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"Crude vaccine effectiveness" is a misleading term in test-negative studies of influenza vaccine effectiveness

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We have been reading with interest the recent reports of interim estimates of influenza vaccine effectiveness (VE) for the 2014/2015 northern hemisphere season.[1–4] The test-negative design has now become established as the standard observational design for timely assessment of influenza VE.[5] Studies following this design often report both a crude and adjusted VE estimate. However, it is important to consider our ultimate goal in reporting VE estimates and whether an unadjusted estimate is useful. The term "vaccine effectiveness" implies a causal effect rather than a mere correlation, and estimation of a causal effect requires confounding to be addressed.[6]

In a typical test-negative study, which is similar to a case-control study, patients with influenza-like illness are enrolled in a clinical setting and tested for influenza. The crude odds ratio is obtained by dividing the odds of vaccination among influenza-positive patients by the odds of vaccination among influenza-negative patients. This measure indicates the *correlation* of vaccination with influenza, but may not be an accurate estimate of the *causal effect* of vaccination on the risk of influenza because that association may be confounded. Confounding variables are associated with, but not the result of, both the exposure and the outcome, conditional on all other variables.[7] In observational studies, statistical adjustment of estimates (e.g. regression or stratification) is usually necessary to overcome confounding and ensure exchangeability between groups. This adjusted estimate will approximate the causal effect, such as the effectiveness of a vaccine. In observational studies of vaccine effectiveness, including the test-negative study, VE is commonly calculated as $1-OR_{adj}\times 100\%$[8].

Absent other biases, the difference between the crude odds ratio and the adjusted odds ratio should show the degree of bias caused by confounding. It can therefore be worthwhile to

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present the crude odds ratio and the adjusted odds ratio. However, we propose here that it is improper to present a “crude VE”, since this value has no causal interpretation and should not be presented as an estimate of VE. Similarly, it should be unnecessary to use the word “adjusted” when reporting VE because adjustment should have been performed in order to present an estimate of a causal effect. We recognise that the differences in crude and adjusted odds ratios may be caused by other biases, including sparse data bias, measurement error or residual confounding. Nevertheless, when reporting an estimate with an implicit causal effect, it can be misleading to report a crude estimate.

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