# CORRESPONDENCE

# The Clinical Effectiveness of Pneumococcal Conjugate Vaccines

by Hannah Ewald, MPH, Matthias Briel, MD, MSc, Danielle Vuichard, MD, Veronika Kreutle, MD, Andriy Zhydkov, MD, and Viktoria Gloy, PhD in issue 9/2016

## **Other Measures of Event Reduction**

The key message that pneumococcal conjugate vaccines "effectively prevent diseases caused by the serotypes in the vaccine [PCV13]," which the authors base only on relative risk reduction (RRR), is in stark contrast to measures of event reduction such as absolute risk reduction (ARR) and the resulting numbers needed to treat (NNTs) (1).

An example of this is the most recent study included in the meta-analysis, the 2015 CAPiTA trial of the PCV13 vaccine, in which the relative risk reduction in participants aged 65 and older shows a pattern of no value (2).

- PCV13 vaccination achieves a protection rate of 0.0638% in terms of reducing community-acquired pneumonia cases (the difference between 33 cases among 42 237 individuals administered PCV13 vaccination = 0.0781% and 60 cases among 42 225 individuals administered placebo vaccination = 0.1419%). The NNT is 1567, and the relative risk reduction (RRR) is 45%.
- For invasive pneumococcal disease (IPD), vaccination achieves a protection rate of 0.05% in terms of event reduction (the difference between 7 IPD cases among 42 240 individuals administered PCV13 vaccination = 0.016% and 28 IPD cases among 42 257 individuals administered placebo vaccination = 0.066%). NNT = 2000, RRR = 75%.

The focus of vaccination in general medical practice is on adult vaccination. Regarding PCV13 pneumococcal vaccination, there should be equal emphasis on findings concerning absolute risk reduction, number needed to treat, and relative risk reduction in order to decide—in conjunction with the patient—to proceed with vaccination in line with relative risk reduction, or not to do so in line with the huge numbers needed to treat.

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#### REFERENCES

- Ewald H, Briel M, Vuichard D, Kreutle V, Zhydkov A, Gloy V: The clinical effectiveness of pneumococcal conjugate vaccines—a systematic review and metaanalysis of randomized controlled trials. Dtsch Arztebl Int 2016; 113: 139–46.
- Bonten MJ, Huijts SM, Bolkenbaas M: Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. New Engl J Med 2015; 372: 1114–25.

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# In Reply:

Many thanks to Dr. Traut for his contribution. As correctly noted, it is important to consider both absolute effects (absolute risk reduction [ARR], number needed to treat [NNT]) and relative effects (e.g. relative risk, relative risk reduction). For all outcomes, we reported relative estimates of effect; for all-cause pneumonia, invasive pneumococcal disease, and acute otitis media, for example, we calculated absolute effects in the form of NNT, from which one can easily deduce ARR (NNT = 1/ARR).

Whereas a relative measure (e.g. relative risk) generally remains stable across various risk groups (1), ARR underestimates the effect for patients with high baseline risk and overestimates the effect for patients with low baseline risk (2). The preferred strategy is therefore to perform a meta-analysis with a relative measure of effect size and then, by population and setting, to apply the relative treatment effect to a specific health risk within a population, as we did in our article for three outcomes, for example (1, 3). Some health risks vary greatly between different populations or settings. NNTs are generally smaller in high-risk populations and larger in low-risk populations. Vaccination is usually performed in low-risk populations that nevertheless typically include a large number of individuals. From a public health perspective, NNTs of 1500 or 2000 individuals to be vaccinated in order to prevent one case of disease therefore certainly do have great practical significance. Population-relevant issues such as herd effects (i.e. the fact that unvaccinated individuals also benefit from vaccination if the vaccination rate is high enough), which are often overlooked by opponents of vaccination, should also be a factor in primary care physicians' decision-making processes. DOI: 10.3238/arztebl.2016.0559b

### REFERENCES

- 1. Higgins JPT GSe: Cochrane handbook for systematic reviews of interventions version 5.1.0 (updated March 2011), chapter 12.5.3 "Expressing absolute risk reductions". The Cochrane Collaboration, 2011 available from www.cochrane-handbook.org.
- Alonso-Coello P, Carrasco-Labra A, Brignardello-Petersen R, et al.: Systematic reviews experience major limitations in reporting absolute effects. J Clin Epidemiol 2016; 72: 16–26.
- Ewald H, Briel M, Vuichard D, Kreutle V, Zhydkov A, Gloy V: The clinical effectiveness of pneumococcal conjugate vaccines—a systematic review and metaanalysis of randomized controlled trials. Dtsch Arztebl Int 2016; 113: 139–46.

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#### **Conflict of interest statement**

The authors of both contributions declare that no conflict of interest exists.