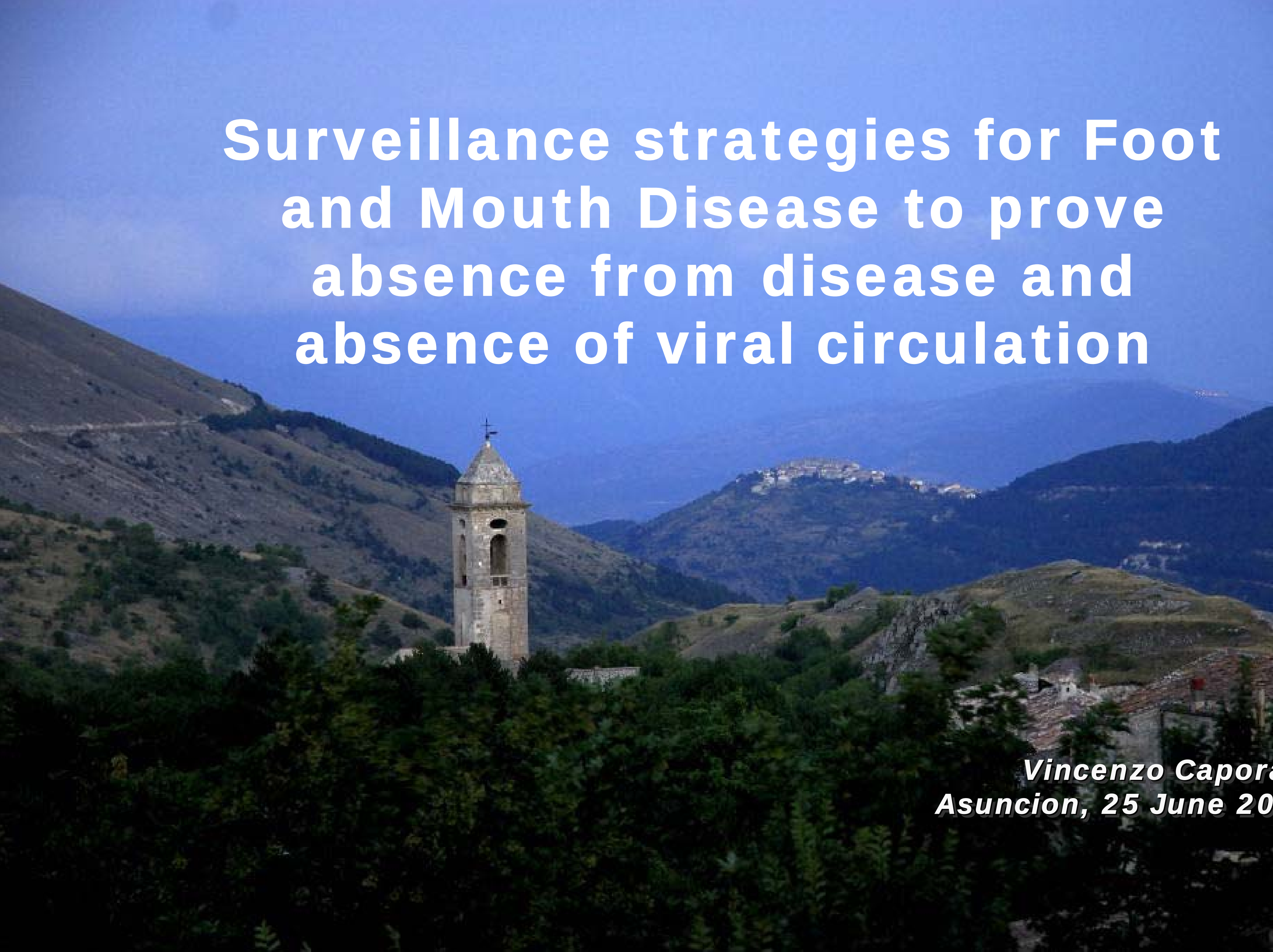
Surveillance strategies for Foot and Mouth Disease to prove absence from disease and absence of viral circulation



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Introduction

- In FMD control the need to prove absence from disease and absence of viral circulation arises mainly when one has

  1. To close an epidemic whether or not emergency vaccination has been employed as a control tool

  2. To assess whether mass vaccination can be phased-out in the process of eradication

  3. To document the health status of a population in relation to trade

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 demonstrate freedom from infection veterinary services have to search actively for any evidence of its presence and exclude it
- The search for infection(s) is one of the main routine tasks of the veterinary services and is performed using a number of approaches and strategies
- The only difference between countries practicing and not practicing vaccination is that
  - in the absence of vaccination the presence of infected animals will eventually lead to virus spread, which makes virtually impossible not to detect the presence of the infection
  - in massively vaccinated populations the presence of a single or a few infected animals might not result in virus circulation and the infection might either be undetected or die off naturally

Approaches in the demonstration of freedom

1. Random surveys with analysis of the survey results using classical statistics

2. Random surveys with analysis of the survey results using hyerarchical Bayesian models

3. Analysis of the relevant components of risk targeted surveillance system


Random survey

Random survey

- 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
- Non-random surveillance activities (e.g. passive surveillance, targeted surveillance, checks on traded animals) were only considered able to provide further non-quantifiable elements ***ancillary*** to the results of the random survey

Random survey

- 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

Random survey
Unvaccinated populations

- The documentation of freedom from FMD is easier when vaccination is not practiced or when a high proportion of unvaccinated animals is present in the population

- In such cases, the presence of FMD infection is easier to detect
  - the spread of the infection rapidly leads to high values of prevalence of infection and disease
  - the risk of infection is for all practical purposes constant across the susceptible populations

- The documentation of FMD freedom might not require the use of any active surveillance activity, if a solid veterinary infrastructure is in place

Random survey
Vaccinated populations

- When vaccination is practiced and a high proportion of the susceptible population is vaccinated

1. The number of false positive in the surveys increases considerably
2. The prevalence of infection between and within herds decreases to very low levels
3. The infection tend to cluster between and within herds

Random survey
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 survey

False positive results

STATISTICAL ASSESSMENT OF THE NUMBER OF POSITIVE

- **Frequentist method** (Cameron and Baldock, 1998)
- **Hyerarchical bayesian method** (Suess et al., 2002; Hanson et al., 2003; Branscum et al., 2004; Mintiens et al., 2005)

Random survey

False positive results

DETAILED INVESTIGATION IN 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
- 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]

Random survey

False positive results

- STATISTICAL ASSESSMENT OF THE NUMBER OF POSITIVE
  - **Frequentist method** (Cameron and Baldock, 1998)
    - ✓ The method gives meaningful results when the difference between the expected prevalence of infection and the expected number of non-specific positive test results is wide (e.g., FMD in an unvaccinated population)
    - ✓ With the levels of infection that might be likely expected in vaccinated populations, the discrimination between false positives and infected herds is often impossible

Random survey
False positive results

- STATISTICAL ASSESSMENT OF THE NUMBER OF POSITIVE
  - **Hyerarchical bayesian method** (Suess et al., 2002; Hanson et al., 2003; Branscum et al., 2004; Mintiens et al., 2005)
    - advanced statistical skills are required to apply HBM properly
    - detailed information has to be collected on each single animal tested in the survey (herd of origin of each tested animal and test results obtained by each animal in each single test applied)
    - accurate prior information is required on the probability distribution of the prevalence of infection within an infected herd
    - **the method is reliable when the expected prevalence within infected herds is high**; therefore it is far less effective in analyzing data from vaccinated than from non-vaccinated populations

Random survey
Clustering of infection

- When vaccination is practiced, the infection tend to cluster between and within herds, with the possible occurrence of endemic foci of infection

- 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

Random survey
Clustering of infection

- Survey design and type of stratification usually adopted:
  - 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 survey
Clustering of infection

- Considering that:
  - the number of units within each stratum varies from thousands to hundreds of thousand, and animals are in the millions
  - the infection is not randomly distributed among the various strata, but usually one single production system (and usually a marginal one) is involved
  - the infection is not randomly distributed within the affected subpopulation

- the odds of detecting the infection through a stratified random survey are poor indeed


ANALYSIS OF THE
RELEVANT COMPONENTS
OF A RISK TARGETED
SURVEILLANCE SYSTEM

Analysis of the relevant components of a risk targeted surveillance system

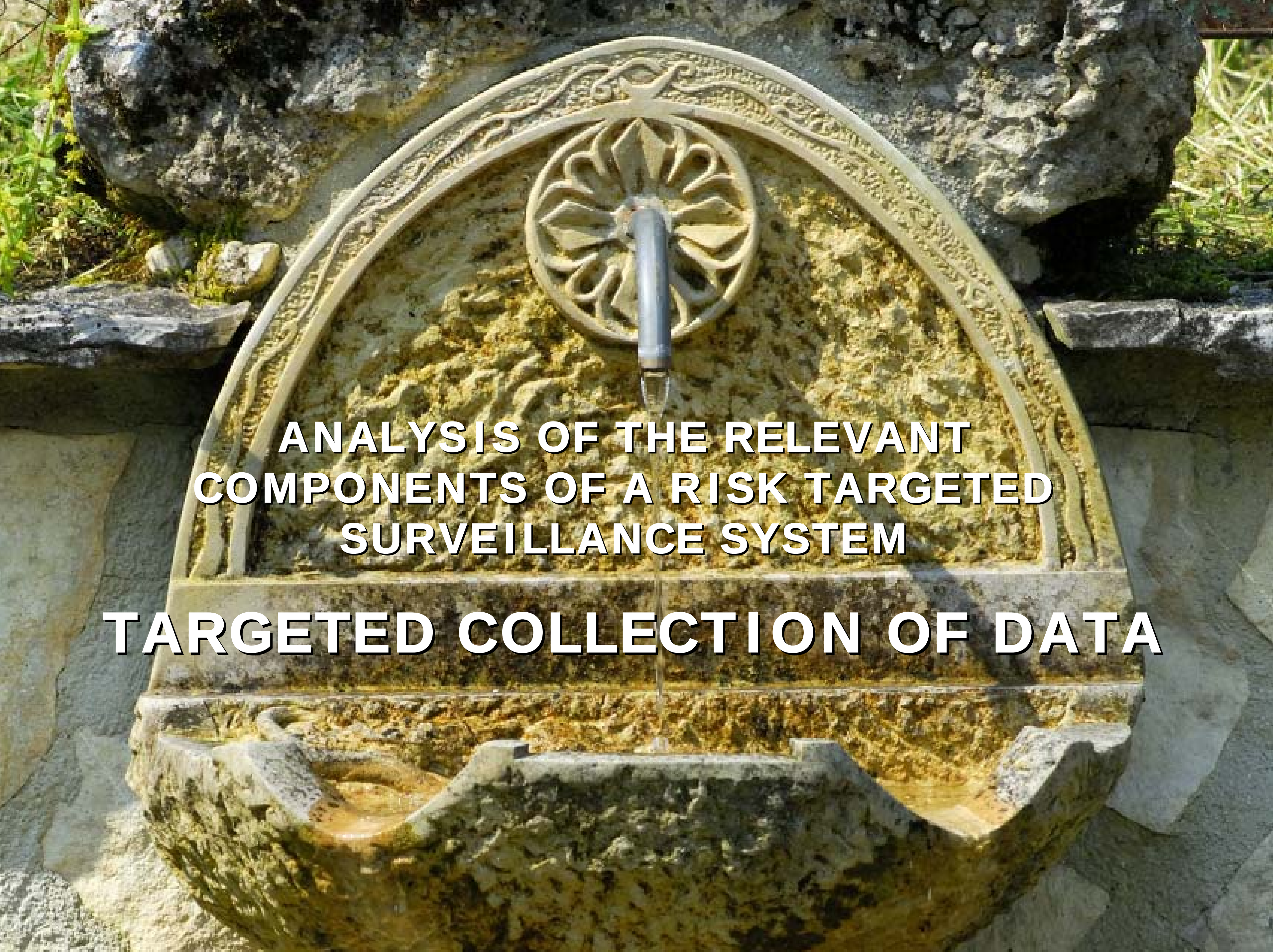
- A number of different activities are conducive to effective data collection IF used in the framework of a sound risk targeted ongoing surveillance system

- Random surveys are/should be but one component of a sound risk targeted ongoing surveillance system

- In general, the sensitivity of the information collected by **non-random** sources
  - is greater than that collected through random surveys
  - is usually poorly exploited in the process of documenting disease freedom

Analysis of the relevant components of a risk targeted surveillance system

- The pillars of the surveillance system of a country wishing to be confident of being and be recognized free from FMD
  1. Targeted (risk based) ongoing surveillance
  2. Early detection system
  3. Disease reporting/notification system
  4. Monitoring of vaccination



ANALYSIS OF THE RELEVANT COMPONENTS OF A RISK TARGETED SURVEILLANCE SYSTEM

TARGETED COLLECTION OF DATA

Analysis of all relevant surveillance components in place

Targeted collection of data

- Regular and frequent clinical inspection of animals in all possible circumstances and places has the highest value in detecting the presence of FMD occurrence, as indicated also by the OIE Terrestrial Animal Health Code
- Ongoing control and testing should be concentrated in high-risk subpopulations
- Serology based targeted sampling of high-risk herds increases confidence in the absence of infection and has a better cost/effectiveness ratio than random sampling

ANALYSIS OF THE RELEVANT COMPONENTS OF A RISK TARGETED SURVEILLANCE SYSTEM

PROPER IDENTIFICATION OF RISK FACTORS

Analysis of all relevant surveillance components in place

Proper 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 to be identified and investigated as possible risk factors are intrinsic to each specific environment
- They should be defined consequent to an accurate retrospective analysis of the disease outbreaks actually occurred
- It is historically proven that when this type of approach is used in mass vaccinated populations, the main risk factors emerging is poor vaccination coverage.

Analysis of all relevant surveillance components in place

Proper identification of risk factors

- Other 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

- The identification of risk factors used in planning “risk based surveillance” has to be based on a proper application of the scientific method

Analysis of all relevant surveillance components in place

Proper identification of risk factors

- It should never rely **solely** on
  - "theoretical" / "literature" / "expert" sources
  - associations detected in the field without any sound biological meaning

Analysis of all relevant surveillance components in place

Proper 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
   a. a deep analysis of available **historical data** on the past epidemics and outbreaks
   b. 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

Analysis of all relevant surveillance components in place

Proper 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


ANALYSIS OF THE RELEVANT COMPONENTS OF A RISK TARGETED SURVEILLANCE SYSTEM
EARLY DETECTION SYSTEM

Analysis of all relevant surveillance components in place

Early detection system

- It is of crucial importance to REACH AND MAINTAIN freedom from an infection (but also to build up a strong confidence into trading partners)

- The results of any survey are valid only for the point in time in which the survey was performed

- A system operating CONTINOUSLY on the basis of clear and sound procedures finalized to early detection - and early reaction in case of infection/disease occurrence - provides a more solid and durable confidence on the level of risk for all stakeholders, including trade partners

Analysis of all relevant surveillance components in place

Early detection system

- An early detection system should, according to the OIE – TAHC
  a. Have a clear *national* chain of command
  b. Provide representative coverage of target animal populations by field services and assure timely reporting to the Veterinary Services
  c. Have the ability to undertake effective disease investigation and reporting
  d. Have access to laboratories capable of diagnosing and differentiating relevant diseases
  e. Provide training for detecting and reporting unusual animal health incidents to veterinarians and others involved in handling animals
  f. Define legal obligations of private veterinarians in relation to the Veterinary Authority

ANALYSIS OF THE RELEVANT COMPONENTS OF A RISK TARGETED SURVEILLANCE SYSTEM

DISEASE REPORTING

Analysis of all relevant surveillance components in place

Disease reporting

- Disease reporting is the central hub of any surveillance system, in particular when vaccination is not applied

- Effective and easily accessible laboratory support is a mandatory component of any reporting system

- Laboratory confirmation has to be based upon tests that have a high specificity, reliable sensitivity

- The documentation of results of passive surveillance systems should never be restricted to confirmed cases, but all instances that prompted an investigation should be *properly* reported and documented

Analysis of all relevant surveillance components in place

Disease reporting

- Information on the occurrence of those conditions presenting similar symptoms to FMD, which must be considered in the differential diagnosis must be collected for a possible quantitative evaluation of the performance of the passive surveillance component

ANALYSIS OF THE RELEVANT COMPONENTS OF A RISK TARGETED SURVEILLANCE SYSTEM

VACCINATION MONITORING

Analysis of all relevant surveillance components in place

Vaccination monitoring

- To assess the vaccination campaign in relation to its objectives (e.g. population coverage, level of herd immunity, proper vaccine distribution and administration, etc.)
- To assess the reliability of information provided by vaccinators
- To detect and analyze possible shortcomings and address them effectively and timely
- To provide the information to assess risk in relation to the consequence of the introduction of the infection in the population
- To provide part of the information needed to target the “risk based surveillance” properly

Conclusions

1. The main goal of a FMD surveillance system is the management of the control of the disease. The proof of the absence of disease and absence of viral circulation is “consequential”

2. The use of random surveys as the main mean to prove absence of disease/infection when FMD occurs at very low level of prevalence has severe limitations, in particular in mass vaccinated populations

3. Ongoing targeted risk based surveillance is he method of choice in case of low prevalence and clustering as in case of mass vaccinated populations

Conclusions

4. When risk based surveillance systems are implemented the use of a proper method to identify risks is mandatory to avoid serious drawbacks

5. Surveillance system should involve all stakeholders in an interactive manner

6. Field and laboratory veterinarians should operate in an integrated mode and have prompt reciprocal access to data

7. No effective surveillance can exist in the absence of a solid veterinary service infrastructure diffusely present in the territory and operating as an integrated system

THANK YOU