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Cultural Drivers of Antibiotic Consumption in High-Income Countries: A Global Ecological Analysis

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Background: Previous studies evaluating the cultural and structural factors underpinning the large variations in the consumption of antibiotics in high-income countries have reached different conclusions. Some studies have found that corruption plays a dominant role, whereas other studies have concluded that cultural factors such as the degree of uncertainty avoidance (UA) and performance-orientation versus cooperation-orientation (POCO) are more important. These studies have been limited to Europe, and we, therefore, aimed to expand this analysis to all high-income countries with available data.
Methods: Using antibiotic consumption data from the IQVIA MIDAS database, linear regression models were constructed with country-level cephalosporin, fluoroquinolone, and macrolide consumption (defined daily doses/1,000 population/year) as the outcome variables and country-specific scores of UA and POCO (obtained from the Hofstede Index), gross domestic product/capita, world region and markers of effective governance (Control of Corruption and Regulatory Quality extracted from the World Bank data) as the explanatory variables. All data, excluding the Hofstede Indices, used country-level averages for the years 2013 to 2015.
Results: Complete data were available for 37 countries from 4 world regions. Consumption of cephalosporins, macrolides, and fluoroquinolones was associated with POCO and UA, but not the markers of effective governance. In the case of macrolide consumption, the association with UA narrowly missed statistical significance. Repeat analyses limited to first European countries and second to non-European countries revealed similar findings.
Conclusions: More thought should be given to construct antibiotic stewardship campaigns that are tailored to the local extent of UA and POCO.

Keywords: antibiotic consumption, antimicrobial resistance, culture, Hofstede model

Introduction

Why does the amount of antibiotics consumed vary to such a large extent between populations around the world? This variation remains over an order of magnitude even when only considering high-income populations.[1,2] Differences in the incidence of infections play only a minor role as has been shown in studies within Western Europe, where differences in the incidence of infections are small but variations in antibiotic consumption vast.[3–5] A large body of work has established that the act of prescribing an antibiotic is a highly social as well as a clinical act.[6–9] Providing an antibiotic represents the health worker's concern for the patient, legitimizes the patient's sick-role, and reinforces the health worker's claim to expert knowledge.[6,7]

Several studies have found that cultural differences mediate some of the differences in antibiotic consumption between European countries.[4,8–13] These studies have mostly used Hofstede's model of cultural dimensions. This highly cited (over 9,000 citations) model defines culture as the collective programming of the mind that distinguishes the members of different groups of people.[10,14] The model is based on an analysis of detailed interviews performed in 53 countries that revealed that cultures vary consistently along six dimensions.[14] Two of these have been found, to varying extents, to be associated with antibiotic consumption—uncertainty avoidance (UA) and performance-orientation versus cooperation-orientation (POCO—also termed the masculinity index).[4,8,10–12]

The UA index indicates the extent to which a society tolerates uncertainty and ambiguity. In high-UA cultures, individuals feel discomfort and stress in unstructured situations that are novel, unknown, or different from usual.[15] It has been hypothesized that in high-UA societies patients

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may be more likely to request, and doctors to provide, antibiotics for illnesses with a low (but uncertain) probability that antibiotics may be beneficial.[4,8,10] This effect of reducing uncertainty may be so much greater in high- than low-UA societies that these societies are less receptive to stewardship messaging.[4]

In performance-oriented cultures, ego needs, assertiveness, targets, and success are emphasized, whereas cooperation-oriented cultures place more focus on caring for all members of society, including the weak.[14] Since one of the key arguments used to not use antibiotics is that this will be good for everyone (via reducing the emergence of antimicrobial resistance [AMR]), performance-oriented societies may be responsive to stewardship messaging.[6,8]

A univariate analysis found a positive association between excessive antibiotic usage (extended use of post-surgical antibiotic prophylaxis) and UA at the levels of countries in Europe.[11] A more detailed analysis assessed if any of the Hofstede dimensions could explain the large country-level variation in the use of antibiotics for colds/flu/sore throats in the past year in Europe (varying between 11% in Finland and 81% in Spain).[10] Multiple regression analyses revealed that both UA and POCO were associated with using antibiotics for these indications.[10] An additional European country-level study used three different sources of antibiotic consumption data and found that both UA and ‘‘power distance’’ (a measure of how power is distributed in a society) were correlated with antibiotic consumption in univariate analysis but that these associations were no longer statistically significant when controlling for gross domestic product (GDP)/capita. Only POCO was significantly associated with consumption after controlling for GDP/capita.[8] More recently, a number of studies have found positive associations between markers of corruption (both national and within the health sector) and antibiotic consumption.[16,17] Of note, the national level of corruption has also been found to be associated with UA, POCO, and power distance.[18] Two studies, both country-level studies within Europe, have tried to disentangle the effects of corruption and cultural factors on consumption. In the first of these, national levels of antibiotic consumption were found to be independently associated with UA, POCO, and markers of corruption.[12] A more recent study found that the ratio of broad- spectrum versus narrow-spectrum antibiotics prescribed was correlated to UA and corruption in univariate, but only UA in multivariate, modeling.[4] UA was found to explain 58% of the variation in prescribing of broad- versus narrow-spectrum antibiotics.

None of these analyses has considered countries outside of Europe. Including countries outside of Europe considerably increases not only the sample size but also the range of variation of antibiotic consumption, corruption, and cultural traits. In this article, we aimed to assess the association between antibiotic consumption, governance, and cultural traits in all high-income countries with available data. Low- and middle-income countries are typically at a different stage in the epidemiological transition, have poorer sanitation (which influences the spread of both infections and AMR),[19,20] frequently have higher infection burdens than high-income countries,[21] and typically have less accurate information about antibiotic consumption.[2,20] For these reasons, the analysis is limited to high-income countries.

Methods

A literature review was conducted to construct a conceptual framework to represent the relationships between the determinants of antibiotic consumption (Fig. 1). Based on this analysis, data for the following variables were extracted.

Data

Culture

Individual scores for UA and POCO were accessed for each country from Hofstede Insights.*

Corruption, institutional strength, and GDP

The World Bank has provided indicators pertaining to six dimensions of governance since 1996. We used two of these that have been theorized or empirically shown to be linked to antimicrobial consumption.[12,16,17,†]

1. Control of Corruption (CoC) measures the extent to which public power is exercised for private gain, including both petty and grand forms of corruption, as well as the capture of the state by elites.
2. Regulatory Quality (RQ) measures the ability of the government to formulate and implement sound policies and regulations that permit private sector development.

The value of both these indices provides each country’s score in units of standard normal distribution, ranging from approximately –2.5 to 2.5. Both are average scores for the years 2013 to 2015.

GDP per capita

The average 2013 to 2015 national GDP per capita based on purchasing power parity and in U.S. dollars for each country was provided by the World Bank.[†]

Antibiotic consumption

Data from IQVIA MIDAS were used as a measure of national antibiotic consumption. IQVIA MIDAS uses national sample surveys that are performed by pharmaceutical sales distribution channels to estimate antimicrobial consumption from the volume of antibiotics sold in retail and hospital pharmacies. The sales estimates from this sample are projected with the use of an algorithm developed by IQVIA MIDAS to approximate total volumes for sales and consumption. Consumption estimates provided by IQVIA MIDAS for three key classes of antibiotics (cephalosporins, macrolides, and fluoroquinolones) are reported as the number of defined daily doses (DDD) per 1,000 population per year. The average annual consumption for the three most recent years of available data was used (2013 to 2015). Data were available for 63 countries.[‡] We used data for the 37 countries that were also classified as high-income countries by the World Bank as of October 2019.**

*https://www.hofstede-insights.com/product/compare-countries/
†http://datatopics.worldbank.org/world-development-indicators/
‡https://resistancemap.cddep.org/AntibioticUse.php
**https://datahelpdesk.worldbank.org/knowledgebase/articles/906519#High_income

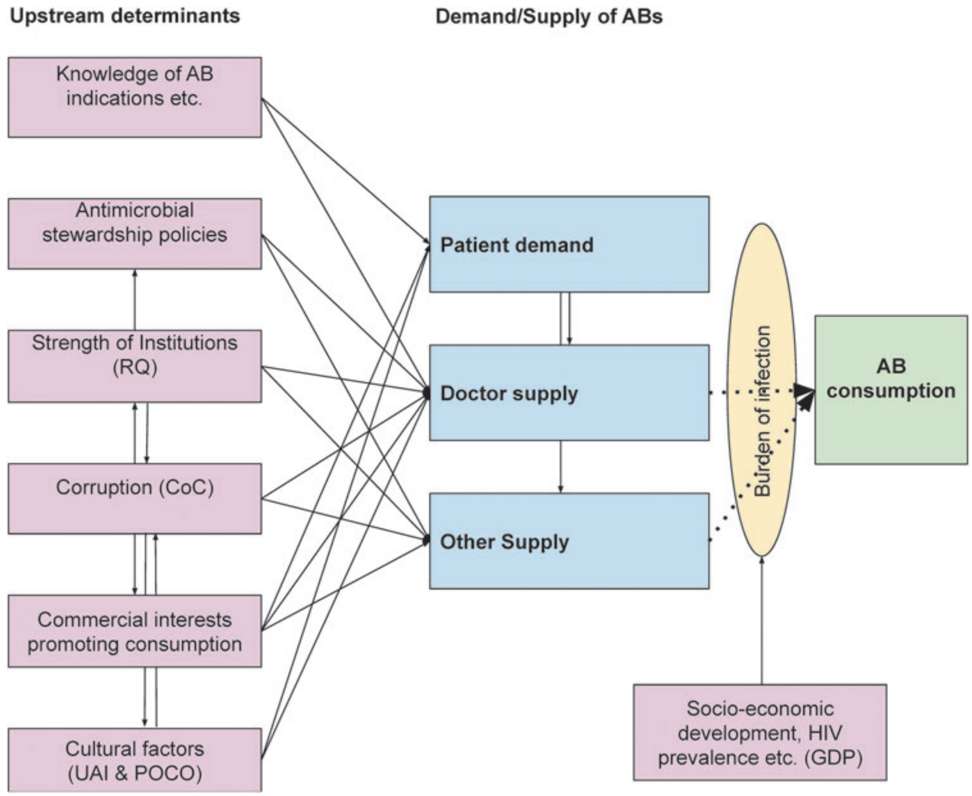

FIG. 1. Conceptual framework to understand the interrelationships between the determinants of country-level antibiotic consumption. CoC, Control of Corruption; GDP, gross domestic product; POCO, performance-orientation versus cooperation-orientation; RQ, Regulatory Quality; UAI, Uncertainty Avoidance Index. Color images are available online.

Data analysis

Univariate and multiple linear regression models were built to establish overall relationships between consumption of antibiotics (cephalosporins, macrolides, and fluoroquinolones) and all the putative explanatory variables. The WHO world region was included as a dummy variable. Sensitivity analyses were conducted that first excluded the world region variable, second were stratified by European countries ($n=25$) versus non-European countries ($n=12$), and third were constructed via backward stepwise selection with significance levels α of 0.01 for variable selection. The analyses were performed in STATA 13. A p-value of less than 0.05 was used as the threshold of statistical significance.

Results

There were large variations in the consumption of antibiotics between the 37 countries: cephalosporins (81 to 3,297 DDD/1,000 population per year), macrolides (270 to 2,921), and fluoroquinolones (254 to 1,501; Fig. 2 and Table 1).

Consumption of cephalosporins, macrolides, and fluoroquinolones was positively associated with POCO (coef. 9.6, 95% confidence interval [CI] 0.6–18.6; coef. 11.2, 95% CI 5.4–17.0; coef. 5.2, 95% CI 1.3–8.9, respectively, Fig. 2 and Table 2).

UA was also positively associated with consumption of cephalosporins (coef. 16.0, 95% CI 2.6–29.4) and quinolones (coef. 6.3, 95% CI 0.7–12.0). In the case of macrolide consumption, this association narrowly missed the statistical significance.

In the univariate analyses, and only in the case of cephalosporin consumption, CoC and RQ were found to be negatively associated with consumption. In multiple regression analyses, the markers of effective governance were not associated with the consumption of antibiotics. GDP/capita was positively associated with fluoroquinolone consumption on multiple regression analysis (coef. 0.01, 95% CI 0.00–0.02).

Sensitivity analyses running the regressions, excluding the regional dummy variable, produced similar results (Supplementary Table S1). On repeating the analyses limited to the only region with a sizable sample size (Europe, $n=25$), only POCO was significantly associated with consumption of all three classes of antibiotics (Supplementary Table S2). Likewise, POCO was the only variable significantly associated with consumption (but only for macrolides) in the analysis limited to non-European countries (Supplementary Table S3). Using backward stepwise regression to build the models did not substantively change the results (Supplementary Table S4).

Discussion

To the best of our knowledge, this is the first global study to evaluate the roles that certain cultural and governance factors play in determining the substantial differences in antibiotic consumption between high-income countries. We found reasonably consistent evidence that the consumption of all three classes of antibiotics investigated was higher in countries that were more performance-oriented and had a lower tolerance of uncertainty. While CoC was always in the expected negative direction, its association with consumption was not statistically significant.

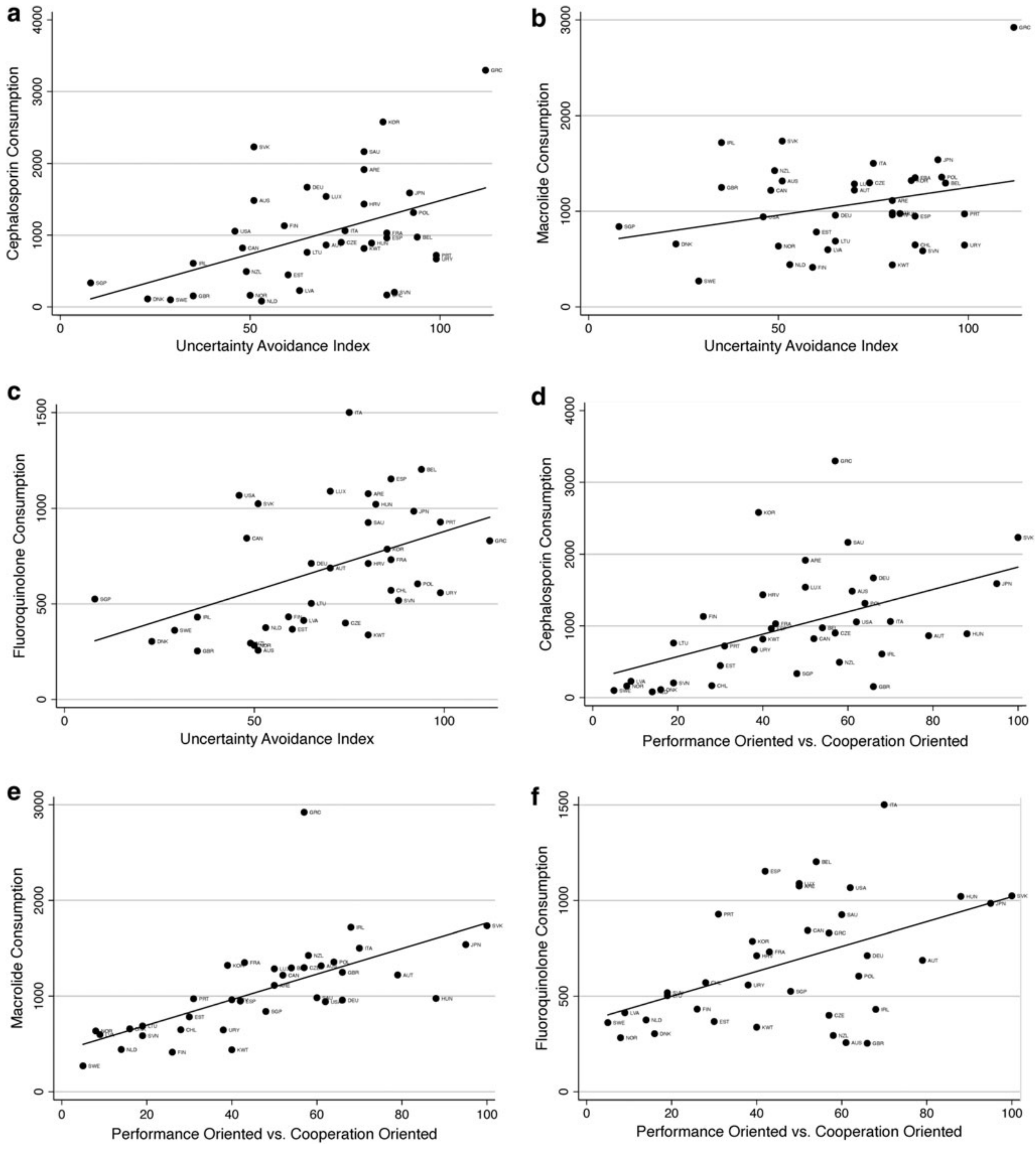

FIG. 2. Scatter diagram of uncertainty avoidance/performance-oriented versus cooperation-oriented scores and consumption of cephalosporins **(a, d)**, macrolides **(b, e)**, and fluoroquinolones **(c, f)** in 37 high-income countries (consumption is measured in defined daily doses/1,000 population/year).

Studies limited to Europe have found that a number of health-related issues differ between low- and high-UA countries. High-UA countries spend relatively more money on doctors than nurses compared with low-UA countries.[14] Health workers in low-UA countries have more eye contact with their patients and pay more attention to building rapport.[22] So too, health workers in high- compared with low-UA countries are more likely to feel uncomfortable with not using antibiotics in the setting of fever, cough, and sore throat.[10,14] They may know that a bacterial cause is unlikely but may be more likely to prescribe antibiotics ''just in case.''[9,13] Likewise, patients in these countries are expected to be less likely to accept a recommendation for symptomatic treatment and rest than low-UA populations.[9]

Table 1. Antimicrobial Consumption, Uncertainty Avoidance, Performance-Orientation Versus Cooperation-Orientation, Gross Domestic Product/Capita, Governance per Country, World Region (Average Values for Years 2013 to 2015)

Country	*Code*	*Region*	*Cephalosporin*	*Macrolide*	*Quinolone*	*UA*	*POCO*	*GDP*	*CoC*	*RQ*
Austria	AUT	Europe	863	1,221	688	70	79	48,800	1.55	1.49
Belgium	BEL	Europe	973	1,295	1,203	94	54	44,605	1.67	1.29
Croatia	HRV	Europe	1,434	962	712	80	40	22,077	0.12	0.46
Czech Republic	CZE	Europe	900	1,298	400	74	57	32,263	0.23	1.09
Denmark	DNK	Europe	111	658	304	23	16	47,901	2.40	1.81
Estonia	EST	Europe	446	783	367	60	30	28,964	1.19	1.45
Finland	FIN	Europe	1,131	414	432	59	26	41,470	2.20	1.85
France	FRA	Europe	1,030	1,351	732	86	43	40,142	1.33	1.16
Germany	DEU	Europe	1,669	959	712	65	66	47,191	1.81	1.55
Greece	GRC	Europe	3,297	2,921	830	112	57	26,839	–0.05	0.63
Hungary	HUN	Europe	890	976	1,021	82	88	25,518	0.32	0.91
Ireland	IRL	Europe	608	1,719	431	35	68	51,068	1.54	1.58
Italy	ITA	Europe	1,061	1,502	1,501	75	70	36,071	0.05	0.78
Latvia	LVA	Europe	228	598	413	63	9	23,808	0.33	1.04
Lithuania	LTU	Europe	761	688	503	65	19	28,174	0.43	1.15
Luxembourg	LUX	Europe	1,540	1,286	1,089	70	50	10,1298	2.12	1.78
Netherlands	NLD	Europe	81	442	376	53	14	49,233	2.05	1.77
Norway	NOR	Europe	161	636	283	50	8	66,015	2.29	1.67
Poland	POL	Europe	1,315	1,357	605	93	64	25,612	0.60	1.05
Portugal	PRT	Europe	719	972	928	99	31	28,747	0.95	0.80
Slovakia	SVK	Europe	2,231	1,734	1,024	51	100	28,928	0.08	0.93
Slovenia	SVN	Europe	204	586	518	88	19	30,845	0.73	0.63
Spain	ESP	Europe	963	948	1,153	86	42	33,710	0.90	0.94
Sweden	SWE	Europe	99	270	362	29	5	46,573	2.29	1.91
The United Kingdom	GBR	Europe	153	1,249	254	35	66	40,868	1.70	1.77
Canada	CAN	Americas	821	1,219	844	48	52	45,646	1.89	1.74
Chile	CHL	Americas	166	648	571	86	28	22,787	1.54	1.49
The United States	USA	Americas	1,055	942	1,067	46	62	55,033	1.31	1.27
Uruguay	URY	Americas	668	646	558	99	38	21,069	1.38	0.54
Kuwait	KWT	Eastern Mediterranean	815	439	338	80	40	52,550	–0.22	–0.13
Saudi	SAU	Eastern Mediterranean	2,165	983	926	80	60	76,703	0.04	0.03
United Arab Emirates	ARE	Eastern Mediterranean	1,915	1,113	1,076	80	50	66,517	1.19	0.96
Australia	AUS	Western Pacific	1,484	1,317	257	51	61	46,880	1.79	1.80
Japan	JPN	Western Pacific	1,589	1,539	985	92	95	39,179	1.66	1.12
Korea	KOR	Western Pacific	2,579	1,322	787	85	39	33,588	0.61	0.99
New Zealand	NZL	Western Pacific	493	1,425	294	49	58	37,261	2.34	1.83
Singapore	SGP	Western Pacific	335	840	525	8	48	86,612	2.08	1.97

CoC, Control of Corruption, GDP, gross domestic product; POCO, performance-orientation versus cooperation-orientation; RQ, Regulatory Quality; UA, Uncertainty Avoidance Index.

In these circumstances, the prescription of antibiotics provides psychological relief to both the health worker and the patient.[9]

When advocating withholding antibiotics, one of the arguments used is that this will reduce the emergence of AMR, which would be beneficial for the whole population. Populations that are more orientated toward cooperation tend to show more concern for other members of society and may thus be more receptive to this message than performance-oriented societies. Several studies have found that more cooperation-oriented societies are more likely to help strangers and support prosocial, egalitarian, and environmental policies.[14,15,23] An alternative explanation is that in performance-oriented societies, higher priority is placed on returning to work as soon as possible, which may translate into more antibiotic use.[8] These considerations generate the hypothesis that cooperation-oriented populations may be more receptive to advice to withhold antibiotics to prevent the emergence of AMR.

The effect sizes of these cultural factors were not small. For example, our model found that the consumption of cephalosporins increased by 16 doses for every 1-point increase in the UA score. If this relationship held for the 104-point UA jump between Singapore (UA-8) and Greece (UA-112), then consumption would increase by 1,664 doses/1,000 population per year. In a similar vein, the 95-point increase in POCO between Sweden and Slovakia would translate into a 912 increase of cephalosporin doses consumed.

The six dimensions of Hofstede's model have been legitimately criticized as being considerable simplifications of

Table 2. Regression Results for National Consumption of Cephalosporins, Macrolides, and Fluoroquinolones (Coefficients [95% Confidence Intervals]; Defined Daily Doses/1,000 Population/Year)

Independent variables	Cephalosporins				Macrolides				Fluoroquinolones			
	Univariate	*p-Value*	*Multivariate*[a]	*p-Value*	*Univariate*	*p-Value*	*Multivariate*[a]	*p-Value*	*Univariate*	*p-Value*	*Multivariate*[a]	*p-Value*
RQ	−577 (−997 to −158)	0.008	399 (−663 to 1,461)	0.469	−120 (−420 to 181)	0.425	339 (−349 to 1,027)	0.327	−226 (−410 to −43)	0.017	−5.9 (−455 to 443)	0.98
CoC	−432 (−721 to 142)	0.005	−484 (−1,083 to 113)	0.181	−166 (−371.5 to 38.5)	0.108	−263 (−650 to 124)	0.213	−147 (−278 to −17)	0.028	−131 (−384 to 121)	0.464
Uncertainty avoidance	14.9 (5.2 to 24.5)	0.004	16.0 (2.6 to 29.4)	0.033	5.8 (−1.1 to 12.7)	0.095	7.6 (−1.0 to 16.3)	0.094	6.2 (2.0 to 10.4)	0.005	6.3 (0.7 to 12.0)	0.046
POCO	15.6 (6.3 to 24.9)	0.002	9.6 (0.6 to 18.6)	0.027	13.3 (8.0 to 18.7)	<0.001	11.2 (5.4 to 17.0)	<0.001	6.5 (2.5 to 10.5)	0.002	5.1 (1.3 to 8.9)	0.008
GDP	0.001 (−0.01 to 0.02)	0.833	0.01 (−0.00 to 0.03)	0.341	0.00 (−0.01 to 0.01)	0.478	0.01 (−0.00 to 0.02)	0.469	0.00 (−0.01 to 0.01)	0.944	0.01 (0.00 to 0.02)	0.037
Region												
Europe	Ref		Ref		Ref		Ref		Ref		Ref	
Americas	−237 (−1,050 to 576)	0.557	−46 (−721 to 628)	0.79	−209 (−754 to 334)	0.441	−111 (−549 to 325)	0.567	86 (−277 to 450)	0.632	157 (−127 to 443)	0.363
Eastern Mediterranean	717 (−205 to 1,640)	0.123	130 (−962 to 1,223)	0.551	−228 (−846 to 390)	0.458	−399 (−1,107 to 308)	0.329	106 (−307 to 519)	0.605	−360 (−822 to 101)	0.265
Western Pacific	381 (−358 to 1,121)	0.302	396 (−225 to 1,019)	0.229	215 (−280 to 711)	0.383	91 (−311 to 494)	0.664	−103 (−435 to 227)	0.528	−129 (−392 to 133)	0.32
Countries	37		37		37		37		37		37	
Adjusted R^2			0.54				0.56				0.56	

[a]The multivariate models were constructed by entering all the independent variables listed in the table into the models.
GDP, gross domestic product per capita (USD).

cultural differences.[24] It is possible that a different cultural classification system would provide a better discriminator of antibiotic consumption.[9,25] Differences in the belief of the self-healing power of the body have, for example, been found to explain part of the large difference in antibiotic consumption between the neighboring countries of the Netherlands and Belgium.[9] Further problems pertaining to the Hofstede data include a lack of clarity as to when the sampling took place in each country, what the sample sizes were, and the sampling methodology used.[14] The analyses are limited to only three classes of antibiotics in high-income countries and are weakened by the small sample size. The combination of the small sample size and the number of independent variables assessed in the multivariable models results in fairly wide CIs. Furthermore, care should be taken in considering all the multivariate point estimates in Table 2 in the same way—as total-effect estimates.[26] The study was purely ecological by design and thus susceptible to the ecological inference fallacy. Furthermore, only country-level data are considered, whereas significant differences in antibiotic prescription habits have been noted between regions within countries.[16] We did not include a measure of burden of infectious diseases in our models largely because other studies have found that this does not play a major role in explaining variations in antibiotic consumption in high-income countries.[4,27] There was little correlation between the independent variables, the largest of which was the well-known negative association between UA and the two measures of governance efficacy (Supplementary Table S5).[18] One potential confounder we did not control for was number of health personnel per capita, which is associated with UA and may be associated with antibiotic consumption. The consumption estimates from IQVIA MIDAS have been found to correlate closely with those from other estimates such as those from the European Surveillance of Antimicrobial Consumption Network data. There was a 93% correlation between these two sources for the consumption estimates from 2015, for example.[1,28]

The strong associations between antibiotic consumption and UA/POCO have been found previously in a number of studies limited to Europe.[4,8,10–12] This study extends these findings to other high-income countries. East Asia, for example, is frequently portrayed as a uniformly high antibiotic consumption region.[1,29] Our analysis included three countries from this region. Japan and South Korea had similarly high consumption of all three classes of antibiotics considered (Table 1). Singapore's consumption of antibiotics was, however, strikingly lower. This finding is commensurate with its considerably lower UA score than Japan and South Korea, as well as its higher CoC and RQ scores (Table 1). The governance efficacy variables were typically significantly associated with antibiotic consumption in the univariate but not in the multiple-regression analyses. This plus their association with UA (Supplementary Table S1)[4,18] suggests that they are confounders or their effect on antibiotic consumption is mediated via UA.

Our analysis, therefore, provides a possible explanation for national variations in antibiotic consumption. It may also help to explain how similar antibiotic stewardship campaigns have been successful in some but not other countries.[6,30] The campaigns may have provided a poor fit to local norms. Our study results build on those of others that suggest that antibiotic stewardship campaigns should be tailored to the local extent of UA and POCO.[4,10] In populations intolerant of uncertainty, it may be particularly efficient to place more emphasis on rapid diagnostic tests that can remove uncertainty about bacterial infections—such as *Streptococcus pyogenes* antigen tests for sore throats and C-reactive protein-type tests for febrile illnesses.[4] In cooperation-oriented populations, raising awareness of population dangers of resistant infections related to taking antibiotics may be more effective than in performance-oriented ones. In the latter group, it may be more effective to raise awareness about the direct and long-term damages that antibiotics have on the recipient's microbiome and resistome.[31–33] The fact that reduced antibiotic consumption is just one of many socially beneficial outcomes associated with cooperation-oriented societies has not escaped our attention.[14,18,23]

Authors' Contributions

C.K. conceptualized the study. C.K. was responsible for the acquisition, analysis, and interpretation of data. C.K. and S.S.M.-B. read and approved the final draft.

Disclosure Statement

No competing financial interests exist.

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Supplementary Material

Supplementary Table S1
Supplementary Table S2
Supplementary Table S3
Supplementary Table S4
Supplementary Table S5

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