

Overview of Vaccine Efficacy and Vaccine Effectiveness

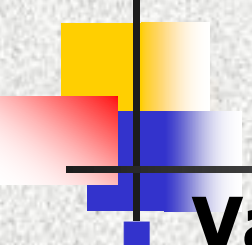


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Efficiency vs Effectiveness

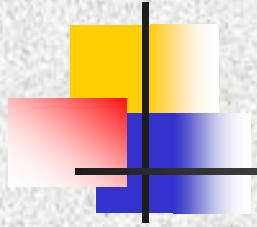
- **Vaccine efficacy-** % reduction in disease incidence in a vaccinated group compared to an unvaccinated group under optimal conditions (eg RCT)
 - Typically use objective outcomes- eg lab-confirmed influenza
 - designed to maximize internal validity (by randomization and allocation concealment)
 - often at the expense of generalizability



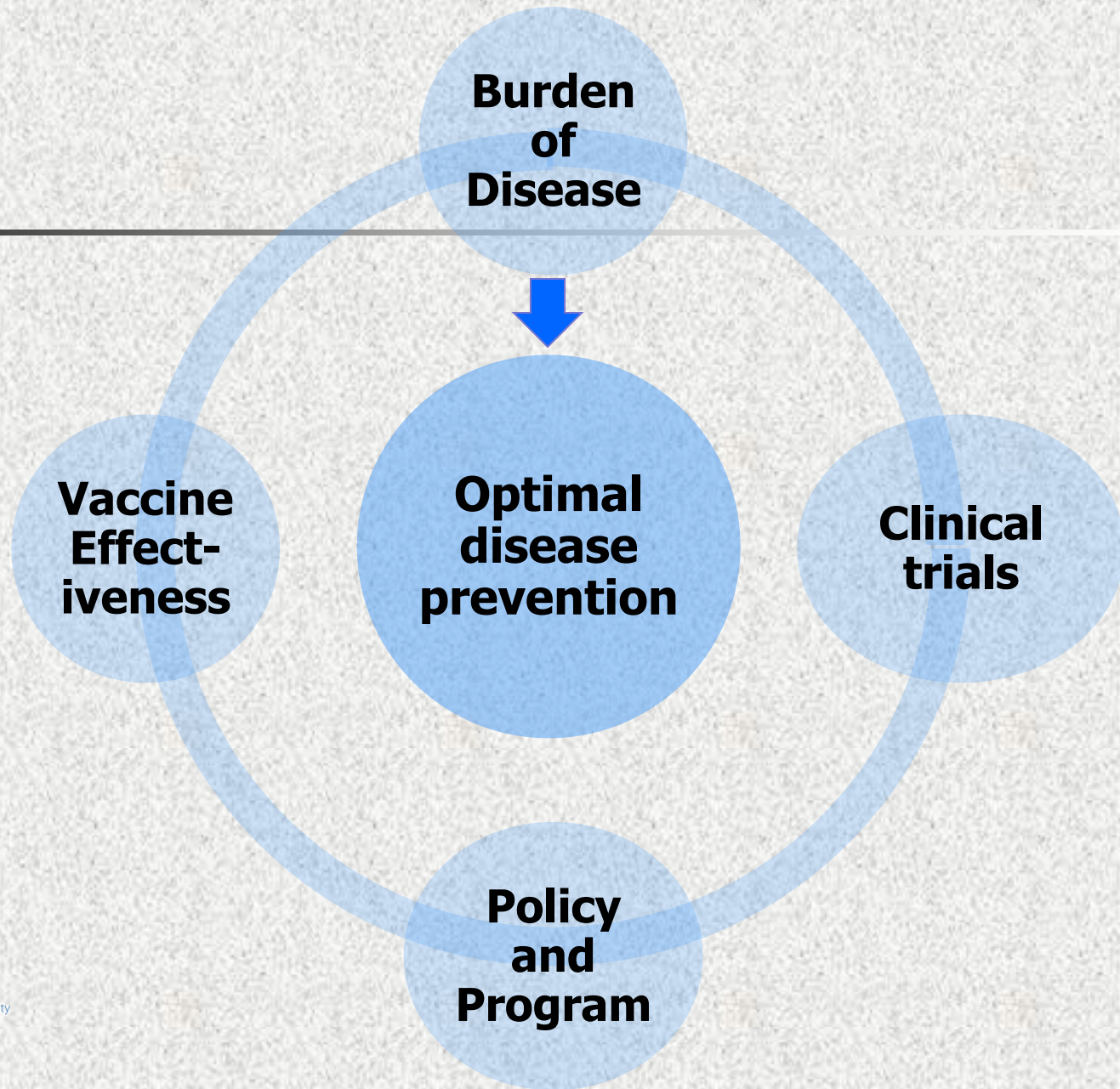
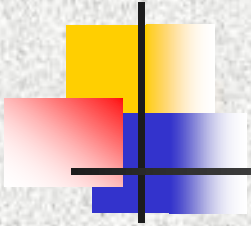
■ **Vaccine effectiveness-** ability of vaccine to prevent outcomes of interest in the “real world”

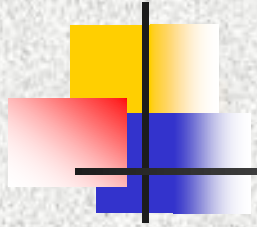
- Primary care settings
- Less stringent eligibility
- Assessment of relevant health outcomes
- Clinically relevant treatment selection and follow-up duration
- Assessment of relevant adverse events
- Adequate sample size to detect clinically relevant differences

■ Intention to treat analysis



Why monitor vaccine effectiveness?

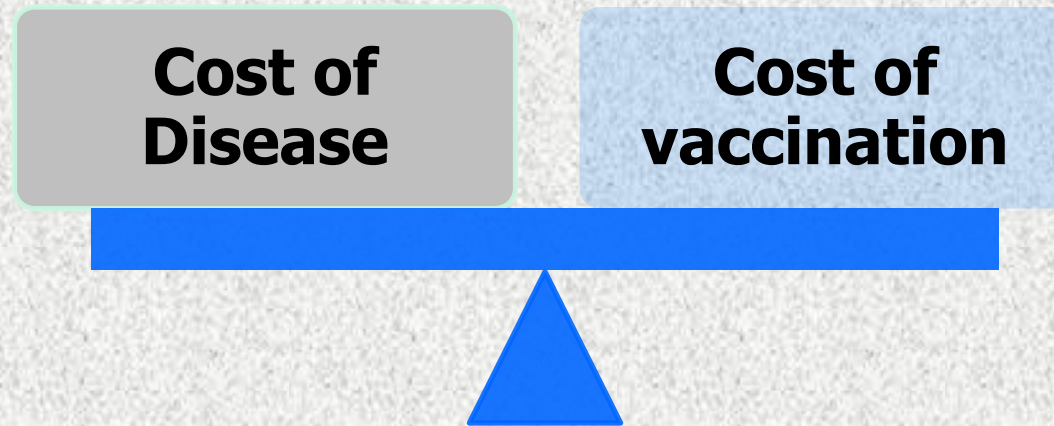




**Demonstrating need
(Burden of disease)
and proving benefit
(Vaccine effectiveness)
is critical to promote immunization,
sustain uptake, and stimulate
development of better vaccines**



Informing Cost effectiveness



- Where the balance rests depends upon understanding the proportion of the disease burden that is vaccine preventable
= **VACCINE EFFECTIVENESS**
- At any vaccine cost, the greater the burden of disease and the greater the proportion that is vaccine preventable, the more **Cost effective** a program will be



Factors impacting vaccine effectiveness

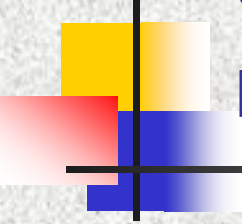
- **Host factors**

- Age
- Comorbidity- including frailty/function
- Prior exposure
- Time since vaccination

- **Vaccine characteristics**

- Mode of delivery
- Live vs inactivated
- Vaccine composition- addition of adjuvant

- **Match to circulating strains**



Optimal VE Data to inform decision-making

- Overall and type/subtype specific (including B-lineages)
- By age group
- Against non-severe and severe outcomes
- In specific at-risk/target populations
- By vaccine type- are new vaccines really better?
- Real-time- throughout season- may predict drift, circulating mismatched strains, duration of protection



Define Outcome- what is important?

- ILI/ARI
- Serious outcomes- hospitalization +/- death, dependence
- Lab-confirmed influenza
- Careful attention/adherence to case definition – specificity more important than sensitivity!



Measuring Vaccine Effectiveness- Data needs

- **Surveillance data** for outcome of interest (case ascertainment)
 - Enhance routine testing for influenza!
- **Immunization data:**
 - Vaccinated?
 - When? (in relation to onset of disease)
 - Which vaccine?
- **Clinical data:** age, gender, comorbidity (including pregnancy), functional status, course and outcome

The problem of BIAS- how do vaccinated and unvaccinated people differ?

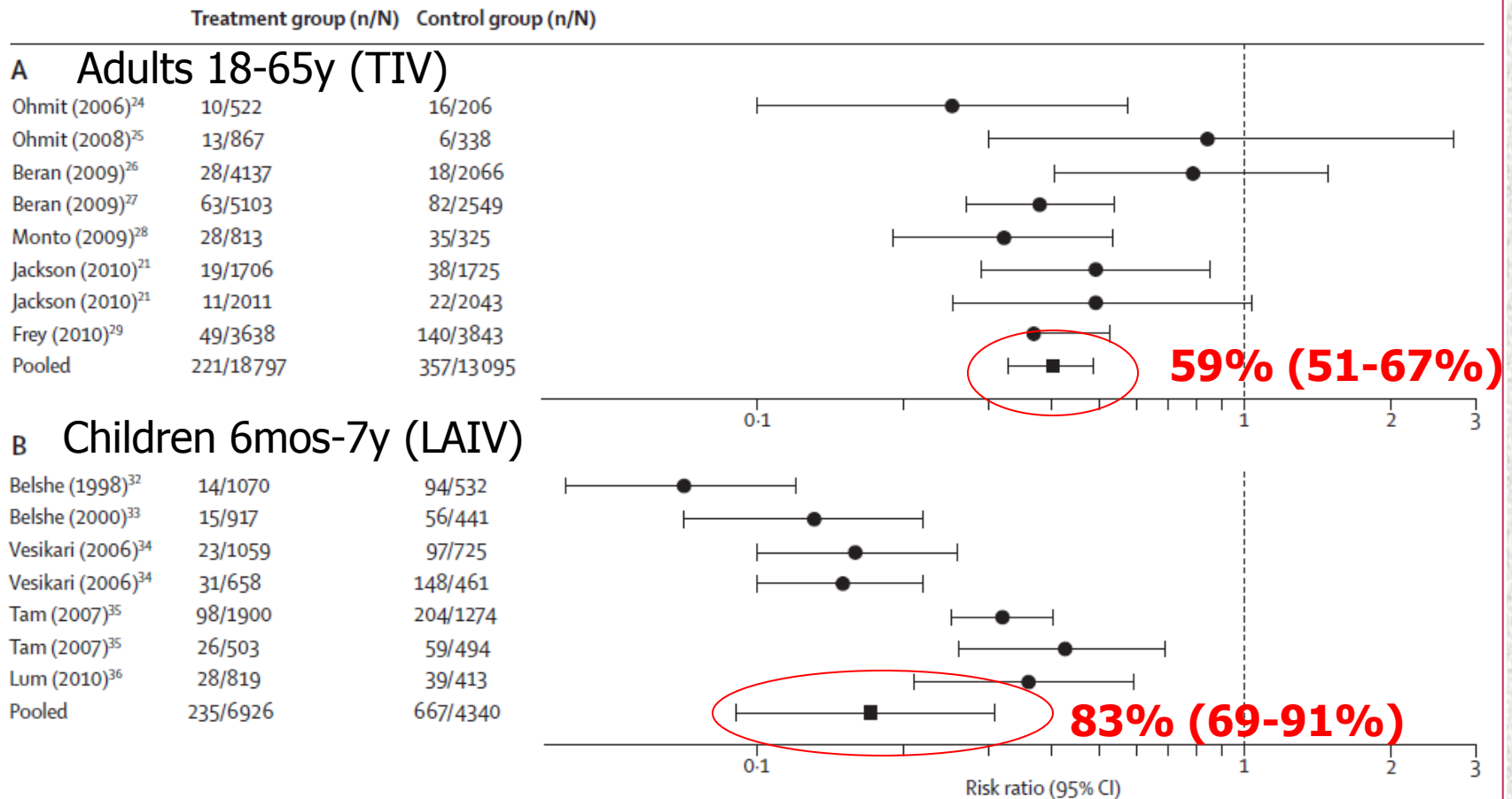
- Bias is any factor independently associated with risk of disease and vaccination status
 - Healthy user bias- persons more likely to be vaccinated are less likely to develop disease- OVER-estimates VE
 - Frailty bias- persons more likely to be vaccinated (frail elderly in LTCF) are more likely to experience adverse influenza outcomes- UNDER-estimates VE

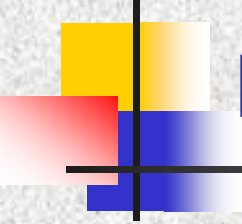


Observational methods for estimating vaccine effectiveness

- **Cohort studies**
- **Case-control studies** (“test-negative” case control)
- **Household contact studies**
- **Screening method**- compare proportion of cases vaccinated to proportion of a comparable group in the population who are vaccinated – useful if vaccination status is only known in people with the outcome- need to know population coverage rates

So... How effective are influenza vaccines?? (Osterholm, Lancet ID Jan 2012)



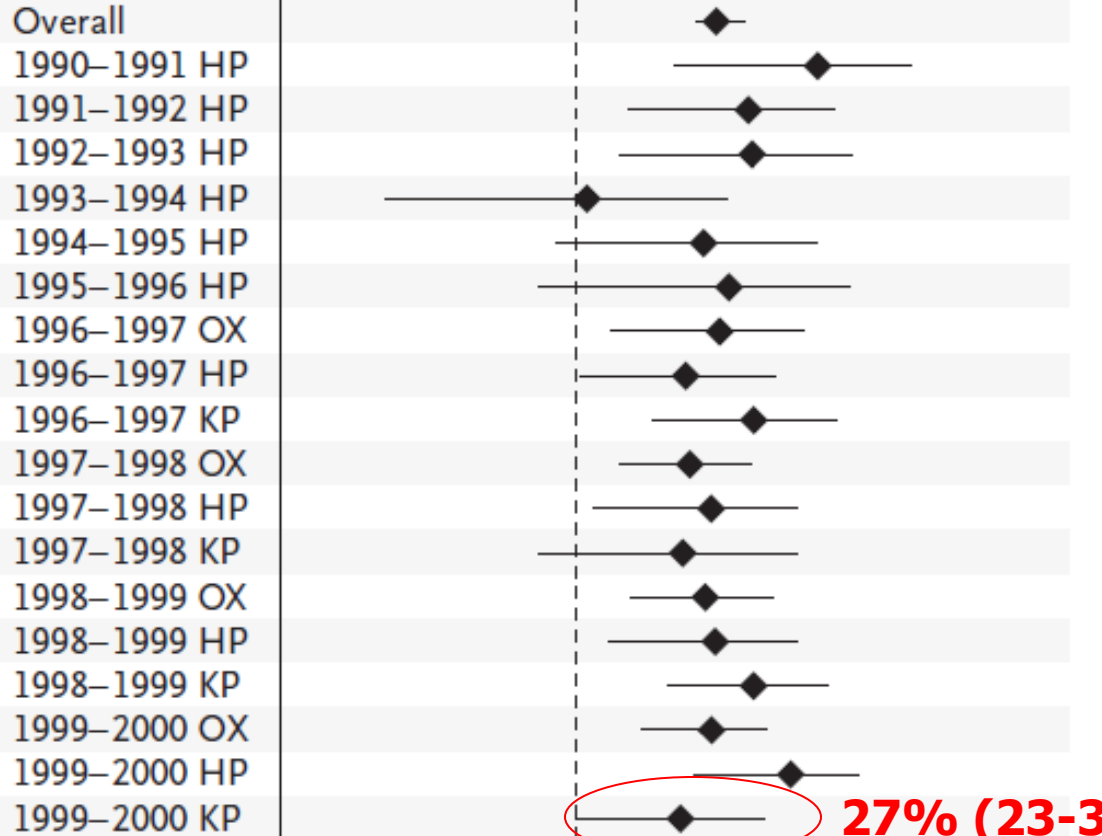


What about the elderly? (Cochrane Library, Feb. 2010)

- Only 1 RCT identified- underpowered to assess efficacy
- Point estimates difficult to interpret due to uncontrolled bias
- No conclusion could be drawn

A

Season



27% (23-32%)

Effectiveness of Vaccine in Reducing the Risk of Hospitalization (%)

B

Season

Overall

1990–1991 HP

1991–1992 HP

1992–1993 HP

1993–1994 HP

1994–1995 HP

1995–1996 HP

1996–1997 OX

1996–1997 HP

1996–1997 KP

1997–1998 OX

1997–1998 HP

1997–1998 KP

1998–1999 OX

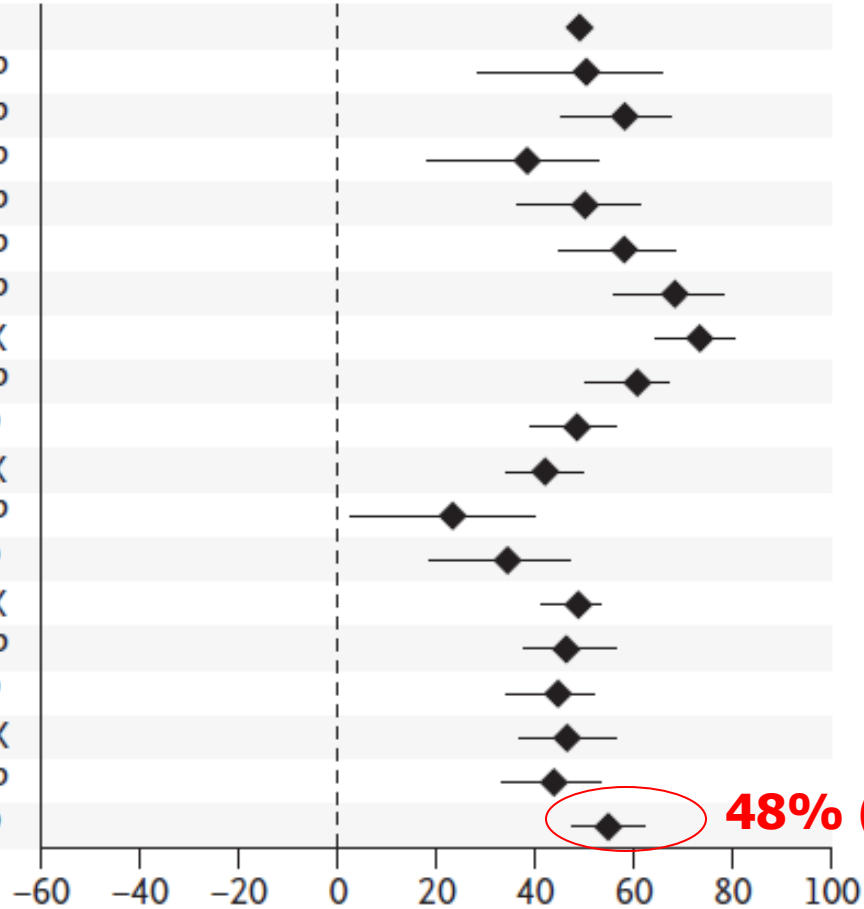
1998–1999 HP

1998–1999 KP

1999–2000 OX

1999–2000 HP

1999–2000 KP



48% (45-50%)



Conclusions

- Monitoring vaccine effectiveness is critical to:
 - Optimize use of limited resources
 - Demonstrate impact of vaccine on health outcomes (justify cost)
 - Optimize vaccine uptake
 - Stimulate development of improved vaccines



Thank you!

