The burden of antimicrobial-resistant infections in black and minority ethnic groups

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Key messages

1. Overuse and misuse of antibiotics is one of the main drivers of antimicrobial resistance (AMR) – particularly prescribing antibiotics for upper respiratory tract infections (URTIs).

2. History of recent travel (particularly to the Indian subcontinent) is correlated with a higher risk of colonisation with antibiotic-resistant bacteria.

3. There is some evidence that ethnic variation in diet could influence the risk of developing an antimicrobial-resistant infection.

4. Public knowledge of antimicrobial resistance and the behaviours contributing to it needs to reach all members of the population, including new entrants to the UK.

5. More research needs to be conducted in the UK pertaining to the burden of AMR in black and minority ethnic groups as the current evidence base is limited and there is a paucity of relevant data.

Introduction

Antimicrobial resistance (AMR) is increasingly being recognized as one of the major threats to human health globally, as outlined by the World Health Organisation, who warned that a “post-antibiotic era – in which common infections and minor injuries can kill…is a very real possibility for the 21st century” (World Health Organisation, 2014). AMR includes resistance to antivirals, antifungals, antiparasitics or, most commonly, antibiotics which are used to treat bacterial infections. Antibiotic resistance, on which this briefing will focus, emerges when an antibiotic is no longer effective against combating a bacterial infection due to the bacteria having acquired genes which allow it to avoid the antibiotic’s therapeutic mechanism of action. Drug-resistance, more generally, is hindering the progress towards control and/or elimination of diseases around the world such as HIV/AIDS, tuberculosis, malaria, pneumonia, diarrhoeal diseases and gonorrhoea. This is exacerbated and accelerated by causes such as increased exposure to antibiotics in the food-chain, a lack of effective rapid diagnostic tests to confirm whether an infection is bacterial or viral, and the misuse and overuse of antibiotics in healthcare settings and in the community.

Infections caused by bacteria resistant to antibiotics are on the rise. In the most recent report from the English Surveillance Program for Antimicrobial Utilisation and Resistance, released by Public Health England in November 2015, the rate of E. coli bloodstream infections (one of the most common and severe healthcare-associated infections) increased by 15.6 per cent between 2010 and 2014, with the proportion of these infections being antibiotic-resistant increasing over the same time period (Public Health England, 2014). Antibiotics are some of the most commonly prescribed drugs not only in the UK but around the world. However up to 50 per cent of all antimicrobial prescriptions are considered to be unnecessary (Centres for Disease Control and Prevention, 2013).

In this briefing, the NIHR Health Protection Research Unit in Healthcare-Associated Infections and Antimicrobial Resistance will explore the evidence base to identify areas where practice could be improved to ensure that all service users are equally aware of the drivers of AMR infections. Countering this global threat cannot be done without the awareness, prudence and participation of all members of society, from healthcare providers to politicians to patients.
Inadequate prescribing, self-medication and over-the-counter antibiotics: stemming the tide

Over the past several decades, people’s natural human gut microbiome has been exposed to extremely high levels of antibiotics which, while vastly improving human health initially and advancing the field of clinical medicine, has led to increased pressure for the natural selection of bacterial strains resistant to these drugs. Poor prescribing and over-the-counter sales of antibiotics without a prescription in many countries have led to massive increases in antimicrobial use (Laxminarayan et al., 2013). It is for this reason that scientific and medical communities now call for prudent use of antibiotics – saving them for infections which are known to be bacterial as opposed to viral.

One of the areas of most concern is the prescribing of antibiotics for coughs, colds and influenza, together known as upper respiratory tract infections (URTIs) – the vast majority of which are viral and therefore do not need an antibiotic prescription. There are many factors that contribute to inappropriate prescribing for URTIs (Avorn and Solomon, 2000):

• a healthcare provider’s uncertainty about whether the infection is bacterial or viral
• a patient’s desire to come away from a medical consultation with a prescription
• a lack of or inadequate communication between patient and healthcare provider about what antibiotics do and do not work against
• or a healthcare provider’s desire to please the patient

One way of reducing the transmission of antibiotic-resistant bacteria is through broad coverage and high uptake of vaccines, particularly pneumococcal conjugate vaccines (PCV) which prevent infection with Streptococcus pneumoniae (a major causative agent of pneumonia). A study by Dagan and Klugman found that most antibiotic-resistant strains of Streptococcus pneumoniae are protected against by a certain type of PCV vaccine (the heptavalent PCV) and infections with antibiotic-resistant Streptococcus pneumoniae in people who had not been vaccinated also reduced via what is known as “herd immunity” (Dagan and Klugman, 2008). Since certain vaccines can help to prevent the transmission of antibiotic-resistant bacteria, it is worrying to see that there is some evidence of differences in black and minority ethnic people’s uptake of vaccines. In the UK, it was found that uptake of another type of pneumococcal vaccine (the pneumococcal polysaccharide vaccine) was lower in areas where the non-white proportion of the population was over 10 per cent compared to areas where 99–100 per cent of the population were white (Pebody et al., 2008). A study in the US found that after accounting for other influencing factors, white patients with diabetes, chronic heart conditions, and cancer had a higher prevalence of influenza vaccination than black patients did with the same conditions (Egede and Zheng, 2003). This highlights the need for further investigation into why these gaps in uptake exist and how to address them to improve vaccine coverage.

Yet how much do patients’ cultural attitudes towards antibiotics, infection and healthcare more generally play a role in health-seeking behaviour? Several studies have been conducted in the US to understand health-seeking behaviours and experiences of antibiotics from ethnically diverse communities (McKee et al 1999, Mainous et al. 2008). In one study, the majority of the participants believed that antibiotics were effective against URTIs, 26 per cent had obtained antibiotics either directly from a pharmacist or from a source outside the US and 31 per cent believed that antibiotics should be available over the counter. Participants from countries where antibiotics were available over the counter were more likely to use antibiotics that had not been prescribed by a physician (Mckee et al. 1999). A significant influence of people seeking antibiotics without a prescription through importation of medication (self-medicating) appeared to be their previous experiences in countries with limited regulation of antibiotic prescribing (McKee et al 1999, Mainous et al. 2008). Moreover, the majority of participants in a study by Mainous et al believed that physician visits were unnecessary when the patient was...
familiar with the symptom and the symptom had previously responded to antibiotic treatment. Almost all were unfamiliar with the role of self-medication in the development of antibiotic resistance (Mainous et al. 2008).

The ease of access to over-the-counter antibiotics without a prescription in many countries worldwide, together with limitations of the health care systems, may influence certain healthcare seeking behaviours and demand for antibiotics for URTIs within minority ethnic groups. There is a lack of corresponding evidence from the UK, as antibiotic use is not generally reported by ethnic group.

2 Returning travellers at a higher risk of multi-drug resistant strain carriage

As people increasingly travel to all parts of the world, so do the gut bacterial strains they carry, be they drug-sensitive, drug-resistant or multi-drug resistant. There is increasing evidence that recent travel, particularly to South and East Asia and the Indian subcontinent, is a major risk factor for colonisation with an antibiotic-resistant bacterial strain leading to the risk of subsequent transmission of these bacteria upon return to the country of residence (Paltansing et al., 2013).

Multi-drug resistant Enterobacteriaceae (a class of bacteria which include the common human coloniser, E. coli), specifically those with extended spectrum beta-lactamases (ESBL)\(^1\), have been highlighted as the key organism group whose acquisition is linked to foreign travel (Figure 1) (Holmes et al.).

![Figure 1. Worldwide travel routes and emergence of antimicrobial resistance.](image)

Data shown includes NDM-positive bacteria from patients with an epidemiological link to the Indian subcontinent, linezolid-resistant enterococci, and reported cefixime/ceftriaxone treatment failures for Neisseria gonorrhoea. Flight path data developed by Dr Jonathan Read and Professor Tom Solomon, based on the number of commercial flight bookings made (number of travellers might be higher). Holmes et al., 2015.

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\(^1\) ESBL is a resistance mechanism which allows bacteria to be resistant to beta-lactam antibiotics, an antibiotic class consisting of penicillins, cephalosporins and carbapenems, among others.
Several studies have been looking into acquisition rates of a certain ESBL-encoding gene in recent travellers. One study conducted in the Netherlands found that prevalence increased from 9 per cent before travel to 34 per cent after travel, with the highest prevalence rates found in those returning from travel to India (58 per cent), North Africa (31 per cent), South Africa (29 per cent) and Southeast Asia (18 per cent) (Christian et al., 2014). A similar study of travellers attending international vaccinations centres in Paris noted a 50 per cent chance of acquiring multi-drug resistant Enterobacteriaceae after international travel (Ruppe et al., 2015). Acquisition rates were highest for travellers returning from Asia (72 per cent) compared to those returning from sub-Saharan Africa (48 per cent) or Latin America (31 per cent) (Ruppe et al., 2015). Geographical area visited was confirmed as being an important risk factor for colonisation with ESBL-encoding Enterobacteriaceae in a similar study – with travel to the Indian subcontinent, Asia and North Africa being the areas of first, second and third highest risk, respectively (Ostholm-Balkhed et al., 2013). This trend has been reiterated in other studies (Tangden et al., 2010, Epelboin et al., 2015).

However, ESBL-producing Enterobacteriaceae are not the only drug-resistant bacteria that put recent travellers at risk. A UK-based study examined antibiotic susceptibility and recent travel histories of patients with enteric fever in two ethnically diverse boroughs of London (Reddy et al., 2011). The investigators collected data for all patients admitted with S. ser. Typhi or S. ser. Paratyphi (the cause of typhoid/enteric fever) in a London hospital over a period of 5 years. Of 138 cases, 26 per cent were multi-drug resistant, 70 per cent were resistant to the antibiotic nalidixic acid and 64 per cent were resistant to the antibiotic ciprofloxacin. Of the patients, 42 per cent were Bangladeshi (British), 26 per cent were Indian (British), 19 per cent were Pakistani (British), 3 per cent were Black British or Black African, 10 per cent were a foreign visitor or new entrant from the Indian subcontinent and 40 had no ethnicity data. Of the cases, 92 per cent were associated with recent foreign travel and 57 per cent of these patients had recently travelled to visit friends and relatives (VFR) in the Indian subcontinent.

Travellers who visit friends and relatives are at a higher risk of acquiring travel-related infections and may be less likely to seek advice before departure or adhere to medications and vaccination precautions if they travel regularly. It is our recommendation that healthcare providers in primary care inquire about the recent travel histories of patients presenting with an infection, paying particular attention to those who have recently travelled or travel regularly (to visit friends and relatives) to the Indian subcontinent, Asia or North Africa. If the infection is suspected of being bacterial, GPs should ensure that antibiotic susceptibility testing takes place to ascertain whether or not the patient is carrying a drug-resistant bacterial strain, with the intention of treating the patient with the appropriate first, second or third-line antibiotic to aid in reducing inappropriate prescribing which could exacerbate antimicrobial resistance.

There is some evidence that ethnic variation in diet could influence the risk of developing an antimicrobial-resistant bacterial infection, although the evidence in this area is limited. A study in the US described resistance patterns among Shigella isolates (one of the main causes of food-borne illness worldwide) using linked data from the Foodborne Diseases Active Surveillance Network (FoodNet) and National Antimicrobial Resistance Monitoring System (NARMS) (Shiferaw et al., 2012). During a 10-year period, the NARMS laboratory tested 1,376 Shigella isolates from FoodNet sites. Of these isolates, 81 per cent linked to FoodNet demographic surveillance data and high percentages of the isolates appeared to be resistant to a variety of antibiotics2. The proportion of Shigella isolates with resistance to a certain kind of antibiotic (trimethoprim-sulfamethoxazole) was

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2 74 per cent were resistant to ampicillin, 58 per cent to streptomycin, 36 per cent to trimethoprim-sulfamethoxazole (TMP-SMX), 32 per cent to sulfamethoxazole-sulfisoxazole, 28 per cent to tetracycline, 2 per cent to nalidixic acid and 0.5 per cent to ciprofloxacin.
40 per cent among white persons, 58 per cent among Hispanic persons, and 75 per cent among persons with a history of international travel. Similarly, a Dutch study showed that amongst biopsy samples from patients positive for *Helicobacter pylori* (a bacterial cause of stomach ulcers and gastric illness), antimicrobial resistance was significantly higher in patients of Turkish descent and in those originating from Africa or the Middle East (combined resistance was 35% to metronidazole and 9.1% to clarithromycin) than in ethnic Dutch people (resistance was 21% to metronidazole and 2.9% to clarithromycin) (Loffeld and Fijen, 2003).

Another study also looked at *Helicobacter pylori* in patients suffering from indigestion who attended endoscopy clinics serving two ethnically diverse central and south London communities (Elviss et al., 2005). They found antibiotic-resistance in the isolates, with a rate of 59 per cent for metronidazole and 11 per cent for clarithromycin, with 8 per cent resistant to both antibiotics. The main risk for resistance to metronidazole was non-UK birth as comparative rates were 68 per cent for non-UK versus 40 per cent for UK-born people. In conclusion, the high overall metronidazole-resistance rate of 59 per cent for *Helicobacter pylori* from inner London was twice the rate found in other UK-based studies and was attributed to the higher risk of resistant strains infecting people born outside the UK. The authors, however, did not account for factors such as living conditions, eating patterns or other factors which could differ between patients living in London vs. other cities in the UK so some caution should be exercised when interpreting these results.

This theme ties in with a new and exciting area of research looking at the gut microbiome (the complex array of symbiotic microbial organisms that inhabit a person’s digestive tract) and the role that diverse microbial interactions in the gut play in how antimicrobial resistance evolves (Perron et al., 2012). It is therefore our recommendation that investigation in this area includes how the role of the gut microbiome may differ with a patient’s ethnicity (and diet) in relation to the risk of developing drug-resistant infections.

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**Public knowledge of antimicrobial resistance is crucial to combatting AMR**

It is widely recognised that the knowledge, behaviour and attitudes of both the prescriber and the patient influence antibiotic prescribing (Daneman, 2015). It is therefore essential that public knowledge and, perhaps more importantly, behaviour change campaigns around the preservation of antibiotics reach all citizens, including new entrants to the UK.

In a UK-based study, a questionnaire was included in the Office for National Statistics’ Omnibus Household Survey in Britain to ascertain the public’s knowledge about and behaviours relating to antibiotics (McNulty et al., 2007). Of the 7,120 participants from England, Scotland and Wales, 79 per cent were aware that antibiotic resistance was a problem in British hospitals, however 38 per cent did not know that antibiotics do not work on most coughs and colds, 4.8 per cent had used an antibiotic without advice from a healthcare provider, 4.7 per cent had obtained an antibiotic in another country without a prescription and 1.7 per cent had given antibiotics to someone for whom they were not prescribed. When ethnicity was taken into consideration, participants of Asian or Black Caribbean ethnicity had a higher percentage of incorrect responses with regards to appropriate antibiotic use and antibiotic resistance than White British participants (Figure 2c) (McNulty et al., 2007).
The relationship between cultural attitudes and antibiotic knowledge, perceived need, use and the nature of the patient/healthcare provider relationship is not straightforward, making national intervention campaigns challenging. In a similar US-based study, it was found that Filipino participants responding to a questionnaire about antibiotic knowledge expressed higher perceived need and reported more frequent use of antibiotics than Hawaiians/Pacific Islanders and White participants (Alden et al., 2006). These results were predicted by the authors as larger percentages of Filipinos in Hawaii were recent immigrants from a country in which antibiotic use is more common. When analysing the preferred physician-patient interaction styles, Filipino and Japanese
American participants preferred the paternalistic decision-making approach of physicians over a shared decision-making approach (when compared to other ethnic groups). Shared decision-making is encouraged in most studies as it appears to be very effective in reducing antibiotic prescriptions through information-sharing.

A recent systematic literature review reported on nine randomised controlled trials investigating the effect of a shared decision-making approach on the rate of antibiotic prescribing for acute respiratory tract infections in primary care (Coxeter et al., 2015). They found that involving patients more in a discussion around the risks and benefits of different treatment options for their respiratory tract infection led to a significant reduction in antibiotic prescribing immediately or within six weeks of the consultation compared with the usual care (47 per cent compared to 29 per cent). This reduction in prescribing did not lead to patient dissatisfaction or patient-initiated re-consultations. They could not, however, ascertain whether this effect was sustained over a longer period of time or whether this reduction in prescribing lead to unintended consequences for the patient.

This highlights that more tailored behaviour change campaigns may be necessary to deliver the correct information to all groups – with particular attention paid to new entrants to the UK coming from countries where attitudes towards antibiotic use may be more relaxed.

It is therefore our recommendation that healthcare providers are given the necessary culturally competent communication training so they can discuss with patients when an antibiotic should or should not be prescribed thereby managing patient expectations and reducing inappropriate demand. They should be able to discuss with patients the wider consequences of inappropriate prescribing, patient safety issues and antimicrobial resistance – paying particular attention to patients for whom this may be a new concept. Educating prescribers is essential to combatting antimicrobial resistance and has been seen to be effective at reducing unnecessary prescribing both in primary care (Little et al., 2013) and secondary care (Davey et al., 2005). We also recommend that healthcare providers stay aware of the most up-to-date antibiotic prescribing guidelines produced by Public Health England (informed by NICE, the British Thoracic Society etc.) in order to prescribe appropriately with respect to local resistance rates in the communities they serve.

**Conclusion**

Prescribers of antibiotics should be provided with adequate levels of communication-based training and support with a view to improve antibiotic prescribing and public knowledge of the uses of antibiotics – highlighting potential differences in health-seeking behaviour and understanding of antimicrobial resistance among new entrants to the UK.

Healthcare professionals should look and test for the potential of antimicrobial resistance among patients with a bacterial infection who have a recent history of travel (particularly to the Indian subcontinent, Asia or North Africa).

More research in relation to varying AMR burden amongst different ethnic groups generally and more specifically due to differences in diet and the microbiome needs to be conducted in the UK.

Public engagement campaigns need to be more heterogeneous in order to improve understanding of the drivers of antimicrobial resistance in a diverse population.
References

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