# Risk-Based Surveillance and the FMD Free Status: Concepts and Application

# Surveillance systems in the EU

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# Introduction

# Introduction

- Freedom from infection implies the absence of the pathogenic agent in the population
- Scientific methods cannot provide absolute certainty of the absence of infection
- The assessment of freedom from infection or disease
  - has a probabilistic nature
  - it involves providing sufficient evidence that the infection, if present in a population, is a very rare event
  - in a globalized society it is impossible to exclude  that an infection has not been introduced recently

# Introduction

- To document freedom from infection, Veterinary Services must actively search for infection and its circulation.
- This search for infection(s) is one of the main routine tasks of Veterinary Services and is carried out using a number of approaches and strategies.
- The cumulative evidence of an absence of infection and virus circulation provided by various surveillance activities can corroborate a hypothesis of absence of infection, in order to document freedom from infection.

# Introduction

- Approaches used to achieve and to demonstrate freedom adopted in the EU
  - Periodical testing of all susceptible animals in the population of interest (census) – adopted to achieve eradication and for a limited time after eradication to provide confidence of the absence of infection
  - Periodical random surveys to provide confidence of the absence of infection
  - Risk-based surveillance and risk based surveys (adopted to achieve eradication and to provide confidence of the absence of infection)

# Approaches to achieve and demonstrate freedom - Census

# Census

- The testing of all susceptible animals in a population is used in the EU for the eradication programs for EBL, bovine TB, sheep and goat brucellosis and bovine brucellosis (in this case only reproduction stock is considered).
- This approach is very resource-intensive and is used only for some diseases that are considered top priorities.
- After the achievement of the officially free status, it is generally replaced by the random survey approach.


Approaches to demonstrate freedom –
Random surveys

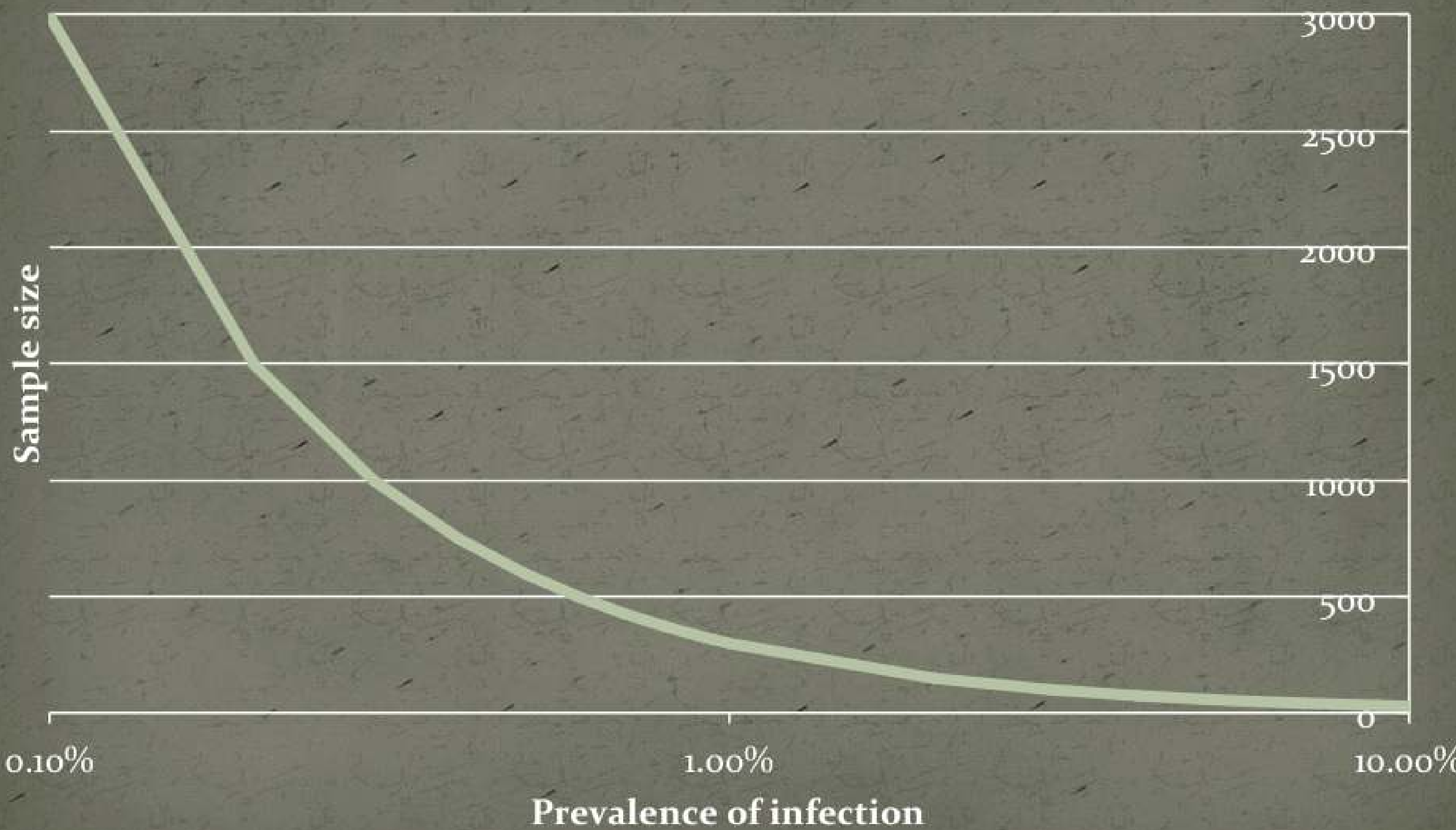
# Random surveys

- The random survey based approach is the most used approach since the years 70's of the 20th century
  - it provide numeric values that per se are considered more objective and more defensible (i.e.: scientific) than any subjective assessment of the risk of disease being absent from the population
  - a quantitative estimation of the confidence of the infection being absent in the population can be easily calculated
  - is the approach requiring the smallest investment in term of resources and veterinary infrastructure

# Random surveys

- The random survey approach is sound when infection/disease is present with a rather high prevalence
- It becomes rapidly insufficient when prevalence tends to become lower, in particular if infection tends to cluster and is not randomly spread in populations, as for instance when mass vaccination is employed

# Number of samples to detect with 95% probability a cartain prevalence of infection



# Random surveys

- Documentation of freedom from highly contagious diseases is thus simple when vaccination is not practiced or where a high proportion of animals in the population are not vaccinated.
- In such cases, the presence of infection is easy to detect; the rapid spread of infection quickly leads to a high prevalence of infection, and the risk of infection is, for all practical purposes, constant across the susceptible population.

# Random surveys

- In such conditions, documentation of FMD freedom is even easier and may not require the use of any active surveillance activities, if a reliable veterinary infrastructure is in place.

# Random surveys

- With FMD, the difficulties arise when vaccination is practiced and a high proportion of the susceptible population is vaccinated. In these conditions:
  - the prevalence of infected herds decreases to a very low level, as does the prevalence of infected animals within the infected herds
  - the infection tends to cluster between and within herds
  - the number of false-positive results in the survey increases considerably (A number of false positive in the surveys is always expected, even in non-vaccinated populations )

# Random surveys

- The overall effect is the possible onset of small endemic foci, which are difficult to detect, in a framework of widespread, randomly scattered animals that falsely test positive. The use of active surveillance therefore becomes necessary.

- So, in summary, we have:
  - Low prevalence
  - Clustering
  - Proportionally high number of false positives

# Random surveys

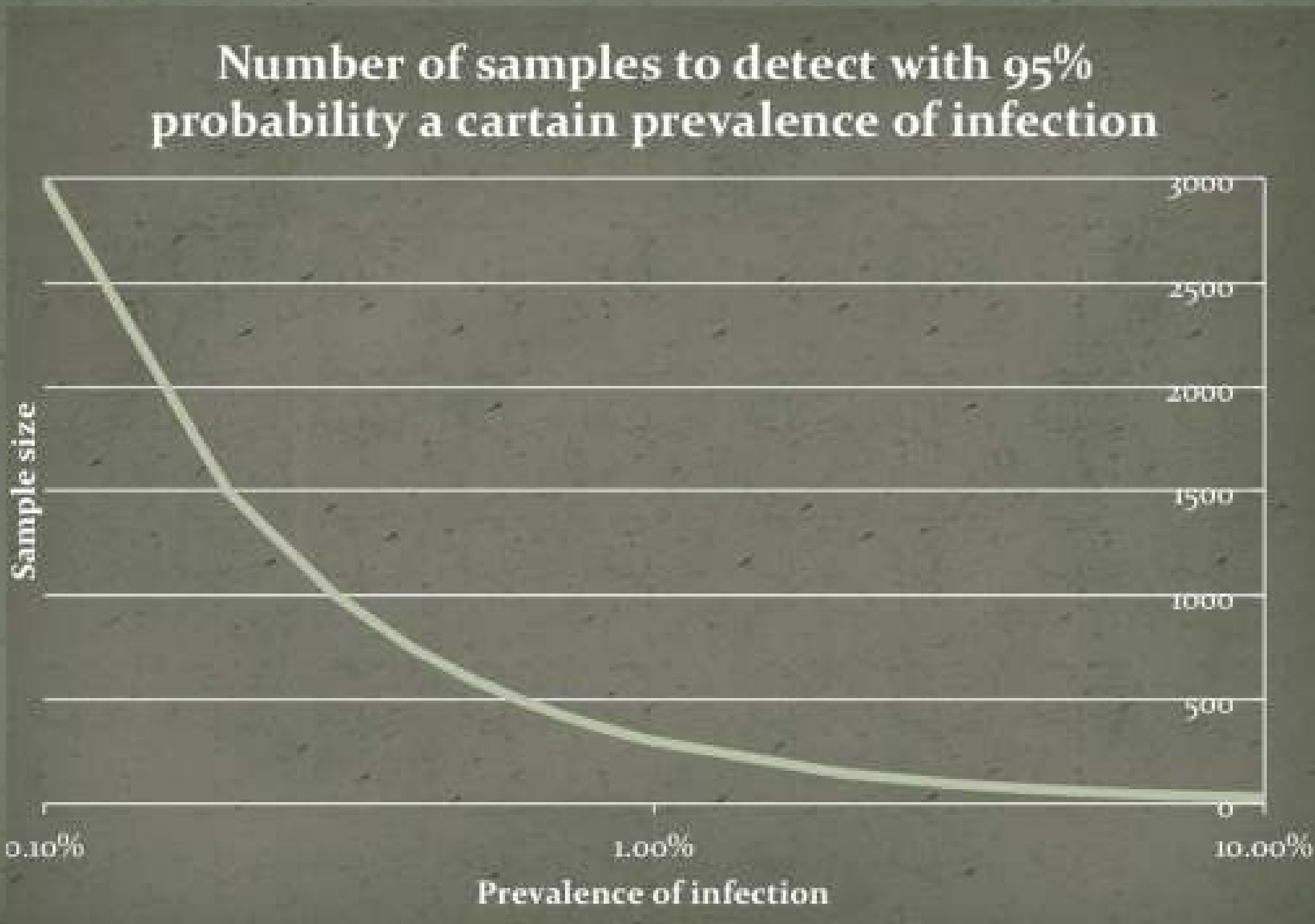
- CLUSTERING
- The way usually followed to overcome this problem was to stratify the random survey to include the sub-population at risk as one of the strata.
- Survey design and type of stratification usually adopted (based on OIE applications for recognition of free status):
  - target prevalence of 1% at the level of epidemiological unit (farm or group of farms)
  - target prevalence of 10% within the epidemiological unit
  - stratification based on geographical criteria
  - when production systems are considered, they are usually within a framework of spatial stratification

# Random surveys

- CLUSTERING
- Considering the size of the populations involved and how tiny usually are the endemic foci, the odds of detecting the infection through a stratified random survey are poor
- The experience of Italy with CBPP in the early $90_{ies}$ is a practical example of the ineffectiveness of random surveys to detect small endemic foci

# Random surveys

- LOW PREVALENCE OF INFECTION



# Random surveys

- FALSE POSITIVE RESULTS
- Possible ways to deal with this problem:
  - assess whether the number of observed positive results is statistically more compatible with false positive results than with true infection
  - perform a detailed investigation in each single herd where positive results are observed and assess whether virus circulation is ongoing or not

# Random surveys

- FALSE POSITIVE RESULTS
- Statistical assessment of the number of positives:
  - Frequentist method
  - Hierarchical Bayesian method

- This type of approach is not considered by the European legislation

# Random surveys

- FALSE POSITIVE RESULTS
- Detailed investigation of all positive herds:
  - The overall effect is to increase the specificity of the diagnosis, aiming at as close to 100% specificity as possible (This is very good indeed, but …)
  - This increase of the specificity has an inherent drawback due to a decrease of sensitivity
  - The decrease of the sensitivity must be compensated by a corresponding increase in the sample size
  - …

# Random surveys

- FALSE POSITIVE RESULTS
- Detailed investigation of all positive herds:
  - …
  - This increase in sample size may rapidly lead to a huge number of samples to be tested [most of the tests and procedures used are independent from each other and, in the context of independent tests, the overall sensitivity is the product of the sensitivities of each procedure applied]


Approaches to achieve and
demonstrate freedom –
RISK BASED SURVEILLANCE

# Risk-based surveillance

- Let's start with an everyday life problem: I am going to the airport and I am a bit late. Where are my car keys? Where did I put them yesterday night?
- I have just 5 minutes to find my keys. I have to possible options to fine them:
  1. The random strategy: I subdivide the volume of my house in 230,000 cubes of 1 cubic dm each, I extract 100 random cubes and inspect the 100 cubes
  2. The targeted strategy: I search in selected places where I think they likely are (on top of the drawer-chest, in the trousers I have put in the laundry basket, etc.)

# Risk-based surveillance

- It is amazing that, in everyday life, nobody would ever dream of adopting a random strategy to search for something (from the car keys when leaving home in the morning, to police investigations), whereas, in the search for animal disease, randomness is usually so highly valued.
- Risk-based surveillance is the most effective way to detect clustered infection and endemic foci.

# Risk-based surveillance

- According to the Terrestrial Code, particular importance should be placed on the targeted collection of data (e.g. based on the increased likelihood of infection in particular localities or species), or on regular and frequent clinical inspection and serological testing of high-risk groups of animals
- In fact, a failure to find infection in a high-risk sub-population (at a given design prevalence) is equivalent to a failure in a random survey with a much lower design prevalence.

# Risk-based surveillance

- Detecting clustered infections and endemic foci is generally important in animal health, for reasons that go beyond the recognition of disease-free status. As already stated, when endemic foci exist, there is always the risk of a new epidemic, due to a change in the more-or-less stable equilibrium (homoeostasis) between the virus and the population, particularly when fluctuations are observed in the level of immune coverage of the animal population.

# Risk-based surveillance

- The first instance in which a risk-based approach was adopted in Italy was in the early 90ies to deal with an incursion of CBPP to Italy:
  - CBPP was highly clustered in a very small area of northern Italy, from which the infection spilled over to farms in the remaining of the country
  - Outside the endemic focus, the prevalence was very low (less than 50 infected farms in 3 years)
  - The test available for the diagnosis at the time had a very poor specificity and an even poorer sensitivity

# Risk-based surveillance

- The eradication was based on a risk based surveillance system, based on:
  - detection of the infection at slaughterhouses (slaughtered and culled animals had the highest probability of including some infected animals)
  - Serological testing of traded animals only (trade of animals was the main way of spread of the infection out of the endemic area)

# Risk based surveillance

- Now, risk-based surveillance is foreseen in the EU legislation for the documentation of the free status for *Echinococcus multilocularis*
- The general approach and the statistical calculations are described in a publication on the EFSA journal (and a companion Excel file for calculations)
- A description of the use of risk-based surveillance for documenting FMD free status has been published on the OIE Scientific and Technical Review

# Risk-based surveillance

- When designing a risk-based surveillance system, the crucial component for the success of the system is the proper identification of risk factors


Identification of risk factors

# Identification of risk factors

- Failure to recognize the PROPER risk factors in "risk base surveillance" may be conducive to very severe problems
- The epidemiological characteristics liable to play the role of risk factors are intrinsic to each specific environment
- They should be defined consequent to an accurate retrospective analysis of the disease outbreaks actually occurred

# Identification of risk factors

- Possible risk factors may be the size of herds, animal movements, age structure of herds, economic conditions and primary source of subsistence of the farmer, production system, intensity of trade and source of supply of farm, etc.
- Risk factors, therefore, MUST be identified on the basis of the local characteristics of both animal husbandry and other local anthropological, social, economical factors

# Identification of risk factors

- The identification of herds at risk SHOULD NOT be based on theoretical check-lists valid all over EU and applied to herds, which may pass or not pass the exam
- The identification of risk factors used in planning “risk based surveillance” has to be based on a proper application of the scientific method

# Identification of risk factors

- It should never rely on either of:
  - “theoretical” / “literature” / “expert” sources
  - associations detected in the field without any sound biological meaning
- On the contrary, it should be based as far as possible on both

# Identification of risk factors

1. A theoretical hypothesis of a set of putative risk factors has to be formulated
2. Each putative risk factor has to be challenged with field data following
   1. a deep analysis of available historical data on the past epidemics and outbreaks
   2. a clearly defined and statistically sound procedure that takes into account also possible confounding factors
3. Only risk factors that are not refuted by the challenge against field data will be used to plan the risk based surveillance component

# Identification of risk factors

- Once risk factors are identified, all holdings sharing the risk factors identified in the investigation performed during the epidemic will be the targeted risk sub-populations

# An example of identification of risk factors

- In the Italian region of Abruzzi, an evaluation of risk factors for bovine TB has been performed in 1996 through a retrospective study of outbreaks occurred in the period 1982-1992
- The study was designed as a case-control study: each infected animal detected during the study period was matched to a healthy animal from a qualified herd of the same province and the presence/absence of exposure to a pre-defined set of risk factors was investigated in both cases and controls
- …

# An example of identification of risk factors

- A set of potential risk factors was defined on the basis of published literature and of common sense
- Potential risk factor NOT associated with the presence of infection was:
  - Grazing (in contrast to what observed elsewhere in Europe and also to the results of a similar study performed for bovine brucellosis in the same region)
- …

# An example of identification of risk factors

- Potential risk factors SIGNIFICANTLY associated with the presence of infection were:
  - The behavior of the veterinary services: animals in districts where delays in the annual testing of healthy herds and in the retesting of infected herds had more chances of being infected
  - Animals imported from other Italian regions or from abroad were more frequently infected than autochthonous animals
  - Animals of dairy breeds were more frequently infected than beef animals
  - …

# An example of identification of risk factors

  - …
  - Chances of infection increased with the age of the animal
  - Chances of infection increased with the size of the herd
- The results of the study were able to identify the herds with the highest chances of becoming infected in the specific environment and husbandry conditions of the region of Abruzzi
- Any extrapolation from the results obtained in the study to other regions would have been completely unwarranted unless confirmed by a specific local study

# An example of identification of risk factors

- From this study it is clearly evident that any error in the identification of risk factors could have catastrophic consequences on the ability to detect the foci of infection
- For example, a surveillance targeted on grazing herds (based on UK experience for bovine TB) would be unable to promptly detect the infection in Abruzzi conditions


In conclusion

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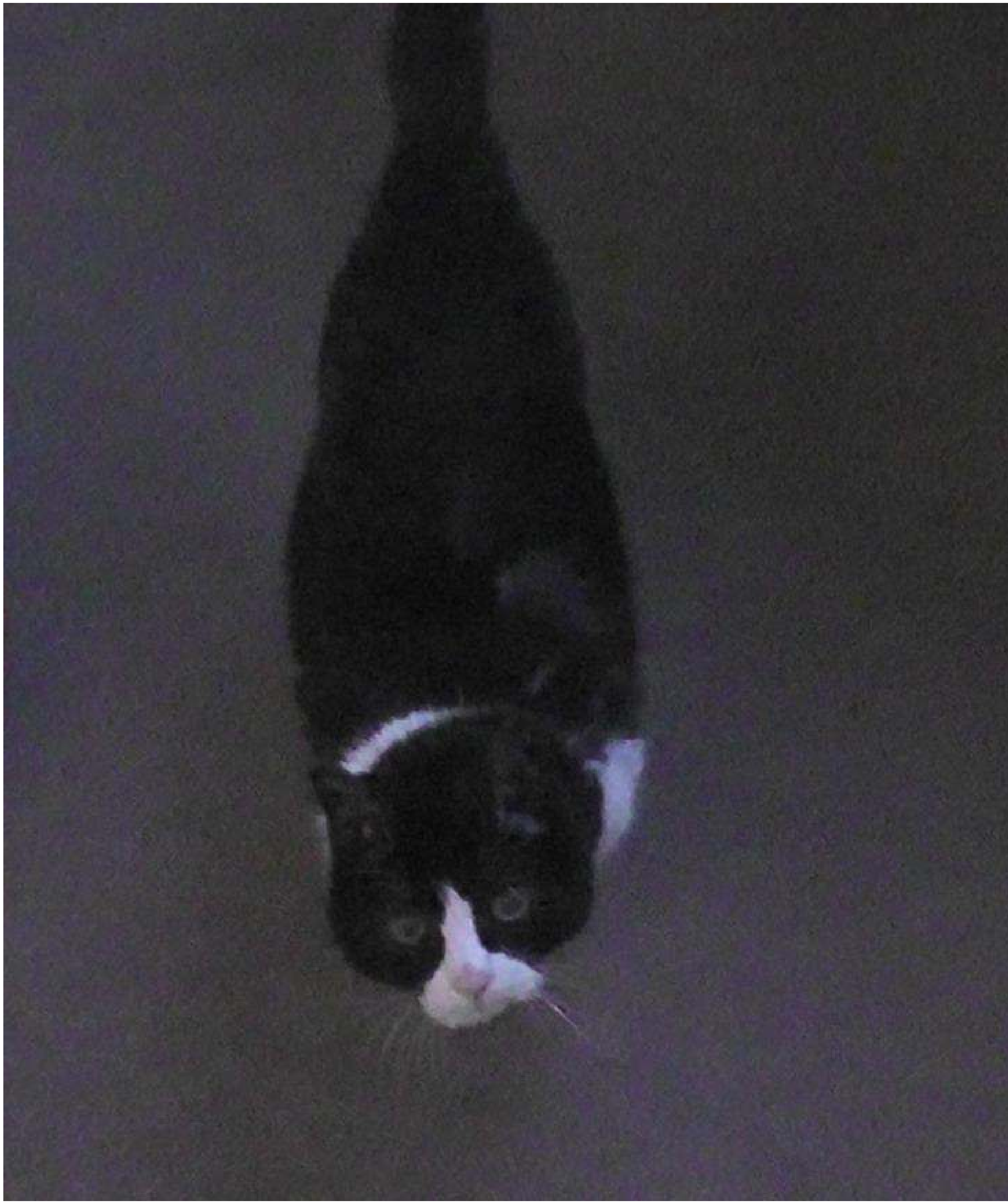
- Risk-based approach is able to provide a much more sensitive surveillance system than the random approach, with the use of a lower sample testing.
- It is much less resource-intensive, but is much more knowledge-intensive: a great deal of information is needed for the proper identification of the risk factors and the design of the system
- In any case, design prevalence and confidence level are far from being the only pillars of the *confidence* in the absence of disease

# In conclusion

- Other elements are crucial in giving confidence in the results of the risk-based surveillance system:
  - existence of an effective notification system and the documentation of suspects not confirmed
  - existence of an effective passive/clinical surveillance system with access to laboratory confirmation
  - existence of an effective early detection and early warning system
  - …

# In conclusion

- Other elements are crucial in giving confidence in the results of the risk-based surveillance system:
  - …
  - in case of the use of vaccines, data and documentation on the effectiveness of the vaccination system and THE USE OF THE DETECTED SHORTCOMINGS as risk factors for the surveillance
  - existence of a reliable laboratory network
  - proper follow up of all positive results detected in any component of the surveillance system (including the passive component)



This was
my cat

Thank you
for the
attention

# For any further information


- V. Caporale, A. Giovannini, C. Zepeda. Surveillance strategies for foot and mouth disease to prove absence of disease and absence of viral circulation. Rev. sci. tech. Off. int. Epiz., 2012, 31 (3), 747-759
- European Food Safety Authority; Scientific and technical assistance on *Echinococcus multilocularis* infection in animals. EFSA Journal 2012;10(11):2973. [22 pp.] doi:10.2903/j.efsa.2012.2973. Available online: www.efsa.europa.eu/efsajournal
- P.A.J. Martin, A.R. Cameron, M. Greiner. Demonstrating freedom from disease using multiple complex data sources 1: A new methodology based on scenario trees. Preventive Veterinary Medicine 79 (2007) 71–97
- A. Giovannini, S. Bellini, M.D. Salman, V. Caporale. Spatial risk factors related to outbreaks of contagious bovine pleuropneumonia in northern Italy (1990-1993). Rev. sci. tech. Off. int. Epiz., 2000, 19 (3), 764-772