Foot-and-mouth disease: Control and vaccination

Theo Knight-Jones

Lecture to 5th year veterinary medicine students

University of Zambia

16 February 2015

ILRI
INTERNATIONAL LIVESTOCK RESEARCH INSTITUTE

CGIAR

Overview

1. Control strategies of FMD

2. Vaccination as a control strategy. Why use this method (Advantages and disadvantages)?

3. Vaccination strategies

4. Available FMD vaccines

5. Vaccine selection for a particular region? How to determine a vaccine to use

6. Period of vaccination in a herd (how long is the protection)

7. Revaccination

8. Possible failures in FMD vaccination

ILRI CGIAR

FMD – Essential info

- Viral disease of “Cloven hoofed animals”

- Picornavirus - 7 serotypes
- High morbidity - low mortality

ILRI CGIAR

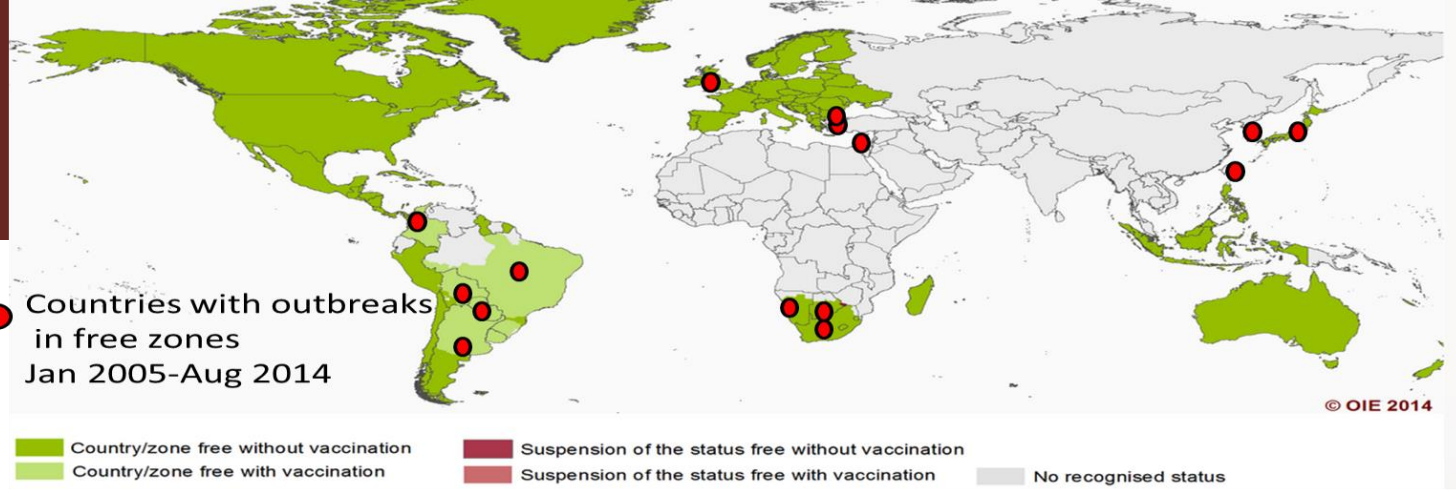
FMD direct impact

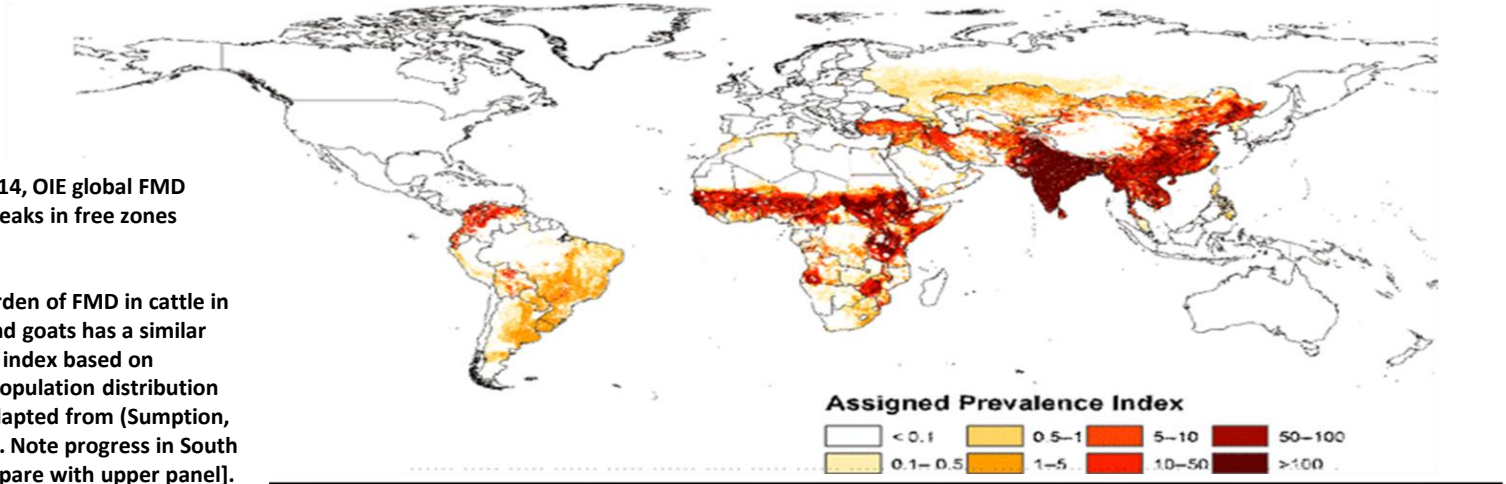
- Highly infectious
  - R_o 2–70 (depending on the setting)
  - High attack rate in outbreaks (>70%)
  - Repeated outbreaks affecting many animals
  - Rapid spread
    - 3-5 day incubation & pre-infectious period
    - UK 2001 - >56 farms infected before disease detected
- Reduced productivity
  - Especially commercial dairy
  - Prevents use of high productivity breeds
  - Reduced traction (beasts of burden)

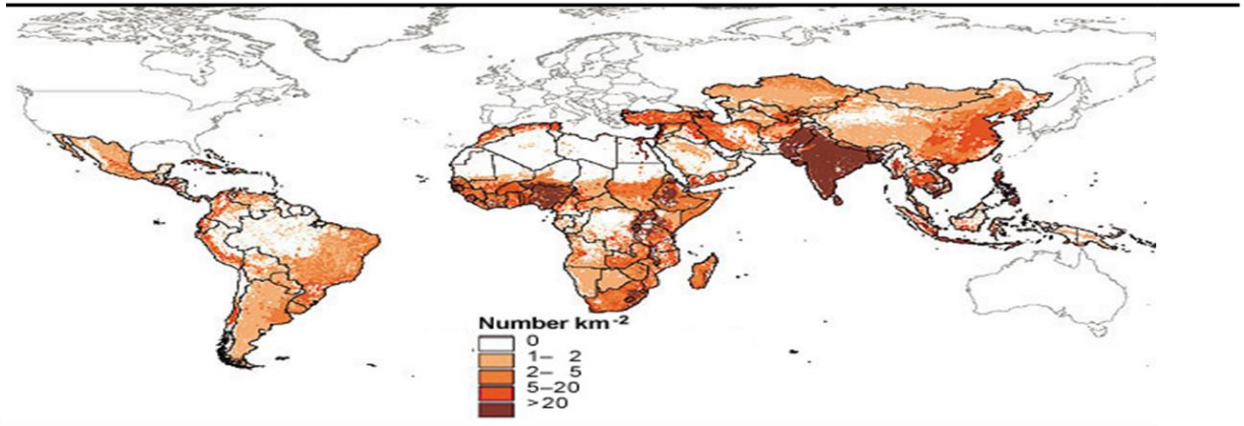
FMD indirect impact

- Trade restrictions
  - FMD free countries block imports from FMD affected countries/zones
    - Disastrous for exporting countries
  - Cost of control
    - Movement/trade restrictions
      - May discourage reporting
    - Vaccination (only measure in most endemic countries)
    - Culling & compensation
      - » Impact on other industries (tourism)

UK 2001
£10billion







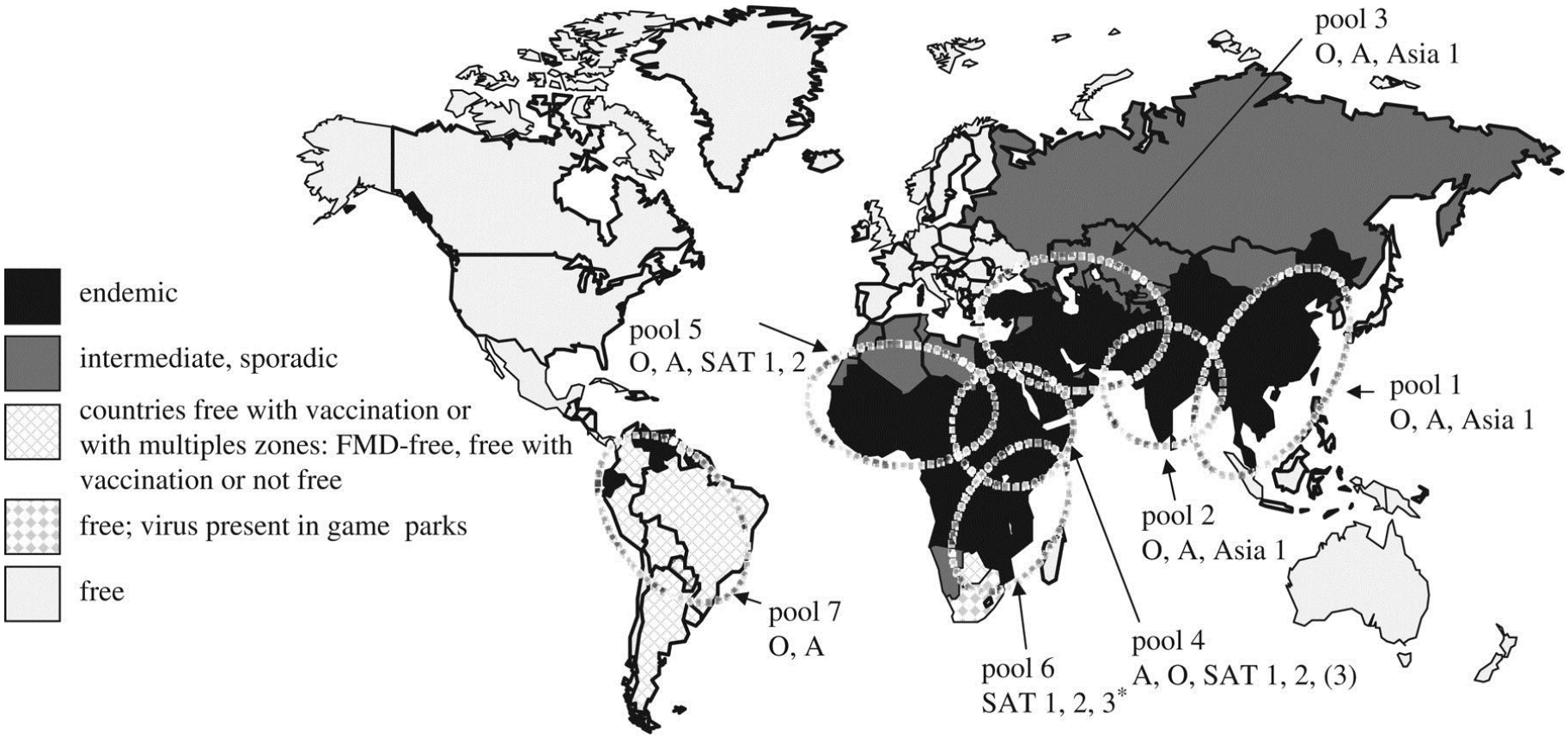
Upper panel – August 2014, OIE global FMD status, with recent outbreaks in free zones identified.

Middle panel - global burden of FMD in cattle in 2008 (burden in sheep and goats has a similar distribution). Prevalence index based on estimates of incidence, population distribution and other risk factors, adapted from (Sumption, Rweyemamu et al. 2008). Note progress in South America since 2008 [compare with upper panel].

Lower panel - density of poor rural livestock keepers from (Thornton, Kruska et al. 2002). Central America, parts of South East Asia and some areas in South America are the few exceptions where FMD was not present in poor livestock keeper populations.

ILRI
CGIAR

FMD conjectured status and serotypes



Paton et al. (2009)

Control measures

Lancisi 1711

http://post.queensu.ca/~forsdyke/rindpst0.htm

a) Movement restrictions
    a) Close markets
    b) Between farms, zones, …
    c) Wildlife
b) Other biosecurity
    a) Fomite control
    b) Vector control (people, insects, objects,….)
c) Cleaning and disinfection of affected premises
d) Culling (affected, dangerous contacts,…)
e) Vaccination
    a) Mass vaccination
    b) Targeted vaccination
        a) Ring/reactive vaccination
        b) Zonal (Cordon Sanitaire)
        c) Specific risk group
    c) Private verses public funded vaccination

- Use of control zones – see Botswana, South Africa

- **Which measures reduce exposure and which reduce susceptibility?**

FMD vaccines

- Inactivated
- Serotype specific protection
  - Variation in protection between strains within serotype
  - Multivalent vaccines used
- Short duration (<6 months?)
  - from serology & challenge studies
- Repeated vaccination throughout life
- Two dose 30 days apart primary course
  - Important but often not given
- Poor stability (3-8°C)
- Sometimes can distinguish infected from vaccinated+uninfected – NSP purified vaccines
    - Non-Structural Protein (NSP) serology

Approximate global FMD vaccination

Region	Million doses/Year	Comments
China	1.6 billion doses	5 government producers
South America	500	Brazil: 350 million doses
Asia (excluding China)	200	India: 150 million doses
Middle East	20	
European region	20	Mainly Turkey
Africa	15	

Hamond (2010)

Used to eradicate FMD from Europe (1991-92)

ILRI CGIAR

What are the advantages and disadvantages of using vaccination to control FMD?

Vaccination

- Vaccination based control:
  - Advantages
    - May not need to cull
    - Protection even if cannot apply other control measures to reduce virus exposure
    - Sounds simple!
  - Disadvantages
    - Short duration of immunity
    - Limited spectrum of protection
    - Population turnover – young are highly susceptible
    - Cost – who pays?
    - Ongoing protection needed
    - False sense of security-affects risk behaviour
    - Vaccine quality/vaccine match
    - Coverage – herd immunity needed
    - Probably need biosecurity as well
    - Incentives for continued vaccination when not working
    - Needs thorough evaluation
    - Logistics of vaccinating million of livestock
    - Strain on veterinary services
    - Top down approach – inconsiderate of field situation needs of farmers
    - Mask infection/transmission – carriers
    - Affects ability to prove disease freedom
    - Affects trading restrictions if free but vaccinate

Current evaluation methods

- Vaccine protection:
  - Challenge studies – $PD_{50,}$ PPG
    - Small numbers
    - Unnatural challenge
  - *In vitro* serological vaccine matching studies
    - r-values, Expected percentage protection
    - Do not actually assess if animals are protected
  - Sero-surveys
    - To assess post-vaccinal antibody response
    - Population immunity (Structural Protein [SP] titre)
      - With antibody titre as a correlate of protection
      - Cannot tell if sero-positive from natural infection or vaccination
        - » High sero-prevalence =good or bad vaccination programme

r-value matching test

Report no:	2dmVNT				
Vaccine: / Field Isolate:	2dmVNT test ref:	A Iran 2005	A22 Irq	A Sau95	A Tur06
A TUR 78/11	mean	0.66	0.52	0.06	0.62
A TUR 3/12	mean	>0.98	0.76	0.08	0.62

In the case of Virus Neutralisation Test (VNT):

r_1 = ≥ 0.3. Suggests that there is a close relationship between field isolate and vaccine strain. A potent vaccine containing the vaccine strain is likely to confer protection.

r_1 = < 0.3. Suggests that the field isolate is so different from the vaccine strain that the vaccine is unlikely to protect.

ND = Not done.

Current evaluation methods

- Sero-prevalence surveys as indicator of burden
- Vaccine protection:
  - Serological correlate of protection
    - Limited protection against different serotypes/strains
    - New strains appear frequently
- Vaccine coverage:
  - Distributed method
    - Number of doses distributed/Estimated population size
- Vaccination programme impact
  - ?

-No effectiveness studies
-Few field trials (RCT)

Protection in the field may vary

Batch variability

Cold chain

Shelf life

Variable animal response

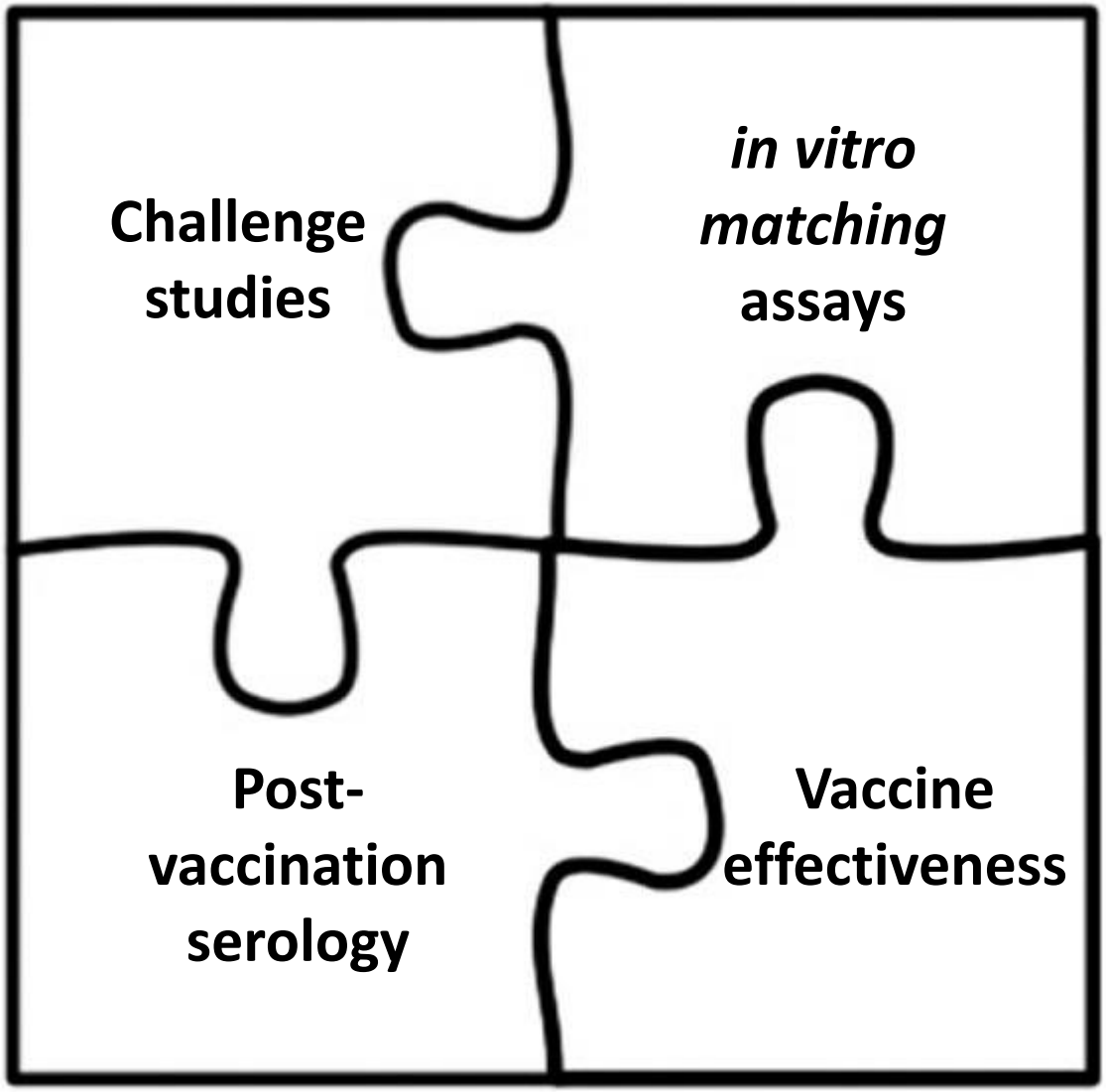
Match with field virus

Field protection:
protection that counts

Time since last vaccinated
Number of doses in lifetime
Level/duration of virus exposure

ILRI CGIAR

FMD vaccine evaluation



Other…

Key questions for a vaccination programme:

1. Are vaccinated animals protected?
   Vaccine effectiveness

2. Are the animals being vaccinated (adequately)?

   Vaccine coverage

Vaccine coverage… questions

- What levels of coverage are achieved?
  - Are there important groups of under-vaccinated stock?
- How does coverage vary over the annual production cycle?
  - Considering population turnover
  - How does this relate to key epidemiological events?
    - Spring turn out to grazing
    - Times of mass trading & livestock movements

Vaccine effectiveness

Reduction in risk in similarly exposed vaccinated compared to unvaccinated animals in the field

FMD vaccine studies in Turkish cattle

Mass vaccination

FMD vaccine protection:

- **Requires several doses (≥3PD_{50})**
- **Declines with time since vaccination**

Mass vaccination

Population immunity ≈ Population vaccination history

[No. of doses, time since last dose]

Population vaccine history ≈ Population age structure

Mass vaccination twice a year:
Population age-sex-vaccination distribution

Beef suckler cattle:

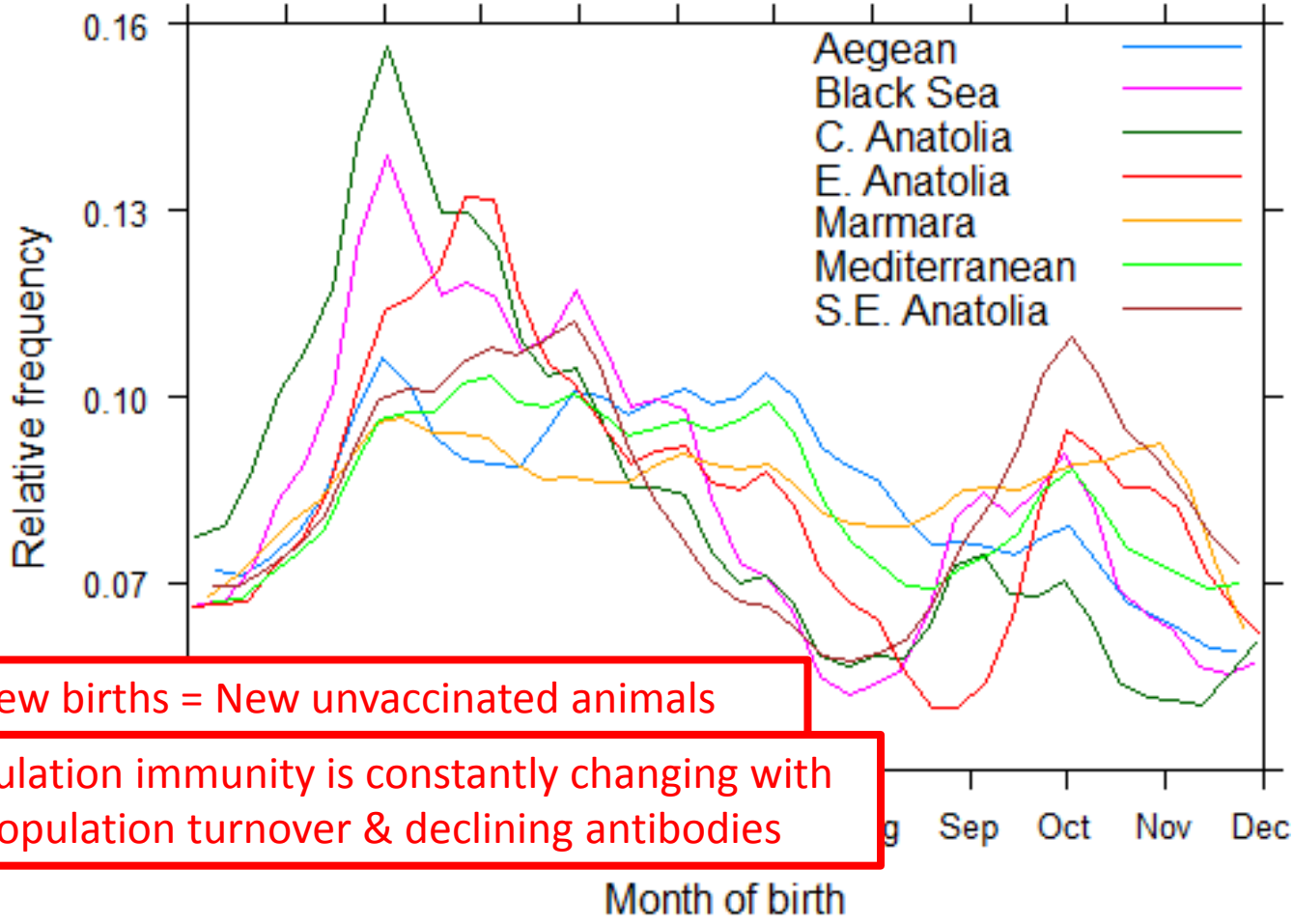
Mass vaccination twice a year:
Population age-sex-vaccination distribution

Beef fattener cattle:

Different production system = different age structure = different population immunity

Population vaccine history & immunity varies by region

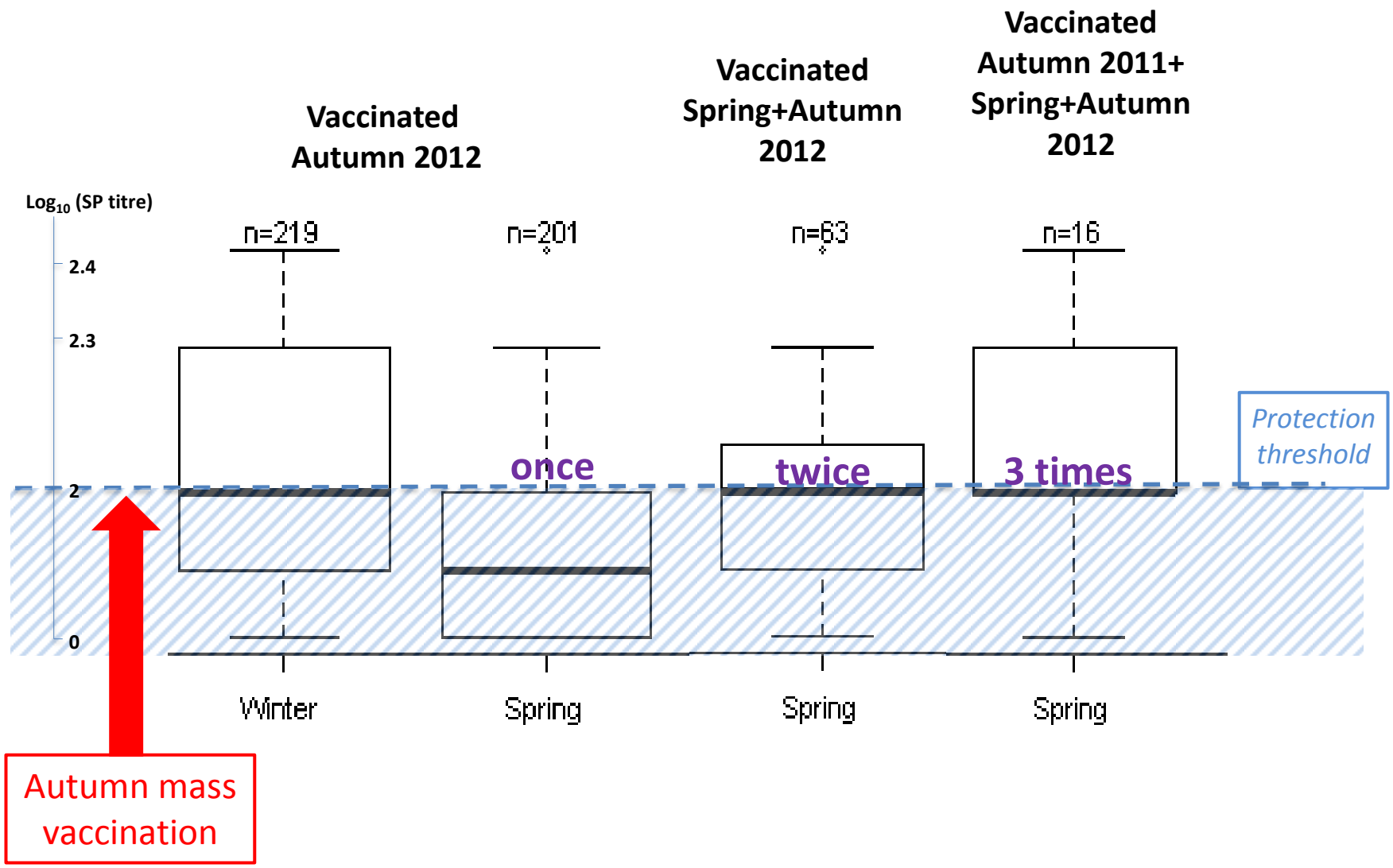
Structure changes with births & deaths over the annual production cycle



New births = New unvaccinated animals

Population immunity is constantly changing with population turnover & declining antibodies

Post-vaccination immunity also declines with time depending vaccine history



If multiple doses needed, variation in immunity resulting from variation in coverage becomes exaggerated

If 3 doses needed for “adequate” protection

District with 100% coverage:

After 3 rounds: 100% of cattle vaccinated 3 times

District with 50% coverage:

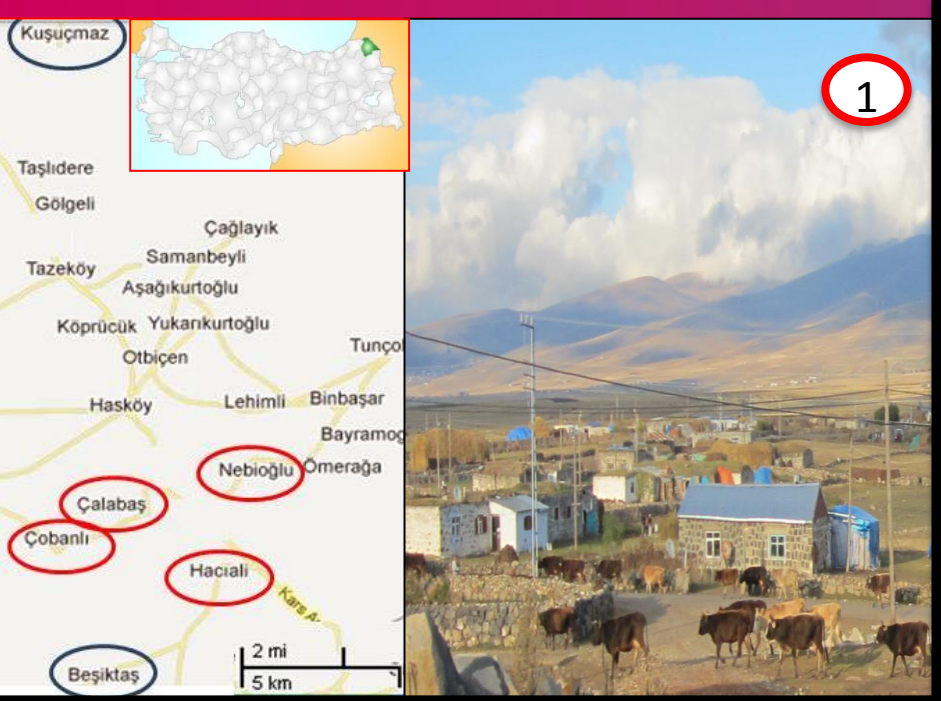
After 3 rounds: 50% x 50% x 50% = 12.5% vaccinated 3 times

Population coverage model

- Describe population immunity over the production cycle with 2012 Turkish mass vaccination policy

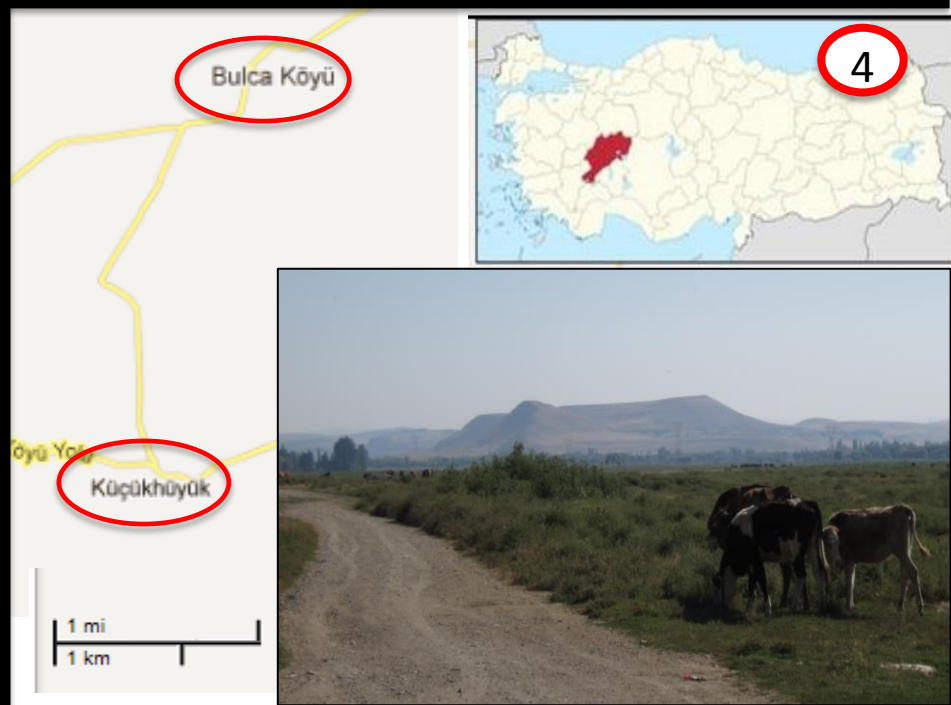
- Simulated the Turkish cattle population for each province
  - Age-structure by day and month of birth
    - Using data from national random surveys for each province and census data

- Dynamic population model representing the changing age structure for each province over the annual production cycle


Kuşuçmaz
Taşlıdere
Gölgeli
Çağlayık
Samanbeyli
Tazeköy
Aşağıkurtoğlu
Köprücük
Yukarıkurtoğlu
Otbiçen
Tunço
Hasköy
Lehimli
Binbaşar
Bayramoğ
Nebioğlu
Ömerağa
Çalabaş
Çobanlı
Hacıali
Beşiktaş
2 mi
5 km
1

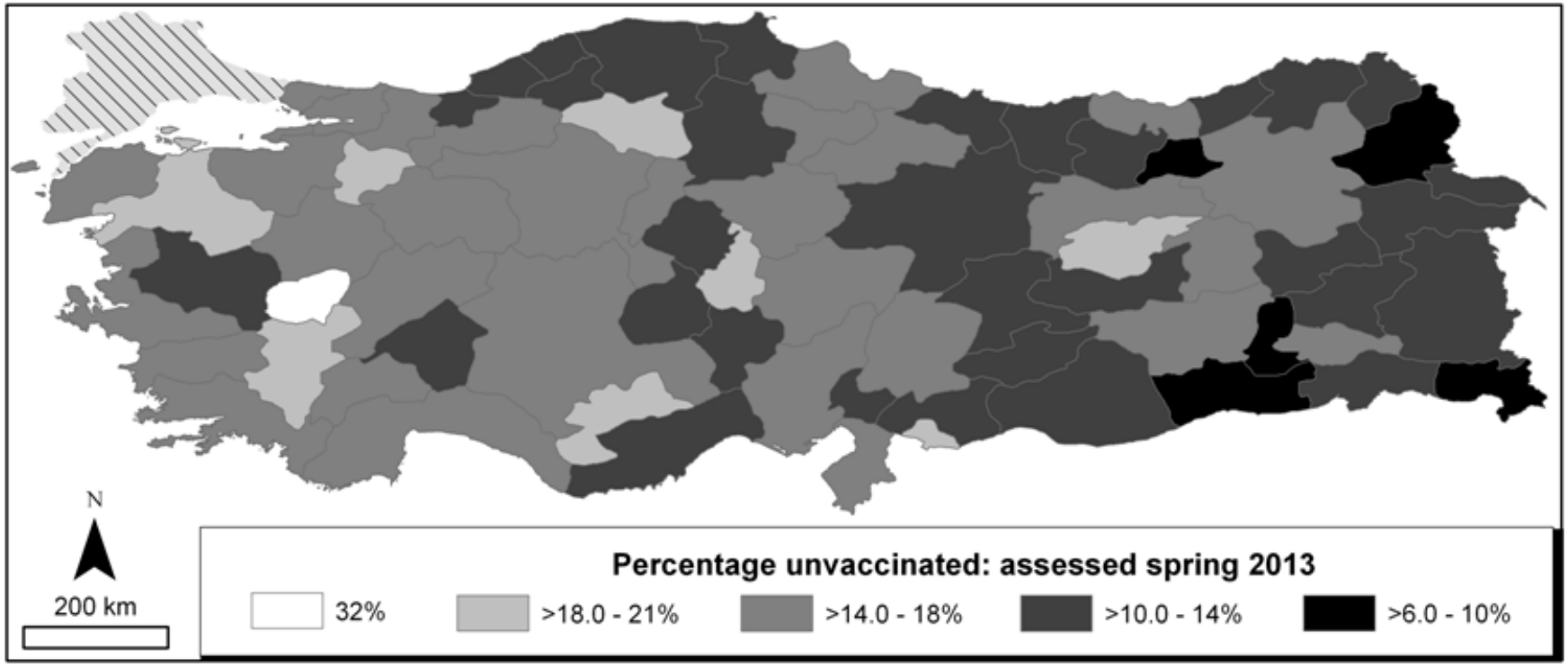

2 mi
5 km
Küçükkalecik
3
Işıklar


3
Akçaköy
Karayahşiler
Tuğlu
Yalınlı
Gümüşsu
Çeltikler
Gökgöl
Sungulu
Irgıllı
Tekke
Çıtak
Kıralan
Karahacılı
Bozdağ
Aşağıseyit
Ataköy
Konak
Özdemirci
Evciler
Dağal
Belenardıç
Uzunpınar
Karakaya
Güzelpınar
Akköy
Pamukkale
Aşağışamlı
Irlıganlı
Kumkısık
Korucuk
Akkale
Pınarkent
Kocabaş
Denizli
Honaz
Emirazizli
Başkarcı
5 mi
10 km
Cankurtaran


Bulca Köyü
4
Küçükhüyük
1 mi
1 km

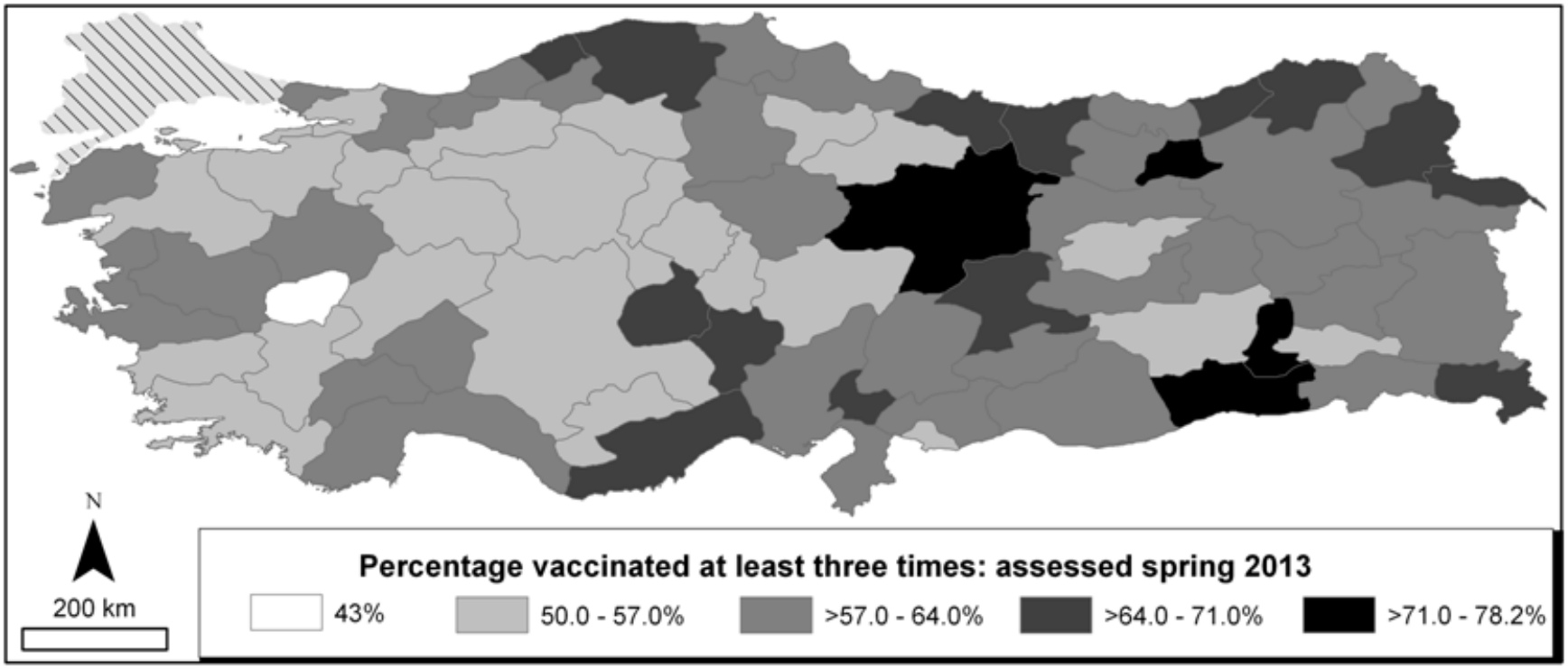
Percentage never vaccinated 6 months after mass vaccination – if eligible cattle always vaccinated

median values reported



Unvaccinated = Cattle too young at prior vaccination
+
New births since prior vaccination

Percentage vaccinated ≥3 times in lifetime – if eligible cattle always vaccinated



Vaccinated ≥3 times = Adult cattle

But not all eligible cattle will be vaccinated

Field studies and routine data found 40–99.9% vaccinated

Betapert distribution (minimum=40%, maximum=100%, most likely=80%)

Results:

- Six months after the last round of vaccination almost half of the cattle aged ≤24 months remain unvaccinated
- Only 50% of all cattle would have been vaccinated more than once with the last dose received ≤6 months ago

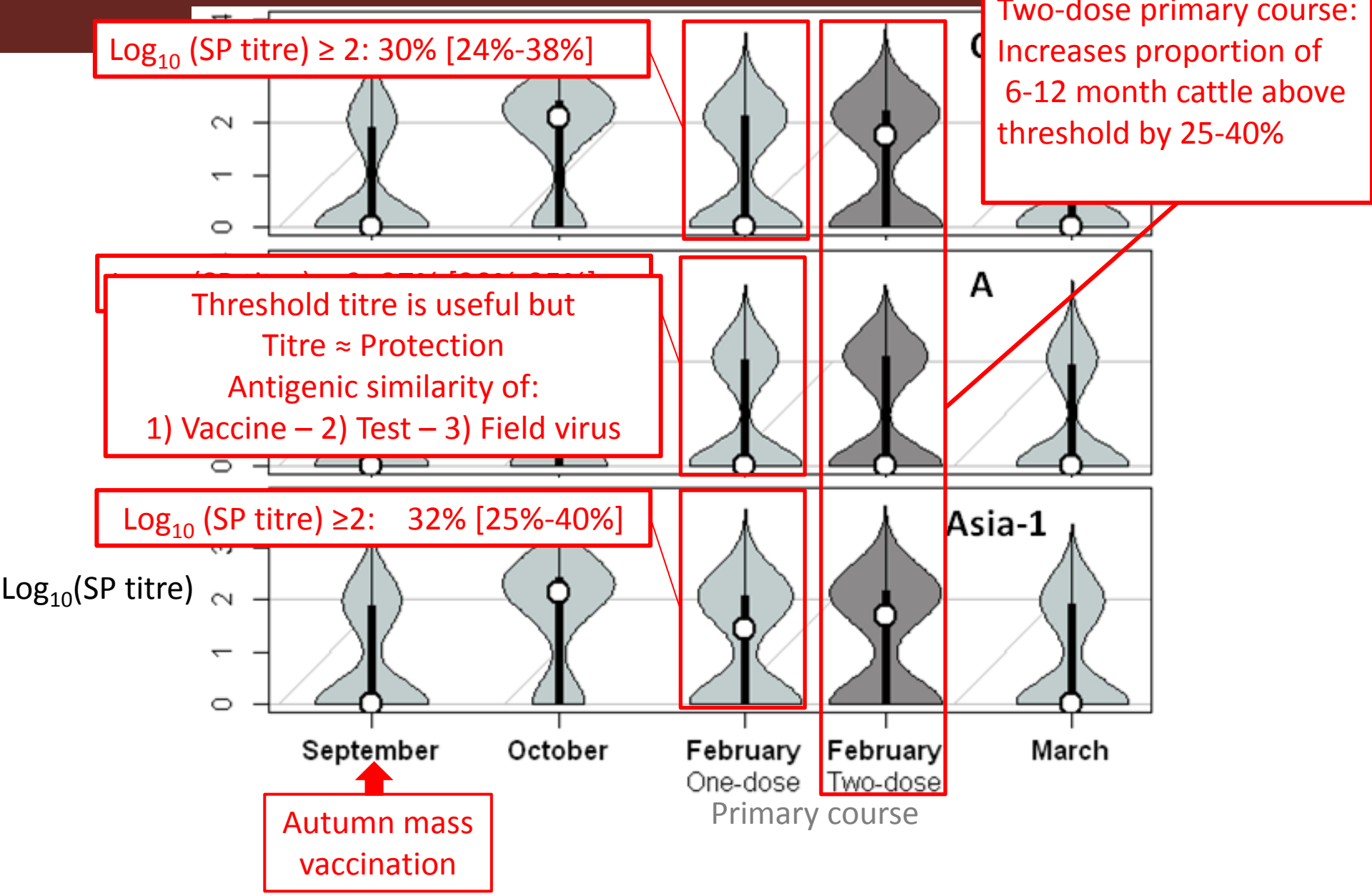
From coverage to immunity

- Predict immunity for simulated population

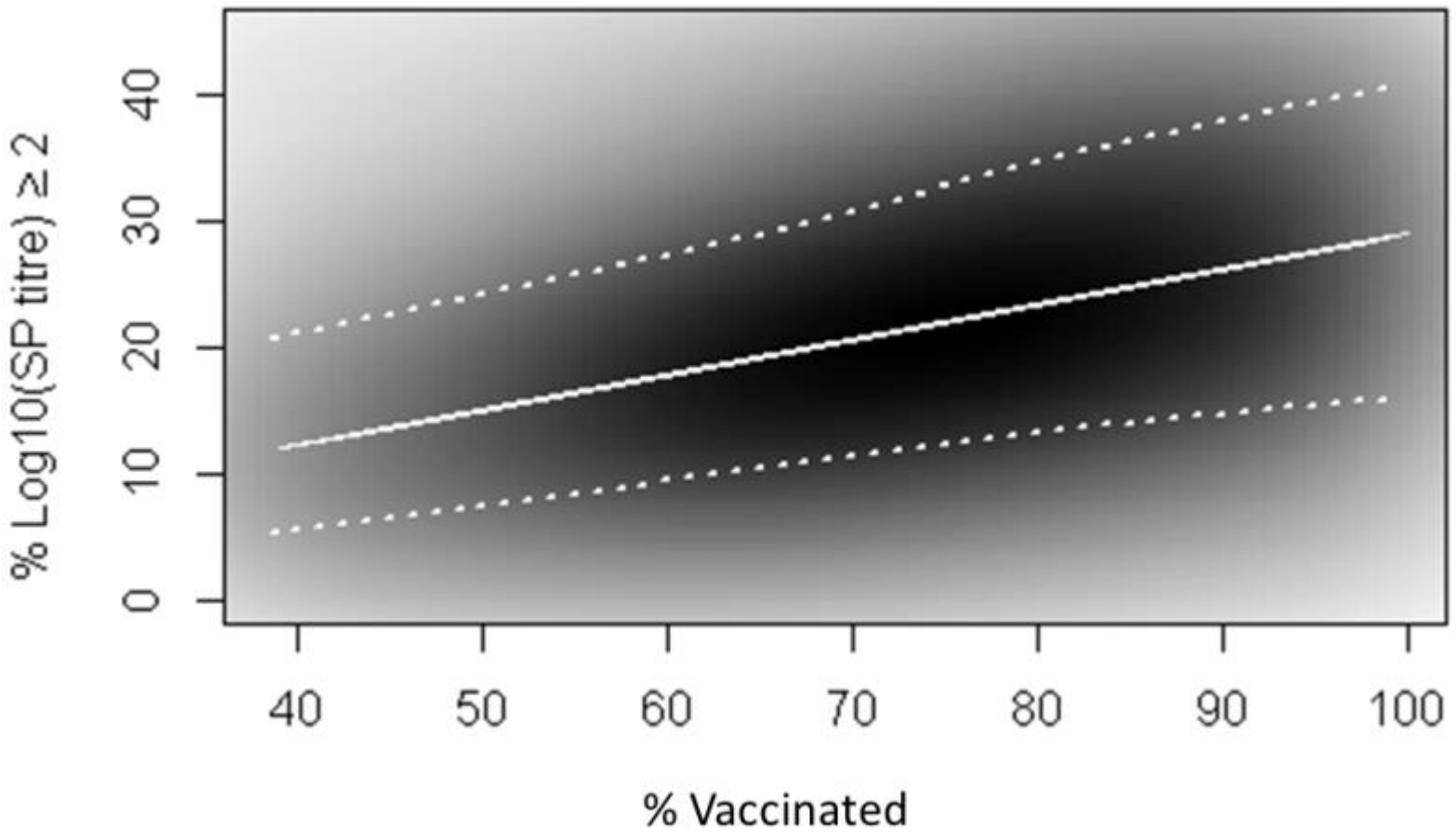
LPBE SP titre = Time since vaccination + No. of times vaccinated

- Using regression models fitted to data from extensive post-vaccination sero-monitoring study [n=647]

Population immunity predictions



District coverage and population immunity



Modelled proportion vaccinated in a district at autumn vaccination against the percentage of cattle with a serotype O SP titre ≥1:10^2 in mid February

Sustained antibodies after single dose

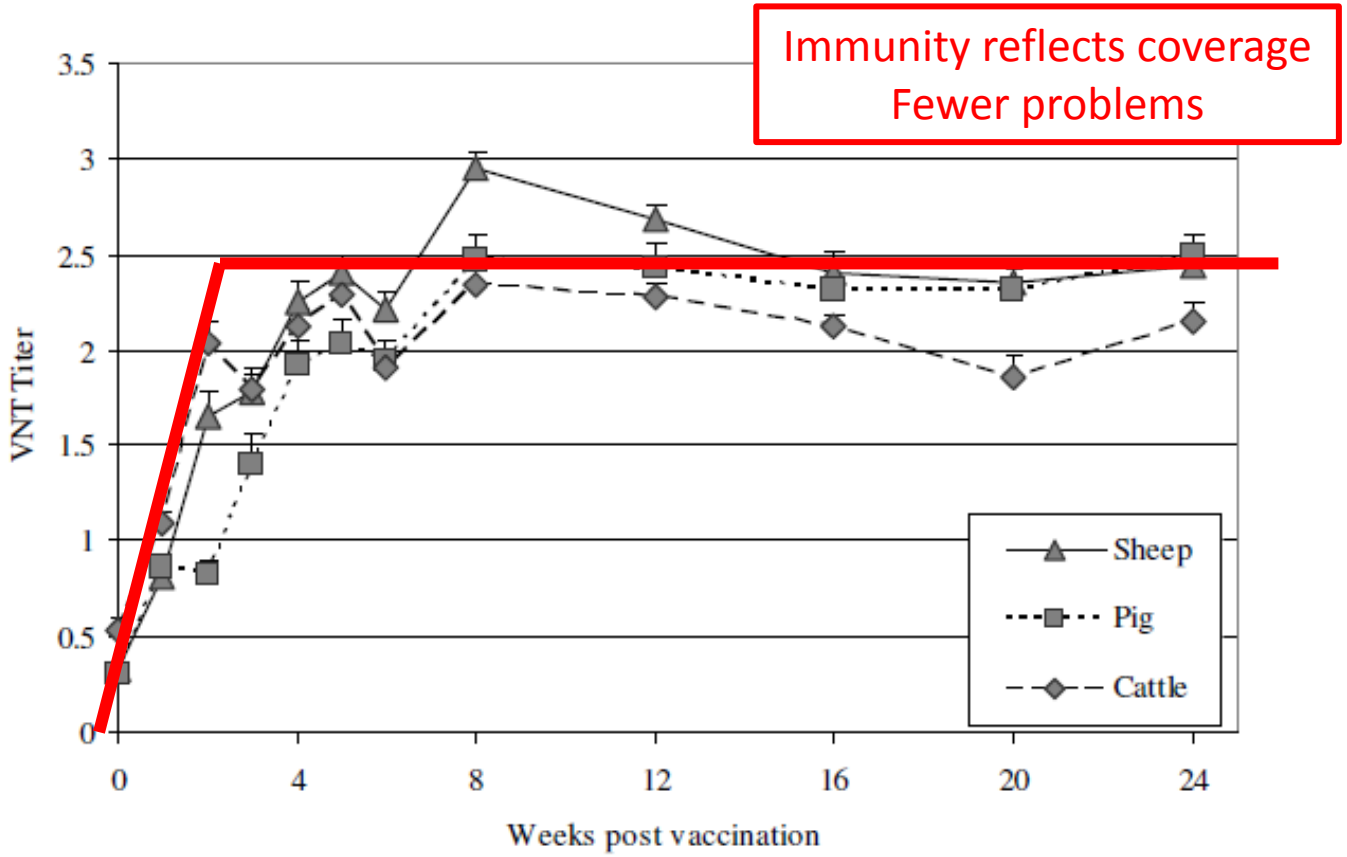


Figure 1. VNT (mean + sem) after vaccination with 6 PD_{50} of O1 Manisa.

From: Selman P, Chénard G, Dekker A (2006) Cedivac-FMD; Duration of Immunity in cattle, sheep and pigs. Open session of the EuFMD, Paphos, Cyprus, 17-19 October 2006

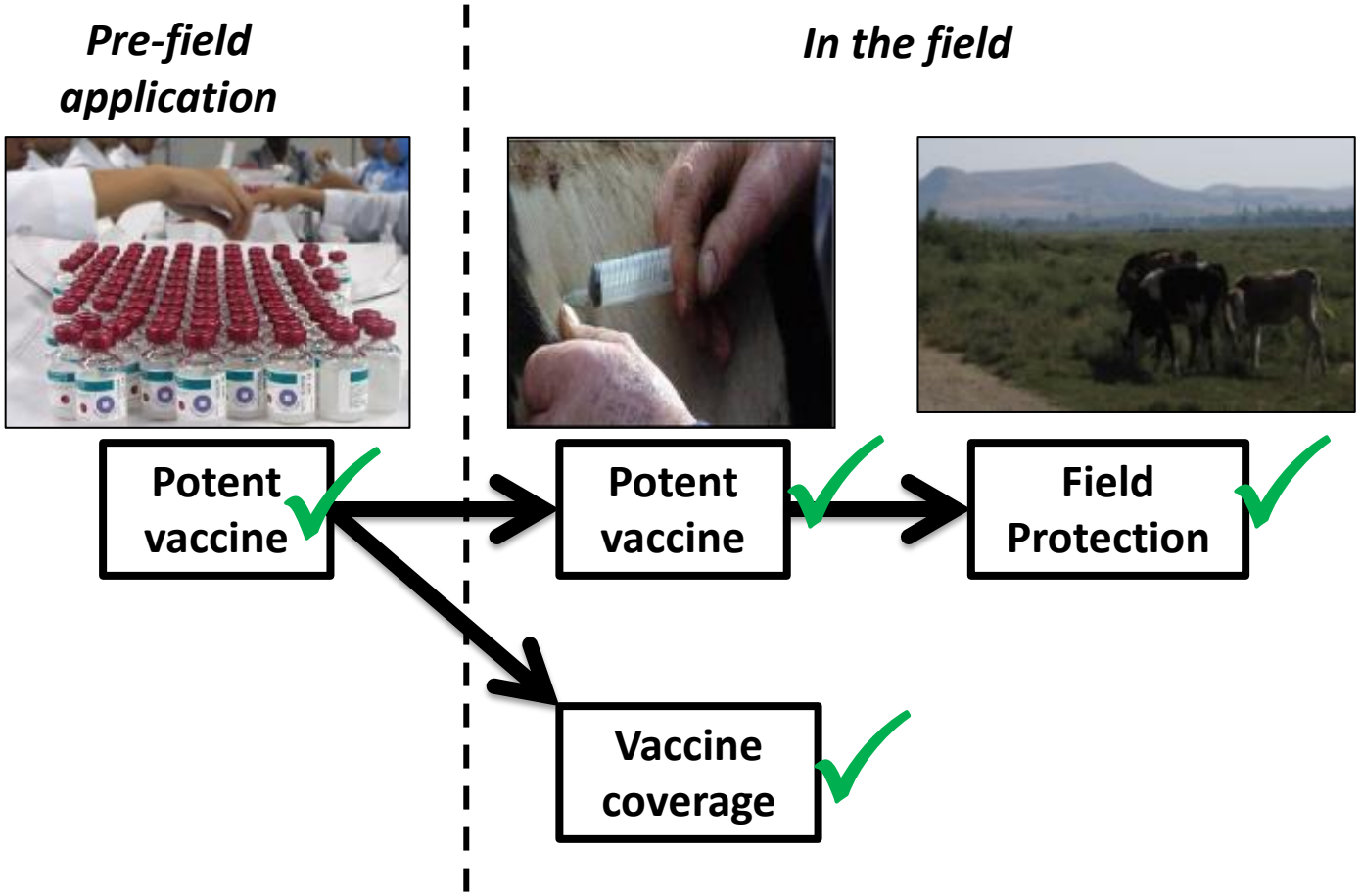
Conclusions: Mass vaccination in Turkey 2012

- Major immunity gaps despite biannual mass vaccination
- Improved vaccine required
  - ≥6PD50 vaccine now routine in Turkey
  - Two-dose primary course used in certain areas
- Immunity gaps will still exist
  - Each round of vaccination may exclude a quarter of all cattle
    - Often unavoidable
- Improved biosecurity measures required
  - Avoid over reliance on vaccine protection

Possible reasons for failures in FMD vaccination programme?

What are they?

Vaccine programme evaluation



Why is FMD control so challenging?

- Highly infectious with rapid transmission
- Multispecies including wildlife
- Multiple serotypes with variation within serotypes
- Some farmers/regions lack motivation to control FMD
- Vaccines:
  - Short lived protection against limited range of strains
  - Expensive & unstable (cold-chain required)
- Subclinical infections
- Livestock population turnover & movements
- Cost/impact of control measures