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Antimicrobial resistance
A global challenge

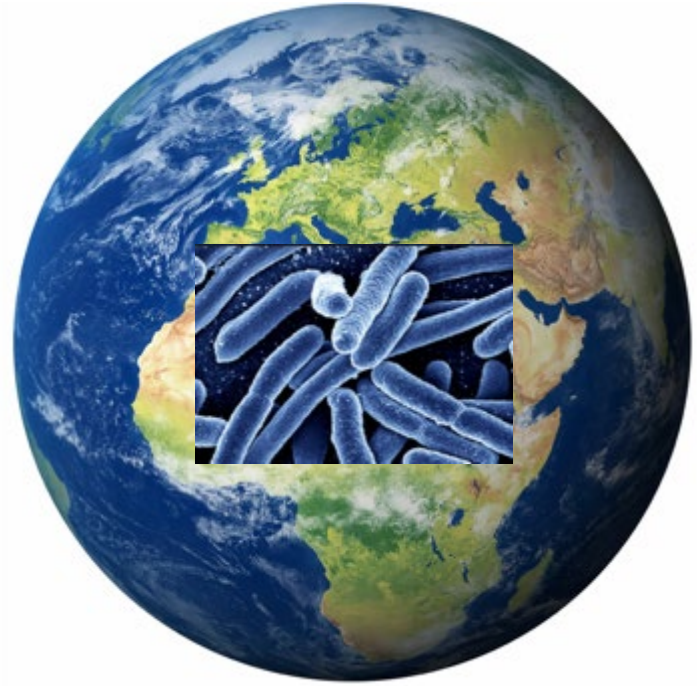
Ernst Kristian Rødland, MD PhD
Norwegian Insitute of Public Health
ernstkristian.rodland@fhi.no

Topics

- What is AMR?
- Usage of antibiotics
- Spread of AMR - One Health
- AMR in LMICs

Microbial biosphere

- Bacteria
  - Environmental
  - Commensal
  - Pathogen
- Natural antibiotics
- Reservoir of antibiotic resistance genes ➡ Resistome



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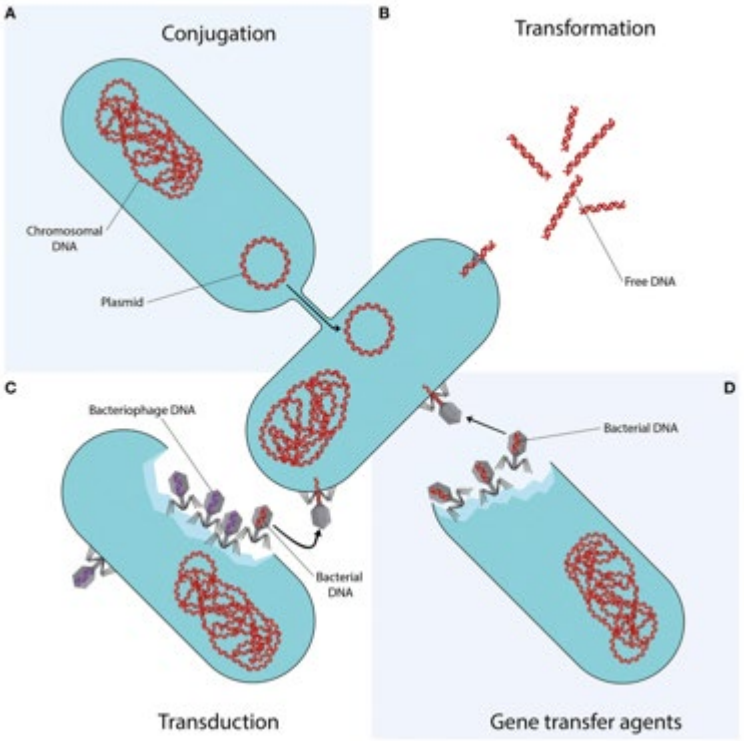
How do bacteria become resistant?

- Vertical
  - Spontaneous mutations
  - Transferred to the bacteria`s progeny
- Horizontal
  - Exchange of genetic elements/plasmids
  - Packages of resistance genes



History of some antibiotics

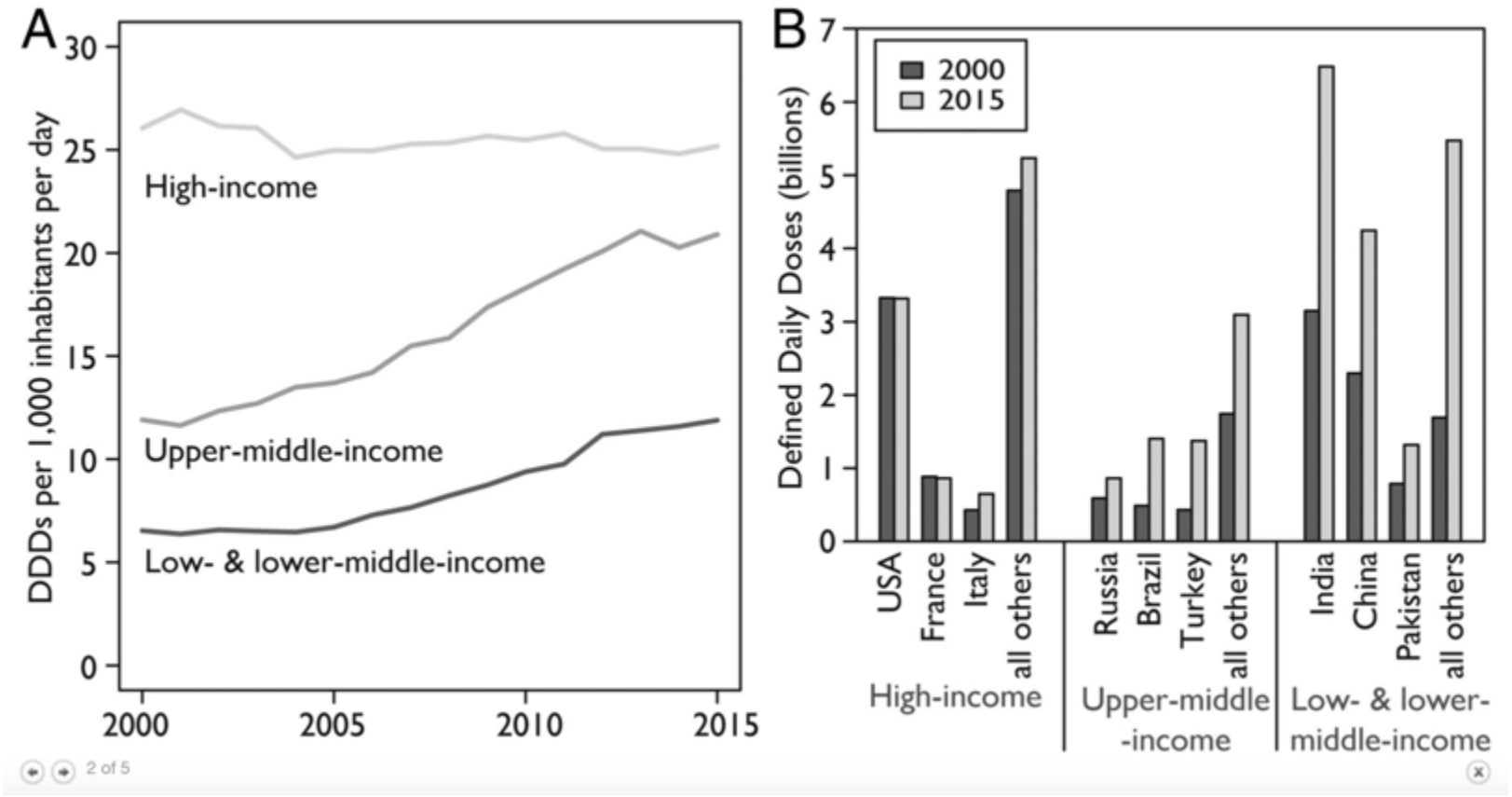
- Penicillin – 1928, regular use in human medicine from the 1940s
- Chlortetracyclin (Aureomycin) – 1945, used as a growth promotor in meat production
- Fluoroquinolones (Nalidixic acid) – 1962

Usage of antibiotics

- 65% increase in human consumption (2000-2015) globally(1)
- Approximately 80% of a.b. consumption is in the animal sector(2)
- Globally: 60-70000 tonnes in agriculture

(1) Klein et al. PNAS 2018
(2) WHO, 2017

Global antibiotic consumption

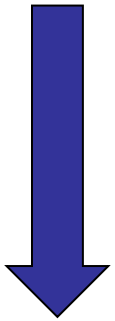


Klein et al. PNAS, 2018

Exposure routes of antibiotics to the environment

- Discharge from manufacturing
- Urine and feces from users of antibiotics
- Antibiotics used in agriculture and aquaculture
- Discarded medicines – lack of take-back programs

Antibiotic selection pressure



Significant impact on the resistome in the microbial biosphere

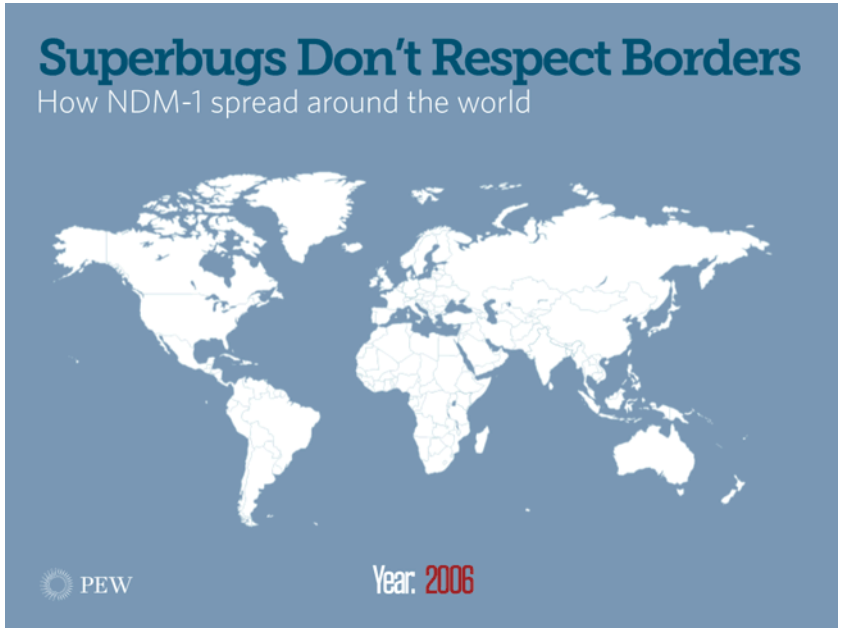
AMR is omnipresent

- E.coli from arctic birds
  - Siberia, Alaska, Greenland
  - AMR detected in 8/97 isolates
  - 17 antimicrobials were tested, resistance to 14 were detected

Sjølund-Karlsson et. al. Emerging Infectious Diseases
www.cdc.gov/eid • Vol. 14, No. 1, January 2008

AMR migration

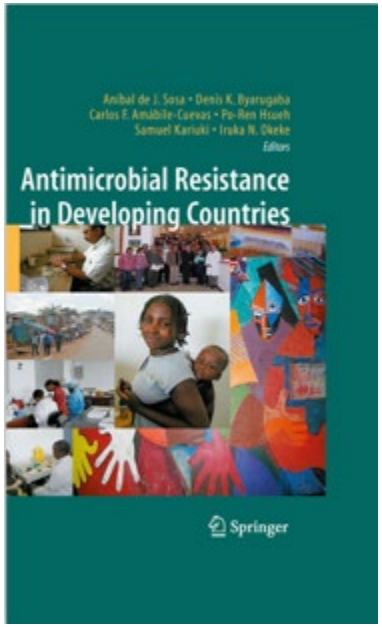
- Approx. 2 billion people move across large distances/year and 1 billion cross international borders
- 20–60% of asylum seekers are colonized with resistant microbes (1,2)
- 50-90% of tourists visiting the tropics get colonized with MDR enterobacteriacea



New Dehli Metallo-beta-lactamase-1 (NDM-1)

(1) de Smalen, A.W., et al., Travel Med Infect Dis, 2017
(2) Heudorf, U., et al.,GMS Hyg Infect Control, 2016

"....If walls have proven insufficient to stop migrating people, it will certainly be so for multi-resistant microbes and their consequences....."



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Journal of Antimicrobial Chemotherapy

Gross national income and antibiotic resistance in invasive isolates: analysis of the top-ranked antibiotic-resistant bacteria on the 2017 WHO priority list

Alessia Savoldi[1,2], Elena Carrara [2]*, Beryl Primrose Gladstone [1], Anna Maria Azzini[2], Siri Göpel[1] and Evelina Tacconelli[1,2]

[1]Division of Infectious Diseases, Department of Internal Medicine I, German Center for Infection Research, University of Tübingen, Otfried Müller Straße 12, 72074 Tübingen, Germany; [2]Division of Infectious Diseases, Department of Diagnostic and Public Health, G. B. Rossi University Hospital, University of Verona, P.le L.A. Scuro 10, 37100 Verona, Italy

*Corresponding author. Tel: +39 0458127396; E-mail: elena.carrara@univr.it

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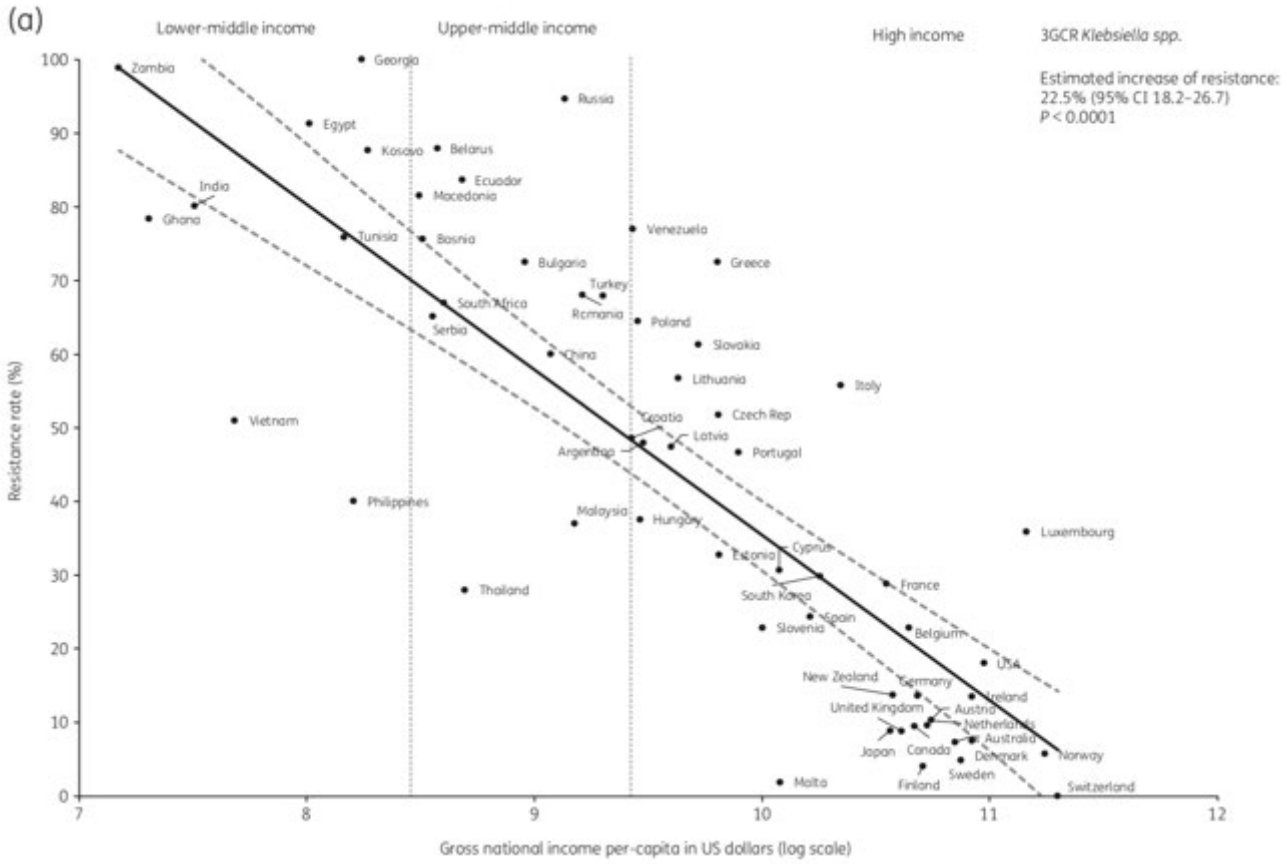
The aim of this study was to collect the most recent data on prevalence of AMR from surveillance networks and to test the hypothesis of an association between lower income status and AMR prevalence in invasive infections.

Materials and methods

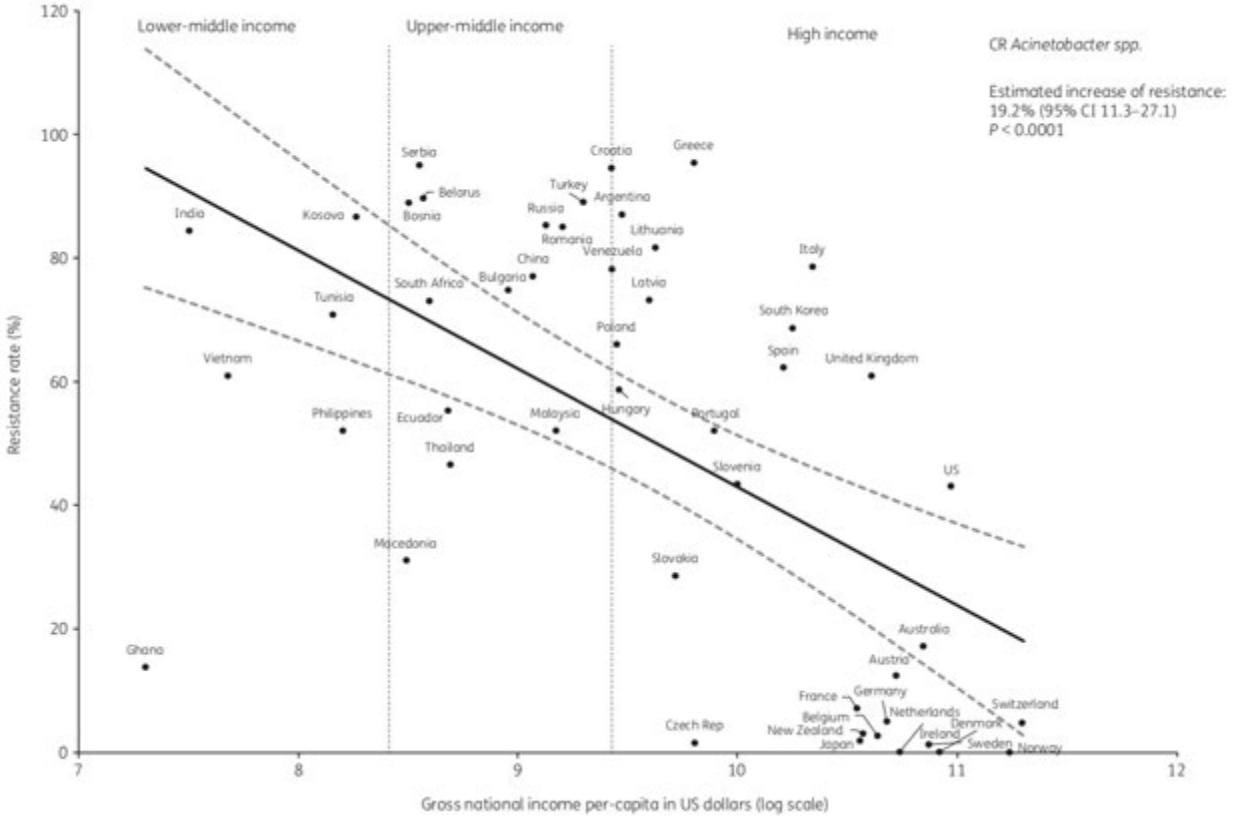
- Countries (HICs, U-MICs, L-MICs, LICs) with data on resistance prevalence for at least on priority pathogen for at least one year
- Only invasive isolates (blood and CSF)
- Validated clinical breakpoints (EUCAST, CLSI)

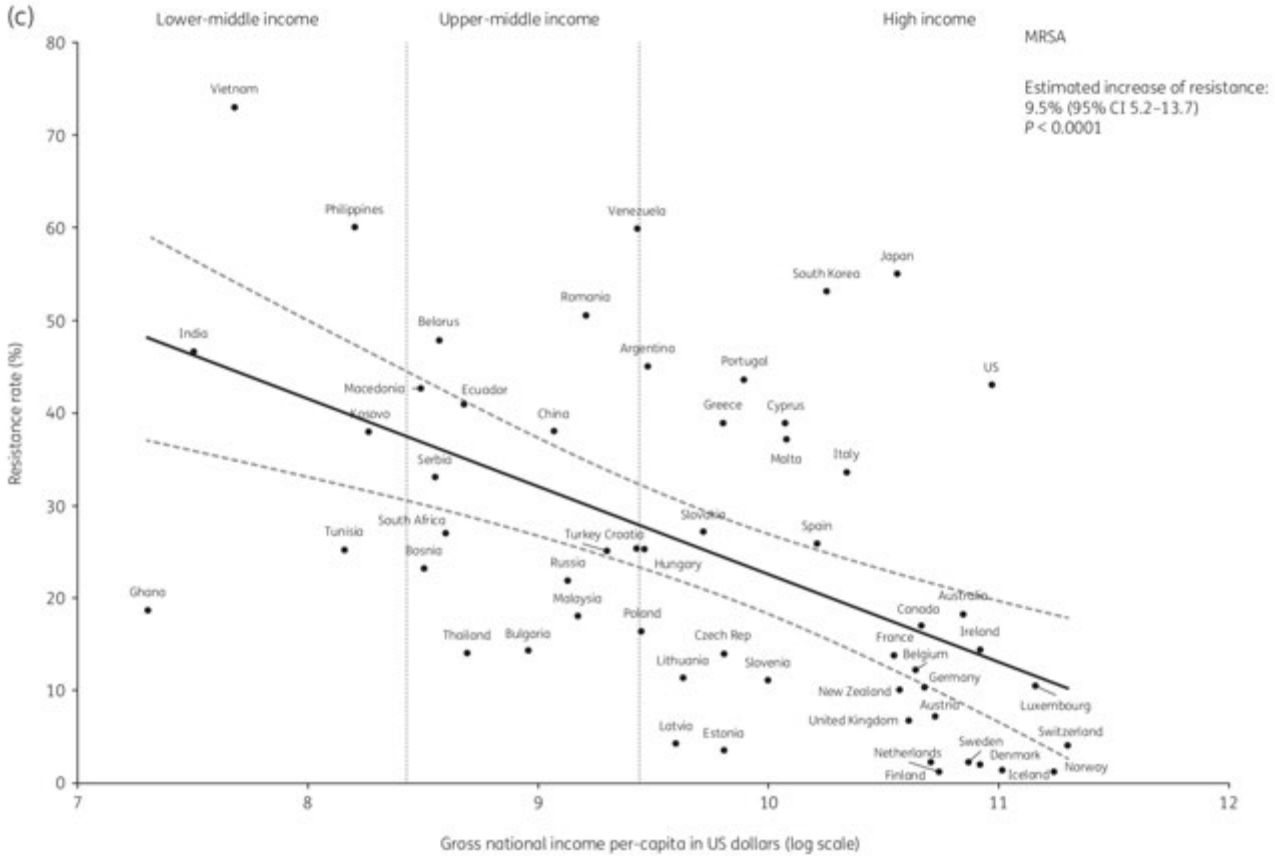
Results

- AMR data from 22 surveillance systems
- 67 countries
  - HICs 57%, 38 countries
  - UMICs 24%, 16 countries
  - LMICs 16%, 11 countries
  - LICs 3%, 2 countries


(a)
Lower-middle income
Upper-middle income
High income
3GCR Klebsiella spp.
Estimated increase of resistance:
22.5% (95% CI 18.2–26.7)
P < 0.0001
Resistance rate (%)
Gross national income per-capita in US dollars (log scale)
Zambia
Georgia
Russia
Egypt
Kosovo
Belarus
Ecuador
Macedonia
India
Ghana
Tunisia
Bosnia
Venezuela
Bulgaria
Greece
Turkey
Romania
South Africa
Serbia
Poland
Slovakia
China
Lithuania
Italy
Vietnam
Croatia
Czech Rep
Latvia
Argentina
Portugal
Philippines
Malaysia
Hungary
Luxembourg
Estonia
Cyprus
France
Thailand
South Korea
Spain
Slovenia
Belgium
USA
New Zealand
Germany
Ireland
United Kingdom
Austria
Netherlands
Australia
Japan
Canada
Denmark
Norway
Malta
Finland
Sweden
Switzerland

(b)


Lower-middle income
Upper-middle income
High income
CR Acinetobacter spp.
Estimated increase of resistance:
19.2% (95% CI 11.3–27.1)
P < 0.0001
Resistance rate (%)
Gross national income per-capita in US dollars (log scale)
120
100
80
60
40
20
0
7
8
9
10
11
12
Serbia
Croatia
Greece
Belarus
Turkey
Argentina
India
Kosovo
Bosnia
Russia
Lithuania
Romania
Venezuela
Italy
China
Bulgaria
South Africa
Latvia
Tunisia
South Korea
Poland
Spain
United Kingdom
Vietnam
Philippines
Ecuador
Malaysia
Hungary
Portugal
Thailand
Slovenia
US
Macedonia
Slovakia
Australia
Ghana
Austria
France
Germany
Switzerland
Belgium
Netherlands
Denmark
New Zealand
Ireland
Sweden
Japan
Czech Rep
Norway


(c)
Lower-middle income
Upper-middle income
High income
MRSA
Estimated increase of resistance:
9.5% (95% CI 5.2–13.7)
P < 0.0001
Resistance rate (%)
Gross national income per-capita in US dollars (log scale)
Vietnam
Philippines
Venezuela
Japan
South Korea
Romania
Belarus
India
Argentina
Portugal
US
Macedonia
Ecuador
Greece
Cyprus
China
Kosovo
Malta
Italy
Serbia
Slovakia
South Africa
Spain
Tunisia
Turkey
Croatia
Bosnia
Russia
Hungary
Ghana
Malaysia
Austria
Canada
Poland
Ireland
Thailand
Bulgaria
Czech Rep
France
Belgium
Lithuania
Slovenia
Germany
New Zealand
Luxembourg
Austria
United Kingdom
Switzerland
Latvia
Estonia
Sweden
Netherlands
Denmark
Finland
Iceland
Norway

Discussion

- A strongly significant inverse association between income status and invasive infections due to MRSA, 3GCR *Klebsiella spp*. and *E. coli*, CR *Acinetobacter spp*., *Klebsiella spp*. and *P. aeruginosa*. Public health officers and policy makers must take determinants of poverty and inequality into account when designing and implementing interventions and infection control policies targeting AMR, especially in LMICs/LICs.

AMR in the WHO African region

- High prevalence of AMR in clinical relevant bacteria
- 2011: WHO publishes a policy package to combat AMR
  - Top priority: strenghten surveillance and laboratory capacity
- No reliable data available from 42,6% of African countries (1)

Table 1 Implementation status of WHO policy package to combat AMR in the WHO African region (2)

Country	*National AMR plan*	*Surveillance on antimicrobial use and resistance*	*Access to quality essential medicines*	*Rational medicine use*	*IPC*	*Innovation, research and development*
Total (47)	2	0	44	43	7	0
%	4.3	0.0	93.6	91.5	14.9	0.0

(1) Tadesse, B.T., et al., BMC Infect Dis, 2017
(2) Essack, S.Y., et al.J Public Health (Oxf), 2017

Available reference labs in Africa

Barbe`et. al, Clinical Microbiology and Infection, 2017

AMR

Developement and spread

- Improper use of antimicrobials
- Lack of microbiological diagnostic services
- Poor sanitation and shortage of clean water
- Crowding – interpersonal spread
- Migration

⇨ Resource limited countries (RLCs)

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Articles

Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis

Peter Collignon, John J Beggs, Timothy R Walsh, Sumanth Gandra, Ramanan Laxminarayan

Summary

Background Understanding of the factors driving global antimicrobial resistance is limited. We analysed antimicrobial resistance and antibiotic consumption worldwide versus many potential contributing factors.

Lancet Planet Health 2018; 2: e398–405

See Comment page e376

Interpretation **Reduction of antibiotic consumption will not be sufficient to control antimicrobial resistance because contagion—the spread of resistant strains and resistance genes—seems to be the dominant contributing factor. Improving sanitation, increasing access to clean water, and ensuring good governance, as well as increasing public health-care expenditure and better regulating the private health sector are all necessary to reduce global antimicrobial resistance.**

My answer has to be fighting poverty