

ENDGAMES

Incidence rates

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The association between use of proton pump inhibitors and risk of hip fracture was investigated in postmenopausal women. Women who were enrolled in the Nurses' Health Study, a prospective cohort study, provided data biennially from 2000 until June 2008. The primary outcome was time until first hip fracture. The incidence rate of hip fracture was higher among regular users of proton pump inhibitors than non-users (2.02 versus 1.51 per 1000 person years).¹

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

- An incidence rate represents the proportion of women who experienced hip fractures.
- Women using proton pump inhibitors had a greater risk per year of hip fracture than non-users.
- The risk of hip fracture is assumed to be equal for each year of follow-up.

Answers

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

The purpose of the study was to establish whether postmenopausal women using proton pump inhibitors were at greater risk of a hip fracture than non-users. However, it would not have been sensible to compare the proportion of users and non-users who had experienced a hip fracture at end of follow-up. It was important to account for varying lengths of time that women were at risk of a hip fracture, which could have occurred for a variety of reasons. By the end of follow-up some women will not have had a hip fracture, while others will have done so at different times during follow-up. Women may have also refused to continue to participate in the study after joining the cohort, moved away, or possibly died.

The incidence rate of hip fractures—the number of hip fractures expressed as a rate—was derived for users and non-users of proton pump inhibitors. The incidence rate accounts for the varying lengths of time that women were at risk of a hip fracture, it being the number of women who experienced a hip fracture divided by the total person years at risk. The total person years at risk is the sum of each woman's length of time they were followed in the cohort. Therefore, the incidence rate does not represent the proportion of women who experienced a hip

fracture (*a* is false) but the risk of a hip fracture per year of exposure. Although incidence rates are often expressed in “per 1000 years” units of time, any convenient unit may be used, including days, weeks, and months.

The researchers reported that a total of 149 hip fractures were recorded in 5341 regular users of proton pump inhibitors over 73 632 person years, compared with 744 hip fractures in 74 558 non-users over 492 154 person years. The incidence rate of hip fracture was therefore 2.02 per 1000 person years among regular users of proton pump inhibitors and 1.51 per 1000 person years among non-users. Therefore, users had a greater risk per year than non-users (*b* is true). Using person years at risk assumes that the risk of a hip fracture is the same for each year of exposure (*c* is true). That is, it is assumed that one person at risk for 10 years is equivalent to 10 people at risk for one year.

The incidence rate ratio, described in a previous question,² would provide a relative measure of the effect of the use of proton pump inhibitors in comparison with non-use. The incidence rate ratio is the incidence rate for the group of women who took proton pump inhibitors divided by the incidence rate for non-users. The incidence rate ratio above is $2.02 \div 1.51 = 1.34$; it is interpreted in a similar fashion to an odds ratio. The incidence rate ratio has no units. Women who took proton pump inhibitors had 1.34 times as many hip fractures as non-users.

The risk of hip fracture and the varying amounts of time that women were exposed to the risk can be described by a hazard ratio. Cox proportional hazard modelling, described in a previous question,³ is used to derive hazard ratios, which can be adjusted for confounding from, for example (but not exclusively), age, smoking status, and body mass index.

Competing interests: None declared.

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- 3 Sedgwick P. Derivation of hazard ratios. *BMJ* 2011;343:d6994.

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