medical sciences forum

MDPI

Proceeding Paper

Antimicrobial Resistance in England 2017 to 2021 (ESPAUR Report 2021–22) †

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† Presented at the ESPAUR 2021/22 Webinar, Antibiotic Guardian, 23 November 2022; Available online: https://antibioticguardian.com/Meetings/espaur-2021-22-webinar/.

Abstract: The English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) antimicrobial resistance (AMR) chapter reports on bacterial, viral, and fungal AMR trends between 2017 and 2021 in England. A 10.8% increase in patient episodes of bacteraemia or fungaemia was observed, and the estimated burden of resistance decreased by 4.2%. Individuals with an antimicrobial-resistant strain (resistant to ≥1 key AMR burden-defined antibiotics) had a higher crude case fatality rate (18.1%) compared to those with a susceptible strain (16.3%). The effect of deprivation on carbapenemase-producing organisms (CPO) incidence, and the impact of the AMR burden across ethnic groups, have been described for the first time. Understanding the impact of ethnicity, deprivation, regional divergence, and potential confounders remains a crucial avenue of enquiry to target appropriate AMR interventions. These findings were presented at the ESPAUR Report webinar on 23 November 2022.

Keywords: antimicrobial; resistance; England; bacterial; fungal; viral; AMR; ethnicity; deprivation; health inequality

Citation: Guy, R.; Higgins, H.; Rudman, J.; Fountain, H.; Bennet, K.F.; Hopkins, K.L.; Demirjian, A.; Gerver, S.M.; Mirfenderesky, M.; Henderson, K.L. Antimicrobial Resistance in England 2017 to 2021 (ESPAUR Report 2021–22). *Med. Sci. Forum* **2022**, *15*, 3. https://doi.org/10.3390/msf2022015003

Academic Editor: David Enoch

Published: 24 March 2023

1. Introduction

Antibiotic resistance is an increasing, established threat to global health, with an estimated 4.9 million associated deaths recorded in 2019 globally [1] and simple surgeries becoming more dangerous due to lack of effective antibiotics [2]. The UK Government has committed to a 5- and 20-year vision to reduce antimicrobial resistance (AMR) [3,4], with a national action plan (NAP) for monitoring progress. The English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report AMR chapter reports on key AMR trends [5,6].

2. Methods

2.1. Data and Data Sources

Bloodstream infections (BSI) caused by key pathogens were taken from routine and reference laboratory data for England for 2017–2021 [5]. Key pathogens included the Gram-negative bacteria: *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Pseudomonas* spp., and *Acinetobacter* spp.; and Gram-positive bacteria: *Enterococcus faecalis*, *Enterococcus faecium*, *Staphylococcus aureus* group, and *Streptococcus pneumoniae*. The carbapenemase-producing Gram-negative bacteria notifications were extracted for 2021 only.

The Gram-negative bacteria were reviewed for susceptibility to each of the following: gentamicin, ciprofloxacin, piperacillin/tazobactam, co-amoxiclav, third-generation cephalosporins (cefotaxime, ceftazidime, ceftriaxone, or cefpodoxime; as applicable) and carbapenems (meropenem, imipenem, or ertapenem, as applicable). The Gram-positive bacteria were reviewed for susceptibility to the following: glycopeptides (vancomycin or teicoplanin), penicillin, macrolides (erythromycin, azithromycin, or clarithromycin), and meticillin (flucloxacillin, oxacillin, or cefoxitin).

Susceptibility reports are given as S (susceptible), I (intermediate; susceptible increased exposure), and R (resistant), as recorded by the local laboratory. The samples were de-duplicated for patients who had more than one blood culture taken (yielding growth of the same pathogen) during a rolling 14-day period from the initial positive blood culture. Where differing susceptibility results were reported, the worst-case scenario susceptibility result was retained, and, for analysis on resistance, S and I were grouped together.

2.2. Data Processing

The burden of resistant infections is a hierarchical measure adapted from the Cassini et al. method [6] and used in publications within England [5]; it incorporates critical treatment antibiotics in key Gram-negative and -positive infections (see ESPAUR report). Ethnicity data were obtained via linkage to NHS Digital's Hospital Episode Statistic (HES) admission data, following the method outlined by the Office for Health Improvement and Disparities [7]. In addition, Index of Multiple Deprivation (IMD) data from the Office for National Statistics (ONS) were linked to the CPO patients' residential postcodes and were analysed by the IMD decile (1 = most deprived; 10 = least deprived) [5].

2.3. Statistical Analyses

Case fatality rates (CFRs) were calculated and stratified by the specimen group and resistance status, using patients successfully matched to the NHS Spine as the denominator. The CFRs were calculated as the percentage of patients who died with or without an antibiotic-resistant infection relative to the total patients in those groups who had been NHS Spine (NHS Digital)-matched. *p*-values were calculated to assess the change in resistance over time; these were generated using an unadjusted binomial regression model with a significant change being defined by $p < 0.05$. Incidence rates were calculated per 100,000 population per year using ONS mid-year populations [5]. Exact binomial 95% confidence intervals were calculated for the percentage resistance for the ethnic group analysis. STATA (version 17; StataCorp, Texas, USA) statistical software was used for this analysis.

3. Results

3.1. The Burden of AMR

There was a 10.8% increase in patient episodes of bacteraemia or fungaemia reported from laboratories in England between 2017 (n = 138,417) and 2021 (n = 153,362), of which 88.9% were monomicrobial in 2021, contrasting with a decrease in overall annual total blood cultures reported across this period [8]. For many of the key pathogens reviewed, the incidence of BSI showed an increase between 2017 and 2021 (*K. pneumoniae* (12.0/100,000 population to 13.5), *Pseudomonas* spp. (8.0 to 8.5), *Acinetobacter* spp. (1.6 to 1.8), and *Enterococcus* spp. (12.4 to 15.8)). Over the same time frame, the incidence of *E. coli* and *S. pneumoniae* BSI decreased (74.3/100,000 population to 66.9 and 8.7 to 4.0, respectively), predominantly in 2020 and 2021.

The burden of AMR decreased by 4.2% between 2017 (n = 16,099) and 2021 (n = 15,446; $p = 0.101$; Figure 1). The burden of antibiotic-resistant BSI predominates within the Enterobacterales family (particularly *E. coli*, of which 40% are resistant to the commonly used co-amoxiclav, and 10% are resistant to piperacillin with tazobactam), comprising 80.3% of the total episodes (with the peak in 2019 at 84.8%). The burden of resistant infections re-

mained relatively unchanged between 2017 and 2021 for Gram-positive infections, although an increase of 2.5% in glycopeptide-resistant *Enterococcus* spp. was recorded ($p < 0.0001$).

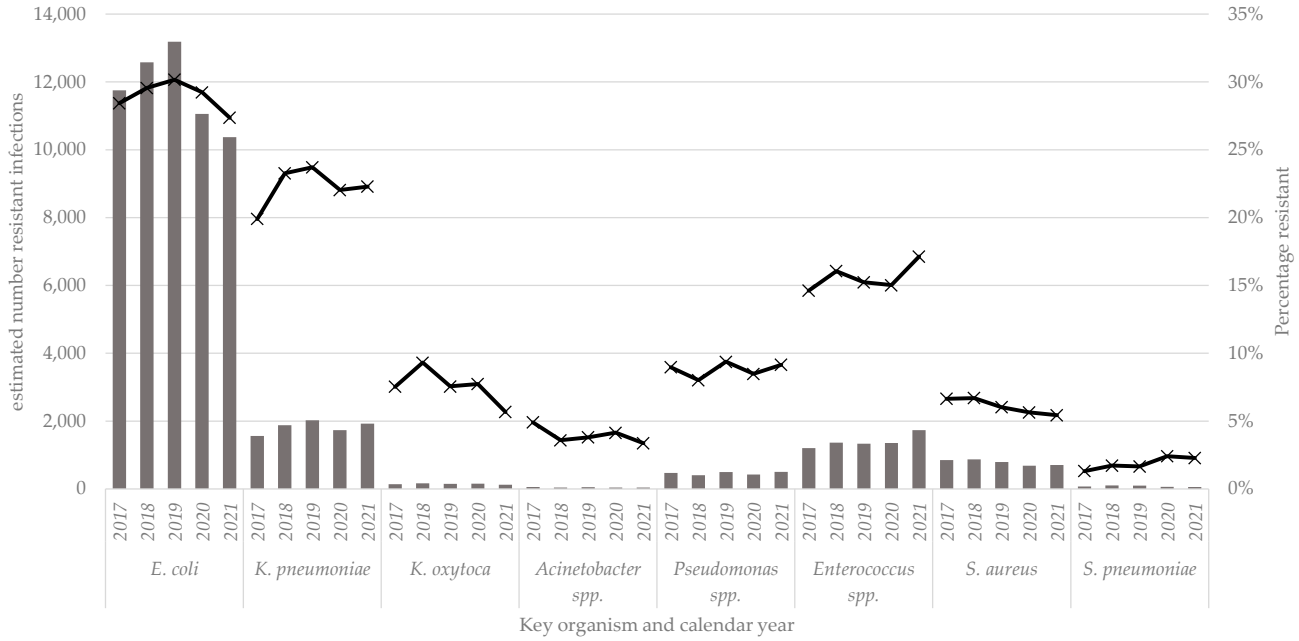

Figure 1. Annual estimated total (of the burden) of antibiotic-resistant bloodstream episodes by species (bar chart, left y-axis) and percentage resistant (line chart, right y-axis); England 2017 to 2021.

The burden of AMR BSI varied by ethnic group. In 2021, the highest number of BSI episodes was recorded in persons within a White ethnic group (80.8%; n = 50,329), of which 20.9% were recorded as resistant to at least one key antimicrobial. Aside from the mix of patients within the 'any other ethnic group' (n = 322; 34.0%), the highest percentage resistance was noted in the 'Asian or Asian British' ethnic group (n = 1243; 32.8%).

The London region reported the highest rate per 100,000 population burden of resistance (55.5/100,000), followed by the North West (44.5) and South East (41.1). The lowest was recorded in the East Midlands (32.1). For the overall incidence of key BSI pathogens, the lowest estimated rate was recorded in the East of England (130.7) and London regions (131.2). The highest rate of key species BSI infection was recorded in the North East (176.5).

When expanded to estimate the number of resistant infections including other infection types (surgical-site infections, urinary tract, and skin/soft-tissue infections), the number of serious antibiotic-resistant infections in England rose by 2.2% in 2021 compared to 2020 (53,985 compared to 52,842; $p < 0.01$), equivalent to 148 severe antibiotic-resistant infections a day in 2021.

3.2. Acquired Carbapenemase-Producing Gram-Negative Bacteria

In 2021, the most frequent carbapenemase family recorded in England was OXA-48-like (915/2244; 40.8%), followed by NDM (563/2244; 25.1%) and KPC (550/2244; 24.5%). In 2021, London and the North West regions reported the largest number of CPOs; however, there is considerable regional variation in both the number and families of carbapenemase being recorded. In the most deprived IMD decile, the rate of CPO notifications was 6.8 per 100,000 population, compared with 2.8 per 100,000 population in the least deprived. The carbapenemase family identified also varied with deprivation; however, the differences may be a result of regional mechanism variations, local screening policies, and outbreaks.

3.3. Thirty-Day All-Cause Mortality

The overall 30-day all-cause CFR in patients with key Gram-negative bacterial BSI (*Escherichia* spp., *Klebsiella* spp., *Pseudomonas* spp., *Acinetobacter* spp.) was 16.7% in 2021

(n = 7627); the CFR was lowest in children aged 1 to 14 years (1.9%, n = 11) and highest in adults aged 85 years and over (21.8%, n = 2053). Individuals with a resistant strain (resistant to $\geq$ 1 key AMR burden-defined antibiotics) had a higher crude CFR (18.1%, n = 1725; $p < 0.05$) compared to those with a susceptible strain (16.3%, n = 5818). In 2021, the crude 30-day all-cause CFR in people with an invasive CPO was 24.5% (n = 25/102).

Detailed summary tables and epidemiological commentary are available in the ESPAUR report. Other topics covered within the AMR chapter include results from the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP), AMR in tuberculosis, antifungal resistance, antiviral resistance, and details of participation in international AMR surveillance.

4. Discussion

Whilst a 10.8% increase in patient episodes of bacteraemia or fungaemia was observed between 2017 and 2021, the incidence rate change varied for different pathogens, particularly with the decrease in *E. coli* and *S. pneumoniae* BSI (74.3/100,000 population to 66.9 and 8.7 to 4.0, respectively) seen in 2020 and 2021. The decreased rates of BSI seen for *E. coli* and *S. pneumoniae* are likely due, at least in part, to the COVID-19 pandemic and associated public health interventions. This resulted in reduced contact between individuals and overall fewer interactions with the healthcare system, such as cancellation of elective surgery or access to GP consultations, although the underlying causes of reductions in BSI rates are likely to be complex and multifactorial. *E. coli* contributes substantially to the total BSI burden, and the marked reduction in BSI incidence may also be due to changes in healthcare interactions in vulnerable populations and antibiotic usage [5], therefore driving the 4.2% decrease in the burden of resistance between 2017 and 2021, although this was not significant. In contrast, other Gram-negative species causing BSI increased between 2017 and 2021, partly due to the more hospital-onset nature of *Klebsiella* spp. and *Pseudomonas aeruginosa* [9]. As we emerge from the COVID-19 pandemic, it will take time to assess the resulting impact on bacterial trends and the AMR burden, particularly in light of the decreasing overall numbers (but the increasing rate per 1000 occupied bed-days) of total blood cultures [8]. The burden of resistant infections remained relatively unchanged for Gram-positive infections overall. The diverging CFR, with higher CFR rates linked with increased resistance, will require further monitoring and investigation, as the true picture is more nuanced than resistance alone and will be affected, for example, by population demographics, comorbidity, time to effective treatment, and pathogenicity.

The detected regional differences in the AMR burden, and carbapenemase family prevalence and distribution, require local and regional knowledge, context, and strategies to understand and target healthcare interventions. Additionally, the effect of deprivation on CPO incidence and the effect of the AMR burden across ethnic groups have been described for the first time in this chapter. While the majority of resistant BSI were recorded in those with White ethnicity (80.8%), this percentage is lower than the national population (84.8%), and 'Asian, Asian British' accounts for 7.4% the population and only 6.1% of the resistant BSI reports; however, ethnic group population rates vary by region and rurality [10]. Understanding the impact of ethnicity, deprivation, and regional divergence, along with potential confounders, remains a crucial avenue of enquiry, and these investigations are currently underway using data linkage and form one of the future actions of this report.

Author Contributions: Conceptualization, R.G. and S.M.G.; methodology, R.G.; validation, R.G., K.L.H. (Katherine L. Henderson), H.H. and J.R.; formal analysis, H.F., K.F.B., H.H., R.G. and J.R.; investigation, H.H., K.L.H. (Katherine L. Henderson) and K.L.H. (Katie L. Hopkins); writing—original draft preparation, R.G.; writing—review and editing, K.L.H. (Katherine L. Henderson), S.M.G., M.M. and H.H.; visualization, R.G.; supervision, S.M.G., A.D. and K.L.H. (Katherine L. Henderson). All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Patient consent was not sought under Section 251 of the National Health Service Act 2006.

Data Availability Statement: The data presented in this study are available in [5].

Acknowledgments: We would like to thank Daniele Meunier, Gauri Godbole, Suzy Sun, Elizabeth Johnson, Riina Rautemaa-Richardson, Daniel Bradshaw, Tamyo Mbisa, Samreen Ljaz, Esther Robinson, and Sharon Cox for their contributions and expertise during the compilation of the annual update on AMR in ESPAUR. In addition, the participation of the NHS laboratories in the routine laboratory surveillance of infections in England is essential for the greater understanding of AMR in England, and they should be thanked.

Conflicts of Interest: The authors declare no conflict of interest.

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