# Serological monitoring of FMD vaccination

# Principles and Practise

David Paton

25 min + 5 min Questions

# Vaccination programmes are complex and so things can go wrong

- Monitor implementation
  - Vaccination coverage
  - Population immunity

- Monitor outcomes
  - Outbreak surveillance and investigation
  - NSP serosurveillance of undisclosed infection

# Population immunity studies

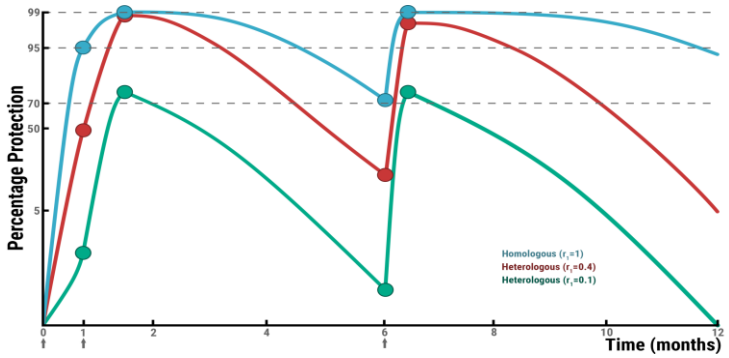
- Questions that can be addressed
  - Have sufficient animals responded to vaccination as expected?
  - How well is the population protected?

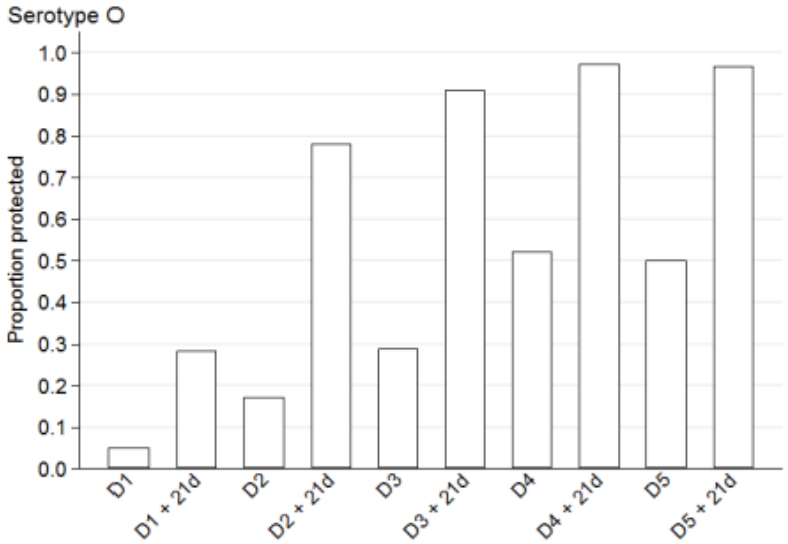
- Immunity is dynamic, but cannot test all animals at all times
  - When to test – vaccination cycle and prior knowledge to inform interpretation
  - Which herds and animals to test – population heterogeneity
  - Synergy from combining coverage and immunity surveys

# What antibody levels should we expect after vaccination?

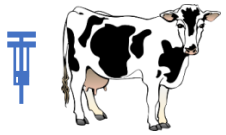
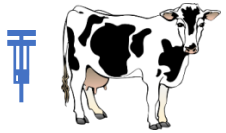
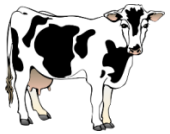
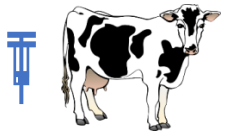
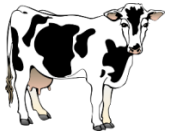
- Simplest approach is to test population in the field at 3-4 weeks after vaccination.
- If not, usually assumed that same test cut-off value will be appropriate at all times.

Schematic representation, based on Pay (1984)




From: FMD in Kenya: Epidemiology, disease impact and vaccine effectiveness on large-scale dairy farms. Nicholas Lyons, PhD, University of London, 2015. D1-5 represents the proportion "protected" at each vaccination with the D+21 representing the proportion 21 days post vaccination

| | | **What is known about Ab levels?** |
|---|---|---|
| 1st vaccination |  | naïve? |
| 2nd vaccination after 28 days |  | data from potency tests |
| 21 days after 2nd vaccination |  | ? |
| 3rd vaccination 6 months after 1st vaccination |  | ? |
| 21 days after 3rd vaccination |  | ? |

Hence, value of

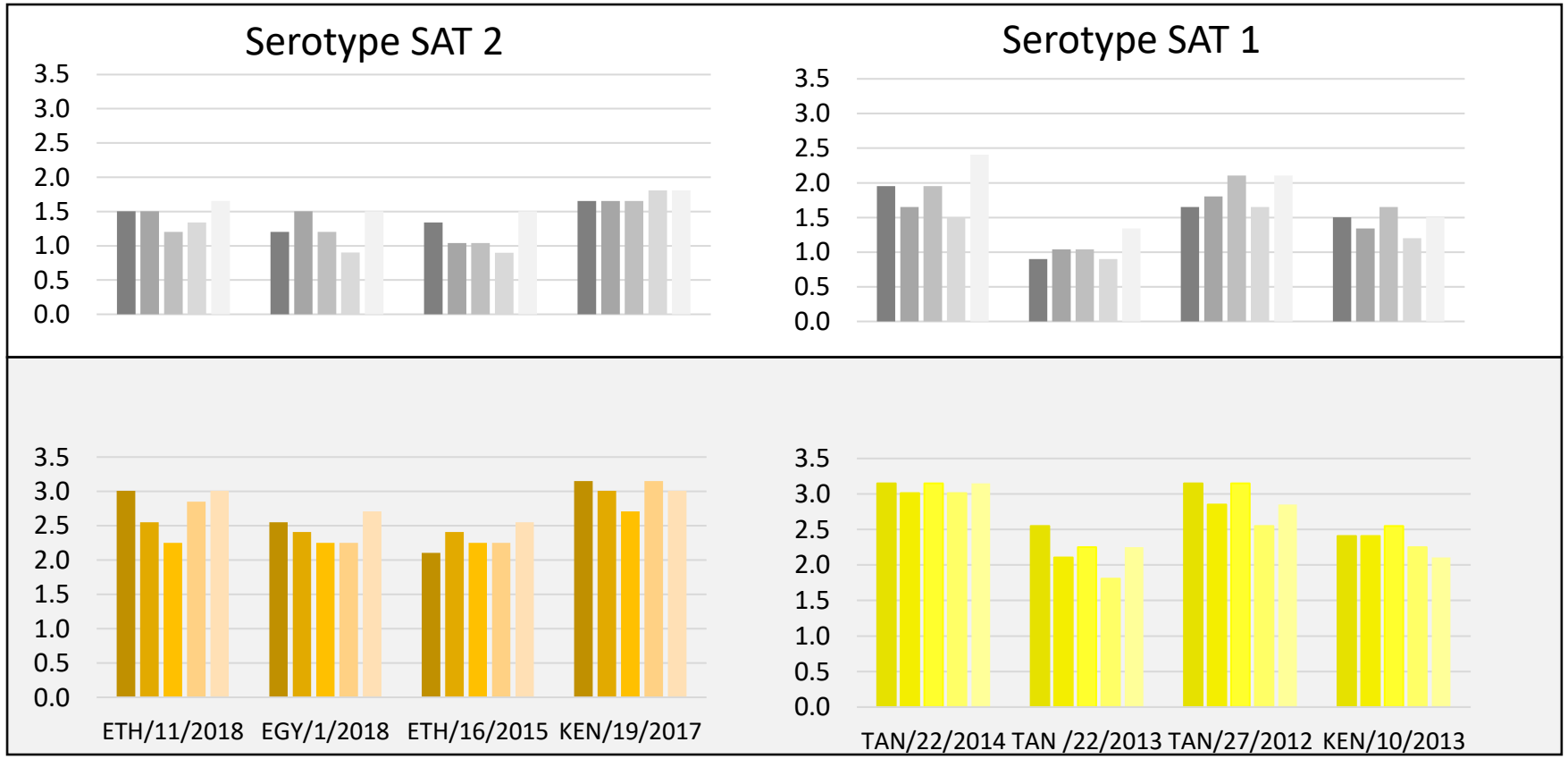
(i) batch release sera and

(ii) small longitudinal studies to sample vaccinated animals in closely managed herds

# The booster effect at first vaccination

**VNT 21 days after first vaccination**

**VNT 10 days after 28 day booster**



# Correlating serology to protection

Many factors can influence the relationship

- Non-antibody mediated immune response
- The type of antibody that you measure – neutralising, opsonising, binding, avidity, isotype
- Confounding variability – animals, viruses, vaccines, tests, timing, protection

# The correlation between serology and homologous protection

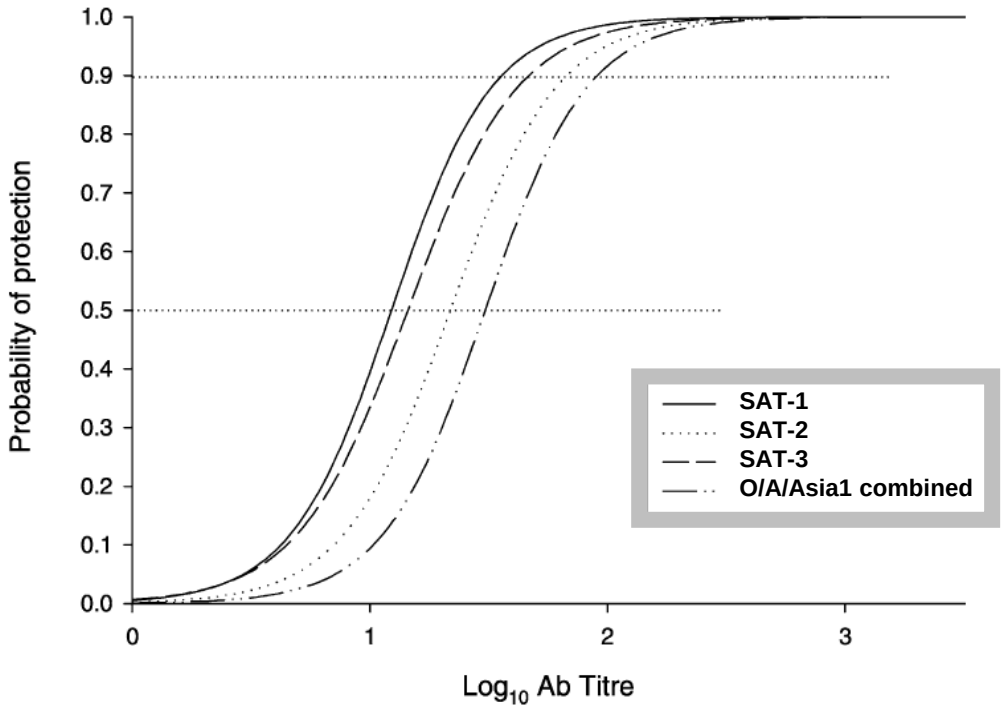
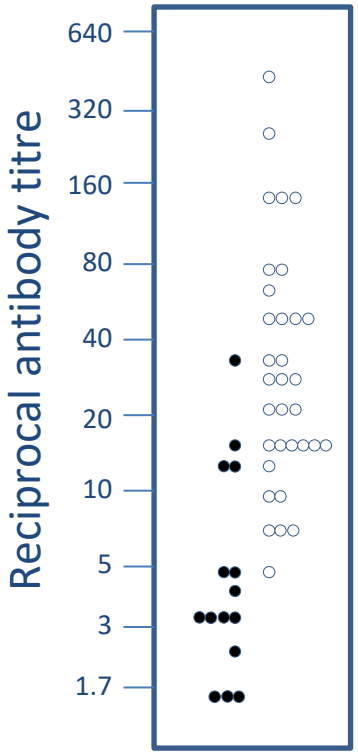



Fig. 2. The best fitting models to four different subsets of the data.

Titre for 75% probability of protection (T75) for O/A/Asia1 combined ≈ $\log_{10}1.7$ (1 in 56)

*Barnett et al (2003) Vaccine 21 3240–48*




Relationship between VNT antibody and protection at 21 dpv for serotype O

● - not protected

○ - protected

*McCullough et al (1992) J Virol 66(4) 1835-40*

Few vaccine challenge studies look at the effects of booster vaccinations and heterologous challenge

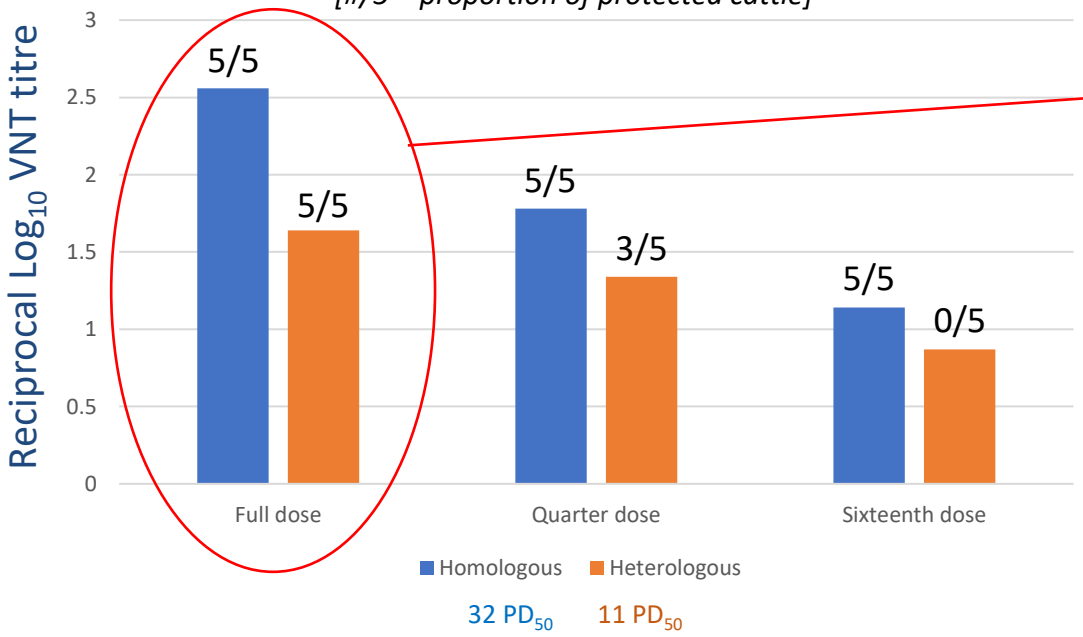
# In real life vaccinated animals are exposed to heterologous viruses

*Brehm KE, Kumar N, Thulke HH, Haas B. (2008) High potency vaccines induce protection against heterologous challenge with foot-and-mouth disease virus. Vaccine 26(13):1681-7.*

A series of challenge studies to compare homologous and heterologous protection for serotype A FMDV

Same $A_{22}$Iraq vaccine: 2 potency tests with homologous and heterologous (A/Egypt/06, $r_1$ = 0.12) challenge

*[#/5 = proportion of protected cattle]*



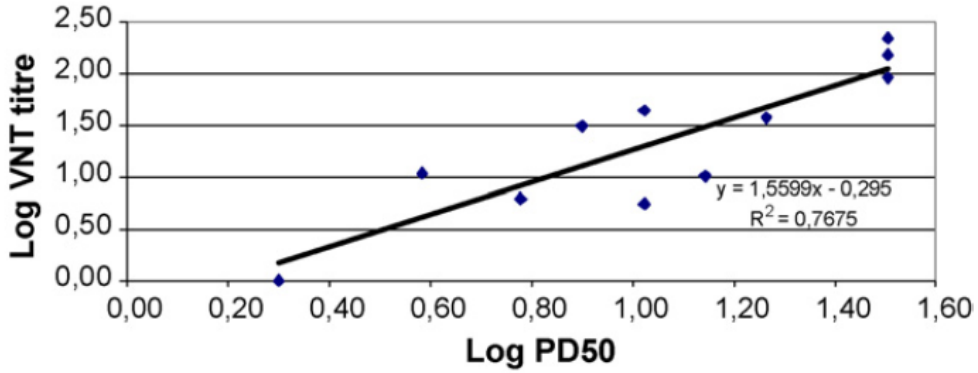
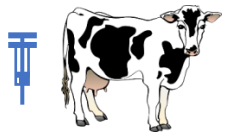
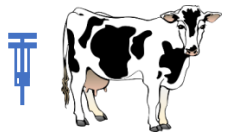
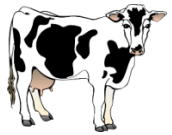
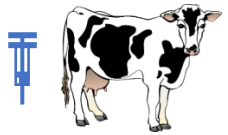
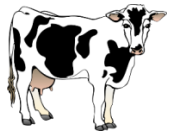




**Figure 2** Regression of protection vs. challenge strain specific full dose mean VNT titres (log PD50 value vs. log titre of full dose group mean).

# Tests for FMD protective antibodies

| TEST | Easy to change virus specificity | Repeatability | Easy/safe to perform and scale up | Corelation to protection |
|---|---|---|---|---|
| VNT | +++ | + | _ | ++ |
| Blocking ELISA | + | +++ | +++ | + |
| Avidity/isotype ELISA | + | +++ | + | +++ |

| | | **What is known about Ab levels?** | **What is known about correlation of Ab to protection?** |
|---|---|---|---|
| 1st vaccination |  | naïve? | unprotected? |
| 2nd vaccination after 28 days |  | data from potency tests | data from potency tests if challenged |
| 21 days after 2nd vaccination |  | ? | ? |
| 3rd vaccination 6 months after 1st vaccination |  | ? | ? |
| 21 days after 3rd vaccination |  | ? | ? |

Small longitudinal studies in closely managed herds can tell you about antibody levels but not protection, unless animals are challenged

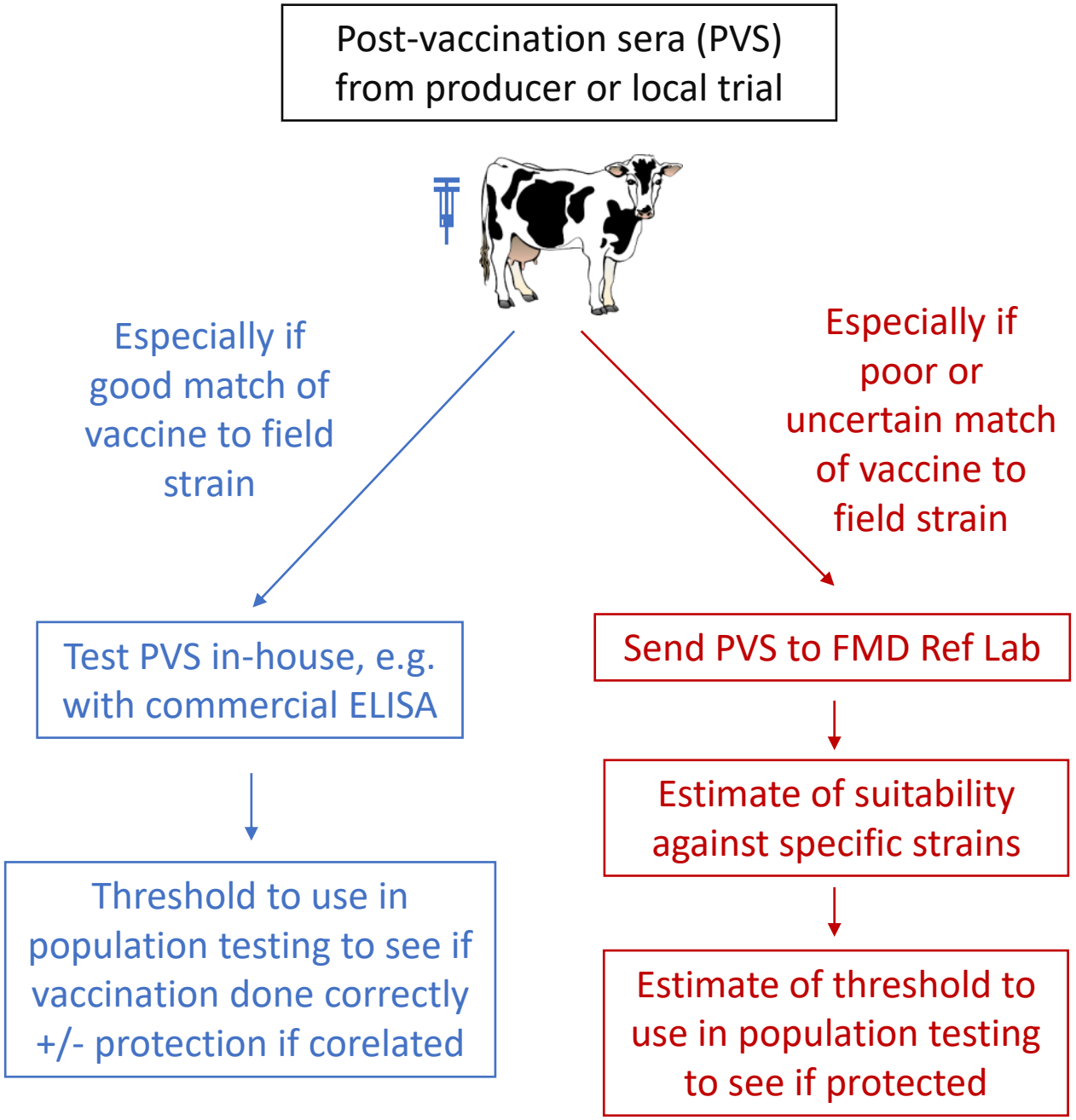
# Practical check list to decide on best approach

*(what are your limitations?)*

- Do you know the field strains against which you are seeking protection and are they available for testing?
- Is the vaccine matched to these field strains?
- Is the potency of the vaccine batch known – how was it deduced?
- Has potency been corelated to serology and do you have access to the test used for this?
- Do you have control sera from vaccinated animals?
- What was the vaccination regime and when were the sera collected?
- What tests are available and can you adjust their virus specificity?

# In practice?

- Vaccine-specific antisera useful to set thresholds for efficiency of vaccination which may or may not be corelated to protection
- Or use heterologous test results to set threshold for field protection
- Or simply assume that almost any level of detectable antibody indicates some protection



# Conclusions

- Need to monitor implementation and effectiveness of vaccination on an ongoing basis
- Population immunity surveys are useful and can be combined synergistically with coverage data
- Various ways to set test thresholds when measuring population immunity depending on what you know and can do
- Usually have to make assumptions due to incomplete information and therefore important to understand the limitations of immunity estimates