The use of math models to improve surveillance and management of infectious diseases in wildlife

CSF => Wild boars
AIV => Dabbling ducks

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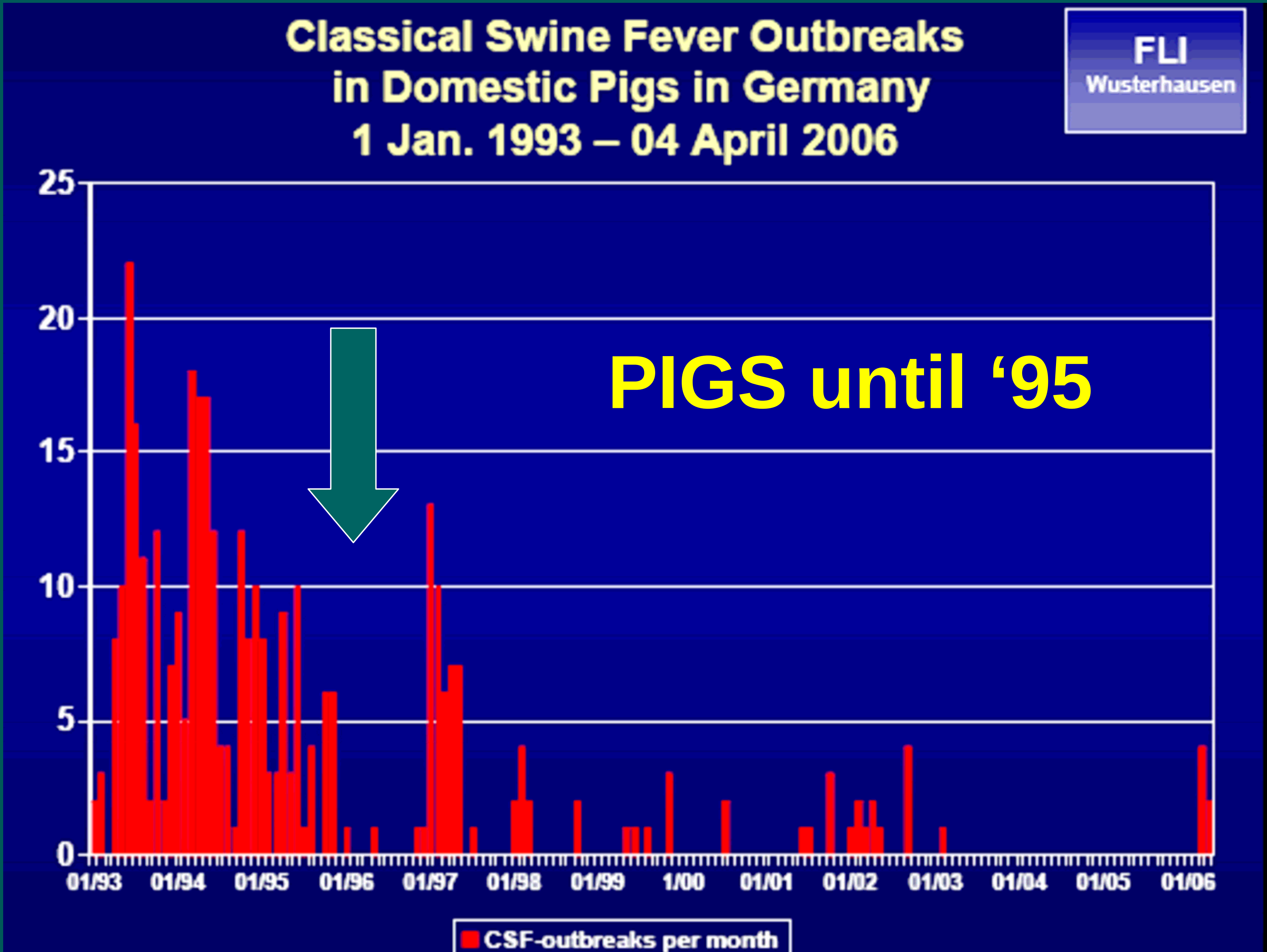
Classical Swine Fever Outbreaks
in Domestic Pigs in Germany
1 Jan. 1993 – 04 April 2006
FLI
Wusterhausen
25
20
15
10
5
0
01/93
01/94
01/95
01/96
01/97
01/98
01/99
1/00
01/01
01/02
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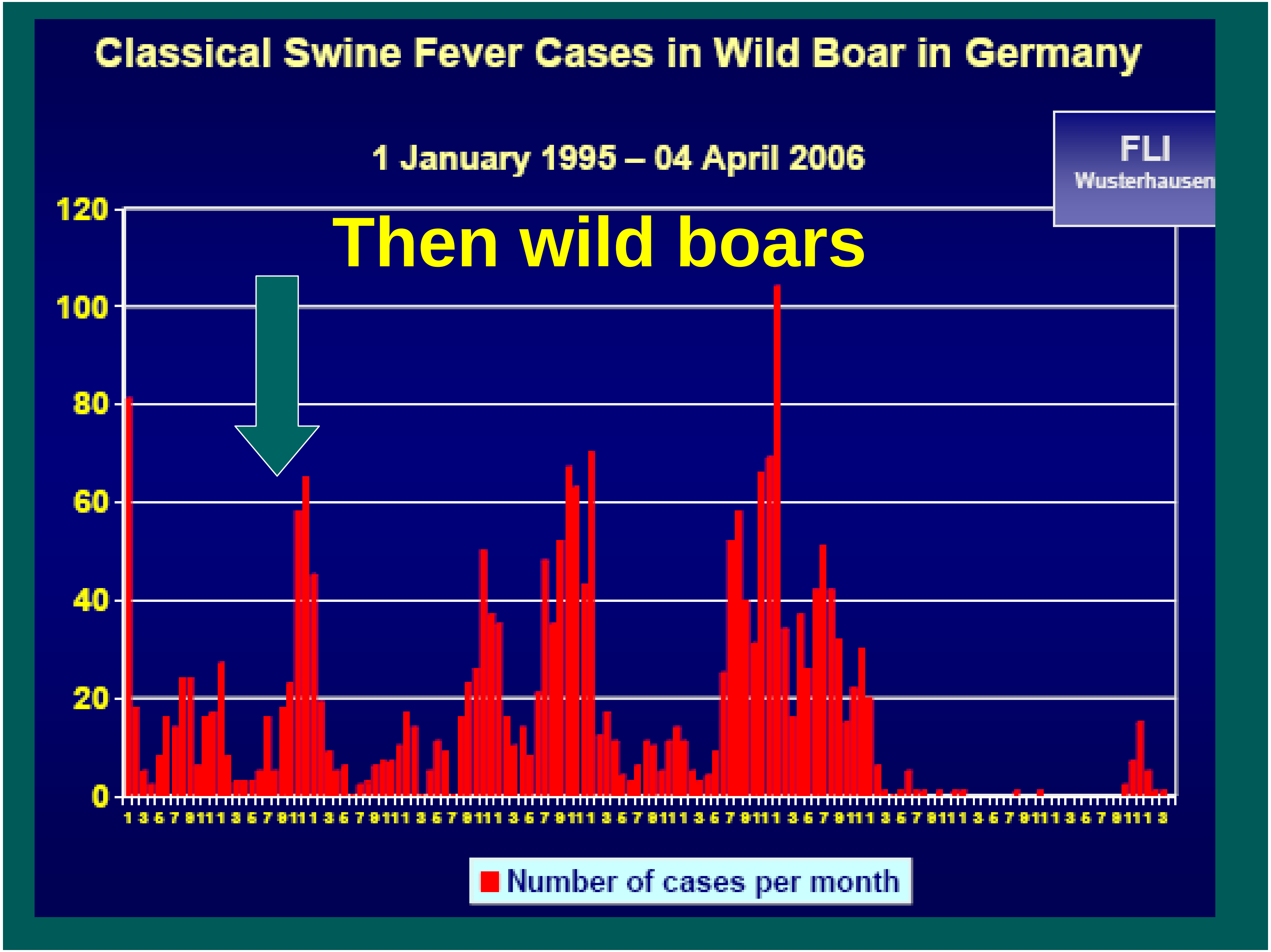
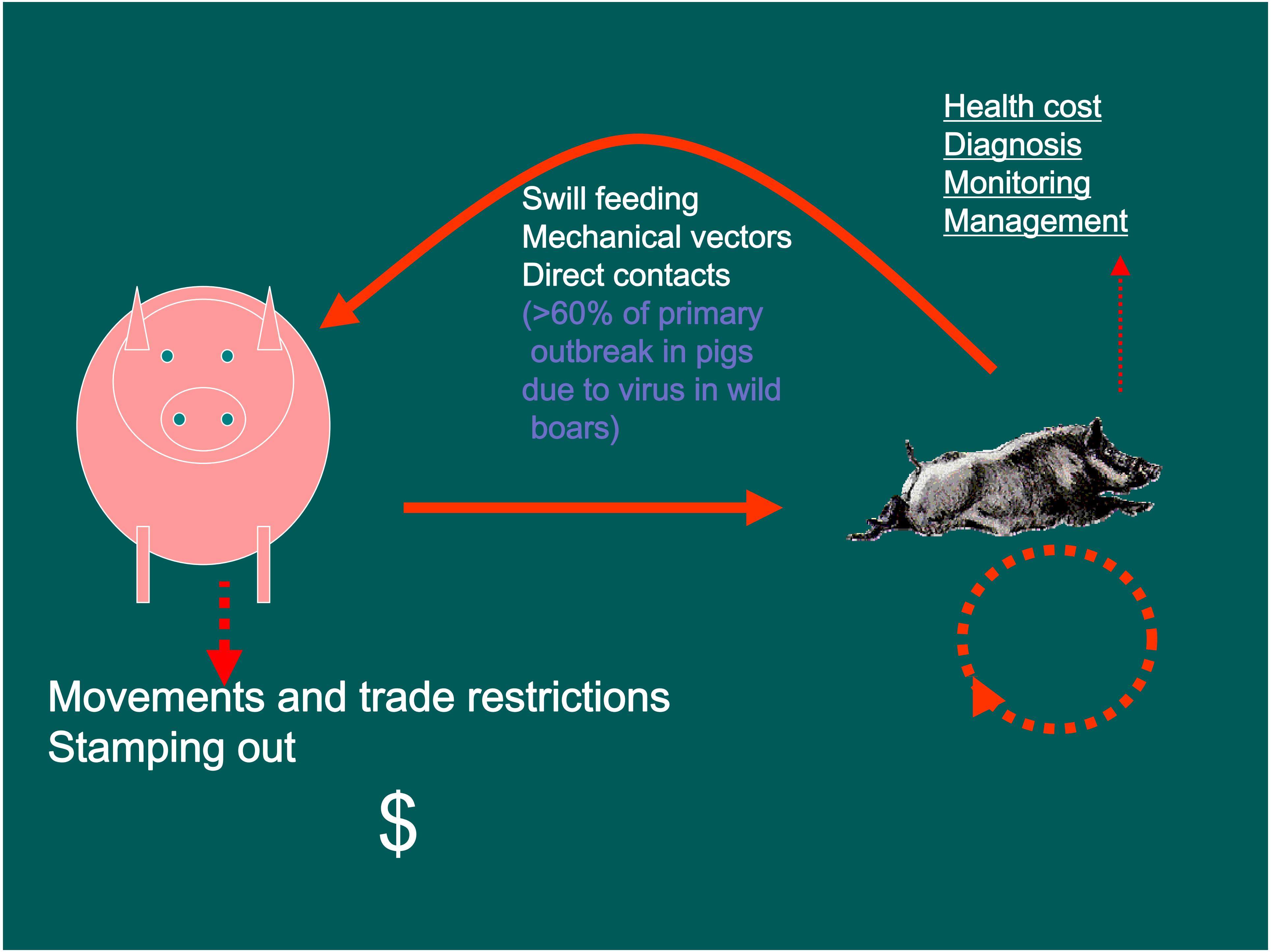
01/06
CSF-outbreaks per month
PIGS until '95


Classical Swine Fever Cases in Wild Boar in Germany
1 January 1995 – 04 April 2006
FLI
Wusterhausen
Then wild boars
120
100
80
60
40
20
0
Number of cases per month


Health cost
Diagnosis
Monitoring
Management
Swill feeding
Mechanical vectors
Direct contacts
(>60% of primary outbreak in pigs due to virus in wild boars)
Movements and trade restrictions
Stamping out
$

Critical points

- CSF virus sometimes fade out spontaneously sometimes not;
- Strong vaccination efforts not always lead to eradication in wild boars;
- Does vaccination work? if so which are the main epidemiological mechanisms?
- Which is the CRITICAL PROPORTION necessary to be vaccinated?
- Why active surveillance very often fails in finding the virus?
- Can we monitor the infection in the wild in a more appropriate manner?

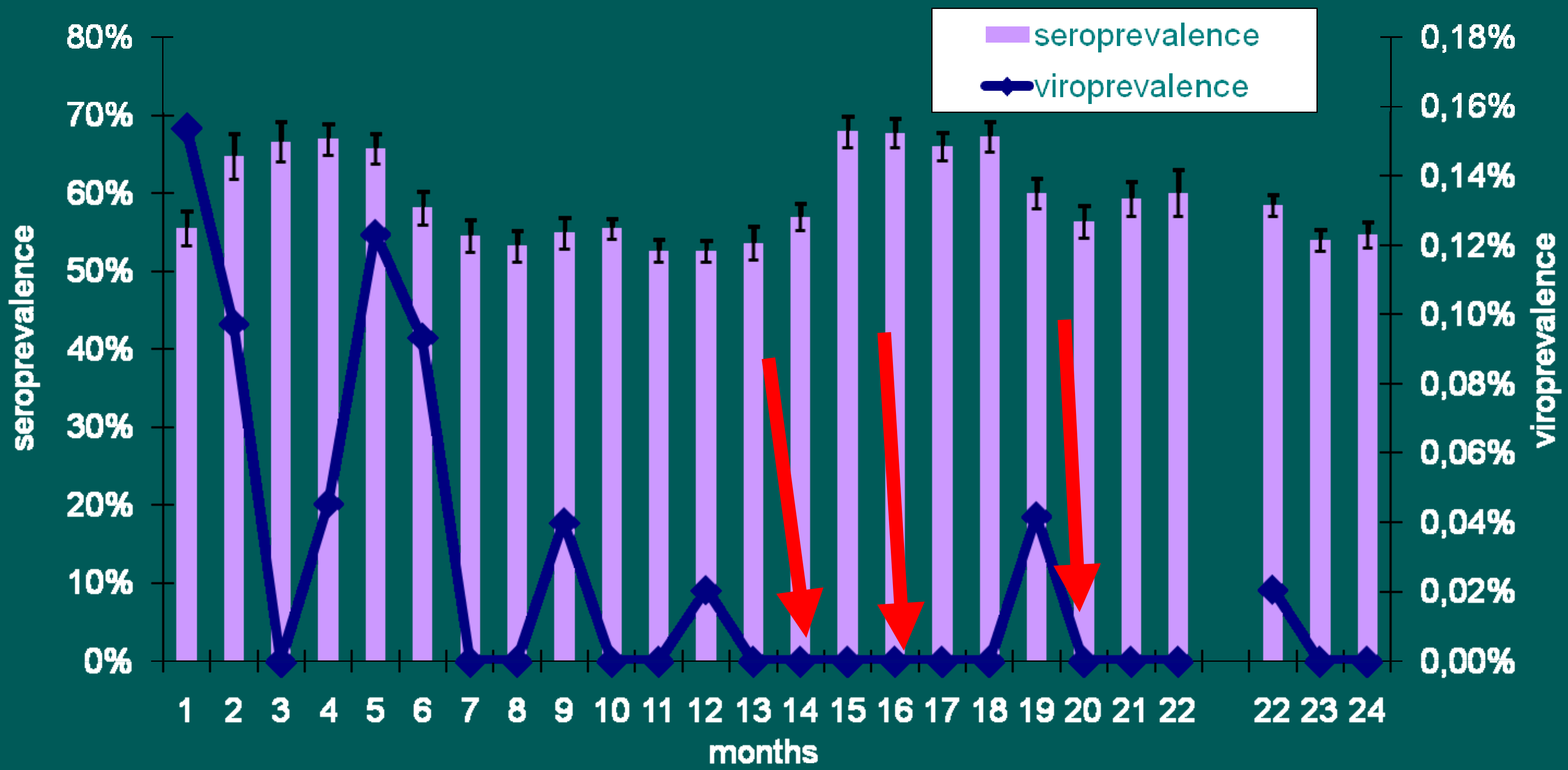
Germany (MWP): Infected area

- 1st February 2003
- 31st January2005 (24 months)
- Vaccination

Area: 5196 SqKM

Pop: 32000 wb

Dens: 6.1 wb/Sqkm



A descriptive epidemiology

- Sero-prevalence is positively associated with age;
- Viroprevalence: at the onset of the infection all age classes are involved; then the 1< year class is the most positive one
- Gender is not very relevant
- Data from literature

The first step

- Force of infection
- Beta
- R0 and Re
- Nt = threshold level of extinction
- Critical Community Size

1.2.2. Infection Parameters

Country	***Beta day^{-1} [IC95%]****	***Beta day^{-1} [IC95%]*****	***Population (individuals kmq^{-1})***	***R_0***	***Nt (individual/kmq^{-1})***
Italy	**0.000336** [0.0000997-0.000636]	**0.272** [0.08-0.52]	**2.7**	**4.7** [1.4-8.9]	**0.58** [0.30-1.94]
Luxemburg	**?**	**0.847** [0.3-1.5]	**?**	**14.5** [5.1-25.7]	**?**
Western Pomerania	**0.0002** [0.00012-0.00028]	**0.367** [0.23-0.51]	**6.1**	**6.3** [3.9-8.8]	**0.97** [0.70-1.56]
RP	n.e.		n.e	n.e	n.e
Belgium	n.e.		n.e	n.e	n.e

**Pseudomass action* *(Force of infection/infected)*
***True Mass action* *(Force of infection*N/infected)*

Force of infection of CSF in Europe during the endemic evolution of the infection

- **Varese/Ticino = 0.002/day;**
- **WMP Germany = 0.0018/day;**
- **Sardinia = 0.0011/day;**
- **Luxembourg = 0.007/day;**

How many susceptible wild boars are needed for maintaining the infection?

- **Varese/Ticino = 0.58/km^2**
- **MWP (Germany) = 0.97/km^2**
- **Sardinia = 0.8/km^2**
- **Luxembourg = 1.12/km^2**

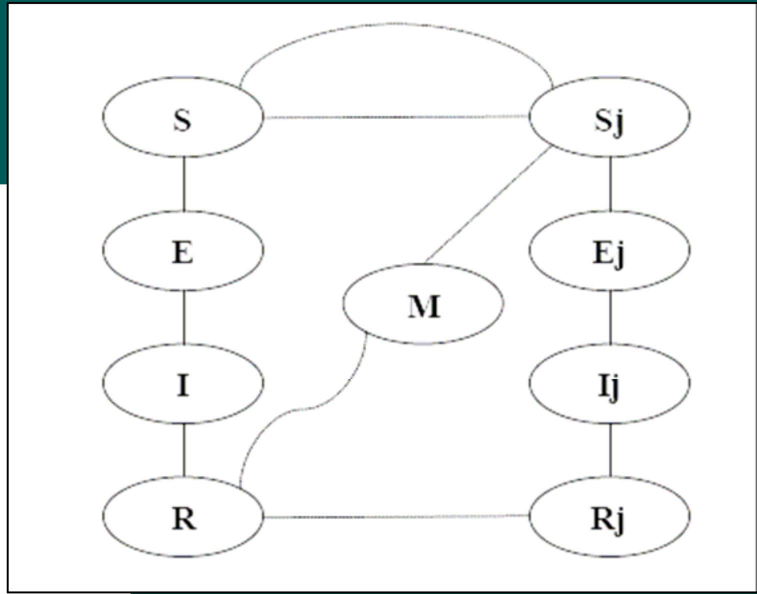
Models framework

18 patches

100 individuals per patch

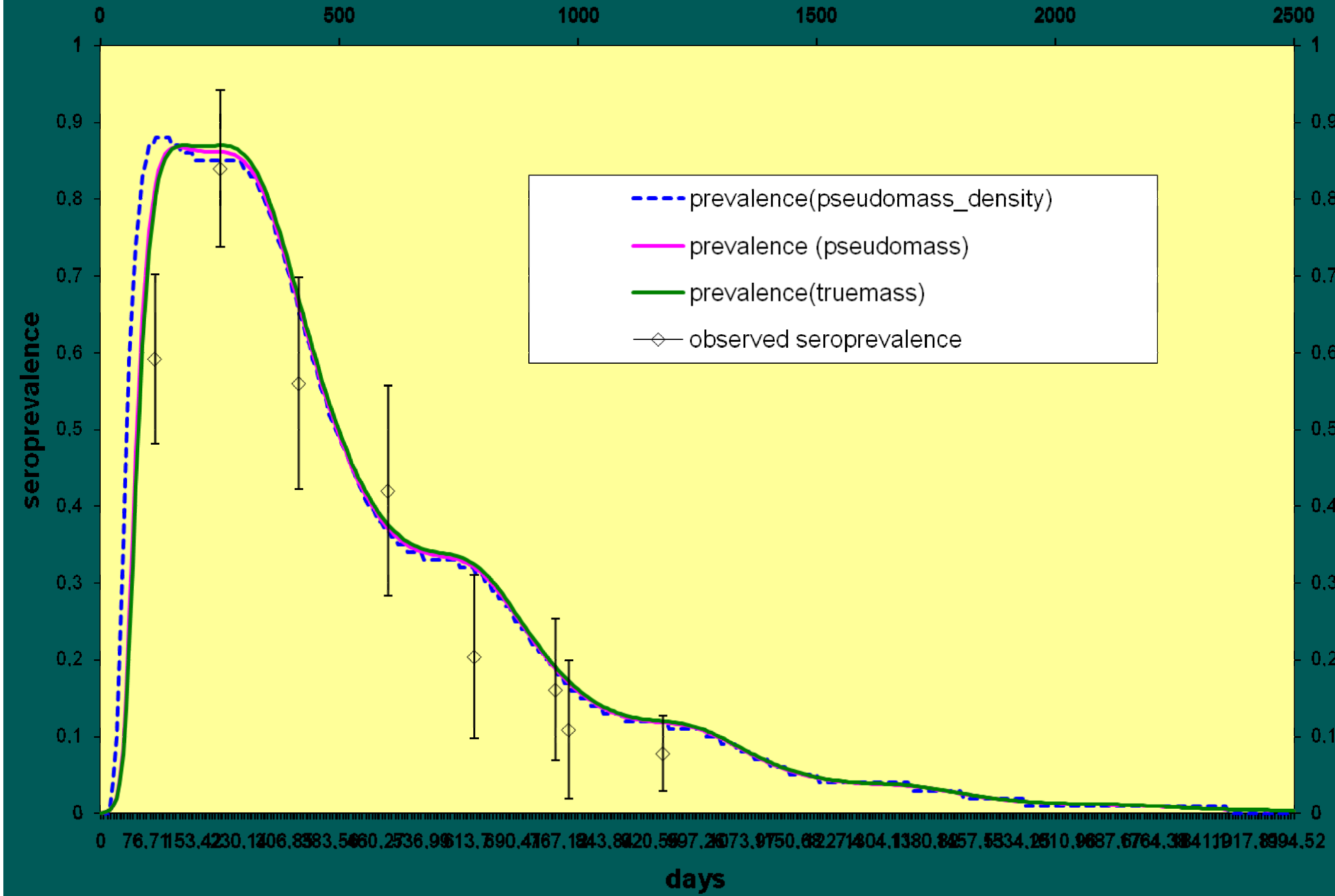
Chain pattern

SEIR

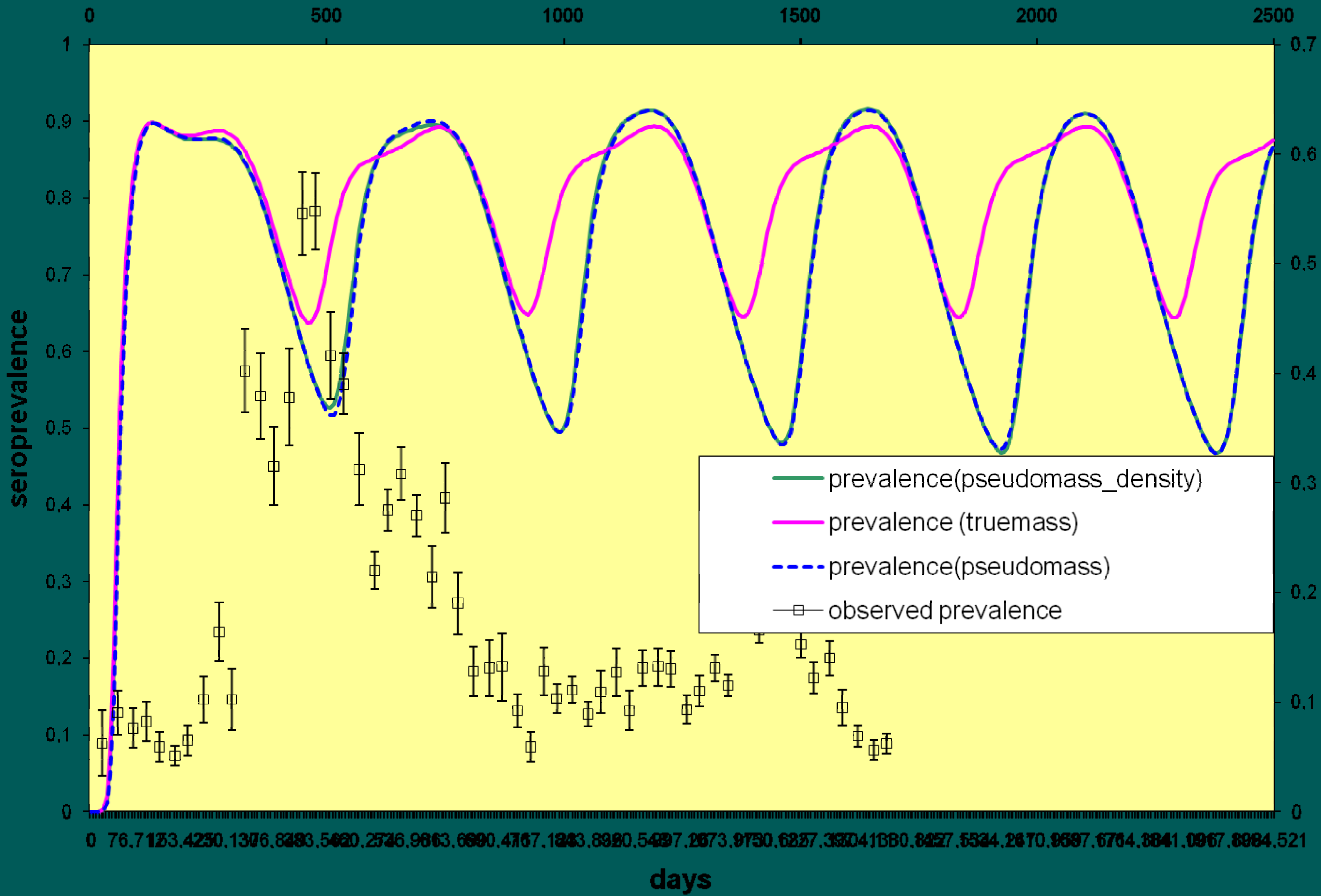


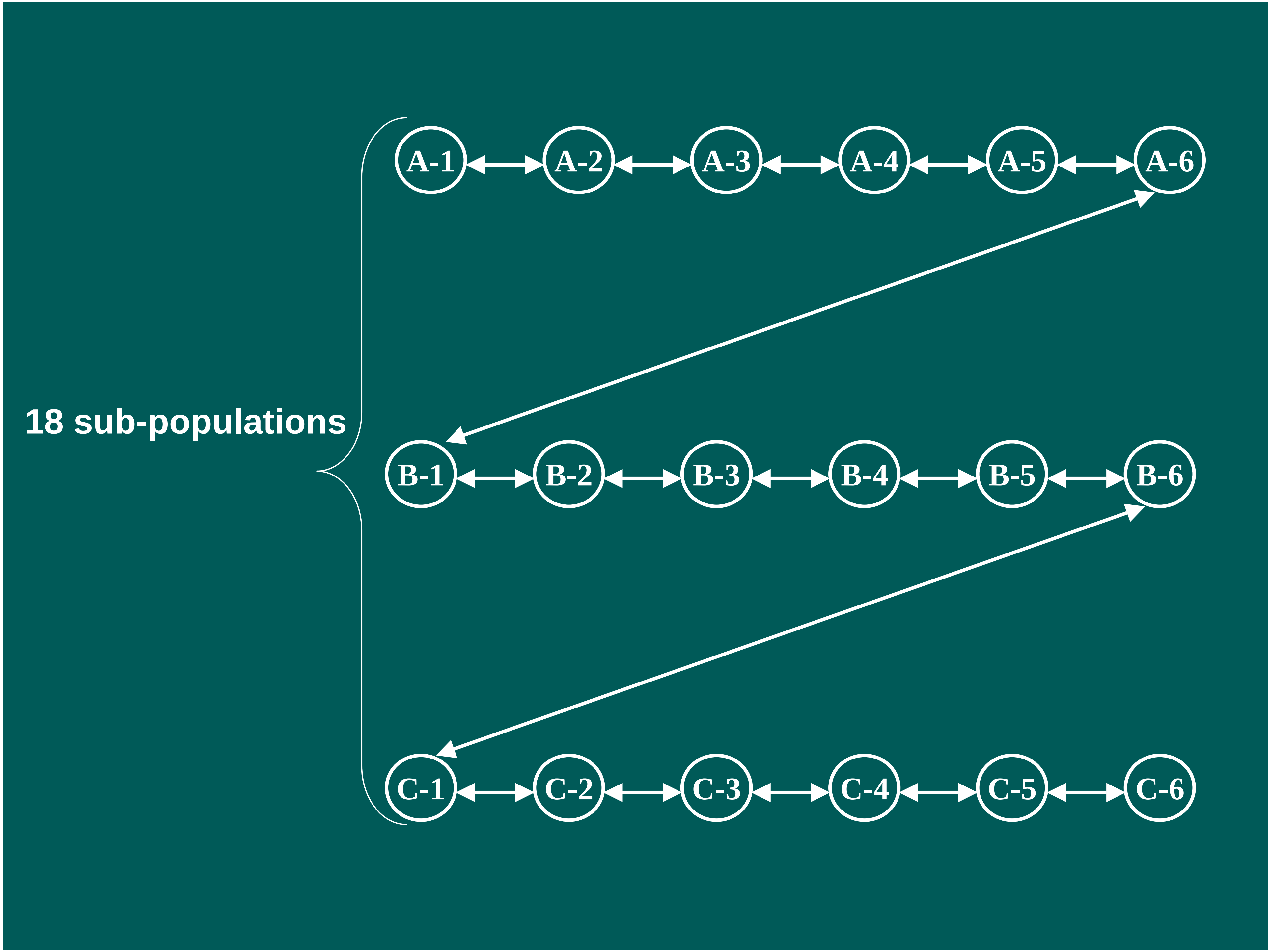
Single population

ITALY (VARESE)Infection models: results



Large areas: infection model




18 sub-populations
A-1
A-2
A-3
A-4
A-5
A-6
B-1
B-2
B-3
B-4
B-5
B-6
C-1
C-2
C-3
C-4
C-5
C-6

Models

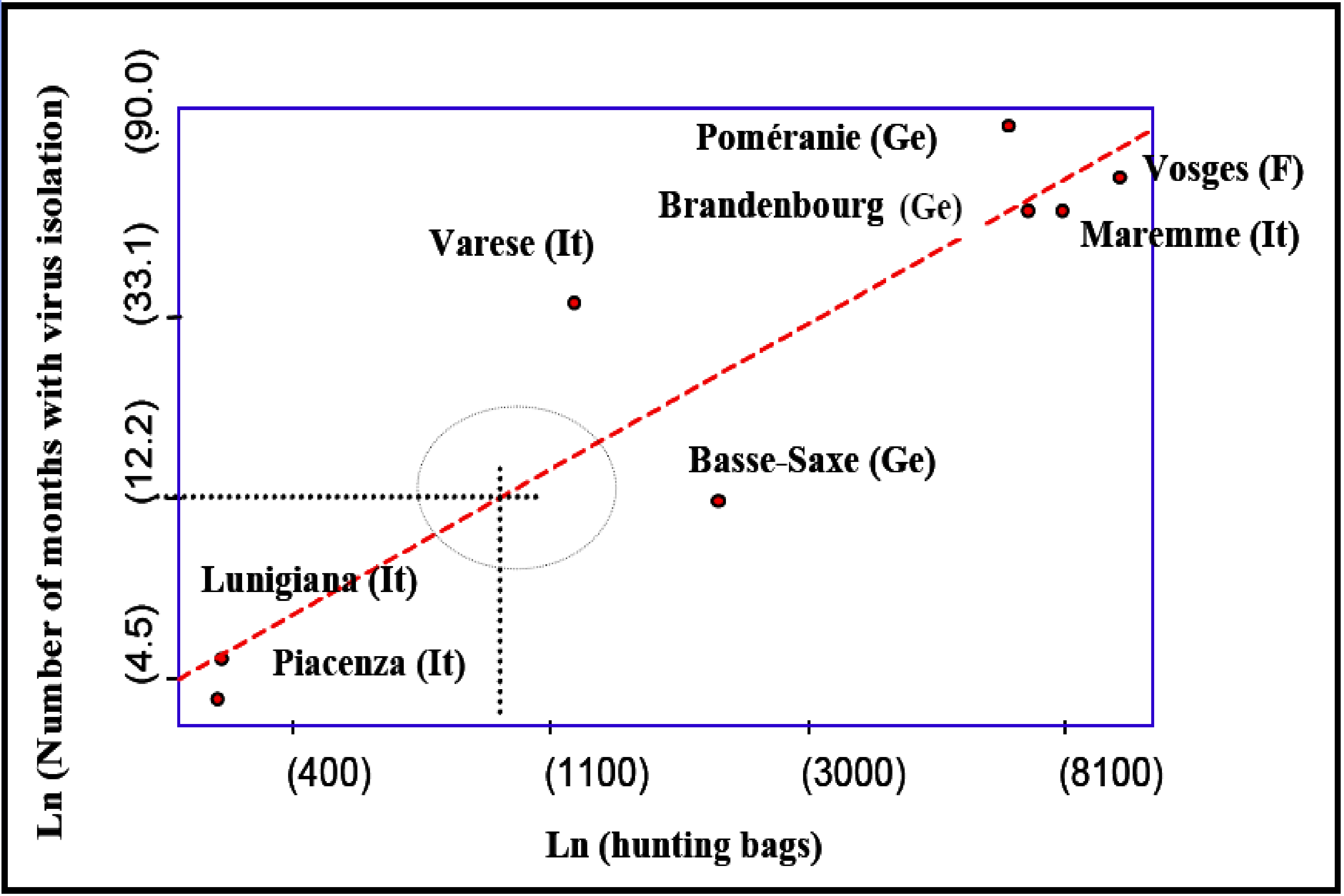
- **METAPOPULATION** -patches approach *(Hanski and Gilpin, 1997)*
- **SEIR** structure
- **2 Age Classes** (young and adults)
- **Homogeneous** mixing inside a single patch
- Patches are connected by a migration rate
- **Frequency dependent** transmission (TRUE MASS ACTION)
- **Deterministic** and **stochastic**

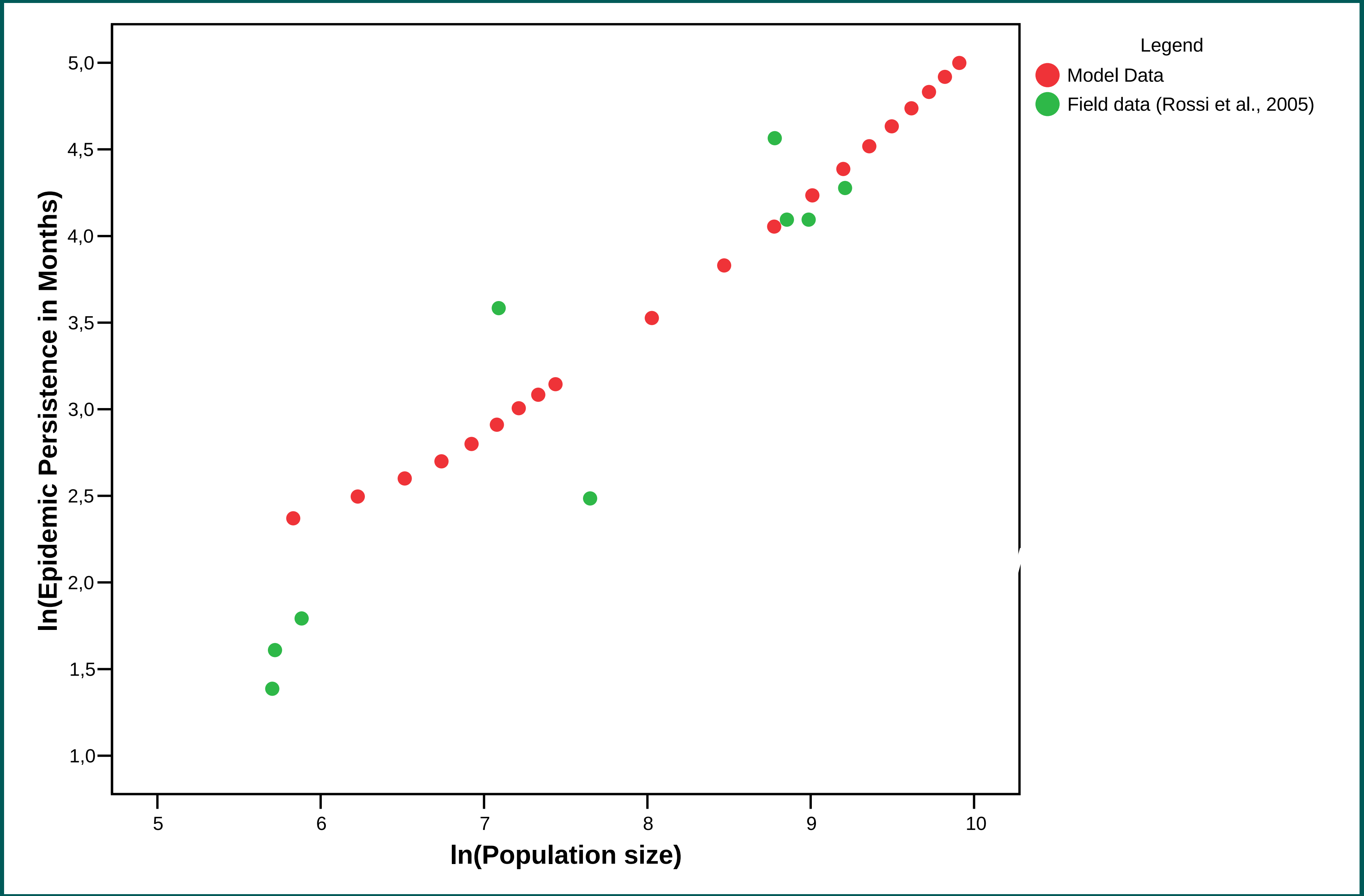
Is the model useful for simulating the infection in large populations?

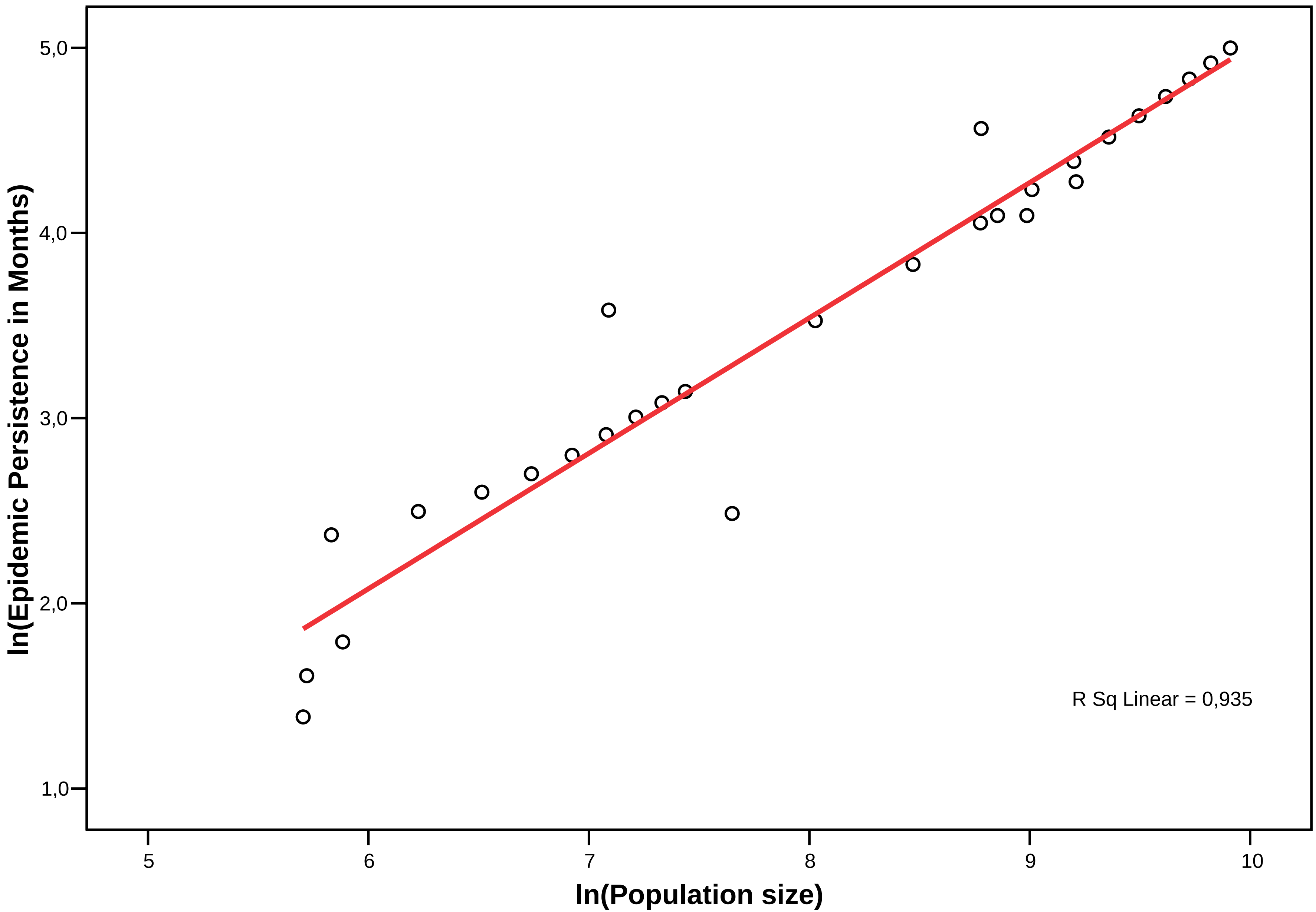
Model validation

- Worst model *vs* optimal model
- How many times the model results lie in the 95%CL of the field results
- Comparison of the model regression *vs* field data regression (Test of Parallelism)

Rossi *et al.* (*2005*) Rev. Epidemiol. Infect.




Legend
Model Data
Field data (Rossi et al., 2005)
ln(Epidemic Persistence in Months)
5,0
4,5
4,0
3,5
3,0
2,5
2,0
1,5
1,0
5
6
7
8
9
10
ln(Population size)

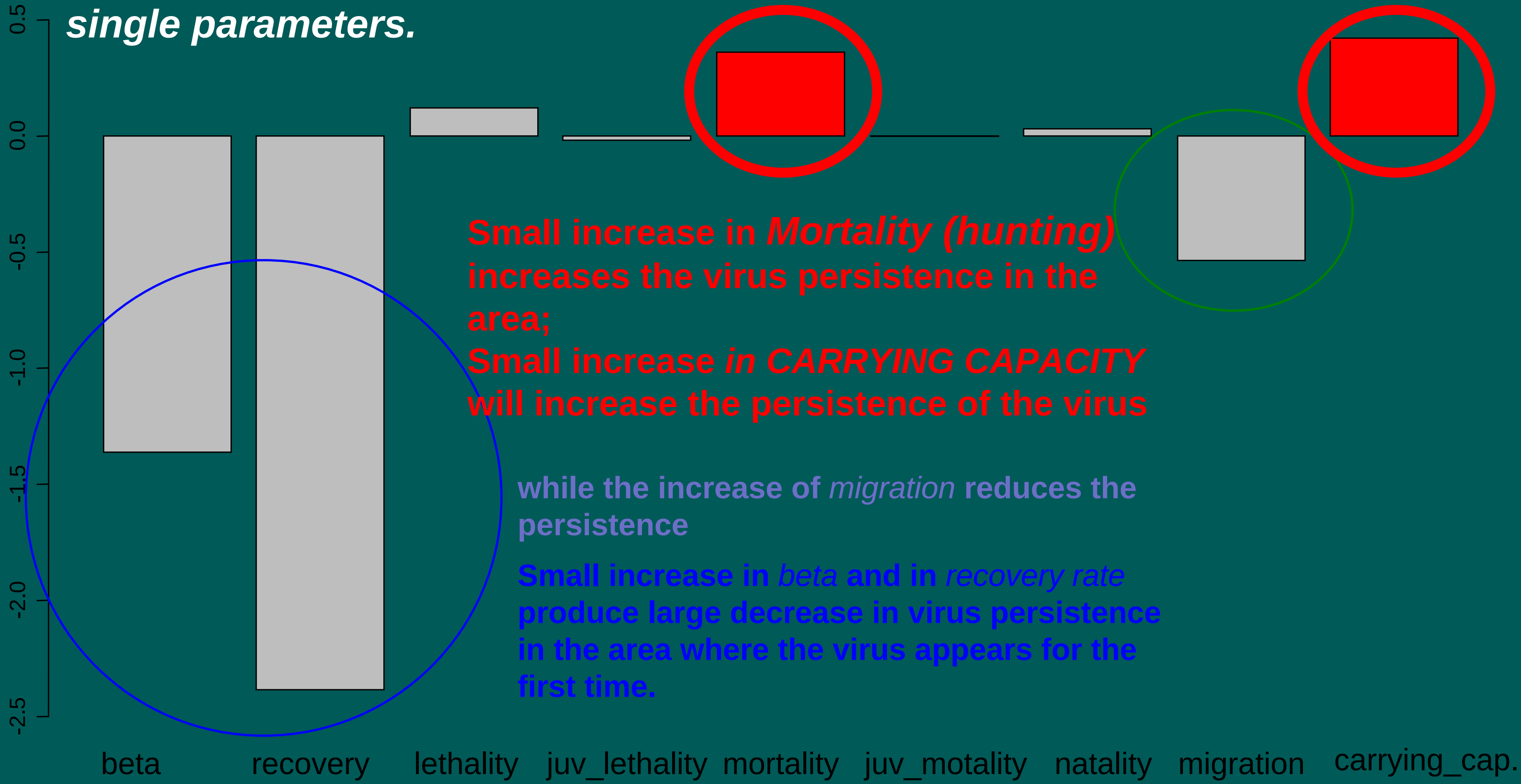


5,0
4,0
3,0
2,0
1,0
ln(Epidemic Persistence in Months)
R Sq Linear = 0,935
5
6
7
8
9
10
ln(Population size)

Our model works!!!.....................

Parameters "sensitivity" to endemic evolution of the infection

Response of epidemic persistence to infinitesimal positive increase of single parameters.

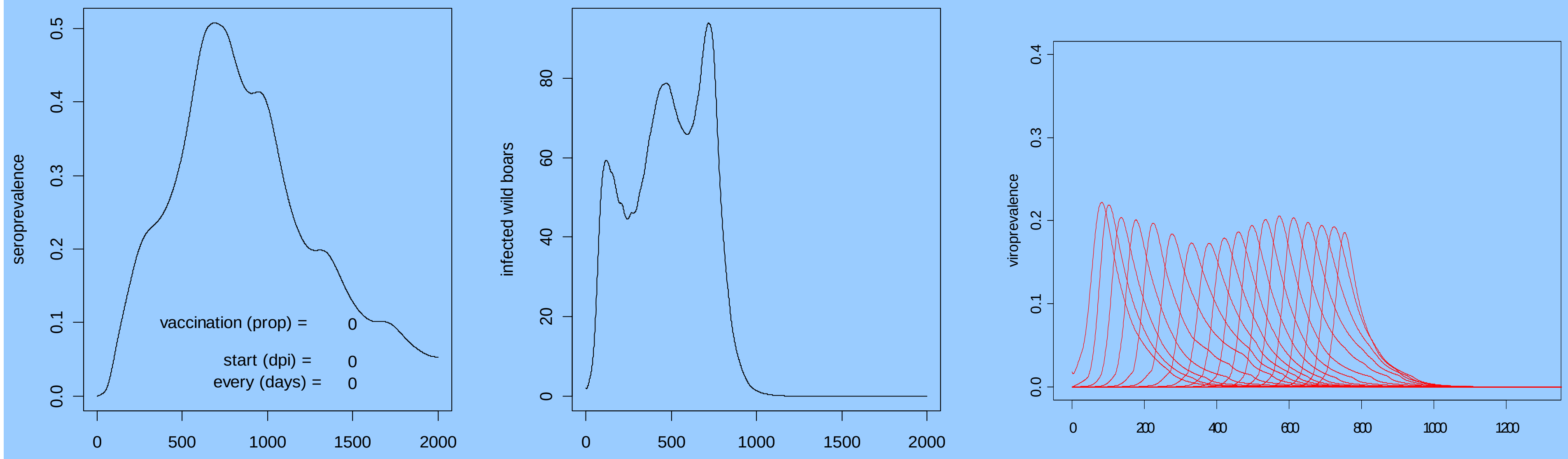


Small increase in *Mortality (hunting)* increases the virus persistence in the area;
Small increase *in CARRYING CAPACITY* will increase the persistence of the virus

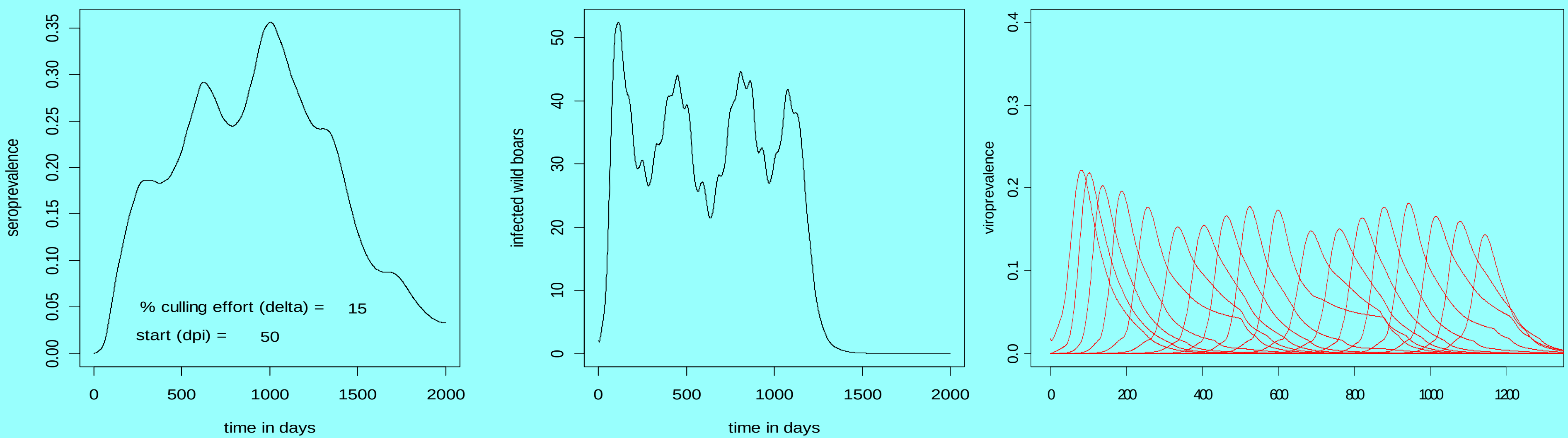
while the increase of *migration* **reduces the persistence**

Small increase in *beta* **and in** *recovery rate* **produce large decrease in virus persistence in the area where the virus appears for the first time.**

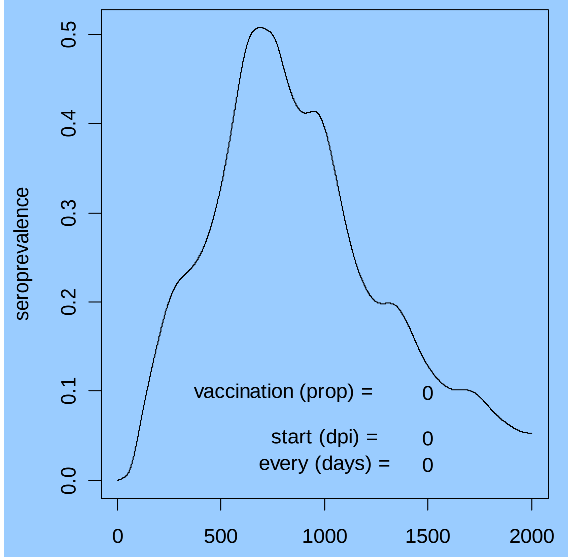
NORMAL

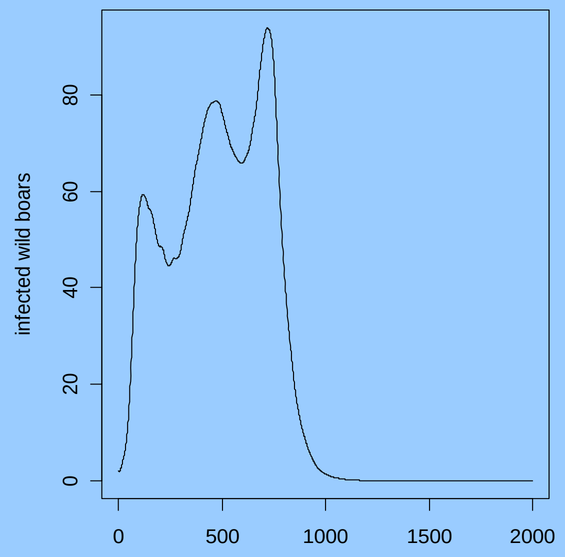


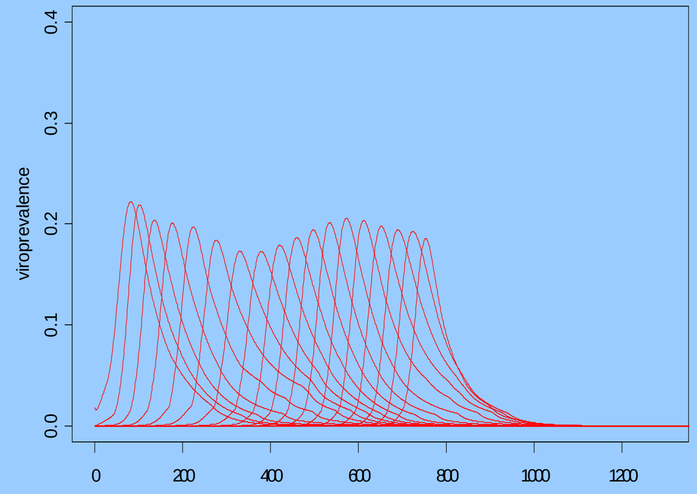
HUNTING +15% (rate = 0.6)



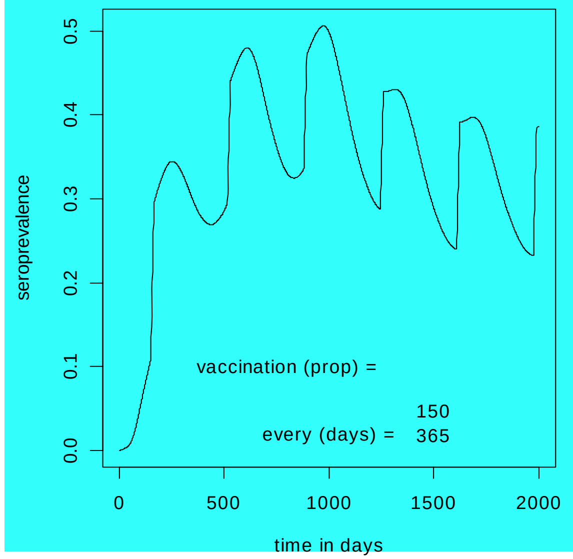
NORMAL

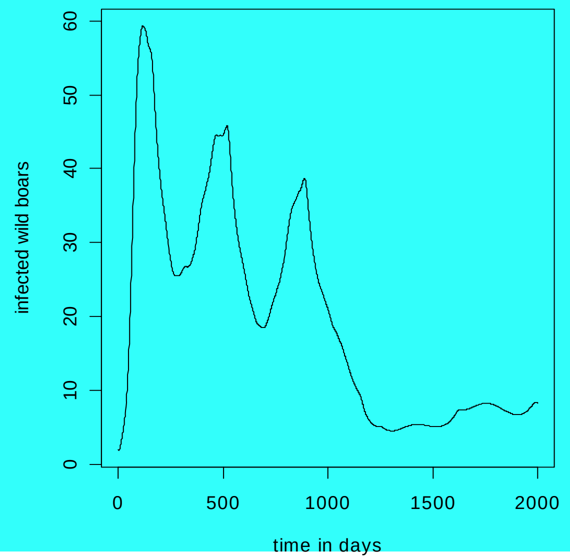


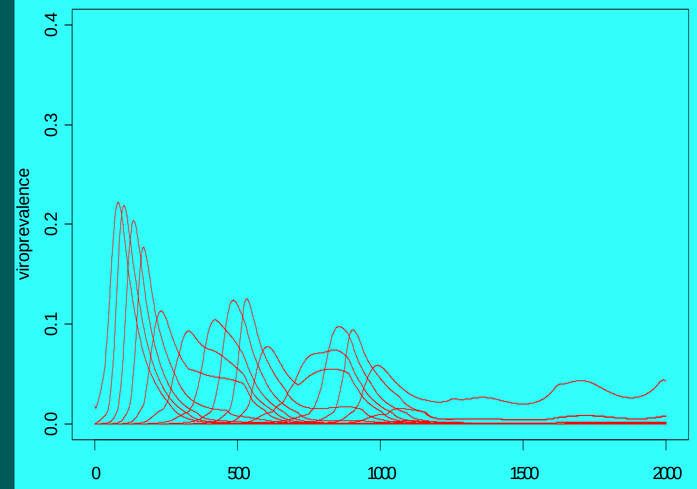




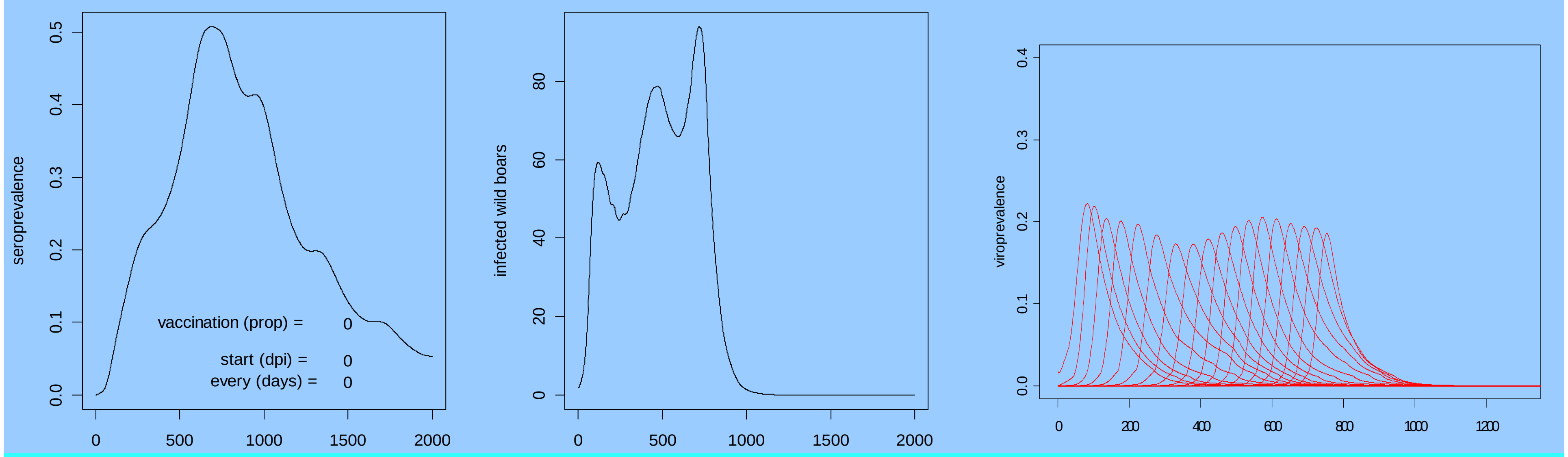
VACCINATION 20% ONCE YEAR^{-1}



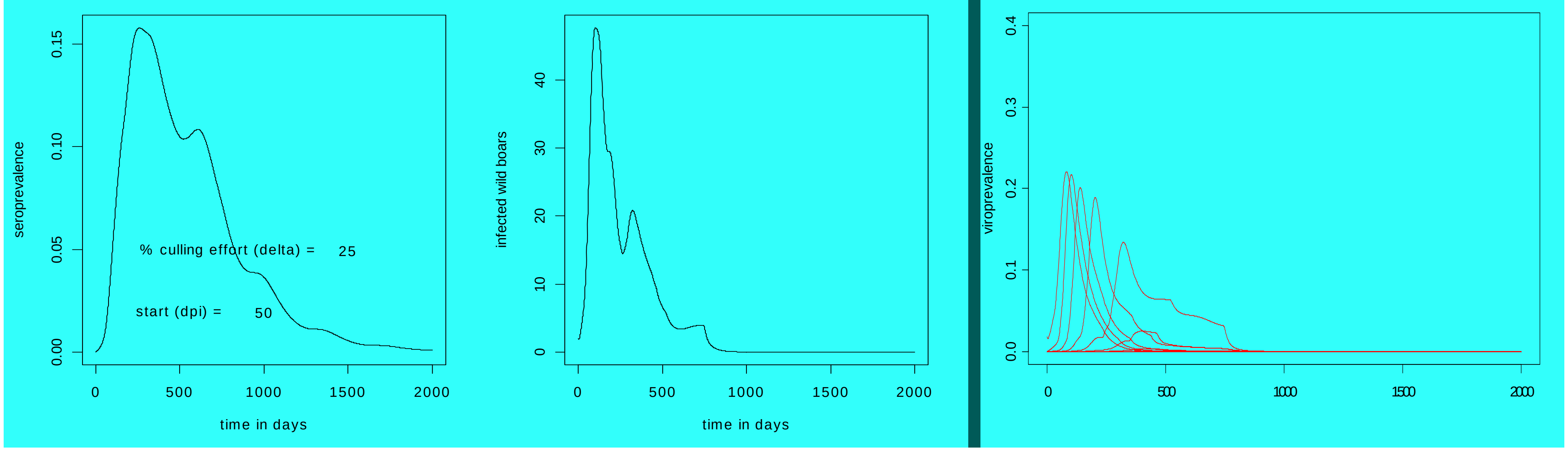




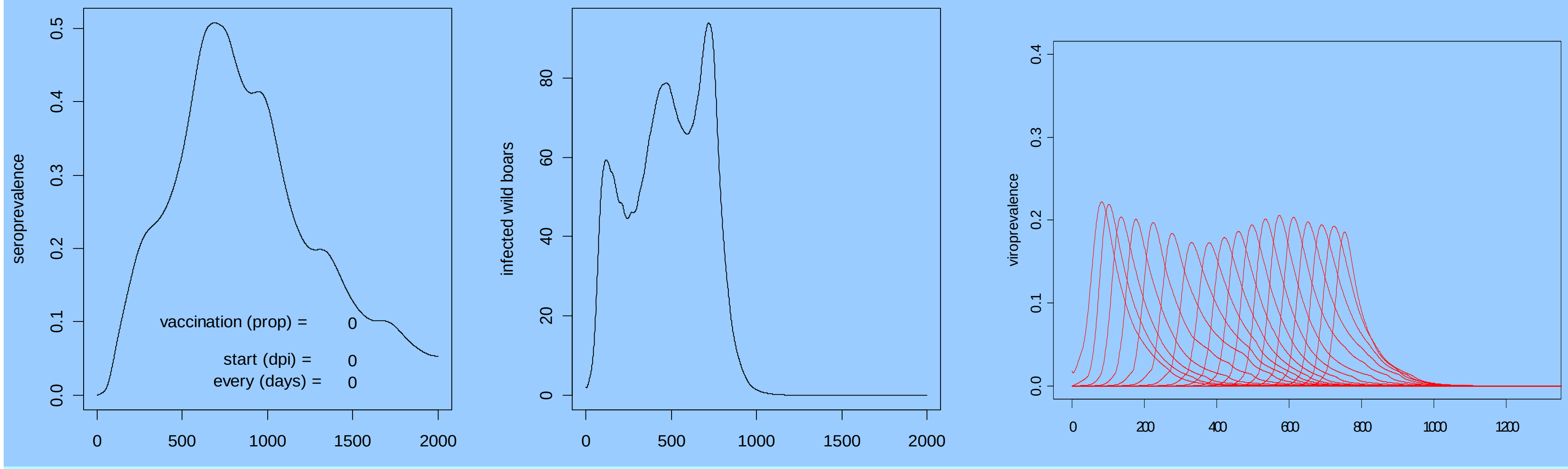
NORMAL



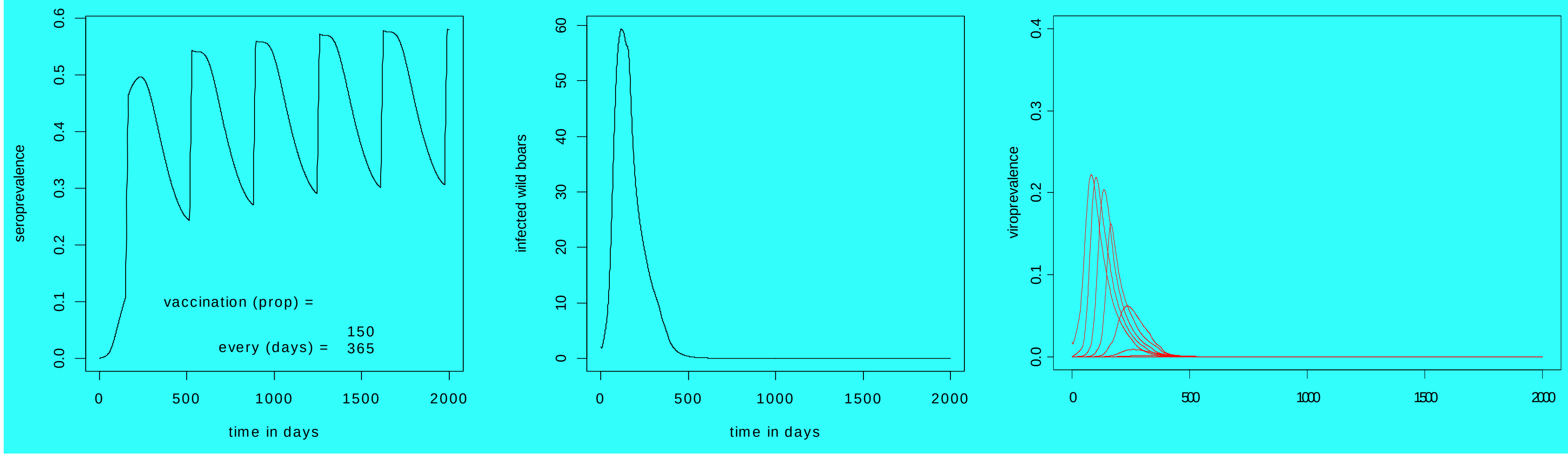
HUNTING +25% (rate = 0.7)



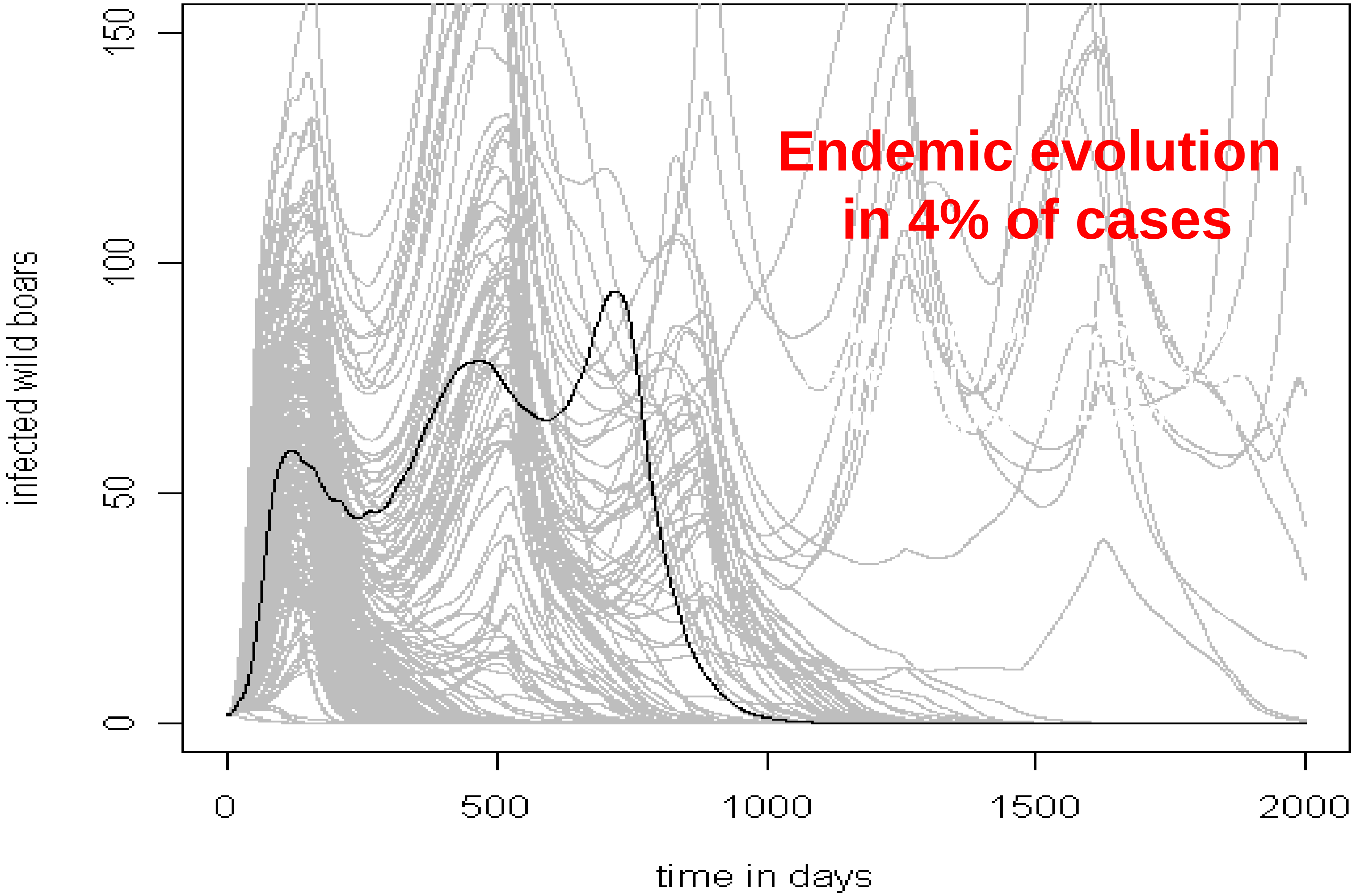
NORMAL



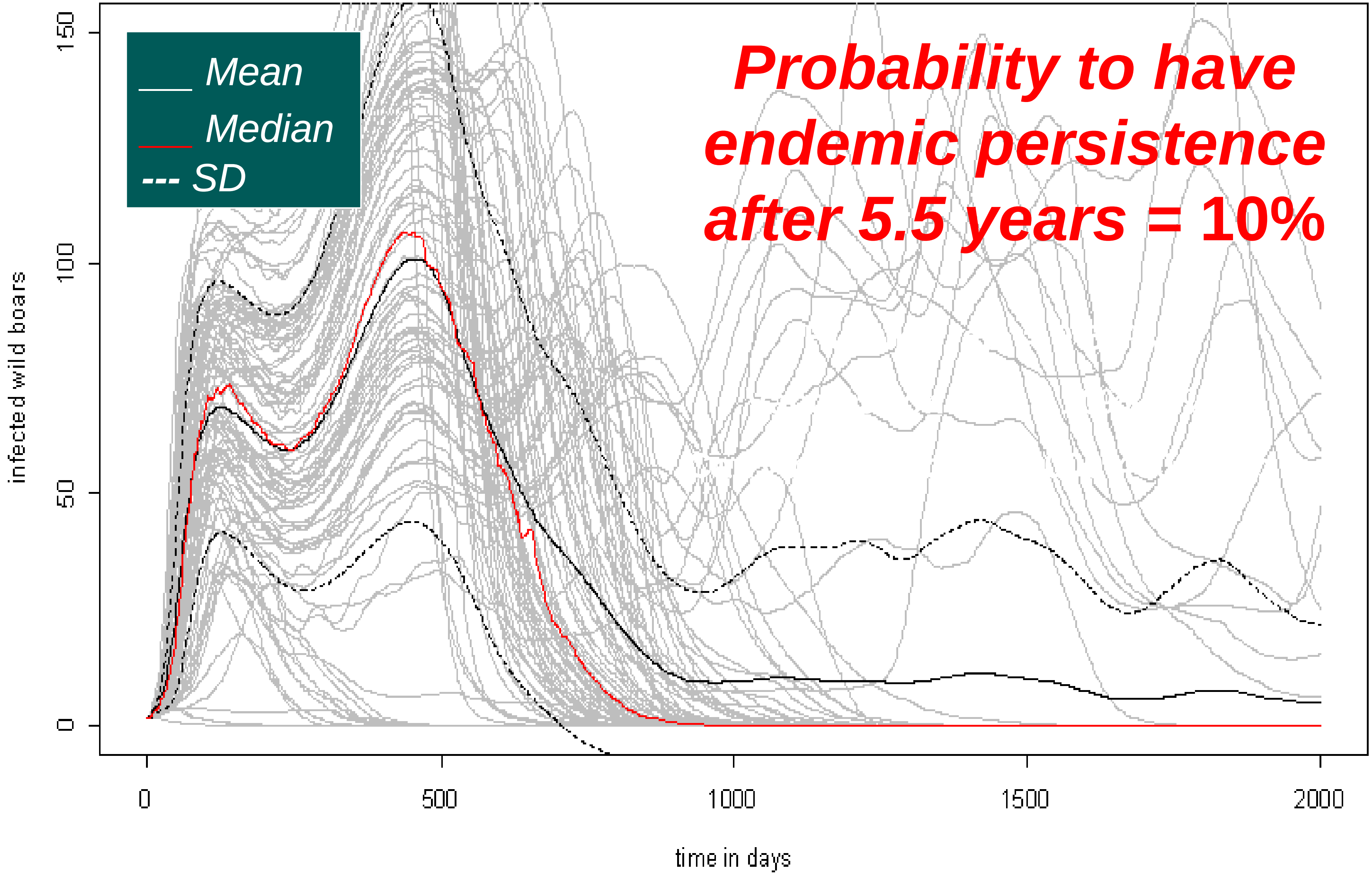
VACCINATION 40% ONCE YEAR^{-1}



Variability in small populations



Variability in large population



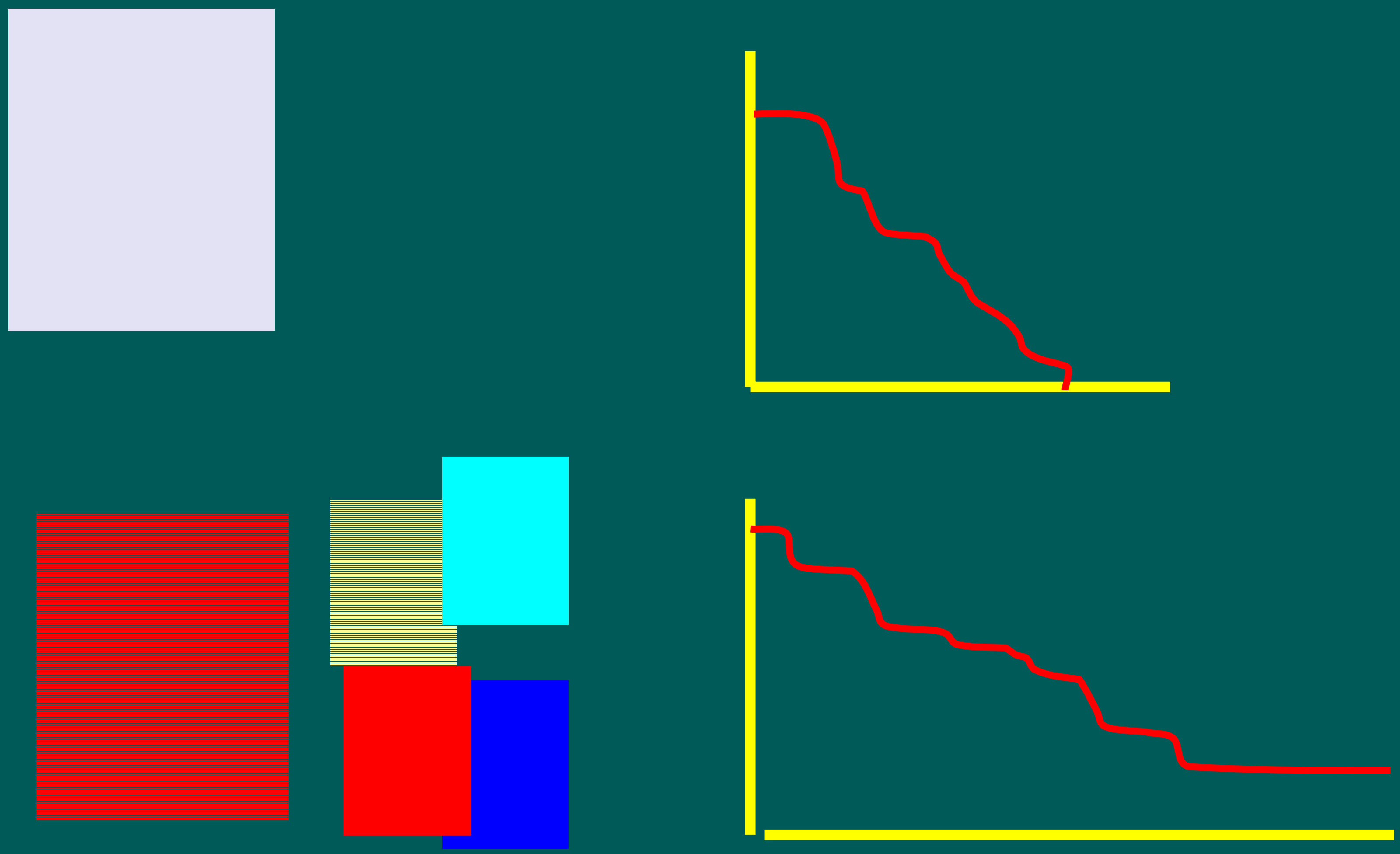
DISCUSSION

Endemic stability might be explained by some factors:

a) Size of the wild boar population as expression of the carrying capacity of the habitat

b) Presence of long virus shedders (chronic or immuno-tollerant animals)

c) Stochastic variations of both infection and management parameters (recovery, latency, beta and passive immunity, hunting and vaccination)



Population and management heterogeneities are increased in large populations

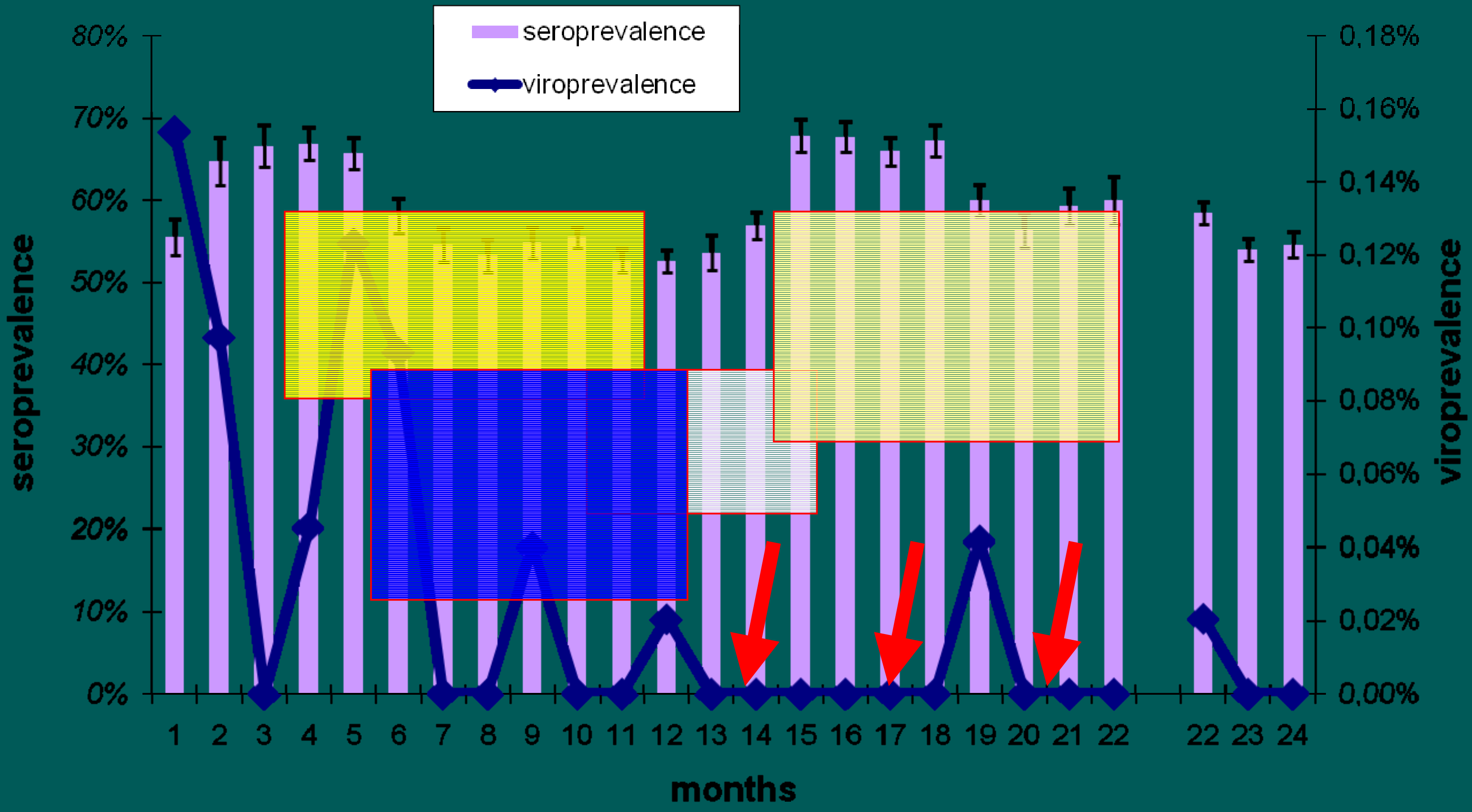
1.1.3 Germany (MWP): Infected area

- 1st February 2003
- 31st January2005 (24 months)
- Vaccination

Area: 5196 SqKM

Pop: 32000 wb

Dens: 6.1 wb/Sqkm



Hunting management

- **Absence of hunting** doesn't produce significant changes in virus persistence or spread;
- Only **high rates** > 70-80% could reduce significantly the virus persistence and spread (local extinction of wild boar)
- **Low rates** (< 45% as default value) reduce slightly the virus persistence but increase the epidemic peak (number of infected);
- **Small increase** in hunting rates (=60%) can promote virus persistence and spread;

Vaccination

- Vaccination is a sensible tool for eradication;
- Rarely vaccination in itself can eradicate the infection inside the outbreak
- Primarily, vaccination prevents the spread of the infection in neighbouring patches (promoting herd immunity in free areas)
- Effectiveness of vaccination increase for **each trial** ;
- Vaccination always reduces the **epidemic peak**;
- Endemic evolution of infection could occur when a low rate of vaccination is achieved in small areas also

Vaccination

- Vaccination of about 20% of susceptible animals results in an increased probability of endemic stability (the infection can spread in neighbouring patches with low incidence)
- Considering the common infection and population parameters a minimum target of 40% of vaccinated should be achieved (40% of susceptible animals);
- 60% of vaccinated animals will solve the infection

THE OPTIMAL VACCINATION

- STARTS AT 150 DAYS AFTER VIRUS DETECTION

- IMMUNISE AT LEAST 40% OF SUSCEPTIBLE INDIVIDUALS DURING THE FIRST TRIAL OF VACCINATION

- HUNTING SHOULD NOT EXCEDE 45% OF THE WHOLE POPULATION (EXCLUDED <4 MONYHS AGE CLASS)

Active Surveillance
the identification of the sampling unit

- The sampling unit is NOT the wild boar population
- The sampling unit is the wild boar metapopulation able to maintain the CSF virus for a certain period of time (CCS/year)
- A possible quantification: 1000-1800 WB in 200-300 KmSq

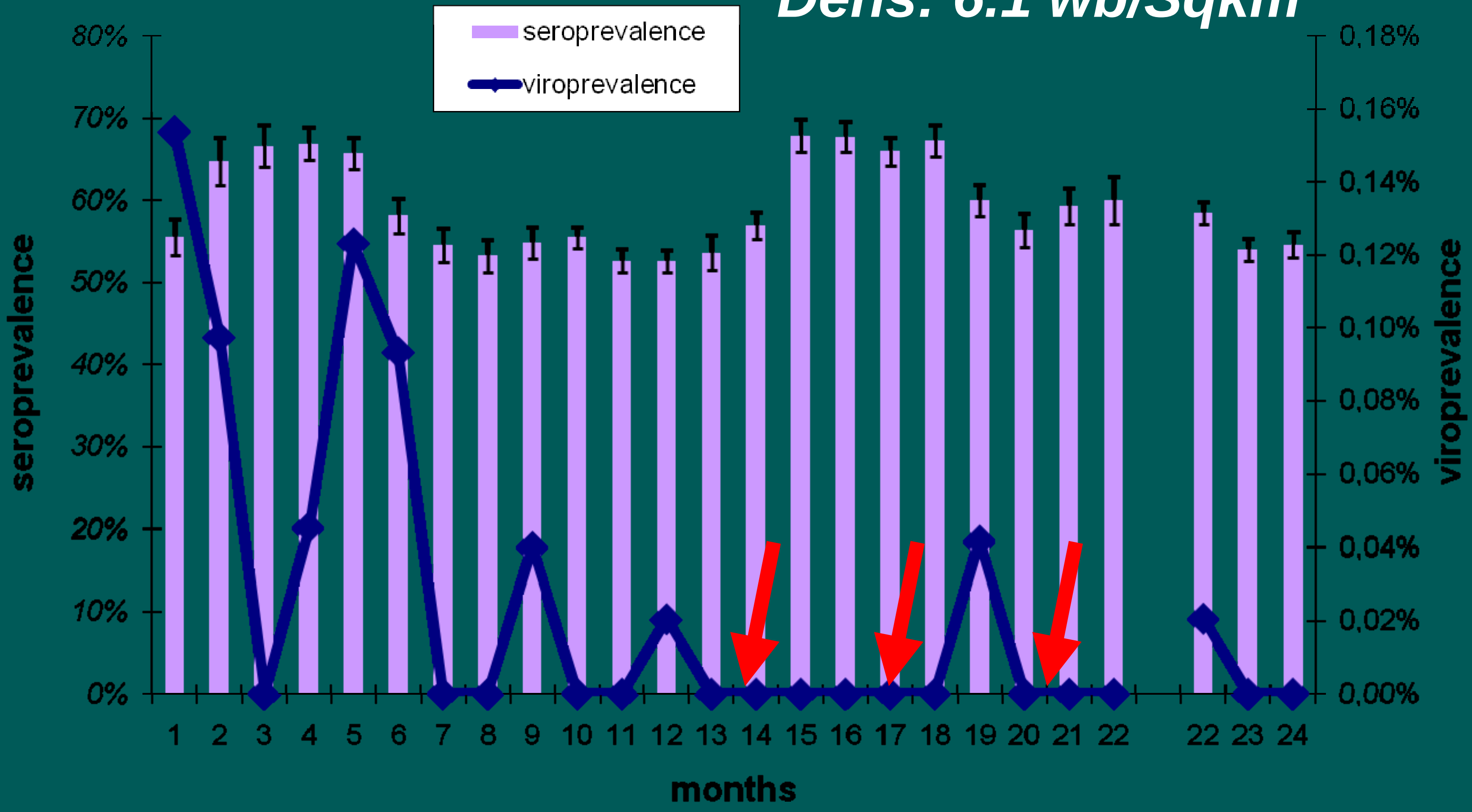
Germany (WMP): Infected area

- 1st February 2003
- 31st January2005 (24 months)
- Vaccination

<u>Area: 5196 KmSq</u>

Pop: 32000 wb

Dens: 6.1 wb/Sqkm



A field example

Involved Area: 5196 KmSq

Pop: 32000 wb

Dens: 6.1 wb/Sqkm

Sampling unit= the whole population

297 samples will detect at least one positive individuals if the infection is prevalent >= 1% (95%LC)

Sampling unit = 17 metapopulations

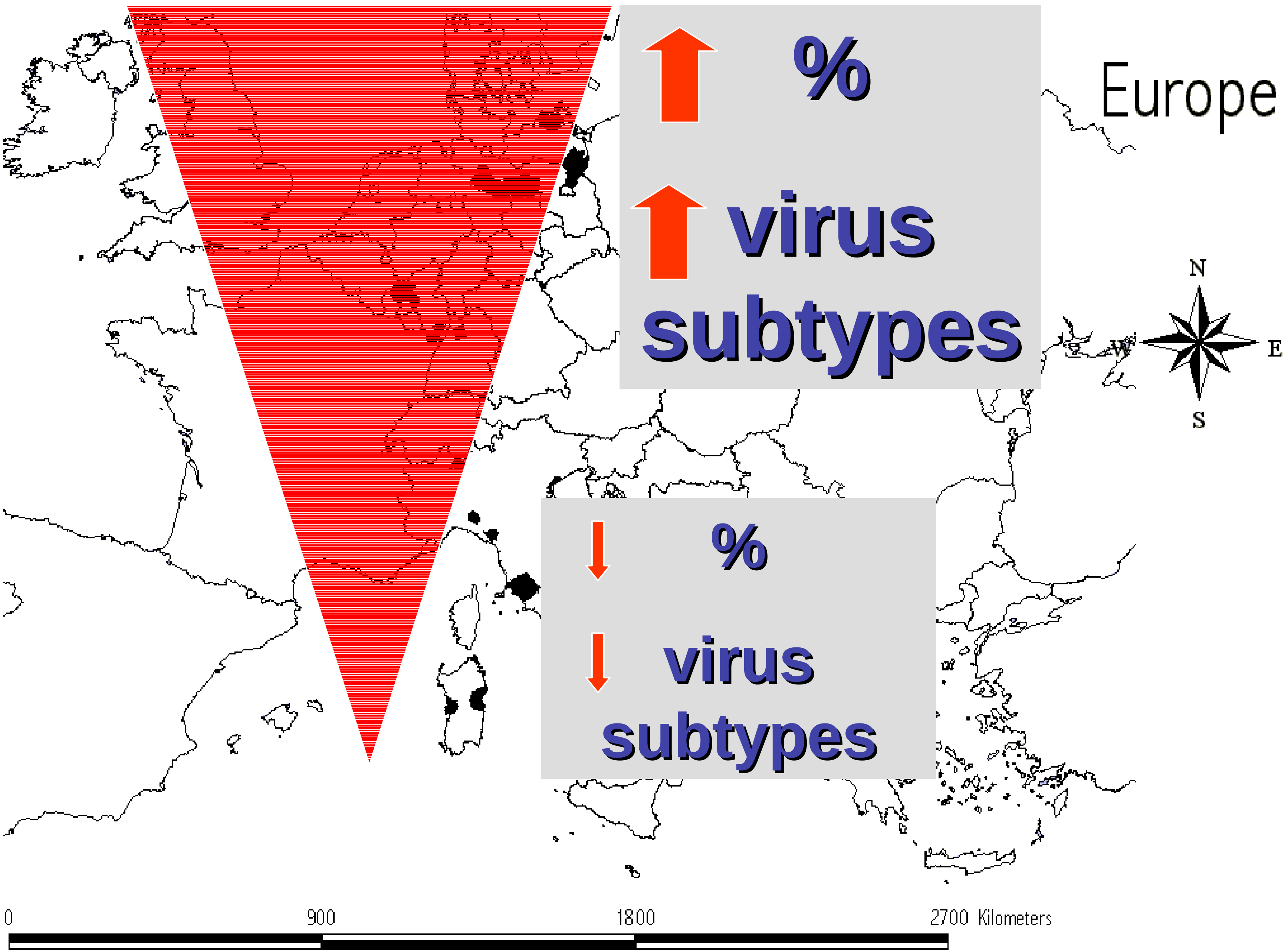
273 samples in each metapopulation will detect at least one positive individuals if the infection is prevalent >= 1%(95%LC)

297 vs 4641 samples

Role of wildlife in AIV epidemiology

AIV epidemiology in wildlife

- LPAI viruses (H5-H7) are widespread in dabbling ducks and juveniles act as the main epidemiological reservoir
- Virus isolates and their prevalence decrease from North East to South West
- Some AI virus subtypes (H5N3, H7N3) can be isolated in the same areas, year after year but more often they disappear and are replaced by different sub-types



↑ %
↑ virus subtypes
Europe
N
E
S
W
↓ %
↓ virus subtypes
0
900
1800
2700 Kilometers

Main epidemiological reservoir of AIV in the wild

Mallard

Teal

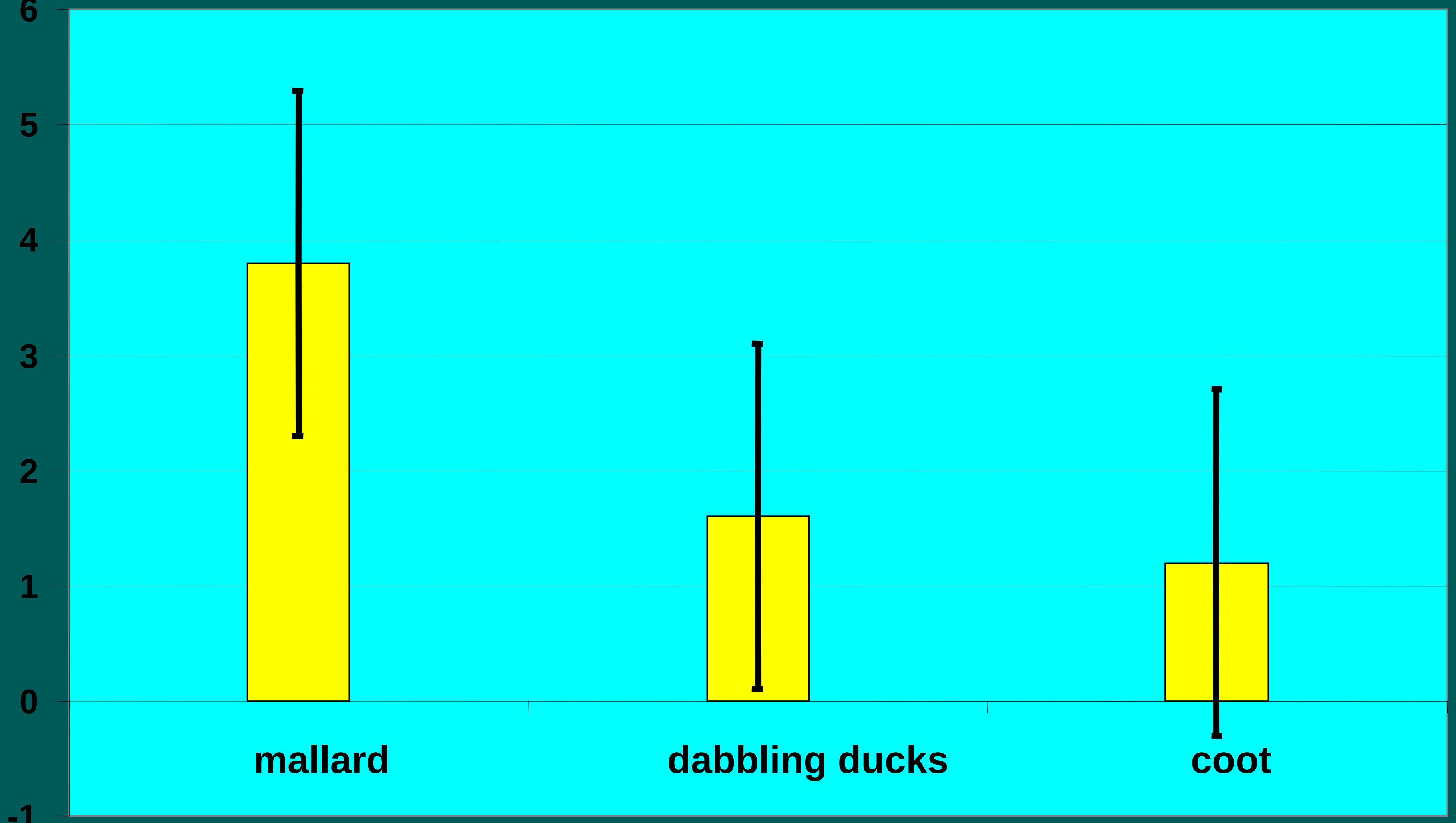
Gawdall

Shoveler

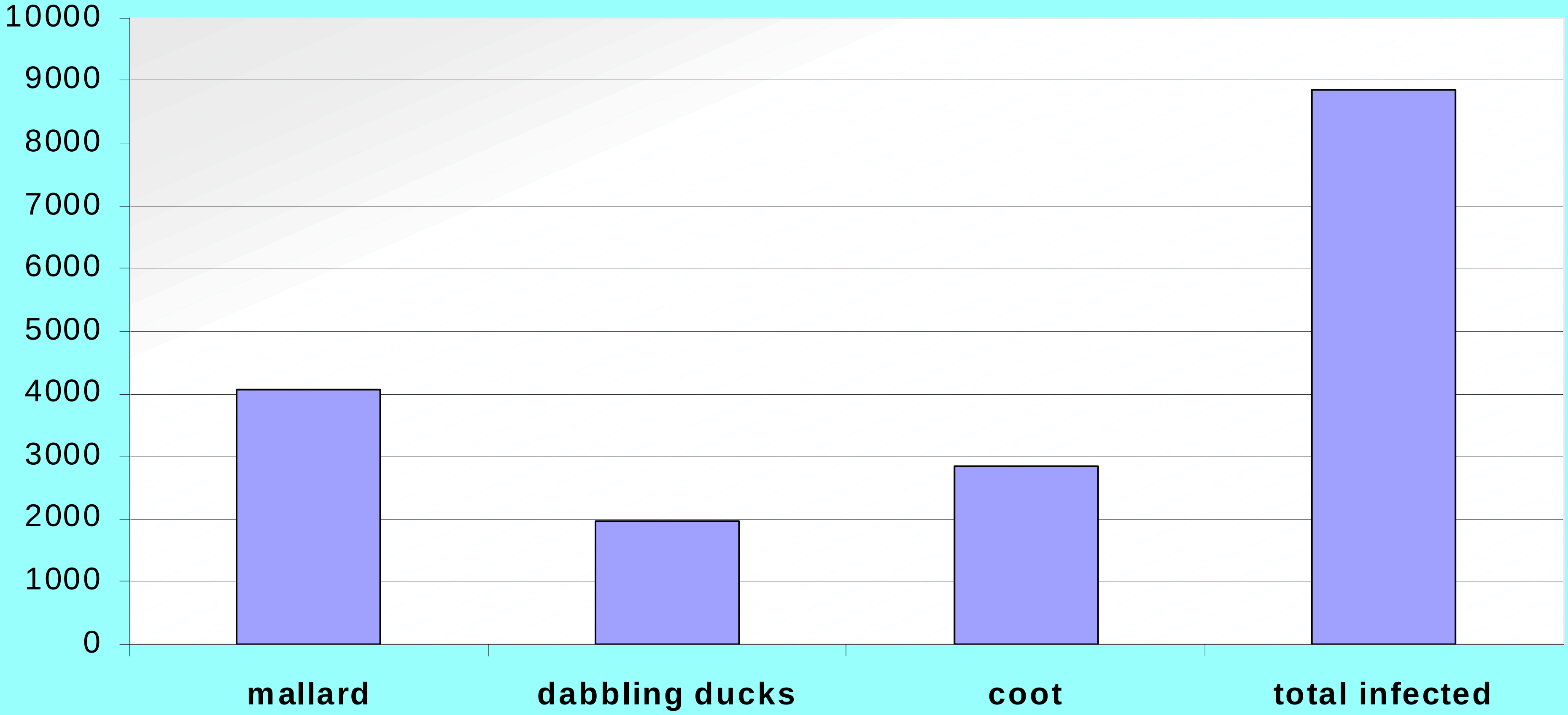
Wigeon

Pintail

Monitoring results: percentage of LPAI viruses detection in wild birds



Estimated number of LPAI virus shedders in the wintering population



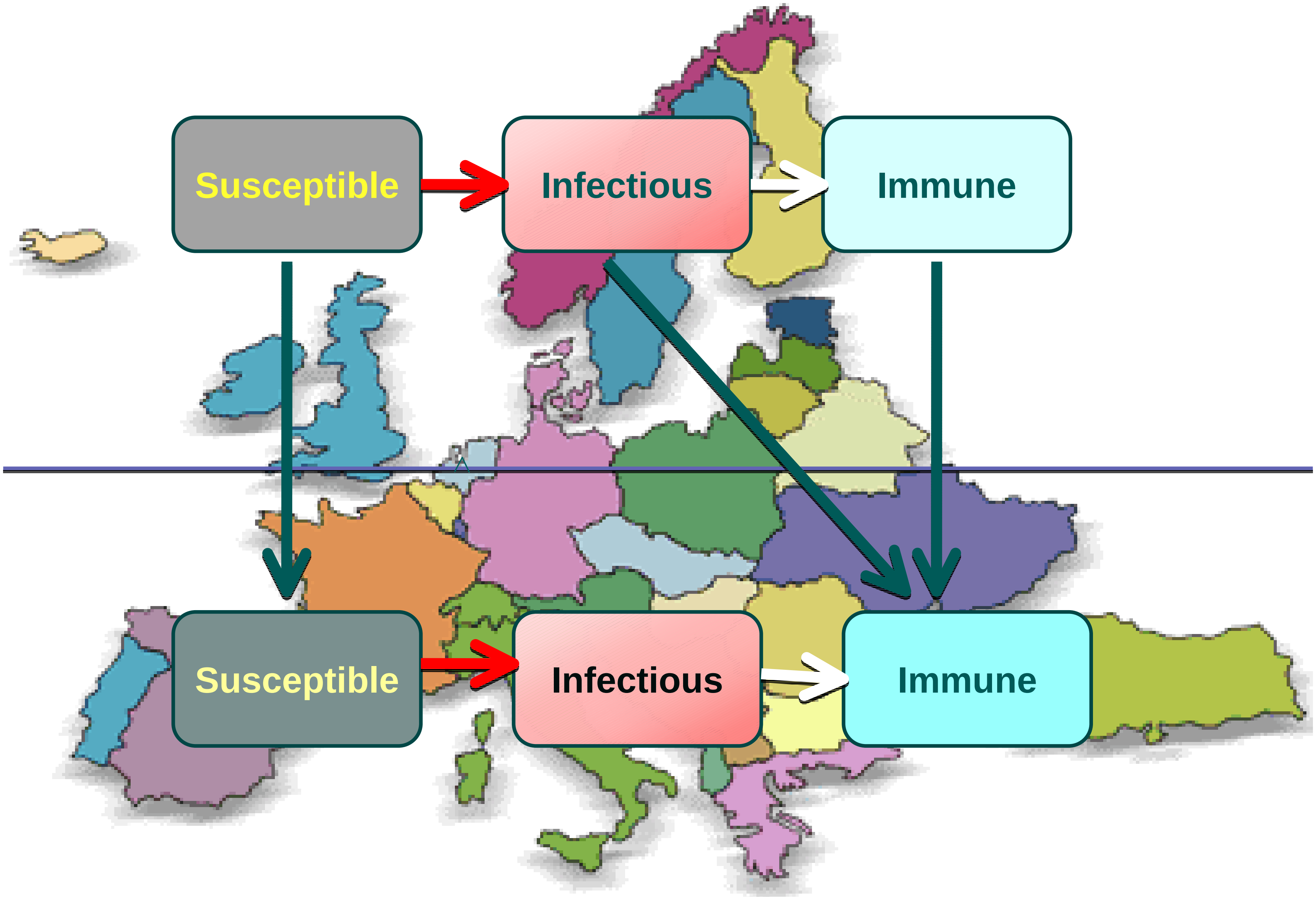
Aims

- To describe the general epidemiology of AIV LPAI

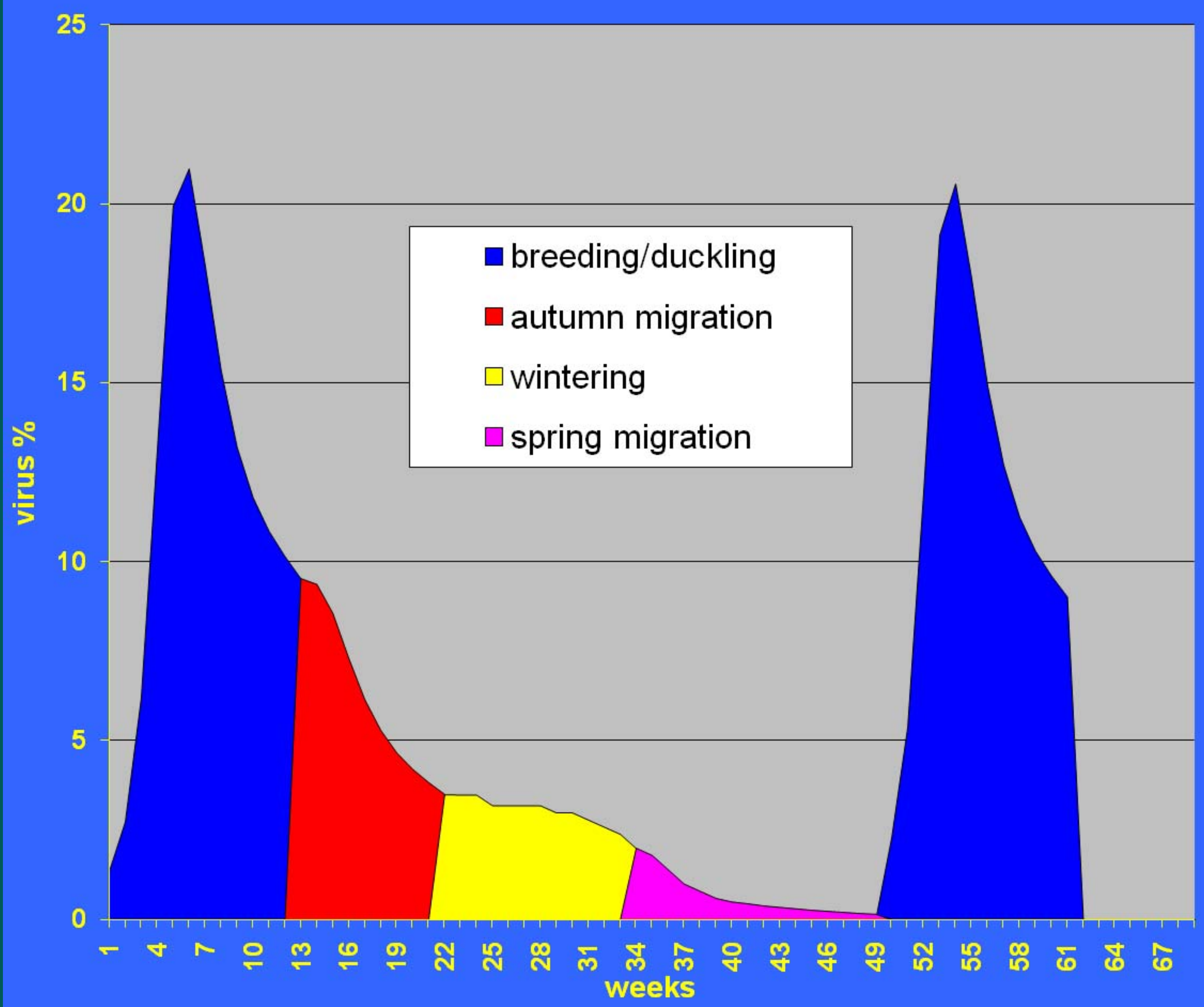
- To offer a surveillance approach in wildlife, also considering the possible spread of some HPAIVs such as H5N1

What is relevant for a Country

- Estimate the minimum number of birds allowing the endemic persistence of the virus(es) in the environment (host threshold density)
- For the Mediterranean basin the relevant period of time is: WINTER (winter" critical community size)
- estimate the capability of the virus of spreading (endemic-epidemic) or not (sporadic infection): Effective reproductive success of the virus
- Determine the relevance of some demographic and epidemiological parameters in describing the general pattern of the infection


Susceptible
Infectious
Immune
Susceptible
Infectious
Immune

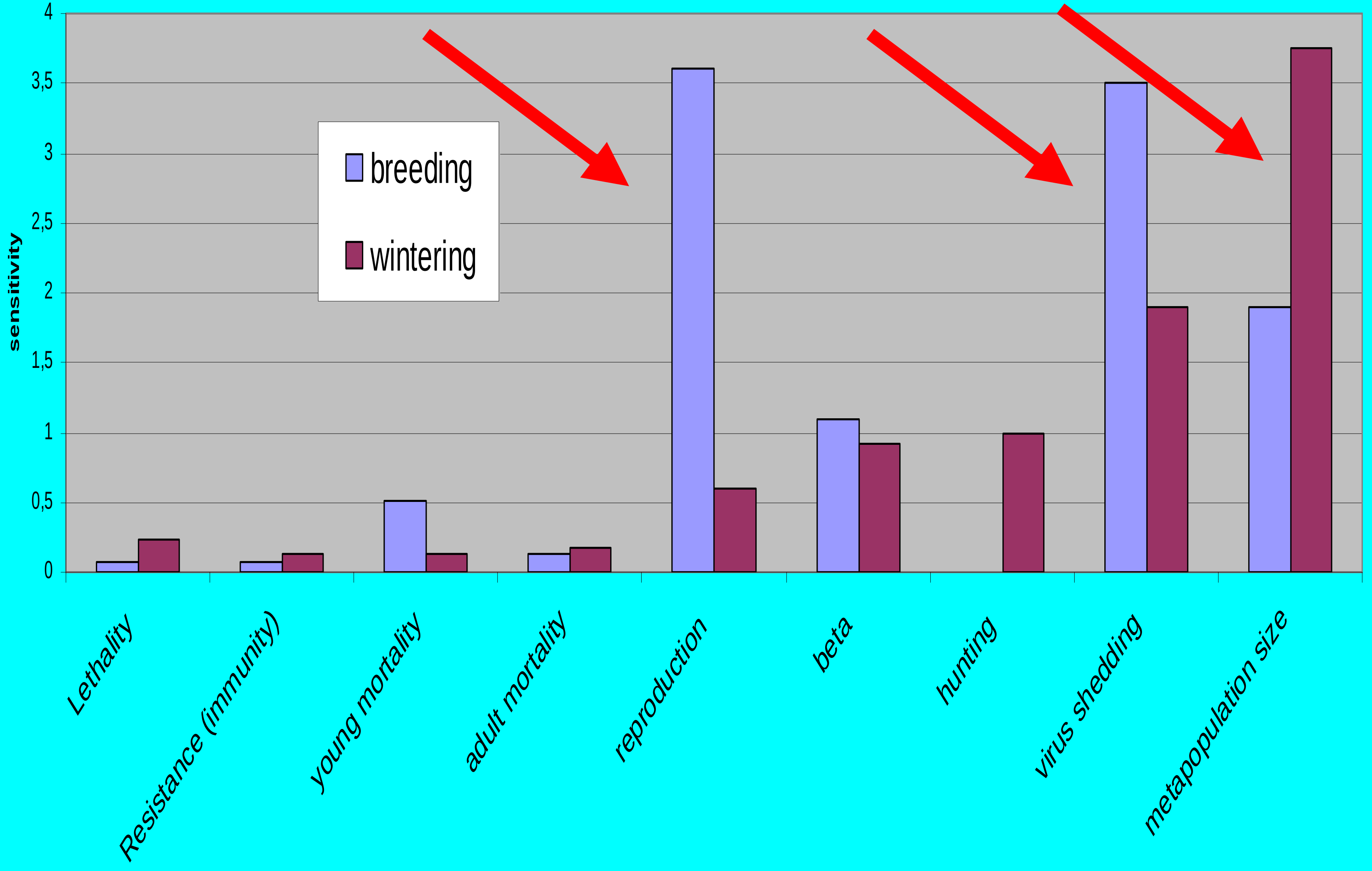
yearly virus prevalence

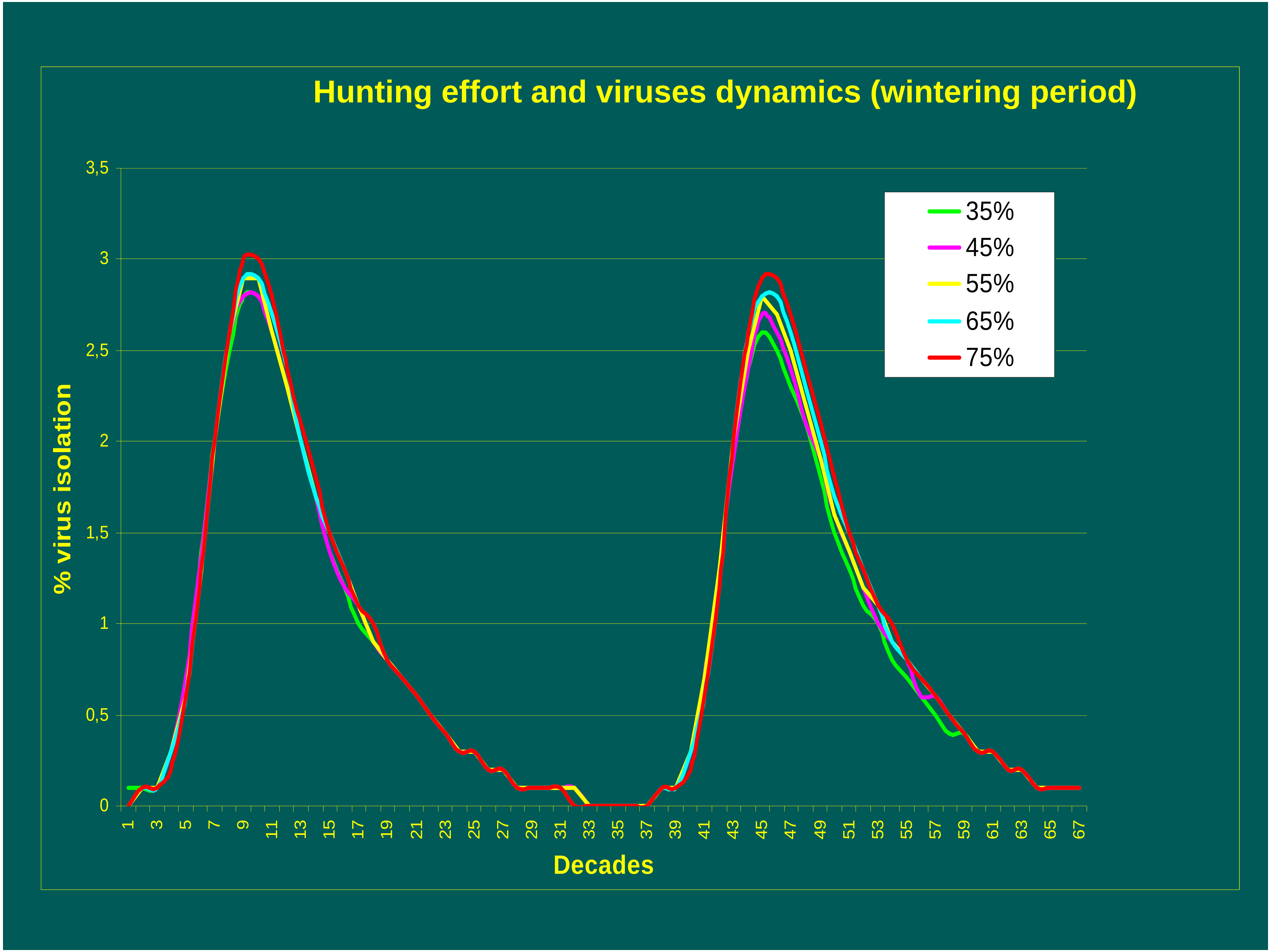


Results LPAI VRUSES

- Host threshold density = 380/individuals/day
- For having endemic LPAI virus during the whole winter (Critical Community Size) ≈ 1200 dabbling ducks
- The Viruses are endemic (R_e = 1.11)

Which factor are relevant?





Hunting effort and viruses dynamics (wintering period)
% virus isolation
Decades
35%
45%
55%
65%
75%
0
0,5
1
1,5
2
2,5
3
3,5
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37 39 41 43 45 47 49 51 53 55 57 59 61 63 65 67

30 millions of birds and thousands of wetlands are involved

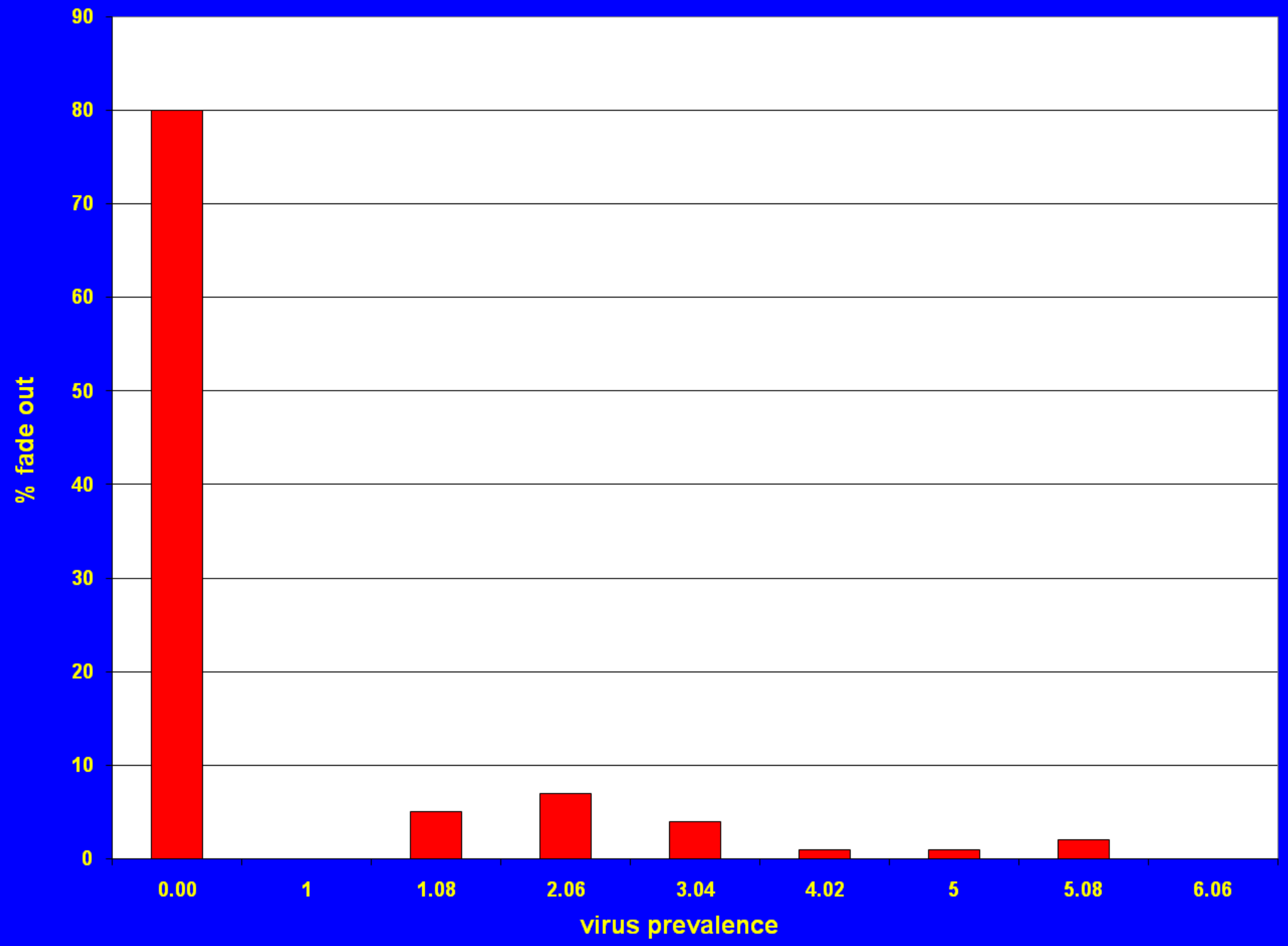
Thousands of wetlands….what can happen?

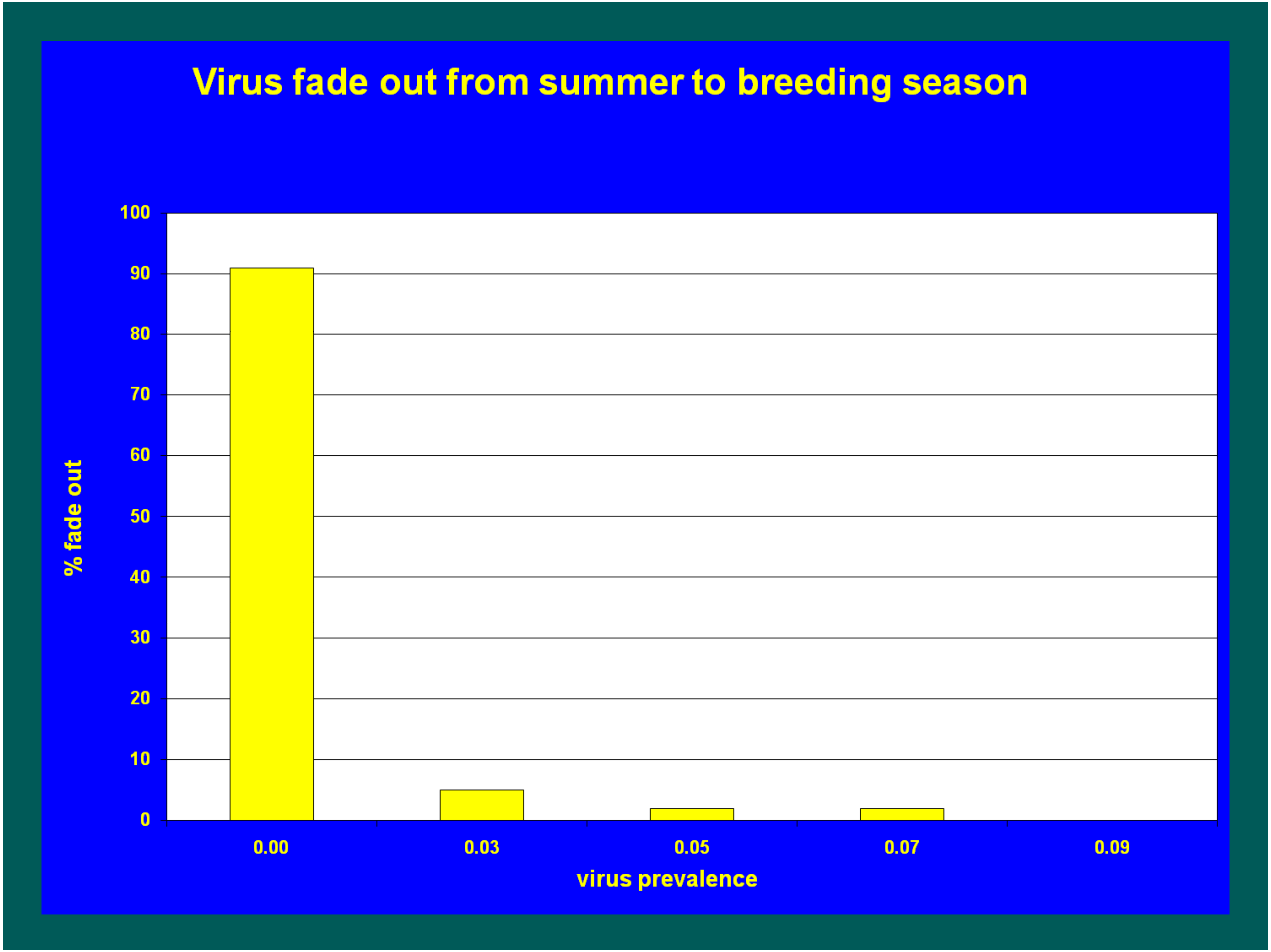
Casual variations on:

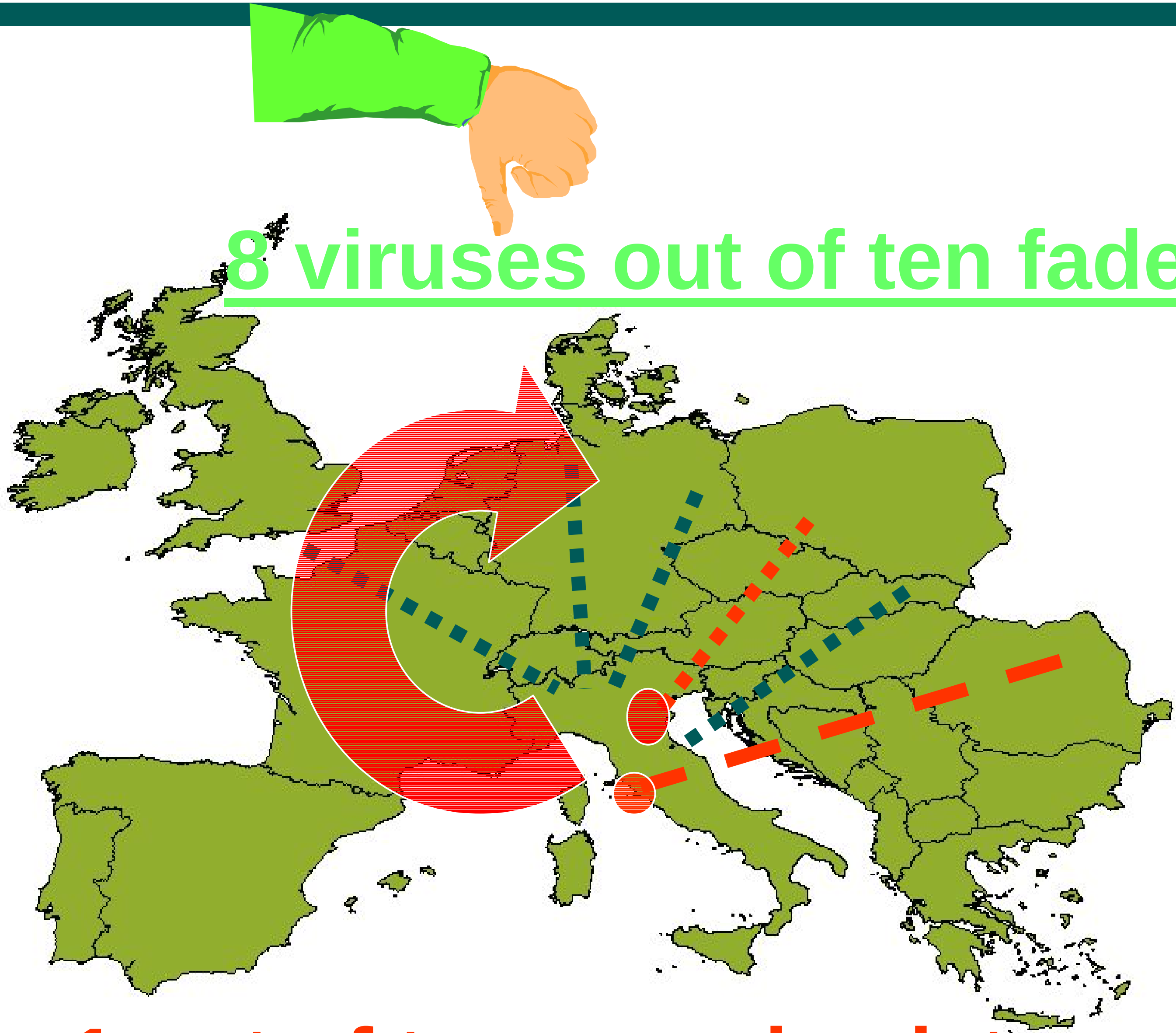
- Local population size (large vs. small wetlands)
- Reproductive success (good in some areas and worse in others)
- hunting intensity (high in some areas, forbidden in others)
- Different transmission coefficient according to the different involved subtypes
- immunity length and protection
- natural mortality

- Stochastic simulation considering the variability of the above parameters

Viruses fade out from summer to wintering




Virus fade out from summer to breeding season
100
90
80
70
60
50
40
30
20
10
0
% fade out
0.00
0.03
0.05
0.07
0.09
virus prevalence



8 viruses out of ten fade out

1 out of ten goes back to the breeding areas

Conclusions

- The size and distribution of dabbling duck LOCAL populations could allow the persistence of a high number of LPAIV in any environment and Country

- The interaction between epidemiological and demographic parameters drives to a local extinction in most of the wetlands

- The viruses dynamic appears mainly based on winter local extinction and summer re-colonisation cycles

- Wintering and spring migration represent the “bottle neck” for the maintenance of genetic variability in both Ducks and LPAI viruses

- Post-breeding high host density will enhance LPAIV transmission and subsequent co-infection of many duck individuals might lead to new “emergent” LPAIV

HOW to survey the presence of AIV in wild birds summarised

- Active surveillance: detecting LPAI viruses trough the examination of alive or healthy hunted birds => wetlands with more than 1200 wintering birds, 20% of positive wetlands with an expected prevalence 2%;

- Passive surveillance: detecting the virus trough examination of dead or sick birds => only for HPAI AIV

Passive surveillance

TYPE OF SAMPLING	ASSU MPTION	APPROACH	LIMITATION	SENSITVITY
All dead birds belonging to the high risk species	HPAI has high lethality rate in high risk species	The probability of detecting the virus in a dead birds is higher in respect to any other type of sampling	If the involved HPAI assumes a LPAI behaviour will not be detected; dead birds are retrieved according to human distribution and search	Extremely high if the HPAI involved retains is lethality **Very effective in early warning**

Passive surveillance

TYPE OF SAMPLING	ASSUNPTION	APPROACH	LIMITATION	SENSITVITY
Passive sampling of mortality clusters of bird species not considered at high risk	H5N1 HPAI has high lethality rate in bird species not considered at high risk	Will reveal H5N1 when it spreads outside wetlands. This type of sampling will reveal secondary outbreaks in bridge species	Uncertain definition of mortality cluster. Huge amount of samples obtained from urban-anthropised areas	Extremely high if H5N1 retains is lethality in not high risk species **Acceptable in early warning**

Active surveillance

TYPE OF SAMPLING	ASSUNPTION	APPROACH	LIMITATION	SENSITVITY
Active sampling in randomly selected areas and bird species	HPAI has an LPAI behaviour in some bird species (lethality low/null). Areas are randomly selected. Individuals live in an homogeneous mixing (same probability to be sampled and infected irrespective of species, age and gender classes)	H5N1 has an LPAI behaviour in some species	Areas and species are likely to be selected with an opportunistic approach. Size of the sampling units and expected prevalence of H5N1 is unknown.	Low or null if H5N1 retains its lethality rate and its sporadic behaviour. Applicable in an early warning strategy exclusively if combined with other type o sampling. **Optimal strategy to detect LPAI Viruses**

Active surveillance

TYPE OF SAMPLING	ASSUNPTION	APPROACH	LIMITATION	SENSITVITY
Active sampling in all areas and birds considered at risk	H5N1 HPAI shows a sporadic/unpredictable behaviour	Each wetland and its ornitho-cenoses is considered at risk.	Practically inapplicable due to the very high number of samples required	High when properly realised. Applicable in an early warning system. Perfect for assessing presence and prevalence of LPAI Viruses.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