NIHR | Manchester Biomedical Research Centre

Using Data to Improve Opportunities for Antimicrobial Treatments

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3rd Year PhD

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Background

As resistance to antimicrobials continues to rise there is a need to reduce overall consumption of antibiotics…

…but this has to balanced with a need to treat patients suspected of sepsis promptly and appropriately

Some studies have looked at timing of treatment and duration of courses – mixed evidence and small cohorts

Electronic Health Records

- Used across primary and secondary care to record patient information
- Increasingly made available for research

Positives	Negatives
Larger cohorts	Messy data with high levels of missing-ness
More generalisable to general population	Difficult to show causality
Quicker and less costly	Variation in how data is recorded

Project Aims

- To integrate sources of routinely collected patient level data to look at how antimicrobials are used in sepsis patients and to identify any areas where this can be optimised

Study 1 – Exploring the antimicrobial burden of sepsis patients admitted to intensive care

Study Aims

- To use observational electronic health record data to….

    1. explore the antimicrobial burden of sepsis patients in intensive care units (ICU)

    2. look at the association between use of antimicrobials and mortality

Methods – Data Source

MIMIC-III database

- Anonymised patient records from a single hospital in the United States from 2001-2012
- 26 tables containing data on all tests, procedures, measurements taken etc. throughout ICU stay

Identifying adults (aged >16) with incident sepsis admitted to ICU between 2008 and 2012

Criteria	Description
Sepsis-3	Sequential Organ Failure Assessment (SOFA) ≥ 2 and suspicion of infection

Extracted all demographic data and data around prescriptions and administration of antimicrobials for 30-day follow up period

Analysis

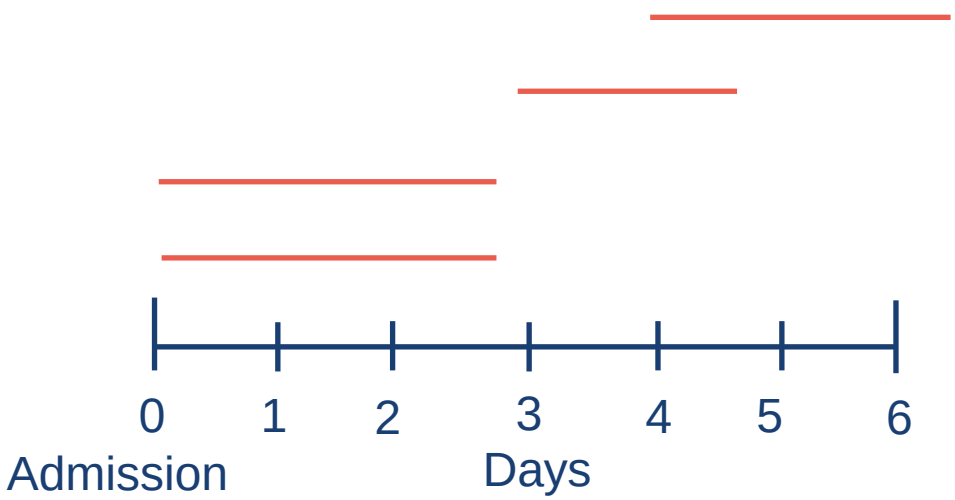
- Descriptive statistics were used to estimate the antimicrobial burden of cohort

- Individual antimicrobial exposure was summarised in 3 ways

Number of courses = 4

Total exposure days = 7

Cumulative exposure days = 11



Analysis

- Descriptive statistics were used to estimate the antimicrobial burden of cohort
- Individual antimicrobial exposure was summarised in 3 ways
- Survival of patients analysed using Kaplan-Meier curves and Cox proportional hazards regression

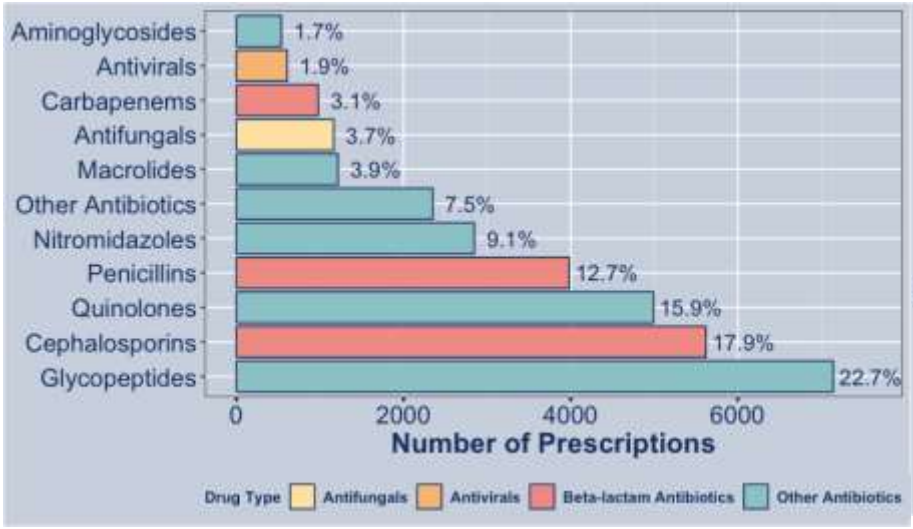
Cohort

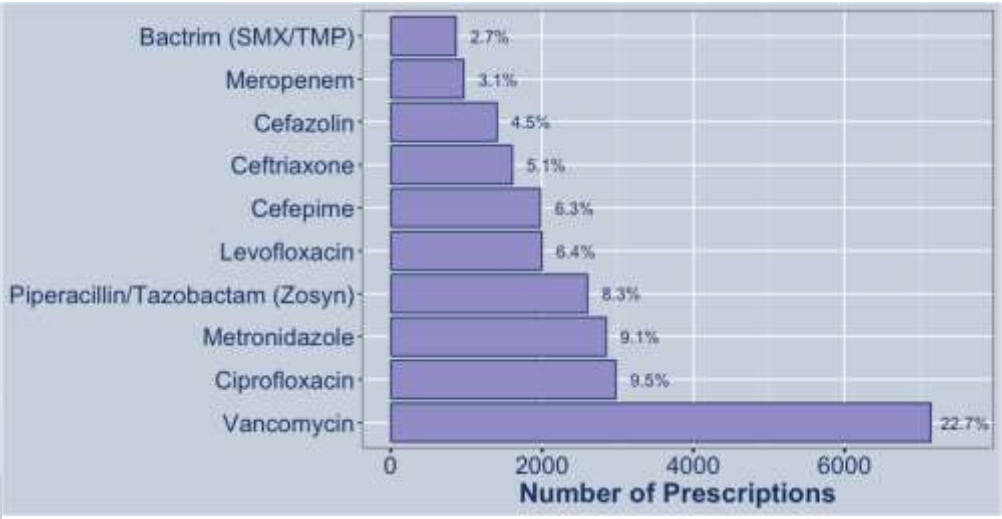
- Of the 23,749 ICU stays, 8,639 patients (36.6%) met the sepsis-3 criteria

	All Patients
No. of ICU stays	8,639
Gender (% male)	56%
Ethnicity (% white)	74%
Age (median)	67.7
SOFA score (median)	5
Elixhauser comorbidity index (median)	4

Antimicrobials

- Antibiotics accounted for 94% of prescriptions
- Vancomycin most frequently used





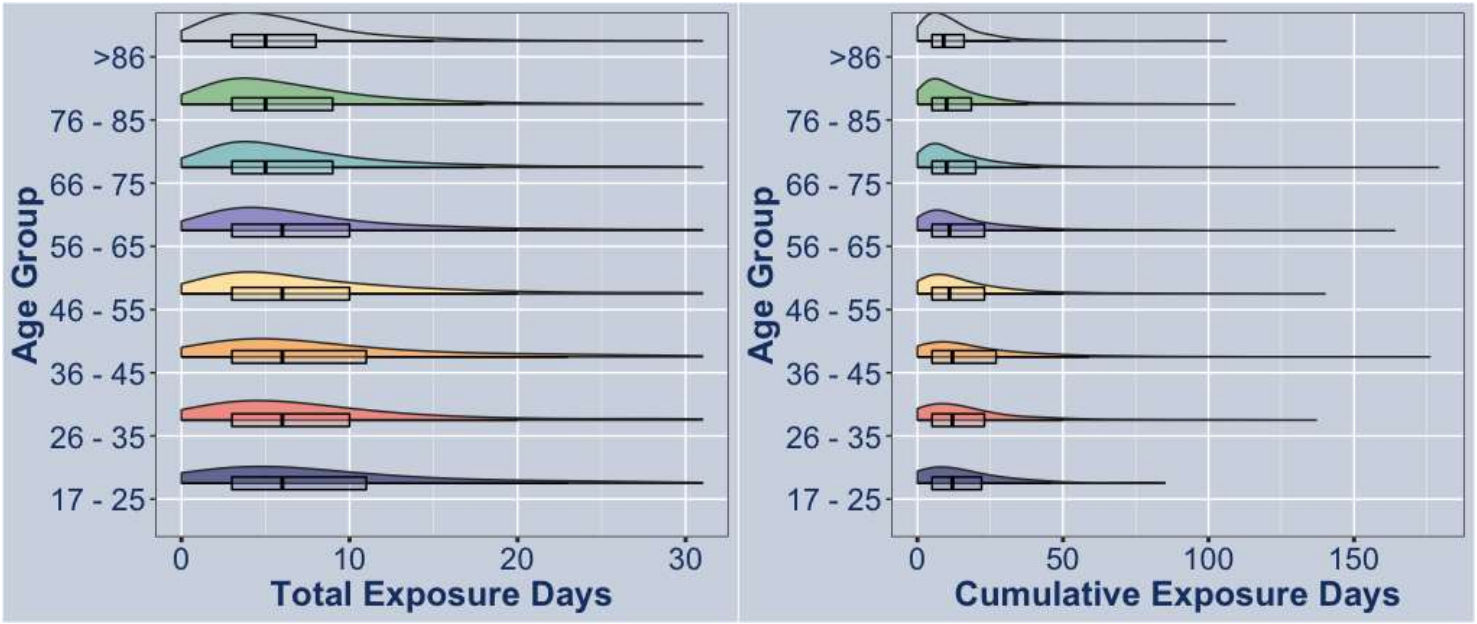
- 76% were administered via IV
- Median length of prescriptions was 3 days

Individual Exposure

	All Patients
No. of courses – median (IQR)	3 (2,5)
Total exposure days - median (IQR)	5 (3-9)
Cumulative exposure days – median (IQR)	10 (5-20)

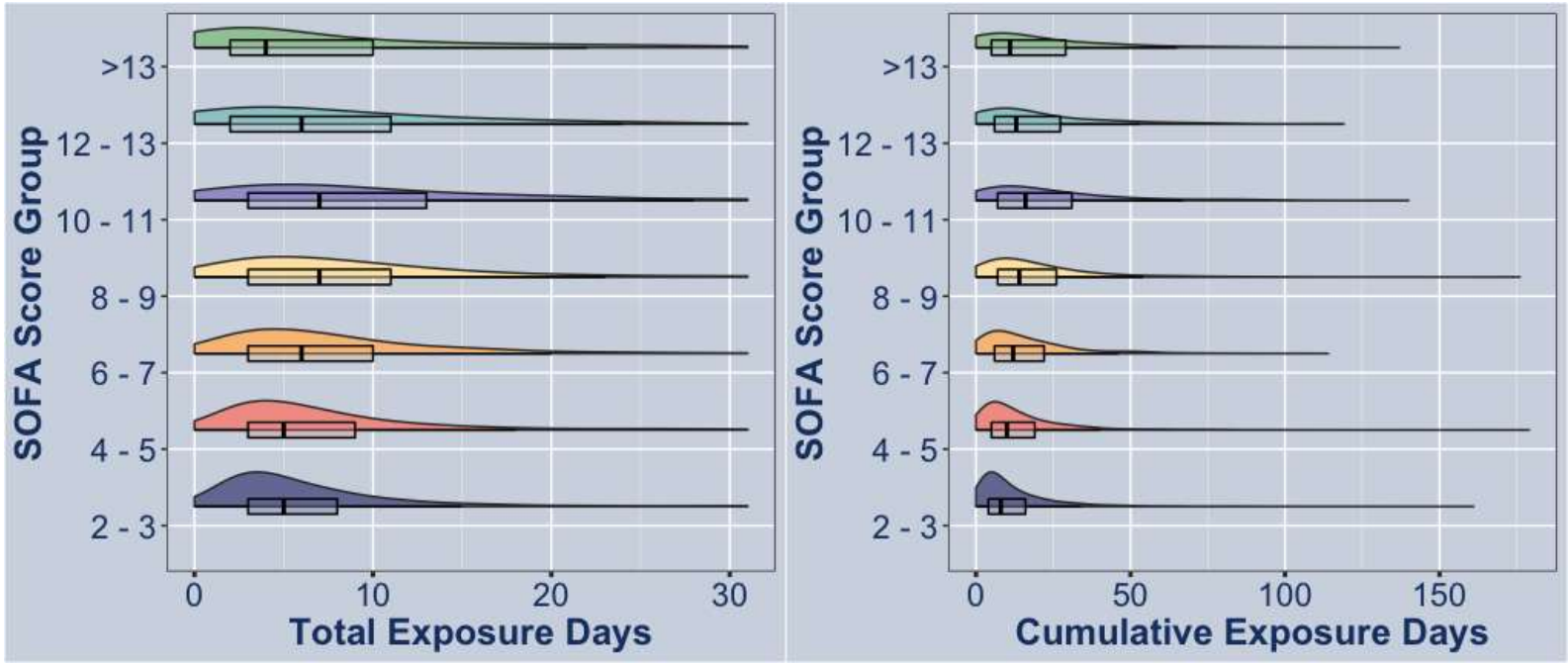
Individual Exposure

	No. of Courses	Total Exposure Days	Cumulative Exposure Days
Age Group (years)			
17-25	3 (2-5)	6 (3-11)	12 (5-22)
56-65	3 (2-5)	6 (3-10)	11 (5-23)
>86	3 (2-5)	5 (3-8)	9 (5-16)



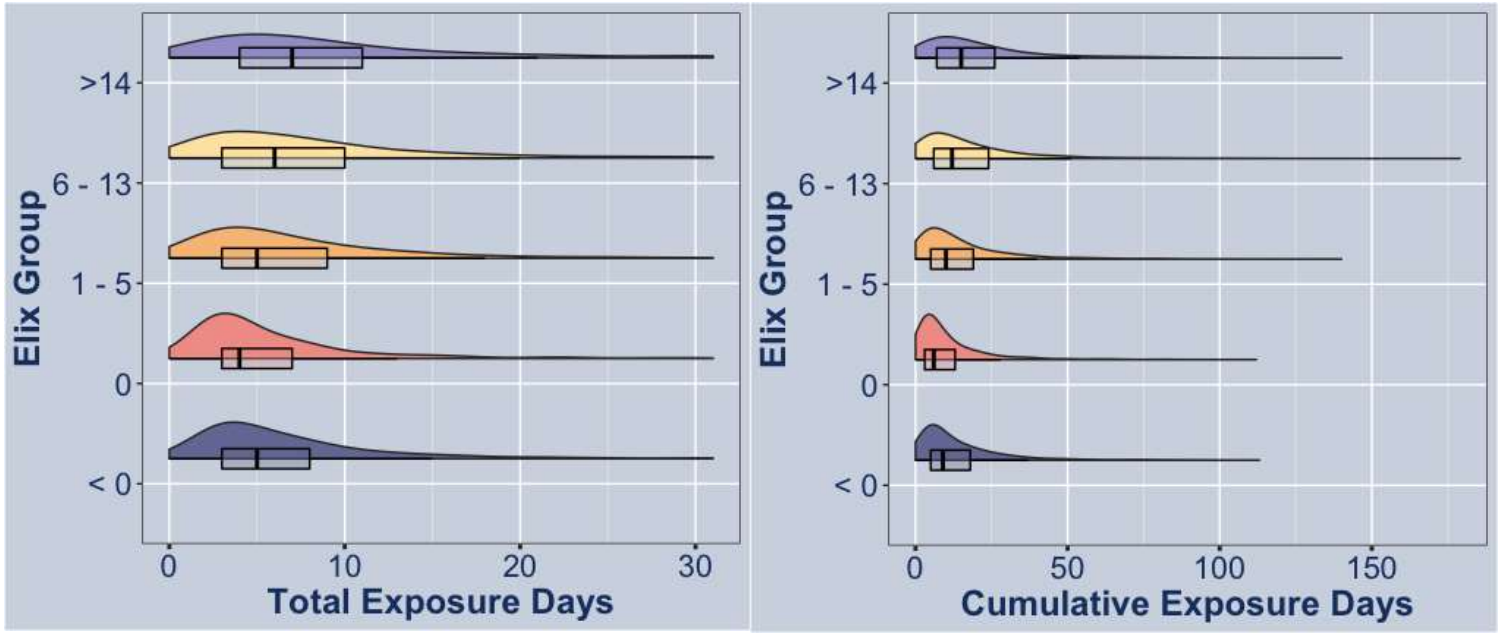
Individual Exposure

	No. of Courses	Total Exposure Days	Cumulative Exposure Days
SOFA Score Group			
2-3	3 (1-4)	5 (3-8)	8 (4-16)
8-9	4 (2-6)	7(3-13)	14 (7-26)
>13	4 (3-6)	4 (2-10)	11 (5-29)

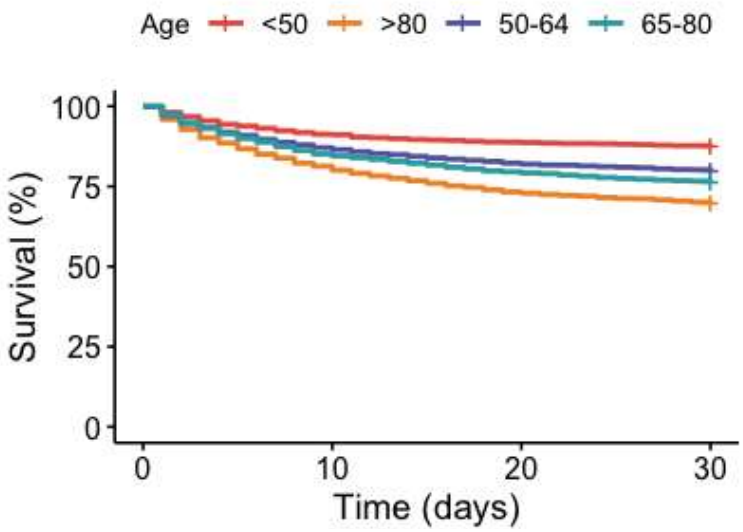


Individual Exposure

	No. of Courses	Total Exposure Days	Cumulative Exposure Days
Elixhauser Index Group			
<0	3 (2-4)	5 (3-8)	9 (5-18)
1-5	3 (2-5)	5 (3-9)	10 (5-19)
>14	4 (3-6)	7 (4-11)	15 (7-26)



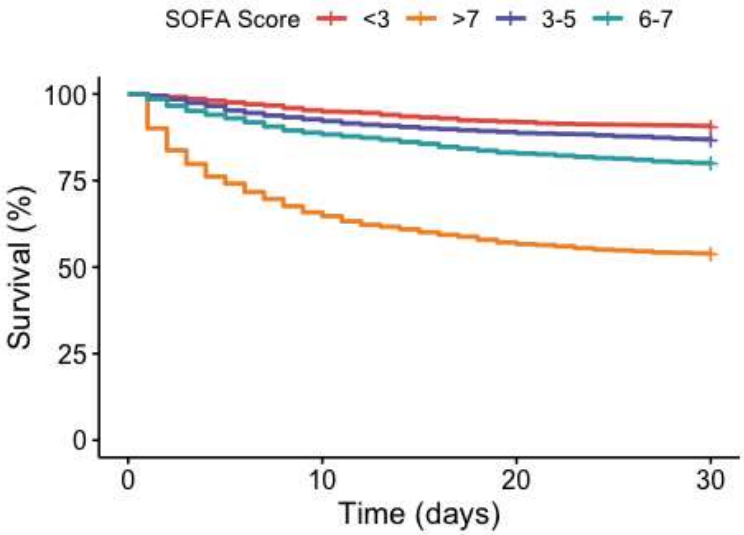
Survival

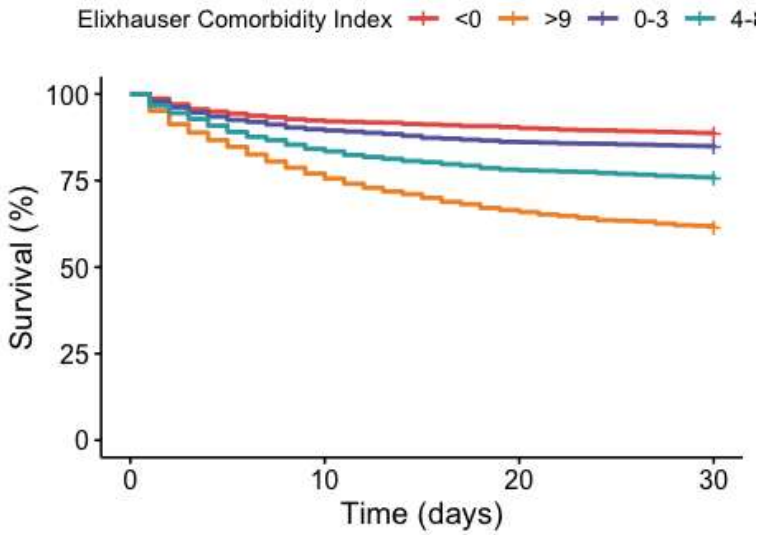


Overall 30-day survival for the cohort was 78%.

Graphs show survival stratified by groups

Lower survival (yellow line) was seen in older patients, those with a higher SOFA score, and a higher comorbidity index





Survival – Cox proportional hazards model

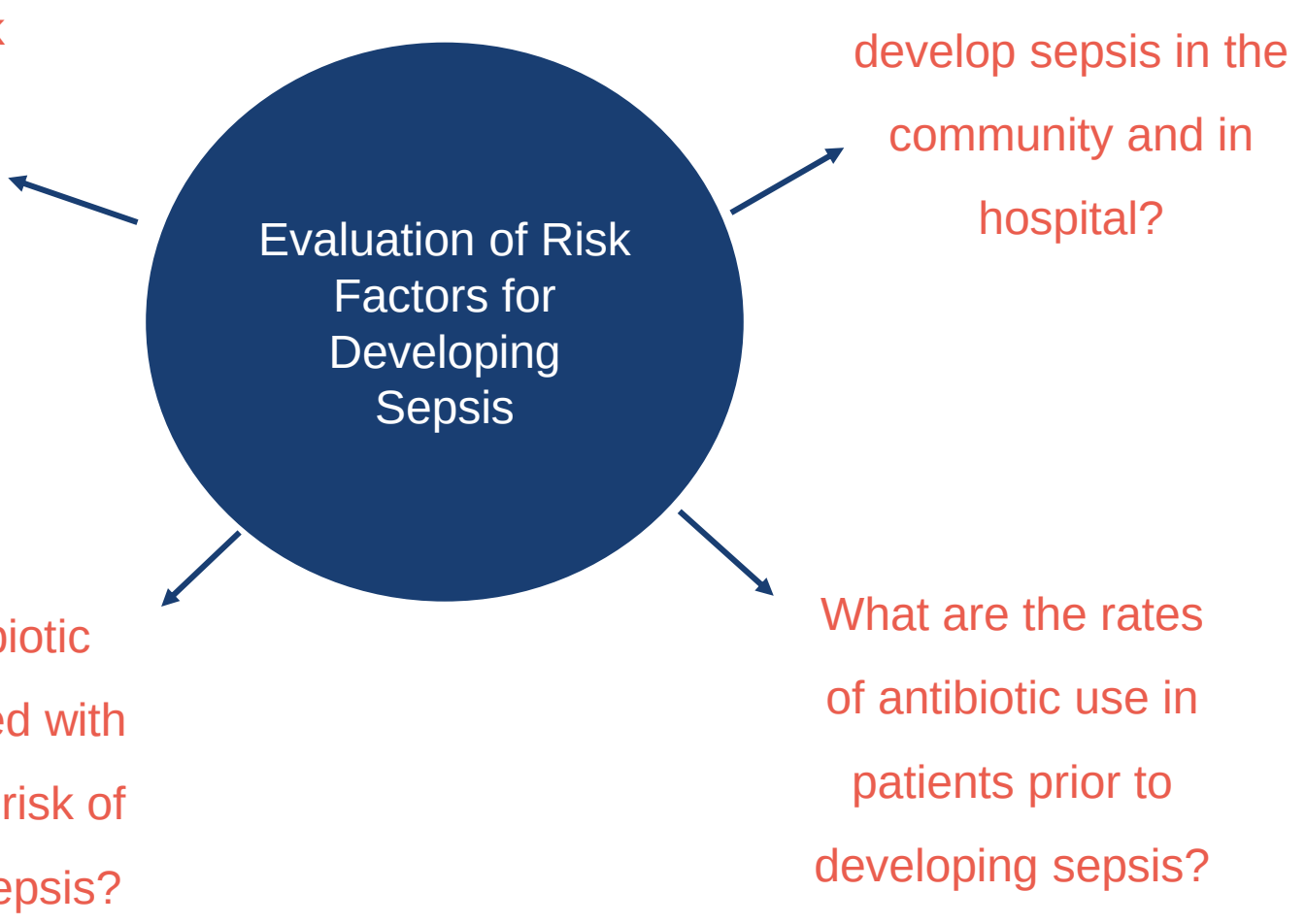
Characteristic	Adjusted Hazard Ratio	95% CI
Age (years)	**1.02**	1.02, 1.02
Gender		
Female	—	—
Male	0.92	0.84, 1.01
Ethnicity		
Black	—	—
Hispanic	1.26	0.94, 1.70
Other	1.2	0.99, 1.45
White	1.14	0.98, 1.34
Admission Type		
Elective	—	—
Emergency	2.4	1.73, 3.33
Urgent	1.88	1.11, 3.19
Elixhauser Comorbidity Index	**0.99**	0.97, 1.01
tt(Elixhauser Comorbidity Index)	1.02	1.02, 1.03
SOFA Score	**1.33**	1.30, 1.37
tt(SOFA score)	0.96	0.95, 0.97
No. of antimicrobials prescribed	**1.2**	1.17, 1.22
No. of exposure days	**0.92**	0.90, 0.93

Summary

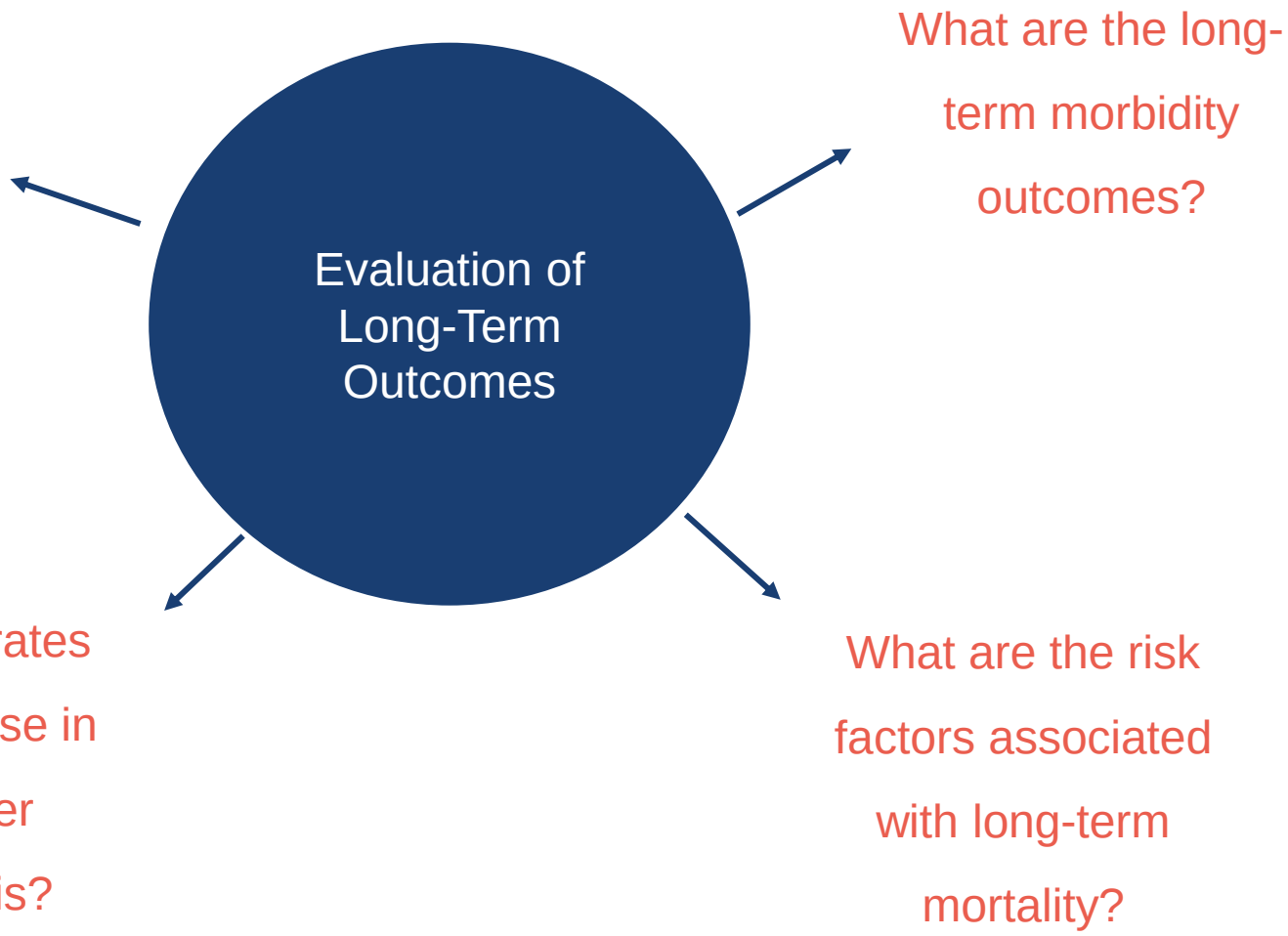
- Antimicrobial use does vary in relation to patient's levels of disease severity and comorbidities
- Cox regression showed that a higher SOFA score and number of antimicrobials prescribed was associated with higher mortality
- BUT a higher number of exposure days was associated with lower mortality

Study 2- The evaluation of risk factors and long-term outcomes in patients with community or hospital- acquired sepsis: a retrospective cohort study using linked primary and secondary care data

Aims


What are the risk factors associated with developing sepsis?
Do these differ between patients who develop sepsis in the community and in hospital?
Evaluation of Risk Factors for Developing Sepsis
Is high antibiotic use associated with an increased risk of developing sepsis?
What are the rates of antibiotic use in patients prior to developing sepsis?

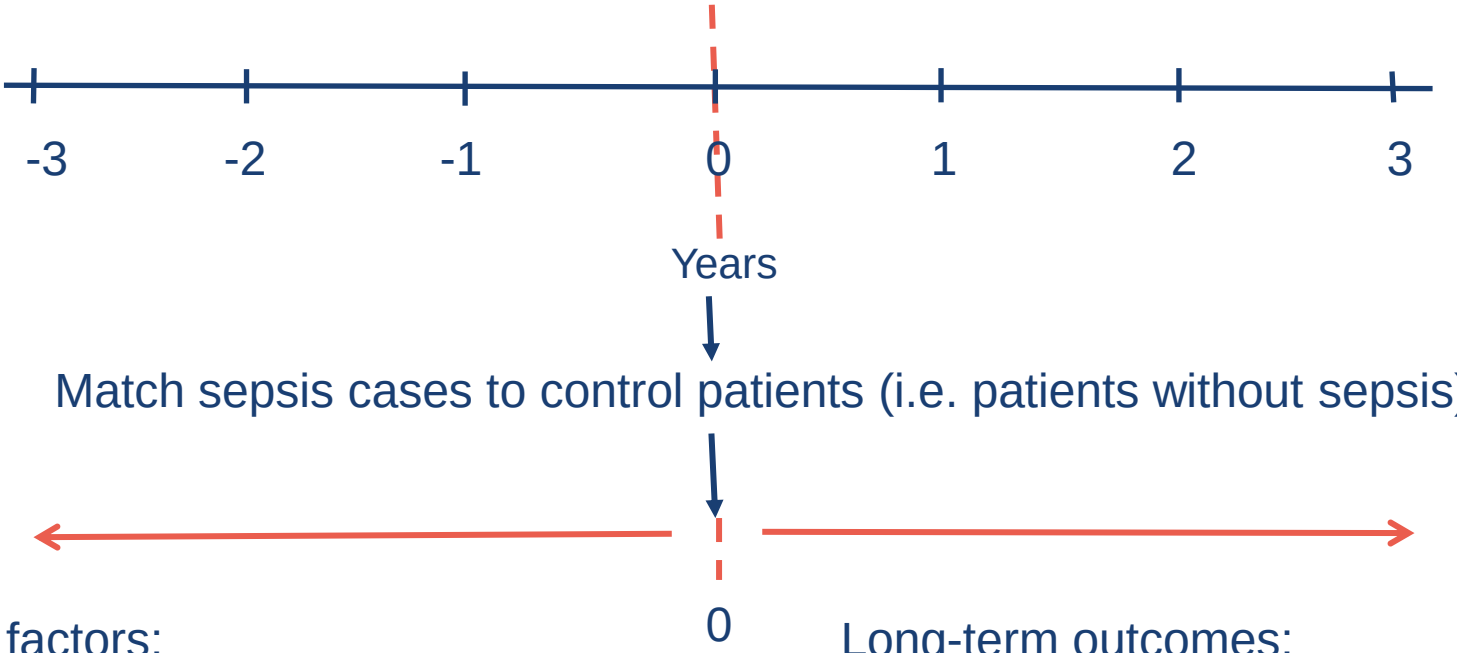
Aims


What are the long-term mortality rates for sepsis patients?
What are the long-term morbidity outcomes?
Evaluation of Long-Term Outcomes
What are the rates of antibiotics use in patients after having sepsis?
What are the risk factors associated with long-term mortality?

Study Design

Data source – CPRD (England) and SAIL (Wales) – linked GP records to hospital admissions

Index date – hospital admission with sepsis



Risk factors:

- Multivariable logistic regression model with development of sepsis as the outcome

Long-term outcomes:

- Survival analysis – Cox regression model

Summary

- There are many different ways we can use routinely collected patient data to explore complex conditions such as sepsis!

- Thank you for listening!