ENDGAMES

STATISTICAL QUESTION

Hazards and hazard ratios

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Researchers investigated the risk of colorectal cancer after screening with flexible sigmoidoscopy. A randomised controlled study was undertaken in Norway with a population based sample. The intervention consisted of once only flexible sigmoidoscopy screening with or without a single round of faecal occult blood testing. The control treatment was no screening. The main outcome measures included length of time from randomisation until death from colorectal cancer.[1]

After a median of six years of follow-up, the hazard ratio for mortality from colorectal cancer, comparing intervention with control, was 0.73 (95% confidence interval 0.47 to 1.13). The researchers concluded that mortality from colorectal cancer was not significantly reduced in the screening group but that it seemed to be lower among participants who attended screening.

Which of the following statements, if any, are true?

a) The hazard of death from colorectal cancer represents the instantaneous rate of death at any time during follow-up.

b) The hazard of death from colorectal cancer represents the proportion of deaths by the end of follow-up.

c) The hazard of death from colorectal cancer was assumed to be constant throughout follow-up in each treatment group.

d) The hazard ratio of death from colorectal cancer was assumed to be constant throughout follow-up.

Answers

Statements *a* and *d* are true, whereas *b* and *c* are false.

The purpose of the trial was to investigate whether once only flexible sigmoidoscopy screening with or without a single round of faecal occult blood testing reduced the risk of colorectal cancer. The main outcome measures included death from colorectal cancer. The researchers reported their initial findings after participants had been followed for a median of six years (range five to seven years). Each participant's survival time was recorded—that is, the time from randomisation until death from colorectal cancer. If death from colorectal cancer occurred during follow-up, the survival time was termed exact; otherwise if the participant was still alive at the end of follow-up their survival time was "censored." Time to event data have been

described in a previous question.[2] Typically the hazard ratio is used to compare two groups' time to event data.

The researchers reported the hazard ratio for death from colorectal cancer, comparing the intervention with control treatment. The hazard ratio, sometimes called a relative hazard, was calculated as the hazard of death for the intervention group divided by the hazard of death for the control group. The hazard of death is the probability of death in a time interval divided by the length of the interval and therefore represents the rate of death. For each group the study period was divided into very short time intervals, and therefore the hazard of death represented the instantaneous rate of death at any time during follow-up (*a* is true).

The hazard of death for each group was not derived as the proportion of participants who had died from colorectal cancer by the end of follow-up (*b* is false). The probability of death by the end of follow-up could have been used to derive a relative risk. Relative risks, described in a previous question,[3] would permit a comparison of the proportion of deaths by the end of follow-up in the screening group relative to the control group. In contrast, the hazard ratio compares the instantaneous risk of death between two groups throughout the study period and does not give any indication of the relative proportion of deaths between the two groups.

The hazard ratio for mortality from colorectal cancer, comparing intervention with control, was 0.73 (95% confidence interval 0.47 to 1.13). The hazard ratio was less than unity, indicating that the hazard of death in the screening group was less than that in the control group. At any time during follow-up participants in the intervention group were 0.73 times as likely to die from colorectal cancer as those in the control group (that is, they had a reduction in risk of 27%). Although the hazard of death in the screening group was lower than in the control group, the 95% confidence for the hazard ratio included unity, and therefore as described in a previous question[4] the ratio of the hazard rates was not significantly different from unity—that is, the two hazard rates were not significantly different.

The hazard rate for either treatment group may not be constant throughout the study period (*c* is false). It is assumed, however, that the ratio of the hazard rates in the two groups was constant

throughout the study period—that is, they were proportional (*d* is true).

Competing interests: None declared.

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2   Sedgwick P. Survival (time to event) data: censored observations. *BMJ* 2011;343:d4816.
3   Sedgwick P, Marston L. Relative risks. *BMJ* 2010;341:c3983.
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