# The Major Factors Driving Global Antibiotic Consumption: A Quantitative Analysis of the Leading Determinants

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## BACKGROUND

- Through natural selection, bacteria have evolved to become increasingly resistant to antimicrobial treatment [1].
- The excessive volume and low-quality usage of antibiotics contributes to the global threat of antimicrobial resistance (AMR).

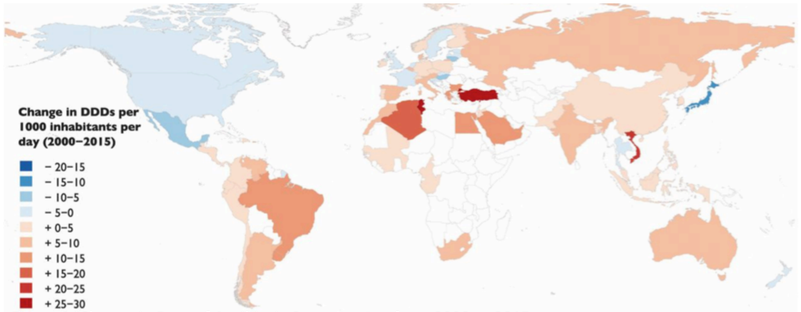


**Figure 1: Change in Rate of Antibiotic Consumption from 2000 to 2015**
Map of national rate of change of antibiotic consumption from 2000 to 2015 in defined daily doses (DDD) per 1,000 people per day [2].

## AIM

- Identify the socioeconomic and cultural factors driving global antibiotic consumption.
- Evaluate the relative influence of these factors on consumption of various antibiotic classes in high-income vs. low- and middle-income countries.

## DATA & METHODS

- Antibiotic consumption in total defined daily doses (DDDs) from 2000 to 2015 in 76 countries was obtained from the CDDEP
- Independent variables were obtained from the World Bank DataBank, the World Health Organization, and Transparency International.
- The complete data set was split in two based on income
- DDD data was logged and independent variables were standardized to a mean of 0 and standard deviation of 1.
- Correlations, PCA biplots, and variance inflation factors, were used to determine the independent variables to include in the multiple linear regression models.

**Table 1: Independent Variable Acronyms**

| Acronym | Data Set |
|---|---|
| HEALTH.EXP | *Health expenditure per capita (current US$)* |
| HOSPBEDS | *Hospital beds (per 1,000 people)* |
| PHYS | *Density of physicians (total number per 1,000 population)* |
| NURSE | *Density of nursing and midwifery personnel (total number per 10,000 population)* |
| PHARMA | *Density of pharmaceutical personnel (total number per 1000 population)* |
| OVER65 | *Population ages 65 and up (% of total)* |
| SANITATION | *People using at least basic sanitation services (% of the population)* |
| DEFECATION | *People practicing open defecation (% of the population)* |
| UNDERNOURISH | *Prevalence of undernourishment (% of the population)* |
| CORRUPTION | *Corruption Perceptions Index* |
| EDU | *Primary school completion rate, total (% of relevant age group)* |

## RESULTS

### PCA Results

- LMIC and HIC PCA biplots (Figures 2 & 3) depict the variance in the independent variables.

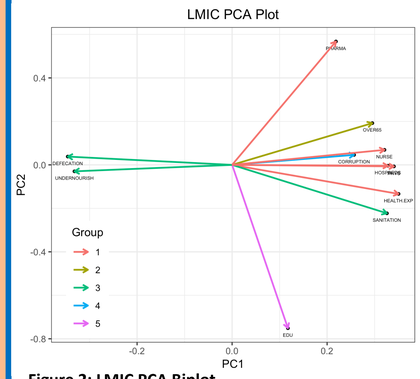


**Figure 2: LMIC PCA Biplot**

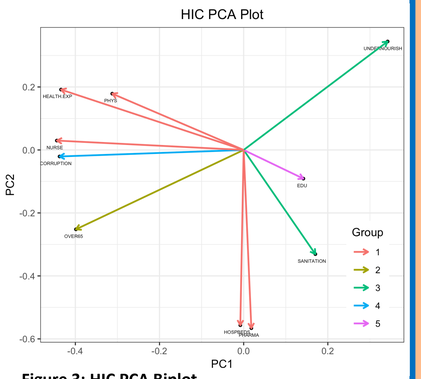


**Figure 3: HIC PCA Biplot**

Visualization of the relative loadings of each variable on independent axes. Colors indicate grouping based on predicted correlation of variables.

### Regression Results

- Regression results (Tables 2) display magnitude and significance of chosen independent variables on log(DDDs) in LMICs and HICs.

**Table 2: LMIC and HIC Multiple Linear Regression Results**

| | *Dependent variable:* | |
|---|---|---|
| | log(DDDs) | |
| | LMIC | HIC |
| | (1) | (2) |
| SANITATION | **-1.231*****| **0.859***** |
| | (0.268) | (0.293) |
| HEALTH.EXP | 0.224 | 0.005 |
| | (0.298) | (0.120) |
| PHARMA | **-0.397**** | **0.882***** |
| | (0.164) | (0.119) |
| EDU | 0.190 | **0.335***** |
| | (0.151) | (0.110) |
| CORRUPTION | 0.134 | |
| | (0.154) | |
| Constant | 19.230*** | 18.074*** |
| | (0.123) | (0.139) |
| Observations | 118 | 122 |
| $R^2$ | 0.333 | 0.468 |
| Adjusted $R^2$ | 0.303 | 0.450 |
| Residual Std. Error | 1.282 (df = 112) | 1.186 (df = 117) |
| F Statistic | 11.188*** (df = 5; 112) | 25.720*** (df = 4; 117) |
| *Note:* | | *p<0.1; **p<0.05; ***p<0.01 |

## CONCLUSIONS

### LMICs

- As SANITATION increases by 10%, total DDDs decreases by 24.7% - Increases in the number of people using basic sanitation facilities leads to decreases in the spread of disease, and thus reduces the demand for antibiotics.
- As PHARMA increases by 10%, total DDDs decreases by 8.74%. - Pharmacists promote better antibiotic consumption practices by optimizing treatment, which leads to less overuse and self-medication of antibiotics in LMICs [2].
- Basted off LMIC PCA biplot, HEALTH.EXP and CORRUPTION are correlated to SANITATION (as well as other variables excluded from the regression model).

### HICs

- SANITATION, PHARMA, and EDU are all positively associated with antibiotic consumption.
- These predictors are all proxies for higher access to healthcare in HICs.
- The HIC PCA biplot indicates less multicollinearity between independent variables compared to in LMICs.
- All significant findings span across most classes of antibiotics.

### Implications

- In LMICs, interventions to both reduce the incidence of disease by increasing use of improved sanitation facilities and to optimize antibiotic treatment by increasing pharmaceutical personnel density would reduce total antibiotic consumption [3].
- To effectively reduce global antibiotic resistance, while taking in to account the current mortality rate and high burden of infectious disease in LMICs, certain antibiotic classes should become widely available while others remain reserved for severe multi-drug resistant cases [4].
- In both LMICs and HICs, surveillance and monitoring of antibiotic prescribing and consumption as well as overall advances in regulatory systems could improve drug quality and treatment plans in order to reduce the incidence of resistance and decrease total consumption

## REFERENCES

1. Klein, E. Y., Van Boeckel, T. P., Martinez, E. M., Pant, S., Gandra, S., Levin, S. A., … Laxminarayan, R. (2018). Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proceedings of the National Academy of Sciences of the United States of America*, *115*(15), E3463–E3470. https://doi.org/10.1073/pnas.1717295115
2. World Health Organization, Global Health Observatory data repository (2016). *Pharmaceutical personnel (per 10,000 population)* [Data file]. Retrieved from http://apps.who.int/gho/data/node.main.HWFGRP_0080?lang=en
3. The World Health Organization. (2015). *Global Action Plan on Antimicrobial Resistance.* Retrieved from www.paprika-annecy.com
4. *WHO Model List of Essential Medicines*. (2017). Retrieved from http://www.who.int/medicines/publications/essentialmedicines/en/

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