

# AMR surveillance using threshold surveys

## Experiences from the OASIS project

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## AMR Surveillance using Innovative Sampling

A JPIAMR project aiming to develop an antimicrobial resistance (AMR) surveillance strategy in a One Health context, which is applicable in high-, middle-, and low-income countries.

OASIS moves from conventionally estimating AMR prevalence to classifying populations/settings as having a “high” or “low” AMR prevalence, by applying a Lot Quality Assurance Sampling approach.



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# Content

- AMR surveillance methodology
  - Role of threshold surveys
- Lot Quality Assurance Sampling (LQAS)
- Validation LQAS methodology in OASIS
- Use of LQAS-based surveillance
- Conclusion

# AMR SURVEILLANCE METHODOLOGY

## Objectives AMR surveillance

- Early warning for new resistance profiles
- Guiding empirical antibiotic treatment based on AMR prevalence
- Assessing changes AMR prevalence
- Assessing impact on interventions
- Assessing local variations in AMR prevalence

# Conventional AMR surveillance

- Predominantly laboratory-based
  - Known to be biased for community setting
- Growing interest population-based surveillance
  - Adding clinical information at sample storage (ACORN project)
  - Syndromic screening at health facility encounter



# Population-based surveillance

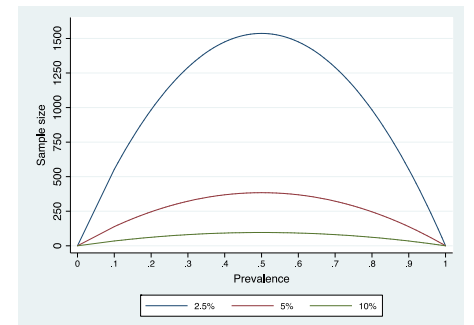
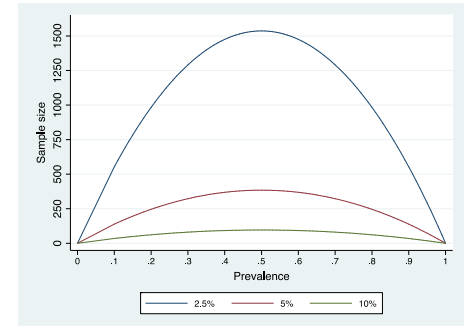
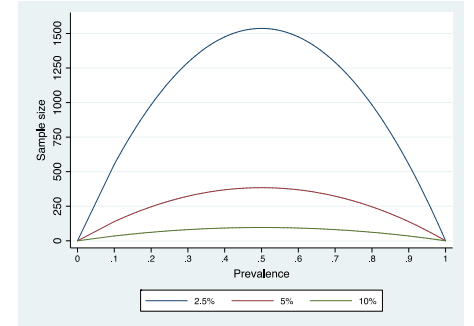
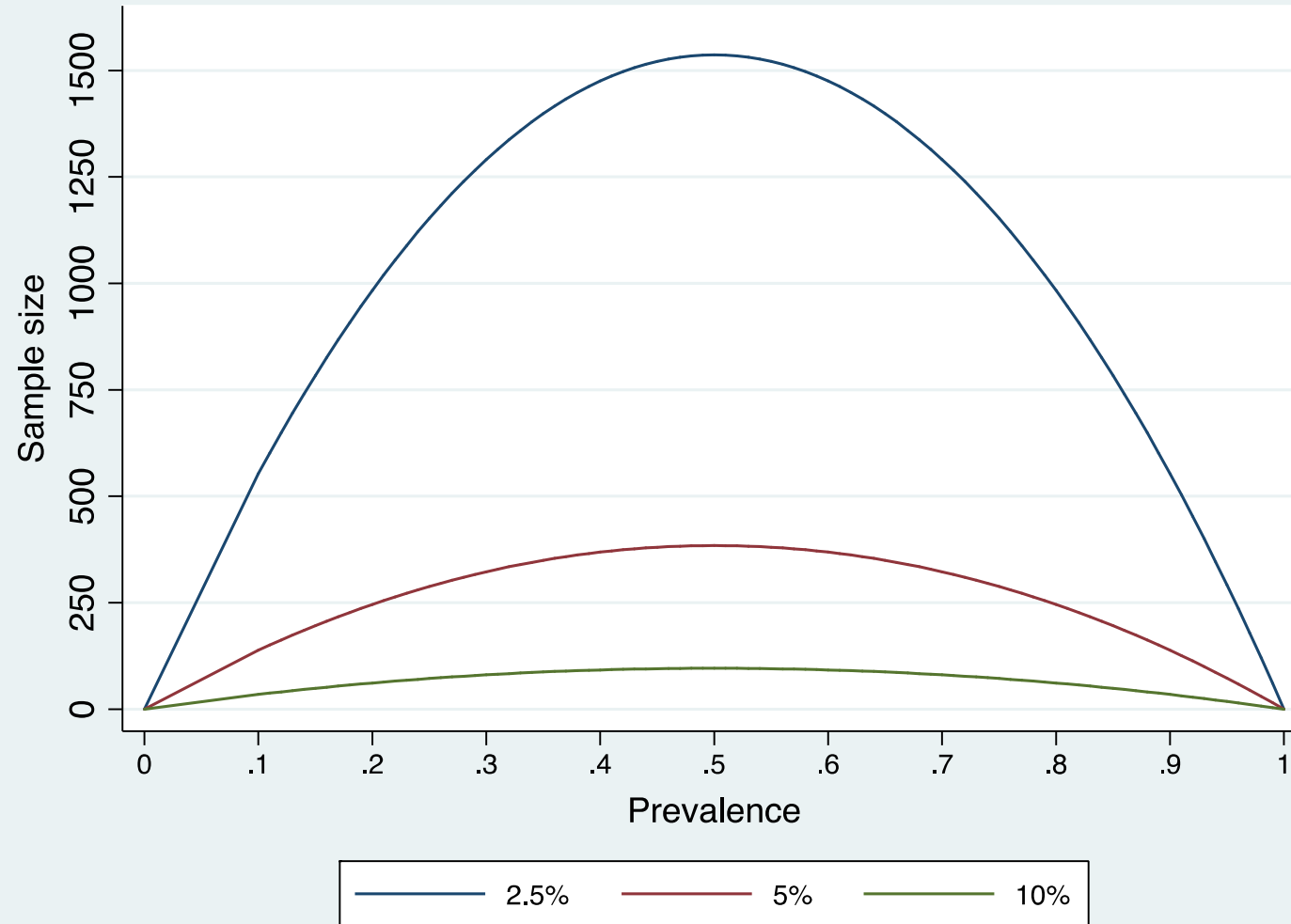


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# Population-based surveillance





# Threshold surveys

- Addresses sample size problem
  - Parallel local surveys
- Based on classification, not estimation
- Change of research question

Is the AMR prevalence above or below x %?

VS

What is the prevalence of AMR in this population?

# Threshold surveys

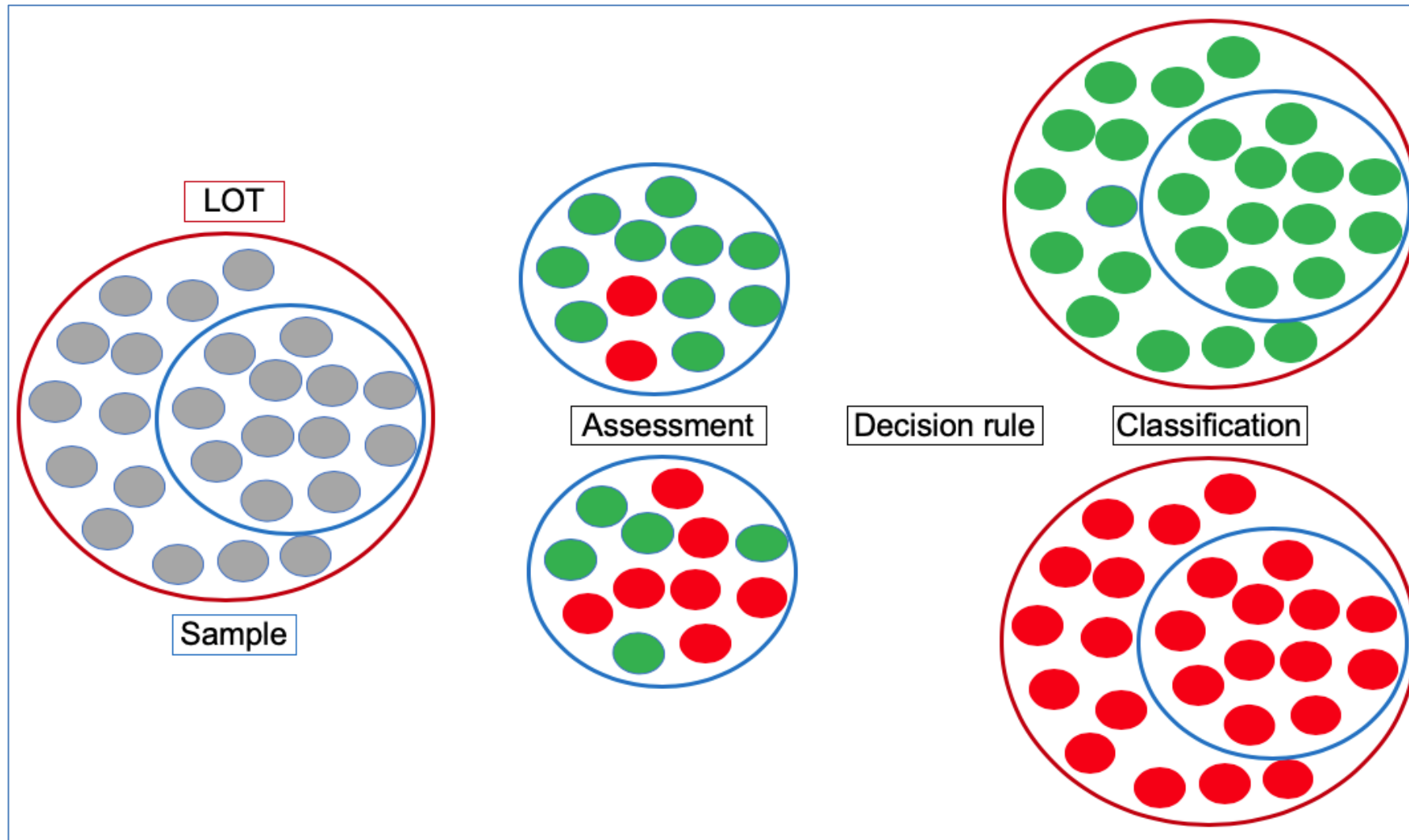
- Lot Quality Assurance Sampling
- Binomial sequential sampling
- Truncated sequential sampling

# LOT QUALITY ASSURANCE SAMPLING (LQAS)

# Lot Quality Assurance Sampling (LQAS)

- Derived from setting of manufacturing
  - Quality assurance strategy
- Used in multiple sectors
  - Vaccine uptake
  - Food safety
  - ....

# Lot Quality Assurance Sampling (LQAS)

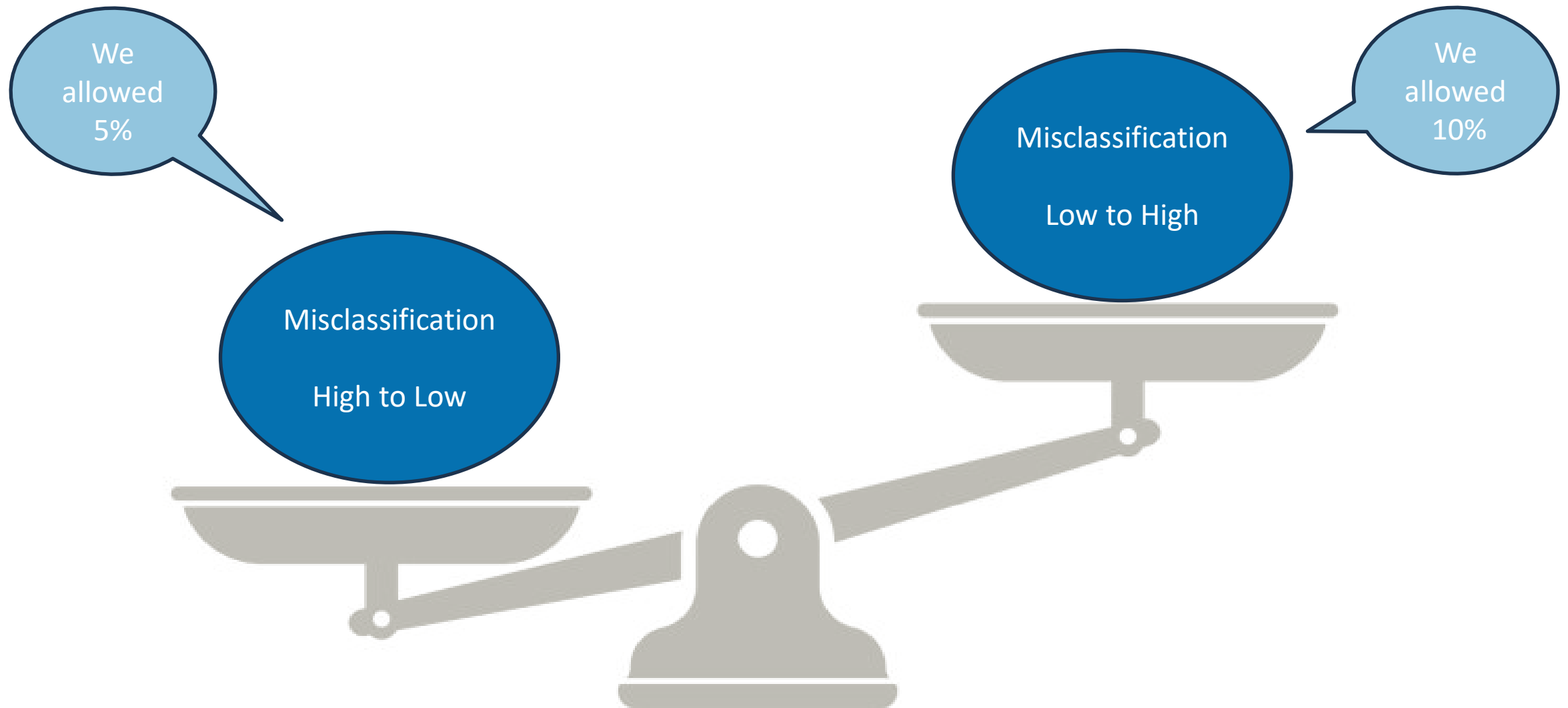


# Component LQAS

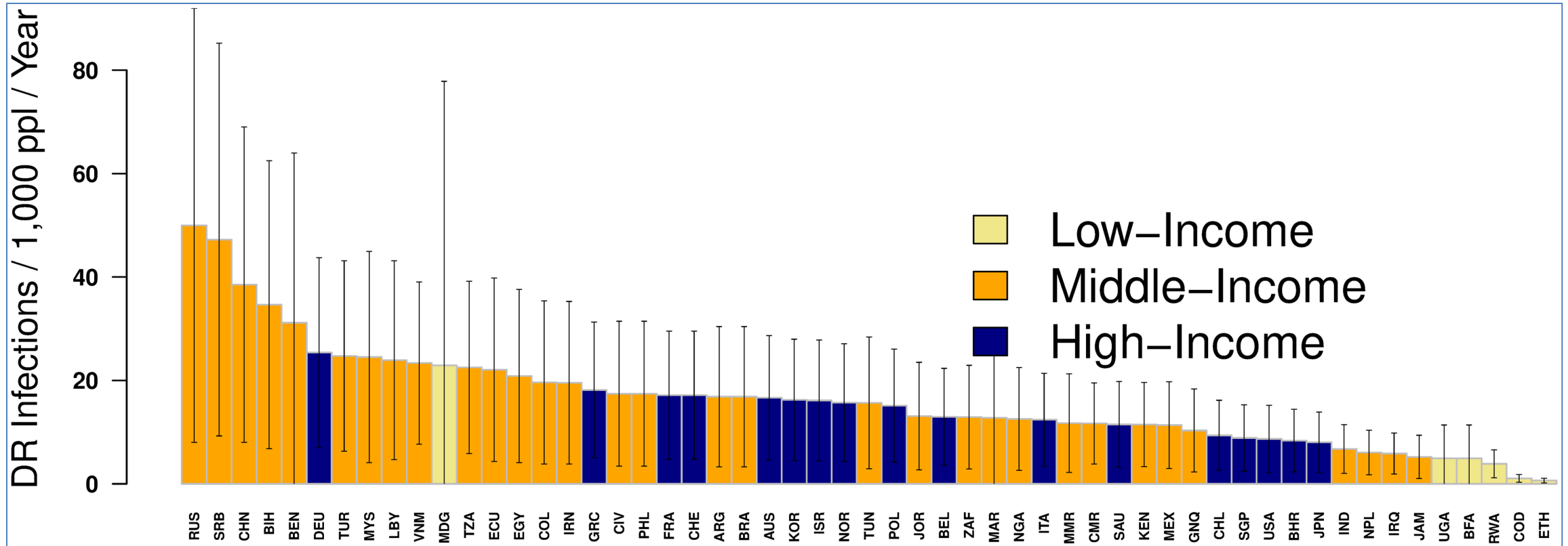
- Lower and upper threshold of outcome (AMR)
  - Above which threshold is action needed
  - Below which threshold is misclassification not allowed
- Allowable misclassification
  - true “low” prevalence classified as “high” and *vice versa*



# Misclassification



# Misclassification and precision



# Component LQAS

- Lower and upper level of outcome (AMR)
- Allowable misclassification
  - true “low” prevalence classified as “high” and *vice versa*
- Both components together drive
  - the sample size
  - the required number of resistant micro-organisms for classification “high prevalence”
- Crucial decisions
  - Requires multi-disciplinary approach

# LQAS sample sizes

Misclassification	High to Low 5% Low to High 10%	
	Sample size	Decision rule
LQAS definition		
1 – 5	153	4
2 – 10	76	4
3 – 15	50	4
5 – 20	44	5
10 – 25	55	10
13 – 30	49	10
20 – 40	45	13
30 – 50	53	21

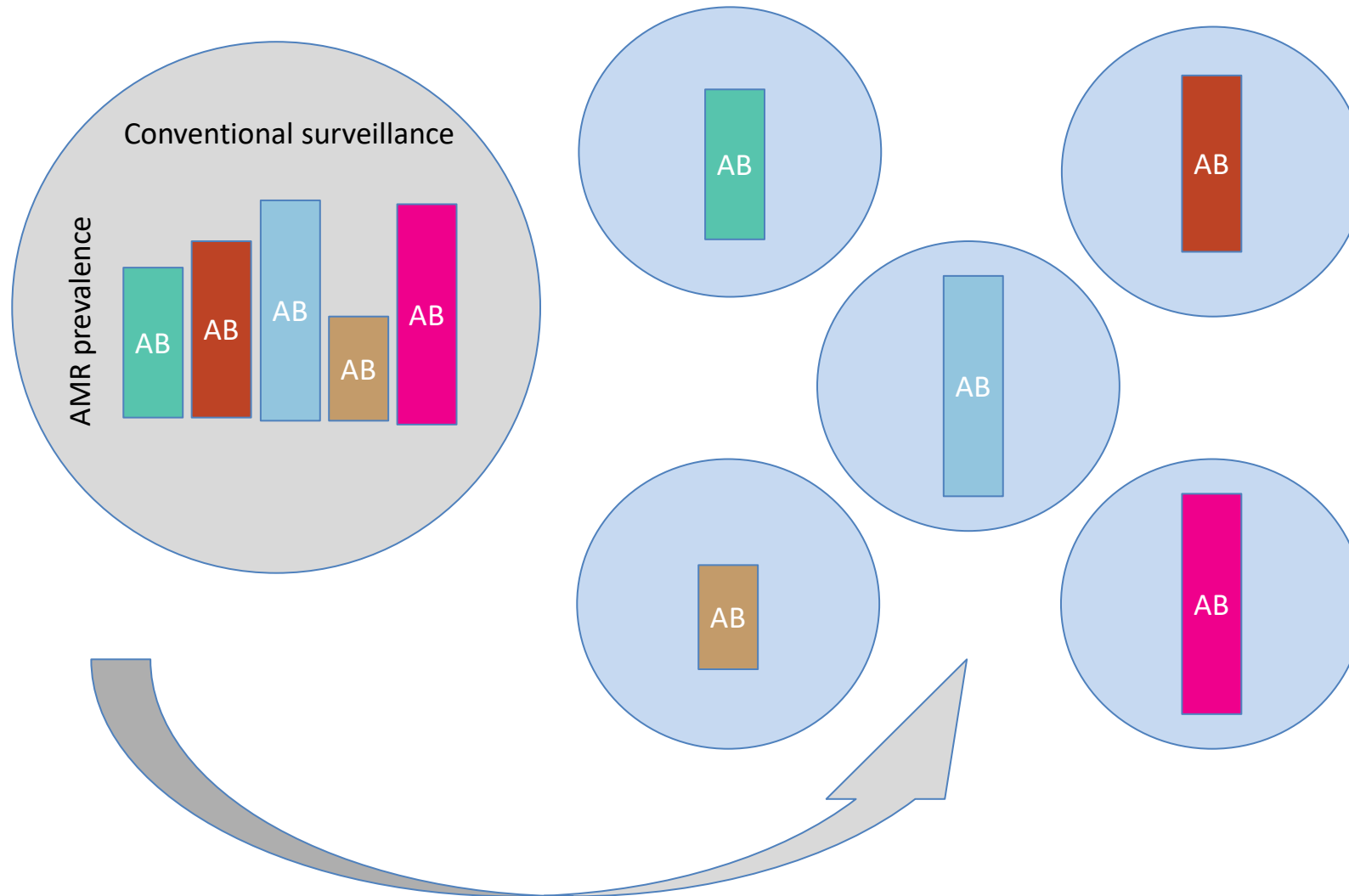
# LQAS sample sizes

Misclassification	High to Low 5% Low to High 10%		High to Low 5% Low to High 5%
LQAS definition	Sample size	Decision rule	Sample size
1 – 5	153	4	na
2 – 10	76	4	89
3 – 15	50	4	59
5 – 20	44	5	50
10 – 25	55	10	70
13 – 30	49	10	61
20 – 40	45	13	60
30 – 50	53	21	67

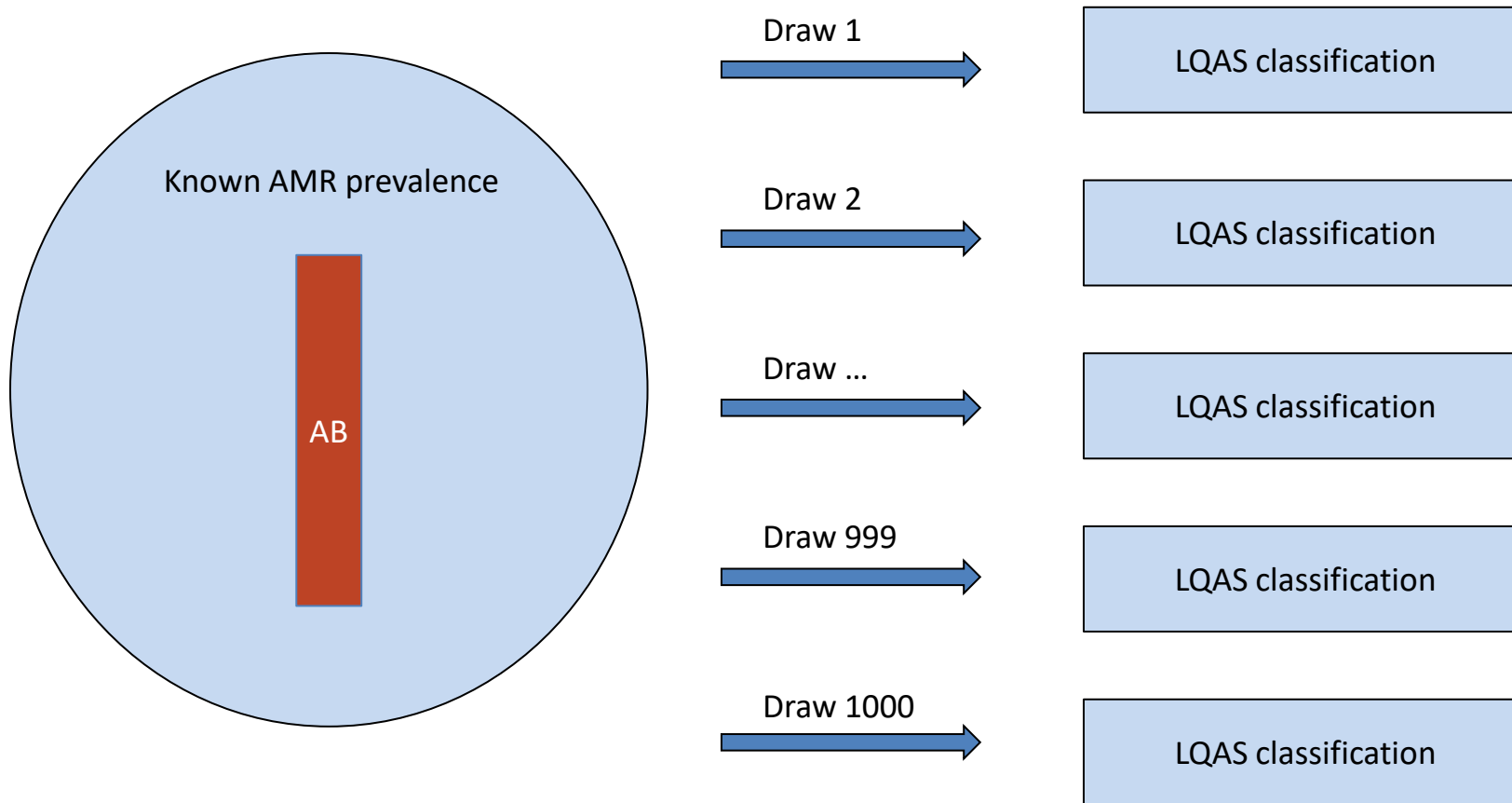
# VALIDATION LQAS METHODOLOGY IN OASIS



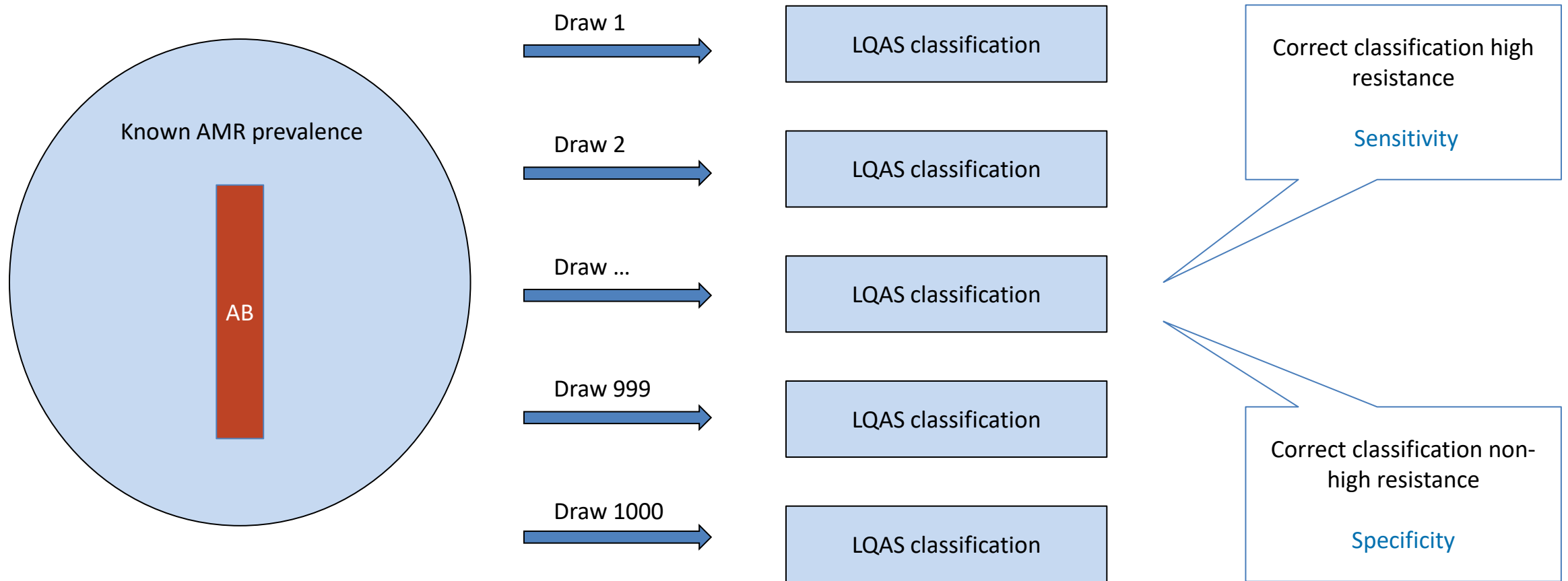
# Theoretical lots from conventional surveillance



# LQAS classifications from repeated draws



# LQAS classifications from repeated draws



# Test characteristics

Definition	Sensitivity	Specificity
1 – 5	100	70.1
2 – 10	100	81.4
3 – 15	100	90.9
5 – 20	100	96.6
10 – 25	99.9	99.9
13 – 30	99.8	97.3
20 – 40	99.7	85.8
30 – 50	99.7	89.2

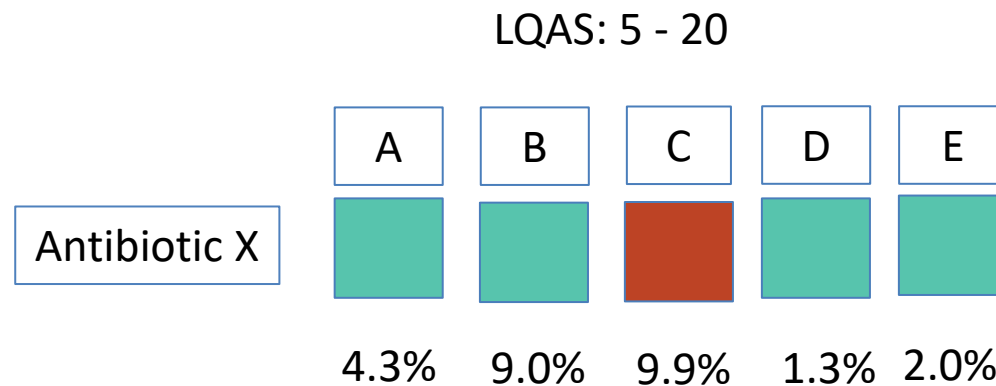
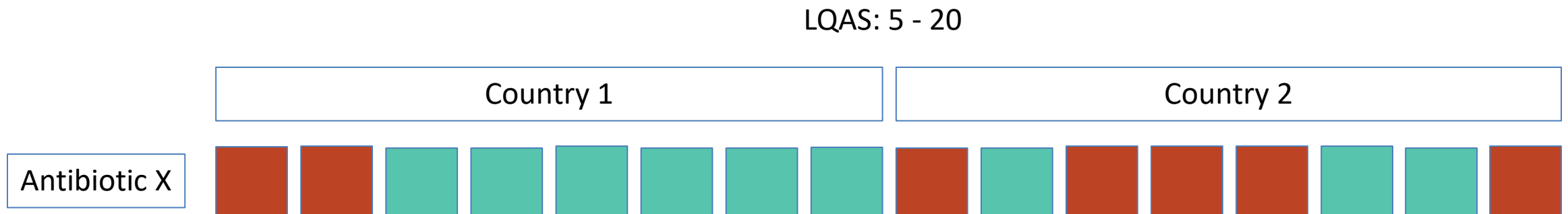
# USE OF LQAS-BASED SURVEILLANCE

# Classification

- LQAS classification is on a single assessment
- Underlying “true” AMR prevalence unknown
- Unknown if misclassification present
- Requires careful design
  - Threshold setting



# Local variation in LQAS classification



# Objectives AMR surveillance

- Guiding empirical antibiotic treatment based on AMR prevalence
  - Flagging areas high AMR prevalence by excellent sensitivity of method
- Assessing changes AMR prevalence
  - Repeat surveys
- Assessing impact on interventions
  - Before – After surveys
- Assessing local variations in AMR prevalence
  - Small sample sizes enable parallel surveys in local areas

## No role LQAS in early warning (very low prevalence)

- Requires large sample size
  - Takes away advantage of method
- Poor test characteristics
  - Reducing allowable misclassification not possible
- Instead: design proper sentinel surveillance

# CONCLUSION AND ACKNOWLEDGEMENT

# Conclusion

- LQAS excellent approach to flag settings with high AMR prevalence
  - High sensitivity
- Suitable for most surveillance objectives
  - Not as an early warning approach
- Facilitates move from laboratory- to population-based surveillance
- Critical design decisions needed for proper interpretation
  - Action needed when exceeding upper threshold
  - Careful threshold setting to manage misclassification

# Acknowledgements

- Research teams in Germany, Togo, Burkina Faso, Netherlands
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