

# A risk assessment of CWD spread in a EU country

C

Ru  
18<sup>th</sup> Annual Meeting of the TSE  
EURL

Torino, 13<sup>th</sup> September 2019



Project funded by Ministry of Health in 2016 aiming at:

- 1) Evaluating the risk of spread of the CWD in a free country.
- 2) Evaluating the Italian Surveillance System.
- 3) Knowing the hunter's awareness of the risk.

## To achieve the goals:

 Literature Systematic review

 Cervids genotyping

 Survey on hunters perception

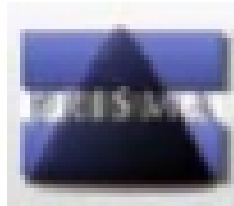
 Official database consultation

 Data collection and monitoring evaluation

 Stochastic modelling thanks to a fault tree analysis

# Material & Methods 1/7

## Systematic Review to collect information about the spread of the disease



Shamseer L, Moher D, Clarke M, Gherzi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ*. 2015 Jan 2;349(jan02 1):g7647.

Section and topic	Item No	Checklist item
<b>ADMINISTRATIVE INFORMATION (OMISSIS)</b>		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
<b>INTRODUCTION</b>		
Rationale	6	Describe the rationale for the review in the context of what is already known: <b>Prima di intraprendere un percorso di valutazione del rischio è essenziale conoscere bene tutte le componenti che ne possono influenzare i singoli passaggi. In questo caso la revisione sistematica è stata condotta per raccogliere in un unico contenitore tutti fattori che possono influenzare l'ingresso, la permanenza e la diffusione della PrP<sup>ewd</sup> in una popolazione libera da malattia.</b>
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO): <b>L'obiettivo generale era quello di revisionare sistematicamente la letteratura per identificare e aggiornare le evidenze scientifiche che dimostrano come la CWD si comporta nelle popolazioni di cervidi e come può essere esportata in luoghi che ne sono privi. Il metodo PICO risulta in questo caso così declinato:</b> <ol style="list-style-type: none"> <li>1) Population= popolazione di cervidi;</li> <li>2) Intervention=CWD con relativi fattori di rischio e percorso diagnostico;</li> <li>3) Control=popolazione esente da malattia;</li> <li>4) Outcome=Valutazione del rischio di introduzione della malattia in Paese apparentemente indenne.</li> </ol>
<b>METHODS</b>		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review: <b>Sono stati considerati eligibili tutti gli articoli (in inglese e in italiano) che riconducessero alle definizioni stabilite a priori: epidemiologia della CWD, trasmissibilità della CWD, fattori di rischio per la CWD, risk assessment, exposure assessment, suscettibilità genetica alla CWD, resistenza del prione nell'ambiente. Tutti i tipi di studio sono stati inclusi;</b>
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage: <b>Medline, google scholar, EFSA.</b>
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated: <b>Dopo vari tentativi di restringere il campo di ricerca a quello prettamente epidemiologico, la chiave più efficace per includere il maggiore numero di lavori possibile è stata: "chronic wasting disease"[All Fields]</b>
Study records:		

CWD <and> Risk  
<or> Risk factors  
<and> spread

# Material & Methods 2/7

Genotyping (N=98)

Haplo type	15 Val <i>gTg/gCg</i>	21 Val <i>gtC/gtG(T)</i>	59 Gly/Ser <i>Ggc/Agc</i>	78 Gln <i>caG/caA</i>	79 Pro <i>ccC/ccT</i>	98 Thr/Ala <i>Acc/Gcc</i>	136 Ala <i>gcT/gcC</i>	168 Pro/Ser <i>Cca/Tca</i>	226 Gln/Glu <i>Cag/Gag</i>
1	T	C	G	G	C	A	T	C	C
2	C	-	-	-	-	-	-	-	-
3	-	G	-	-	-	-	-	-	-
4	-	T	-	-	-	-	-	-	-
5	-	-	A	-	-	-	-	-	-
6	-	-	-	A	-	-	-	-	-
7	-	-	-	-	T	-	-	-	-
8	-	-	-	-	-	G	-	-	-
9	-	-	-	-	-	-	-	T	-
10	-	-	-	-	-	-	C	-	G
11	-	-	-	-	-	-	C	-	C
12	-	-	-	-	-	-	T	-	G

# Material & Methods 3/7

## Survey on hunters perception (N=30)

Data: \_\_\_/\_\_\_/\_\_\_\_\_

Intervistatore: \_\_\_\_\_

1. Hai mai sentito parlare di una malattia dei cervi chiamata Chronic Wasting Disease, o Malattia del deperimento cronico? SI NO

(Spiegare nel caso dicessero no: è una malattia infettiva che colpisce i cervi ed è diffusa in USA e Canada e, dal 2016, in Nord Europa.)

2. Se sì, sai quali altre specie possono essere colpite oltre al cervo?

-----  
-----  
-----

3. Se sì alla 1, sai che problema potrebbe causare alle popolazioni di cervi?

-----  
-----  
-----

4. Sai come si trasmette?

-----  
-----  
-----  
-----

# Material & Methods <sup>4/7</sup>

Searching deer population data

 Import:

 **Italian population:** <http://www.isprambiente.gov.it/it>.

# Material & Methods 5/7

## Evaluation of the surveillance system

- $$M = \frac{\left(1 - \alpha \frac{1}{n'}\right) * \left(\frac{N-1}{2}\right)}{Se} \quad \text{(Cannon \& Roe, 1982)}$$

M= maximum number of escaped animals

M= maximum number of escaped animals

$\alpha$  = type 1 error  
n' = number of negatives

N = whole population

Se = diagnostic sensitivity

Se = diagnostic sensitivity

$$dSe = 1 - \left(1 - \sum \frac{dSe}{N}\right)^{P * M} \quad \text{(Viljugrein H., et al., 2018)}$$

dSe = diagnostic sensitivity for single test

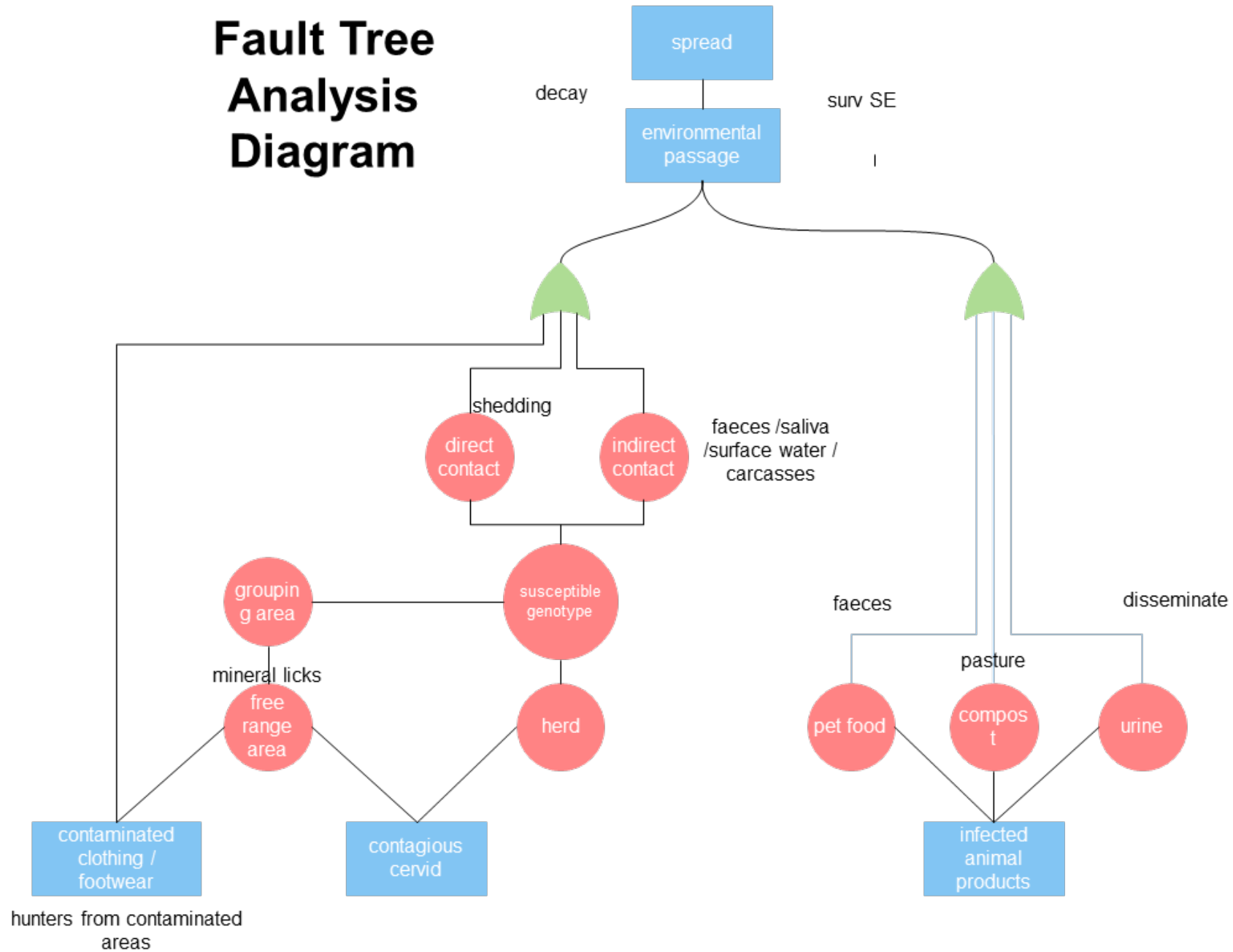
N = whole population

P = design prevalence



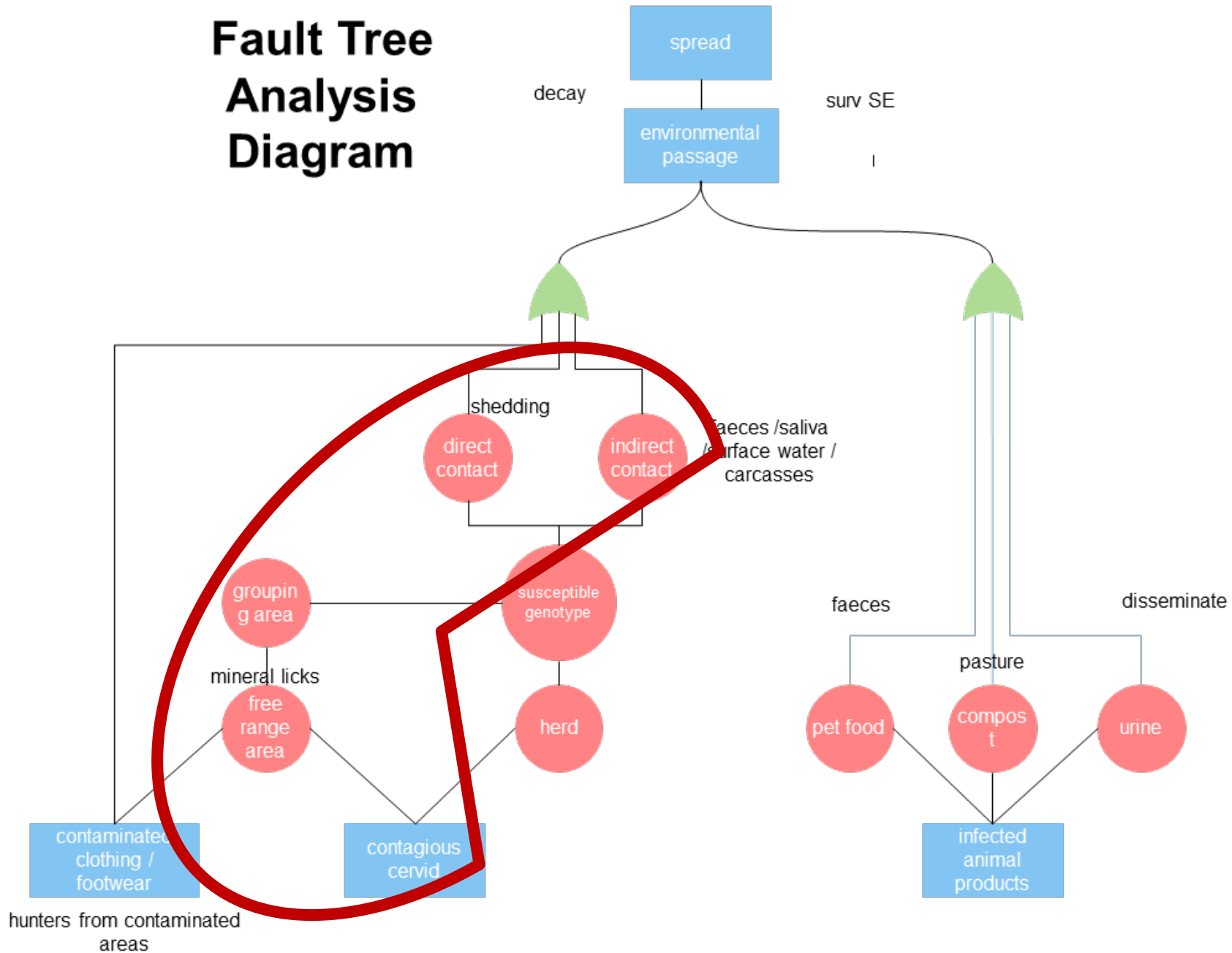
# Material & Methods 6/7

## Fault Tree Analysis Diagram



# Material & Methods 6/7

## Fault Tree Analysis Diagram



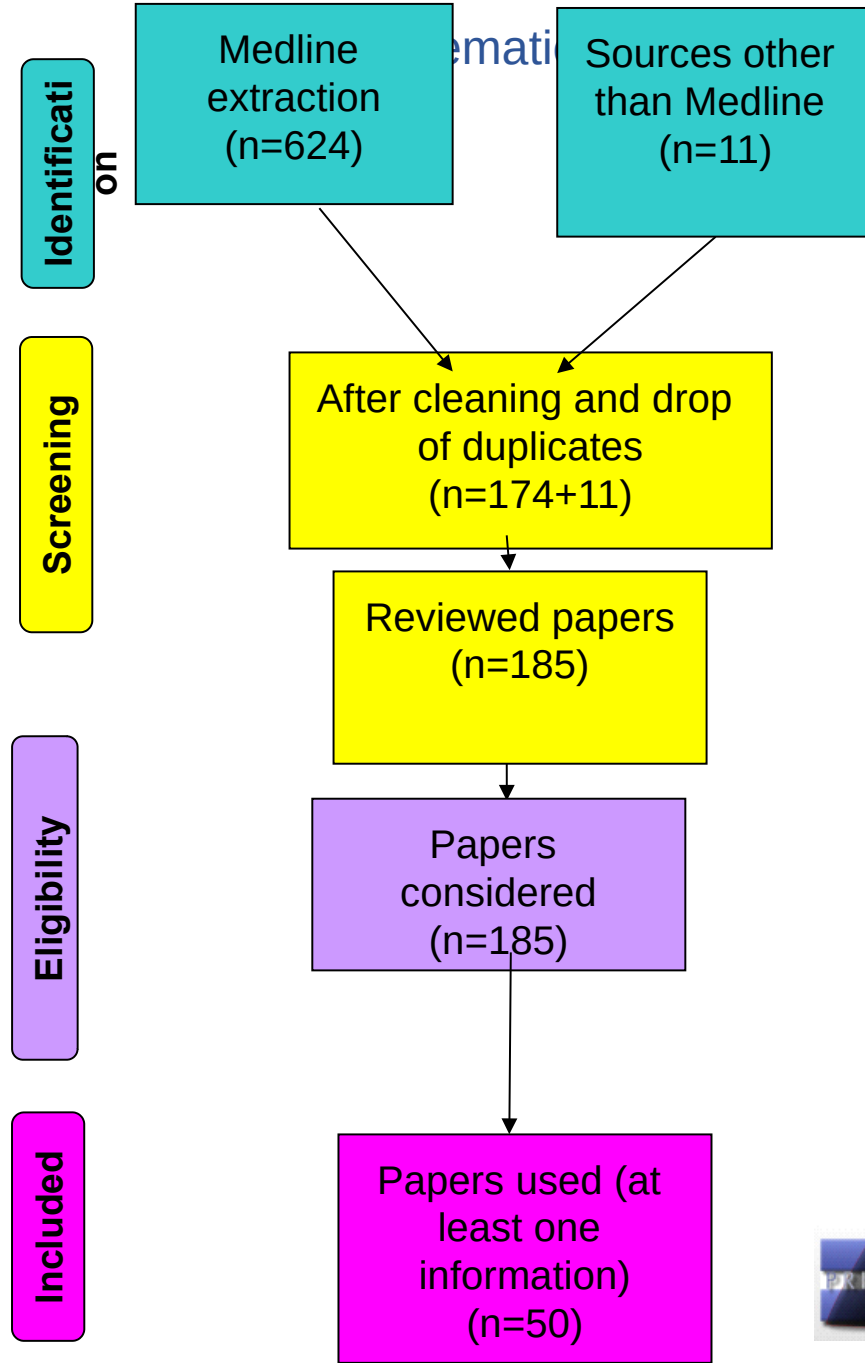
# Material & Methods 7/7

## Stochastic import risk model

### 1. Introduction of an infected animal in a free-range area:

- C1) N° of imported animals from Norway: **N=1/2 years**
- C2) Prevalence of disease in Norway: **P=0.05% (CI95% 0.03-0.07), Beta(38394, 20)**
- C3) N° of infected animals introduced in a free-range area: **C1\*C2**
- C4) N° of autochthonous animals: **67788**
- C5) Area for free ranging animals: **54000 Km<sup>2</sup>**
- C6) Density (heads/Km<sup>2</sup>): **C4/C5**
- C7) Density (heads/Km<sup>2</sup>) of infected animals: **C3/C5**
- C8) Probability of at least one head/ Km<sup>2</sup> in a free-range area: **1-Poisson(C6,0)**
- C9) Probability of at least one infected head/ Km<sup>2</sup> in a free-range area: **1-Poisson(C7,0)**
- C10) Deer home-range: 50 Km<sup>2</sup>
- C11) Probability of contact between a deer and an infected head / Km<sup>2</sup>:  
$$1-[(1-C8)^{C10} * (1-C9)^{C10}]$$
- C12) Percentage of susceptible animals: 90%, Beta(91,9)
- C13) Transmission rate: 3.26%, Beta(524,15507)
- C14) Probability of an effective contact/year:  $(1-(C11*C12*C13))$
- C15) N° of contacts nose-to- nose/year:  $(C7*C10)*C14$

# Results <sup>1/7</sup>



# Results <sup>2/7</sup>

## genotyping

In the red deer PRNP, one single-nucleotide polymorphism (SNP) encoding amino acid change was identified: Q226E. Silent mutations were found at codons 78 and 136. All these polymorphisms were already reported by Peletto et al. (2009) in Italian red deer.

Four haplotypes can be inferred:

- the wild-type haplotype, with a frequency of 53.8%;
- two haplotypes with the silent mutations 78 and 136 (5.8% and 38.5%, respectively);
- the haplotype with the 226E allele (1.9%).

# Results <sup>3/7</sup>

Survey on hunters perception

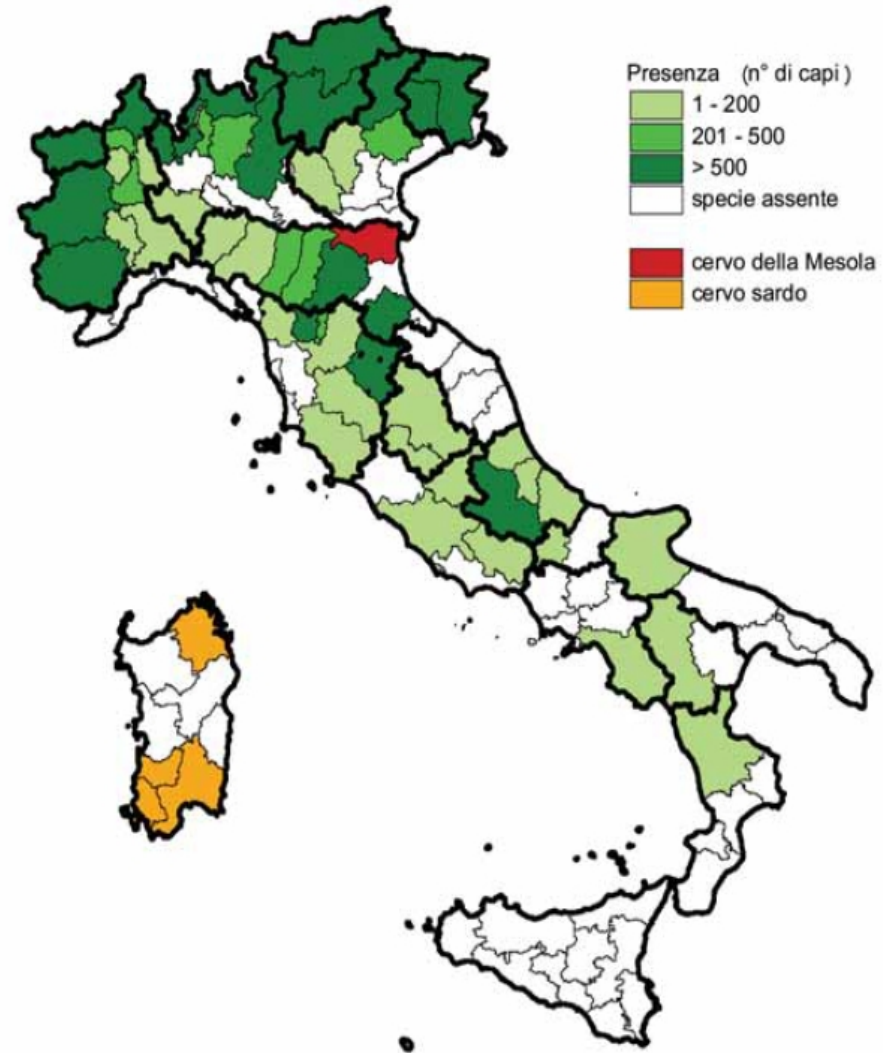
## Questionnaire:

Very unknown disease!

- Only 26.7% knows the existence of a neurological disease affecting cervids!
- 100% of hunters uses the same clothes and instruments both in Italy and abroad (included USA);
- 93% of hunters leaves the offal at the kill site;
- No use of artificial salt licks.

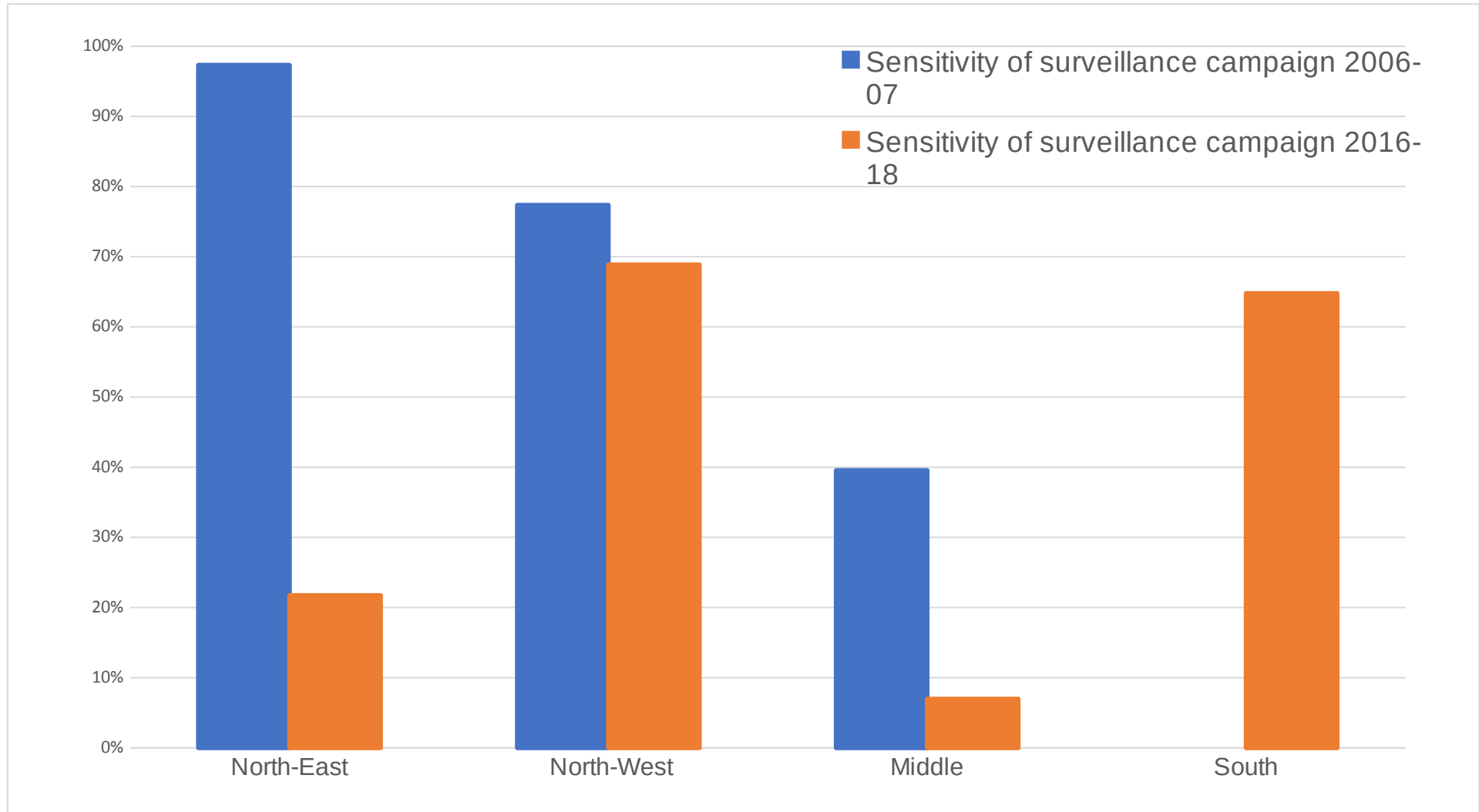
# Results <sup>4/7</sup>

Geographical distribution of deer population



# Results <sup>5/7</sup>

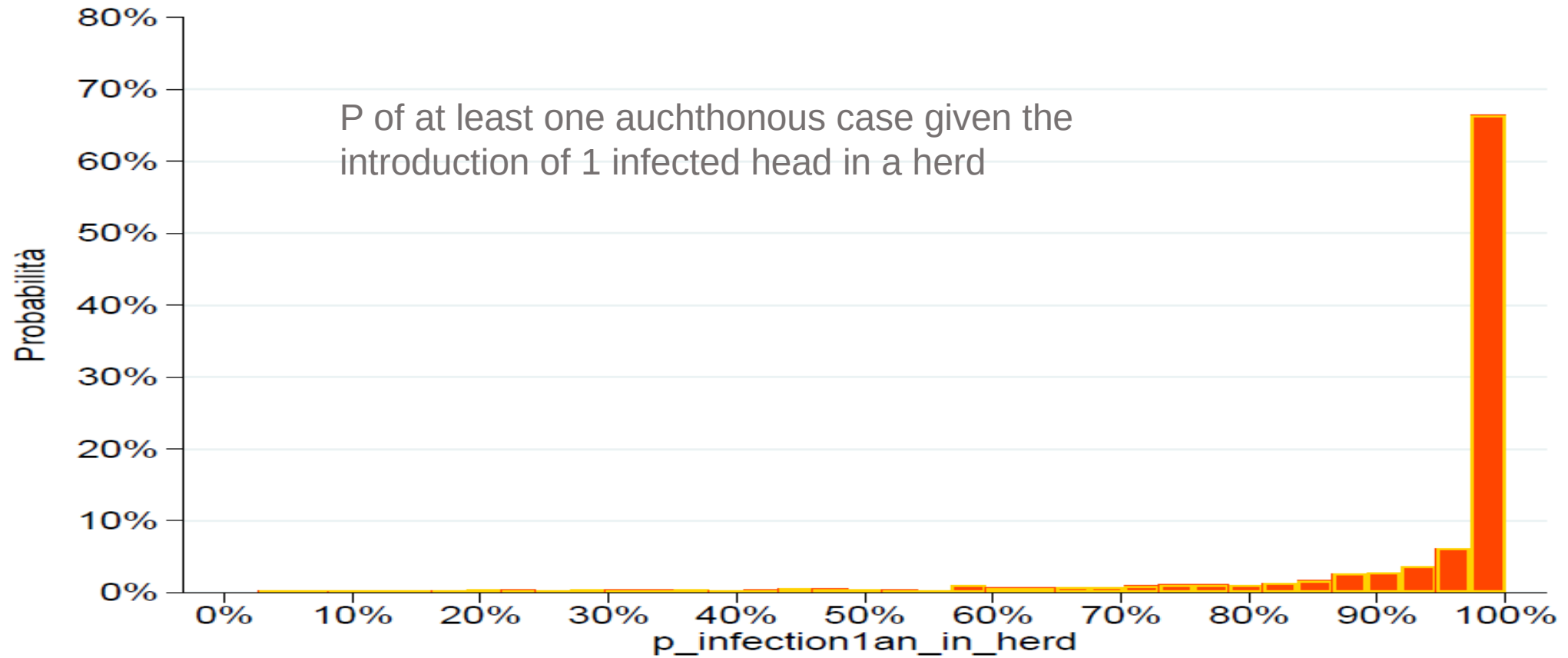
## Surveillance system sensitivity





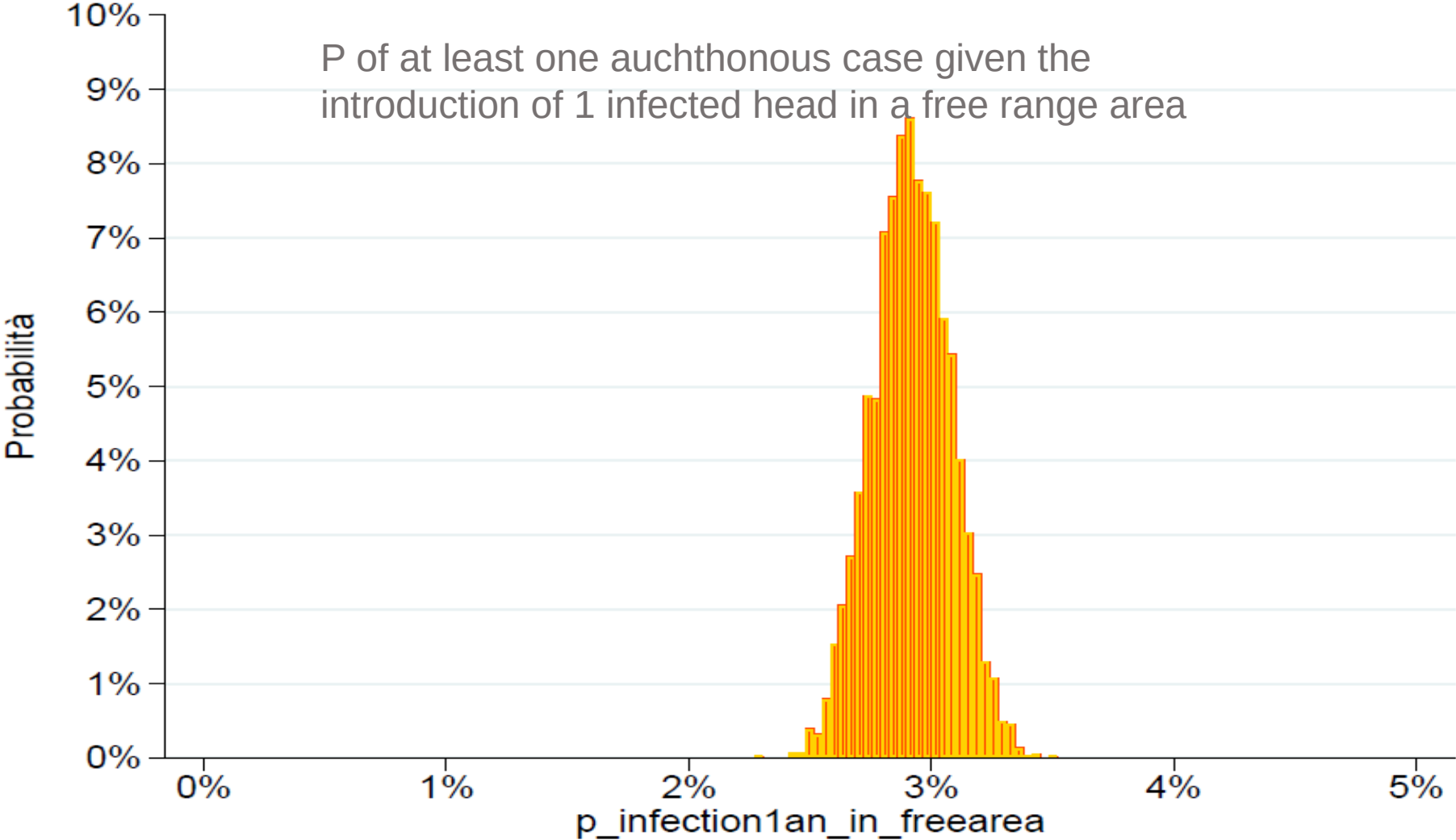
# Results <sup>6/7</sup>

Probability distribution



# Results 7/7

Probability distribution



# Conclusions

- Great effort for data search and too many assumptions for the model (ie: uncertainty)
- High probability of spreading if disease enters Italy.
- Disease monitoring activity was well conducted in terms of the number of animals tested, but not always targeting the species;
- It would have been useful to know the stratification by gender of the deer population and also to have available all the data needed to model the dynamics of the population and the seasonality;
- As expected, in absence of any selective pressure on the PRNP gene, the frequencies found in 2017 were not different from those found by Peletto et al., in 2009;
- Hunters awareness very poor.

THANKS FOR YOUR ATTENTION

