able people or to select those with the right personality can be valuable if used in addition to other selection procedures, both at the undergraduate stage and later in the doctor's career.

During clinical training students should be allocated to a named tutor with whom regular meetings would take place to discuss progress and to determine aspects that need strengthening. A record book might be kept in which practical procedures and functions (like breaking bad news to relatives) are listed and dates of achievements are recorded; comments and assessments by teachers could be added.

Medical students and house officers have found support and discussion groups helpful.[13] Firth-Cozens found that nearly half of house officers agreed that "....a counselling service should be provided for medical staff...."[3] Overwork is the most stressful aspect of being a junior doctor. Regional health authorities advertise part time posts for those who cannot pursue a full time career owing to domestic commitments, disability, or ill health. But ill health (even if it means leaving medicine) caused by the stress of being a full time junior house officer is not sufficient reason for creating a part time post (Yorkshire Health Authority, personal communication).

Doctors pursuing a career in hospital medicine need training in the personnel and management aspects of the job.[14] Time should be set aside to discuss problems, to set achievable goals, and to review progress.[15] Allowance must be made for such meetings in the timetables of both consultants and juniors. This may not be easy with present staffing levels in some acute specialties (the ones where stresses may be greatest).

Although a doctor will probably work for the National Health Service for life, mobility in training is such that moving to another hospital is like leaving the company. For this reason commitment by consultants to the welfare and training of juniors is often viewed as wasted effort. Junior doctors in turn feel unsettled and disjointed by short term contracts; relationships with consultants are viewed as haphazard and arbitrary. An obvious solution would be rotations which last several years, as in psychiatry, general practice, and some medical and surgical schemes.

The attitude of doctors to the personnel aspects of their job reflects the low priority the NHS as a whole places on it. A change of emphasis need not be at the expense of patients. At IBM the customer is the number one priority,[16] yet it is recognised that staff are the most valuable asset. When IBM was founded in 1914 the first principle was that the individual must be respected—and that still holds true today. Perhaps the most telling comments come from an IBM marketing executive. "The least that can be done for an employee who does something nice for a customer is to thank him. I almost deleted the preceding sentence because it seemed so obvious, but the truth is that many employers and managers take genuine contributions of their staff for granted and rarely express their appreciation."[17]

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Statistics in Medicine

Calculating confidence intervals for survival time analyses

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It is common in follow up studies to be concerned with the survival time between entry to the study and a subsequent event. The event may be death in a study of cancer, the disappearance of pain in a study comparing different steroids in arthritis, or the return of ovulation after stopping a long acting method of contraception. These studies often generate some so called "censored" observations of survival time. Such an observation would occur, for example, on any patient who is still alive at the time of analysis in a trial where death is the end point. In this case the time from allocation to treatment to the latest follow up visit would be the patient's censored survival time.

The Kaplan-Meier product limit technique is the recognised approach for calculating survival curves in such studies.[1] An outline of this method is given here with details of how to calculate a confidence interval for the population value of the survival proportion at any time during the follow up. The situations of a single group of patients and of the difference in survival proportions between two groups are considered. For the latter case confidence interval calculations are also described for the hazard ratio between groups—for example, the relative death rate, relapse rate, etc.

A worked example is included for each method. The calculations have been carried out to full arithmetical precision, as is recommended practice,[2] although intermediate steps are shown as rounded results. The rationale behind the use of confidence intervals has been described previously.[3] Confidence intervals

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convey only the effects of sampling variation on the precision of the estimated statistics and cannot control for any non-sampling errors such as bias in the selection of patients or in losses to follow up.

Survival proportions and their differences

SINGLE SAMPLE

Suppose that the survival times after entry to the study (ordered by increasing duration) of a group of n subjects are $t_1, t_2, t_3, \ldots t_n$. The proportion of subjects (p) surviving beyond any follow up time (t) is estimated by the Kaplan-Meier technique as:

$$p=\Pi\frac{r_i-d_i}{r_i},$$

where r_i is the number of subjects alive just before time t_i (the ith ordered survival time), d_i denotes the number who died at time t_i, and Π indicates multiplication over each time a death occurs up to and including time t.

The standard error (SE) of p is given by:

$$SE=\sqrt{\frac{p(1-p)}{n'}},$$

where n′ is the "effective" sample size at time t. When there are no censored survival times n′ will be equal to n, the total number of subjects in the study group. When censored observations are present it is necessary to calculate the effective sample size as:

$$n'=\frac{r_i-d_i}{p}$$

each time a death occurs.[4]

The $100(1-\alpha)\%$ confidence interval for the population value of the survival proportion p at time t is calculated as:

$$p-(N_{1-\alpha/2}\times SE) \quad \text{to} \quad p+(N_{1-\alpha/2}\times SE),$$

where $N_{1-\alpha/2}$ is the appropriate value from the standard Normal distribution for the $100(1-\alpha/2)$ percentile. This is widely available in tables. Thus for a 95% confidence interval $\alpha=0{\cdot}05$ and $N_{1-\alpha/2}=1{\cdot}96$.

The times at which to estimate survival proportions and their confidence intervals should be determined in advance of the results. They can be chosen according to practical convention—for example, the five year survival proportions which are often quoted in cancer studies—or according to previous similar studies. The formulas for confidence intervals given in this paper are not reliable for small sample sizes and for p close to 0 or 1. If n′ is less than about 10 or p outside the range 0·1 to 0·9 the confidence intervals should be interpreted with caution.

Worked example

Consider the survival experience of the 25 patients randomly assigned to receive γ linolenic acid for the treatment of colorectal cancer of Dukes's stage C.[5] The ordered survival times (t), the calculated survival proportions (p), and the effective sample sizes (n′) are shown in the table.

The data come from a comparative trial, but it may be of interest to quote the two year survival proportion and its confidence interval for the group receiving γ linolenic acid. The survival proportion to any follow up time is taken from the entries in the table for that time if available or for the time immediately preceding. Thus for two years the survival proportion is $p=0{\cdot}5498$ and the effective sample size is $n'=12{\cdot}7$.

The standard error of this survival proportion is:

$$SE=\sqrt{\frac{0{\cdot}5498\times(1-0{\cdot}5498)}{12{\cdot}7}}=0{\cdot}1394.$$

The 95% confidence interval for the population value of the survival proportion is then given by:

$$0{\cdot}5498-(1{\cdot}96\times0{\cdot}1394) \quad \text{to} \quad 0{\cdot}5498+(1{\cdot}96\times0{\cdot}1394)$$

that is, from 0·28 to 0·82.

The estimated percentage of survivors to two years is thus 55% with a 95% confidence interval of 28% to 82%.

TWO SAMPLES

The difference between survival proportions at any time t in two study groups of sample sizes n_1 and n_2 is measured by p_1-p_2, where p_1 and p_2 are the survival proportions at time t in groups 1 and 2 respectively.

The standard error of p_1-p_2 is:

$$SE_{diff}=\sqrt{\frac{p_1(1-p_1)}{n_1'}+\frac{p_2(1-p_2)}{n_2'}},$$

where n_1' and n_2' are the effective sample sizes at time t in each group. The $100(1-\alpha)\%$ confidence interval for the population value of p_1-p_2 is:

$$p_1-p_2-(N_{1-\alpha/2}\times SE_{diff}) \quad \text{to} \quad p_1-p_2+(N_{1-\alpha/2}\times SE_{diff}),$$

where $N_{1-\alpha/2}$ is found as for a single sample.

Worked example

The survival experience of the patients receiving γ linolenic acid and the controls can be compared from the results given in the table. At two years, for example, $p_1=0{\cdot}5498$ and $p_2=0{\cdot}5136$ with $n_1'=12{\cdot}7$ and $n_2'=13{\cdot}6$. The estimated difference in two year survival proportions is thus $0{\cdot}5498-0{\cdot}5136=0{\cdot}0362$.

The standard error of this difference in survival proportions is:

$$\sqrt{\frac{0{\cdot}5498\times(1-0{\cdot}5498)}{12{\cdot}7}+\frac{0{\cdot}5136+(1-0{\cdot}5136)}{13{\cdot}6}}=0{\cdot}1943.$$

The 95% confidence interval for the population value of the difference in two year survival proportions is then given by:

$$0{\cdot}0362-(1{\cdot}96\times0{\cdot}1943) \quad \text{to} \quad 0{\cdot}0362+(1{\cdot}96\times0{\cdot}1943)$$

that is, from −0·34 to 0·42.

Thus the study estimate of the increased survival proportion at two years for the patients given γ linolenic acid compared with the control group is

Survival data by month for 49 patients with Dukes's C colorectal cancer randomly assigned to receive either γ linolenic acid or control treatment[5]

Group treated with γ linolenic acid				Controls			
Case No	Survival time* (months) t	Survival proportion p	Effective sample size n′	Case No	Survival time* (months) t	Survival proportion p	Effective sample size n′
1	1+	1	25	26	3+	1	24
2	5+	1	25	27	6		
3	6	0·9130	23·0	28	6		
4	6			29	6	0·8261	23·0
5	9+	,,	,,	30	6		
6	10			31	8		
7	10	0·8217	21·9	32	8	0·7391	,,
8	10+			33	12		
9	12			34	12	0·6522	,,
10	12			35	12+		
11	12	0·6284	20·7	36	15+	,,	,,
12	12			37	16+	,,	,,
13	12+			38	18+		
14	13+	,,	,,	39	18+	,,	,,
15	15+	,,	,,	40	20	0·5870	15·3
16	16+	,,	,,	41	22+	,,	,,
17	20+	,,	,,	42	24	0·5136	13·6
18	24	0·5498	12·7	43	28+		
19	24+			44	28+	,,	,,
20	27+	,,	,,	45	28+		
21	32	0·4399	9·1	46	30	0·3852	7·8
22	34+	,,	,,	47	30+		
23	36+			48	33+	,,	,,
24	36+	,,	,,	49	42	0	—
25	44+	,,	,,				

*Survival times are shown in each group by month to either death or to censoring. Figures with plus signs show that patient follow up was censored.

only about 4%. Moreover, the imprecision in the estimate from this small study is indicated by the 95% confidence interval ranging from −34% to 42%, suggesting little benefit if any from γ linolenic acid.

The hazard ratio

The ratio of failure—for example, death or relapse—rates in a follow up study of two groups is termed the "hazard ratio" and is a common measure of the relative effect of treatment, exposure, etc. If O_1 and O_2 are the observed numbers of deaths at time t in the two groups then the expected numbers of deaths (E_1 and E_2) assuming an equal risk of dying at each time in both groups may be calculated as:

$$E_1=\Sigma\frac{r_{1i}d_i}{r_i} \quad \text{and} \quad E_2=\Sigma\frac{r_{2i}d_i}{r_i},$$

where r_{1i} and r_{2i} are the numbers of subjects alive and not censored in groups 1 and 2 just before time t_i with $r_i=r_{1i}+r_{2i}$; $d_i=d_{1i}+d_{2i}$ is the number who died at time t_i in the two groups combined; and Σ indicates addition over each time of death up to and including t.

The hazard ratio (h) is then estimated by:

$$h=\frac{O_1/E_1}{O_2/E_2}.$$

To obtain a $100(1-\alpha)\%$ confidence interval for the population value of the hazard ratio first calculate the two quantities:

$$X=\frac{O_1-E_1}{V} \quad \text{and} \quad Y=\frac{N_{1-\alpha/2}}{\sqrt{V}}$$

$$\text{where} \quad V=\Sigma\frac{r_{1i}r_{2i}d_i(r_i-d_i)}{r_i(r_i-1)}$$

and $N_{1-\alpha/2}$ is the appropriate value from the standard Normal distribution for the $100(1-\alpha/2)$ percentile. Thus for a 95% confidence interval $\alpha=0{\cdot}05$ and $N_{1-\alpha/2}=1{\cdot}96$.

The confidence interval for the hazard ratio is then given by:

$$e^{X-Y} \quad \text{to} \quad e^{X+Y}.$$

Worked example

For all the data in the table $O_1=10$, $E_1=11{\cdot}37$, $O_2=12$, $E_2=10{\cdot}63$, and $V=4{\cdot}99$.

The hazard ratio is thus estimated as:

$$h=\frac{10/11{\cdot}37}{12/10{\cdot}63}=0{\cdot}78.$$

The values of X and Y for $\alpha=0{\cdot}05$ are:

$$X=\frac{10-11{\cdot}37}{4{\cdot}99}=-0{\cdot}28 \quad \text{and} \quad Y=\frac{1{\cdot}96}{\sqrt{4{\cdot}99}}=0{\cdot}88.$$

The 95% confidence interval for the population value of the hazard ratio is then given by:

$$e^{-1{\cdot}15} \quad \text{to} \quad e^{0{\cdot}60} \text{ that is, from } 0{\cdot}32 \text{ to } 1{\cdot}83.$$

The results indicate that treatment with γ linolenic acid has been associated with an estimated reduction in mortality to 78% of that for the control treatment. This reduction, however, is imprecisely estimated as shown by the wide confidence interval of 32% to 183%, which almost equally suggests that γ linolenic acid has no benefit over the control treatment.

Comment

Further discussion and examples are given by Simon.[6] He shows also how to calculate a confidence interval for the median survival time, which is a less commonly used statistic. The computations for the confidence intervals described here can be carried out conveniently using an appropriate statistical computer package.[7]

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ANY QUESTIONS

Is there any justification in continuing to teach the Holger Neilson method of resuscitation in first aid classes to the general public?

The Holger Neilson method of artificial respiration was first described in 1932. With the victim in the prone position it requires the rescuer to press alternately on the victim's back and to raise and lower his flexed arms. It is one of the manual methods of resuscitation. In the 1950s there was renewed interest in the expired air method of respiration (mouth to mouth or mouth to nose). Several clinical trials compared the efficiency of the various manual and expired air methods; the former failed badly in trials on human volunteers.[1] Safar *et al* showed that the major reason for this was that the airway was not maintained throughout the manoeuvre.[2] In the expired air methods the airway was maintained continuously by head tilt and jaw support. He concluded that borderline respiratory values resulted with the manual methods and doubted whether these methods should be taught in the future. In another study by Nolte a direct comparison of the manual and expired air methods showed Holger Neilson to be the least effective of the manual methods while the expired air methods excelled over all the other procedures in terms of tidal volume and arterial blood gas tensions.[3]

Despite these findings the Holger Neilson method is widely taught as an alternative to mouth to mouth ventilation. The stated indications for Holger Neilson have little or no validation. If there are severe facial injuries the most probable reason for the victim not breathing is airway obstruction. Proper clearing and control of the airway will allow the victim to breathe. If the casualty is trapped face downwards mouth to mouth ventilation is still possible although not easy. If the chest or arms are trapped the Holger Neilson method is not possible. Finally, in cases of poisoning with corrosive substances the airway is probably extensively damaged and requires proper and careful clearing and control to enable the victim to breathe. There is no contraindication to performing mouth to mouth ventilation on victims of poisoning from substances such as cyanide, provided that the mouth is first cleared of any obvious debris or chemical material.

If the Holger Neilson method is ineffective the victim will remain apnoeic and hypoxic and will eventually require cardiac resuscitation. The Holger Neilson method is of no use when a combination of expired air respiration and external chest compressions is required. So there would seem to be no indication to teach first aiders any alternative to mouth to mouth or mouth to nose ventilation. Training in the Holger Nielson method confuses the first aider, lengthens his or her training, and provides an alternative that has been shown in clinical experiments not to work.—D A ZIDEMAN, consultant anaesthetist, London.

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