

The Relationship Between Antimicrobial Consumption and Human Emerging Infectious Disease

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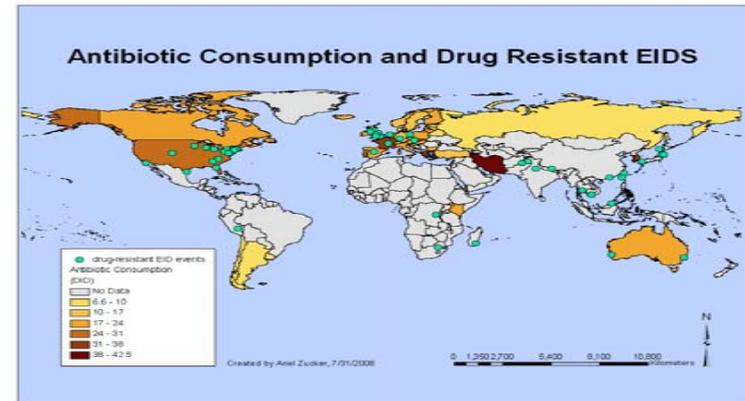
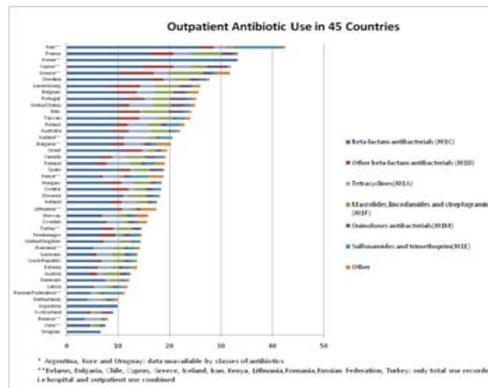
- Human emerging infectious diseases (EIDs) are diseases that have recently increased in incidence, impact or geographic range. They include diseases caused by newly evolved strains of existing pathogens (e.g., multi-drug resistant TB) and those that have recently entered the human population for the first time (e.g., HIV/AIDS, SARS, Ebola).
- Although the relationship between antimicrobial consumption and antimicrobial resistance has been established, this is the first study to explore the relationship between the antimicrobial consumption on a large scale and EID events
- Our findings suggest that efforts in surveillance and containment of drug-resistant EIDs should be refocused to areas of high population density and high antimicrobial consumption, while better data should be collected on antimicrobial consumption in low-income countries to establish the true relationship between drug consumption and EID events.

Introduction

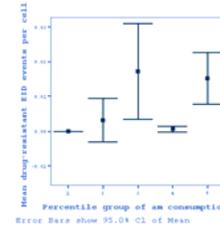
- As literature builds about how anthropogenic forces change the environment around us, this project aims to determine how these forces change the microbial environment within us. We investigate worldwide antibiotic consumption rates at the national level and explore how they connect to patterns of emerging infectious diseases (EIDs).
- Antimicrobial resistance is a global health threat. The spread of resistance has already been linked to antimicrobial consumption; this study attempts to link the emergence of resistance to consumption.

Methods: Data Collection

- Biological, temporal and spatial data on human EID events were collected from 1940 to 2003 (391 EID events, 355 pathogens) from a previous analysis (1).
- Data on health and Economic Indicators were gathered from WDI online (2)
- Data on antibiotic consumption for humans in the inpatient and outpatient setting and for animals were gathered from over fifty sources, creating the most comprehensive antibiotic use database to date. (3)
- Consumption data is divided into antimicrobial class — as microbes have unique resistance mechanisms for each class.



Discussion



- Finding appropriate proxies for antimicrobial consumption has proved difficult. One unexplored possibility is national drug consumption.
- Antimicrobial consumption is a significant predictor of total EIDs, but not of drug-resistant EIDs. This may be due to the low number of data points for d-r EIDs, which decreases the power of the model.
- The low d-r EID count of Canada has a large effect on our analysis due to Canada's size. An exploration Canada's EID count may shed light on our analysis.
- Our data suggests that low-income countries may account for most extremes in antibiotic consumption, and antimicrobial reporting bias. E.g. of the third-world countries with consumption data, none have any EIDs reported; this may have more to do with reporting infrastructure than real differences in EID events.

Conclusion

- Our study provides evidence that population density is a fundamental driver of drug-resistant EIDs and antimicrobial consumption is a driver of total EIDs; surveillance and containment efforts for drug resistance should be refocused to world population centers with high antimicrobial consumption, such as India and Indonesia.
- There are many sources of bias in this study that future research might overcome: EID reporting bias, measurement bias in antimicrobial consumption, and antimicrobial consumption reporting bias. E.g. of the third-world countries with consumption data, none have any EIDs reported; this may have more to do with reporting infrastructure than real differences in EID events.
- There has been an acceleration in countries reporting information on antimicrobial consumption, and systems for reporting EIDs are rapidly developing infrastructure and attention. This will help address issues of reporting bias in the future. Also, as countries begin to report antimicrobial consumption in multiple units, the different measures can be compared in a sensitivity analysis to test the accuracy of any observed relationship.
- The plausibility of a relationship between drug consumption and zoonotic or vector-borne EIDs should be explored in further research, as our study suggests a causal relationship.

References

- (1) Bronzwaer S, Cars O, Buchholz U, et al. A European Study on the Relationship between Antimicrobial Use and Antimicrobial Resistance. *Emerging Infectious Diseases* 8:3, 278-282 (2002)
- (2) Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, Daszak P. Global Trends in Emerging Infectious Diseases. *Nature* 451, 990-993, 2008
- (3) The World Bank Group. World Development Indicators Online. Accessed July 08. www.worldbank.org
- (4) Most consumption data from: European Surveillance of Antimicrobial Consumption: Interactive Database. Accessed 15/6/08. <http://www.esac.uia.ac.be>

Methods: Data Analysis

- A map of drug resistant EID events was plotted over antimicrobial drug use data.
- A log-linear predictive model of antibiotic consumption was developed using economic and health indicators from the World Development Indicators Online: GDP/capita PPP, total health expenditure, % private health expenditure, % public health expenditure, hospital beds/1000 inhabitants, and physicians/1000 inhabitants.
- A linear predictive model of EIDs was developed using a gridded human EID event database and the observed antibiotic consumption data. The predictors included were: population density, mammalian diversity, and level of antibiotic consumption.

Results

- The predictive model of antibiotic consumption was weak, although some of the health indicators were statistically significant predictors.
- Outpatient antibiotic consumption correlated significantly with total EID events, including drug-resistant, zoonotic, and vector-borne EIDs ($b=.001$, $p=.016$).
- As one can see on the graph to the right, the fourth quintile group of antimicrobial consumption—Canada, Australia, Iceland and Israel—had abnormally few EIDs.
- Population density was a significant predictor of drug-resistant EIDs ($b=0.008$, $p\text{-value}<0.001$).
- Antibiotic consumption in the outpatient setting correlated positively but insignificantly ($b = 0.02$, $p > .25$) with drug-resistant EID events. Inpatient consumption correlated negatively and insignificantly with drug-resistant EIDs.

