Use of experts' beliefs in the evaluation of complex and early stage interventions

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Project background

Case study: an economic evaluation of two antimicrobials (AMs), conducted to inform a novel funding model by NHS England & NHS Improvement

"Netflix" subscription model piloted to dissociate manufacturers' revenue from antibiotic usage

- Subscription charge based on the total health benefit of the AMs at population level, over 10 years

- Health benefits included additional elements of value of AMs: **S**pectrum, **T**ransmission, **E**nablement, **D**iversity, **I**nsurance

Modelling approach

Modelling patient-level INHEs in HVCS

Estimation of costs and benefits of introducing CAZ-AVI at the patient-level using decision analytic modelling

Modelling population-level INHEs in HVCS over time

Forecasting population size and resistance over time

Extrapolation from HVCS to expected usage

Rescaling to reflect usage within and outside the HVCS

INHE = incremental net health effects; HVCS = high value clinical scenarios

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What were the HVCSs?

	CAZ-AVI	Cefiderocol
Pathogen	Carbapenem-producing *Enterobacterales* (**CPE**)	**CPE** *Pseudomonas aeruginosa*
Mechanism of resistance	OXA-48	Metallo-beta-lactamases (**MBL**)
Treatment setting	Microbiology-directed setting (**MDS**) Empiric setting (**ES**)	
Site of infection	**ES**: HAP/VAP **MDS**: cUTI, HAP/VAP?	

cUTI = complicated urinary tract infections

HAP/VAP = Hospital-acquired pneumonia/ventilator-associated pneumonia

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What were the challenges for SEE?

1. Time constraints

2. Complex parameters

3. Repetitive questions (experts' engagement)

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How did elicitation fit with the wider project?

	Jan-21	Feb-21	Mar-21	Apr-21	May-21	Jun-21	Jul-21	Aug-21	Sep-21
Evidence mapping and literature reviews	███	███	███	███	███				
Establishing the model structure	███	███	███	███	███				
Identifying evidence to populate the decision-model				███	███				
Structured expert elicitation to supplement literature reviews				███	███	███			
Building, validating and running the model						███	███	███	███

SEE under time constraints

- Strong communication with the evidence review team to narrow down potential parameters early on

- Established a small sample of experts to advise on SEE

- Plan methods where possible

- Plan dates for conducting SEE (and stick with the schedule)

Timelines for conducting SEE

SEE training delivered via webinar
(1hour)

↓
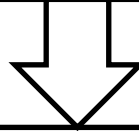
Elicited experts' beliefs individually using a web app
(2 weeks)

↓
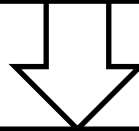
Experts shown group summaries and provided with
opportunity to update their answers (1 week)

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What were the challenges for SEE?

1. Time constraints

2. **Complex parameters required in the model**

3. Expert motivation though repetitive questions

Parameters required for the analysis

Model structure: Modelled patients' outcomes conditional on in-vitro susceptibility to antimicrobials

Outcomes of interest: survival, quality of life and resource use (consider infection, comorbidities and drug toxicity)

To simplify the exercise, we selected questions based on literature gaps and likely impact on model results…

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Elicitation questions

Question 1. In this patient population, what proportion of patients will **still be alive 30 days after** starting microbiology-directed treatment?

Question 2. In this patient population, what will be the **average length of stay**?

Question 3. In this patient population, **what proportion of hospital stay** would be spent on each of the following wards?

- Intensive Care Unit

- High Dependency/Critical Care Unit

- Other

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Question 1. In this patient population, what proportion of patients will still be alive 30 days after starting microbiology-directed treatment ?

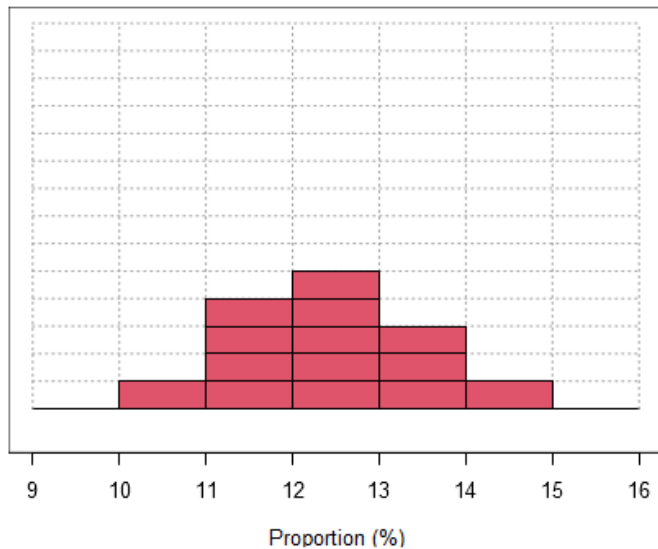I believe that the proportion is very unlikely to be:

- less than [10] %,

- more than [15] %.

You can update your range by entering new values and clicking 'Update range'.

[Update range]

Please add 14 chips to the grid below to express your uncertainty. The more chips you place in a particular bin the more certain you are that the proportion lies in that bin.

You can use **0** more chips.

Proportion (%)

What were the challenges for SEE?

1. Time constraints

2. Complex parameters required in the model

3. **Expert motivation though repetitive questions**

Parameters requires in the decision model

Three different outcomes

  …in two patient populations (susceptible and resistant)

    …for three separate sites of infection

     …and three different pathogens/mechanisms of resistance.

Up to 48 elicitation questions!

How did we motivate experts to complete the exercise?

Simplifications: we assumed that outcomes are not conditional on the pathogen, as long as they are susceptible/resistant to treatment.

Shorter questions: only elicited uncertainty where necessary.

Exercise structure: clear background information, questions broken down using tabs, text, formatting.

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Assessing the value of novel antimicrobials

EEPRU: Policy Research Unit in Economic Methods of Evaluation in Health & Social Care Interventions

NICE and NHS England and NHS Improvement have commissioned a project to assess the feasibility of innovative models for reimbursing antimicrobials.

As part of the project, the University of Sheffield and the University of York are modelling the outcomes and value of two antimicrobials that have particular clinical advantages in targeting infections caused by **carbapenem-resistant gram negative bacteria** . For this modelling we are focusing on patients with infections caused by the following pathogens:

- **Cefiderocol (Fetcroja)** targetting carbapenem-producing Enterobacterales (CPE) and *Pseudomonas* with metalo-beta-lactamase (MBL); and
- **Ceftazidime with avibactam (CAZ-AVI, Zavicefta)** targeting CPE with OXA-48.

The bug and resistance mechanisms were identified by our clinical experts as having the highest clinical value due to limited alternative treatment options.

This modelling work and subsequent NICE Committee deliberations will provide guidance on the value of each product to the NHS.

There are several model inputs for which data are limited or unavailable. As an alternative we require your expert opinion to inform the quantification of these inputs. We are also interested in how uncertain you are about your opinions. The training seminar gave you guidance on how to express your uncertainty, but a reminder is also provided later in the 'Instructions' section.

To begin, please click on 'Continue'.

Continue

EEPRU: Policy Research Unit in Economic Methods of Evaluation in Health & Social Care Interventions

Patients susceptible to treatment   Patients not susceptible to treatment

The following questions refer to outcomes in patients with **HAP** caused by CPE with an OXA-48 or MBL resistance mechanism, or by *Pseudomonas* with a MBL resistance mechanism, who receive a treatment to which they are **susceptible** (as treatment is informed by microbiological tests).

Note that we are assuming that 22% of the patients experience an acute kidney injury, and that, if the bug is susceptible to the administered antibiotic, outcomes of HAP caused by CPE with OXA48 or MBL are comparable to outcomes of HAP caused by Pseudomonas with MBL.

Question 1. In this patient population, what proportion of patients will still be alive 30 days after starting microbiology-directed treatment ?

I believe that the proportion is very unlikely to be:

- less than [   ] %,

- more than [   ] %.

When you are happy with your answers please click on 'Continue'.

[Continue]

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EEPRU: Policy Research Unit in Economic Methods of Evaluation in Health & Social Care Interventions

The following questions refer to exactly the same patients as the previous section - with HAP caused by CPE with an OXA-48 or MBL resistance mechanism, or by *Pseudomonas* with a MBL resistance mechanism.

In these patients, what would be their outcomes if they were **not susceptible to any existing antibiotics (including CAZ-AVI and cefiderocol)** , and they received multi-drug salvage therapy instead?

You can view your previous answers about patients who are susceptible to treatment by clicking on the relevant 'Patients susceptible to treatment' tab above.

Note that we are assuming that 22% of the patients experience an acute kidney injury and that, if the bug is not susceptible to any existing antibiotics, outcomes of HAP caused by CPE with OXA48 or MBL are comparable to outcomes of HAP caused by Pseudomonas with MBL.

Question 1. In this patient population, what proportion of patients will still be alive 30 days after starting multi-drug salvage therapy ?

I believe that the proportion is very unlikely to be:

- less than [ ] %,

- more than [ ] %.
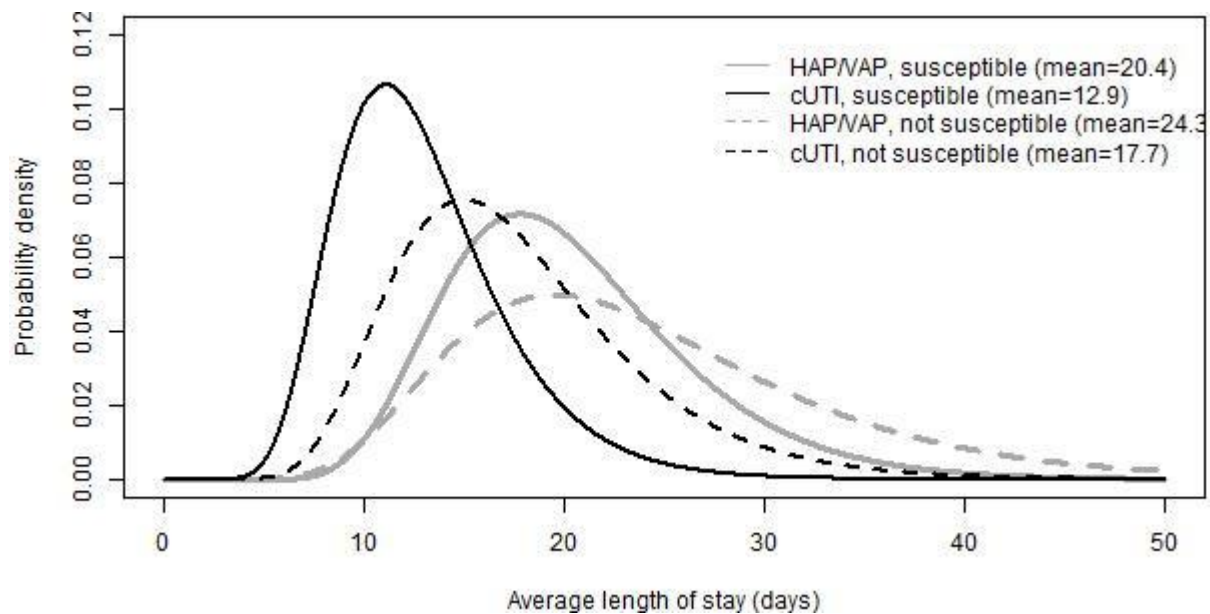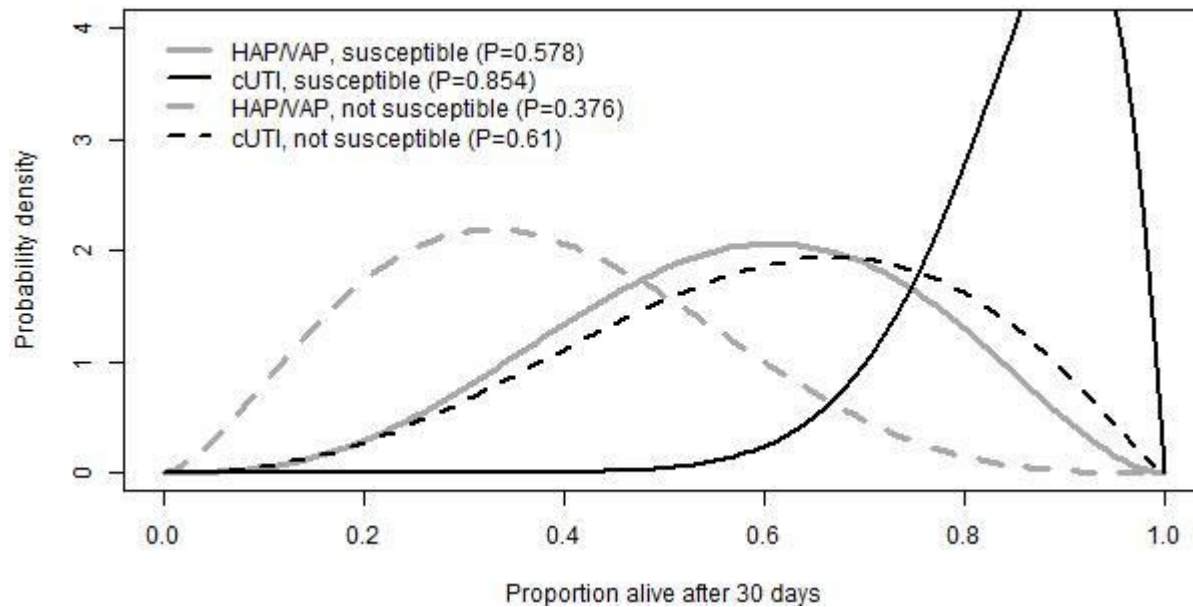
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Results

Sample of experts: 9 experts started, 7 completed.

Two experts revised their responses following group feedback.

Aggregate priors consistent with prior expectations.

SEE results used in the base case… but were found not to be the key drivers of treatment effect.

Top panel legend:
- HAP/VAP, susceptible (P=0.578)
- cUTI, susceptible (P=0.854)
- HAP/VAP, not susceptible (P=0.376)
- cUTI, not susceptible (P=0.61)

X-axis: Proportion alive after 30 days
Y-axis: Probability density

Bottom panel legend:
- HAP/VAP, susceptible (mean=20.4)
- cUTI, susceptible (mean=12.9)
- HAP/VAP, not susceptible (mean=24.3)
- cUTI, not susceptible (mean=17.7)

X-axis: Average length of stay (days)
Y-axis: Probability density

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Results

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Aggregate priors consistent with prior expectations.

SEE results used in the base case… but were found not to be the key drivers of treatment effect.

Lessons learnt

1. Plan early, plan ahead!

2. Involve a sample of experts in the process to ensure optimum design.

3. Pragmatic approach to selecting parameters for elicitation

Thank you