS research and development programme on evaluating methods to promote the implementation of research and development. We thank Nick Freemantle for his contribution to this paper.

Funding: This work was partly funded by the European Community funded Eur-Assess project. The Cochrane Effective Practice and Organisation of Care Review Group is funded by the Chief Scientist Office of the Scottish Office Home and Health Department; the NHS Welsh Office of Research and Development; the Northern Ireland Department of Health and Social Services; the research and development offices of the Anglia and Oxford, North Thames, North West, South and West, South Thames, Trent, and West Midlands regions; and by the Norwegian Research Council and Ministry of Health and Social Affairs in Norway. The Health Services Research Unit is funded by the Chief Scientist Office of the Scottish Office Home and Health Department. The views expressed are those of the authors and not necessarily the funding bodies.

Conflict of interest: None.

- 1 Eddy DM. Clinical policies and the quality of clinical practice. *N Engl J Med* 1982;307:343-7.
- 2 Grimshaw JM, Freemantle N, Langhorne P, Song F. *Complexity and systematic reviews: report to the US Congress Office of Technology Assessment*. Washington, DC: Office of Technology Assessment, 1995.
- 3 Mulrow CD. Rationale for systematic reviews. *BMJ* 1994;309:597-9.
- 4 Bero L, Grilli R, Grimshaw JM, Harvey E, Oxman AD, eds. *Effective professional practice and organisation of care module*, Cochrane Database of Systematic Reviews. *The Cochrane Library*. The Cochrane Collaboration; Issue 4. Oxford: Update Software; 1997.
- 5 Implementing clinical guidelines: can guidelines be used to improve clinical practice? *Effective Health Care* 1994; No 8.
- 6 Grimshaw JM, Russell IT. Effect of clinical guidelines on medical practice: a systematic review of rigorous evaluations. *Lancet* 1993;342:1317-22.
- 7 Oxman AD, Guyatt GH. The science of reviewing research. *Ann N Y Acad Sci* 1993;703:123-31.
- 8 Oxman AD. Checklists for review articles. *BMJ* 1994;309:648-51.

- 9 Lomas J. Words without action? The production, dissemination, and impact of consensus recommendations. *Annu Rev Public Health* 1991;12:41-65.
- 10 Grilli R, Lomas J. Evaluating the message: the relationship between compliance rate and the subject of a practice guideline. *Med Care* 1994;32:202-13.
- 11 Oxman AD, Thomson MA, Davis DA, Haynes RB. No magic bullets: a systematic review of 102 trials of interventions to help health care professionals deliver services more effectively or efficiently. *Can Med Assoc J* 1995;153:1423-31.
- 12 Beaudry JS. The effectiveness of continuing medical education: a quantitative synthesis. *J Continuing Education Health Professions* 1989;9:285-307.
- 13 Davis DA, Thomson MA, Oxman AD, Haynes RB. Changing physician performance: a systematic review of the effect of continuing medical education strategies. *JAMA* 1995;274:700-5.
- 14 Mugford M, Banfield P, O'Hanlon M. Effects of feedback of information on clinical practice: a review. *BMJ* 1991;303:398-402.
- 15 Buntinx F, Winkens R, Grol R, Knottnerus JA. Influencing diagnostic and preventive performance in ambulatory care by feedback and reminders: a review. *Fam Pract* 1993;10:219-28.
- 16 Johnston ME, Langton KB, Haynes RB, Mathieu A. Effects of computer-based clinical decision support systems on clinician performance and patient outcome: a critical appraisal of research. *Ann Intern Med* 1994;120:135-42.
- 17 Austin SM, Balas EA, Mitchell JA, Ewigman BG. Effect of physician reminders on preventive care: meta-analysis of randomized clinical trials. *Proceedings—the Annual Symposium on Computer Applications in Medical Care* 1994;121-4.
- 18 Wensing M, Grol R. Single and combined strategies for implementing changes in primary care: a literature review. *Int J Quality Health Care* 1994;6:115-32.
- 19 Waddell DL. The effects of continuing education on nursing practice: a meta-analysis. *J Continuing Education Nurs* 1991;22:113-8.
- 20 Yano EM, Fink A, Hirsch SH, Robbins AS, Rubenstein LV. Helping practices reach primary care goals: lessons from the literature. *Arch Intern Med* 1995;155:1146-56.
- 21 Soumerai SB, McLaughlin TJ, Avorn J. Improving drug prescribing in primary care: a critical analysis of the experimental literature. *Milbank Q* 1989;67:268-317.
- 22 Lomas J, Haynes RB. A taxonomy and critical review of tested strategies for the application of clinical practice recommendations: from "official" to "individual" clinical policy. *Am J Prev Med* 1987;4:77-94.
- 23 Gyorkos TW, Tannenbaum TN, Abrahamowicz M, Bédard L, Carsley J, Franco ED, et al. Evaluation of the effectiveness of immunization delivery methods. *Can J Public Health* 1994;85(suppl 1):14-30S.
- 24 Mandelblatt J, Kanetsky PA. Effectiveness of interventions to enhance physician screening for breast cancer. *J Fam Pract* 1995;40:162-71.
- 25 Silagy C, Lancaster T, Gray S, Fowler G. The effectiveness of training health professionals to provide smoking cessation interventions: systematic review of randomised controlled trials. *Qual Health Care* 1995;3:193-8.
- 26 Lomas J, Anderson GM, Domnick-Pierre K, Vayda E, Enkin MW, Hannah WJ. Do practice guidelines guide practice? The effect of a consensus statement on the practice of physicians. *N Engl J Med* 1989;321:1306-11.
- 27 Whiting-O'Keefe QE, Henke C, Simborg DW. Choosing the correct unit of analysis in medical care experiments. *Med Care* 1984;22:1101-14.
- 28 Grol R. Implementing guidelines in general practice care. *Qual Health Care* 1992;1:184-91.
- 29 Donner A, Birkett N, Buck C. Randomisation by cluster: sample size requirements and analysis. *Am J Epidemiol* 1981;114:906-14.
- 30 NHS Research and Development Programme. *Methods to promote the implementation of research findings in the NHS: priorities for evaluation*. Leeds: Department of Health, 1995.
- 31 Freemantle N, Grilli R, Grimshaw JM, Oxman A. Implementing the findings of medical research: the Cochrane Collaboration on effective professional practice. *Qual Health Care* 1995;4:45-7.

The articles in this series are adapted from *Getting Research Findings into Practice*, edited by Andrew Haines and Anna Donald and published by BMJ Books.

Statistics Notes

Time to event (survival) data

Douglas G Altman, J Martin Bland

In many medical studies an outcome of interest is the time to an event. Such events may be adverse, such as death or recurrence of a tumour; positive, such as conception or discharge from hospital; or neutral, such as cessation of breast feeding. It is conventional to talk about survival data and survival analysis, regardless of the nature of the event. Similar data also arise when measuring the time to complete a task, such as walking 50 metres.

The distinguishing feature of survival data is that at the end of the follow up period the event will probably not have occurred for all patients. For these patients the survival time is said to be censored, indicating that the observation period was cut off before the event occurred. We do not know when (or, indeed, whether) the patient will experience the event, only that he or she has not done so by the end of the observation period.

Correspondence to: Mr Altman

continued over

BMJ 1998;317:468-9

Censoring may also occur in other ways. Patients may be lost to follow up during the study, or they may experience a "competing" event which makes further follow up impossible. For example, patients being followed to a cardiac event may die from some other disease or in an accident.

In most survival studies patients are recruited over a period and followed up to a fixed date beyond the end of recruitment. Thus the last patients recruited will be observed for a shorter period than those recruited first and will be less likely to experience the event. An important assumption, therefore, is that patients' survival prospects (prognosis) stay the same throughout the study (although this will not matter too much in a randomised trial). We also assume that patients lost to follow up have the same prognosis as those remaining in the study.

Table 1 shows the survival times of 44 patients in a randomised trial. Several patients in each group were still alive at the end of the study, while one was lost to follow up. In such a study we wish to compare the survival times of the two groups of patients. Statistical methods such as *t* tests cannot cope with the uncertainty in the data caused by censoring. Patients with censored data contribute valuable information and they should not be omitted from the analysis. It would also be wrong to treat the observed time (at censoring) as the survival time. We cannot tell, for example, whether the patient in the control group who was still alive at 127 months would have lived longer than the patient in the prednisolone group who died after 143 months. Rather we need recourse to a specialised set of statistical methods that have been developed for handling such data. We shall consider methods for graphical display and analysis of survival data in subsequent Statistics Notes.

Implicit in the preceding discussion is that survival should be evaluated in a cohort of patients followed forwards in time from a particular time point, such as diagnosis or randomisation, even if the cohort is identified retrospectively. An alternative, and potentially highly misleading, approach is to take a group of people experiencing the event of interest, perhaps in a certain time interval, and ascertain the elapsed time since the start of the relevant preceding time span. For example, we might take all newly diagnosed diabetics and find out when they first experienced certain symptoms. Similarly we might take birth as the start of the time period of interest for a group of individuals who have died and investigate associations between age at death and other variables.

Analyses of such data can cause serious problems. A good example is the highly dubious finding that left handed people die on average seven years younger than right handed people.² In this study those dying at old ages were survivors from a cohort born 70 or more years ago while those dying young may have been born at any time, and so on average will have been born later. Such studies make strong implicit assumptions—in essence that the prevalence of the risk factor(s), the characteristics of the population at risk, and the survival (prognosis) remain unchanged over many decades.³ These assumptions will usually be untenable and may also be untestable. Using this study design we would certainly find that people who use electric guitars or even personal computers die

much younger than those who do not. The differing longevity in relation to handedness² would have arisen if the prevalence of left handedness had increased over the past 80 years. Proper prospective studies have found no evidence of an effect of handedness on lifespan.^{4,5}

The same design was used in a study of long term survival in prostate cancer. All patients dying in a three year period who had been treated with palliative intent were "followed from death to diagnosis,"⁶ a period of up to 30 years. The authors reported that the proportion of deaths due to cancer increased with length of survival. This finding cannot be trusted because of the problems noted above, which are common to all such studies.³ Subjects with long survival times must have been diagnosed decades ago, whereas those with short survival times may include some patients diagnosed recently. The observed association could be a spurious consequence of improved treatment, earlier diagnosis, or some other change over time. The same error was seen recently in the *BMJ*.⁷

Retrospective studies can be valuable, but this design should be avoided when studying survival times. Whenever possible times to an event of interest should be studied in a definable cohort of individuals followed forwards in time.

- 1 Kirk AP, Jain S, Pocock S, Thomas HC, Sherlock S. Late results of the Royal Free Hospital prospective controlled trial of prednisolone therapy in hepatitis B surface antigen negative chronic active hepatitis. *Gut* 1980;21:78-83.
- 2 Halpern DF, Coren S. Handedness and life span. *N Engl J Med* 1991;324:998.
- 3 Abrahamsson PA, Adami HO, Taube A, Kim K, Zelen M, Kulldorff M. Re: Long-term survival and mortality in prostate cancer treated with noncurative intent. *J Urol* 1996;155:296-7.
- 4 Cerhan JR, Folsom AR, Potter JD, Prineas RJ. Handedness and mortality risk in older women. *Am J Epidemiol* 1994;140:368-74.
- 5 Aggleton JP, Bland JM, Kentridge RW, Neave NJ. Handedness and longevity: an archival study of cricketers. *BMJ* 1994;309:1681-4.
- 6 Aus G, Hugosson J, Norlén L. Long-term survival and mortality in prostate cancer treated with noncurative intent. *J Urol* 1995;154:460-5.
- 7 MacManus I. Which doctors die first? *BMJ* 1997;314:1132.

Endpiece

Hopefully, the last word

Since at least the 17th century, certain adverbs in -ly have acquired the ability to qualify a predication or assertion as a whole. Such adverbs are elliptical uses of somewhat longer phrases. ... In the 20th century there has been a swift and immoderate increase in the currency of [such] adverbs [which] include actually, basically, frankly, hopefully, regretfully, strictly, and thankfully. Suddenly, round about the end of the 1960s, and with unprecedented venom, a dunce's cap was placed on the head of anyone who used just one of them—hopefully—as a sentence adverb. ... Conservative speakers, taken unawares by the sudden expansion of an unrecognised type of construction, have exploded with resentment that is unlikely to fade away before at least the end of the 20th century.

Robert Burchfield,
The New Fowler's Modern English Usage
(Oxford: Clarendon Press, 1996)

ICRF Medical Statistics Group,
Centre for Statistics in Medicine,
Institute of Health Sciences, Oxford
OX3 7LF

Douglas G Altman,
head

Department of Public Health
Sciences, St George's Hospital Medical School,
London SW17 0RE

J Martin Bland,
professor of medical statistics

Table 1 Survival times (months) of 44 patients with chronic active hepatitis randomised to receive prednisolone or no treatment¹

Prednisolone (n=22)	Control (n=22)
2	2
6	3
12	4
54	7
56†	10
68	22
89	28
96	29
96	32
125*	37
128*	40
131*	41
140*	54
141*	61
143	63
145*	71
146	127*
148*	140*
162*	146*
168	158*
173*	167*
181*	182*

*Still alive at time of analysis.

†Lost to follow up.