UK Health Security Agency

Laboratory surveillance of paediatric bacterial bloodstream infections and antimicrobial resistance in England: 2018 to 2022

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Contents

1. Introduction

This is the second edition of a series of health protection reports highlighting trends in laboratory-reported incidence and antimicrobial resistance (AMR) of bacterial bloodstream infections (BSI) in the paediatric population (0 to 17 year olds inclusive) in England. This report covers the years between 2018 and 2022. It should be viewed as supplementary to the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) report 2022 to 2023 (1). Paediatric data are included in the main ESPAUR report, and further AMR data by age group are provided here.

This report is based upon ESPAUR methodology (1). Please note that the incidence of some organisms causing BSIs in children is very low, which can limit resistance trend interpretation. For this reason, resistance rates for certain antimicrobial and organism combinations are not graphically displayed where the number of infection episodes was below 20 for that age group and year. Data reference tables featuring the BSI rates and susceptibility data behind the findings in this report can all be found in the data tables (appendices) associated with this report.

In the AMR BSI section, frequently reported BSI-causing organisms (Appendices 11 to 15) for each age-group were used to report AMR rates for key antimicrobials (defined for each organism in Table 3 of the Methods). While AMR for Coagulase-negative staphylococci (CoNS) and *Micrococcus* spp. are reported for infants (up to 3 months old), this is not reported for older children as reports are less likely to be clinically relevant. However, CoNS and *Micrococcus* spp. remain the most frequently reported organisms detected from blood samples across all age groups and are therefore included in the BSI rates (see Caveats, page 5).

The age groups used in the rates of laboratory-reported BSI rates and antimicrobial susceptibility trends differ slightly due to incidence, and therefore susceptibility testing, being low for some age groups (outlined in Table 2 of the Methods section).

2. Main points

2.1 Bloodstream infection rates

Main results were that:

- bloodstream infection (BSI) reports in all paediatric age groups in England increased between 2018 (n=15,123) and 2022 (n=19,050), with a 27.8% increase in the overall rate (0 to 17 year olds), mainly driven by increases in group A streptococci (GAS) (54.9% increase) and CoNS and Micrococcus spp. (35.4% increase)
- the increase in CoNS and Micrococcus spp. occurred predominantly in the older age groups (≥1 year olds) where reports are less likely to be clinically relevant
- there was a decrease in BSI rates in most age groups in 2020 (from 1 month olds upwards), likely due to the impact of non-pharmaceutical interventions and disruptions to elective healthcare during the coronavirus-2019 (COVID-19) pandemic; this decrease did not occur in 0 to 3 day old neonates and 4-day to 1 month old neonates and infants
- the rate of BSI was highest in 4-day to 1 month-old neonates and infants (2,940 per 100,000), as was the percentage increase between 2018 and 2022 (26.1%)

2.2 Antimicrobial resistance

Main results were that:

- group B streptococci (GBS) bacteraemia cases diagnosed in infants up to 3 months old remain highly susceptible to the first-line treatment, penicillin
- data from neonates 0 to 3 days old indicated an increase in GBS resistance to clindamycin from 23.0% (n=56/244 tested) in 2018 to 33.0% (n=53 per 161 tested) in 2022 and erythromycin from 26.8% (n=71 per 265 tested) in 2018 to 43.0% (n=74 per 172 tested)
- *Listeria* spp. BSI were rare in children older than one month, and no amoxicillin resistance was reported in *Listeria* spp. isolates
- between 2018 to 2022, GAS was universally susceptible to penicillin and resistance to commonly used key antibiotics (glycopeptides and co-trimoxazole) remained low (<6%)
- *Escherichia coli* BSI resistance to amoxicillin/clavulanate remained high at approximately 40% over the 2018-2022 period, while resistance to third-generation cephalosporins, ciprofloxacin, and gentamicin remains below 20%, and resistance to amikacin and piperacillin with tazobactam at less than 10%
- *E. coli* meropenem resistance was low (<1%) in all paediatric age groups between 2018 and 2022
- *Enterococcus faecalis* remains susceptible to amoxicillin, glycopeptides, and linezolid

- meticillin-resistant *Staphylococcus aureus* (MRSA) comprised <7% of *S. aureus* BSI isolates in all age groups
- *Streptococcus pneumoniae* resistance to penicillin remained low (<3%) throughout the period in 3 month to 4-year-old children
- in 3 month to 4-year-old children, there were concerning patterns of *Klebsiella pneumoniae* resistance to piperacillin with tazobactam (31.7% in 2022), third-generation cephalosporins (32.4%), gentamicin (15.2%), ciprofloxacin (31.5%)
- among meticillin-sensitive *S. aureus* (MSSA) isolates, resistance to macrolides and clindamycin increased from 17.1% (n=36 per 210 tested) in 2018 to 23.9% (n=24 per 226 tested) in 2022 and from 9.9% (n=17 per 171 tested) in 2018 to 20.6% (n=40 per 194 tested) in 2022, respectively, in 3 month to 4-year-old children

2.3 Caveats

Caveats are that:

- the overall incidence of BSI in the paediatric population is low; caution should therefore be taken when interpreting resistance rates due to small sample sizes and resistance rates are not reported where the number tested is <20 samples
- the COVID-19 pandemic affected the general case-mix of hospital patients during much of 2020 and 2021, this has likely impacted trends for the 5-year period
- clinical data are not captured in the UKHSA laboratory reporting surveillance system used in this report, and thus clinical significance of blood culture isolates cannot be determined
- antibiotic susceptibility results reported here have not been confirmed by UKHSA's national reference laboratory

3. Results

3.1 Incidence of bloodstream infections

Overall rates of bloodstream infections (BSIs) in England increased between 2018 and 2022 for all paediatric age groups (Figure 1 and Appendix 1), from 63.4 to 81.0 per 100,000 population (an increase of 27.8%). This represents a total of 19,050 bacterial bloodstream infections in children aged 0 to 17 years old in 2022. When broken down by organism, this increase occurred predominantly in CoNS and *Micrococcus* spp. (35.4% increase between 2018 and 2022), particularly in the older age groups (≥1 year old) where they are commonly considered as commensals or contaminants and are therefore less likely to be clinically relevant. There was also an increase in reported group A streptococci (GAS; 54.9% increase between 2018 and 2022), corresponding with a national surge of GAS infection in 2022. A breakdown of the most commonly isolated pathogens is provided in Appendix 1 and provides a structure for resistance rates described below.

BSI rates were higher each year in neonates aged 4 days to 1 month than other paediatric age groups; the rate increased from 2,330.9 to 2,939.9 per 100,000 population (an increase of 26.1%) between 2018 and 2022. The BSI rate increase observed between 2018 and 2022 in 0 to 3 day old neonates was marginal at 4.6% (246.5 to 257.9 per 100,000 population). Large increases in the BSI rate occurred for infants aged 1 month to 1 year (35.9% increase (420.5 to 571.6 per 100,000 population)) and 5 to 17 year olds (35.8% increase (23.6 to 32.1 per 100,000 population)). However, the largest increase occurred in 1 to 4 year old children (44.7 to 68.2 per 100,000 population, 52.5% increase).

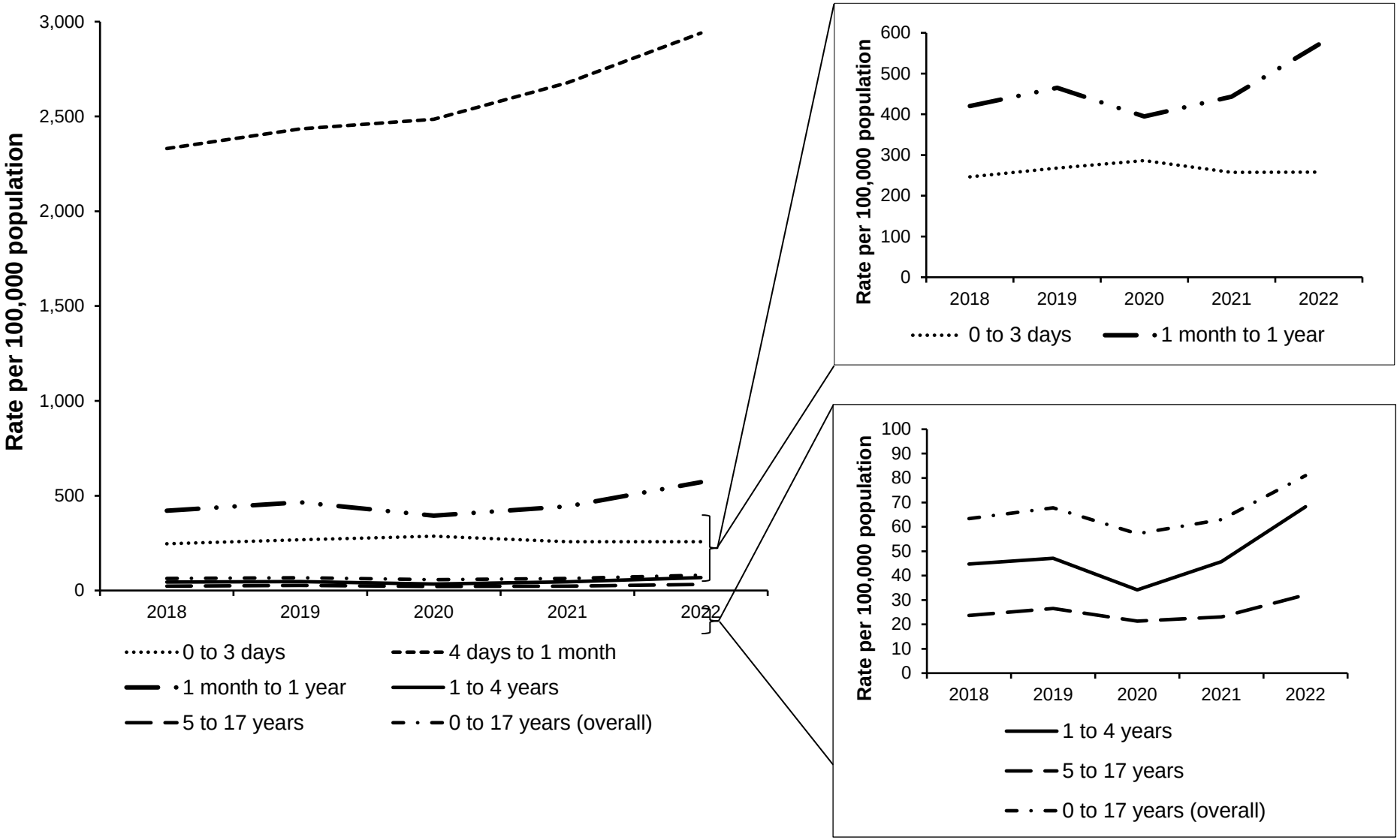
The BSI rate decreased in 2020 compared to 2018 across most age groups, except for children up to 1 month old, before subsequently surpassing 2018 rates in 2022 (Figure 1 and Appendix 1). In 4 days to 1 month old children, the reported BSI rate remained unaffected by the COVID-19 pandemic and continued to increase annually. In contrast, in 0 to 3 day old children, the rate peaked in 2020 (286.4 per 100,000 population), before decreasing to 257.4 per 100,00 and 257.9 per 100,000 in 2021 and 2022; this is still higher than in 2018.

The 4 most commonly isolated organisms by age group in 2022 were:

- 0 to 3 days old: CoNS and *Micrococcus* spp. (n=709), Group B streptococci (GBS; n=219), *Escherichia coli* (n=110), and *Staphylococcus aureus* (n=90) (Appendix 12)
- 4 days to 1 months old: CoNS and *Micrococcus* spp. (n=1,450), *E. coli* (n=174), *S. aureus* (n=128), and non-pyogenic streptococci (n=108) (Appendix 13)
- 1 month to 1 year old: CoNS and *Micrococcus* spp. (n=2,670), non-pyogenic streptococci (n=487), *E. coli* (n=364), and *S. aureus* (n=328) (Appendix 14)
- 1 to 4 years old: CoNS and *Micrococcus* spp. (n=1,505), non-pyogenic streptococci (n=300), GAS (n=201), and *S. aureus* (n=146) (Appendix 15)

- 5 to 17 years old: CoNS and *Micrococcus* spp. (n=2,408), *S. aureus* (n=432), non-pyogenic streptococci (n=326), and GAS (n=223) (Appendix 16)

Figure 1. BSI rates per 100,000 paediatric population for each paediatric age group (aged 0 to 17 years) in England: 2018 to 2022



3.2 Antimicrobial resistance of bloodstream infections

3.2.1 Neonates (0 to 3 day olds)

3.2.1.1 Gram-positive bloodstream infections

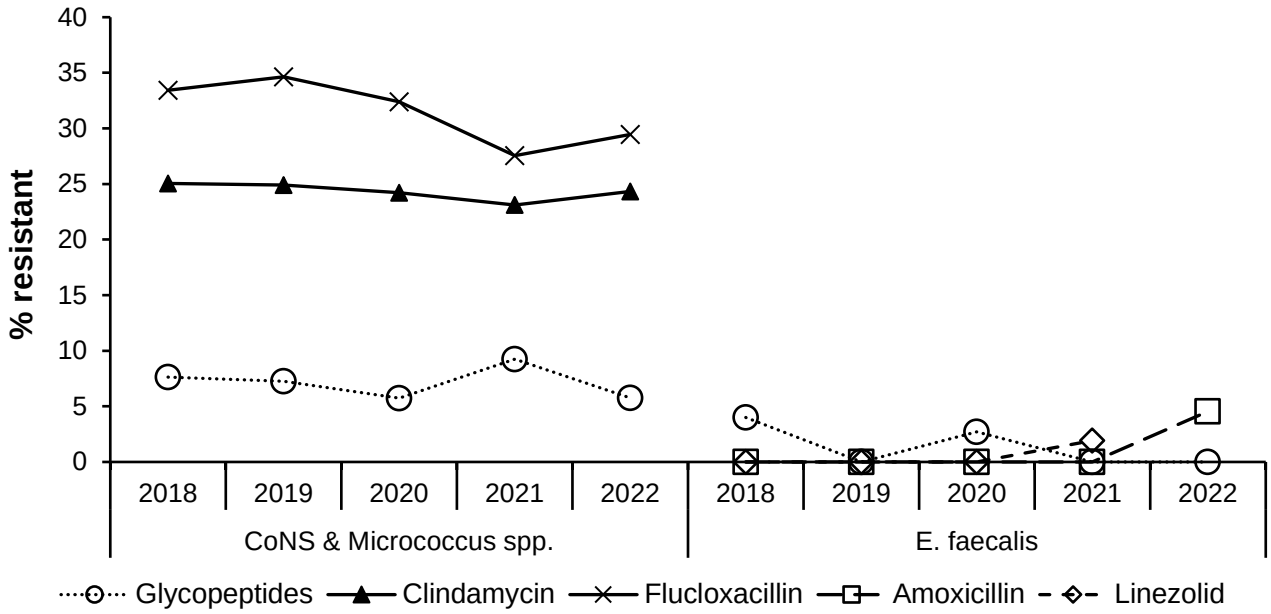
GBS remained universally susceptible to the first-line treatment, penicillin. Resistance to clindamycin and erythromycin increased between 2018 and 2022 (Figure 2c and Appendix 2). Clindamycin resistance increased from 23.0% (n=56 per 244 tested) in 2018 to 33.0% (n=53 per 161 tested) in 2022. Erythromycin resistance increased from 26.8% (n=71 per 265 tested) in 2018 to 43.0% (n=74 per 172 tested) in 2022.

Small numbers of *S. aureus* BSI were reported; resistance to flucloxacillin remained low and stable between 2018 (6.7%, n=2 per 30 tested) and 2022 (6.1%, n=2 per 33 tested) (Figure 2b and Appendix 2). Low numbers of meticillin-susceptible *S. aureus* (MSSA) BSIs were reported, however a third (33.3%, n=11 per 33 tested) of MSSA BSI isolates were resistant to macrolides in 2022, in comparison to 10.7% (n=3 per 28 tested) resistance in 2018, similar to the adult population. In MSSA reports, resistance to all other commonly used antibiotics (glycopeptides, clindamycin, co-trimoxazole, mupirocin and fusidic acid) remained below 16% (Figure 2b, Appendix 2). Mupirocin or glycopeptide resistance was not detected in MSSA isolates reported between 2018 and 2022. Further interpretation of resistance amongst meticillin-resistant *S. aureus* (MRSA) isolates was not evaluated due to the low (≤3) annual number of isolates. *Enterococcus faecalis* resistance to the key antibiotics (amoxicillin, glycopeptides, and linezolid) was low (<6%) over the 2018-2022 period (Figure 2a and Appendix 2).

Non-pyogenic streptococci (*Streptococcus* spp. except for *Streptococcus* groups A, B, C, and G, and *S. pneumoniae*) resistance to macrolides was 41.3% (n=31 per 75 tested) in 2018 and 48.6% (n=18 per 37 tested) in 2022. Clindamycin resistance was 7.9% (n=8 per 101 tested) in 2018 and 21.9% (n=14 per 64 tested) in 2022. Resistance to penicillin and glycopeptides remained low, with 5% resistance to penicillin in 2022 (n=4 per 75 tested) and only 2 isolates resistant to glycopeptides between 2018 and 2022 (Figure 2c and Appendix 2).

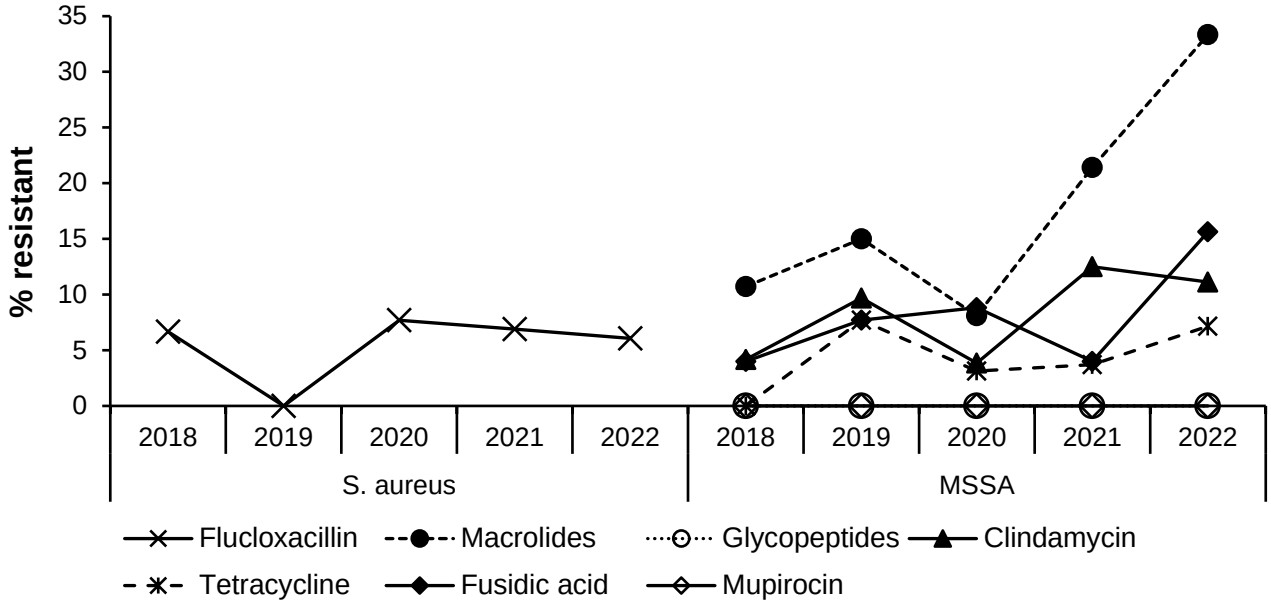
Figure 2. AMR of Gram-positive BSI for children aged 0 to 3 days in England, 2018 to 2022 for: (a) CoNS and *Micrococcus* spp. and *E. faecalis (b) *S. aureus* (all) and MSSA** (c) GBS and *Streptococcus* non-pyogenic*****

(a)



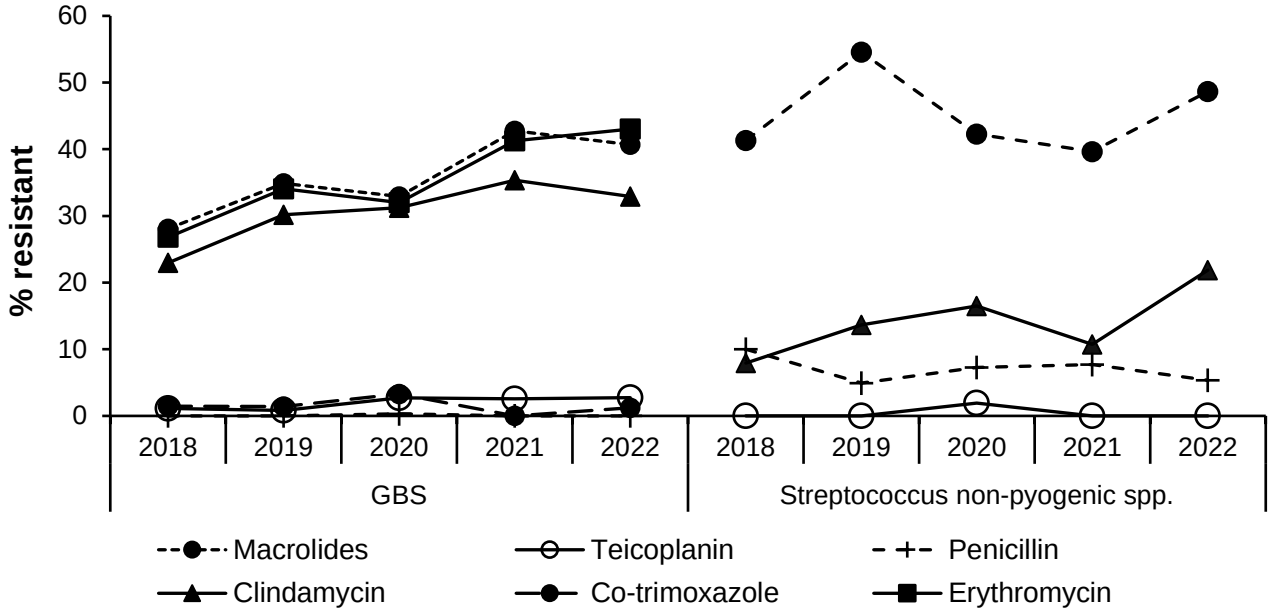
* Resistance not displayed for *E. faecalis* for linezolid in 2022 due to low (<20) numbers of reported BSIs.

(b)



** Resistance not displayed for MRSA, and for MSSA (co-trimoxazole (2018 to 2022 and linezolid (2022)), due to low (<20) numbers of reported BSIs.

(c)



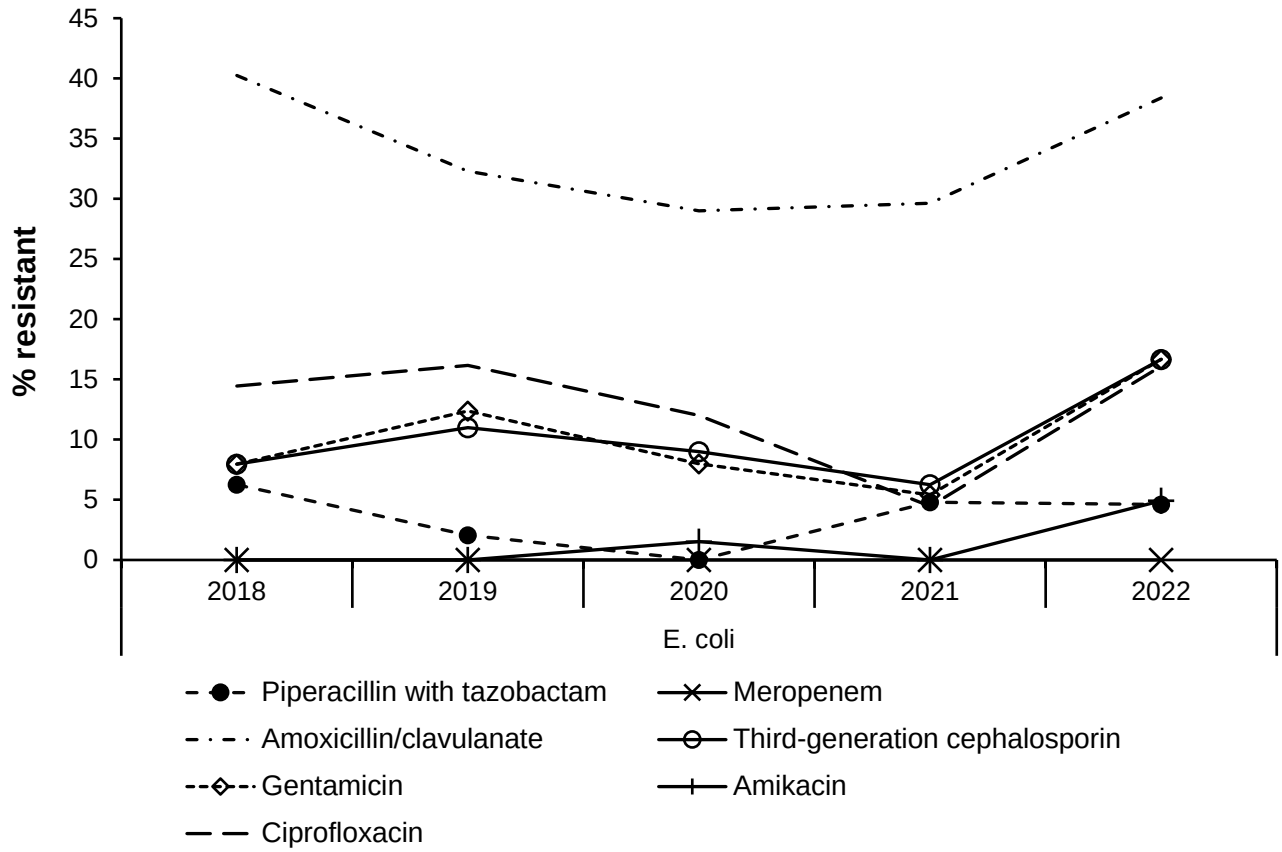
*** Resistance to co-trimoxazole not displayed for non-pyogenic *Streptococcus* due to low (<20) numbers of reported BSIs

3.2.1.2 Gram-negative bloodstream infections

E. coli resistance to amoxicillin/clavulanate was 40.2% (n=33 per 82 tested) in 2018 and 38.4% (n=33 per 86 tested) in 2022. *E. coli* resistance to third-generation cephalosporins was 8.0% (n=7 per 88 tested) in 2018 and 16.7% (n=15 per 90 tested) in 2022 (Figure 3 and Appendix 3). Resistance to piperacillin with tazobactam was low (<7%) and stable over the period.

Ciprofloxacin resistance was stable over the period, with reported resistance at 14.5% (n=12 per 83 tested) in 2018 and 16.1% (n=14 per 87 tested) in 2022. Gentamicin resistance was 8.0% (n=7 per 88 tested) in 2018 and 16.7% (n=15 per 90 tested) in 2022. Amikacin resistance remained stable and low (<5%) over the 2018-2022 period. Meropenem resistance was not detected in this age group between 2018 and 2022.

Figure 3. AMR of Gram-negative BSI for children aged 0 to 3 days in England, 2018 to 2022 for *E. coli*



3.2.2 Neonates and infants (4 days to 3 months old)

3.2.2.1 Gram-positive bloodstream infections

In bacteraemia detected in neonates and infants aged 4 days to 3 months old, *S. aureus* resistance to flucloxacillin has increased slightly from 2.1% (n=4 per 190 tested) in 2018 to 5.6% (n=11 per 196 tested) in 2022 (Figure 4b and Appendix 4). MSSA resistance to macrolides and clindamycin increased over the 2018 to 2022 period; from 10.5% (n=19 per 181 tested) in 2018 to 18.7% (n=35 per 197 tested) in 2022 for macrolides, and from 8.7% (n=13 per 150 tested) in 2018 to 17.0% (n=27 per 159 tested) in 2022 for clindamycin. In reports of MSSA, resistance to glycopeptides, co-trimoxazole, tetracycline, and mupirocin was low (<5%) over the period. Resistance to fusidic acid was 7.8% (n=13 per 166 tested) in 2018 and 9.1% (n=16 per 176 tested) in 2022. Further interpretation of resistance amongst MRSA isolates was not evaluated due to the low (≤3) annual number of isolates.

GBS remained universally susceptible to the first-line treatment, penicillin (with zero resistant isolates reported between 2018 and 2022) (Figure 4c and Appendix 4). Clindamycin and erythromycin resistances increased between 33.5% (n=54 per 161 tested) in 2018 and 37.5% (n=42 per 112 tested) in 2022 for clindamycin, and between 36.9% (n=62 per 168 tested) in 2018 and 45.5% (n=56 per 123 tested) in 2022 for erythromycin.

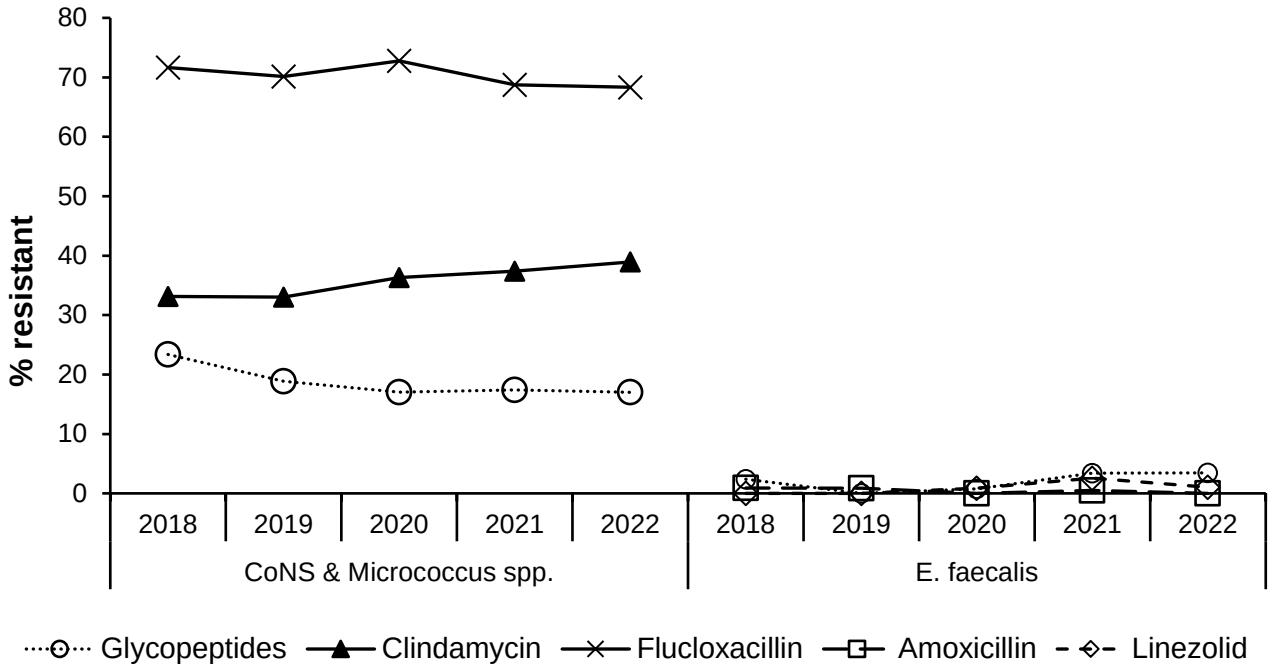
E. faecalis resistance has remained stable and low (<5%) over the 2018-2022 period for all antibiotics (amoxicillin, linezolid, and glycopeptides) (Figure 4a and Appendix 4).

CoNS and *Micrococcus* spp. resistance to flucloxacillin was stable between 2018 (71.7%, n=1,168 per 1,630 tested) and 2022 (68.3%, n=1,165 per 1,705 tested) (Figure 4a and Appendix 4). Glycopeptide resistance was also stable between 2018 (23.4%, n=261 per 1,117 tested) and 2022 (17.0%, n=193 per 1,135 tested). There was a marginal increase in clindamycin resistance, from 33.1% in 2018 (n=423 per 1,277 tested) to 38.9% (n=568 per 1,459 tested).

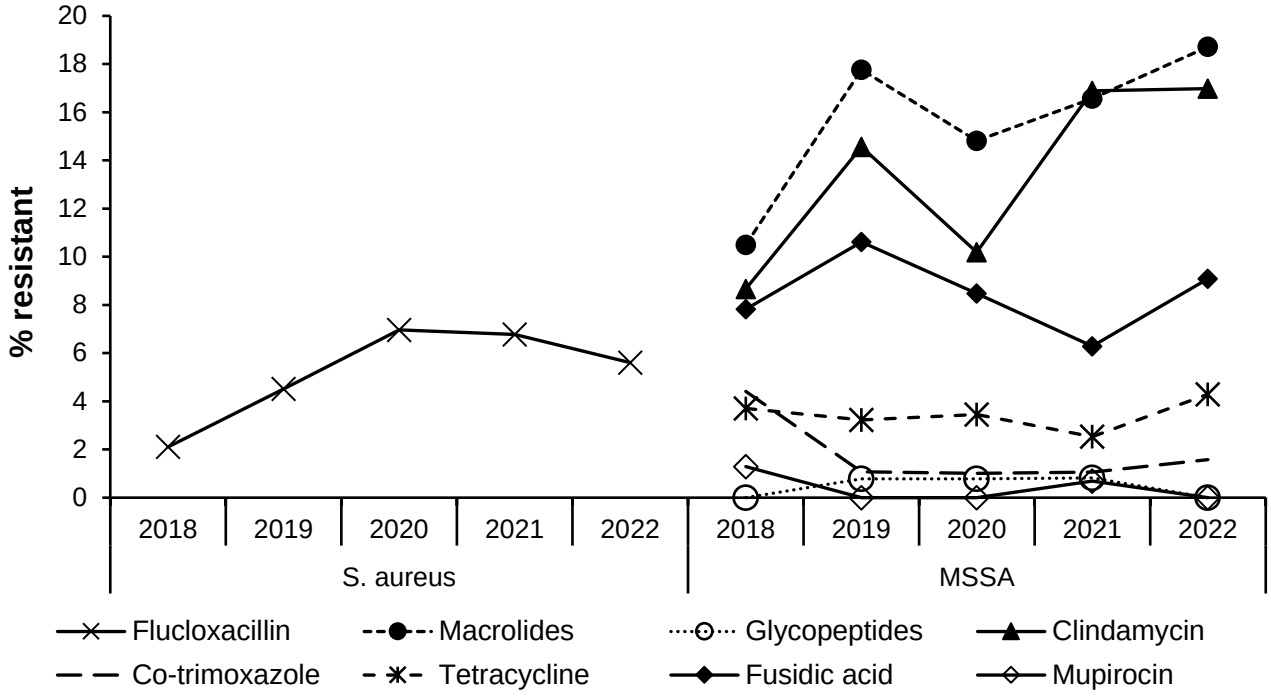
Finally, non-pyogenic streptococci resistance to macrolides was 53.9% (n=76 per 141 tested) in 2018 and 48.9% (n=46 per 94 tested) in 2022 (Figure 4c and Appendix 4). Resistance to co-trimoxazole was stable and low (<4%) over the period. Resistance to penicillin was stable between 18.4% (n=15 per 143 tested) in 2018 and 14.0% (n=27 per 193 tested) in 2022. Resistance to clindamycin was also stable at 10.5% (n=15 per 143 tested) in 2018 and 8.9% (n=13 per 146 tested) in 2022.

Figure 4. AMR of Gram-positive BSI for children aged 4 days to 3 months in England, 2018 to 2022 for: (a) CoNS and *Micrococcus* spp. and *E. faecalis* (b) *S. aureus* (all) and MSSA* (c) GBS and *Streptococcus* non-pyogenic spp.**

(a)

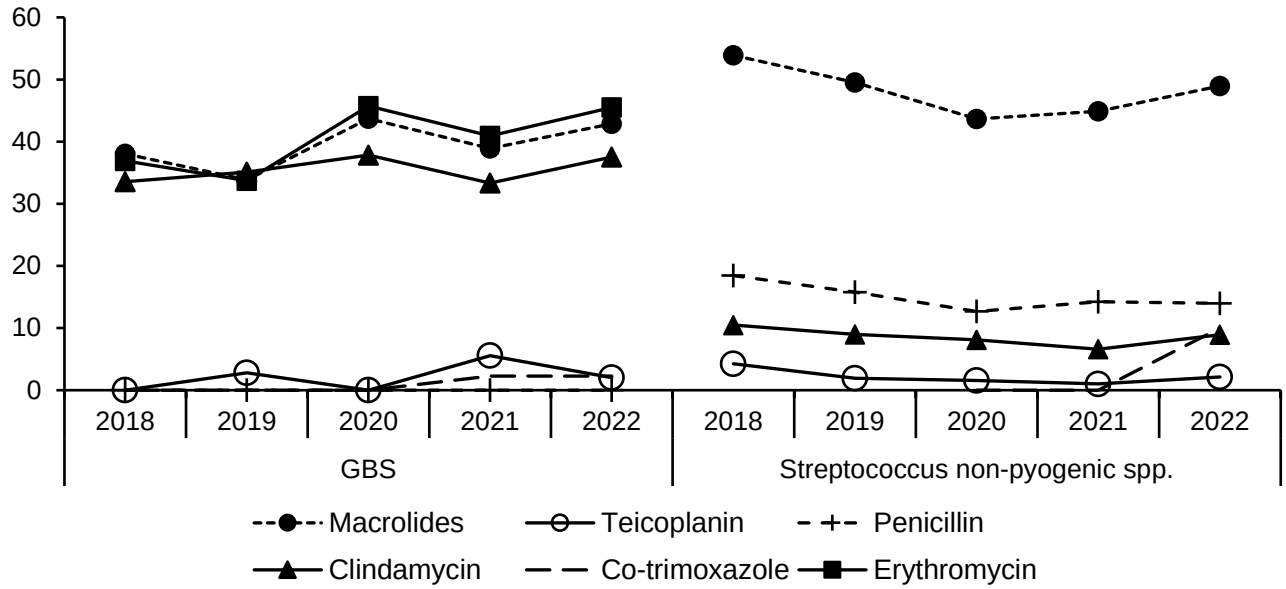


(b)



* Resistance not displayed for MRSA due to low (<20) numbers of reported BSIs.

(c)



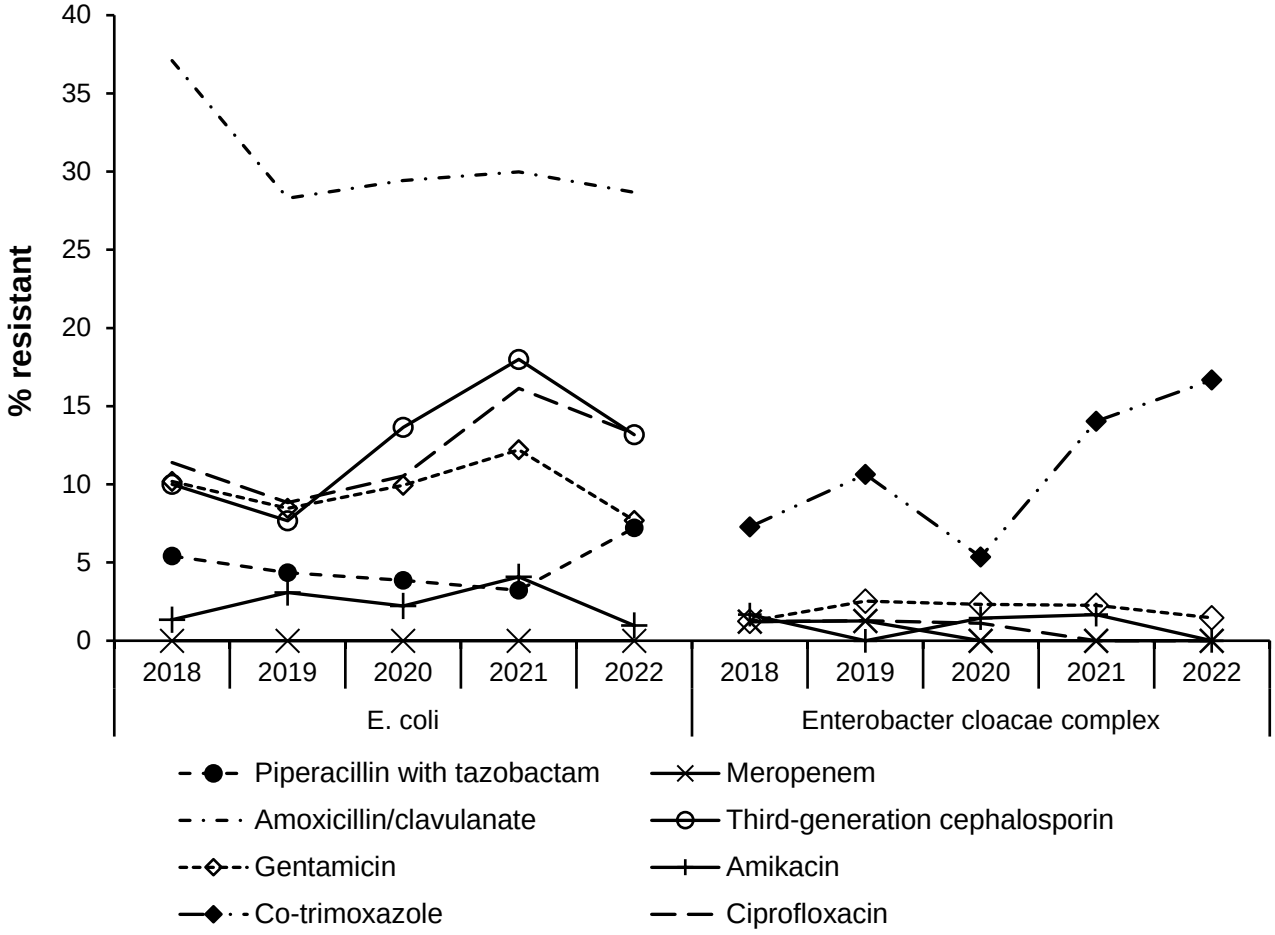
** Resistance not displayed for non-pyogenic Streptococcus (co-trimoxazole (2018 and 2019)) due to low (<20) numbers of reported BSIs.

3.2.2.2 Gram-negative bloodstream infections

E. coli resistance to amoxicillin/clavulanate ranged between 37.1% in 2018 (n=115 per 310 tested) to 28.7% in 2022 (n=84 per 293 tested). Resistance to third-generation cephalosporins remained fairly constant over the 5-year period, currently at 13.2 % (n=2 per 206 tested) in 2022 (Figure 3 and Appendix 3). Resistance to gentamicin (7.7%, n=24 per 312 tested), and piperacillin with tazobactam (7.2%, n=21 per 291 tested) remains at less than 10%, with resistance to amikacin currently at 1.0% (n=2 per 206 tested). Meropenem resistance was not detected.

Enterobacter cloacae complex resistance to gentamicin, amikacin, and meropenem remained stable and low (<3%) between 2018 and 2022 (Figure 5 and Appendix 5). Resistance to ciprofloxacin was 1.2% (n=1 per 82 tested) in 2018 and 0.0% (n=0 per 62 tested) in 2022.

Figure 5. AMR of Gram-negative BSI for children aged 4 days to 3 months in England, 2018 to 2022 for *E. coli* and *Enterobacter cloacae* complex



3.2.3 Infants and children (3 months to 4 years)

3.2.3.1 Gram-positive bloodstream infections

In infants and children aged 3 months to 4 years old, there was a low prevalence of resistance in *E. faecalis* to amoxicillin, glycopeptides, and linezolid (<5%). *E. faecium* resistance to amoxicillin was common throughout the period at 90.6% (n=48 per 53 tested) in 2018 and 81.8% (n=54 per 66 tested) in 2022. Resistance to vancomycin was 25.9% (n=15 per 58 tested) in 2018 and 16.2% (n=12 per 74 tested) in 2022. Resistance to teicoplanin was 28.6% (n=14 per 49 tested) in 2018 and 16.7% (n=12 per 72 tested) in 2022. Resistance to linezolid was low (<4%) throughout the period.

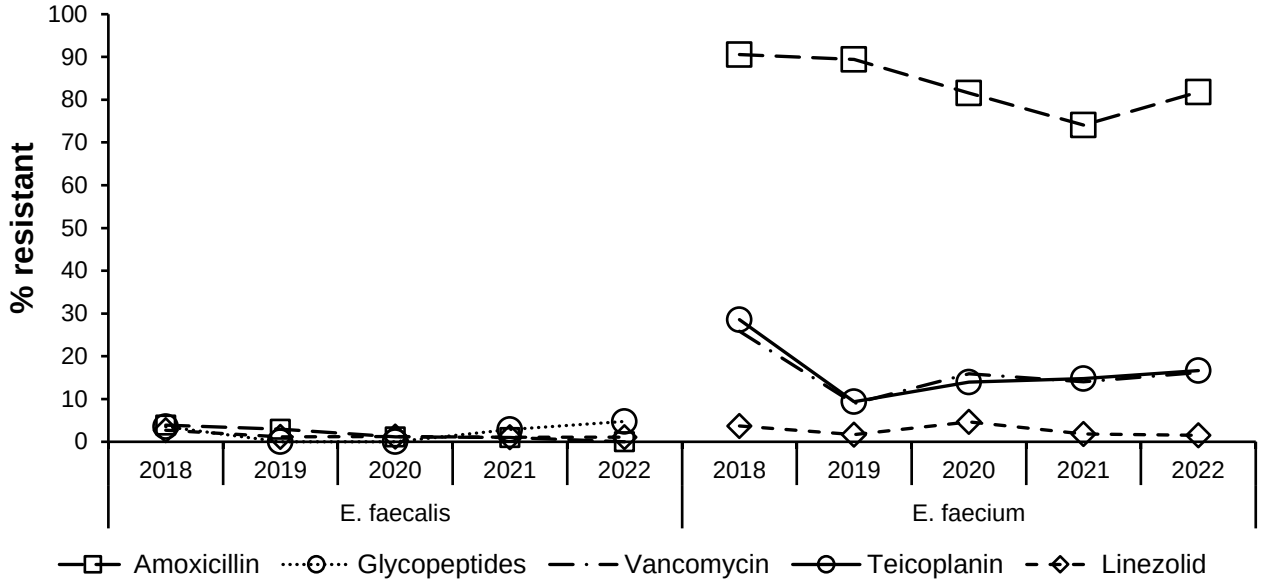
Between 2018 to 2022, resistance to penicillin in GAS was not detected. GAS co-trimoxazole resistance remained low (<6%) and generally stable. Resistance to macrolides and clindamycin was also low (<6%) from 2018 to 2020 and in 2022, however, higher resistance to these antibiotics was reported in 2021 (Figure 6b and Appendix 6), associated with circulating strain types. Trends and demographics of GAS are discussed in more detail in the seasonal and annual reports (2, 3, 4).

S. aureus resistance to flucloxacillin remained low at 8.0% (n=18 per 226 tested) in 2018 and 10.0% (n= 23 per 230 tested) in 2022. MSSA resistance to macrolides and clindamycin increased from 17.1% (n=36 per 210 tested) in 2018 to 23.9% (n=24 per 226 tested) in 2022 and from 9.9% (n=17 per 171 tested) in 2018 to 20.6% (n=40 per 194 tested) in 2022, respectively. Resistance to glycopeptides, co-trimoxazole and mupirocin remained low (<5%) throughout the period. MSSA resistance to fusidic acid remained stable at 18.8% (n=36 per 192 tested) in 2018 and 14.1% (n=3 per 213 tested) in 2022. Further interpretation of resistance amongst MRSA isolates was not evaluated due to the low (≤3) annual number of isolates.

S. pneumoniae resistance to penicillin remained low throughout the 5-year period at 2.1% (2.1%, n=4 per 188 tested in 2018; 2.1%, n=4 per 189 tested, in 2022). Resistance to both macrolides and clindamycin remained low and stable over the 5-year period at 7% and 5% respectively. Macrolide resistance was 7.0% (n=14 per 199 tested) in 2018 and 7.7% (n=16 per 208 tested) in 2022. Clindamycin resistance was 3.2% (n=2 per 63 tested) in 2018 and 4.8% (n=4 per 84 tested) in 2022.

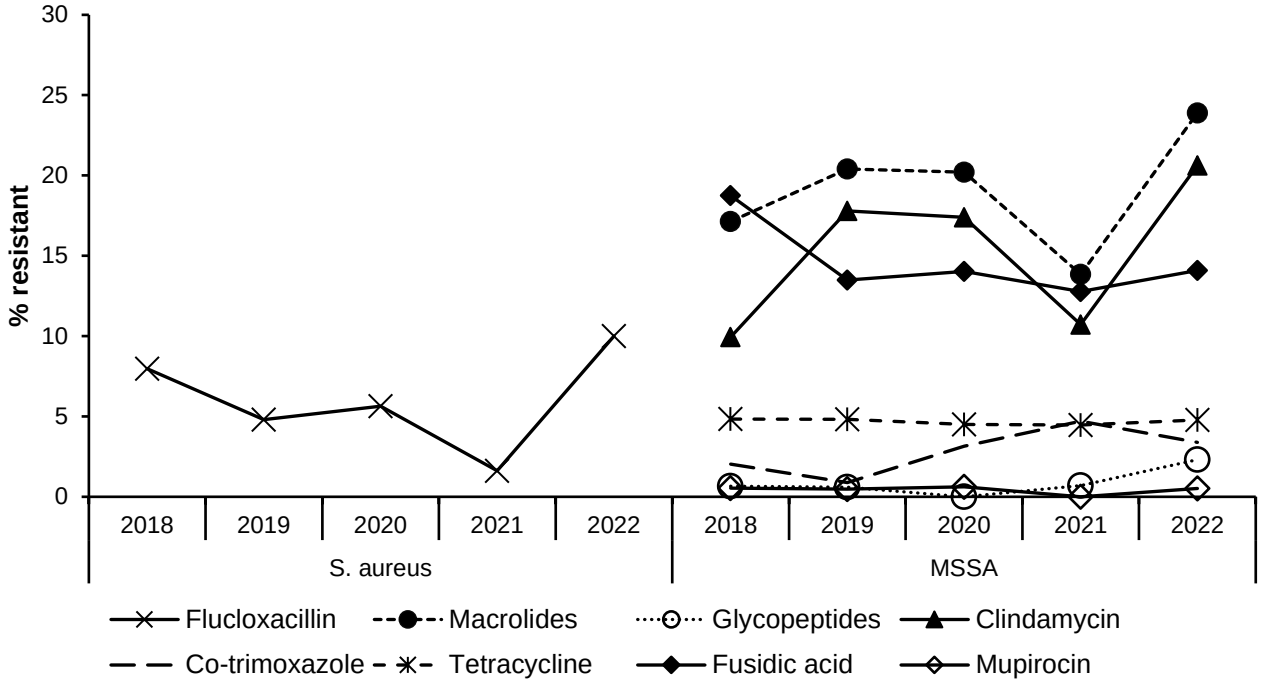
Figure 6. AMR of Gram-positive BSI for children aged 3 months to 4 years in England, 2018 to 2022 for: (a) *E. faecalis* and *E. faecium (b) *S. aureus* (all) and MSSA** (c) GAS***, *S. pneumoniae**** and *Streptococcus* non-pyogenic spp.**

(a)



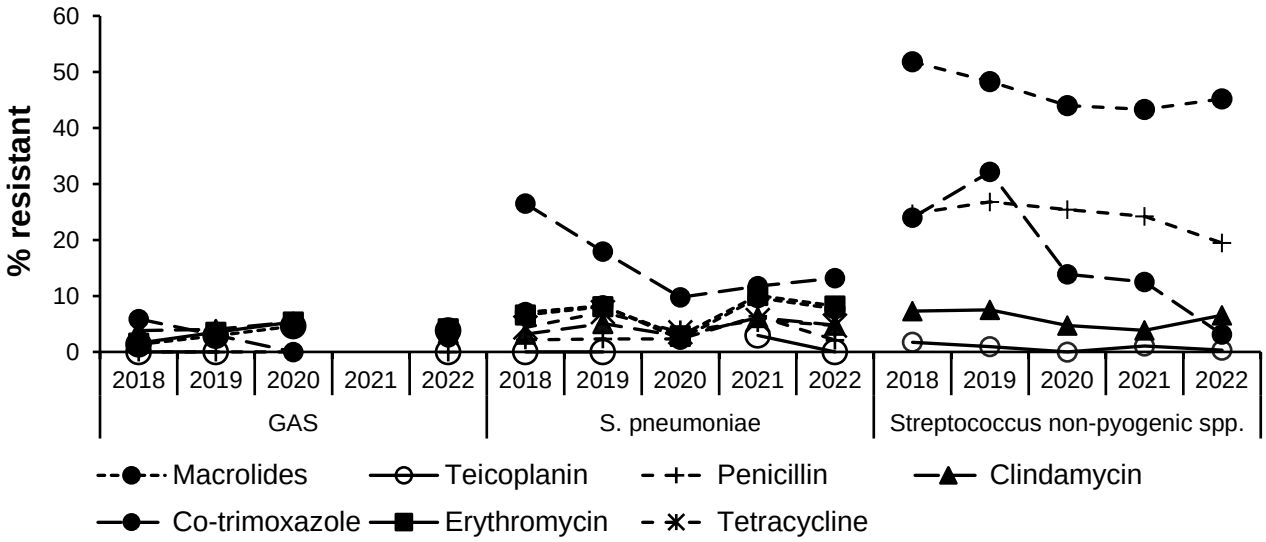
* Resistance not displayed for *E. faecium* (daptomycin (2018 to 2022)) due to low (<20) numbers of reported BSIs.

(b)



** Resistance not displayed for MRSA due to low (<20) numbers of reported BSIs.

(c)



*** Resistance not displayed for GAS (teicoplanin [2020 and 2021]) and in 2021 due to low (<20) numbers of reported BSIs.

**** Resistance not displayed for *S. pneumoniae* (teicoplanin [2020]) due to low (<20) numbers of reported BSIs.

3.2.3.2 Gram-negative bloodstream infections

Overall, *E. coli* resistance to the most common antibiotics remained broadly stable between 2018 to 2022 in the 3 month to 4 year old infants and children (Figure 7a). *E. coli* resistance to amikacin was low over the period, ranging from a minimum of 0% in 2018 (n=0 per 112 tested) to a maximum of 4.1% in 2019 (n=5 per 122 tested). Third-generation cephalosporin resistance was stable at 17.0% (n=27 per 159 tested) in 2018 and 17.5% (n=31 per 177 tested) in 2022. Resistance to amoxicillin per clavulanate ranged from a peak of 46.6% (n=83 per 178 tested) in 2019 to a low of 36.6% (n=63 per 172 tested) in 2022. Resistance to piperacillin with tazobactam and ciprofloxacin were also stable over the period; 13.0% (n=20 per 154 tested) resistance in 2018 and 14.9% (n=25 per 168 tested) resistance in 2022 for piperacillin with tazobactam, and 18.0% (n=28 per 156 tested) resistance in 2018 and 14.3% (n=25 per 175 tested) resistance in 2022 for ciprofloxacin. Resistance to meropenem was low, with only 3 isolates reported resistant over the period (one in 2018 and 2 in 2020).

Enterobacter cloacae complex resistance to gentamicin ranged from a minimum of 3.3% (n=3 per 92 tested) in 2019 to a maximum of 8.3% (n=9 per 109 tested) in 2022 (Figure 7a). Resistance to amikacin was low (<1.5%) throughout the period. Resistance to co-trimoxazole ranged from 17.0% (n=8 per 47 tested) in 2018 to 27.5% (n=25 per 91 tested) in 2022. Resistance to ciprofloxacin ranged from 6.0% (n=5 per 84 tested) in 2018 to 13.9% (n=15 per 108 tested) in 2022. Meropenem resistance was low (<3.0%).

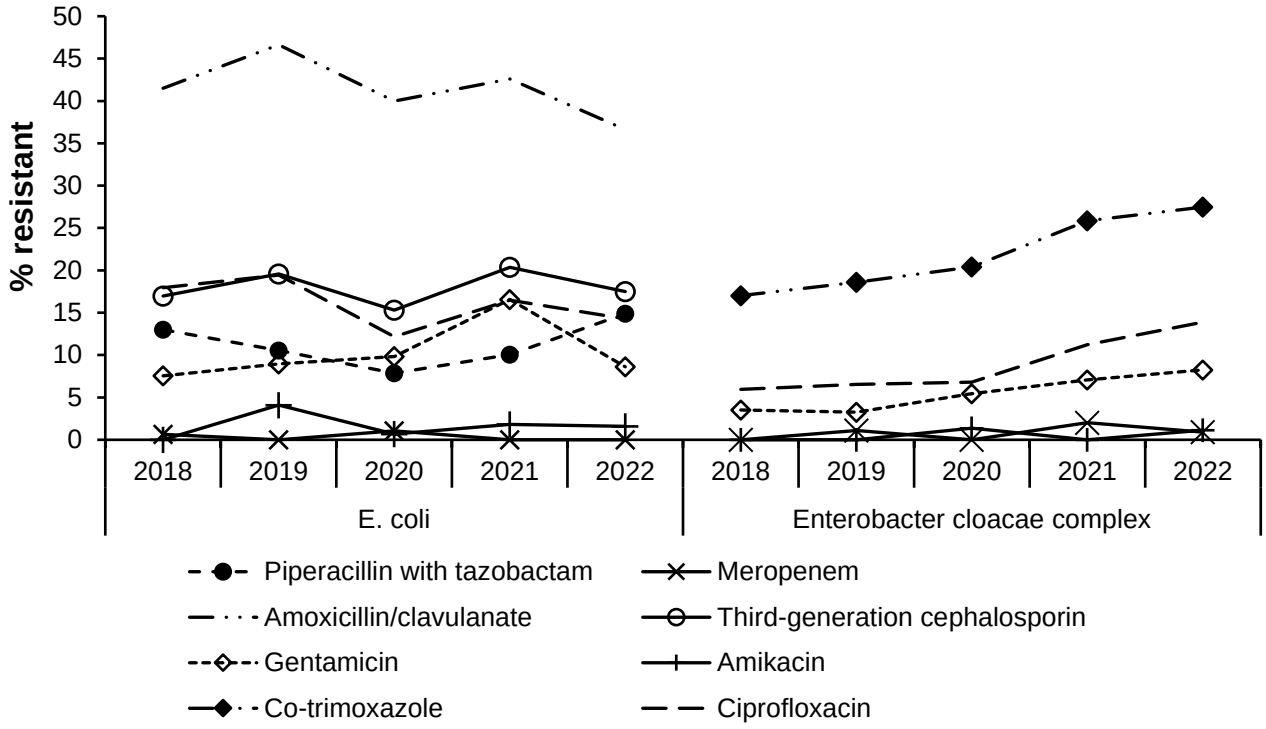
K. pneumoniae resistance to gentamicin ranged from 11.6% (n=8 per 69 tested) in 2018 to a peak of 19.6% (n=20 per 102 tested) in 2021, with resistance at 15.2% (n=17 per 112 tested) in 2022 (Figure 7b). Amikacin resistance ranged from 0% (n=0 per 86 tested) in 2019, to 7.3% (n=6 per 82 tested) in 2021, with resistance at 5.9% (n=5 per 85 tested) in 2022. Third-

generation cephalosporin resistance ranged from a minimum of 19.4% (n=18 per 93 tested) in 2020 to a maximum of 38.8% (n=40 per 103 tested) in 2021. Amoxicillin/clavulanate resistance was 39.6% (n=40 per 101 tested) in 2022, and resistance to piperacillin with tazobactam and ciprofloxacin was 31.7% and 31.5%, respectively, in 2022. Resistance to meropenem was low (<6%), with a maximum of 6 resistant isolates reported per year during the period.

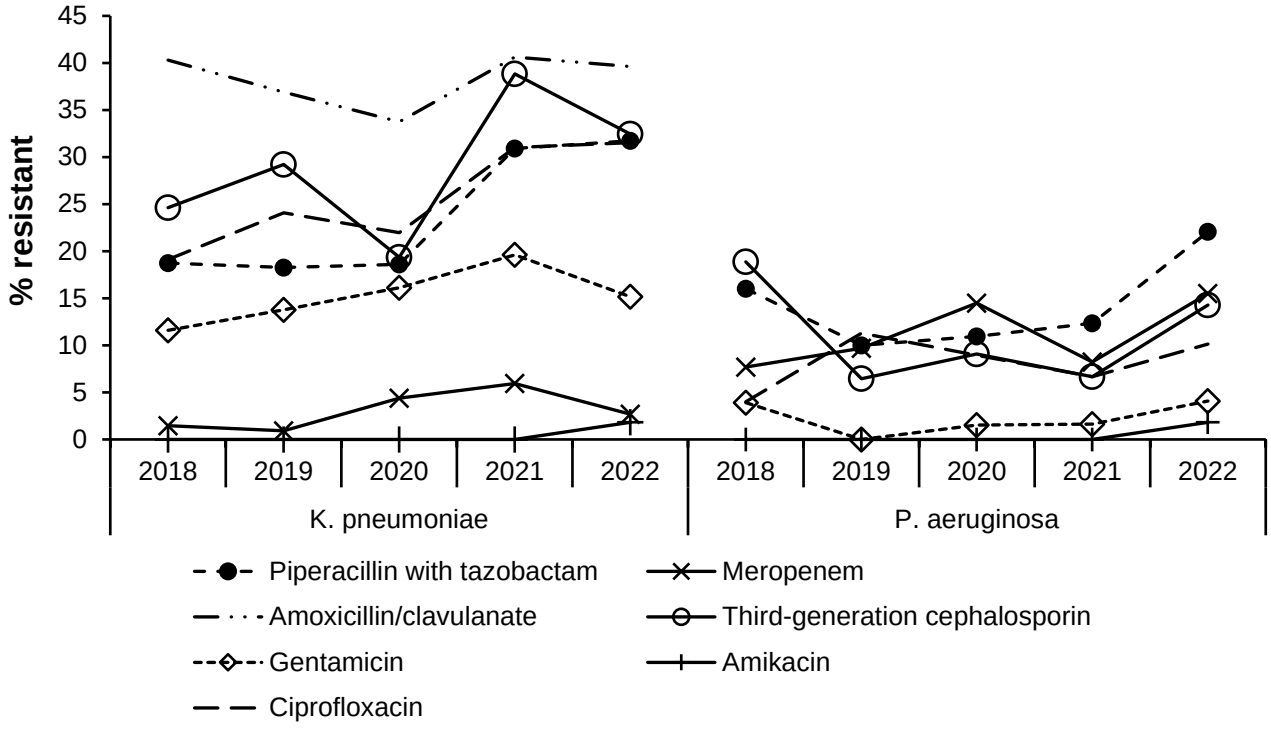
P. aeruginosa resistance to gentamicin was low (<5%) during this period, with no more than 2 resistant isolates reported per year (Figure 7b). Amikacin resistance was also low, with only one resistant isolate reported in this period, in 2022 (1.8% resistance, n=1 per 55 tested). Resistance to third-generation cephalosporins ranged from a minimum of 6.5% (n=4 per 62 tested) in 2019 to a maximum of 18.9% (n=10 per 53 tested) in 2018, with resistance at 14.3% (n=10 per 70 tested) in 2022. Piperacillin with tazobactam resistance ranged from 10.0% (n=6 per 60 tested) in 2019 to 22.1% (n=15 per 68 tested) in 2022. Ciprofloxacin resistance ranged from 4.0% (n=2 per 50 tested) in 2018 to 11.3% (n=7 per 62 tested) in 2019 with resistance at 10.1% (n=7 per 69 tested) in 2022. Meropenem resistance ranged from 7.7% (n=4 per 52 tested) in 2018 to 15.5% (n=11 per 71 tested) in 2022.

Figure 7. AMR of Gram-negative BSI for children aged 3 months to 4 years in England, 2018 to 2022 for: (a) *E. coli* and *Enterobacter cloacae complex* (b) *K. pneumoniae* and *P. aeruginosa*

(a)



(b)


% resistant
45
40
35
30
25
20
15
10
5
0
2018
2019
2020
2021
2022
K. pneumoniae
P. aeruginosa
Piperacillin with tazobactam
Amoxicillin/clavulanate
Gentamicin
Ciprofloxacin
Meropenem
Third-generation cephalosporin
Amikacin

3.2.4 Children (5 to 17 years)

3.2.4.1 Gram-positive bloodstream infections

S. aureus resistance to flucloxacillin was stable between 2018 (5.0%, n=16 per 320 tested) and 2022 (5.1%, n=16 per 316 tested) in children aged 5 to 17 years old (Figure 8a and Appendix 8). MSSA resistance to macrolides increased marginally over the 2018-2022 period; from 15.1% (n=46 per 305 tested) in 2018 to 20.1% (n=62 per 309 tested) in 2022. Clindamycin and fusidic acid resistance were stable over the 2018-2022 period; clindamycin resistance was 12.3% (n=32 per 260 tested) in 2018 and 13.3% (n=35 per 263 tested) in 2022, fusidic acid resistance was 13.4% (n=38 per 283 tested) in 2018 and 12.5% (n=35 per 280 tested) in 2022. MSSA resistance to glycopeptides, co-trimoxazole, tetracycline, and mupirocin was low (<5%) over the period. Further interpretation of resistance amongst meticillin-resistant MRSA isolates was not evaluated due to the low (≤3) annual number of isolates.

Between 2018 and 2022, *E. faecalis* resistance to commonly used antibiotics (amoxicillin, glycopeptides, and linezolid) was stable and low (<5%) (Figure 8b and Appendix 8). *E. faecium* resistance to amoxicillin was high between 81% to 92% over the period, whereas resistance to linezolid was stable and low (<9%). *E. faecium* vancomycin resistance was 22.5% (n=9 per 40 tested) in 2018 and 27.8% (n=15 per 54 tested) in 2022.

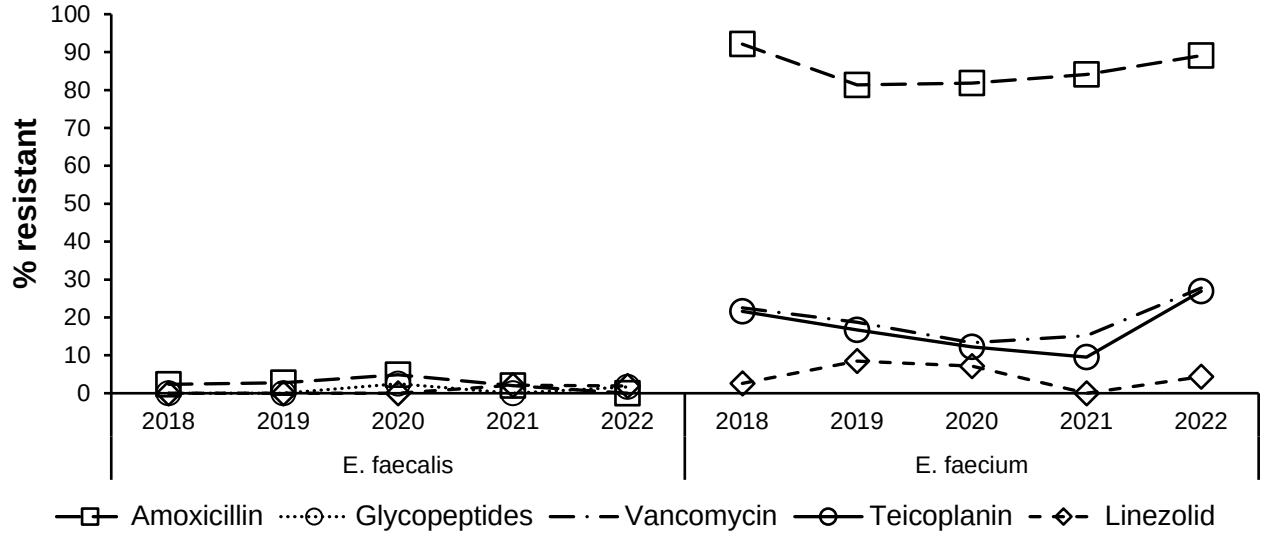
GAS resistance to commonly used antibiotics (glycopeptides, penicillin, clindamycin, co-trimoxazole) remained below 15.0% between 2018 and 2022 (Figure 8c and Appendix 8). Macrolide resistance was 3.7% (n=4 per 109 tested) in 2018 and 6.7% (n=11 per 165 tested) in 2022. Low incidence of GAS BSI in 2021 makes resistance estimates difficult to interpret for that year.

S. pneumoniae resistance to penicillin was 2.9% (n=2 per 69 tested) in 2018 and 6.7% (n=4 per 60 tested) in 2022. Macrolide resistance was 8.1% (n=6 per 74 tested) in 2018 and 8.3% (n=5 per 60 tested) in 2022. Between 2018 and 2022, co-trimoxazole resistance fluctuated between 9.5% and 25.0% due to low incidence (28 isolates tested in 2022) (Figure 8c and Appendix 8). Resistance to tetracycline was stable and low (<5%) over the period.

Non-pyogenic streptococci macrolide resistance decreased from 49.3% (n=101 per 205 tested) in 2018 to 37.6% (n=50 per 133 tested) in 2022 (Figure 8c and Appendix 8). Glycopeptide resistance was stable and low (<2%) over the period. Penicillin resistance was higher, fluctuating between 15.2% (n=54 per 354 tested) and 21.1% (n=52 per 247 tested) over the period.

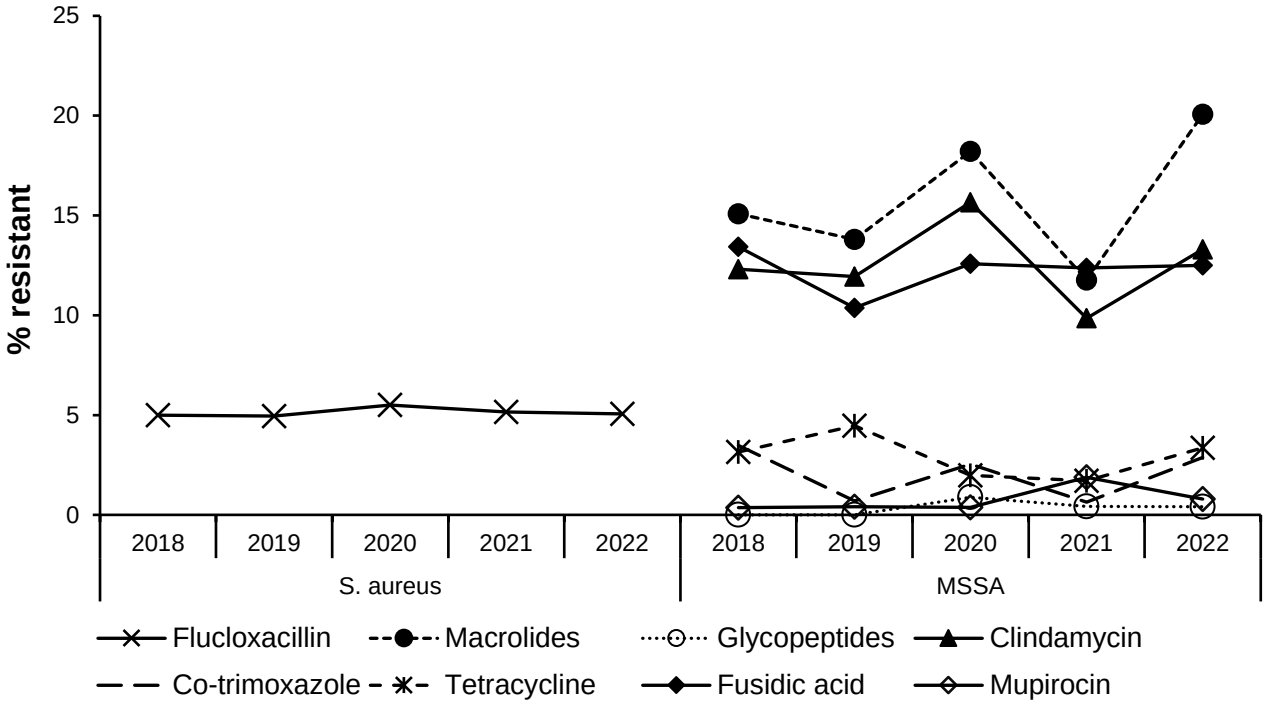
Figure 8. AMR of Gram-positive BSI for children aged 5 to 17 years in England, 2018 to 2022 for: (a) *E. faecalis* and *E. faecium (b) *S. aureus* (all) and MSSA** and (c) GAS***, *S. pneumoniae*****, and *Streptococcus* non-pyogenic spp.*******

(a)



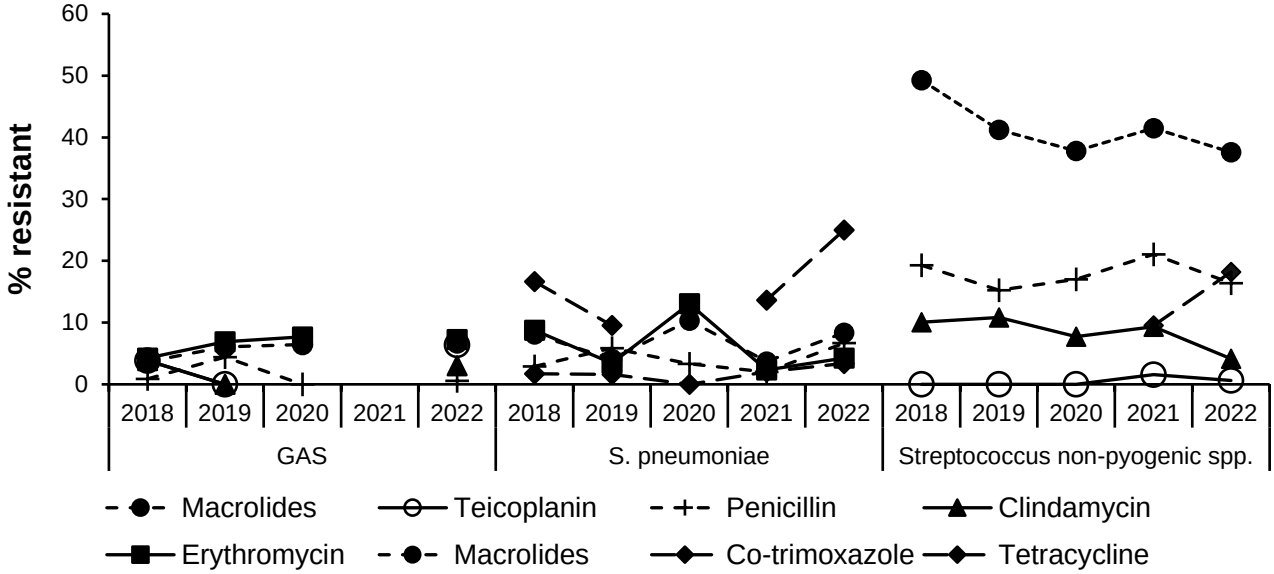
* Resistance not displayed for *E. faecium* (daptomycin [2018-2022]) due to low (<20) numbers of reported BSIs.

(b)



** Resistance not displayed for MRSA due to low (<20) numbers of reported BSIs.

(c)



*** Resistance not displayed for GAS (2021), GAS (co-trimoxazole [2018-2022]) and GAS (clindamycin and teicoplanin [2020 and 2021]) due to low (<20) numbers of reported BSIs.
**** Resistance not displayed for *S. pneumoniae* (clindamycin and teicoplanin [2018-2022]) and co-trimoxazole [2020]) due to low (<20) numbers of reported BSIs.
***** Resistance not displayed for non-pyogenic *Streptococcus* spp. (co-trimoxazole (2018-2020)) due to low (<20) numbers of reported BSIs.

3.2.4.2 Gram-negative bloodstream infections

In children aged 5 to 17 years old, *E. coli* gentamicin resistance increased from 6.6% (n=12 per 181 tested) in 2018 to 12.4% (n=22 per 178 tested) in 2022. *E. coli* resistance to amikacin was low (<4%) over the period. Third-generation cephalosporin resistance increased from 9.2% (n=17 per 184 tested) in 2018 to 17.0% (n=31 per 182 tested) in 2022. Resistance to amoxicillin/clavulanate was stable, ranging from a peak of 42.4% (n=64 per 151 tested) in 2020 to a low of 34.1% (n=57 per 167 tested) in 2019. Resistance to piperacillin with tazobactam was 7.7% (n=13 per 170 tested) in 2018 and 11.0% (n=18 per 164 tested) in 2022. Ciprofloxacin resistance was stable at 19.0% (n=34 per 169 tested) in 2018 and 20.8% (n=37 per 178) in 2022. Meropenem resistance was low (<1%) each year, with a total of 4 resistant isolates reported across the period.

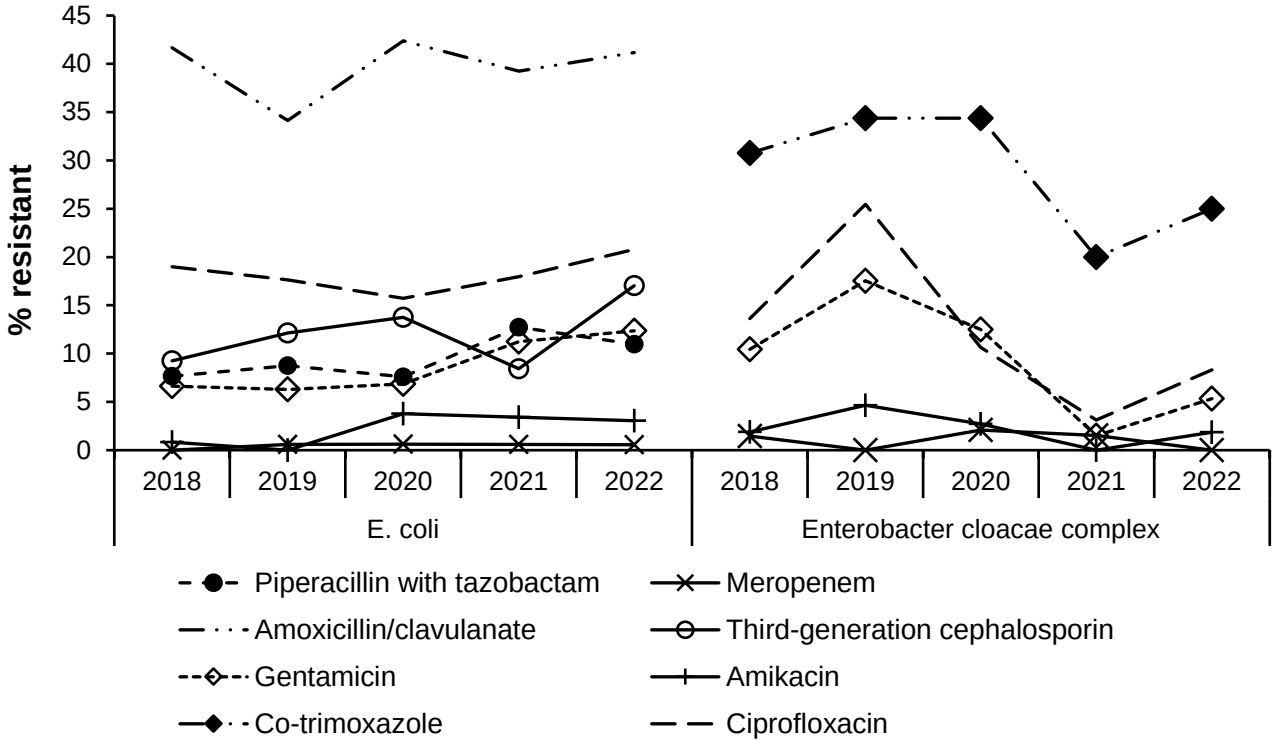
Enterobacter cloacae complex resistance to gentamicin was 10.5% (n=7 per 67 tested) in 2018 and 5.3% (n=4 per 75 tested) in 2022 (Figure 9a and Appendix 9). Resistance to amikacin was low (<5%) throughout the period. Resistance to co-trimoxazole ranged from 20.0% (n=8 per 40 tested) in 2021 to 34.4% (n=11 per 32 tested) in 2020. Resistance to ciprofloxacin ranged from 3.1% (n=2 per 72 tested) in 2021 to 25.5% (n=14 per 55 tested) in 2019. Meropenem resistance was low (<3%).

K. pneumoniae resistance to gentamicin was stable between 11 and 16% over the 2018-2022 period (Figure 9b and Appendix 9). Amikacin resistance was low (<3%) and stable. Third-generation cephalosporin resistance was also broadly stable between 23.1% (n=12 per 52 tested) in 2018 and 25.3% (n=19 per 75 tested) in 2022. Amoxicillin/clavulanate resistance fluctuated between 2019 and 2021 but was broadly similar between 2018 and 2022 (36.0% (n=18 per 50 tested) in 2018 and 35.2% (n=25 per 71 tested) in 2022). Piperacillin with tazobactam resistance was 18.4% (n=9 per 54 tested) in 2018 and 26.4% (n=19 per 72 tested) in 2022. Ciprofloxacin resistance increased from 14.8% (n=8 per 54 tested) in 2018 to 28.0% (n=21 per 75 tested) in 2022. Meropenem resistance was low (<5%).

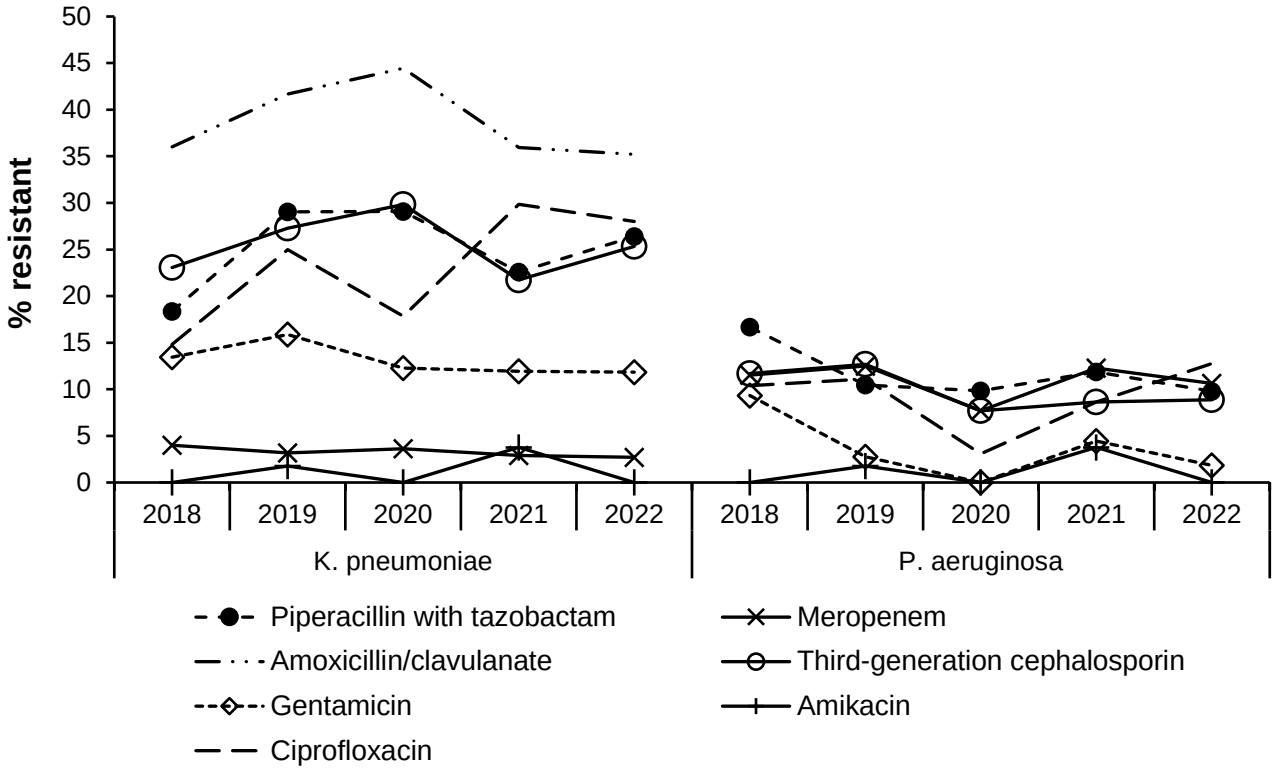
Finally, *P. aeruginosa* resistance to gentamicin and amikacin was low (<10%) over the 2018-2022 period (Figure 9b and Appendix 9). Third-generation cephalosporin resistance was broadly stable, with a minimum of 7.7% (n=5 per 65 tested) in 2020 and a maximum of 12.7% (n=9 per 71 tested). Piperacillin with tazobactam resistance was 16.7% (n=12 per 72 tested) in 2018 and 9.8% (n=9 per 92 tested) in 2022. Ciprofloxacin resistance was 10.4% (n=8 per 77 tested) in 2018 and 10.6% (n=12.94 tested) in 2022. Meropenem resistance was 11.5% (n=9 per 78 tested) in 2018 and 10.6% (n=10 per 94 tested) in 2022.

Figure 9. AMR of Gram-negative BSI for children aged 5 to 17 years in England, 2018 to 2022 for: (a) *E. coli* and *Enterobacter* spp. (b) *K. pneumoniae* and *P. aeruginosa*

(a)



(b)



3.3 *Listeria* spp.

Listeria spp. has been included in this report due to its occurrence in infants under 6 weeks of age. Isolation of *Listeria* from sample types other than blood cultures is not included in this report.

3.3.1 Bloodstream infection rates of *Listeria* spp. in paediatric population (0 to 17 years)

While infants under 6 weeks of age (as well as the immunosuppressed in other age groups) are particularly vulnerable to *Listeria*, the incidence of *Listeria* spp. BSI is low in the paediatric population (Table 1). The highest number of cases was in the 0 to 3 day old neonates across all years - this has been broadly stable between 2018 and 2022 with a peak of 1.9 BSIs per 100,000 in 2020, however, small numbers make meaningful trend interpretation difficult. Between 2018 and 2020, there were no reports of *Listeria* spp. BSI in 4 days to 1 month old neonates and infants. In 2021 there were 3 reported BSIs and 2 in 2022. Annual reports of all reported *Listeria monocytogenes* infection are available elsewhere (5).

Table 1. BSI rates per 100,000 paediatric population (aged 0 to 17 years) for Listeria spp. in England: 2018 to 2022 (n stands for number)

Age category	2018 rate	2018 (n)	2019 rate	2019 (n)	2020 rate	2020 (n)	2021 rate	2021 (n)	2022 rate	2022 (n)
0 to 3 days	1.4	9	0.5	3	1.9	11	1.3	8	1.4	8
4 days to 1 month	0.0	0	0.0	0	0.0	0	4.7	4	2.3	2
1 month to 1 years	0.1	1	0.0	0	0.0	0	0.0	0	0.0	0
1 to 4 years	0.0	0	0.0	0	0.0	0	0.0	1	0.0	0
0 to 17 years	0.0	10	0.0	3	0.0	11	0.1	13	0.0	10

3.3.2 AMR of *Listeria* spp. in paediatric population (0 to 17 years)

There was no reported resistance to amoxicillin in *Listeria* spp. isolates in children aged 0 to 17 years between 2018 and 2022. During this period, 3 isolates were resistant to co-trimoxazole out of 24 tested.

4. Data sources and methods

This report focuses on the paediatric population (0 to 17 years). The age groups used in the rates of laboratory-reported BSI rates and antimicrobial susceptibility trends differ slightly due to susceptibility testing being low for some (smaller) age groups (Table 2).

Table 2. Age categories used in the analysis for BSI rates and AMR of BSI

Age category for BSI rates	Age category for AMR of BSI
0 to 3 days	0 to 3 days
4 days to 1 month 1 month to 1 years 1 to 4 years	4 days to 3 months 3 months to 4 years
5 to 17 years	5 to 17 years

This report is based upon ESPAUR methodology (1). In summary, voluntary surveillance data on the antibiotic susceptibility of pathogens causing bacteraemia was obtained from SGSS (Second Generation Surveillance System) for the period 2018 to 2022. The SGSS is a national database maintained by UK Health Security Agency (UKHSA) that contains laboratory data supplied electronically by approximately 98% of hospital microbiology laboratories in England. SGSS comprises 2 modules, a communicable disease reporting (CDR; formerly CoSurv/LabBase2) module and an antimicrobial resistance (AMR; formerly AmSurv) module. The CDR module includes antimicrobial susceptibility test results for bloodstream isolates of the key pathogens being monitored as part of the UK 5-year AMR Strategy, although any test results suppressed from clinical reports by the sending laboratories are not captured when the data is submitted. In contrast, the AMR module contains more comprehensive antibiogram information as it includes results for all antibiotics tested (including results suppressed from clinical reports) for isolates from all clinical sources. The antimicrobial resistance trends included within this report use data from the AMR module and the rates of laboratory reported BSI from the CDR module; as this data is provided on a voluntary basis, case ascertainment will have been incomplete. However, ascertainment of notifiable infections, such as invasive GAS, will be high.

In previous ESPAUR reports (6), hospital microbiology laboratories have reported antimicrobial susceptibility test results as ‘susceptible’, ‘intermediate’ or ‘resistant’. These categories were defined as follows:

1. Susceptible: a bacterial strain is said to be susceptible to a given antibiotic when its growth is inhibited in vitro by a concentration of the drug that is associated with a high likelihood of therapeutic success.
2. Intermediate: a bacterial strain is said to be intermediate when the concentration of antibiotic required to inhibit its growth in vitro is associated with an uncertain therapeutic

outcome at standard antibiotic doses. It implies that an infection due to the isolate may be appropriately treated in body sites where the antibiotic is physically concentrated or when a high dosage of drug can be used.

3. Resistant: a bacterial strain is said to be resistant to a given antibiotic when the concentration required to inhibit its growth in vitro is associated with a high likelihood of therapeutic failure.

The breakpoint criteria for categorising clinical isolates as susceptible, intermediate or resistant to individual antibiotics have changed over time. As noted in the ESPAUR report 2019, in 2019 the EUCAST definitions were amended to rename the ‘intermediate’ category to ‘susceptible, increased exposure’ (with an adjusted increased dose), as the antibiotic should still work for treatment (6). The definition changes cannot be retrospectively applied.

As patients may have more than one positive blood culture taken, blood cultures taken from the same patient that yielded growth of the same pathogen during a rolling 14-day period from the initial positive blood culture were regarded as comprising the same episode of infection and were de-duplicated, retaining the worst-case scenario susceptibility result for each antibiotic tested (resistant > intermediate > susceptible).

Rates of laboratory-reported BSI per 100,00 were calculated using 2 methods depending on the age group, with the population denominator source differing. The BSI rate in the 0 to 3 days age group was calculated using the relevant year’s Office for National Statistics (ONS) live birth data for England (7). All other age groups (4 days to 1 month, 1 month to 1 year, 1 to 4 years, 5 to 17 years, and 0 to 17 years) used the ONS mid-year resident population estimates for the respective year for each respective age group as the denominator, with under 1 month rates calculated using one-twelfth of the 0 years age group and 1 to 11 months rates using eleven-twelfths of the 0 years age group (8). At the time of analysis, there was no 2022 mid-year population estimate, therefore, the 2021 mid-year population estimate was used as a proxy. All reported BSI episodes to SGSS were included in calculating reported BSI rates.

The AMR BSI section includes the most frequently reported BSI-causing bacteria for each age group (Appendices 11 to 15) and key antibiotics for each organism (defined in Table 3).

Table 3. Organisms and key antibiotics included in the AMR analysis by age category

Organisms	0 to 3 days	4 days to 3 months	3 months to 4 years	5 to 17 years
CoNS and *Micrococcus* spp.	- Glycopeptides - Clindamycin - Flucloxacillin	- Glycopeptides - Clindamycin - Flucloxacillin	Organism not included for age group	Organism not included for age group
E. faecalis	- Amoxicillin - Linezolid - Glycopeptides	- Amoxicillin - Linezolid - Glycopeptides	- Amoxicillin - Linezolid - Glycopeptides	- Amoxicillin - Linezolid - Glycopeptides
E. faecium	Organism not included for age group	Organism not included for age group	- Amoxicillin - Linezolid - Teicoplanin - Vancomycin - Daptomycin	- Amoxicillin - Linezolid - Teicoplanin - Vancomycin - Daptomycin
GAS	Organism not included for age group	Organism not included for age group	- Penicillin - Co-trimoxazole - Clindamycin - Erythromycin - Tetracycline - Macrolides - Teicoplanin	- Penicillin - Co-trimoxazole - Clindamycin - Erythromycin - Tetracycline - Macrolides - Teicoplanin
GBS	- Penicillin - Clindamycin - Erythromycin - Co-trimoxazole - Macrolides	- Penicillin - Clindamycin - Erythromycin - Co-trimoxazole - Macrolides	Organism not included for age group	Organism not included for age group

Organisms	0 to 3 days	4 days to 3 months	3 months to 4 years	5 to 17 years
	- Teicoplanin	- Teicoplanin		
S. aureus	- Flucloxacillin	- Flucloxacillin	- Flucloxacillin	- Flucloxacillin
MRSA	- Glycopeptides - Co-trimoxazole - Clindamycin - Macrolides - Tetracycline - Mupirocin - Fusidic acid	- Glycopeptides - Co-trimoxazole - Clindamycin - Macrolides - Tetracycline - Mupirocin - Fusidic acid	- Glycopeptides - Co-trimoxazole - Clindamycin - Macrolides - Tetracycline - Mupirocin - Fusidic acid	- Glycopeptides - Co-trimoxazole - Clindamycin - Macrolides - Tetracycline - Mupirocin - Fusidic acid
MSSA	- Glycopeptides - Co-trimoxazole - Clindamycin - Macrolides - Tetracycline - Mupirocin - Fusidic acid	- Glycopeptides - Co-trimoxazole - Clindamycin - Macrolides - Tetracycline - Mupirocin - Fusidic acid	- Glycopeptides - Co-trimoxazole - Clindamycin - Macrolides - Tetracycline - Mupirocin - Fusidic acid	- Glycopeptides - Co-trimoxazole - Clindamycin - Macrolides - Tetracycline - Mupirocin - Fusidic acid
Listeria spp.	- Amoxicillin - Co-trimoxazole - Meropenem - Moxifloxacin	- Amoxicillin - Co-trimoxazole - Meropenem - Moxifloxacin	- Amoxicillin - Co-trimoxazole - Meropenem - Moxifloxacin	- Amoxicillin - Co-trimoxazole - Meropenem - Moxifloxacin

Organisms	0 to 3 days	4 days to 3 months	3 months to 4 years	5 to 17 years
S. pneumoniae	Organism not included for age group	Organism not included for age group	- Penicillin - Clindamycin - Co-trimoxazole - Macrolides - Tetracycline - Erythromycin - Teicoplanin	- Penicillin - Clindamycin - Co-trimoxazole - Macrolides - Tetracycline - Erythromycin - Teicoplanin
Streptococcus non-pyogenic spp.	- Teicoplanin - Penicillin - Clindamycin - Co-trimoxazole - Macrolide	- Teicoplanin - Penicillin - Clindamycin - Co-trimoxazole - Macrolide	- Teicoplanin - Penicillin - Clindamycin - Co-trimoxazole - Macrolide	- Teicoplanin - Penicillin - Clindamycin - Co-trimoxazole - Macrolide
E. coli	- Amikacin - Meropenem - Co-amoxiclav - Third-generation cephalosporins - Gentamicin - Piperacillin with tazobactam - Ciprofloxacin	- Amikacin - Meropenem - Co-amoxiclav - Third-generation cephalosporins - Gentamicin - Piperacillin with tazobactam - Ciprofloxacin	- Amikacin - Meropenem - Co-amoxiclav - Third-generation cephalosporins - Gentamicin - Piperacillin with tazobactam - Ciprofloxacin	- Amikacin - Meropenem - Co-amoxiclav - Third-generation cephalosporins - Gentamicin - Piperacillin with tazobactam - Ciprofloxacin
Enterobacter cloacae complex	Organism not included for age group	- Amikacin - Gentamicin - Ciprofloxacin	- Amikacin - Gentamicin - Ciprofloxacin	- Amikacin - Gentamicin - Ciprofloxacin

Organisms	0 to 3 days	4 days to 3 months	3 months to 4 years	5 to 17 years
		- Co-trimoxazole - Meropenem	- Co-trimoxazole - Meropenem	- Co-trimoxazole - Meropenem
K. pneumoniae	Organism not included for age group	Organism not included for age group	- Amikacin - Meropenem - Amoxicillin/ clavulanate - Third-generation cephalosporins - Gentamicin - Piperacillin with tazobactam - Ciprofloxacin	- Amikacin - Meropenem - Amoxicillin/clavulanate - Third-generation cephalosporins - Gentamicin - Piperacillin with tazobactam - Ciprofloxacin
P. aeruginosa	Organism not included for age group	Organism not included for age group	- Amikacin - Meropenem - Ceftazidime - Gentamicin - Piperacillin with tazobactam - Ciprofloxacin	- Amikacin - Meropenem - Ceftazidime - Gentamicin - Piperacillin with tazobactam - Ciprofloxacin

The antimicrobials included in the antimicrobial susceptibility reporting are clinically important in the treatment of Gram-positive or Gram-negative paediatric infections. The following antimicrobial groupings were used:

- flucloxacillin (comprised of meticillin, oxacillin, cefoxitin, and flucloxacillin)
- third-generation cephalosporins (comprised of cefotaxime, ceftazidime, ceftriaxone, and cefpodoxime; except for *Pseudomonas* spp. where only ceftazidime was included)
- glycopeptides (comprised of teicoplanin and vancomycin)
- amoxicillin (comprised of ampicillin/amoxicillin, except for in *Listeria* spp. where only amoxicillin used)
- macrolides (comprised of azithromycin, clarithromycin, and erythromycin)

Several organism species were grouped together during data processing:

- CoNS with *Micrococcus* spp. because they form part of the normal skin flora and are common contaminants of blood cultures
- non-pyogenic *Streptococcus* spp., which comprises all *Streptococcus* spp. except for *Streptococcus* groups A, B, C, and G, and *S. pneumoniae*
- *Enterobacter cloacae* complex includes *Enterobacter asburiae, Enterobacter bugandensis, Enterobacter cloacae, Enterobacter cloacae* complex, *Enterobacter hormaechei*, *Enterobacter kobei*, *Enterobacter xianfangensis,* and unspeciated *Enterobacter* spp. (approximately 9% in 2022)
- all *Listeria* spp.
- *S. aureus* includes MRSA, MSSA and *S. aureus* that did not have a resistant, susceptible, or intermediate to flucloxacillin and cefoxitin test result in SGSS
- MRSA is any *S. aureus* isolate that had a resistant test result to flucloxacillin and cefoxitin in SGSS
- MSSA is any *S. aureus* isolate that had a susceptible or intermediate test result to flucloxacillin and cefoxitin in SGSS

Data reference tables featuring the data behind the findings in this report are provided in an appendix feature.

5. Acknowledgements

These reports would not be possible without the weekly contributions from microbiology colleagues in laboratories across England, without whom there would be no surveillance data. The support from colleagues within the UKHSA and UKHSA AMRHAI Reference Unit (9) in particular, is valued in the preparation of the report. Feedback and specific queries about this report are welcome and can be sent to hcai.amrdepartment@ukhsa.gov.uk.

6. References

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9. UKHSA (2014) 'Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit'

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