Summer Institute for Public Health Practice
Public Health Today: New Strategies. New Tools.

Basic Epidemiology: Vaccine Safety and Effectiveness

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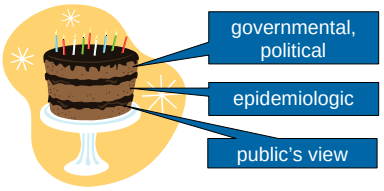
Modern vaccines

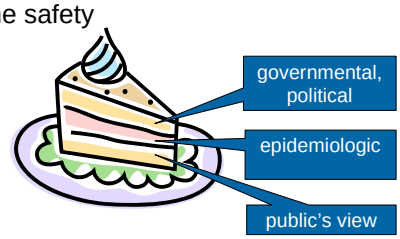
- Modern vaccines are safe and effective
- However, they are neither perfectly safe nor perfectly effective
- Some persons who receive vaccines will have adverse events
- Some persons who receive vaccines will not be protected

Public health is like a cake with many layers



Each public health problem is a slice of the cake

Vaccine safety



Perspectives on Vaccine Safety

- Epidemiologic Perspective on Risk
- Public Perspective on Risk
- Risk vs Benefits
- Government work in Vaccine Safety

Epidemiologic Risk

<u># new cases during a specified period</u>
size of population at start of period

= "Attack rate"
= Probability of getting disease
= Risk of disease

Example of Risk Calculation

1. **Deaths in diabetic men**
   100 deaths
   189 men at start of follow-up period
   Risk = 100/189 = 0.529 = 52.9%

2. **Deaths in nondiabetic men**
   811 deaths
   3151 men at start of follow-up period
   Risk = 811/3151 = 0.257 = 25.7%

Risk Ratio / Relative Risk

$$\text{RR} = \frac{\text{Risk in "exposed" group}}{\text{Risk in "unexposed" group}}$$

EXAMPLE:

Relative risk of death among diabetic men vs. nondiabetic men

$$\text{RR} = \frac{100/189}{811/3151} = \frac{0.529}{0.257} = 2.1$$

Efficacy *vs* Effectiveness - 1

- Vaccine efficacy – performance of vaccine under ideal conditions
- Vaccine effectiveness – performance of vaccine in the field

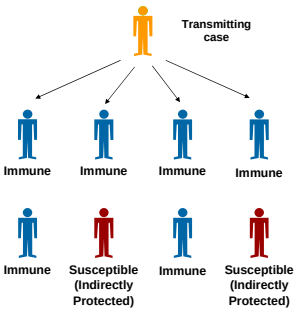
Efficacy *vs* Effectiveness - 2

- Differences in recipients (e.g., nutrition)
- Vaccine storage & administration
- Interference from drugs/other things administered at same time (e.g., breast milk & OPV)
- Herd immunity

Herd Immunity - 1

Resistance of a group to spread of an infectious agent, based on the immunity of a high proportion of individuals of that group...

Herd Immunity - 2



Herd Immunity - 3

"..the proportion of the population required to be immune varies accord to the agent, its transmission characteristics, the distribution of immunes and susceptibles, and other (e.g., environmental) factors."

Source: Last, Dictionary of Epidemiology

Herd Immunity - 4

- Herd immunity threshold for polio
  ~80%
- Herd immunity threshold for measles
  ~95%

Vaccine efficacy - 1

- In spite of immunization levels of 90%, an outbreak of 100 cases of measles occurs in a high school with 1,000 students
- Since 1/2 of cases occurred in students who had previously been vaccinated, the principal feels vaccine has not been effective

Vaccine efficacy - 2

1,000 students, 90% vaccinated =
900 vaccinated, 100 unvaccinated

100 cases, 1/2 in vaccinated =
50 vaccinated, 50 unvaccinated

Vaccine efficacy - 3

How much protection from disease does vaccine provide?

$$VE\ (\%) = \frac{ARU - ARV}{ARU} \times 100$$

VE = vaccine efficacy
ARU = attack rate in unvaccinated
ARV = attack rate in vaccinated

Vaccine efficacy - 4

Attack rate in vaccinated (ARV) =
50/900 X 100 = 5.5%

Attack rate in unvaccinated (ARU) =
50/100 X 100 = 50.0%

Vaccine efficacy - 5

VE (%) = $\frac{ARU - ARV}{ARU} \times 100$

= $\frac{50.0 - 5.5}{50.0} \times 100$ = $\frac{44.5}{50.0} \times 100$

= 89%

Vaccine efficacy - 6

VE = $\frac{ARU - ARV}{ARU} \times 100$

= $\frac{ARU}{ARU} - \frac{ARV}{ARU} \times 100$

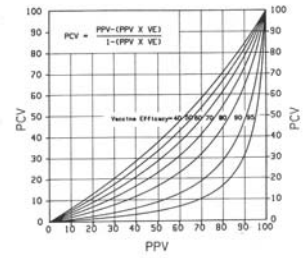
= (1 – ARV/ARU) X 100

= (1 – RR) X 100

Immunity levels after 1 dose

	Efficacy		
	90%	95%	98%
Coverage	% immune		
90%	81.0	85.5	88.2
95%	85.5	90.2	93.1
98%	88.2	93.1	96.0

Percentage of Cases Vaccinated (PCV) per Percentage of Population Vaccinated (PPV), for 7 Values of Vaccine Efficacy (VE)



Governmental perspectives on Effectiveness and Safety

Pre-Licensure Vaccine Safety Studies

- Laboratory
- Animals
- Humans

Pre-Licensure Human Studies

- Phase I, II, III trials
- Common reactions are identified
- Vaccines are tested in thousands of people before being licensed and on the market allowed
- Poorly detected reactions:
  - Rare
  - Delayed onset
  - Subpopulations

Post-Licensure Surveillance

- Identify rare reactions
- Monitor increases in known reactions
- Identify risk factors for reactions
- Identify vaccine lots with increased rates of reactions
- Identify signals

Vaccine Adverse Event Reporting System (VAERS)

- Jointly administered by CDC and FDA
- National reporting system
- Passive (depends on health care providers and others to report)
- Receives ~10,000 reports per year

Vaccine Adverse Event Reporting System (VAERS)

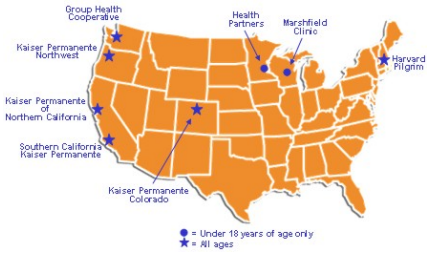
- Detects
  - new or rare events
  - increases in rates of known events
  - patient risk factors
- Additional studies required to confirm VAERS signals
- Not all reports of adverse events are causally related to vaccine

Vaccine Safety Datalink

- Large-linked database
- Links vaccination and health records
- Population under “active surveillance”
  - 7 HMOs
  - 2.5% of the U.S. population
- Powerful tool for monitoring vaccine safety

Vaccine Safety Datalink

- 8 Managed Care Organizations
- 9 Million Individuals



Vaccine Safety Datalink

- Immunization histories on 5 million people
- Data on vaccine type, dates, concurrent vaccinations
- Medical outcomes (outpatient visits, emergency room visits, hospitalizations)
- Birth data, census data
- Studies on hypotheses generated by VAERS, medical literature, changes in immunization schedule, introduction of new vaccines
- 75 scientific articles since 1990

Vaccine Safety Datalink Studies

- Aseptic meningitis after MMR
- Safety of second dose of MMR
- Chronic arthropathy in women after rubella vaccination
- Safety of revaccination with pneumococcal polysaccharide
- Impact of sequential IPV/OPV schedule on vaccination coverage
- Varicella serology among school-age children with negative/uncertain history of chickenpox

The Public and Risk Communication

- When making decisions in their lives, people generally do not use quantitative measures, such as probabilities
- A risk from something people feel that they cannot control (West Nile Virus) is usually of more concern than a risk they think they can control (smoking, drinking)
- This is one reason why adverse reactions to vaccine may be of greater concern

The Public and Risk Communication

- People respond better to positive, rather than negative messages (If you do this you will be healthy. Vs. If you do this you will die.)
- People respond better to risk communication if it is personalized. (This is what I am doing. This is what I am doing for my children.)
- This is one reason why it is important to involve leaders or “champions” in vaccination programs

Comparison of Risk vs Benefits of Vaccination United States

Disease	Pre-vaccine Era*	2002**	% change
Diphtheria	175,885	1	99.99
Measles	503,282	37	99.99
Mumps	152,209	238	99.80
Pertussis	147,271	8,296	94.40
Polio paralytic)	16,316	0	100.00
Rubella	47,745	14	99.97
Cong. Rubella Synd.	823	3	99.60
Tetanus	1,314	22	97.90
H flu b & unk (<5 yrs)	20,000+	167	98.60
Total	1,064,854	8,894	-99.16
Vaccine Adverse Events	0	7,773	+++

* Typically, average during 3 years before vaccine licensure
\+ Estimated because no national reporting existed in the prevaccine era
** Provisional (01/06/2003)

Problem with Risks vs Benefits

- Balance may change with time.
- Balance may change with place.
- Discussion: compare use of IPV vs OPV in the US vs India.

References:

- Orenstein, W et. al. “Field evaluation of vaccine efficacy.” Bulletin of the World Health Organization, 63 (6), 1055-1068 (1985).
- www.cdc.gov/vaccinesafety - see VAERS, VSD, Scientific Agenda