Global Antimicrobial Resistance and Use Surveillance System (GLASS 2022):

Investigating the relationship between antimicrobial resistance and antimicrobial consumption data across the participating countries.

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Outline

- Background information
- Objective of the study
- Data source and statistical analysis
- Results
- Summary and Conclusion

Image source: https://www.who.int/initiatives/glass

Background information 1

- Antimicrobial resistance (AMR) was responsible for about 1.3 million deaths in 2019 (*Murray et al.*, 2022)
- This trend will increase and may result in about 10 million deaths annually by 2050 if nothing is done about it (*Jim O.N et al.*, 2016)
- Antimicrobial selection pressure favors the development and persistence of AMR
- The misuse of antimicrobials further accelerates this selection pressure and aggravates the development and dissemination of AMR (*Davies, J.et al.*, 2010)

Image source: bioMérieux Connection, https://www.biomerieuxconnection.com/2018/07/12/explain-antimicrobial-resistance-friends-family-infographics/

Background information 2

- Certain antimicrobials are classified as classified as critically important by WHO to human medicine to tackle AMR.
- Within the class mentioned above, a subclass considered as the highest priority to treat multi-drug resistant (MDR) bacterial infection are quinolones, third and fourth-generation cephalosporins, macrolides and ketolides, and glycopeptides (*WHO*, 2019)
- It is alarming that there are increasing reports of resistance to these highest-priority antimicrobials too (*Collignon et. al*, 2016)

Background information 3

- In 2015, as part of the global fight against AMR, the Global Antimicrobial Resistance and Use Surveillance System (GLASS) was established by the World Health Organization (WHO) (*WHO*, 2015).
- In the 2022 report, for the first time WHO reported both AMC and AMR data from participating countries, although only a few countries participated in reporting both AMR and AMC data (*WHO*, 2022).
- This framework was aimed to harmonize the reporting of quality and representative data of AMR and AMU on a global scale.
- The GLASS has also led to improvements in surveillance systems in several countries, territories, and areas (CTAs), however, many CTAs still have poor surveillance systems and are still associated with data underreporting.

Study Objective

- The objective of this study was to associate the reported AMR data with the AMC data in different countries and regions based on the reported GLASS data, focusing on beta-lactam/cephalosporin and quinolones AMC data and beta-lactam/cephalosporin and quinolones resistant *E. coli* and *Klebsiella pneumoniae* and also explore the relationship and differences between the AMC data reported among the participating countries.

Data source and statistical analysis 1

- The data used in this study was extracted from the WHO GLASS report published for 2022 (*WHO, 2022*)
- 216 countries, territories, and areas (CTAs) were enrolled in the GLASS program however, data availability varied from country to country.
- Only 26 CTAs presented AMC data for the data collection cycle and data were presented as both adjusted and unadjusted measurements.
- AMR data were presented as percentage-resistant bacteria isolated from total bacteriologically confirmed infections.
- The data collection round for this report was designated 2020 but spanned till 2021.

Data source and statistical analysis 2

- For this study we extracted AMC data expressed as a defined daily dose (DDD) adjusted by the population size of each participating country for Beta-lactam antibacterials, penicillins group (J01C), Other beta-lactam antibacterials group (J01D), and Quinolone antibacterials group (J01M)
- For the AMR data, we extracted data on bloodstream infection for beta-lactam and fluoroquinolone-resistant Escherichia coli and Klebsiella pneumoniae

Data source and statistical analysis 2

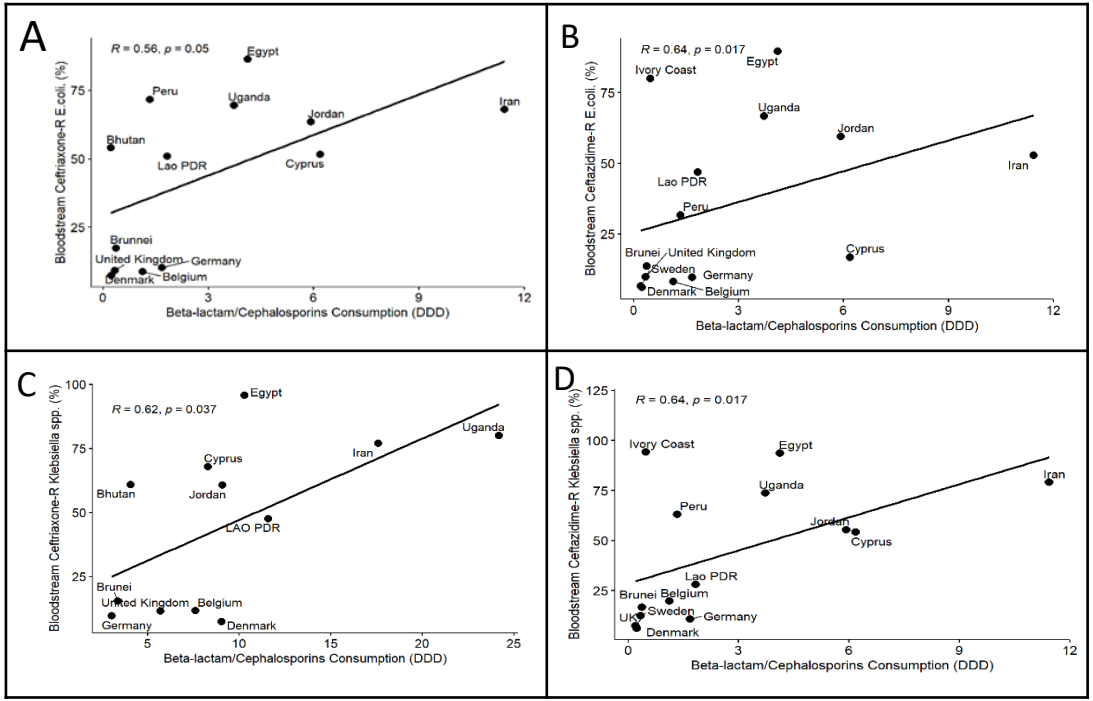
- **Datasets**
- AMC data expressed as a defined daily dose (DDD) adjusted by the population size of each participating country for
    - Beta-lactam antibacterials, penicillins group (J01C),
    - Other beta-lactam antibacterials group (J01D), and
    - Quinolone antibacterials group (J01M)
- AMR data on bloodstream infection for beta-lactam and fluoroquinolone-resistant Escherichia coli and Klebsiella pneumoniae

- **Statistical Analysis**
- mixed-effect regression model with the beta distribution:
    - Effect of AMC on the prevalence of beta-lactam and fluoroquinolone-resistant E. coli and Klebsiella pneumoniae
- multivariable linear regression model and adjustment for multiple comparisons using Tukey's method:
    - Explore the relationship and differences in the antimicrobial consumption data (DDD) reported among the participating countries
- Statistical significance was set at $P<0.05$, and all statistical analyses were performed using R software (R version 4.1.1)

Table 1: Beta regression mixed models of the effect of antimicrobial consumption on the prevalence of beta-lactam and fluoroquinolone-resistant E. coli and Klebsiella spp. from bloodstream infections (the country was taken as a random effect)

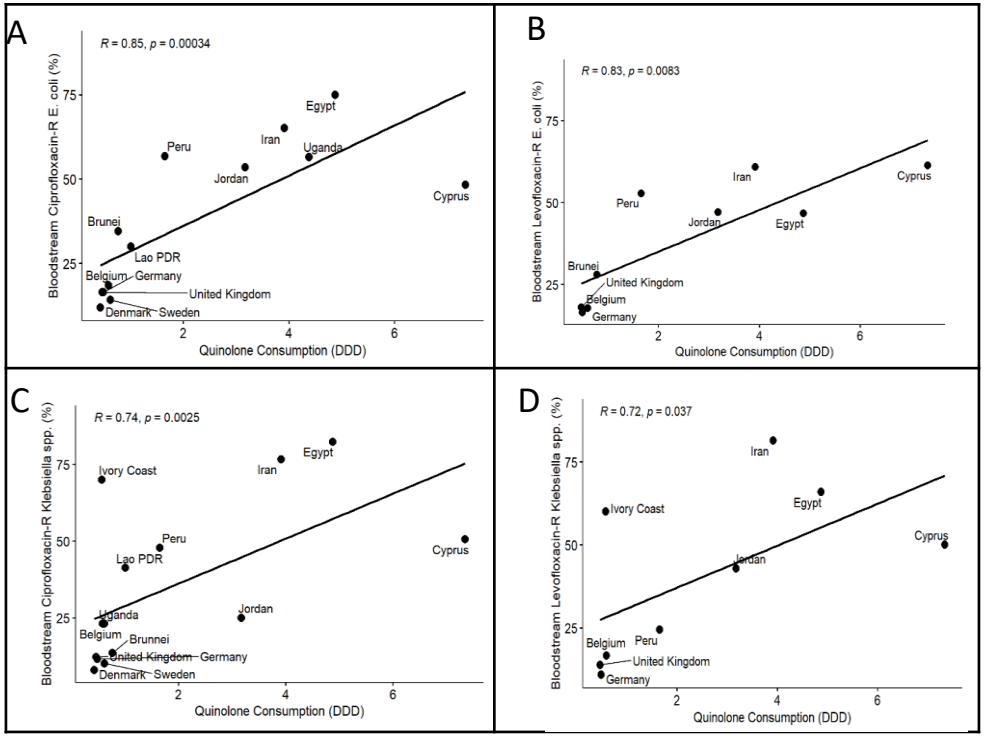
Antimicrobial consumption (Variable)	Antimicrobial resistance (Outcome)	Regression estimates		
		Odds ratio	95% Confidence interval	P-value
Beta-lactam/Cephalosporins Consumption	Bloodstream Ceftriaxone-R *E. coli*	1.22	1.01-1.48	**0.0395**
Beta-lactam/Cephalosporins Consumption	Bloodstream Ceftazidime-R *Klebsiella* spp.	1.20	0.98-1.47	0.0737
Beta-lactam/Cephalosporins Consumption	Bloodstream Ceftriaxone-R *Klebsiella* spp.	1.11	0.99-1.25	0.0522
Quinolone Consumption	Bloodstream Ciprofloxacin-R *E. coli*	1.40	1.17-1.67	**0.0002**
Quinolone Consumption	Bloodstream Levofloxacin-R *E. coli*	1.31	1.15-1.50	**<0.0001**
Quinolone Consumption	Bloodstream Ciprofloxacin-R *Klebsiella* spp.	1.37	1.07-1.76	**0.0118**
Quinolone Consumption	Bloodstream Levofloxacin-R *Klebsiella* spp.	1.31	1.02-1.68	**0.0341**

Figure 1: Linear association and Spearman correlation coefficients between selected extended-spectrum cephalosporin-resistant bacteria from bloodstream infections and beta-lactam/cephalosporin consumption among the countries.



- We observed a statistically significant positive linear association between bloodstream-associated ceftriaxone-resistant *E. coli* or *Klebsiella* and bloodstream-associated ceftazidime-resistant *E. coli* or *Klebsiella* and beta-lactam drug consumption among the countries.
- Clustering observed in countries based on AMC pattern

Figure 2: Linear association and Spearman correlation coefficients between selected fluoroquinolone-resistant bacteria from bloodstream infections and quinolone consumption among the countries.



- we observed a statistically significant positive linear association between bloodstream-associated ciprofloxacin-resistant *E. coli or Klebsiella*, *and* bloodstream-associated levofloxacin-resistant *E. coli or Klebsiella* and quinolone consumption among the countries.
- Clustering observed in countries based on AMC pattern

Figure 2: Linear association and Spearman correlation coefficients between selected fluoroquinolone-resistant bacteria from bloodstream infections and quinolone consumption among the countries.

Antimicrobial group comparison	DDD difference	Standard error	P-value
Beta-lactam antibacterials, penicillins (J01C) - Aminoglycoside antibacterials (J01G)	8.13	0.79	**<0.0001**
Other antibacterials (J01X) - Beta-lactam antibacterials, penicillins (J01C)	-7.70	0.78	**<0.0001**
Intestinal antiinfectives (A07A) - Beta-lactam antibacterials, penicillins (J01C)	-8.26	0.90	**<0.0001**
Sulfonamides and trimethoprim (J01E) - Beta-lactam antibacterials, penicillins (J01C)	-7.44	0.80	**<0.0001**
Beta-lactam antibacterials, penicillins (J01C) - Agents against amoebiasis and other protozoal diseases (P01A)	7.06	0.78	**<0.0001**
Beta-lactam antibacterials, penicillins (J01C) - Amphenicols (J01B)	8.32	0.95	**<0.0001**
Tetracyclines (J01A) - Beta-lactam antibacterials, penicillins (J01C)	-6.62	0.79	**<0.0001**
Quinolone antibacterials (J01M) - Beta-lactam antibacterials, penicillins (J01C)	-6.28	0.78	**<0.0001**
Combinations of antibacterials (J01R) - Beta-lactam antibacterials, penicillins (J01C)	-8.70	1.25	**<0.0001**
Macrolides, lincosamides and streptogramins (J01F) - Beta-lactam antibacterials, penicillins (J01C)	-5.23	0.78	**<0.0001**
Other beta-lactam antibacterials (J01D) - Beta-lactam antibacterials, penicillins (J01C)	-5.13	0.78	**<0.0001**
Other beta-lactam antibacterials (J01D) - Aminoglycoside antibacterials (J01G)	2.99	0.79	0.010
Macrolides, lincosamides and streptogramins (J01F) - Aminoglycoside antibacterials (J01G)	2.89	0.79	0.017
Other beta-lactam antibacterials (J01D) - Intestinal antiinfectives (A07A)	3.14	0.90	0.028
Macrolides, lincosamides and streptogramins (J01F) - Intestinal antiinfectives (A07A)	3.03	0.90	0.040
Other beta-lactam antibacterials (J01D) - Amphenicols (J01B)	3.19	0.95	0.044
Other beta-lactam antibacterials (J01D) - Other antibacterials (J01X)	2.57	0.78	0.051
Macrolides, lincosamides and streptogramins (J01F) - Amphenicols (J01B)	3.09	0.95	0.061
Other antibacterials (J01X) - Macrolides, lincosamides and streptogramins (J01F)	-2.46	0.78	0.075

Summary and Conclusion

- There was a consistently significant positive linear association between antimicrobial consumption and resistance in beta-lactam and fluoroquinolone-resistant *E. coli* and *Klebsiella spp.* from bloodstream infections.
- These findings also emphasize the need to implement effective antimicrobial stewardship programs and policies to optimize antimicrobial use and lower the prevalence of resistant bacterial infections.
- Also, this study emphasizes the importance of combined analysis of AMC and AMR data to effectively make policy decisions and take effective measures to fight the AMR menace.

Summary and Conclusion

- A key limitation of this study is based on the inconsistencies of the data from different CTAs. CTAs with robust surveillance were able to give robust reports, while CTAs with poor surveillance systems are associated with underreporting of either or both AMC and AMR data.
- Although, this is the first time WHO will be reporting together both AMC and AMR data since GLASS started, with time this approach will get better and help to generate more insight to making more robust policies to fight AMR.

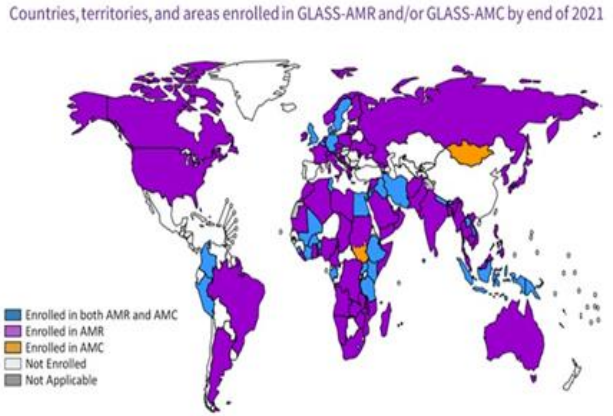


Image source: https://www.who.int/initiatives/glass

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