Elicitation Protocol:
Expert Judgment Evaluation of the Future Risk of Antimicrobial Resistance

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Expert Judgment Evaluation of the Future Risk of Antimicrobial Resistance: France

Introduction

Structured expert judgment is an accepted tool in risk analysis for supplementing data shortfalls, quantifying uncertainty, and building rational consensus. It has been used in studies sponsored by many private and public entities, including the European Union, World Health Organization, several agencies in the United States, and the Robert Wood Johnson Foundation. Structured expert judgment has been used to characterize uncertainty in a wide variety of applications not amenable to repeated experimentation or rigorous data collection. Examples include studying the effectiveness of medical procedures in low-resource settings, the relationship between breastfeeding and cognitive development, risks from nuclear power plants, and the risks of invasive species.

This elicitation is about predicting future rates of resistance for different bug/drug combinations in France. Although national surveillance systems regularly provide information on resistance rates, translating that information into predictions is a challenge due to the large number of factors affecting the spread and emergence of resistance. Expert judgment can provide valuable information about future resistance rates.

In the classical model of structured expert judgment, experts quantify their uncertainty with regard to variables of interest and calibration variables from the subject area. Calibration variables are questions for which the true values are unknown to the experts but will be known to the study team within the timeframe of the study. They allow for combinations of the experts' assessments to be validated against empirical data. The variables of interest questions are the objective of the elicitation exercise: data does not exist for these questions, so we must rely on expert judgment. Experts are treated as statistical hypotheses and combined so as to maximize the statistical accuracy and informativeness of the "decision maker," or combination of expert judgments.

Expert names

Expert names are preserved to enable competent peer review, but are not associated with responses in any open documentation. Expert reasoning is captured during the elicitation and becomes, part of the published record. Both the quantitative estimates and the qualitative reasoning from the experts are anonymous in any published report or article.

Elicitation format

The elicitation consists of specifying percentiles of uncertain quantities, as illustrated below.

You are presented with an uncertainty quantity:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
5%	25%	50%	75%	95%

Although the true value to this example question based on the data is known, presumably you don't know the number off the top of your head, so the number you have in mind is uncertain.

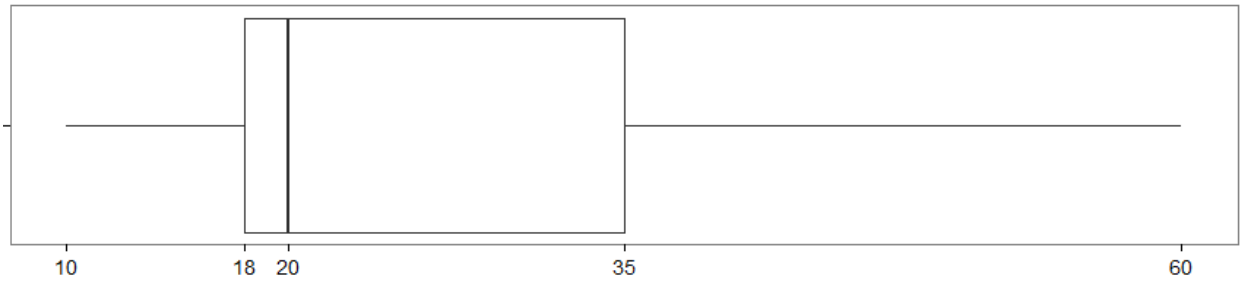
You are asked to provide numbers that quantify your uncertainty by specifying these five percentiles.

- The 5th percentile is the number for which you think there is a 5% chance the true value is *below* and a 95% chance the true value is *above*.
- The 25th percentile is the number for which you think there is a 25% chance the true value is *below* and a 75% chance the true value is *above*.
- The 50th percentile is the number for which you think there is a 50% chance the true value is *below* and a 50% chance the true value is *above*.
- The 75th percentile is the number for which you think there is a 75% chance the true value is *below* and a 25% chance the true value is *above*.
- The 95th percentile is the number for which you think there is a 95% chance the true value is *below* and a 5% chance the true value is *above*.

The values you provide for a question must always be increasing, such that:
5th percentile < 25th percentile < 50th percentile < 75th percentile < 95th percentile

Suppose you answer as shown below:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
10	18	20	35	60
5%	25%	50%	75%	95%

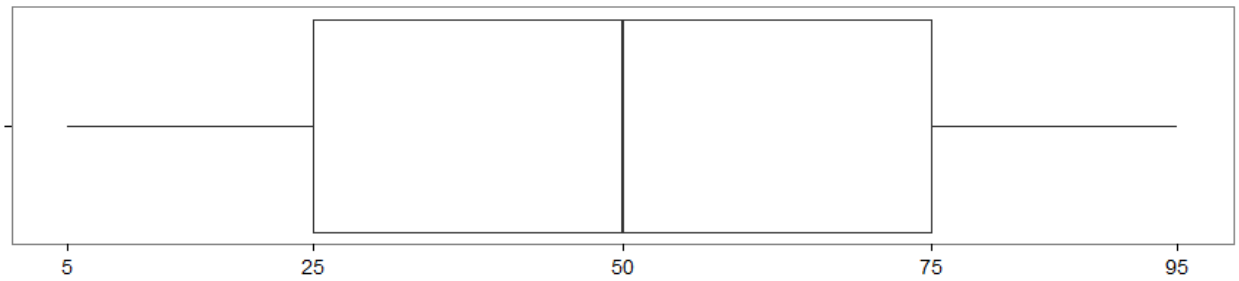


This means you believe the true value is equally likely to be above or below 20%. You believe there is a 50% chance the true percent of isolates that tested resistant falls between 15% and 30%. You believe there is a 90% the true value falls between 10% and 60%.

The actual value for this question is **30%**. This falls within your specified 90% confidence band, so you are not surprised by the answer. However, you would have been surprised to hear the true value were 5% or 75%.

Suppose you had answered:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
5	25	50	75	95
5%	25%	50%	75%	95%



The true value falls between the 25th and 50th percentiles you provided, so you are still not surprised by this answer. However, this response is less informative than the first because the range between percentiles is greater.

An expert is a *good probability assessor* if the provided assessments capture the true values with the long run correct relative frequencies (**statistically accurate**), with distributions that are as narrow as possible (**informative**). Statistical accuracy means that, for a large number of questions, half of the true values fall above the 50th percentiles and half fall below, 90% of the true values fall within the provided 90% intervals (between the 5th and 95th percentiles), and 50% of the true values fall within the provided 50% intervals (between the 25th and 75th percentiles). Informativeness is based on how far apart or concentrated the percentiles are.

In gauging overall performance, statistical accuracy is more important than informativeness. Non-informative but statistically accurate assessments are useful, as they sensitize us to how large the uncertainties may be. Highly informative but statistically inaccurate assessments are not useful. Do not shy away from wide distributions if that reflects your real uncertainty.

If you have little knowledge about an item, this fact by itself does NOT disqualify you as an uncertainty assessor. Knowing little means that your percentiles should be "far apart." If other experts are more informative, without sacrificing accuracy, then they will exert more influence on the combined decision maker assessment. If there are no statistically accurate experts with more informative assessments, then the uninformative assessments accurately depict the uncertainty. That itself is VERY important information.

Training

Below are a few practice questions to familiarize you with the format and performance concepts.

The following questions are based on TSN data for the United States in 2012.

T1. What percent of tested *Staphylococcus aureus* isolates were resistant to methicillin?				
5%	25%	50%	75%	95%

T2. What percent of tested *Streptococcus pneumoniae* isolates were resistant to penicillins?				
5%	25%	50%	75%	95%

T3. What percent of tested *Klebsiella pneumoniae* isolates were resistant to third generation cephalosporins?				
5%	25%	50%	75%	95%

Elicitation

Calibration questions

All questions concern France.

Questions 1-8 concern data reported by the European Antimicrobial Resistance Surveillance Network (EARS-Net). EARS-Net data come from invasive isolates (i.e., blood and cerebrospinal fluid). The laboratories reporting data may not be nationally representative or constant from year to year. Within a country, the clinical guidelines used may not be consistent between laboratories or across years. Additionally, clinical breakpoints are occasionally revised. As EARS-Net only contains the susceptible (S), intermediate (I), or resistant (R) results and not the underlying disc diffusion zone diameters or minimum inhibitory concentrations (MIC), data cannot be updated or re-analyzed as guidelines on breakpoints are revised. Antimicrobial susceptibility results can thus vary over time.

Questions 9-10 concern data reported by the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP).

Many of the questions ask about the difference in the rate of resistance from 2011 to 2015, which is defined as:

2015 rate – 2011 rate

1. What was the difference in the rate of *Escherichia coli* isolates resistant to fluoroquinolones from 2011 to 2015?				
5%	25%	50%	75%	95%

2. What was the difference in the rate of *Escherichia coli* isolates resistant to third generation cephalosporins from 2011 to 2015?				
5%	25%	50%	75%	95%

3. What was the difference in the rate of *Klebsiella pneumoniae* isolates resistant to third generation cephalosporins from 2011 to 2015?				
5%	25%	50%	75%	95%

4. What was the difference in the rate of *Staphylococcus aureus* isolates resistant to methicillin from 2011 to 2015?				
5%	25%	50%	75%	95%

5. What was the difference in the rate of *Streptococcus pneumoniae* isolates non-susceptible (i.e., intermediate or resistant) to penicillins from 2011 to 2015?				
5%	25%	50%	75%	95%

6. What was the difference in the rate of *Streptococcus pneumoniae* isolates non-susceptible (i.e., intermediate or resistant) to macrolides from 2011 to 2015?				
5%	25%	50%	75%	95%

7. What was the difference in the rate of *Pseudomonas aeruginosa* isolates resistant to fluoroquinolones from 2011 to 2015?				
5%	25%	50%	75%	95%

8. What was the difference in the rate of *Pseudomonas aeruginosa* isolates resistant to carbapenems from 2011 to 2015? Note: Data is based only on imipenem and meropenem.				
5%	25%	50%	75%	95%

9. What was the difference in the rate of *Neisseria gonorrhoeae* isolates resistant to azithromycin from 2011 to 2014?				
5%	25%	50%	75%	95%

10. What was the difference in the rate of *Neisseria gonorrhoeae* isolates resistant to ciprofloxacin from 2011 to 2014?				
5%	25%	50%	75%	95%

Variables of interest

All questions concern France.

For the following questions, assume isolates are collected and tested according to current EARS-Net and EUCAST guidelines (available here).

In 2014 17.6% of *Escherichia coli* isolates were resistant to fluoroquinolones. What percent of *Escherichia coli* isolates will be resistant to fluoroquinolones …				
11. … in 2018 (two years)?				
5%	25%	50%	75%	95%
12. … in 2021 (five years)?				
5%	25%	50%	75%	95%
13. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 9.9% of *Escherichia coli* isolates were resistant to third generation cephalosporins.

What percent of *Escherichia coli* isolates will be resistant to third generation cephalosporins …

14. … in 2018 (two years)?				
5%	25%	50%	75%	95%

15. … in 2021 (five years)?				
5%	25%	50%	75%	95%

16. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 less than 0.1% of *Escherichia coli* isolates were resistant to carbapenems.

What percent of *Escherichia coli* isolates will be resistant to carbapenems (including ertapenem) …

17. … in 2018 (two years)?				
5%	25%	50%	75%	95%

18. … in 2021 (five years)?				
5%	25%	50%	75%	95%

19. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 29.6% of *Klebsiella pneumoniae* isolates were resistant to third generation cephalosporins.

What percent of *Klebsiella pneumoniae* isolates will be resistant to third generation cephalosporins …

20. … in 2018 (two years)?				
5%	25%	50%	75%	95%

21. … in 2021 (five years)?				
5%	25%	50%	75%	95%

22. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 0.5% of *Klebsiella pneumoniae* isolates were resistant to carbapenems.

What percent of *Klebsiella pneumoniae* isolates will be resistant to carbapenems (including ertapenem) …

23. … in 2018 (two years)?				
5%	25%	50%	75%	95%

24. … in 2021 (five years)?				
5%	25%	50%	75%	95%

25. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 17.4% of *Staphylococcus aureus* isolates were resistant to methicillin. What percent of *Staphylococcus aureus* isolates will be resistant to methicillin …				
26. … in 2018 (two years)?				
5%	25%	50%	75%	95%
27. … in 2021 (five years)?				
5%	25%	50%	75%	95%
28. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 22.3% of *Streptococcus pneumoniae* isolates were non-susceptible to penicillins. What percent of *Streptococcus pneumoniae* isolates will be non-susceptible (i.e., intermediate or resistant) to penicillins …				
29. … in 2018 (two years)?				
5%	25%	50%	75%	95%
30. … in 2021 (five years)?				
5%	25%	50%	75%	95%
31. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 13.7% of *Pseudomonas aeruginosa* isolates were multidrug resistant (that is, resistance to three or more antimicrobial groups among piperacillin + tazobactam, ceftazidime, fluoroquinolones, aminoglycosides, and carbapenems).

What percent of *Pseudomonas aeruginosa* isolates will be pan-resistant, that is, resistant to all available antibiotics …

32. ... in 2018 (two years)?

5%	25%	50%	75%	95%

33. ... in 2021 (five years)?

5%	25%	50%	75%	95%

34. ... in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 0.9% of *Neisseria gonorrhoeae* isolates were resistant to cefixime (Euro-GASP).

What percent of *Neisseria gonorrhoeae* isolates will be resistant to third generation cephalosporins …

35. ... in 2018 (two years)?

5%	25%	50%	75%	95%

36. ... in 2021 (five years)?

5%	25%	50%	75%	95%

37. ... in 2026 (ten years)?

5%	25%	50%	75%	95%

The final questions concern isolates from other sites, not included in the EARS-Net or Euro-GASP data.

38. What percent of *Staphylococcus aureus* isolates from skin and soft tissue will be resistant to methicillin in 2021 (five years from now)?				
5%	25%	50%	75%	95%

39. What percent of *Escherichia coli* isolates from urine will be resistant to fluoroquinolones in 2021 (five years from now)?				
5%	25%	50%	75%	95%

40. What percent of *Escherichia coli* isolates from urine will be resistant to third generation cephalosporins in 2021 (five years from now)?				
5%	25%	50%	75%	95%

Expert Judgment Evaluation of the Future Risk of Antimicrobial Resistance: Italy

Introduction

Structured expert judgment is an accepted tool in risk analysis for supplementing data shortfalls, quantifying uncertainty, and building rational consensus. It has been used in studies sponsored by many private and public entities, including the European Union, World Health Organization, several agencies in the United States, and the Robert Wood Johnson Foundation. Structured expert judgment has been used to characterize uncertainty in a wide variety of applications not amenable to repeated experimentation or rigorous data collection. Examples include studying the effectiveness of medical procedures in low-resource settings, the relationship between breastfeeding and cognitive development, risks from nuclear power plants, and the risks of invasive species.

This elicitation is about predicting future rates of resistance for different bug/drug combinations in Italy. Although national surveillance systems regularly provide information on resistance rates, translating that information into predictions is a challenge due to the large number of factors affecting the spread and emergence of resistance. Expert judgment can provide valuable information about future resistance rates.

In the classical model of structured expert judgment, experts quantify their uncertainty with regard to variables of interest and calibration variables from the subject area. Calibration variables are questions for which the true values are unknown to the experts but will be known to the study team within the timeframe of the study. They allow for combinations of the experts' assessments to be validated against empirical data. The variables of interest questions are the objective of the elicitation exercise: data does not exist for these questions, so we must rely on expert judgment. Experts are treated as statistical hypotheses and combined so as to maximize the statistical accuracy and informativeness of the "decision maker," or combination of expert judgments.

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Elicitation format

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In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
5%	25%	50%	75%	95%

Although the true value to this example question based on the data is known, presumably you don't know the number off the top of your head, so the number you have in mind is uncertain.

You are asked to provide numbers that quantify your uncertainty by specifying these five percentiles.

- The 5th percentile is the number for which you think there is a 5% chance the true value is *below* and a 95% chance the true value is *above*.
- The 25th percentile is the number for which you think there is a 25% chance the true value is *below* and a 75% chance the true value is *above*.
- The 50th percentile is the number for which you think there is a 50% chance the true value is *below* and a 50% chance the true value is *above*.
- The 75th percentile is the number for which you think there is a 75% chance the true value is *below* and a 25% chance the true value is *above*.
- The 95th percentile is the number for which you think there is a 95% chance the true value is *below* and a 5% chance the true value is *above*.

The values you provide for a question must always be increasing, such that:
5th percentile < 25th percentile < 50th percentile < 75th percentile < 95th percentile

Suppose you answer as shown below:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
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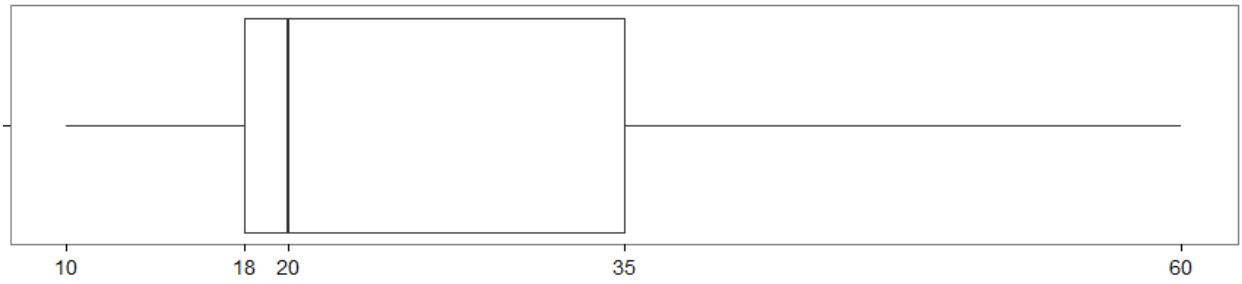

This means you believe the true value is equally likely to be above or below 20%. You believe there is a 50% chance the true percent of isolates that tested resistant falls between 15% and 30%. You believe there is a 90% the true value falls between 10% and 60%.

The actual value for this question is **30%**. This falls within your specified 90% confidence band, so you are not surprised by the answer. However, you would have been surprised to hear the true value were 5% or 75%.

Suppose you had answered:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
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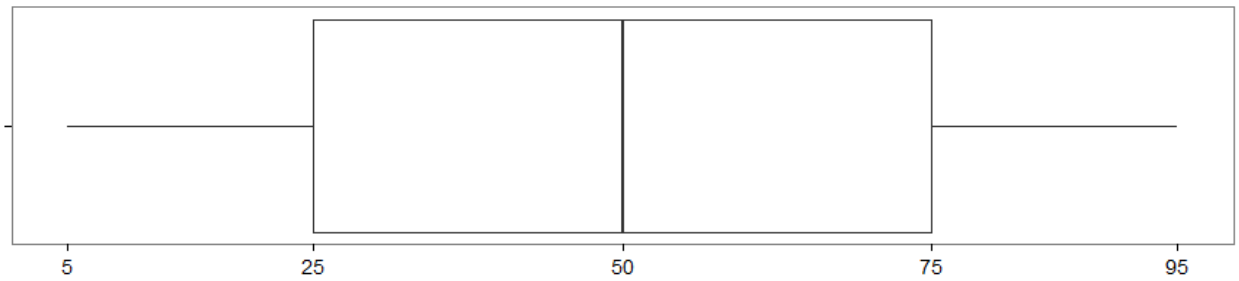

The true value falls between the 25th and 50th percentiles you provided, so you are still not surprised by this answer. However, this response is less informative than the first because the range between percentiles is greater.

An expert is a *good probability assessor* if the provided assessments capture the true values with the long run correct relative frequencies (**statistically accurate**), with distributions that are as narrow as possible (**informative**). Statistical accuracy means that, for a large number of questions, half of the true values fall above the 50th percentiles and half fall below, 90% of the true values fall within the provided 90% intervals (between the 5th and 95th percentiles), and 50% of the true values fall within the provided 50% intervals (between the 25th and 75th percentiles). Informativeness is based on how far apart or concentrated the percentiles are.

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5%	25%	50%	75%	95%

T2. What percent of tested *Streptococcus pneumoniae* isolates were resistant to penicillins?				
5%	25%	50%	75%	95%

T3. What percent of tested *Klebsiella pneumoniae* isolates were resistant to third generation cephalosporins?				
5%	25%	50%	75%	95%

Elicitation

Calibration questions

All questions concern Italy.

Questions 1-8 concern data reported by the European Antimicrobial Resistance Surveillance Network (EARS-Net). EARS-Net data come from invasive isolates (i.e., blood and cerebrospinal fluid). The laboratories reporting data may not be nationally representative or constant from year to year. Within a country, the clinical guidelines used may not be consistent between laboratories or across years. Additionally, clinical breakpoints are occasionally revised. As EARS-Net only contains the susceptible (S), intermediate (I), or resistant (R) results and not the underlying disc diffusion zone diameters or minimum inhibitory concentrations (MIC), data cannot be updated or re-analyzed as guidelines on breakpoints are revised. Antimicrobial susceptibility results can thus vary over time.

Questions 9-10 concern data reported by the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP).

Many of the questions ask about the difference in the rate of resistance from 2011 to 2015, which is defined as:

2015 rate – 2011 rate

1. What was the difference in the rate of *Escherichia coli* isolates resistant to fluoroquinolones from 2011 to 2015?				
5%	25%	50%	75%	95%

2. What was the difference in the rate of *Escherichia coli* isolates resistant to third generation cephalosporins from 2011 to 2015?				
5%	25%	50%	75%	95%

3. What was the difference in the rate of *Klebsiella pneumoniae* isolates resistant to third generation cephalosporins from 2011 to 2015?				
5%	25%	50%	75%	95%

4. What was the difference in the rate of *Staphylococcus aureus* isolates resistant to methicillin from 2011 to 2015?				
5%	25%	50%	75%	95%

5. What was the difference in the rate of *Streptococcus pneumoniae* isolates non-susceptible (i.e., intermediate or resistant) to penicillins from 2011 to 2015?				
5%	25%	50%	75%	95%

6. What was the difference in the rate of *Streptococcus pneumoniae* isolates non-susceptible (i.e., intermediate or resistant) to macrolides from 2011 to 2015?				
5%	25%	50%	75%	95%

7. What was the difference in the rate of *Pseudomonas aeruginosa* isolates resistant to fluoroquinolones from 2011 to 2015?				
5%	25%	50%	75%	95%

8. What was the difference in the rate of *Pseudomonas aeruginosa* isolates resistant to carbapenems from 2011 to 2015? Note: Data is based only on imipenem and meropenem.				
5%	25%	50%	75%	95%

9. What was the difference in the rate of *Neisseria gonorrhoeae* isolates resistant to azithromycin from 2011 to 2014?				
5%	25%	50%	75%	95%

10. What was the difference in the rate of *Neisseria gonorrhoeae* isolates resistant to ciprofloxacin from 2011 to 2014?				
5%	25%	50%	75%	95%

Variables of interest

All questions concern Italy.

For the following questions, assume isolates are collected and tested according to current EARS-Net and EUCAST guidelines (available here).

In 2014 43.9% of *Escherichia coli* isolates were resistant to fluoroquinolones. What percent of *Escherichia coli* isolates will be resistant to fluoroquinolones …				
11. … in 2018 (two years)?				
5%	25%	50%	75%	95%
12. … in 2021 (five years)?				
5%	25%	50%	75%	95%
13. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 28.7% of *Escherichia coli* isolates were resistant to third generation cephalosporins.

What percent of *Escherichia coli* isolates will be resistant to third generation cephalosporins …

14. … in 2018 (two years)?

5%	25%	50%	75%	95%

15. … in 2021 (five years)?

5%	25%	50%	75%	95%

16. … in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 0.2% of *Escherichia coli* isolates were resistant to carbapenems.

What percent of *Escherichia coli* isolates will be resistant to carbapenems (including ertapenem) …

17. … in 2018 (two years)?

5%	25%	50%	75%	95%

18. … in 2021 (five years)?

5%	25%	50%	75%	95%

19. … in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 56.5% of *Klebsiella pneumoniae* isolates were resistant to third generation cephalosporins.

What percent of *Klebsiella pneumoniae* isolates will be resistant to third generation cephalosporins …

20. … in 2018 (two years)?				
5%	25%	50%	75%	95%

21. … in 2021 (five years)?				
5%	25%	50%	75%	95%

22. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 32.9% of *Klebsiella pneumoniae* isolates were resistant to carbapenems.

What percent of *Klebsiella pneumoniae* isolates will be resistant to carbapenems (including ertapenem) …

23. … in 2018 (two years)?				
5%	25%	50%	75%	95%

24. … in 2021 (five years)?				
5%	25%	50%	75%	95%

25. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 33.6% of *Staphylococcus aureus* isolates were resistant to methicillin. What percent of *Staphylococcus aureus* isolates will be resistant to methicillin …				
26. … in 2018 (two years)?				
5%	25%	50%	75%	95%
27. … in 2021 (five years)?				
5%	25%	50%	75%	95%
28. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 14.8% of *Streptococcus pneumoniae* isolates were non-susceptible to penicillins. What percent of *Streptococcus pneumoniae* isolates will be non-susceptible (i.e., intermediate or resistant) to penicillins …				
29. … in 2018 (two years)?				
5%	25%	50%	75%	95%
30. … in 2021 (five years)?				
5%	25%	50%	75%	95%
31. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 23.0% of *Pseudomonas aeruginosa* isolates were multidrug resistant (that is, resistance to three or more antimicrobial groups among piperacillin + tazobactam, ceftazidime, fluoroquinolones, aminoglycosides, and carbapenems).

What percent of *Pseudomonas aeruginosa* isolates will be pan-resistant, that is, resistant to all available antibiotics …

32. ... in 2018 (two years)?

5%	25%	50%	75%	95%

33. ... in 2021 (five years)?

5%	25%	50%	75%	95%

34. ... in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 2.0% of *Neisseria gonorrhoeae* isolates were resistant to cefixime (Euro-GASP).

What percent of *Neisseria gonorrhoeae* isolates will be resistant to third generation cephalosporins …

35. ... in 2018 (two years)?

5%	25%	50%	75%	95%

36. ... in 2021 (five years)?

5%	25%	50%	75%	95%

37. ... in 2026 (ten years)?

5%	25%	50%	75%	95%

The final questions concern isolates from other sites, not included in the EARS-Net or Euro-GASP data.

38. What percent of *Staphylococcus aureus* isolates from skin and soft tissue will be resistant to methicillin in 2021 (five years from now)?				
5%	25%	50%	75%	95%

39. What percent of *Escherichia coli* isolates from urine will be resistant to fluoroquinolones in 2021 (five years from now)?				
5%	25%	50%	75%	95%

40. What percent of *Escherichia coli* isolates from urine will be resistant to third generation cephalosporins in 2021 (five years from now)?				
5%	25%	50%	75%	95%

Expert Judgment Evaluation of the Future Risk of Antimicrobial Resistance: Spain

Introduction

Structured expert judgment is an accepted tool in risk analysis for supplementing data shortfalls, quantifying uncertainty, and building rational consensus. It has been used in studies sponsored by many private and public entities, including the European Union, World Health Organization, several agencies in the United States, and the Robert Wood Johnson Foundation. Structured expert judgment has been used to characterize uncertainty in a wide variety of applications not amenable to repeated experimentation or rigorous data collection. Examples include studying the effectiveness of medical procedures in low-resource settings, the relationship between breastfeeding and cognitive development, risks from nuclear power plants, and the risks of invasive species.

This elicitation is about predicting future rates of resistance for different bug/drug combinations in Spain. Although national surveillance systems regularly provide information on resistance rates, translating that information into predictions is a challenge due to the large number of factors affecting the spread and emergence of resistance. Expert judgment can provide valuable information about future resistance rates.

In the classical model of structured expert judgment, experts quantify their uncertainty with regard to variables of interest and calibration variables from the subject area. Calibration variables are questions for which the true values are unknown to the experts but will be known to the study team within the timeframe of the study. They allow for combinations of the experts' assessments to be validated against empirical data. The variables of interest questions are the objective of the elicitation exercise: data does not exist for these questions, so we must rely on expert judgment. Experts are treated as statistical hypotheses and combined so as to maximize the statistical accuracy and informativeness of the "decision maker," or combination of expert judgments.

Expert names

Expert names are preserved to enable competent peer review, but are not associated with responses in any open documentation. Expert reasoning is captured during the elicitation and becomes, part of the published record. Both the quantitative estimates and the qualitative reasoning from the experts are anonymous in any published report or article.

Elicitation format

The elicitation consists of specifying percentiles of uncertain quantities, as illustrated below.

You are presented with an uncertainty quantity:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
5%	25%	50%	75%	95%

Although the true value to this example question based on the data is known, presumably you don't know the number off the top of your head, so the number you have in mind is uncertain.

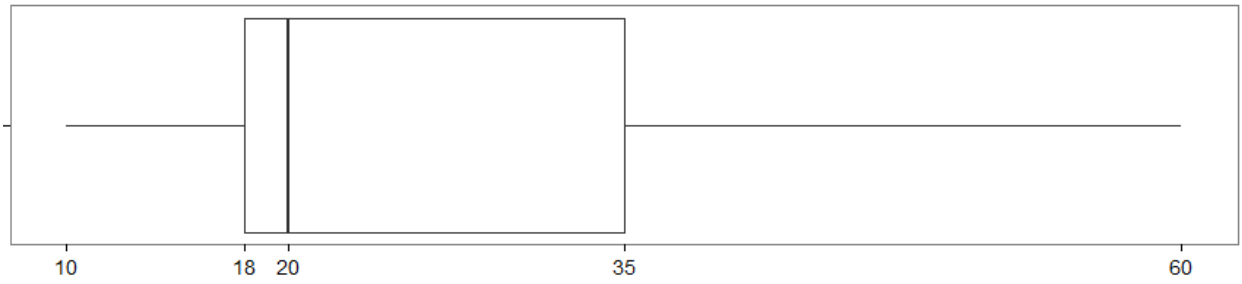
You are asked to provide numbers that quantify your uncertainty by specifying these five percentiles.

- The 5th percentile is the number for which you think there is a 5% chance the true value is *below* and a 95% chance the true value is *above*.
- The 25th percentile is the number for which you think there is a 25% chance the true value is *below* and a 75% chance the true value is *above*.
- The 50th percentile is the number for which you think there is a 50% chance the true value is *below* and a 50% chance the true value is *above*.
- The 75th percentile is the number for which you think there is a 75% chance the true value is *below* and a 25% chance the true value is *above*.
- The 95th percentile is the number for which you think there is a 95% chance the true value is *below* and a 5% chance the true value is *above*.

The values you provide for a question must always be increasing, such that:
5th percentile < 25th percentile < 50th percentile < 75th percentile < 95th percentile

Suppose you answer as shown below:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
10	18	20	35	60
5%	25%	50%	75%	95%

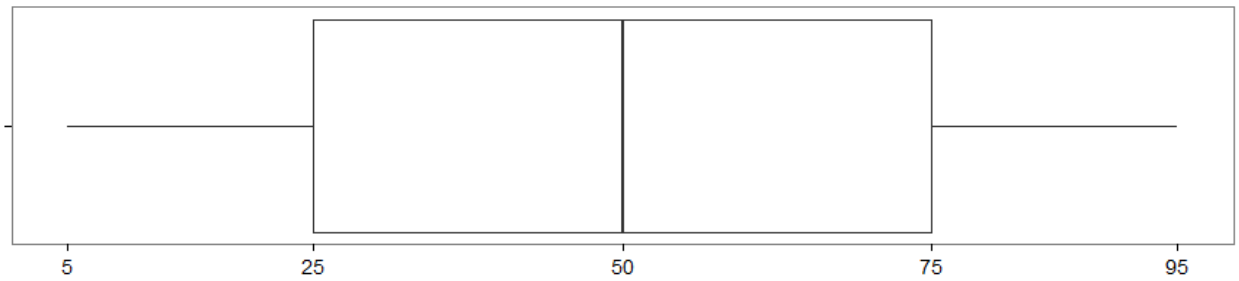


This means you believe the true value is equally likely to be above or below 20%. You believe there is a 50% chance the true percent of isolates that tested resistant falls between 15% and 30%. You believe there is a 90% the true value falls between 10% and 60%.

The actual value for this question is **30%**. This falls within your specified 90% confidence band, so you are not surprised by the answer. However, you would have been surprised to hear the true value were 5% or 75%.

Suppose you had answered:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
5	25	50	75	95
5%	25%	50%	75%	95%



The true value falls between the 25th and 50th percentiles you provided, so you are still not surprised by this answer. However, this response is less informative than the first because the range between percentiles is greater.

An expert is a *good probability assessor* if the provided assessments capture the true values with the long run correct relative frequencies (**statistically accurate**), with distributions that are as narrow as possible (**informative**). Statistical accuracy means that, for a large number of questions, half of the true values fall above the 50th percentiles and half fall below, 90% of the true values fall within the provided 90% intervals (between the 5th and 95th percentiles), and 50% of the true values fall within the provided 50% intervals (between the 25th and 75th percentiles). Informativeness is based on how far apart or concentrated the percentiles are.

In gauging overall performance, statistical accuracy is more important than informativeness. Non-informative but statistically accurate assessments are useful, as they sensitize us to how large the uncertainties may be. Highly informative but statistically inaccurate assessments are not useful. Do not shy away from wide distributions if that reflects your real uncertainty.

If you have little knowledge about an item, this fact by itself does NOT disqualify you as an uncertainty assessor. Knowing little means that your percentiles should be "far apart." If other experts are more informative, without sacrificing accuracy, then they will exert more influence on the combined decision maker assessment. If there are no statistically accurate experts with more informative assessments, then the uninformative assessments accurately depict the uncertainty. That itself is VERY important information.

Training

Below are a few practice questions to familiarize you with the format and performance concepts.

The following questions are based on TSN data for the United States in 2012.

T1. What percent of tested *Staphylococcus aureus* isolates were resistant to methicillin?				
5%	25%	50%	75%	95%

T2. What percent of tested *Streptococcus pneumoniae* isolates were resistant to penicillins?				
5%	25%	50%	75%	95%

T3. What percent of tested *Klebsiella pneumoniae* isolates were resistant to third generation cephalosporins?				
5%	25%	50%	75%	95%

Elicitation

Calibration questions

All questions concern Spain.

Questions 1-8 concern data reported by the European Antimicrobial Resistance Surveillance Network (EARS-Net). EARS-Net data come from invasive isolates (i.e., blood and cerebrospinal fluid). The laboratories reporting data may not be nationally representative or constant from year to year. Within a country, the clinical guidelines used may not be consistent between laboratories or across years. Additionally, clinical breakpoints are occasionally revised. As EARS-Net only contains the susceptible (S), intermediate (I), or resistant (R) results and not the underlying disc diffusion zone diameters or minimum inhibitory concentrations (MIC), data cannot be updated or re-analyzed as guidelines on breakpoints are revised. Antimicrobial susceptibility results can thus vary over time.

Questions 9-10 concern data reported by the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP).

Many of the questions ask about the difference in the rate of resistance from 2011 to 2015, which is defined as:

2015 rate – 2011 rate

1. What was the difference in the rate of *Escherichia coli* isolates resistant to fluoroquinolones from 2011 to 2015?				
5%	25%	50%	75%	95%

2. What was the difference in the rate of *Escherichia coli* isolates resistant to third generation cephalosporins from 2011 to 2015?				
5%	25%	50%	75%	95%

3. What was the difference in the rate of *Klebsiella pneumoniae* isolates resistant to third generation cephalosporins from 2011 to 2015?				
5%	25%	50%	75%	95%

4. What was the difference in the rate of *Staphylococcus aureus* isolates resistant to methicillin from 2011 to 2015?				
5%	25%	50%	75%	95%

5. What was the difference in the rate of *Streptococcus pneumoniae* isolates non-susceptible (i.e., intermediate or resistant) to penicillins from 2011 to 2015?				
5%	25%	50%	75%	95%

6. What was the difference in the rate of *Streptococcus pneumoniae* isolates non-susceptible (i.e., intermediate or resistant) to macrolides from 2011 to 2015?				
5%	25%	50%	75%	95%

7. What was the difference in the rate of *Pseudomonas aeruginosa* isolates resistant to fluoroquinolones from 2011 to 2015?				
5%	25%	50%	75%	95%

8. What was the difference in the rate of *Pseudomonas aeruginosa* isolates resistant to carbapenems from 2011 to 2015? Note: Data is based only on imipenem and meropenem.				
5%	25%	50%	75%	95%

9. What was the difference in the rate of *Neisseria gonorrhoeae* isolates resistant to azithromycin from 2011 to 2014?				
5%	25%	50%	75%	95%

10. What was the difference in the rate of *Neisseria gonorrhoeae* isolates resistant to ciprofloxacin from 2011 to 2014?				
5%	25%	50%	75%	95%

Variables of interest

All questions concern Spain.

For the following questions, assume isolates are collected and tested according to current EARS-Net and EUCAST guidelines (available here).

In 2014 34.0% of *Escherichia coli* isolates were resistant to fluoroquinolones. What percent of *Escherichia coli* isolates will be resistant to fluoroquinolones …				
11. … in 2018 (two years)?				
5%	25%	50%	75%	95%
12. … in 2021 (five years)?				
5%	25%	50%	75%	95%
13. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 12.3% of *Escherichia coli* isolates were resistant to third generation cephalosporins.

What percent of *Escherichia coli* isolates will be resistant to third generation cephalosporins …

14. … in 2018 (two years)?

5%	25%	50%	75%	95%

15. … in 2021 (five years)?

5%	25%	50%	75%	95%

16. … in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 0.1% of *Escherichia coli* isolates were resistant to carbapenems.

What percent of *Escherichia coli* isolates will be resistant to carbapenems (including ertapenem) …

17. … in 2018 (two years)?

5%	25%	50%	75%	95%

18. … in 2021 (five years)?

5%	25%	50%	75%	95%

19. … in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 18.0% of *Klebsiella pneumoniae* isolates were resistant to third generation cephalosporins.

What percent of *Klebsiella pneumoniae* isolates will be resistant to third generation cephalosporins …

20. … in 2018 (two years)?				
5%	25%	50%	75%	95%

21. … in 2021 (five years)?				
5%	25%	50%	75%	95%

22. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 2.3% of *Klebsiella pneumoniae* isolates were resistant to carbapenems.

What percent of *Klebsiella pneumoniae* isolates will be resistant to carbapenems (including ertapenem) …

23. … in 2018 (two years)?				
5%	25%	50%	75%	95%

24. … in 2021 (five years)?				
5%	25%	50%	75%	95%

25. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 22.1% of *Staphylococcus aureus* isolates were resistant to methicillin. What percent of *Staphylococcus aureus* isolates will be resistant to methicillin …				
26. … in 2018 (two years)?				
5%	25%	50%	75%	95%
27. … in 2021 (five years)?				
5%	25%	50%	75%	95%
28. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 27.9% of *Streptococcus pneumoniae* isolates were non-susceptible to penicillins. What percent of *Streptococcus pneumoniae* isolates will be non-susceptible (i.e., intermediate or resistant) to penicillins …				
29. … in 2018 (two years)?				
5%	25%	50%	75%	95%
30. … in 2021 (five years)?				
5%	25%	50%	75%	95%
31. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 12.4% of *Pseudomonas aeruginosa* isolates were multidrug resistant (that is, resistance to three or more antimicrobial groups among piperacillin + tazobactam, ceftazidime, fluoroquinolones, aminoglycosides, and carbapenems).

What percent of *Pseudomonas aeruginosa* isolates will be pan-resistant, that is, resistant to all available antibiotics …

32. ... in 2018 (two years)?

5%	25%	50%	75%	95%

33. ... in 2021 (five years)?

5%	25%	50%	75%	95%

34. ... in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 0.0% of *Neisseria gonorrhoeae* isolates were resistant to cefixime (Euro-GASP).

What percent of *Neisseria gonorrhoeae* isolates will be resistant to third generation cephalosporins …

35. ... in 2018 (two years)?

5%	25%	50%	75%	95%

36. ... in 2021 (five years)?

5%	25%	50%	75%	95%

37. ... in 2026 (ten years)?

5%	25%	50%	75%	95%

The final questions concern isolates from other sites, not included in the EARS-Net or Euro-GASP data.

38. What percent of *Staphylococcus aureus* isolates from skin and soft tissue will be resistant to methicillin in 2021 (five years from now)?				
5%	25%	50%	75%	95%

39. What percent of *Escherichia coli* isolates from urine will be resistant to fluoroquinolones in 2021 (five years from now)?				
5%	25%	50%	75%	95%

40. What percent of *Escherichia coli* isolates from urine will be resistant to third generation cephalosporins in 2021 (five years from now)?				
5%	25%	50%	75%	95%

Expert Judgment Evaluation of the Future Risk of Antimicrobial Resistance: UK

Introduction

Structured expert judgment is an accepted tool in risk analysis for supplementing data shortfalls, quantifying uncertainty, and building rational consensus. It has been used in studies sponsored by many private and public entities, including the European Union, World Health Organization, several agencies in the United States, and the Robert Wood Johnson Foundation. Structured expert judgment has been used to characterize uncertainty in a wide variety of applications not amenable to repeated experimentation or rigorous data collection. Examples include studying the effectiveness of medical procedures in low-resource settings, the relationship between breastfeeding and cognitive development, risks from nuclear power plants, and the risks of invasive species.

This elicitation is about predicting future rates of resistance for different bug/drug combinations in the United Kingdom. Although national surveillance systems regularly provide information on resistance rates, translating that information into predictions is a challenge due to the large number of factors affecting the spread and emergence of resistance. Expert judgment can provide valuable information about future resistance rates.

In the classical model of structured expert judgment, experts quantify their uncertainty with regard to variables of interest and calibration variables from the subject area. Calibration variables are questions for which the true values are unknown to the experts but will be known to the study team within the timeframe of the study. They allow for combinations of the experts' assessments to be validated against empirical data. The variables of interest questions are the objective of the elicitation exercise: data does not exist for these questions, so we must rely on expert judgment. Experts are treated as statistical hypotheses and combined so as to maximize the statistical accuracy and informativeness of the "decision maker," or combination of expert judgments.

Expert names

Expert names are preserved to enable competent peer review, but are not associated with responses in any open documentation. Expert reasoning is captured during the elicitation and becomes, part of the published record. Both the quantitative estimates and the qualitative reasoning from the experts are anonymous in any published report or article.

Elicitation format

The elicitation consists of specifying percentiles of uncertain quantities, as illustrated below.

You are presented with an uncertainty quantity:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
5%	25%	50%	75%	95%

Although the true value to this example question based on the data is known, presumably you don't know the number off the top of your head, so the number you have in mind is uncertain.

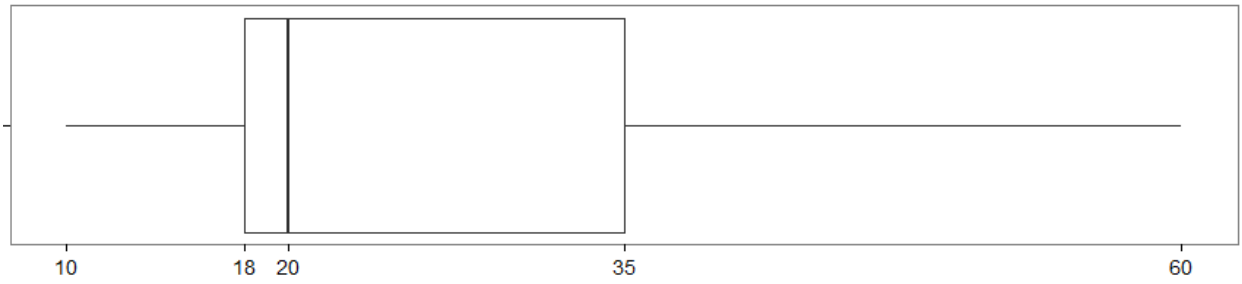
You are asked to provide numbers that quantify your uncertainty by specifying these five percentiles.

- The 5th percentile is the number for which you think there is a 5% chance the true value is *below* and a 95% chance the true value is *above*.
- The 25th percentile is the number for which you think there is a 25% chance the true value is *below* and a 75% chance the true value is *above*.
- The 50th percentile is the number for which you think there is a 50% chance the true value is *below* and a 50% chance the true value is *above*.
- The 75th percentile is the number for which you think there is a 75% chance the true value is *below* and a 25% chance the true value is *above*.
- The 95th percentile is the number for which you think there is a 95% chance the true value is *below* and a 5% chance the true value is *above*.

The values you provide for a question must always be increasing, such that:
5th percentile < 25th percentile < 50th percentile < 75th percentile < 95th percentile

Suppose you answer as shown below:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
10	18	20	35	60
5%	25%	50%	75%	95%

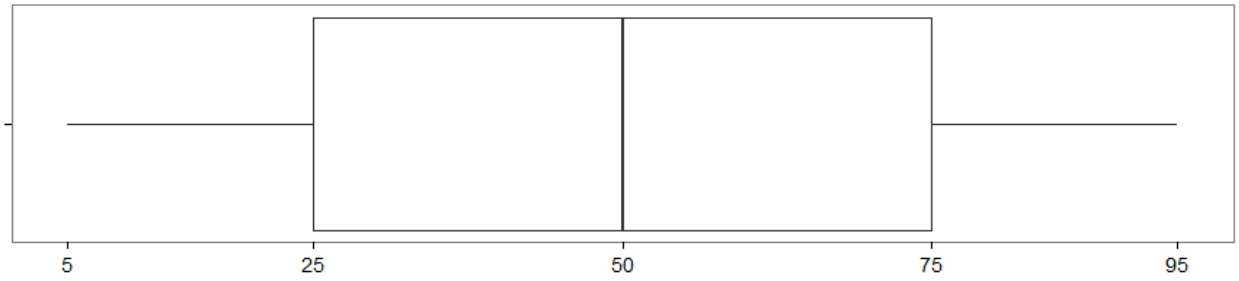


This means you believe the true value is equally likely to be above or below 20%. You believe there is a 50% chance the true percent of isolates that tested resistant falls between 15% and 30%. You believe there is a 90% the true value falls between 10% and 60%.

The actual value for this question is **30%**. This falls within your specified 90% confidence band, so you are not surprised by the answer. However, you would have been surprised to hear the true value were 5% or 75%.

Suppose you had answered:

In the United States in 2012, what percent of the 4,104 tested *Escherichia coli* isolates included in data from The Surveillance Network (TSN) were resistant to fluoroquinolones?				
5	25	50	75	95
5%	25%	50%	75%	95%



The true value falls between the 25th and 50th percentiles you provided, so you are still not surprised by this answer. However, this response is less informative than the first because the range between percentiles is greater.

An expert is a *good probability assessor* if the provided assessments capture the true values with the long run correct relative frequencies (**statistically accurate**), with distributions that are as narrow as possible (**informative**). Statistical accuracy means that, for a large number of questions, half of the true values fall above the 50th percentiles and half fall below, 90% of the true values fall within the provided 90% intervals (between the 5th and 95th percentiles), and 50% of the true values fall within the provided 50% intervals (between the 25th and 75th percentiles). Informativeness is based on how far apart or concentrated the percentiles are.

In gauging overall performance, statistical accuracy is more important than informativeness. Non-informative but statistically accurate assessments are useful, as they sensitize us to how large the uncertainties may be. Highly informative but statistically inaccurate assessments are not useful. Do not shy away from wide distributions if that reflects your real uncertainty.

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Training

Below are a few practice questions to familiarize you with the format and performance concepts.

The following questions are based on TSN data for the United States in 2012.

T1. What percent of tested *Staphylococcus aureus* isolates were resistant to methicillin?				
5%	25%	50%	75%	95%

T2. What percent of tested *Streptococcus pneumoniae* isolates were resistant to penicillins?				
5%	25%	50%	75%	95%

T3. What percent of tested *Klebsiella pneumoniae* isolates were resistant to third generation cephalosporins?				
5%	25%	50%	75%	95%

Elicitation

Calibration questions

All questions concern the United Kingdom.

Questions 1-8 concern data reported by the European Antimicrobial Resistance Surveillance Network (EARS-Net). EARS-Net data come from invasive isolates (i.e., blood and cerebrospinal fluid). The laboratories reporting data may not be nationally representative or constant from year to year. Within a country, the clinical guidelines used may not be consistent between laboratories or across years. Additionally, clinical breakpoints are occasionally revised. As EARS-Net only contains the susceptible (S), intermediate (I), or resistant (R) results and not the underlying disc diffusion zone diameters or minimum inhibitory concentrations (MIC), data cannot be updated or re-analyzed as guidelines on breakpoints are revised. Antimicrobial susceptibility results can thus vary over time.

Questions 9-10 concern data reported by the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP).

Many of the questions ask about the difference in the rate of resistance from 2011 to 2015, which is defined as:

2015 rate – 2011 rate

1. What was the difference in the rate of *Escherichia coli* isolates resistant to fluoroquinolones from 2011 to 2015?				
5%	25%	50%	75%	95%

2. What was the difference in the rate of *Escherichia coli* isolates resistant to third generation cephalosporins from 2011 to 2015?				
5%	25%	50%	75%	95%

3. What was the difference in the rate of *Klebsiella pneumoniae* isolates resistant to third generation cephalosporins from 2011 to 2015?				
5%	25%	50%	75%	95%

4. What was the difference in the rate of *Staphylococcus aureus* isolates resistant to methicillin from 2011 to 2015?				
5%	25%	50%	75%	95%

5. What was the difference in the rate of *Streptococcus pneumoniae* isolates non-susceptible (i.e., intermediate or resistant) to penicillins from 2011 to 2015?				
5%	25%	50%	75%	95%

6. What was the difference in the rate of *Streptococcus pneumoniae* isolates non-susceptible (i.e., intermediate or resistant) to macrolides from 2011 to 2015?				
5%	25%	50%	75%	95%

7. What was the difference in the rate of *Pseudomonas aeruginosa* isolates resistant to fluoroquinolones from 2011 to 2015?				
5%	25%	50%	75%	95%

8. What was the difference in the rate of *Pseudomonas aeruginosa* isolates resistant to carbapenems from 2011 to 2015? Note: Data is based only on imipenem and meropenem.				
5%	25%	50%	75%	95%

9. What was the difference in the rate of *Neisseria gonorrhoeae* isolates resistant to azithromycin from 2011 to 2014?				
5%	25%	50%	75%	95%

10. What was the difference in the rate of *Neisseria gonorrhoeae* isolates resistant to ciprofloxacin from 2011 to 2014?				
5%	25%	50%	75%	95%

Variables of interest

All questions concern the United Kingdom.

For the following questions, assume isolates are collected and tested according to current EARS-Net and EUCAST guidelines (available here).

In 2014 16.8% of *Escherichia coli* isolates were resistant to fluoroquinolones. What percent of *Escherichia coli* isolates will be resistant to fluoroquinolones …				
11. … in 2018 (two years)?				
5%	25%	50%	75%	95%
12. … in 2021 (five years)?				
5%	25%	50%	75%	95%
13. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 10.3% of *Escherichia coli* isolates were resistant to third generation cephalosporins.

What percent of *Escherichia coli* isolates will be resistant to third generation cephalosporins …

14. … in 2018 (two years)?

5%	25%	50%	75%	95%

15. … in 2021 (five years)?

5%	25%	50%	75%	95%

16. … in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 0.1% of *Escherichia coli* isolates were resistant to carbapenems.

What percent of *Escherichia coli* isolates will be resistant to carbapenems (including ertapenem) …

17. … in 2018 (two years)?

5%	25%	50%	75%	95%

18. … in 2021 (five years)?

5%	25%	50%	75%	95%

19. … in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 9.3% of *Klebsiella pneumoniae* isolates were resistant to third generation cephalosporins.

What percent of *Klebsiella pneumoniae* isolates will be resistant to third generation cephalosporins …

20. … in 2018 (two years)?

5%	25%	50%	75%	95%

21. … in 2021 (five years)?

5%	25%	50%	75%	95%

22. … in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 0.8% of *Klebsiella pneumoniae* isolates were resistant to carbapenems.

What percent of *Klebsiella pneumoniae* isolates will be resistant to carbapenems (including ertapenem) …

23. … in 2018 (two years)?

5%	25%	50%	75%	95%

24. … in 2021 (five years)?

5%	25%	50%	75%	95%

25. … in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 11.3% of *Staphylococcus aureus* isolates were resistant to methicillin. What percent of *Staphylococcus aureus* isolates will be resistant to methicillin …				
26. … in 2018 (two years)?				
5%	25%	50%	75%	95%
27. … in 2021 (five years)?				
5%	25%	50%	75%	95%
28. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 5.1% of *Streptococcus pneumoniae* isolates were non-susceptible to penicillins. What percent of *Streptococcus pneumoniae* isolates will be non-susceptible (i.e., intermediate or resistant) to penicillins …				
29. … in 2018 (two years)?				
5%	25%	50%	75%	95%
30. … in 2021 (five years)?				
5%	25%	50%	75%	95%
31. … in 2026 (ten years)?				
5%	25%	50%	75%	95%

In 2014 1.6% of *Pseudomonas aeruginosa* isolates were multidrug resistant (that is, resistance to three or more antimicrobial groups among piperacillin + tazobactam, ceftazidime, fluoroquinolones, aminoglycosides, and carbapenems).

What percent of *Pseudomonas aeruginosa* isolates will be pan-resistant, that is, resistant to all available antibiotics …

32. ... in 2018 (two years)?

5%	25%	50%	75%	95%

33. ... in 2021 (five years)?

5%	25%	50%	75%	95%

34. ... in 2026 (ten years)?

5%	25%	50%	75%	95%

In 2014 0.0% of *Neisseria gonorrhoeae* isolates were resistant to cefixime (Euro-GASP).

What percent of *Neisseria gonorrhoeae* isolates will be resistant to third generation cephalosporins …

35. ... in 2018 (two years)?

5%	25%	50%	75%	95%

36. ... in 2021 (five years)?

5%	25%	50%	75%	95%

37. ... in 2026 (ten years)?

5%	25%	50%	75%	95%

The final questions concern isolates from other sites, not included in the EARS-Net or Euro-GASP data.

38. What percent of *Staphylococcus aureus* isolates from skin and soft tissue will be resistant to methicillin in 2021 (five years from now)?				
5%	25%	50%	75%	95%

39. What percent of *Escherichia coli* isolates from urine will be resistant to fluoroquinolones in 2021 (five years from now)?				
5%	25%	50%	75%	95%

40. What percent of *Escherichia coli* isolates from urine will be resistant to third generation cephalosporins in 2021 (five years from now)?				
5%	25%	50%	75%	95%