Diagnostic needs for different regions and stages of FMD control

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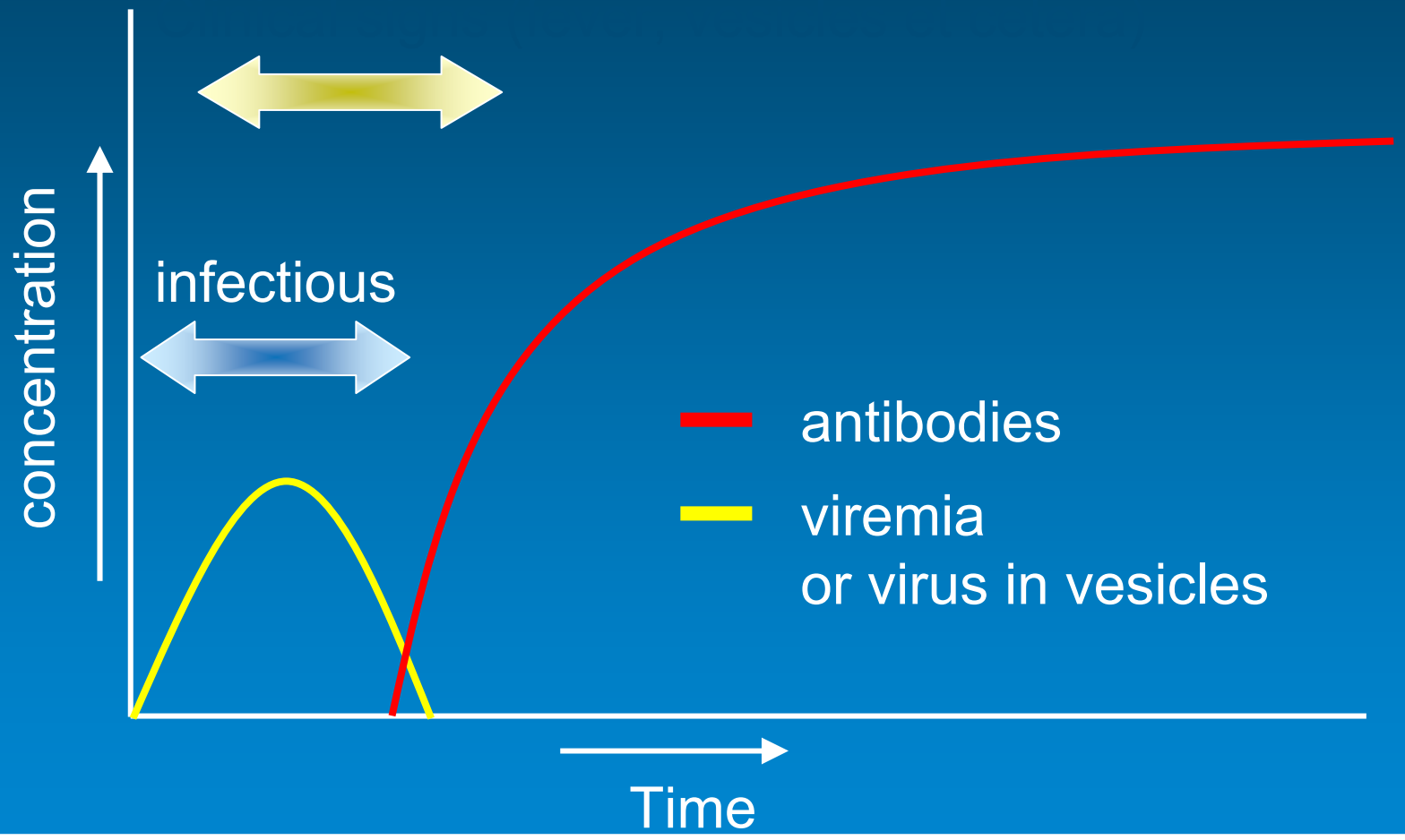
Be prepared

- Diagnostic possibilities
- Fit for purpose (OIE principles of validation)
- Situation different for every country and control strategy
- Example of modelling study in the Netherlands

General scheme of a virus infection



Possible tests (not complete)

- Infectious virus (short lived)
  - Virus isolation
  - RT-PCR (preferable real-time)
  - Antigen detection ELISA
  - Lateral flow device
- Antibodies (later after infection)
  - Virus neutralisation test
  - ELISA (LPBE, SPBE, commercial)
  - NS-ELISA (in-house or commercial)
  - EITB (specific blot for each NSP)

Fit for purpose (OIE chapter 1.1.3)

1. Demonstrate freedom from infection in a defined population (country/zone/compartment/herd) (prevalence apparently zero)
   a) 'Free' with and/or without vaccination
   b) Historical freedom
   c) Re-establishment of freedom after outbreaks
2. Certify freedom from infection or agent in individual animals or products for trade / movement purposes
3. Eradication of infection from defined populations
4. Confirmatory diagnosis of suspect or clinical cases (includes confirmation of positive screening test)
5. Estimate prevalence of infection or exposure to facilitate risk analysis (surveys, herd health status, disease control measures)
6. Determine immune status of individual animals or populations (post-vaccination).

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OIE validation pathway; laboratory perspective

1. **Selection of an assay fit for its intended purpose**
2. **Validation part 1**
    1. **Optimisation and standardisation of reagents**
    2. **Repeatability**
    3. **Determination of analytical specificity and sensitivity**
3. Validation part 2
    1. **Determining assay performance**
    2. **Threshold determination**
    3. **Assay performance estimates**
    4. **Comparison and harmonisation of assays**
4. Validation part 3
    1. **Establishing reproducibility and augmenting repeatability estimates of the assay**
    2. **Programme implementation**
    3. **Monitoring validity of assay performance**

Test selection should not be initiated by lab

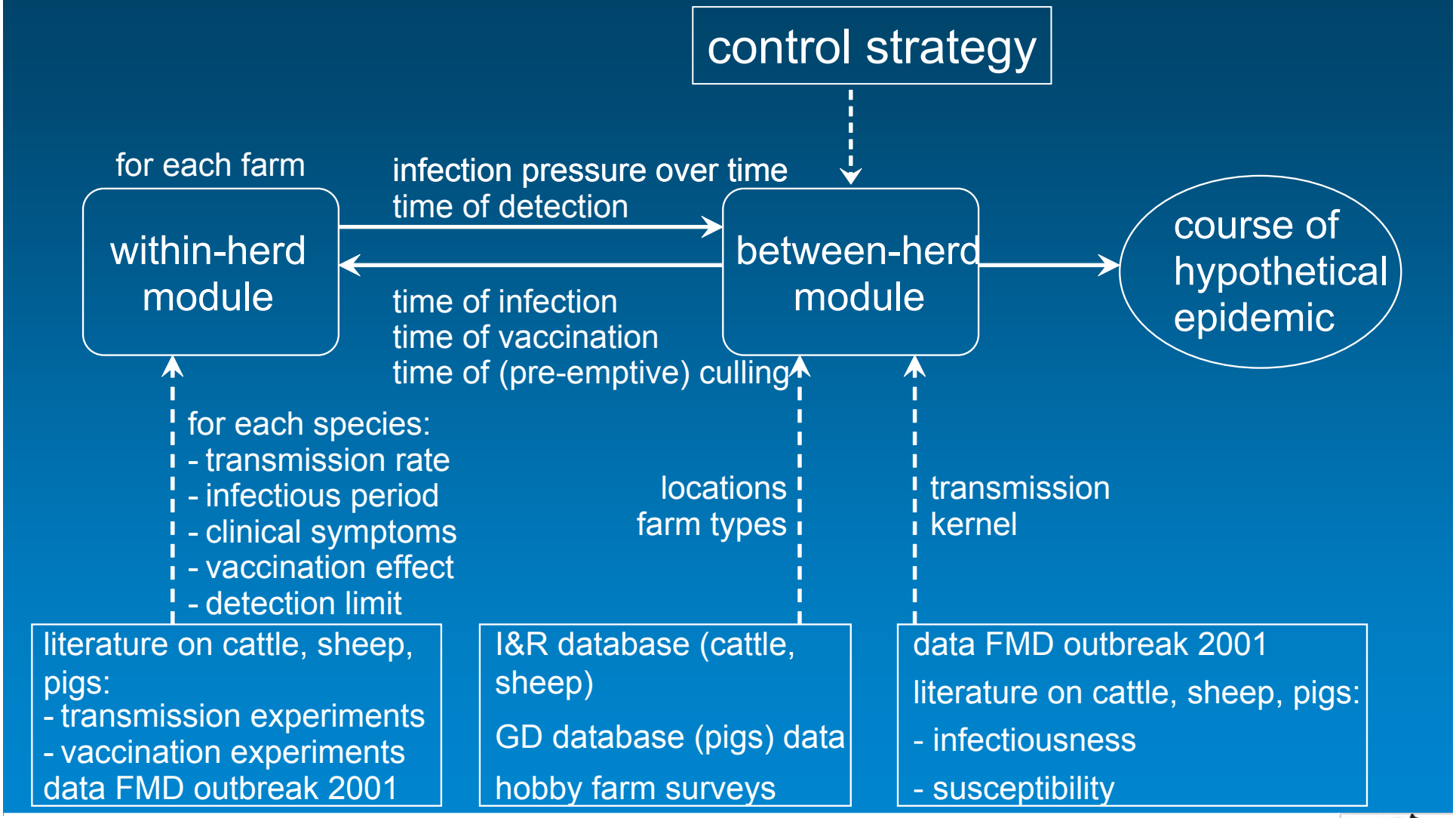
- Start with the programme objective
- Validation data have been published
- Jump from selection of assay to implementation
- Is a ***precise*** estimate of analytical and diagnostic sensitivity essential?
- Is determining a threshold essential?
- Repeatability/reproducibility is shown when charting the controls

Epidemiological modelling in the Netherlands

Based on published tests the efficiency of a control programme can be evaluated

- Lab based epidemiologists and mathematical epidemiologist worked together
- Clear input from the ministry of Agriculture
- Economics not included in presentation

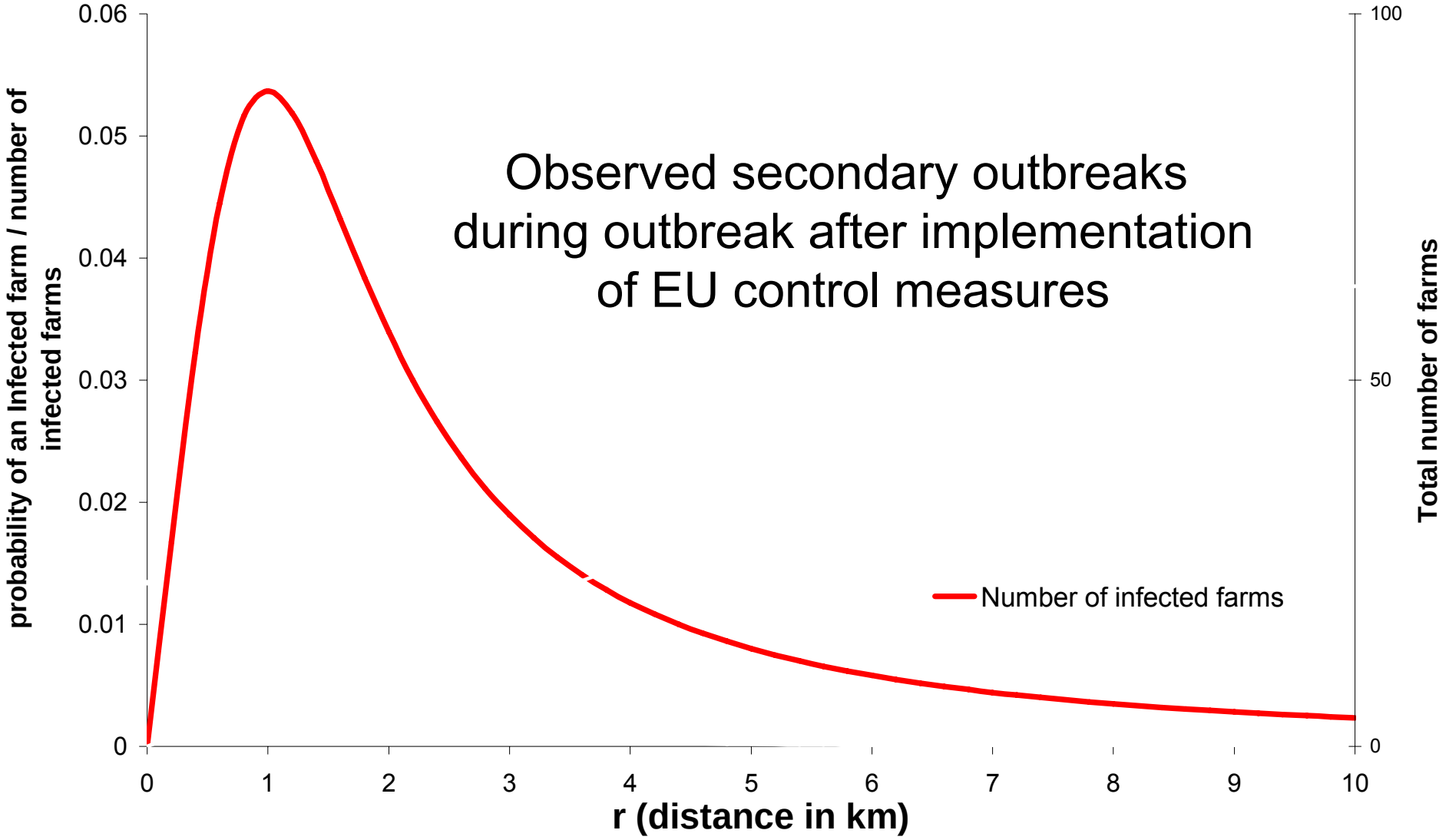
Scheme of the model



Within-herd module

- Susceptible Exposed Infectious Removed model
- Transmission rate in various species based on published data
- Time till first clinical symptoms from experiments
- Detection threshold for clinical disease
  - 3 cattle, 6 sheep, 7 pigs
  - Sheep 50% subclinical
- Different lengths of latent period for various species
- Effect of vaccination linear decrease of transmission rate from day 4 to 11 in cattle and from day 7 to 14 in pigs

Between-herd module



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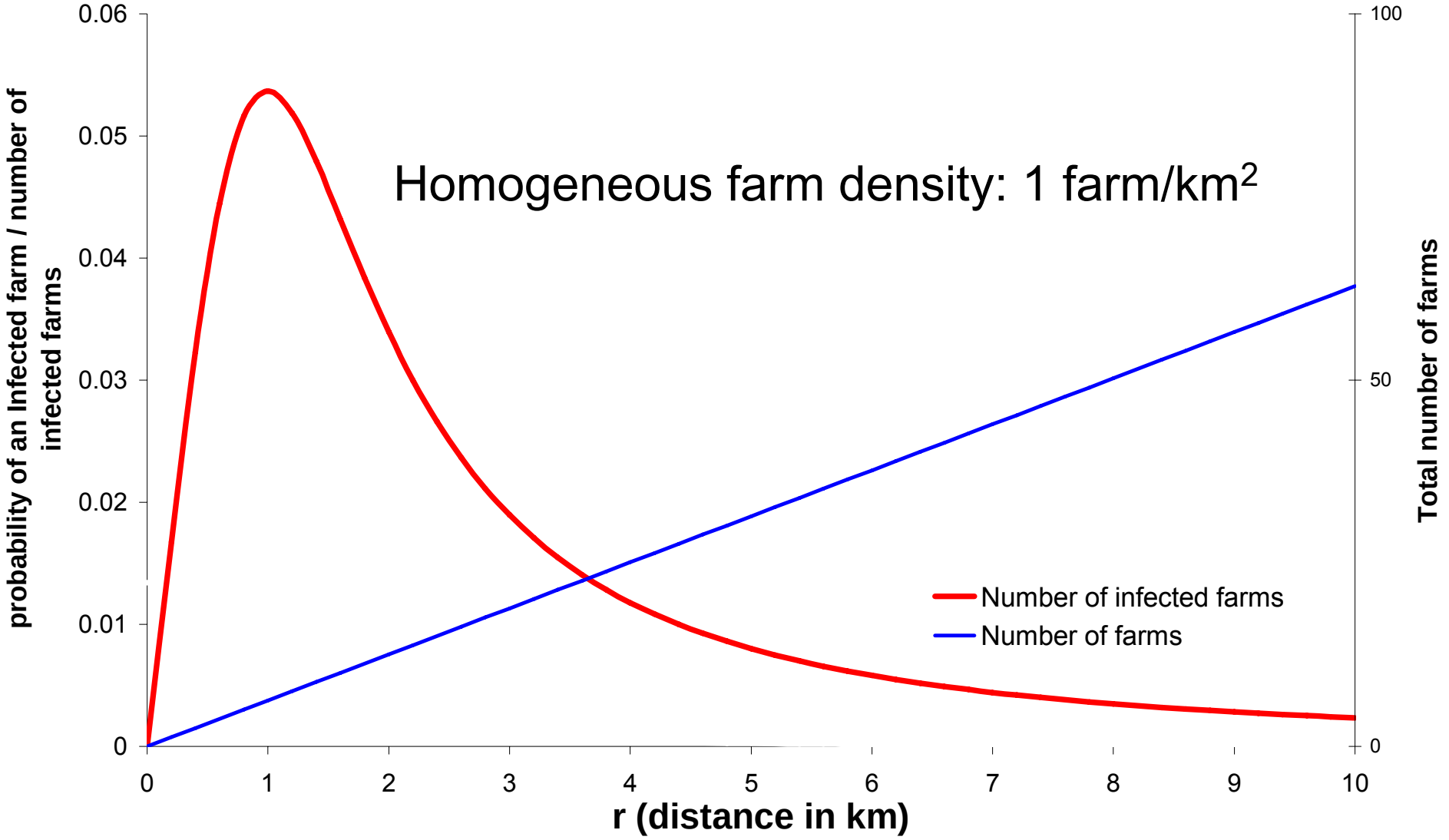

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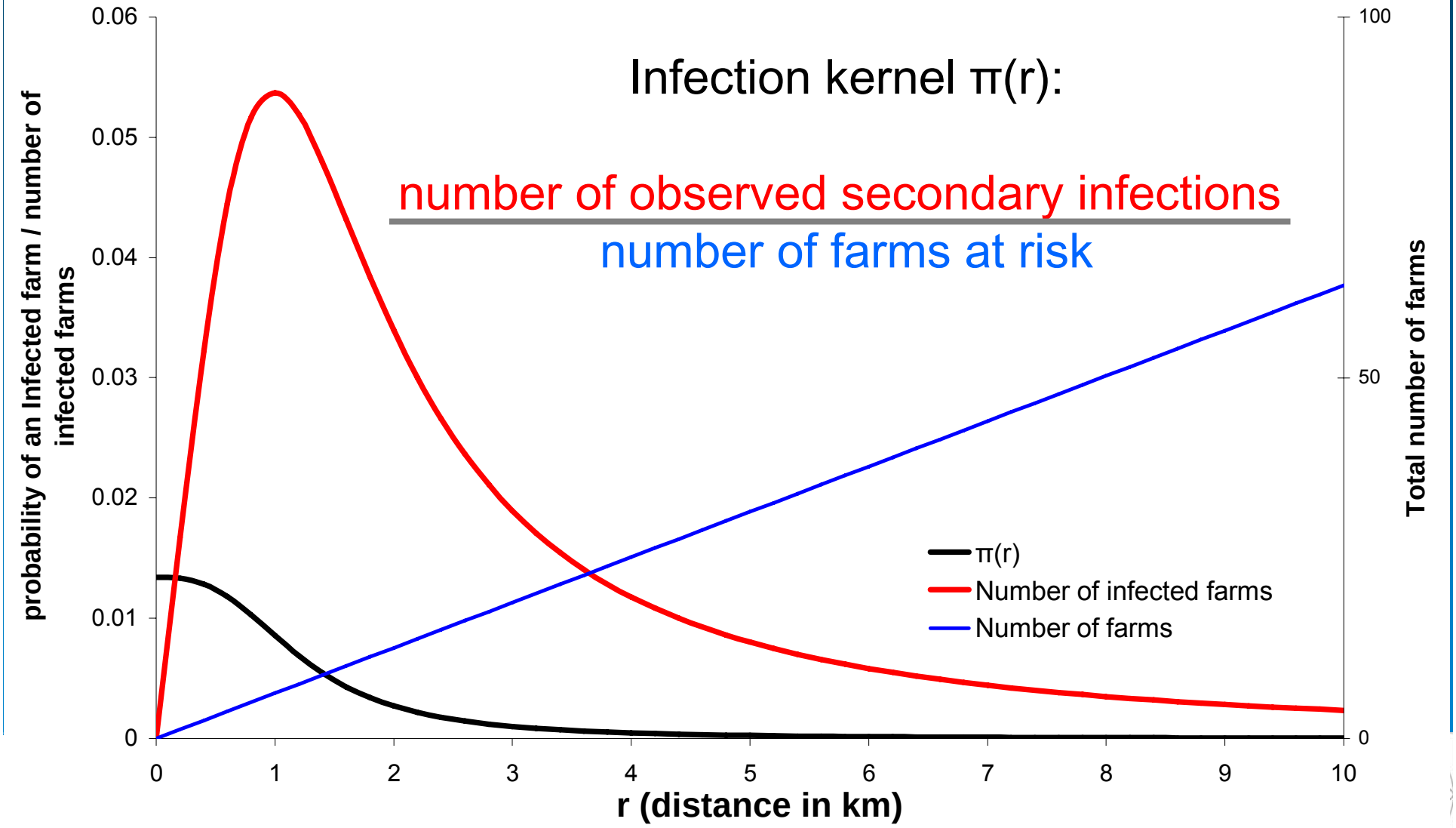


Between-herd module

- Infection Kernel from the Netherlands 2001
- Similar to infection Kernel in UK 2001
- Different in infectivity and susceptibility for various species (supported by outbreak data and experimental data)
- Probability of infection based on the number of infectious animals
- Actual farm locations were used

Farm density map of the Netherlands

0 farms/km^2 grey

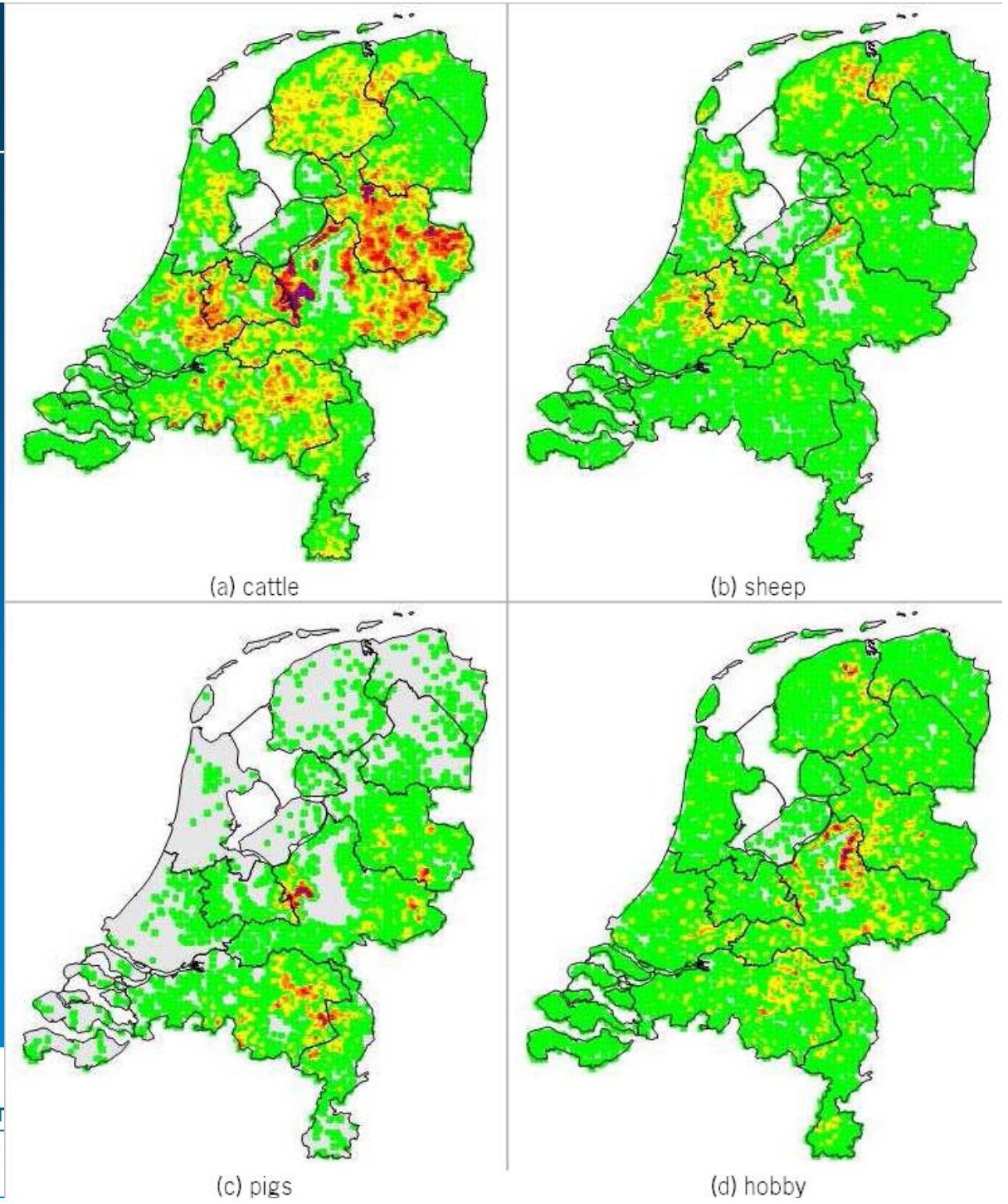
0-1 farms/km^2 green

1-2 farms/km^2 yellow

2-3 farms/km^2 orange

3-4 farms/km^2 red

> 4 farms/km^2 purple



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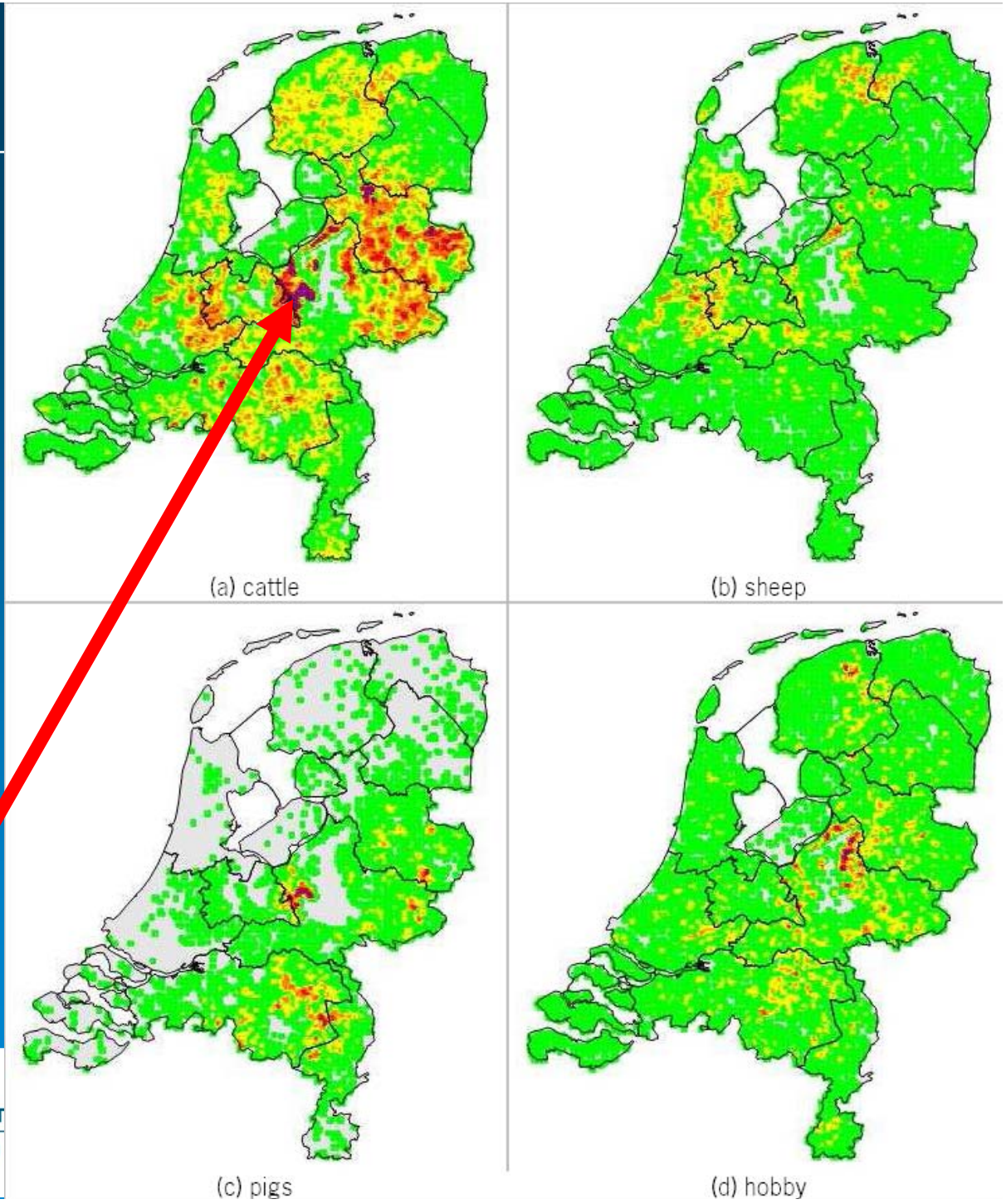
Infection starts on cattle farm in this area



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Monitoring according to EU directive

- No-vaccination
  - Clinical surveillance sufficient in cattle and pig holdings
  - Serological surveillance in sheep herds within 10 km of an outbreak to be able to detect 5% prevalence with 95% confidence
- 2 km ring vaccination
  - All susceptible animals on vaccinated farms
  - All sheep farms within 10 km of an outbreak (see above)

Diagnostic sensitivity and specificity

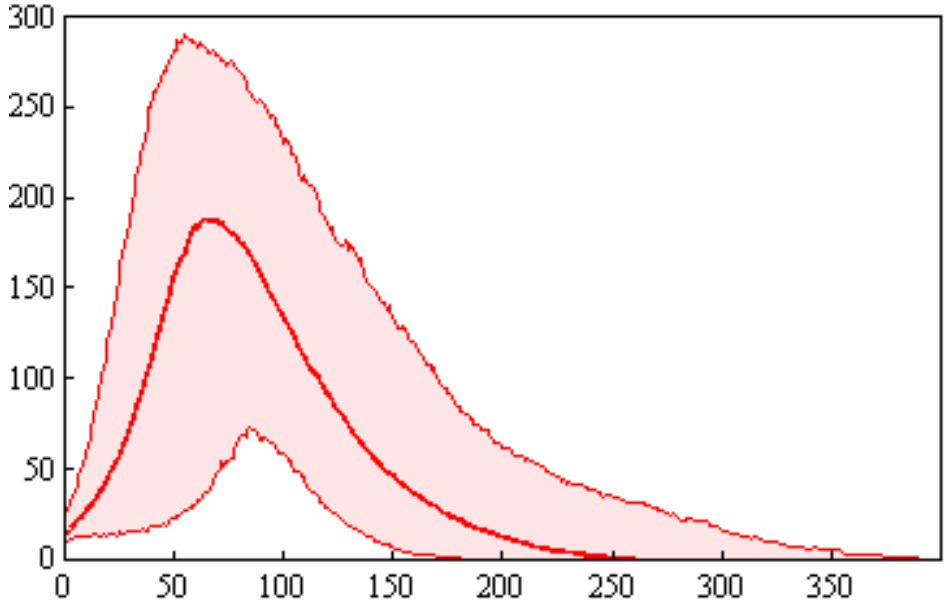
- No vaccination (LPBE ELISA)
  - 98% sensitive
  - 97% specific
- Vaccination (NS-ELISA)
  - 70% sensitive
  - 99% specific

Results (1000 iterations, median [90% interval])

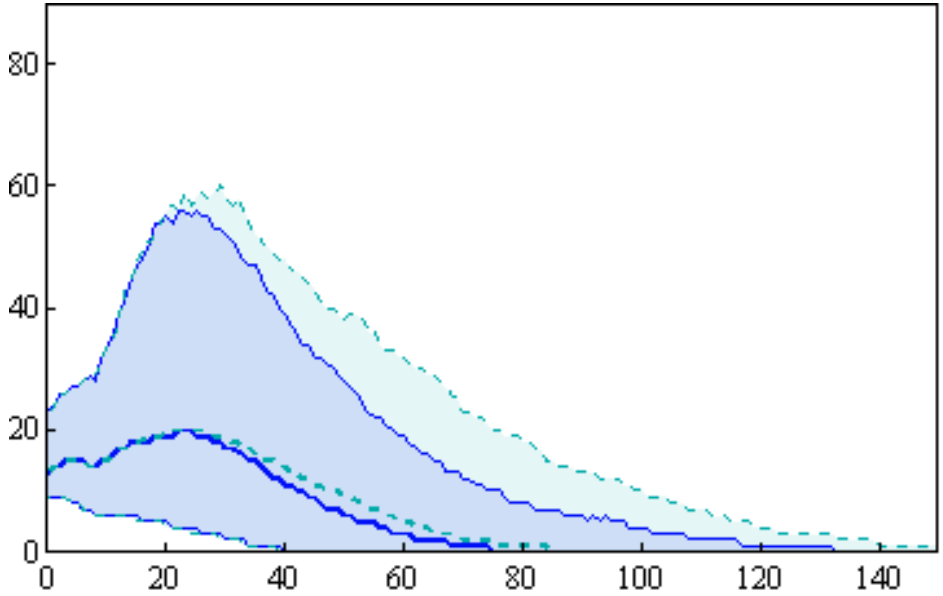
	No vaccination	2 km ring vaccination
Number of infected farms	**1640** [1126, 2145]	**72** [23, 162]
Duration (days)	**259** [181, 390]	**76** [41, 133]
# infected farms not detected	**146** [93, 197]	**17** [2, 47]
# infected animals before screening	**767** [466, 1090]	**50** [7, 148]

Epidemiological curve

No vaccination



2 km ring vaccination



Average (and 90% percentile) of infectious farms per day

Final screening (median, [90% interval])

	No vaccination	2 km ring vaccination
Number of farms	**19 880** [16 101, 22 759]	**5 463** [2 122, 10 420]
Number of samples (x 1 000)	**379** [302, 441]	**669** [20, 1 196]
Number of farm retested	**7 869** [6 316, 9 085]	**2 691** [1 027, 5 062]
# infected animals after final screening	**62** [33, 94]	**3.5** [0.3, 14.8]

Conclusion from model

- Lower risk for transmission (to neighbouring countries) when using emergency vaccination
- Lower number of non-detected infected animals after outbreak
- Sensitivity of NS ELISA is sufficient
- OIE waiting period should not be based on control strategy only but should be risk based

NB! slight bias towards large outbreaks due to the fact that only iterations were included in which the first farm infected 10 other farms

Is this model applicable in other situations?

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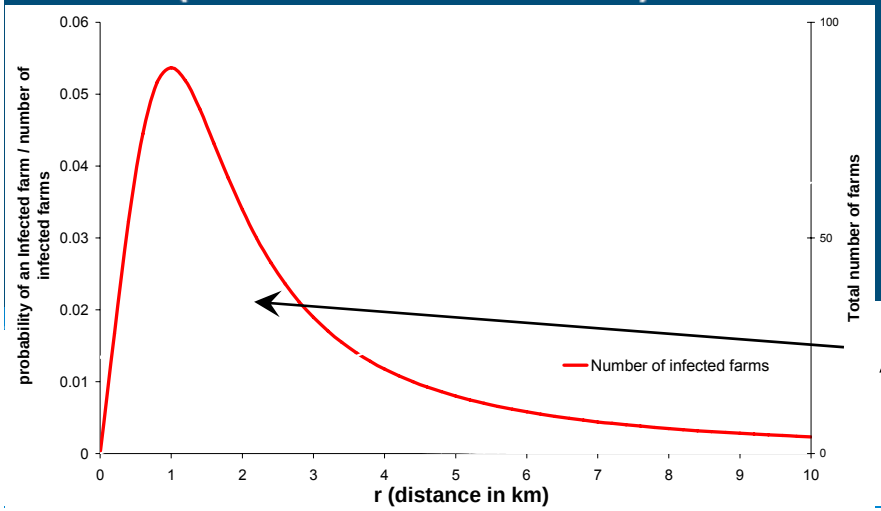
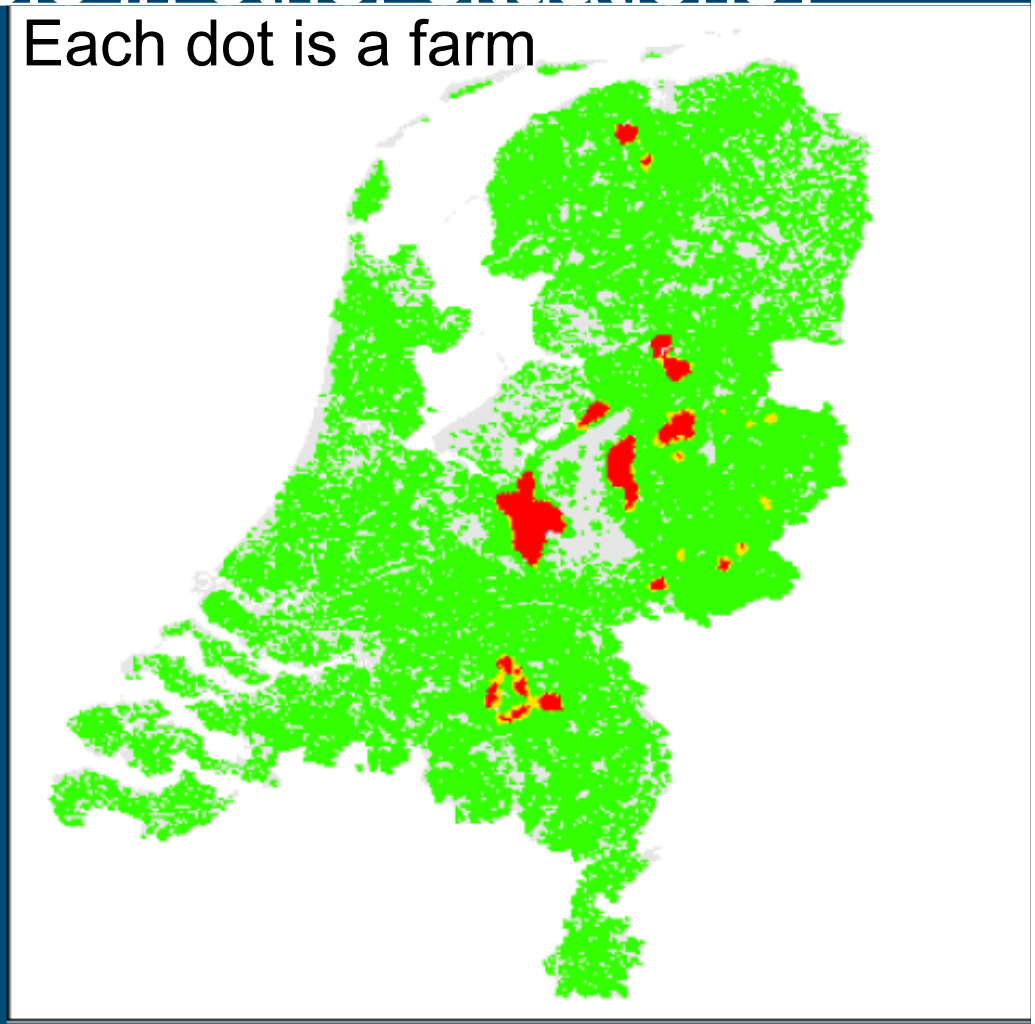
Risk maps with 3 colours:

- Red: '1 km culling' not sufficient to avoid large outbreaks (= R_0>1)
- Orange: '1 km culling' sufficient
- Green: 'no ring culling' already sufficient (= EU-measures)



Each dot is a farm



Area under the curve: < 1 green

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Is this model applicable in other situations?

- The Netherlands is small all samples arrive within a few hours in the lab
- Effect of emergency vaccination based on high quality FMD emergency vaccines
- No doubt about cold-chain during vaccination
- The Netherlands depend on export, short duration of an outbreak is economic favorable
- **Yes** model can be adapted to other situations

Discussion on diagnostic needs

BE PREPARED

- make an inventory of the needs in your country
- Start with the desired end result
- Select the adequate diagnostic tools
- Set-up a quality control system
- Buy international standards
- Set-up secondary/tertiary standards to be included in each test
- Participate in proficiency tests