

# Concepts of surveillance for early warning and demonstration of disease freedom in vaccinated populations

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EpiMundi



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POPULATION HEALTH MANAGEMENT

# New name

Ausvet Europe is now EpiMundi



**AUSVET**  
Europe



**EpiMundi**  
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# Surveillance classification

Disease  
present

Disease  
absent

Same proportion

Estimating  
occurrence

At least  
one case

Demonstrating  
freedom

Every case

Case finding

The first case

Early detection





# Freedom from disease

Detecting at least one case



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# Demonstration of freedom: Principles

- Proving freedom – not practically possible
  - Test every unit
  - Perfect test
  - Simultaneous
- Approach
  - Compare 2 hypothetical populations

1

Infected at  $P^*$

$$P \geq P^*$$

2

Not infected at  $P^*$

$$P < P^*$$



# Design prevalence ( $P^*$ )

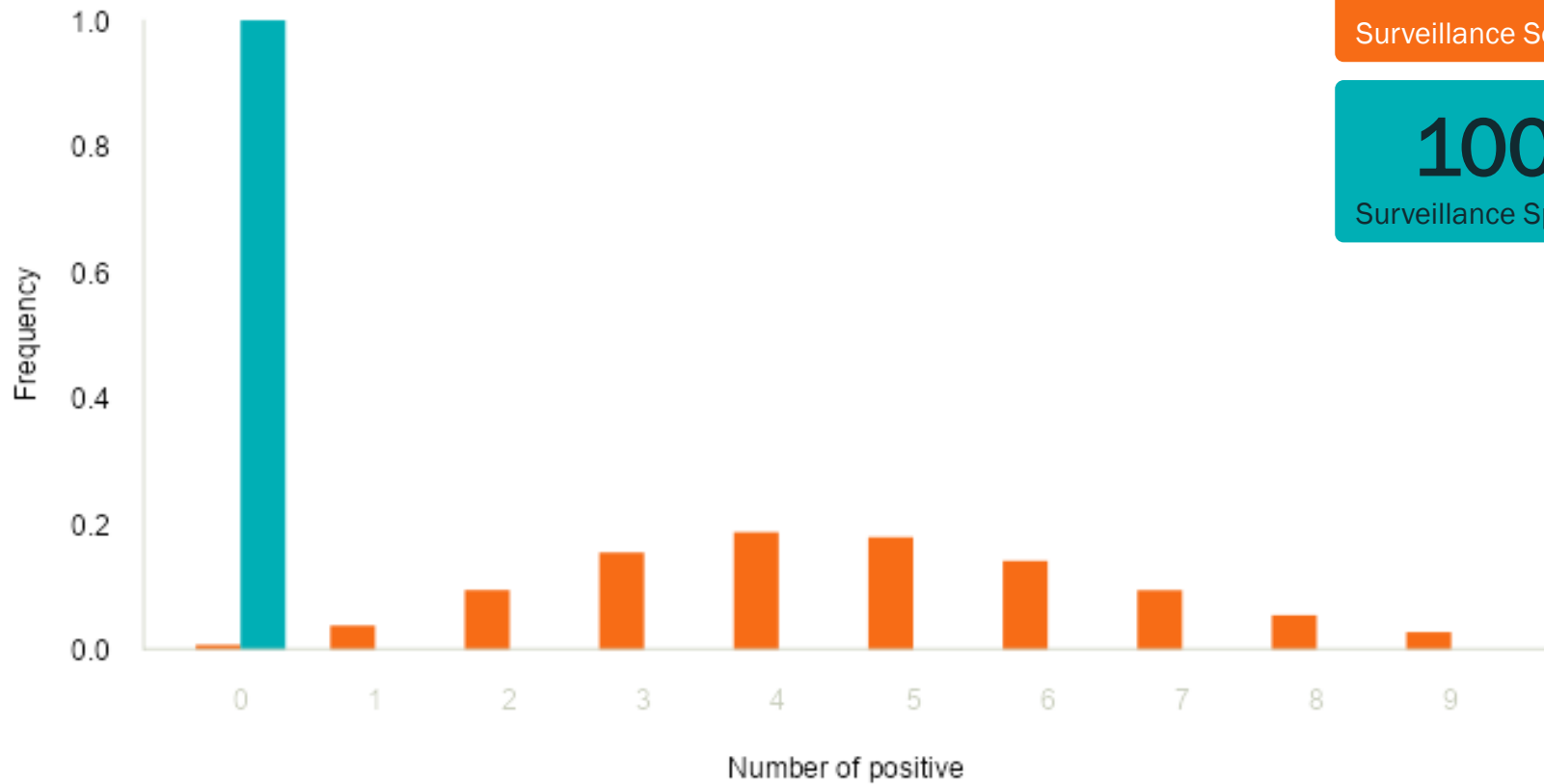
- Hypothetical prevalence
  - If the population was infected
- Major impact on sensitivity of surveillance
  - Easy to find disease with high  $P^*$
- Sets the standard for surveillance
  - Allows comparison between
    - Studies
    - Approaches
    - Countries
- Agree, then stick to it



# Demonstration of freedom: Practice

- Surveillance sensitivity
  - Probability of a positive result, if disease is present
  - $\Pr(S+ | D+)$
- Surveillance specificity
  - Probability of a negative result, if disease is absent
  - $\Pr(S- | D-)$
- Cut point
  - Number of positive test results required to conclude positive





**1**  
Cut point

**99.23%**  
Surveillance Se

**100%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

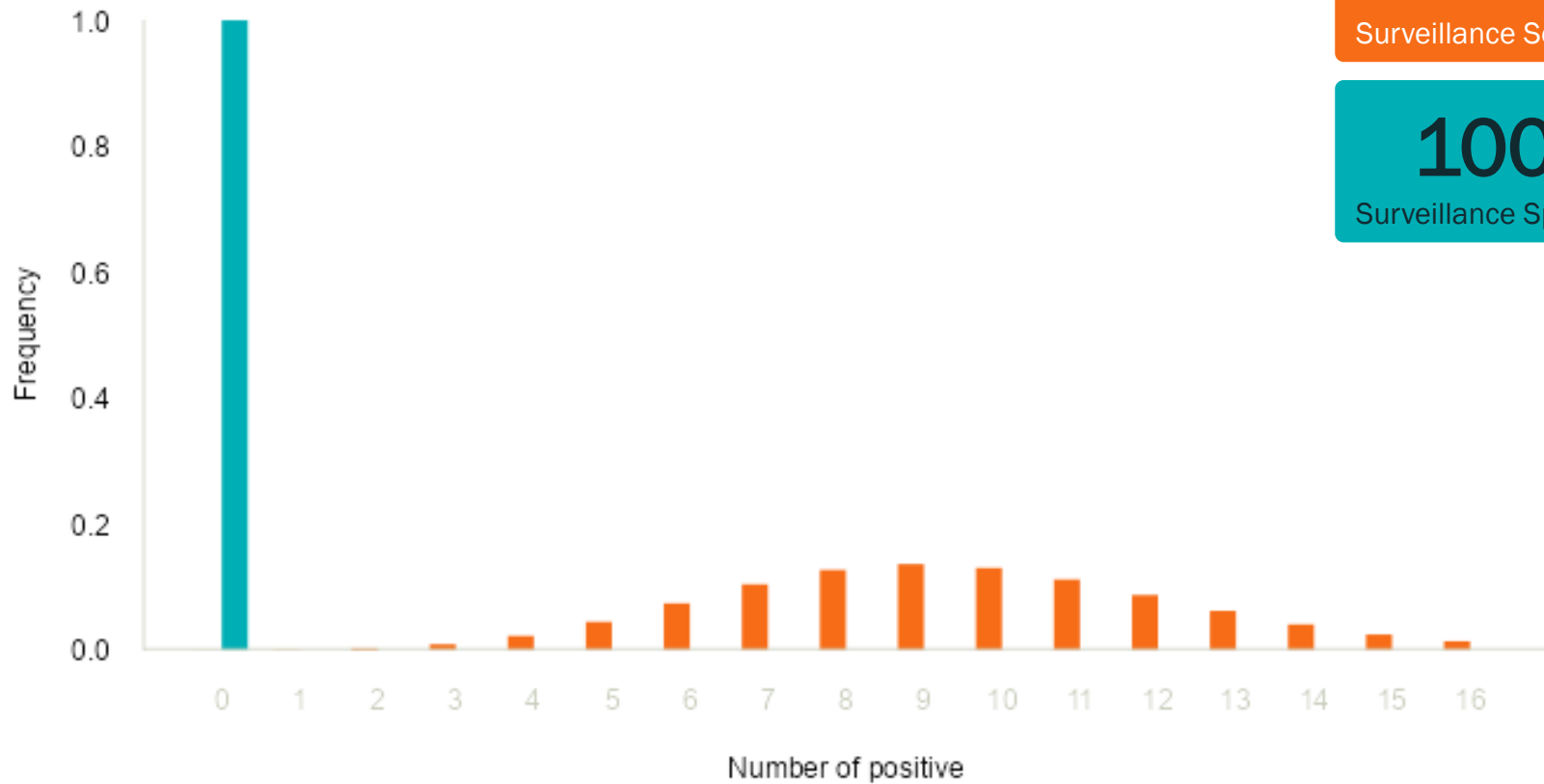
**100%**  
Test Specificity

**5%**  
Design prevalence

# Design prevalence

What impact does the choice have?





**1**  
Cut point

**100%**  
Surveillance Se

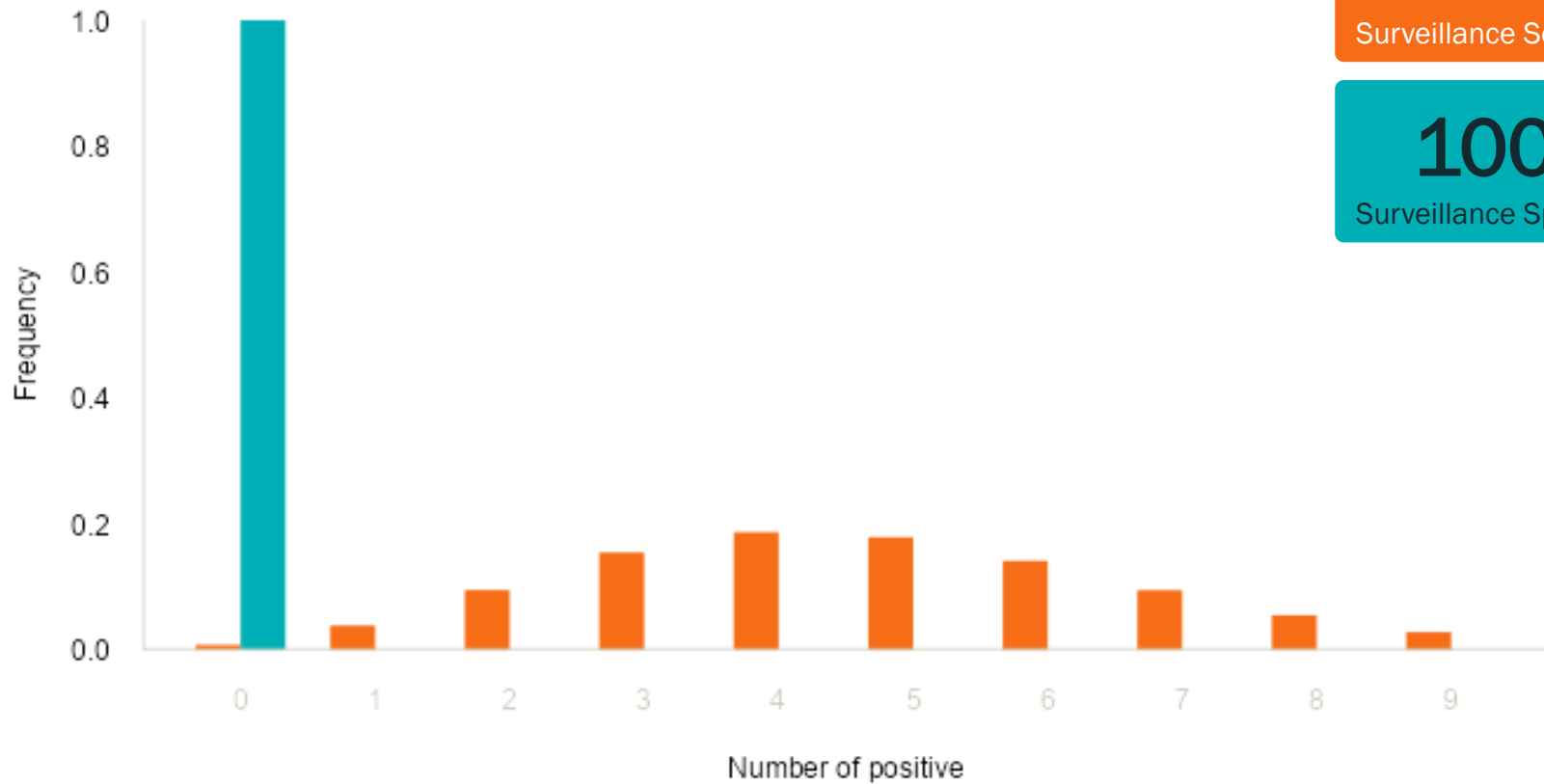
**100%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

**100%**  
Test Specificity

**10%**  
Design prevalence



**1**  
Cut point

**99.23%**  
Surveillance Se

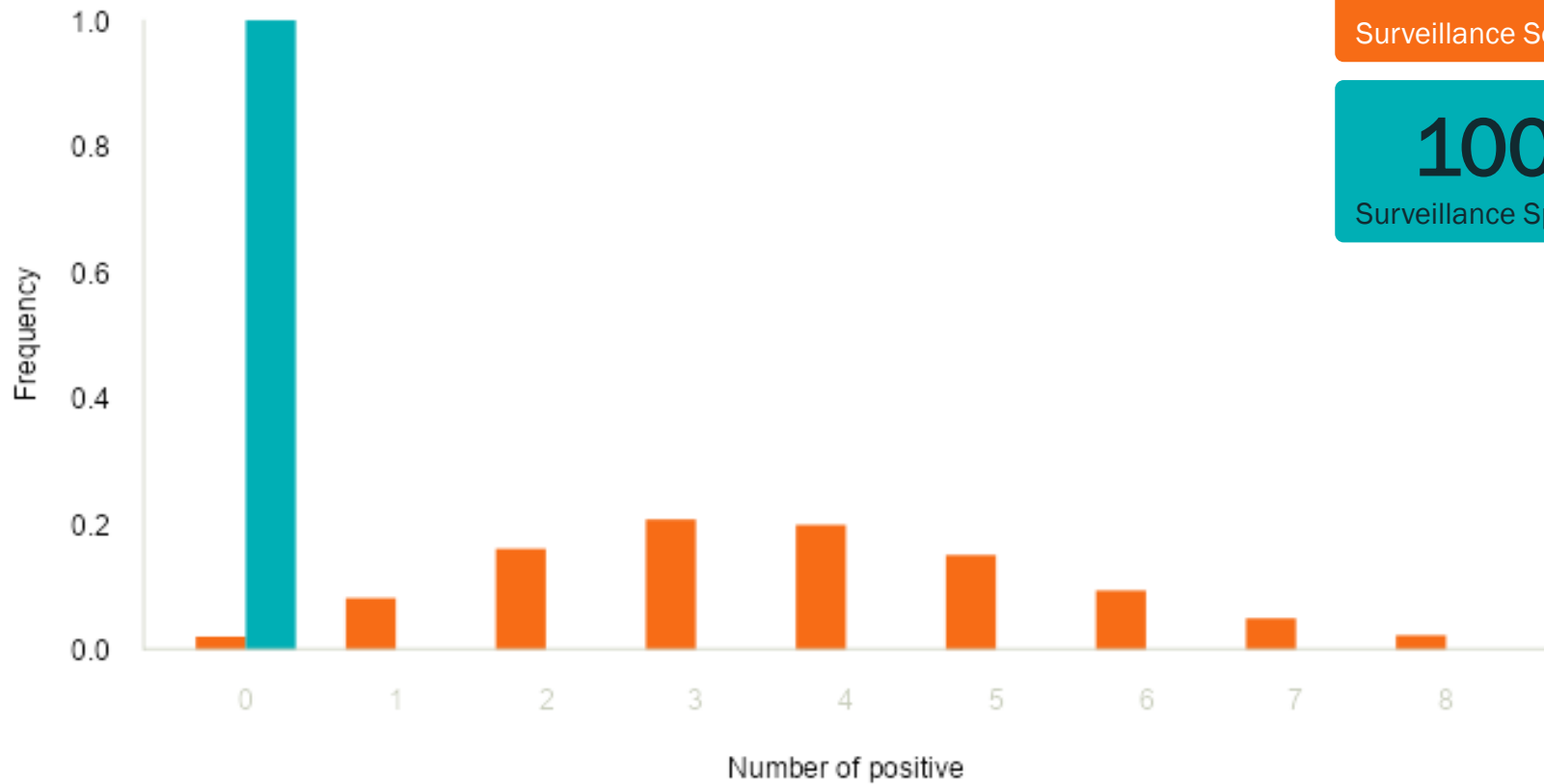
**100%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

**100%**  
Test Specificity

**5%**  
Design prevalence



**1**  
Cut point

**97.92%**  
Surveillance Se

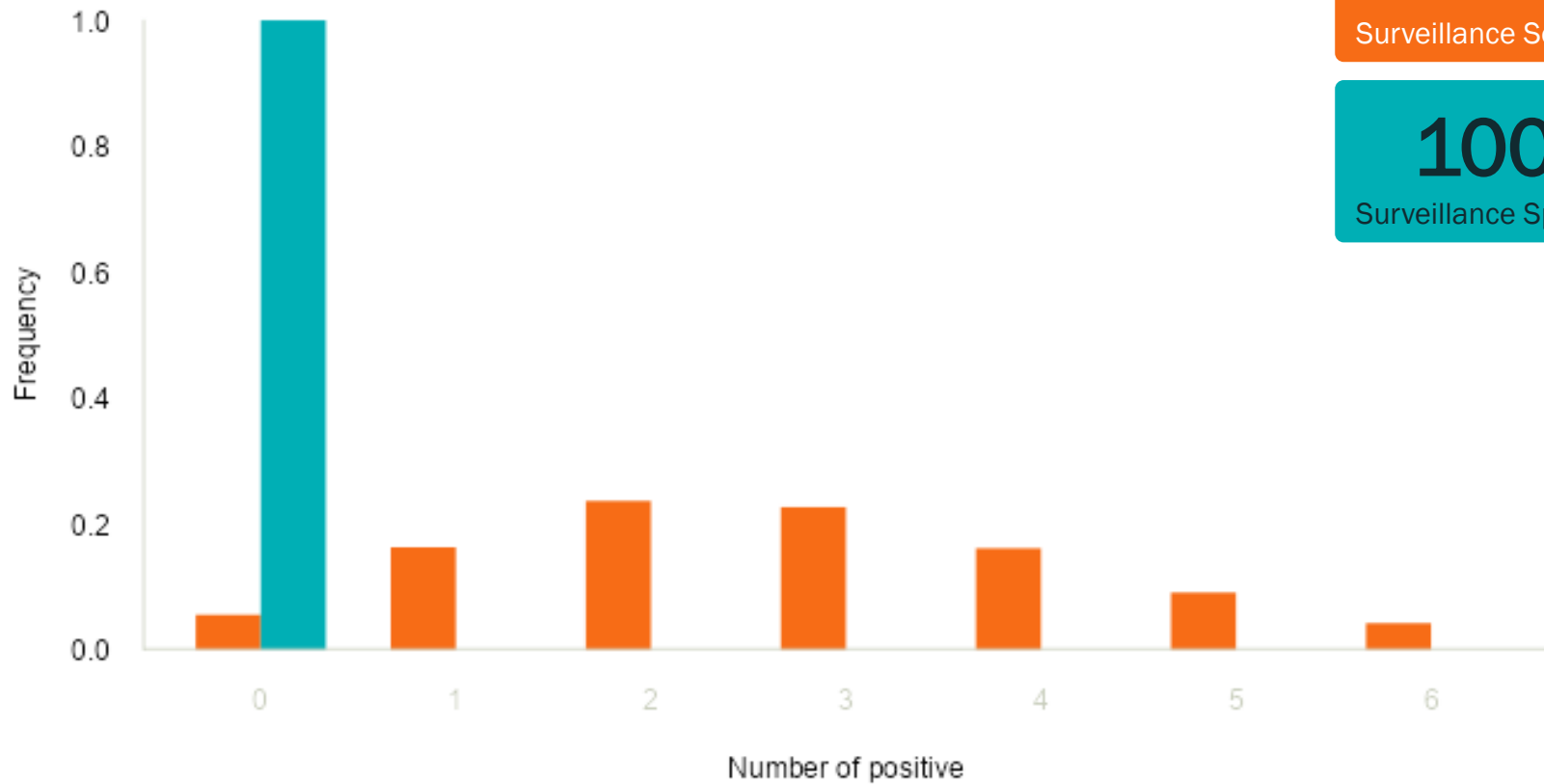
**100%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

**100%**  
Test Specificity

**4%**  
Design prevalence



**1**  
Cut point

**94.45%**  
Surveillance Se

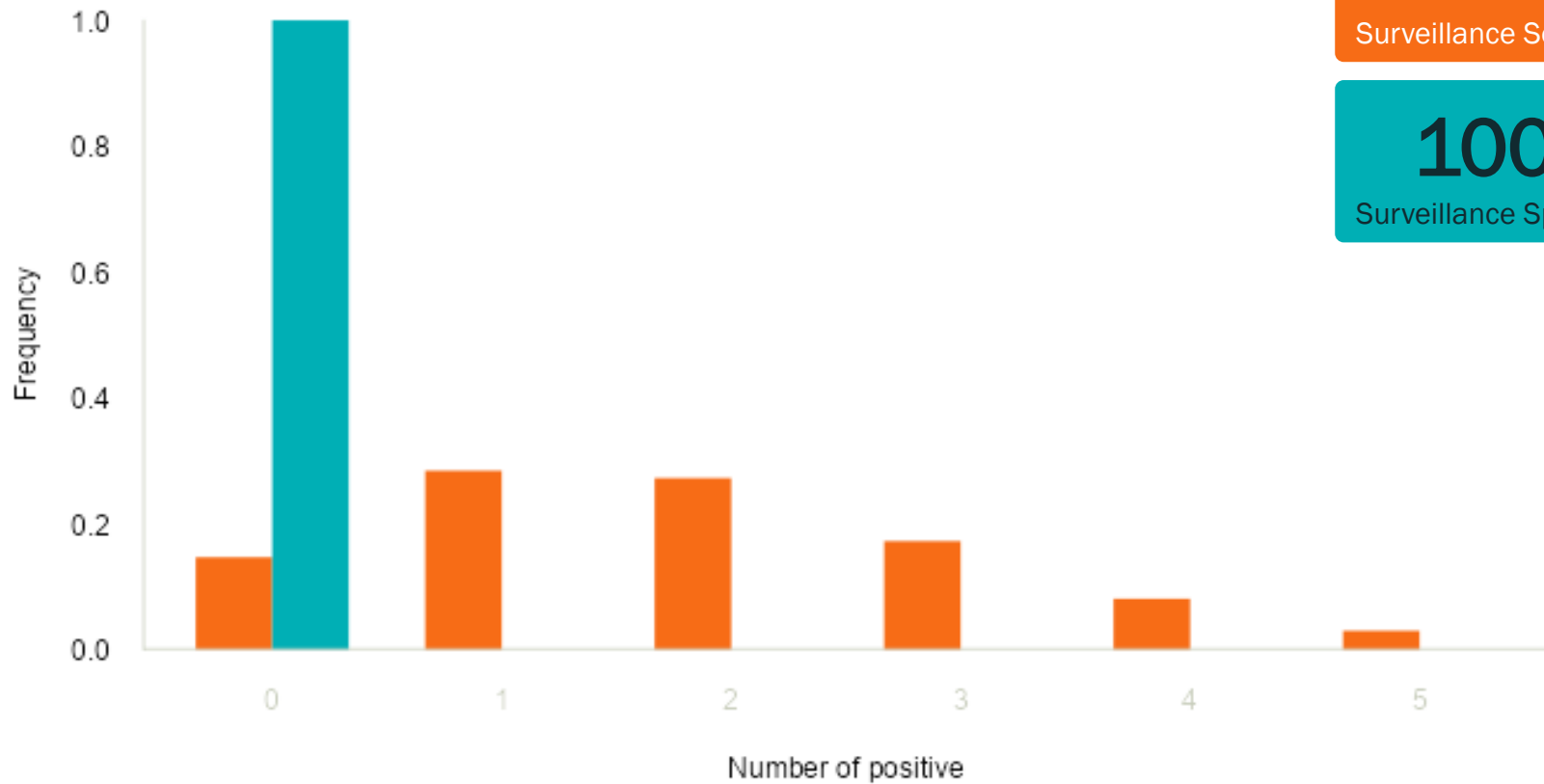
**100%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

**100%**  
Test Specificity

**3%**  
Design prevalence



**1**  
Cut point

**85.31%**  
Surveillance Se

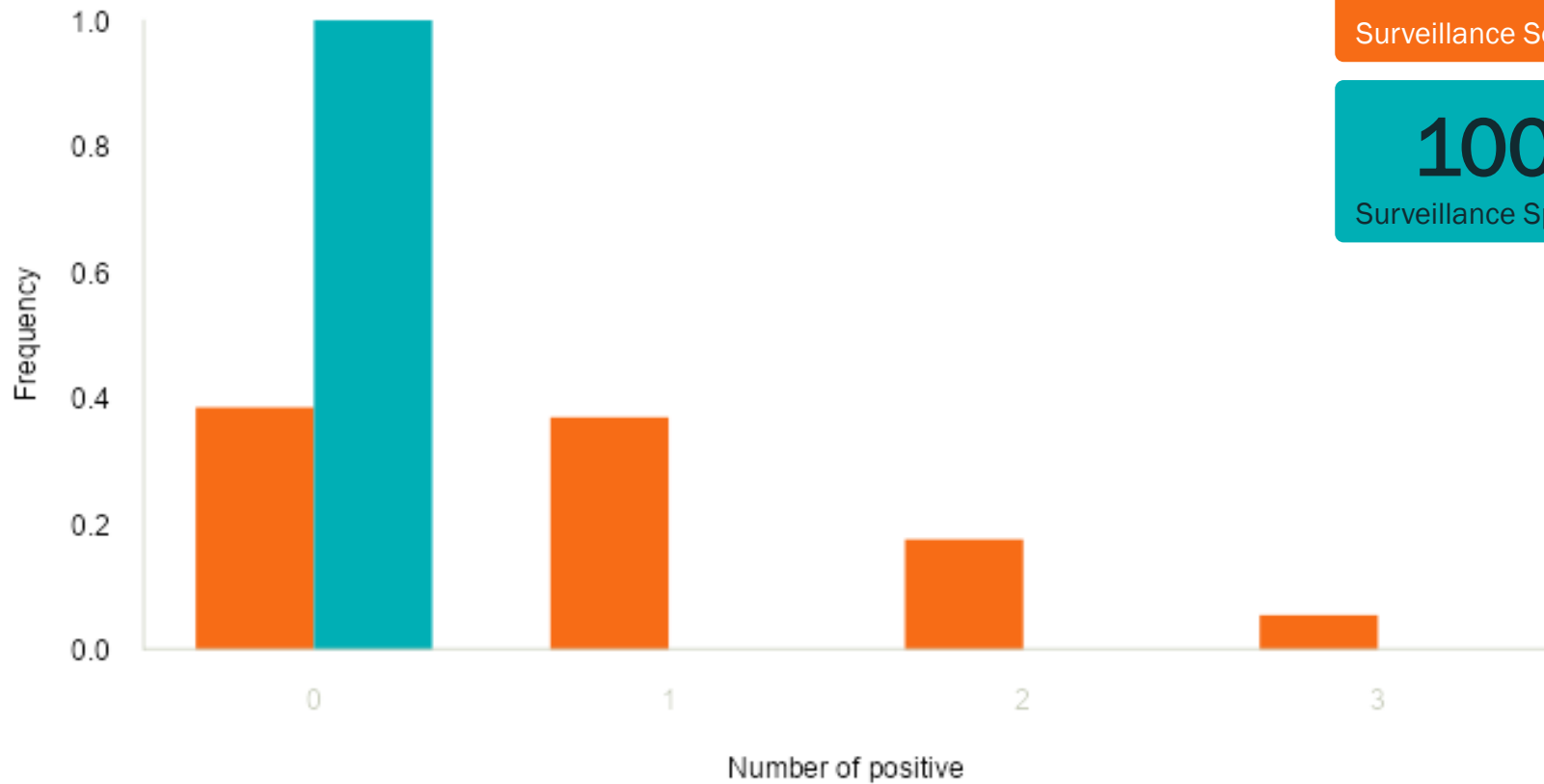
**100%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

**100%**  
Test Specificity

**2%**  
Design prevalence



**1**  
Cut point

**61.50%**  
Surveillance Se

**100%**  
Surveillance Sp

**100**  
Sample size

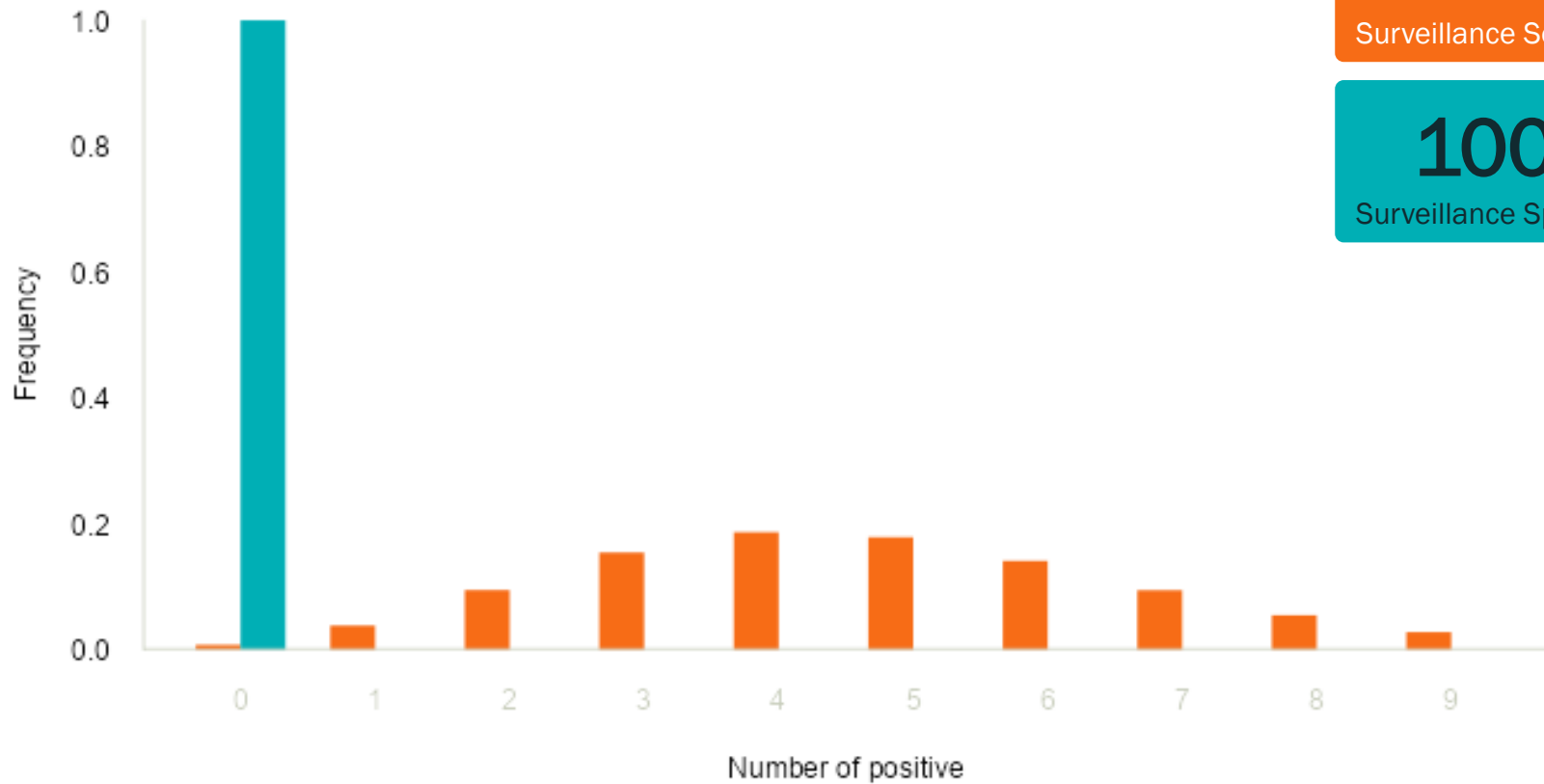
**95%**  
Test Sensitivity

**100%**  
Test Specificity

**1%**  
Design prevalence

# Test sensitivity





**1**  
Cut point

**99.23%**  
Surveillance Se

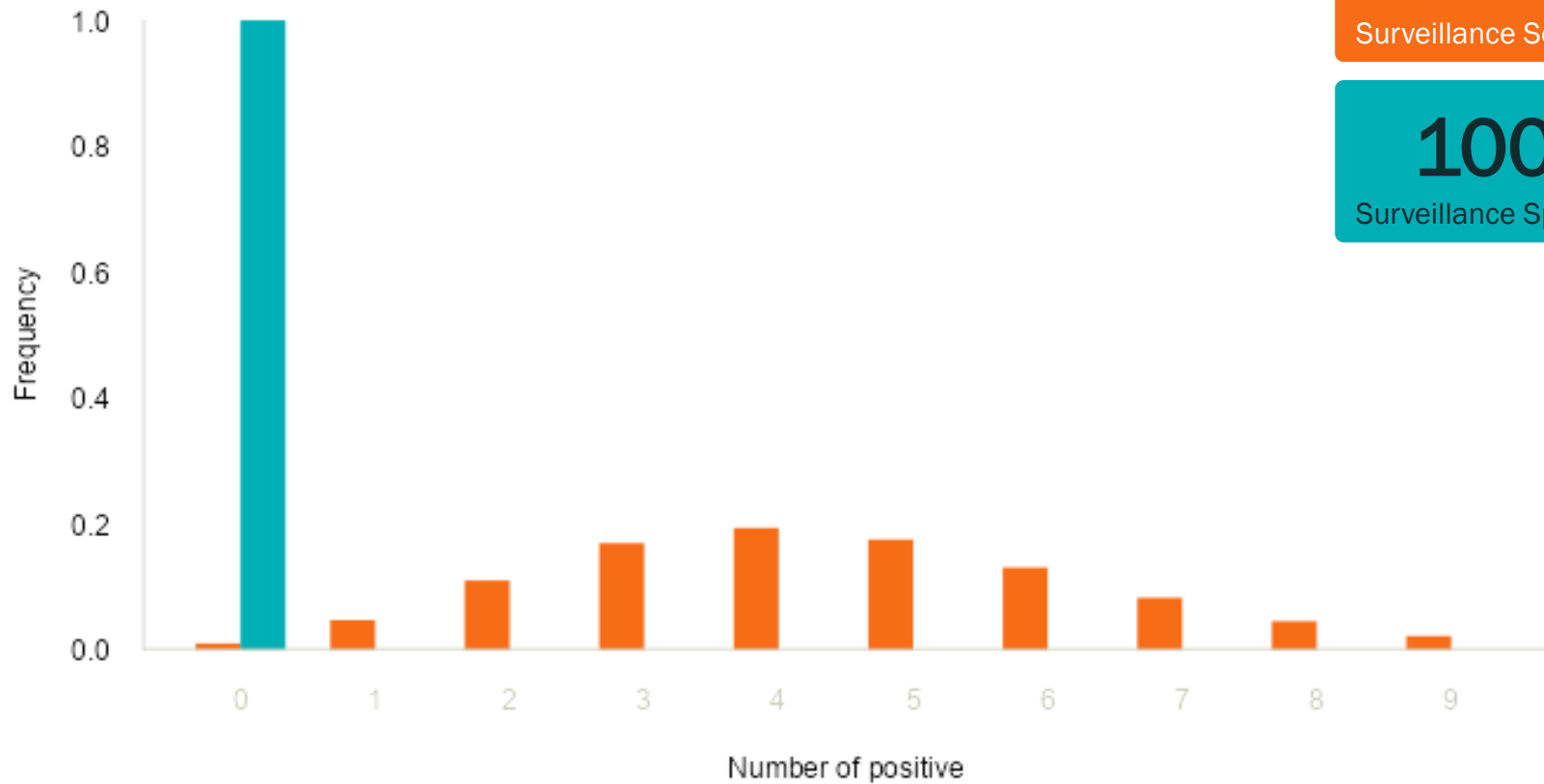
**100%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

**100%**  
Test Specificity

**5%**  
Design prevalence



**1**  
Cut point

**99.00%**  
Surveillance Se

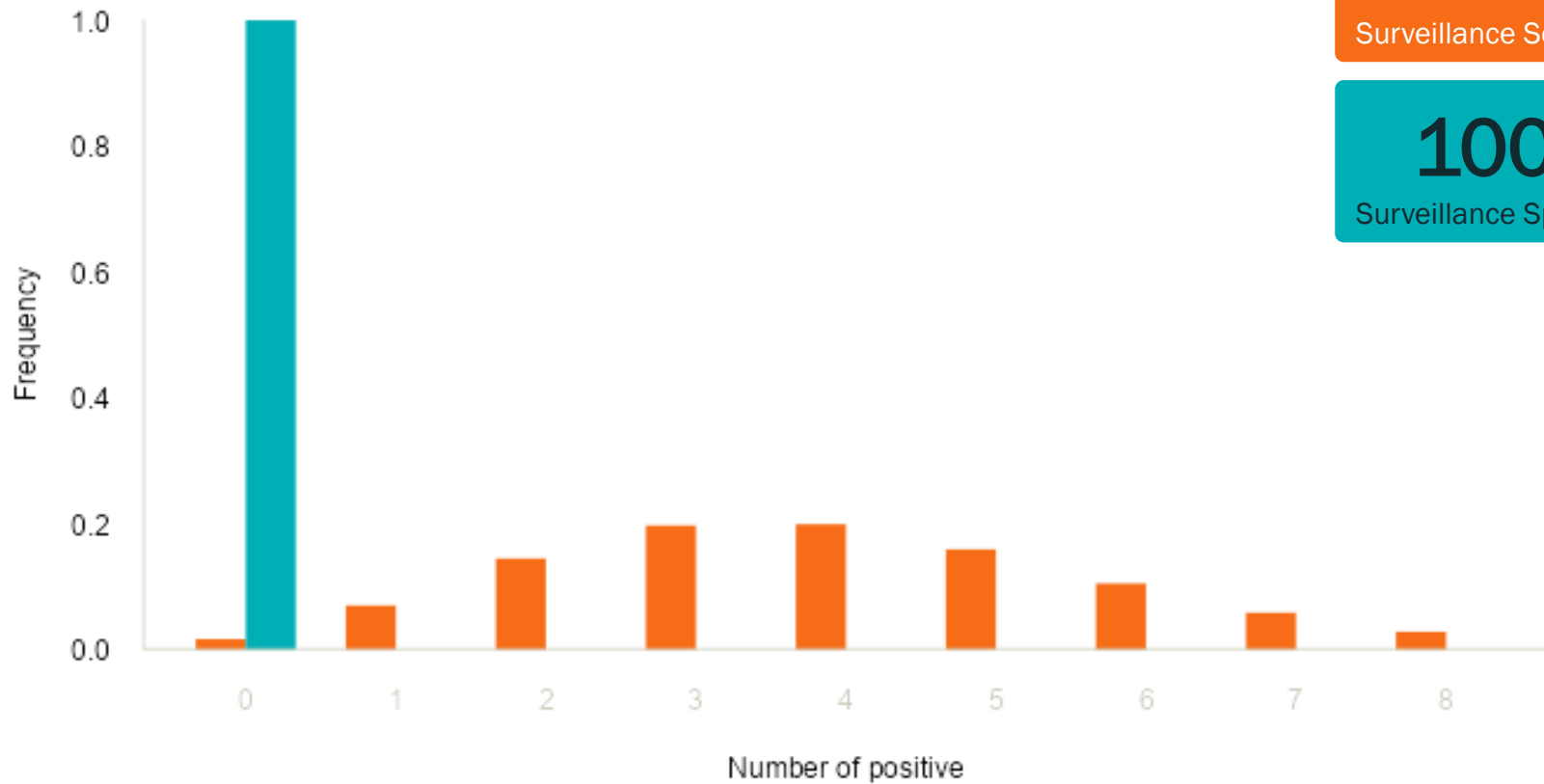
**100%**  
Surveillance Sp

**100**  
Sample size

**90%**  
Test Sensitivity

**100%**  
Test Specificity

**5%**  
Design prevalence



**1**  
Cut point

**98.31%**  
Surveillance Se

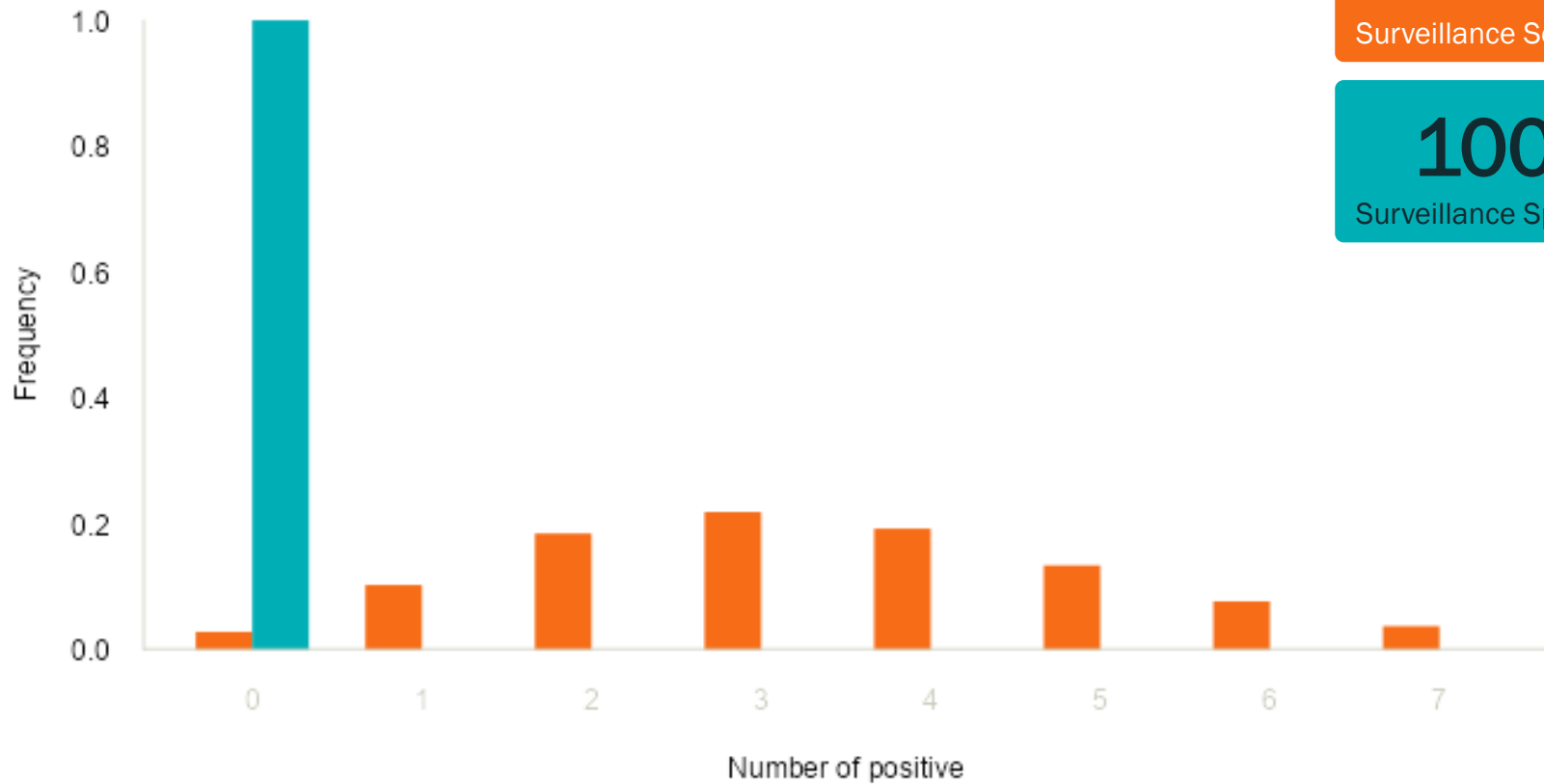
**100%**  
Surveillance Sp

**100**  
Sample size

**80%**  
Test Sensitivity

**100%**  
Test Specificity

**5%**  
Design prevalence



**1**  
Cut point

**97.16%**  
Surveillance Se

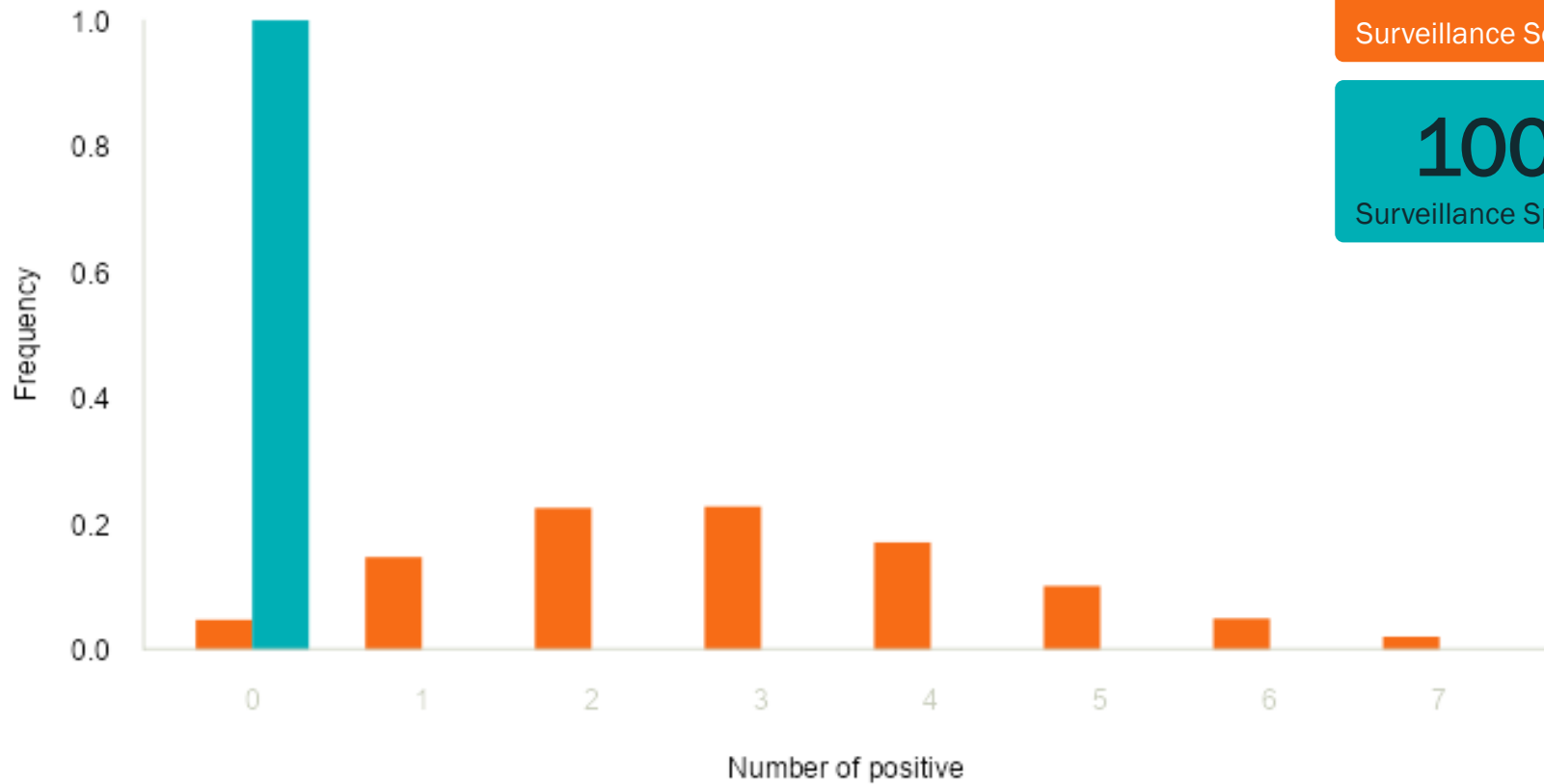
**100%**  
Surveillance Sp

**100**  
Sample size

**70%**  
Test Sensitivity

**100%**  
Test Specificity

**5%**  
Design prevalence



**1**  
Cut point

**95.24%**  
Surveillance Se

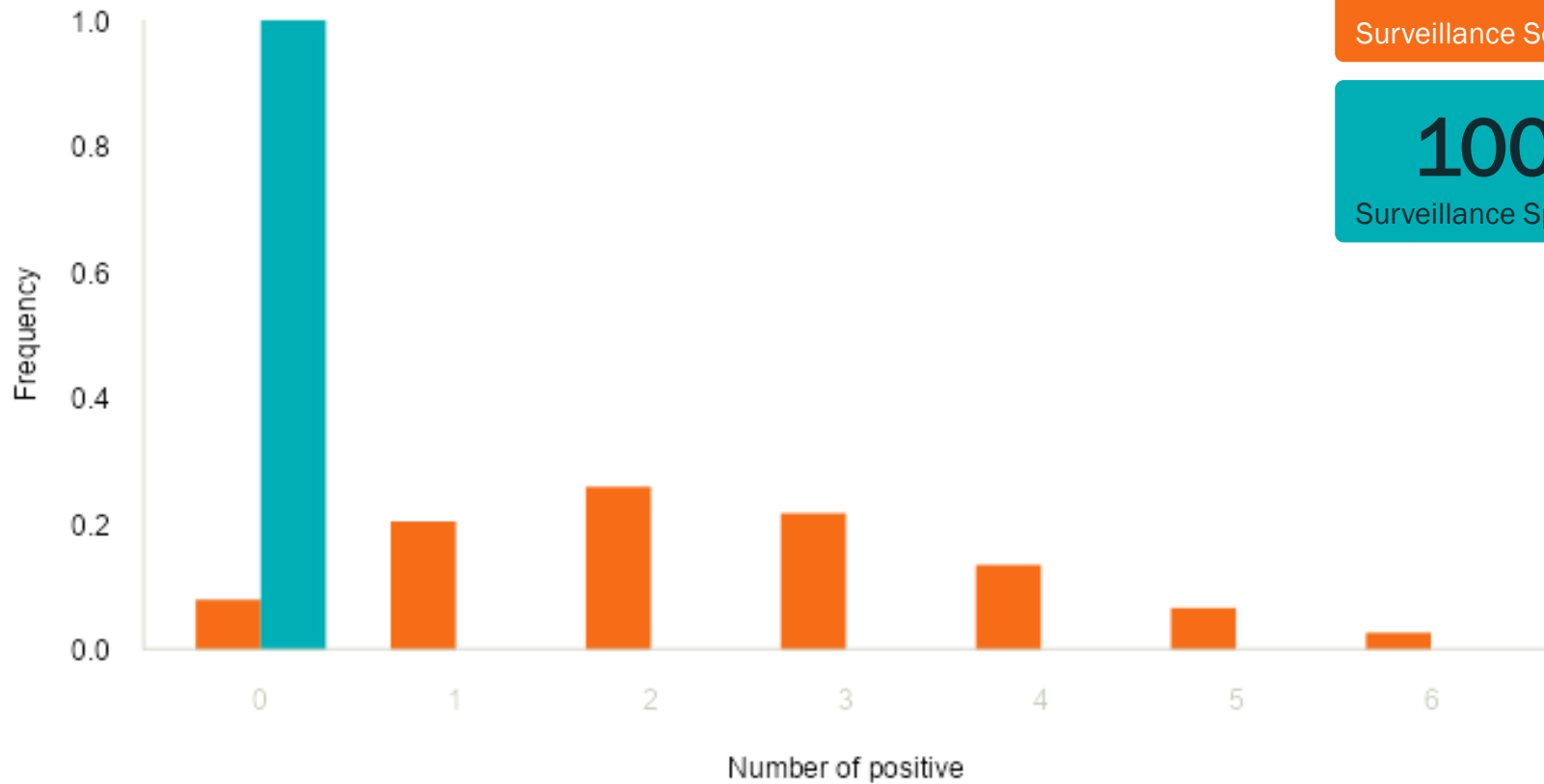
**100%**  
Surveillance Sp

**100**  
Sample size

**60%**  
Test Sensitivity

**100%**  
Test Specificity

**5%**  
Design prevalence



**1**  
Cut point

**92.05%**  
Surveillance Se

**100%**  
Surveillance Sp

**100**  
Sample size

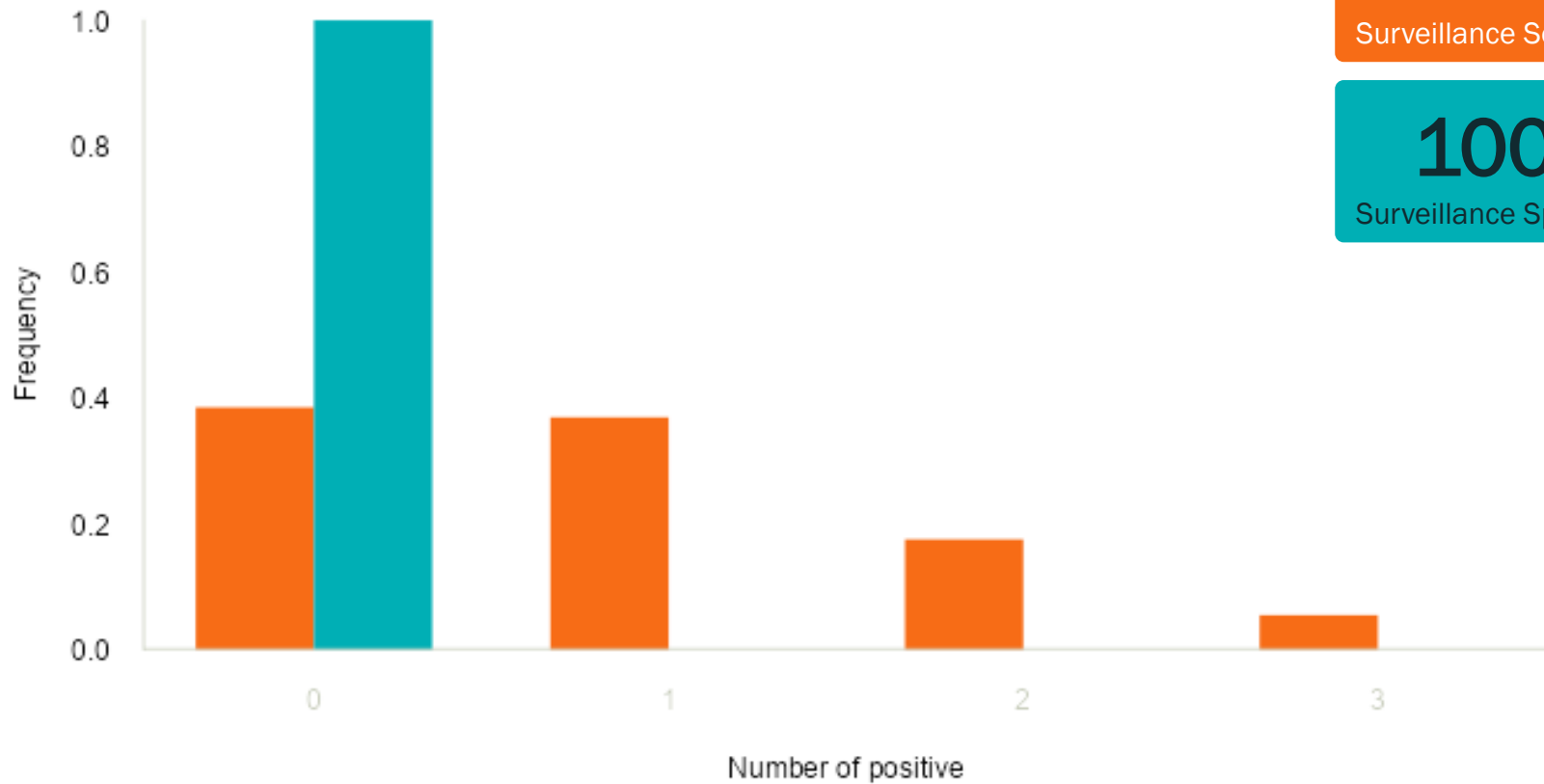
**50%**  
Test Sensitivity

**100%**  
Test Specificity

**5%**  
Design prevalence

# Sample size





**1**  
Cut point

**61.50%**  
Surveillance Se

**100%**  
Surveillance Sp

**100**

Sample size

**95%**

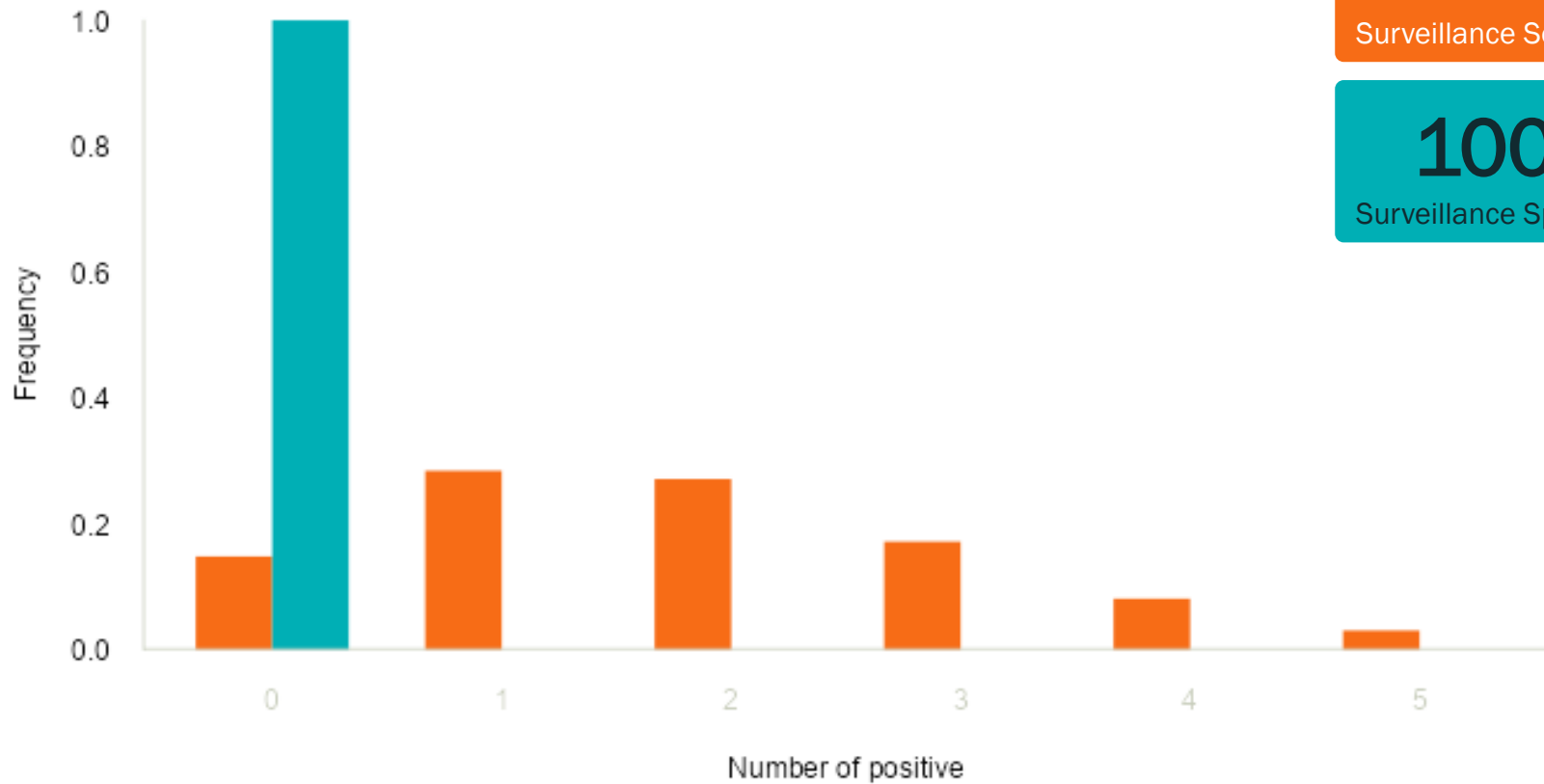
Test Sensitivity

**100%**

Test Specificity

**1%**

Design prevalence



**1**  
Cut point

**85.18%**  
Surveillance Se

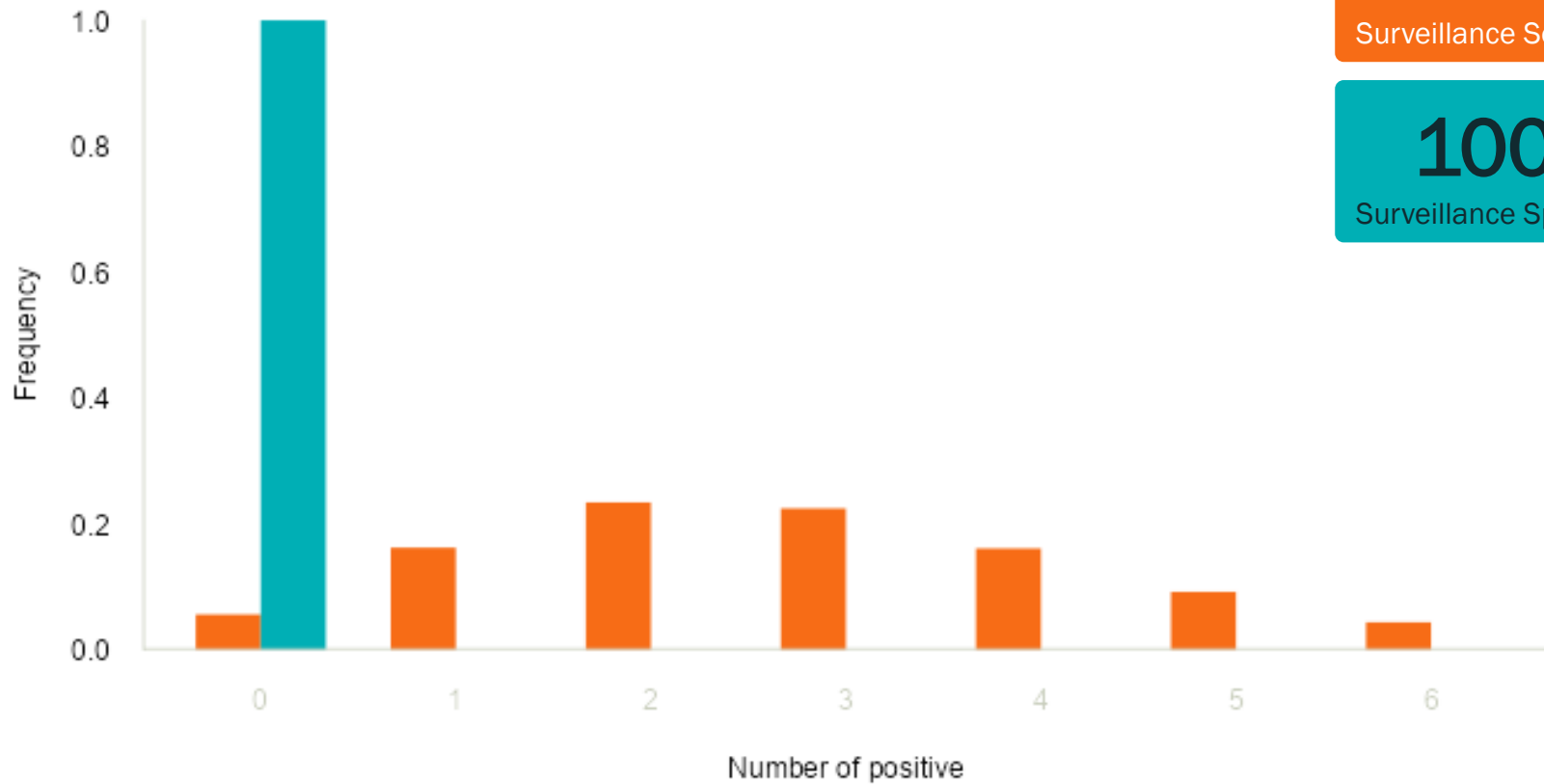
**100%**  
Surveillance Sp

**200**  
Sample size

**95%**  
Test Sensitivity

**100%**  
Test Specificity

**1%**  
Design prevalence



**1**  
Cut point

**94.29%**  
Surveillance Se

**100%**  
Surveillance Sp

**300**

Sample size

**95%**

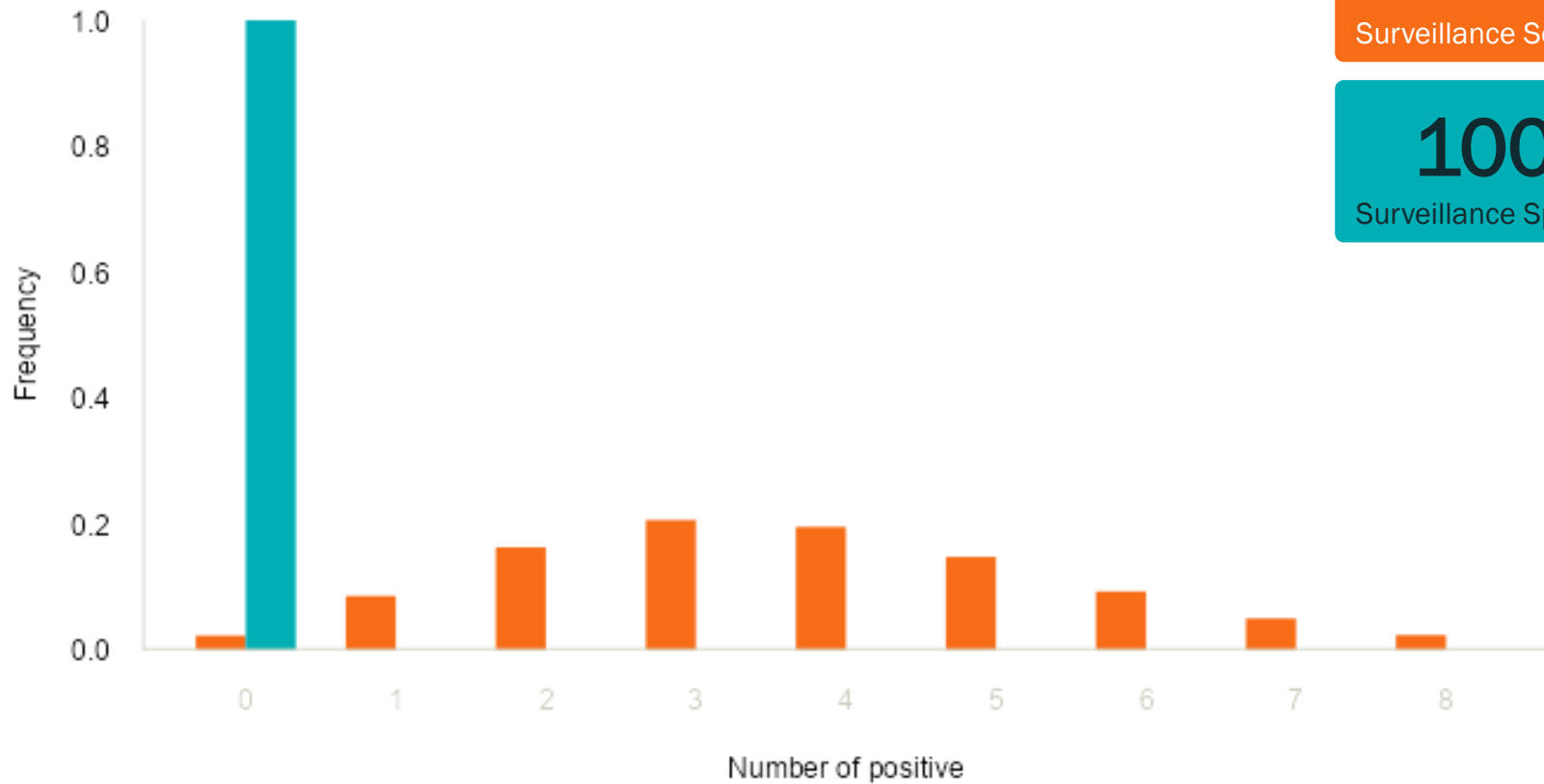
Test Sensitivity

**100%**

Test Specificity

**1%**

Design prevalence



**1**  
Cut point

**97.80%**  
Surveillance Se

**100%**  
Surveillance Sp

**400**  
Sample size

**95%**  
Test Sensitivity

**100%**  
Test Specificity

**1%**  
Design prevalence

# Test specificity

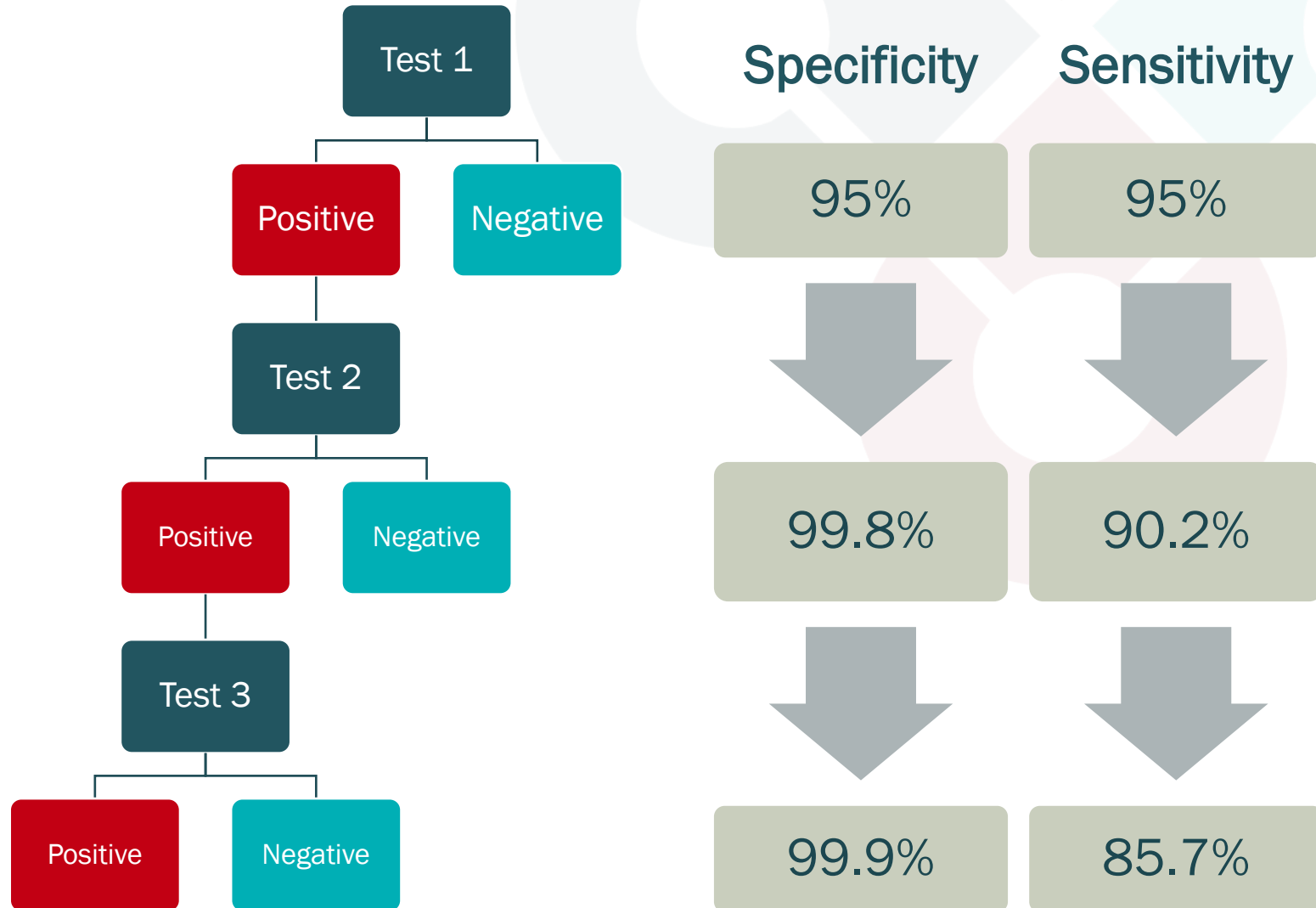


# Imperfect specificity

- Previous examples assume perfect specificity
  - No false positives
- Options
  - Confirmatory testing
  - Policy decisions
  - Change the cut point



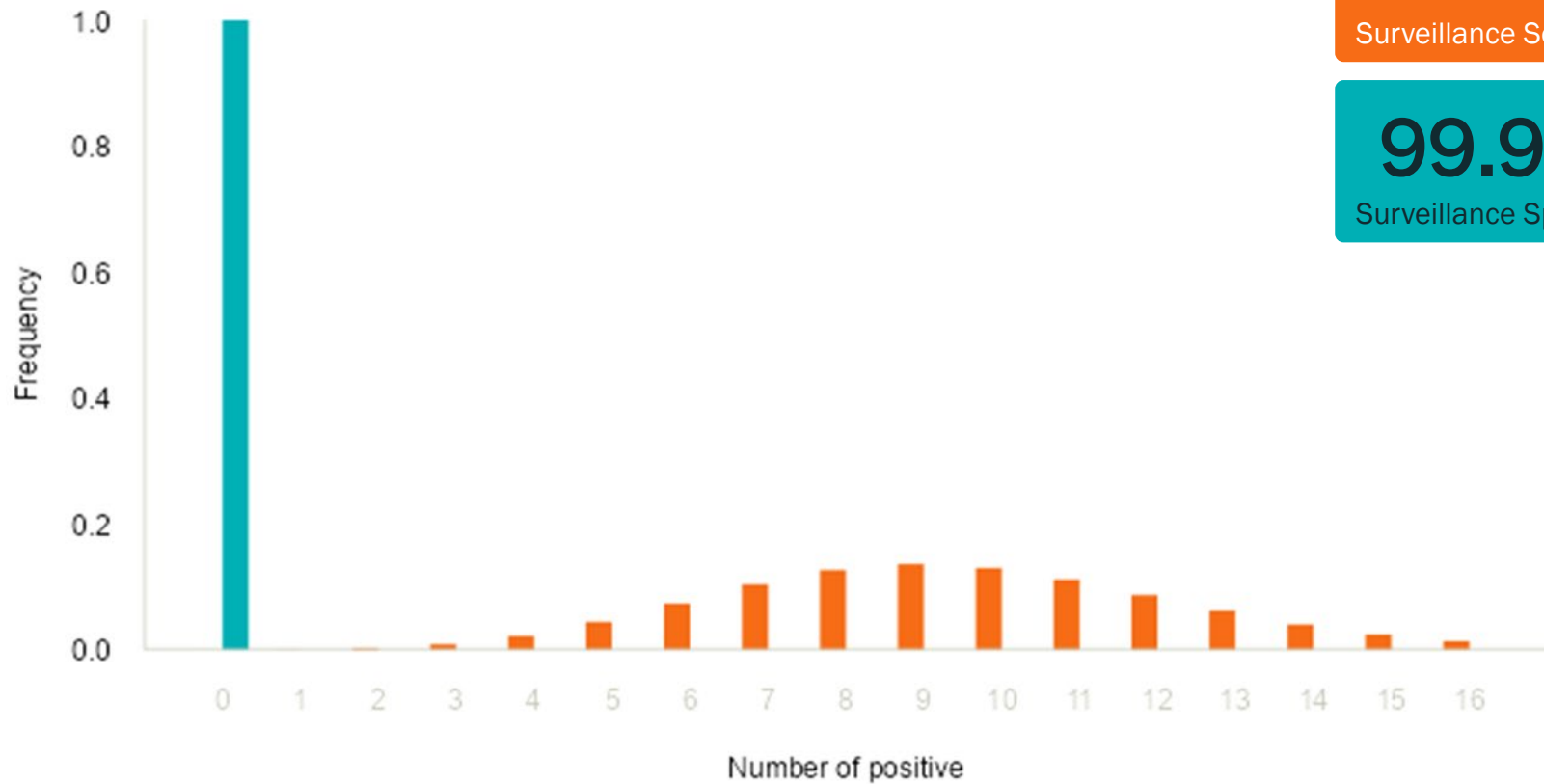
# Improving specificity



# Changing the cut point

- Define a threshold to consider a population diseased
- Recognises expected false positives





**1**  
Cut point

**100.0%**  
Surveillance Se

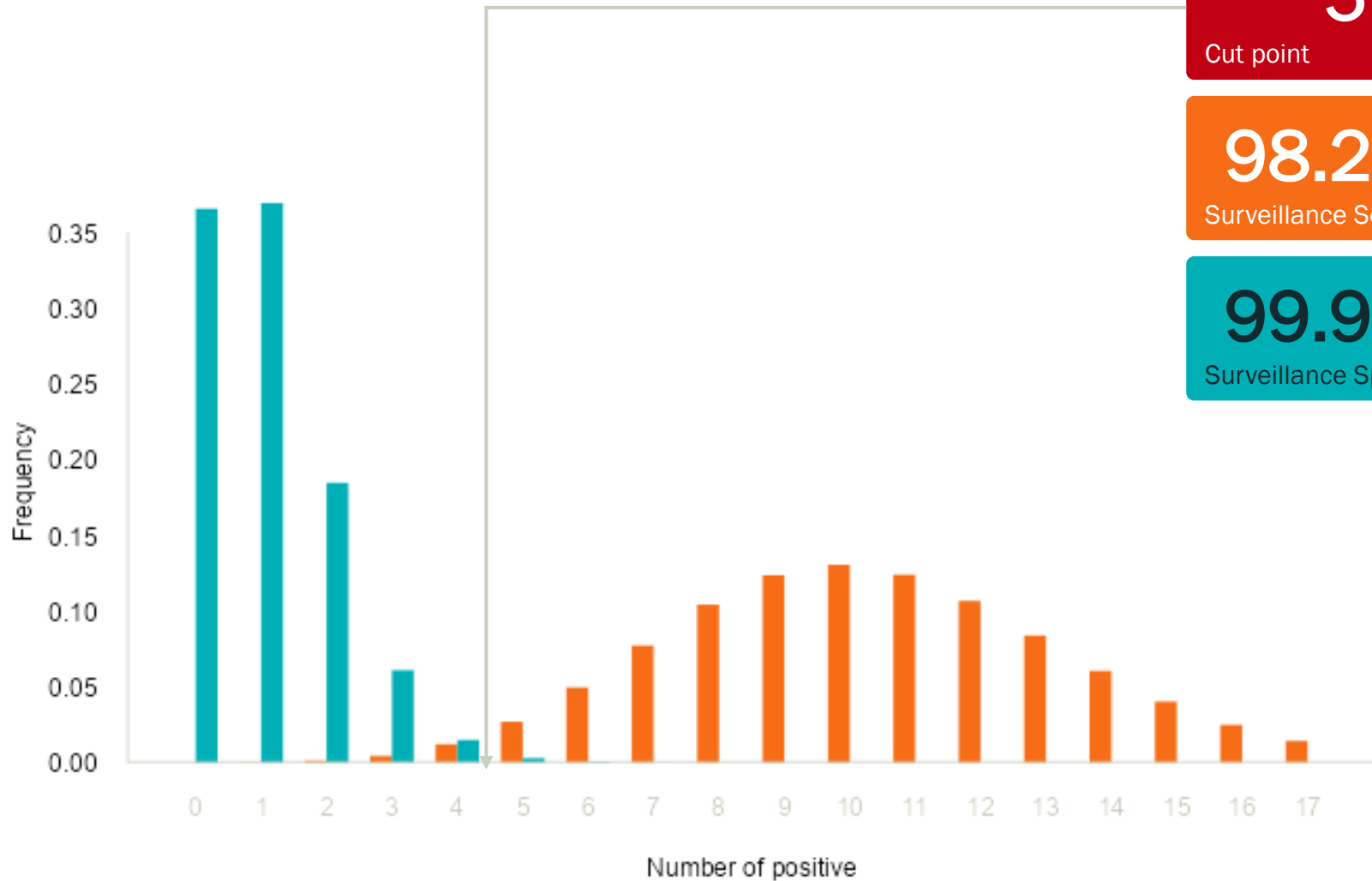
**99.91%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

**100%**  
Test Specificity

**10%**  
Design prevalence



**5**  
Cut point

**98.22%**  
Surveillance Se

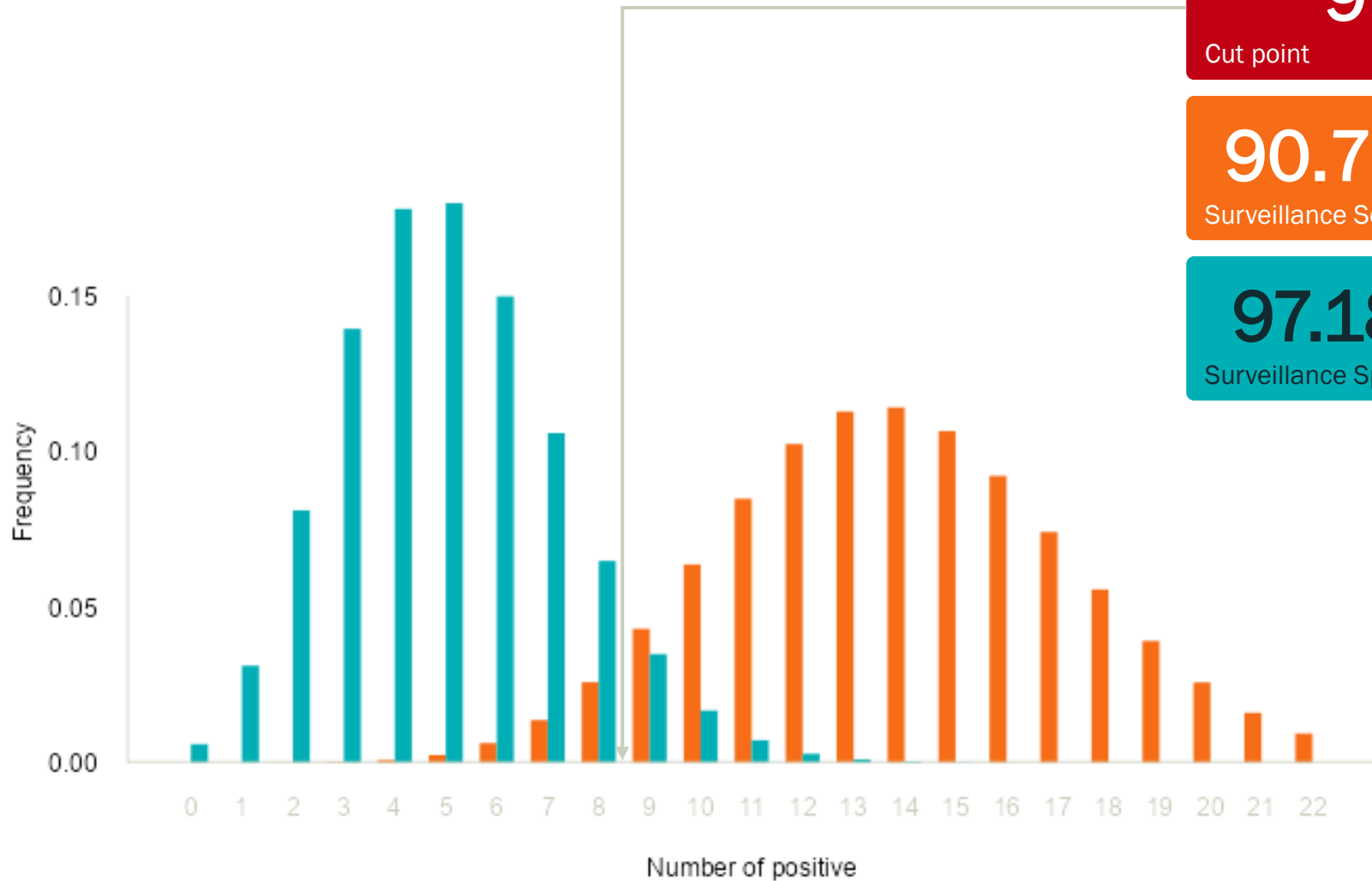
**99.95%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

**99%**  
Test Specificity

**10%**  
Design prevalence



**9**  
Cut point

**90.78%**  
Surveillance Se

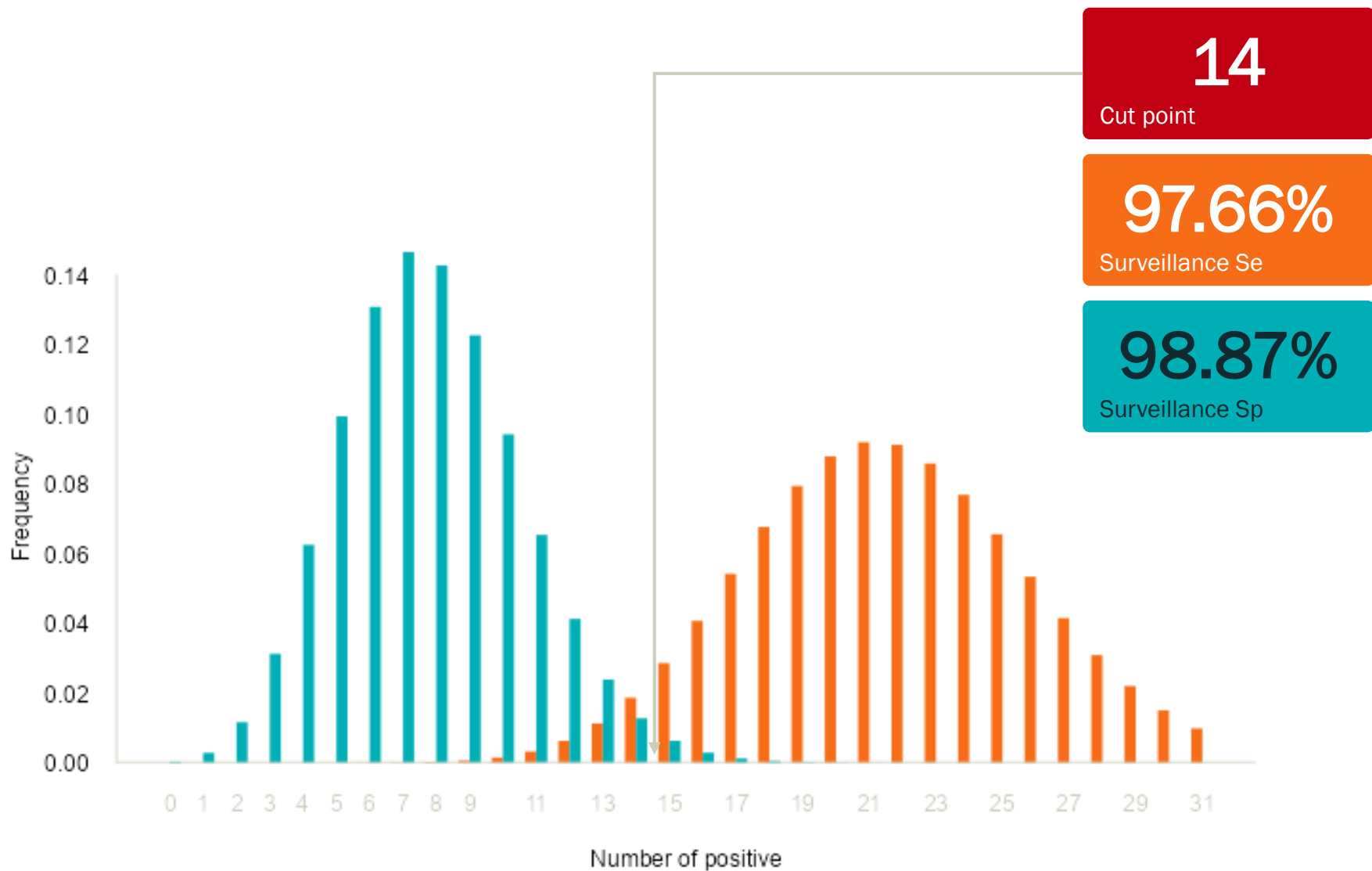
**97.18%**  
Surveillance Sp

**100**  
Sample size

**95%**  
Test Sensitivity

**95%**  
Test Specificity

**10%**  
Design prevalence

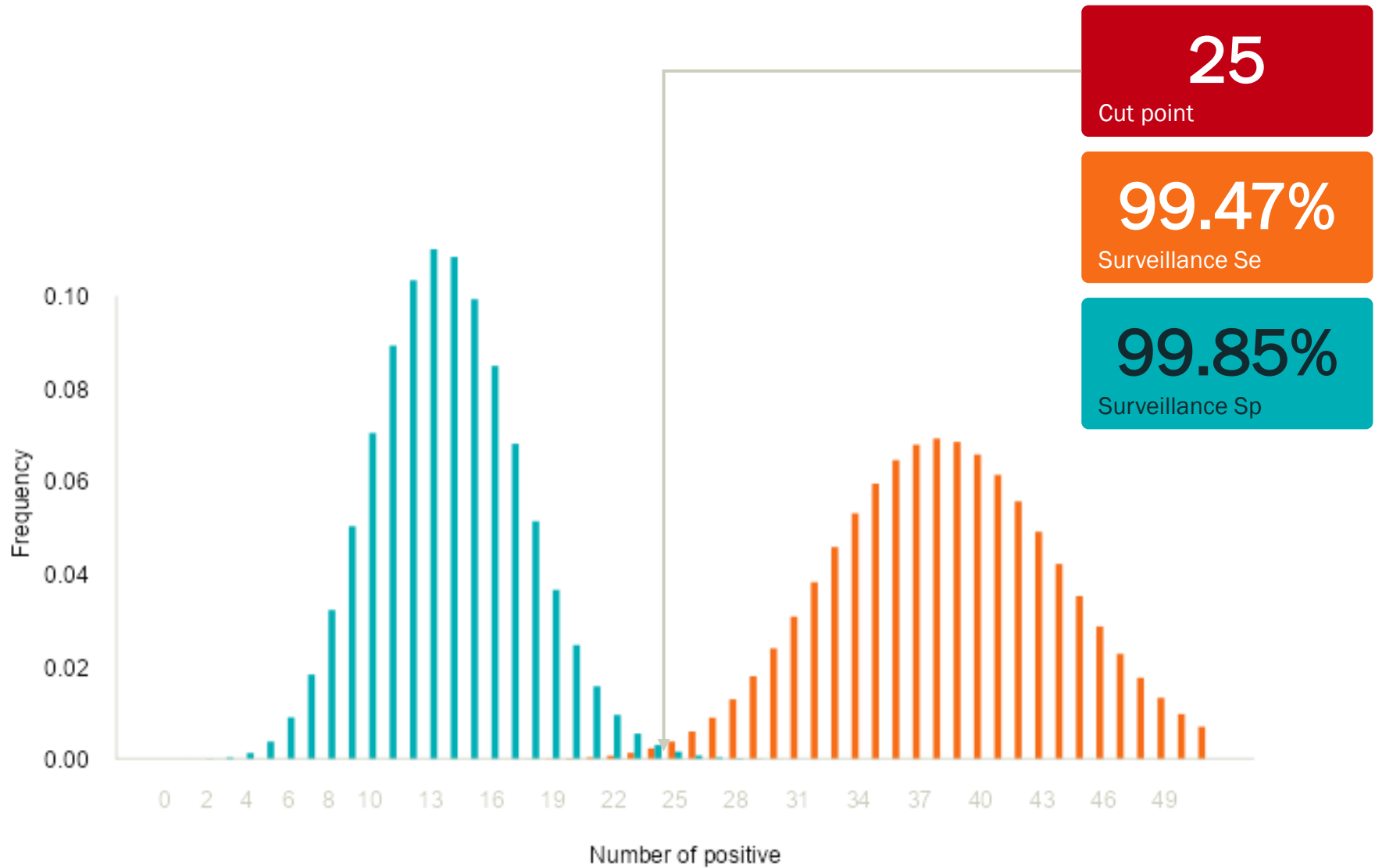


**155**  
Sample size

**95%**  
Test Sensitivity

**95%**  
Test Specificity

**10%**  
Design prevalence



275

Sample size

95%

Test Sensitivity

95%

Test Specificity

10%

Design prevalence

# Changing the cut point

- Approach rarely used in practice
- Communication challenge:
  - “ Only 20 positive in a sample of 275, therefore the population is considered free from disease...”
- Requires robust estimate of specificity



# Demonstration of freedom: Increasing efficiency

- Risk-based sampling
- Small populations
- Combining evidence from multiple surveillance components
- Accounting for lack of independence
- Incorporating the value of historical evidence



# Demonstration of freedom: Vaccinated populations

- Test specificity
  - May be lower for some tests
- Design prevalence
  - Undetected disease present in vaccinated population
    - Prevalence lower than in naïve population





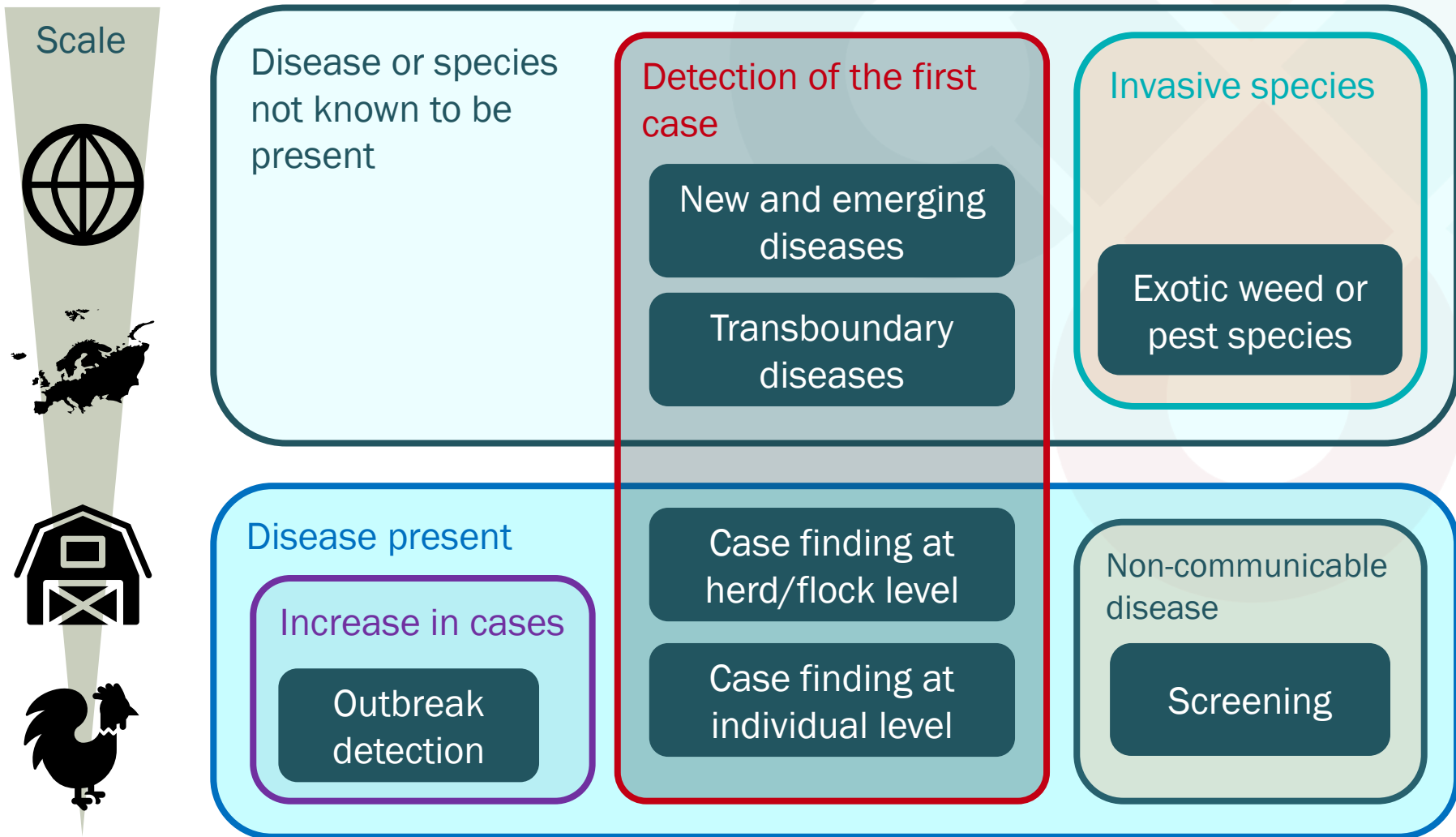
# Early detection

Detecting the first case



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# What is early detection?



# What is 'early'?

## Unit

- First wild bird?
- First domestic bird?
- First barn?
- First farm?
- First district?

## Pathogenesis

- When infected?
- When viraemic?
- When seroconverted?
- When clinical?
- When dead?

## Pragmatic answer

- Early enough for interventions to prevent or minimise adverse consequences
- Must be feasible and cost-effective



# Target early detection sensitivity

- Proportion of incursions that we would like to successfully detect?

**100%**

- Less is unlikely to be acceptable
- Rarely able to achieve this target



# Quantifying sensitivity

Early detection surveillance sensitivity (SSe)

- Population coverage ( $C_P$ )
  - % of population under surveillance
- Temporal coverage ( $C_T$ )
  - Frequency of observations relative to target time to detection
- Detection sensitivity ( $Se_D$ )
  - For test system

$$SSe = C_P \times C_T \times Se_D$$



# Implications

- Ideal early detection surveillance needs to:
  - ✓ Include the **entire population**
  - ✓ Be **continuous**
  - ✓ Use a **highly sensitive** detection system
- Approaches to early detection surveillance

Approach	Suitability	Comments
Sample surveys	✗	Poor population coverage
Sentinel sites	✗	Poor population coverage
Periodic surveillance (annual, quarterly)	✗	Poor temporal coverage
Producer reporting with laboratory investigation	✓	May have poor detection sensitivity
Syndromic pattern detection based on production data	✓	Requires follow-up investigation



# Improving early detection surveillance

- Risk-based detection of

doi:10.2903/sp.efsa.2022.EN-7762

- Pos

## Development of a prototype early warning system for avian



SCIENTIFIC OPINION | Open Access | CC BY ND

## Vaccination of poultry against highly pathogenic avian influenza – Part 2. Surveillance and mitigation measures

EFSA Panel on Animal Health and Animal Welfare (AHAW)

European Union Reference Laboratory for Avian Influenza, Søren Saxmose Nielsen ... See all authors

First published: 18 April 2024 | <https://doi.org/10.2903/j.efsa.2024.8755> | Citations: 1

Adopted: 25 March 2024

This article was originally published on the EFSA website [www.efsa.europa.eu](http://www.efsa.europa.eu) on 17 April 2024 as part of EFSA's urgent publication procedures.

Note: A plain language summary of this scientific opinion is available at <https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2024.p220401>



# Early detection in vaccinated populations

- Decreased sensitivity of detection systems based on clinical or production-related observations
  - Producer reporting
  - Syndromic pattern analysis
- Cost and logistic implications of increased reliance on laboratory-based surveillance
  - Higher detection sensitivity
  - More difficult to achieve high temporal and population coverage



# Conclusions: Freedom

- Methodology well established
- Cost optimisation
  - Low sensitivity, low cost, large sample size
  - Better than high sensitivity, high cost, small sample size
- Imperfect specificity continues to pose challenges
- Do we need to establish relevant standard design prevalence ( $P^*$ ) ?



# Conclusions: **Early detection**

- Principles are straightforward

$$\text{Early detection sensitivity} = \text{Population coverage} \times \text{Temporal coverage} \times \text{Detection sensitivity}$$

- Application more complex
  - What unit? How early?
  - Population dynamics modelling
  - Very hard to achieve high sensitivity affordably





**Thank you**



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