Vaccine efficacy: The implication of using odds ratio and relative risk for the calculation. Which one would you choose?

by Andrea Manfrin & Miland Joshi

Abstract

During the last 12 months, COVID-19 became a global problem. Universities and drug companies are working together for the development of treatments. Vaccines appear to be one of the most promising treatments, and trials are completed, and other are ongoing. All these studies tend to use a common comparator, the percentage of vaccine efficacy (VE%), calculated using the following formula VE=(1-RR) x100. A recent study published in a renowned medical journal presented large trial results using a different formula VE=(1-OR) x100. We compared the analysis using relative risk (RR) versus an odds ratio (OR), and we did not find any large difference in the results. Nevertheless, we would advise using RR instead of OR in the interests of accuracy, for best practice.

Text

Logunov et al. (2021) conducted an interim analysis of a randomised controlled phase 3 trial evaluating the safety and efficacy of a vector-based heterologous prime-boost COVID-19 vaccine (1). To calculate the vaccine efficacy, they used the following formula: VE=(1-OR) x100. The odds ratio (OR) is calculated by the formula OR = ad/bc, where a is the number of cases in the vaccinated arm, b is the number of non-cases in the arm, c is the number of cases in the control group, and d is the number of non-cases in this arm.

The Department of Epidemiology of the School of Public Health, UCLA, however, suggests that the formula for the calculation of the vaccine efficacy is VE=(1-RR) (2), where the relative risk (RR) =[a/(a+c)]/[b/(b+d)]. The authors also added that RR must be less than 1 for the vaccination to be preventive.

Vaccine efficacy has been explained by Hodgson et al. (2020)(3); in simple term, it represents the percentage reduction in disease incidence in a vaccinated group compared to a non-vaccinated group under optimal conditions. The UCLA definition is consistent with the one provided by Spiegelhalter and Masters (4).

Difference between OR and RR

RR represents a ratio of the probabilities (p) or risks of an event or outcome across two groups; OR is a ratio of the odds of an event or outcome across two groups (5). OR is the ratio of two odds; RR is the ratio of two probabilities (P); odds of an event = P/(1-P).

Recommendations

We recommend using RR instead of the OR to calculate efficacy because efficacy is the reduction in the risk effected by the vaccine. To calculate the log-transformed RR standard errors, we used the formula in Altman's *Statistics with Confidence* (6). We have compared the table in their publication with a table that we created using the formula VE=(1-RR) x100. As shown in Table 1, the differences are small. The only noticeable discrepancy lies in the lower confidence interval for the >60 groups. It should be said that with the large numbers involved in a clinical trial, the prevalence or risk is low, and in such circumstances OR and RR are approximately equal. Nevertheless, we believe that it is important to use the correct formula for the calculation to provide not only the best evidence but also for following best practice.

Table 1 Interim results of vaccine efficacy using VE=(1-OR) x 100 (1) vs VE=(1-RR) x 100

1st occurrence 21 days after dose 1	**VE=(1-OR) x 100**	**VE=(1-RR) x 100**
	Vaccine efficacy % (95% CI)	**Vaccine efficacy % (95% CI)**
Overall	91·6 (85·6–95·2)	91.5 (85.4, 95.1)
Age Group		
18-30	91·9 (51·2–99·3)	91.8 (27.1, 99.1)
31-40	90·0 (71·1–96·5)	89.9 (69.2, 96.7)
41-50	91·3 (73·7–96·9)	91.3 (73.7, 97.1)
51-60	92·7 (81·1–97·0)	92.6 (80.4, 97.2)
>60	91·8 (67·1–98·3)	91.7 (61.2, 98.2)
Sex		
Female	87·5 (73·4–94·2)	87.3 (72.6, 94.1)
Male	94·2 (87·2–97·4)	94.1 (86.8, 97.3)
Moderate/Severe Cases	100 (94·4–100·0)	100.0 (95.1*****,100.0)
First COVID-19 occurrence after dose 1		
Any time after dose 1	73·1 (63·7–80·1)	72.8 (63.4, 79.8)
From 14 days after dose 1	87·6 (81·1–91·8)	87.5 (80.9, 91.8)
First COVID-19 occurrence after dose 2 (28 days after dose 1)		
All	91·1 (83·8–95·1)	91.0 (83.3, 95.1)

***** To calculate the lower limit, we used the "rule of 3": with zero events out of 14964, an upper bound for the rate of occurrences is 3/14964.

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