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Risk factors for resistant bacteraemia in patients with community onset suspected sepsis: a cohort study using linkage of routinely collected national data

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Background

Sepsis is the body's response to severe infection. It is a prevalent and harmful condition, with over 150,000 cases in the UK every year resulting in 44,000 deaths, which is more than for bowel, breast and prostate cancer combined. (http://sepsistrust.org/)

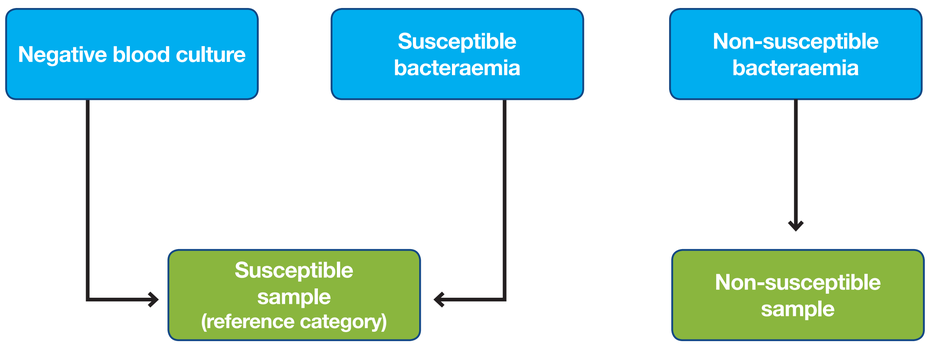
Essential to initial treatment of suspected sepsis is early administration of appropriate antibiotics. Initial antibiotic treatment is usually empirical and choice is based on local prescribing guidelines. These guidelines generally do not take account of patient characteristics and the likelihood of antibiotic resistance in individual patients.

The empiric regimen for initial treatment of suspected sepsis on admission to hospital varies amongst NHS boards in Scotland but the most commonly recommended combination is amoxicillin plus gentamicin plus metronidazole. We aimed to characterise risk factors for having a bacteraemia non-susceptible to this regimen among adults who have a blood culture taken on admission to hospital or within the first two days of their admission.

Methods

We defined suspected sepsis as patients having had a blood culture taken, irrespective of result. Using culture and susceptibility results, positive cultures were defined as non-susceptible if the isolate was non-susceptible to both amoxicillin and gentamicin, or non-susceptible to metronidazole. Susceptible organisms and negative blood cultures were combined to form the comparator group (figure 1).

Figure 1: Categorisation of blood cultures



Following approval from the Public Benefit and Privacy Panel for Health & Social Care, blood culture data from the Health Protection Scotland Electronic Communication of Surveillance in Scotland (ECOSS) dataset were initially linked with patient-level hospitalisations data from the National Services Scotland (NSS) General/Acute Inpatient dataset (SMR01) to select cases of interest.

A summary of case selection and data processing is shown below:

- Blood cultures selected from ECOSSS for samples taken between 01/01/2016 to 30/09/2017 for patients aged ≥16 years.
- Using culture and susceptibility results, samples were defined as either blood culture negative, susceptible or non-susceptible.
- Blood culture data matched with SMR01 Hospital Activity data and samples taken from day three of an admission onwards were excluded
- Where more than one sample was taken during an admission, de-duplication was carried out to select only one sample per admission. The European Centre for Disease Control protocol for the submission of data to the European Antimicrobial Resistance Surveillance Network was used to ensure the most resistant sample was selected.
- Cases were further de-duplicated to include only one case per patient in the final dataset, using the ECDC protocol and random sampling.
- Final cases data were linked to SMR01 and community NHS prescriptions from NSS Prescribing Information System (PIS) to determine demographics, co-morbidity and previous antibiotic exposure.

Multivariable logistic regression was undertaken to determine risk factors for non-susceptibility. All analysis was carried out in R version 3.2.3.

Results

A total of 102,760 samples were analysed: 1,064 (1.0%) were non-susceptible to the empiric regimen. Of those cases, 839 (79%) were non-susceptible to amoxicillin and gentamicin and 225 (21%) to metronidazole. Table 1 provides a summary of the cases included in the analysis.

All covariates, excluding SIMD quintile (measuring relative deprivation), were found to be significant at univariate levels and were therefore included in the multivariable analysis. Summarised results of the multivariable analysis are shown in Table 2.

Table 1: Study population

Characteristic	Non-susceptible bacteraemia n (%)	Susceptible sample n (%)	Total n (% of cohort)
Total samples in study population	1064 (1.0)	101696 (99.0)	102760
Gender			
Female	484 (0.9)	52258 (99.1)	52742 (51.3)
Male	580 (1.2)	49438 (98.8)	50018 (48.7)
Age group			
16-24	15 (0.3)	5228 (99.7)	5243 (5.1)
25-34	20 (0.3)	6705 (99.7)	6725 (6.5)
35-44	45 (0.6)	7696 (99.4)	7741 (7.5)
45-54	80 (0.6)	12254 (99.4)	12334 (12.0)
55-64	149 (0.9)	15871 (99.1)	16020 (15.6)
65-74	270 (1.3)	20773 (98.7)	21043 (20.5)
75-84	298 (1.4)	21391 (98.6)	21689 (21.1)
85+	187 (1.6)	11778 (98.4)	11965 (11.6)
Care home residence			
No	925 (0.9)	96492 (99.1)	97417 (94.8)
Yes	139 (2.6)	5204 (97.4)	5343 (5.2)
SIMD Quintile			
1-most deprived	291 (1.0)	27434 (99.0)	27725 (27.0)
2	249 (1.1)	23456 (98.9)	23705 (23.1)
3	209 (1.0)	19837 (99.0)	20046 (19.5)
4	164 (1.0)	16808 (99.0)	16972 (16.5)
5-least deprived	151 (1.1)	14161 (98.9)	14312 (13.9)
Charlson score			
0	213 (0.7)	28736 (99.3)	28949 (28.2)
1-2	326 (1.1)	29191 (98.9)	29517 (28.7)
3-4	209 (1.8)	11686 (98.2)	11895 (11.6)
≥5	210 (2.0)	10163 (98.0)	10373 (10.1)
Unknown[a]	106 (0.5)	21920 (99.5)	22026 (21.4)
Number of hospital stays in previous 12 months			
0	285 (0.6)	47930 (99.4)	48215 (46.9)
1	225 (1.0)	22063 (99.0)	22288 (21.7)
2	149 (1.2)	11942 (98.8)	12091 (11.8)
3	126 (1.9)	6394 (98.1)	6520 (6.3)
4+	279 (2.0)	13367 (98.0)	13646 (13.3)
Drug classes prescribed in previous 12 months[b]			
0	38 (0.6)	6247 (99.4)	6285 (6.1)
1-4	111 (0.6)	18432 (99.4)	18543 (18.0)
5-9	266 (0.9)	29061 (99.1)	29327 (28.5)
10-14	313 (1.2)	26053 (98.8)	26366 (25.7)
15+	336 (1.5)	21903 (98.5)	22239 (21.6)
Exposure to antibiotics in the community in previous 3 months			
No	580 (0.9)	64726 (99.1)	65306 (63.6)
Yes	484 (1.3)	36970 (98.7)	37454 (36.4)

a An unknown Charlson score suggests the patient had no hospital admissions in the previous 5 years, therefore a Charlson score could not be calculated.
b Drug classes defined as the number of different British National Formulary paragraphs.

Table 2: Summarised results of multivariable analysis

Characteristic	Summarised result
Gender	Risk of non-susceptibility greater in males than females.
Increasing age	Risk of non-susceptibility increased with age.
Care home residence	Risk of non-susceptibility greater in those who had resided in a care home.
Charlson score	Risk of non-susceptibility increased with Charlson score.
Hospitalisations in previous 12 months	Risk of non-susceptibility increased with number of stays.
Drug classes prescribed in previous 12 months	No increased risk of non-susceptibility.
Antibiotic exposure in the community in previous 3 months	Risk of non-susceptibility increased with exposure to antibiotics.

Multivariable logistic regression found increasing age was associated with non-susceptibility. Those aged ≥85 years were 3.57 (95%CI 2.15-6.39) times more likely to be non-susceptible compared to those aged 16-24, as were males (OR 1.24; 95%CI 1.10-1.40) and those residing in a care home (OR 2.01; 95%CI 1.66-2.43). Increasing comorbidity was associated with increased likelihood of non-susceptibility – those with a Charlson score of ≥5 were 1.44 (95%CI 1.15-1.79) times more likely to be non-susceptible than those with a score of zero and those with ≥4 previous hospitalisations were 2.61 (95%CI 2.11-3.22) times more likely than those with no previous hospitalisations.

Exposure to any antibiotic in the community in the previous three months was found to be associated with non-susceptibility and those previously prescribed an antibiotic were 1.20 times (95%CI: 1.06-1.37) more likely to be non-susceptible.

Discussion

Risk factors for non-susceptibility to the antibiotic regimen commonly used in Scotland for suspected sepsis have been characterised. Exposure to any antibiotic in the three months prior to admission is a risk factor for non-susceptibility; next we will examine cumulative exposure to all antibiotics and to specific antibiotics in the three, six and 12 months prior to blood culture. Following this, we aim to develop risk prediction models as the next step towards developing a clinical decision support tool to help clinicians identify patients at risk of being non-susceptible to the commonly recommended empirical treatment for sepsis in NHS Scotland for whom different empiric antibiotics may be required.