Assessing vaccine effectiveness

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Vaccine efficacy

- How well does it work in clinical trials?
  - pre-licensure double blind RCTs
  - % reduction in incidence in vaccinated vs unvaccinated, under ideal conditions

Vaccine effectiveness

- How well did it work in a community setting?
  - post-licensure, in the field under non-ideal conditions
  - the same calculation, but different study methods
Why do efficacious vaccines sometimes fail?

- **Host**
  - Biological variation in immune response
  - Immune response differing with age
  - Interference from other microorganisms
  - Immunocompromised recipient
  - Interference from maternal antibody
  - Decrease in immune response over time

- **Pathogen**
  - Change in antigenic structure

- **Vaccine/delivery**
  - Cold chain failure
  - Error in vaccine manufacture
  - Error in vaccine administration
Triggers for measuring vaccine effectiveness

- Disease incidence increases, or does not decrease as expected after vaccination
- Vaccine used in ways not assessed pre-licensure
  - eg. Number of doses, age groups, countries, time since vaccination, change in vaccine makeup
Calculating VE

\[ VE \ (\%) = \left\{ 1 - \left( \frac{ARV}{ARU} \right) \right\} \times 100 \]

\[ = (1 - RR) \times 100 \]

ARV: Attack rate in vaccinated
ARU: Attack rate in unvaccinated
RR: Relative Risk of disease in vaccinated vs unvaccinated
Methods for estimating vaccine effectiveness

- Special observational studies
- Disease outbreak investigations
- Analysis of routinely collected data
Observational studies

- Cohort
  - usually prospective
    - start with an exposure, observe for disease

- Case control
  - usually retrospective
    - start with disease, look back for exposure
Cohort study example

- Prospective Cohort Study on the Effectiveness of Influenza and Pneumococcal Vaccines in Preventing Pneumonia Development and Hospitalization
  - Song JY et al. Clinical and Vaccine Immunology 2015

- Included 2,217 patients presenting to ED with Influenza-like Illness (ILI)
  - 31.9% had influenza vaccine, 9.7% had pneumococcal vaccine
  - 329 (14.8%) hospitalised, 69 (21.0%) with pneumonia
  - VE of influenza vaccine: against pneumonia 64.0%, against hospitalisation 35.0%
  - Pneumococcal vaccine was not effective against pneumonia and hospitalisation
Case Control study example

- Effectiveness of 13-valent pneumococcal conjugate vaccine for prevention of invasive pneumococcal disease in children in the USA: a matched case-control study

- Cases identified through active surveillance in 13 sites and controls identified via birth registries; matched to cases by age and postal code.
  - Included 722 children pneumococcal disease and 2991 controls
  - Vaccine effectiveness against pneumococcal serotypes in the vaccine was 86.0%
  - Vaccine effectiveness against any pneumococcal serotype was 65.6%
Outbreak investigations - Household contact studies

- Measure 2° attack rate in household contacts
- Combine population of households to form vaccinated and unvaccinated cohorts
- Corrects for potential differences in exposure, but has some unique biases that need to be considered
Outbreak investigations - Household contact studies

- Mumps vaccine effectiveness and risk factors for disease in households during an outbreak in New York City
  - Livingston KA et al. Vaccine 2014

- Included 2,176 residents from 311 households; 462 (21%) met the case definition for mumps
  - 17.4% had 1 dose and 44.1% had 2 doses of mumps vaccine
  - VE of mumps vaccine: 1 dose 82.9%, 2 dose 86.3%
Use of routinely collected data - the screening method

- Compares vaccination status of cases with population coverage

\[
VE = 1 - \left\{ \left( \frac{PCV}{1 - PCV} \right) \left( \frac{1 - PPV}{PPV} \right) \right\}
\]

PCV = Proportion of cases vaccinated
PPV = Proportion of population vaccinated
Use of routinely collected data - the screening method

- Simple and rapid method of VE estimation
- Useful for monitoring changes over time
- Not good for precise estimates

Use of routinely collected data - the screening method

- Strong Additional Effect of a Second Varicella Vaccine Dose in Children in Germany, 2009-2014

- 8153 reported varicella cases aged 1-4 years collected from 900 medical practice sentinel surveillance sites
  - 403 (4.9%) cases had 1 dose and 285 (3.5%) had 2 doses of varicella vaccine
  - Population coverage from health insurance claims estimated at 28.8% for 1 dose and 58.8% for 2 doses
  - VE of varicella vaccine: 1 dose 86.6%, 2 dose 97.3%
What happens when VE isn’t high?

- No
  - Influenza, US, 1940s
  - OPV, Brazil, 1986
  - Pertussis, US, 2010s
Summary

- Important to measure and monitor VE
  - provide valuable tools for evaluation of vaccination programs

- Importance of public health data
  - disease notifications, ACIR
  - outbreak investigations

- VE measured using imperfect observational methods
  - consider potential biases

- Method depends on the situation
  - resources
  - data sources