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ENDGAMES

STATISTICAL QUESTION

Odds and odds ratios

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Researchers evaluated the efficacy of intravitreous injections of bevacizumab for the treatment of neovascular age related macular degeneration. A prospective, double blind, multicentre, randomised controlled trial study design was used. The intervention was intravitreous bevacizumab 1.25 mg, given as three loading injections at six week intervals and followed by further treatment if needed (again at six week intervals). The control was standard treatment—photodynamic therapy, intravitreal injections of pegaptanib, or intravitreal injections of placebo. Study participants were 131 patients (mean age 81 years) with wet age related macular degeneration.[1]

The primary outcome measure was a gain of 15 letters or more of visual acuity at one year from baseline assessed with an ETDRS (Early Treatment Diabetic Retinopathy Study) visual acuity chart. Of 65 participants allocated to the intervention, 21 (32%) gained 15 letters or more of visual acuity from baseline compared with two (3%) of the control group (n=66). The odds of a gain of 15 letters or more of visual acuity at one year were 21/44 for the intervention group and 2/64 for the control group. The unadjusted odds ratio for the primary outcome when comparing the intervention with the control was 15.3 (95% confidence interval 3.4 to 68.5). When adjusted for age, sex, and baseline visual acuity, the odds ratio for the primary outcome when comparing the treatments remained significant (adjusted odds ratio 18.1, 95% confidence interval 3.6 to 91.2). The authors concluded that the intervention (bevacizumab 1.25 mg intravitreous injections given as part of a six weekly variable retreatment regimen) was superior to standard care.

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

a) It was possible to estimate the population at risk

b) The odds ratio of gaining 15 letters or more of visual acuity at one year estimates the population relative risk of the primary outcome when comparing the intervention with the control

c) The odds of gaining 15 letters or more of visual acuity at one year is the absolute probability of the primary outcome occurring

d) When compared with the control, the intervention was independently associated with the primary outcome

Answers

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

The trial evaluated the efficacy of intravitreous bevacizumab injections for the treatment of neovascular age related macular degeneration. The intervention was compared with standard treatment (control). Because the study was prospective in design, the population at risk could be estimated using sample estimates (*a* is true). Estimating the population at risk has been described in a previous question.[2] In particular, the observed risk (probability) of a gain of 15 letters or more of visual acuity at one year estimated the probability of the primary outcome occurring in the population for each of the treatment groups. Although not presented, the sample unadjusted relative risk would equal the ratio of the risk of a gain of 15 letters or more of visual acuity at one year for the intervention group relative to the control group. This sample estimate would estimate the population relative risk, a measure of the association between treatment (intervention compared with control) and the primary outcome. Relative risks have been described in previous questions.[3 4]

It is not possible to derive adjusted relative risks—that is, adjust for confounding and allow for the simultaneous effects of other variables studied. However, it is possible to derive an odds ratio that estimates the population relative risk (*b* is true). Odds ratios can be adjusted for confounding using a statistical method known as logistic regression, described in a previous question.[5] It has been proposed that the sample odds ratio is a good estimate of the population relative risk when the disease or outcome is rare in the population, typically when the prevalence is less than 10%. It is not obvious if the odds ratio is a good estimate of the population relative risk in the example above because the primary outcome for the intervention group is not rare.

To calculate the odds ratio of a gain of 15 or more letters of visual acuity at one year for the intervention compared with the control, the odds of the primary outcome for the intervention group were divided by the odds of the primary outcome for the control group. The odds of a gain of 15 or more letters of visual acuity at one year is not the probability of the primary outcome

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occurring (*c* is false); the odds is an alternative way of expressing probability, as described previously.[6]

The odds of a gain of 15 or more letters of visual acuity at one year was derived as the probability of the primary outcome occurring divided by the probability of the primary outcome not occurring. Of 65 participants allocated to the intervention, 21 had a gain of 15 letters or more of visual acuity at one year and 44 did not. Therefore, for those participants who received the intervention, the odds of the primary outcome was: (21/65)÷(44/65)=(21/65)×(65/44)=21/44. Hence, the odds of the primary outcome for the intervention group was the ratio of participants with a gain of 15 letters or more of visual acuity at one year to those without such a gain. The odds of a gain of 15 letters or more of visual acuity at one year for the control group was calculated in a similar way—the ratio of the number of participants with a gain of 15 letters or more of visual acuity at one year to those without: 2/64.

The odds ratio provides a measure of the association between treatment (intervention compared with control) and the primary outcome. The unadjusted odds ratio was derived as the odds of a gain of 15 letters or more of visual acuity at one year for the intervention divided by the odds for the control treatment: (21/44)÷(2/64)=(21/44)×(64/2)=(21×64)÷(44×2)=15.3. Therefore, the odds of the primary outcome occurring was greater in the intervention group than in the control group. Hence, the intervention group was more likely to experience a gain of 15 letters or more of visual acuity at one year. The 95% confidence interval for the population odds ratio was 3.4 to 68.5; because it excluded unity (1.0) the intervention group experienced a significant increase in the primary outcome compared with the control group. When adjusted for potential confounding, the odds ratio was 18.1 (95% confidence interval 3.6 to 91.2). The association between treatment (intervention compared with control) and the primary outcome remained significant after adjusting for confounding, so the intervention group was said to be independently associated with the primary outcome (*d* is true).

Competing interests: None declared.

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