Antimicrobial resistance (AMR) increasing, presenting complex and urgent threat to global health

- AMR →
  - Longer duration of infection,
  - Increased healthcare costs
  - Ongoing risk of transmission
  - Increased mortality
  - 700,000 deaths per year
  - ABR → $20 billion of excess healthcare costs, with additional costs to society up to $35 billion a year in the United States alone (CDC)

- Large gap in knowledge of magnitude of AMR, driving mechanisms, outcomes

Following discovery of penicillin, Alexander Fleming warned of improper antibiotic use in Nobel Lecture:

> It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body. The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant.

Antimicrobial resistance now widespread; increasingly challenging to treat infections caused by bacteria, viruses, parasites and fungi

Antimicrobial resistance (AMR) increasing, presenting complex and urgent threat to global health

- Increasing resistance to antimicrobials worldwide
- Community and healthcare settings
- Resistance reported for every major class of antibiotics
- Challenging to prevent or treat key infectious diseases
  - Common bacterial infections
  - Healthcare associated infections (HAIs)
  - Infectious diseases causing greatest burden of mortality worldwide, such as TB, HIV, and malaria

Threat to universal healthcare coverage and the sustainable development goals

- Social, economic, health impact, need for cross-sectoral 'One Health' approach
- Burden of morbidity, mortality, and associated costs: low- and middle-income countries (LMICs)
  - Limited hygiene, health service infrastructure, sanitation
  - Limited antimicrobial stewardship and surveillance
  - Countries with greatest burden, least capacity and resources to respond

Compromising achievement of Universal Healthcare Coverage (UHC):

- "Ensuring that all people have access to needed promotive, preventive, curative and rehabilitative health services, of sufficient quality to be effective, while also ensuring that people do not suffer financial hardship when paying for these services. Universal health coverage has therefore become a major goal for health reform in many countries and a priority objective of WHO."
- Migrants should have universal and equitable access to healthcare regardless of immigration status
Global Action Plan on AMR

2015: WHO endorsed global action plan to tackle AMR

Five key pillars of action1
1) improving awareness and understanding of antimicrobial resistance through effective communication, education and training;
2) strengthening the knowledge and evidence base through surveillance and research;
3) reducing the incidence of infection through effective sanitation, hygiene, and infection prevention measures;
4) optimizing the use of antimicrobial medicines in human and animal health; and
5) developing the economic case for sustainable investment taking into account the needs of all countries, and increasing investment in new medicines, diagnostic tools, vaccines, and other interventions.


Globalisation and AMR

- Travel, tourism, migration, inter-hospital transfer, movement of animals or agricultural products
- Research focus predominantly on travellers and patients returning from hospitals abroad
- Concern migration contributing to global spread of AMR – limited evidence

Global migration

Unprecedented rates of migration

- 244m migrants worldwide; 65.3m forced migrants – refugees, asylum seekers, or IDPs worldwide
- 1 in 113 people on the planet displaced
- Over 2m forced migrants to Europe since 2015;
  - Highest rates since records began
- 61.4% have health problems during journey; 93% of those with health issue on arrival had symptom onset during migration; Median travel time: 100 days
- AMR risk factors: High-incidence country, social inequalities/living conditions (e.g., camps, detention centres), cost of healthcare/Rx, barriers to care, disrupted health systems, poor quality Rx

Previous focus on infectious diseases in migrants predominantly in HIV and TB

Migrants experience burden of TB in high-income countries

- 73.4% of MDR-TB cases in EU and EEA member states in foreign-born
- Evidence of MDR-TB being imported as well as acquired or transmitted in host countries

Concerns increasing MDR-TB attributed to poor treatment adherence

Systematic review and meta-analysis on MDR-TB treatment adherence in migrants:

- Migrant adherence to MDR-TB treatment regimens is approaching global treatment targets (71% vs 75%)
- Migrant adherence and non-adherence to MDR-TB treatment regimens is comparable to non-migrant populations

Limited evidence on relationship between migration and drug-resistance

- Increasing AMR; migration contributing to burden in host countries?
- Not known whether migrants experience high rates of AMR or where acquired
  - Higher due to increased incidence in countries of origin, poor social conditions, barriers to care?
  - Lower due to more limited access/exposure to antibiotics or healthcare facilities?
- Limited surveillance/data collection
Systematic review and meta-analysis
- Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines
- Databases: MEDLINE, Embase, PubMed, Scopus
- Primary data (2000-2017) on carriage or infection in migrants (foreign-born) from observational studies reporting antibacterial resistance in common bacterial pathogens
- Migrants to EU/EEA
- Data extraction and quality assessment using piloted standardised forms
- Random effects models to calculate pooled prevalence
- PROSPERO CRD42016043681

Results
- 23 observational studies reporting on antibiotic resistance in 2319 migrants
- Pooled prevalence of any AMR carriage or infection: 25.4% (95% CI: 19.1 – 31.8)
  - Meticillin-resistant Staphylococcus aureus (MRSA) (7.8%, 4.8 – 10.7)
  - Antibiotic resistant Gram-negative bacteria (27.2%, 17.6 – 36.8)
- Elevated rates among refugees and asylum seekers
  - 33.0% (95% CI: 18.3 – 47.6) compared to ‘other’ migrants (6.8%; 95% CI: 2.1 – 11.5)
- High prevalence in high migrant community settings
  - 33.1% (95% CI: 11.1 – 55.1) compared to 24.4% (95% CI: 16.2 – 32.6) in hospital settings
- Migrants overrepresented among community acquired MRSA
  - 62.7% (95% CI: 50.2 – 75.3) PVL positive MRSA isolates (marker for CA-MRSA).
- Evidence antibiotic resistant organisms being acquired during migration trajectory in transit or host countries
  - Limited evidence of onward transmission

MDRO screening: asylum seekers admitted to university hospital or presenting to emergency department
- 273 patients
  - Carriage rate of 31%: E.coli most common Duration of MDRO carriage in asylum seekers
  - Duration of MDROs in asylum seekers in the Netherlands
  - Screening and clinical samples from asylum seekers in the Netherlands; Rates of MRSA and MDR detected every four weeks after arrival
  - 2093 asylum seekers
  - No decline in MDROs in first obtained sample was observed after arrival in Netherlands
  - Carriage rate of MDRO in asylum seekers remains high even after prolonged stay
AMR in the context of increasingly restrictive health services

- Calls to improve knowledge and surveillance on AMR in migrants
  - Increasingly restrictive health systems and multiple barriers to care
- Not engaging with migrants early enough →
  - Delays in access to high quality care (detection, treatment, prevention)
  - Not improving awareness and understanding of AMR and antibiotic use
- Poor and inconsistent data collection

Restrictive health systems will prevent us from achieving Global Action Plan on AMR

“...I used to struggle with prescriptions – sometimes I was required to pay, but then I wouldn’t take it.”
- Refused asylum seeker, England

AMR in the context of increasingly restrictive health services

- NHS England one of most restrictive healthcare systems in Europe
  
- ‘Overseas visitors’ chargeable for NHS care
  - Upfront charging – 150% tariff before receiving care
  - Exemptions:
    - GP
    - ‘urgent’ or ‘immediately necessary’ care
    - Infectious diseases of public health significance
- NHS surcharge £200 per year

Memorandum of Understanding

- Patient information shared with Home Office for immigration enforcement purposes
- Debts above £500 referred to Home Office after 2 months
  - £2244-3282 for uncomplicated birth/delivery

Entitlement to healthcare scores

Data from [E Van Ginneken, Healthcare access for undocumented migrants in Europe. EuroHealth 2014; 20 (4)].

- Most undocumented migrants have access to emergency healthcare only
- There is clear evidence to suggest these more restrictive policies impact on other migrant groups and deter them from seeking healthcare
- This compromises early detection and treatment of infections, treatment adherence, and prevention

Entitlement to free statutory healthcare

Data on AMR and migration

- GAP-AMR called to strengthen knowledge and evidence on AMR worldwide through research and surveillance
- Robust evidence needed to inform evidence-based approaches to prevention and control
- WHO Global Antimicrobial Resistance Surveillance System (GLASS)
  - 8 key bacteria causing common infections worldwide; introducing surveillance on fungal resistance
- Mobile (migrant/displaced) populations not routinely captured by national surveillance systems
- Innovative platforms, e.g. data collection networks for surveillance of travel-related morbidity (GeoSentinel)
Tackling AMR

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<thead>
<tr>
<th>Barriers</th>
<th>Facilitators</th>
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<tr>
<td>Individual barriers</td>
<td>Well-trained and dedicated staff</td>
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<tr>
<td>- Discrimination, fear of accessing care</td>
<td>- Confidentiality, communication, culturally</td>
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<tr>
<td>- Anxiety about breaches in confidentiality</td>
<td>- Sensitive and appropriate services, language support</td>
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<tr>
<td>- Lack of professionalism</td>
<td>- Migrant involvement</td>
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<tr>
<td>- Lack of staff training and support</td>
<td>- Patient involvement in delivery</td>
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<tr>
<td>- Language barriers</td>
<td>- Increasing migrant community ownership and collaborations</td>
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<td>- Financial barriers</td>
<td>- Outreach</td>
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<tr>
<td>- Health system infrastructure; prescribing</td>
<td>- Tailored awareness-raising in migrant communities</td>
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<tr>
<td>- Funding</td>
<td>- Accessible outreach settings</td>
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<tr>
<td>- Holistic and linked in care</td>
<td>- Preventive care, health promotion, screening</td>
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<td>- Inclusive and enabling care</td>
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Barriers → delay in diagnosis & Rx, morbidity / mortality; spread of infection, increased costs.

[Seedat, Hargreaves, Nellums et al. The Lancet Infect Dis; 2018]

Implications for policy and guidelines

- Improve access to care and availability of screening for migrants, particularly forced migrants
- Need to target infection prevention and control initiatives in high-migrant community settings
  - Refugee camps, reception centres, detention centres, not only hospitals, particularly in light of significant barriers to accessing formal care
  - Poor social conditions, limited access to services may be more significant determinants of AMR – particularly in refugees and asylum seekers – than importation
- Call for improved prevention efforts in community settings (ECDC), including hygiene and targeted interventions to prevent spread of AMR in camp settings
- Calls for more robust evidence to guide policies around microbiological screening
- Demand for more harmonised and evidence-based infection prevention and control measures in Europe

Thank you

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