The Role of Structural Factors in Antibiotic Use Among European Union Citizens: A Multilevel Analysis

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The Role of Structural Factors in Antibiotic Use Among European Union Citizens: A Multilevel Analysis

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Using the 2016 European Commission's Eurobarometer survey, this study analyzed how a multitude of factors are associated with identification and intention of following proper antibiotic treatment. Multilevel analyses showed that knowledge and information from medical professionals and mass media (individual-level predictors), and advanced access to education (a structural-level factor) are associated with identification. For intention, structural factors (Access to Information & Communications, Health & Wellness, Nutrition & Basic Medical Care) contributed significant variances to the model, in addition to the individual-level effects (sources and trust in medical professionals and mass media). Results demonstrate a need to consider these structural-level influences to shed light on the process though which antibiotic resistance preventions and interventions might impact individuals' health literacy and behavioral outcomes.

Keywords: antibiotic resistance, multilevel analyses, health literacy, health information seeking, Eurobarometer survey

"Act now to tame the superbugs that are killing 700,000 a year."
—Ed Whiting, *Guardian* opinion writer

Since 1999, the British newspaper *The Guardian* has produced a series of entries on the urgent crisis of antimicrobials. Headlines in *The Guardian* paint a gloomy picture. One reads, "Antimicrobial Resistance: A Greater Threat Than Cancer by 2050," highlighting the impact of overprescription of antibiotics on global health (Watt, 2016). Another says, "Antimicrobial Resistance: What You Need to Know," underscoring the importance of accurate information (Weaver, 2016).

Fast forward to 2019; *antimicrobial resistance* (AMR)—a broad term that includes antibiotic and antiviral resistance—continues to threaten global health. Antimicrobials inhibit the growth of harmful microbial infections (Centers for Disease Control and Prevention [CDC], 2017a; Michael, Dominey-Howes, & Labbate, 2014; World Health Organization [WHO], 2017). Antimicrobial resistance (AMR) occurs naturally. Misuses of antimicrobials (e.g., using antibiotics designed to treat bacterial infections to treat viral infections)

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have accelerated the rate at which microbes rapidly change in response to these medicines (WHO, 2017), causing 700,000 deaths each year globally (Carlet, Pulcini, & Piddock, 2014). Antimicrobial agents, which include antibiotic and antiviral medicines, are developed to treat these harmful microbes (CDC, 2017a; Michael et al., 2014).

Antibiotic resistance, one of the categories in AMR and the primary focus of this article, receives the most attention as new resistance is rapidly emerging and spreading at a global scale (WHO, 2017). In Europe, antibiotic resistance is killing 25,000 people and causing a loss of €1.5 billion (US$1.7 billion) each year (European Commission, 2017). In the United States, 2 million people infected with bacteria are resistant to antibiotics, resulting in 23,000 deaths annually (CDC, 2017a; Kuehn, 2013). It is estimated that by 2050, antibiotic resistance will lead to 10 million deaths per year, costing around US$100 trillion (de Kraker, Stewardson, & Harbarth, 2016).

The effects of antibiotic resistance, including prolonged hospital stay, use of expensive drugs for treatment, and increased healthcare resources for treating resistance, have already burdened global health and the global economy (European Commission, 2017; WHO, 2017). Despite large-scale public awareness and education campaigns, such as European Antibiotic Awareness Day, research continues to show cases of misunderstanding (e.g., using antibiotics to treat the flu or colds) or abuse (e.g., sharing leftover antibiotics) among users (Scanfeld, Scanfeld, & Larson, 2010). Focusing on individual-level changes, therefore, is insufficient in confronting the antibiotic resistance crisis.

Indeed, health behaviors are complex. Increasingly, studies have recognized how behavioral outcomes are a product of complex individual and structural interactions (Kondo et al., 2009; Longo, 2005; Pickett & Pearl, 2001; Squiers, Peinado, Berkman, Boudewyns, & McCormack, 2012). Empirical research has found significant relationships between structural factors (e.g., healthcare system, healthcare expenditures, gross domestic product [GDP], and income inequality) and health outcomes (Kondo et al., 2009; Macinko, Starfield, & Shi, 2003; Nixon & Ulmann, 2006) as posited in the theoretical frameworks of health literacy skills and health-information-seeking behaviors (Longo, 2005; Squiers et al., 2012). Exploring individual-level health outcomes as predicted by a multitude of individual and structural factors in the context of antibiotic resistance may provide policy-level implications for large-scale changes in the long run.

This study examines the influence of multilevel factors on individual outcomes that are proxies for behavior change (Ajzen, 2011; Webb & Sheeran, 2006). These factors include (1) European Union (EU) citizens' identification of proper antibiotic use and (2) their behavioral intention to follow proper treatment using the 2016 European Commission's Eurobarometer survey. It contributes to antibiotic resistance research by identifying structural factors that may enhance the effectiveness and sustainability of future prevention and intervention efforts on a multinational scale.

Increasing Cases of Drug Resistance or Antibiotic Resistance

To understand antibiotic resistance, a category under the umbrella term *antimicrobial resistance*, one must understand what micros are. Micros (e.g. fungi, bacteria, viruses, and some parasites) are organisms that are part of the ecological system. They cannot be seen with the naked eye. Although there are beneficial micros, a select few can cause life-threatening infections (Michael et al., 2014).

Antimicrobial agents, which include antibiotic and antiviral medicines, are developed to treat these harmful microbes (CDC, 2017a; Michael et al., 2014). Antibiotics are used for bacterial infections such as pneumonia, tuberculosis, blood poisoning, gonorrhea, and foodborne diseases, whereas antiviral medicines are used to treat viral infections such as influenza and HIV. Microorganism resistance can render treatments of infectious diseases and illnesses (e.g., tuberculosis, HIV, and malaria) ineffective (Michael et al., 2014; USAID, 2016; WHO, 2017), which could burden the public health and economic systems. In this article, we focus on antibiotic resistance, which receives more attention from international health organizations and is more broadly discussed than antiviral resistance.

Factors Contributing to the Rising Problem of Antibiotic Resistance

Several factors can accelerate antibiotic resistance (Bjorkman, Erntell, Roing, & Lundborg, 2011; Hart & Kariuki, 1998; Kuehn, 2013; Michael et al., 2014), including overprescription and inappropriate use of antibiotics. For example, Kuehn (2013) finds that physicians overprescribed antibiotics for sore throats, prescribing them when only 10% of the patient populations needed them. Patients also misused antibiotics to treat viral infections (e.g., colds, the flu, and sore throats), hoping for an immediate solution (Michael et al., 2014; Reardon, 2014). It is also common that some patients who use antibiotics to treat bacterial infections do not finish prescribed doses, increasing the risks of "misapplication of antimicrobial therapy to non-susceptible organisms" (Michael et al., 2014, p. 4).

Scholars have warned of widespread consequences of an antibiotic resistance crisis that limits treatment options for diseases because new antibiotics usually take decades to develop (Reardon, 2014; Taylor, Lichten, & Smith, 2016). Assessing the perspectives of patients and the general public, and the influence of structural factors therefore may further our understanding of the crisis and help find prevention solutions and interventions.

Campaigns to Reduce Rising Antibiotic Resistance

Many countries have launched campaigns to combat antibiotic resistance. These campaigns target individuals and focus on educating the public, patients, or healthcare providers using print and Web materials (CDC, 2017b; Earnshaw et al., 2009; McNulty & Johnson, 2008). This approach has garnered some success in raising awareness and changing prescription behavior. In England, it was found that written instructions helped reduce antibiotic use in patients with acute bronchitis (Macfarlane et al., 2002). Similarly, results from the Netherlands indicated a significant reduction in antibiotic prescription for respiratory tract symptoms after primary physicians, pharmacists, and patients received training about proper antibiotic prescription procedure (Welchen, Kuyvenhoven, Hoes, & Verheij, 2004).

Despite their success, these campaigns are often implemented in isolation, focusing on one country/community or one health issue at a time, thus limiting their broad impact. More recently, an integrated approach called for by the WHO (2016) has been gaining traction. This approach prioritizes joint communication and research responses on local, national, regional, and global levels, further echoing an integrated theoretical framework of health literacy (Squiers et al., 2012) and health information seeking (Longo, 2005; Longo et al., 2010).

An Integrated Theoretical Framework of Health Literacy and Information Seeking

Behavioral change models have increasingly recognized ecological and structural influences on individuals' health behaviors. Indeed, health behaviors do not happen in a vacuum. Take obesity as an example. Not only is it impacted by an individual's dietary choices and physical activities (immediate factors), but it is also influenced by structural factors (e.g., built environments, healthy food availability, neighborhoods, and cultural norms; Ohri-Vachaspati et al., 2015). The inclusion of these multilevel factors in assessing antibiotic resistance and its determinants could provide insights into strategizing future antibiotic resistance prevention and intervention efforts on a global scale (Dahlberg & Krug, 2002; Longo, 2005; Squiers et al., 2012; Stokols, 1996). Health literacy skills (HLS; Squiers et al., 2012) and individual health-information-seeking behaviors (HISB) models (Longo, 2005; Longo et al., 2010) offer meaningful conceptual frameworks to do this. They incorporate communication determinants (e.g., health literacy and information seeking) within the larger, ecological influences. Combining these two models allows for capturing multilevel influences and the complexities of human behaviors regarding antibiotic use. Figure 1 shows the combined theoretical framework.

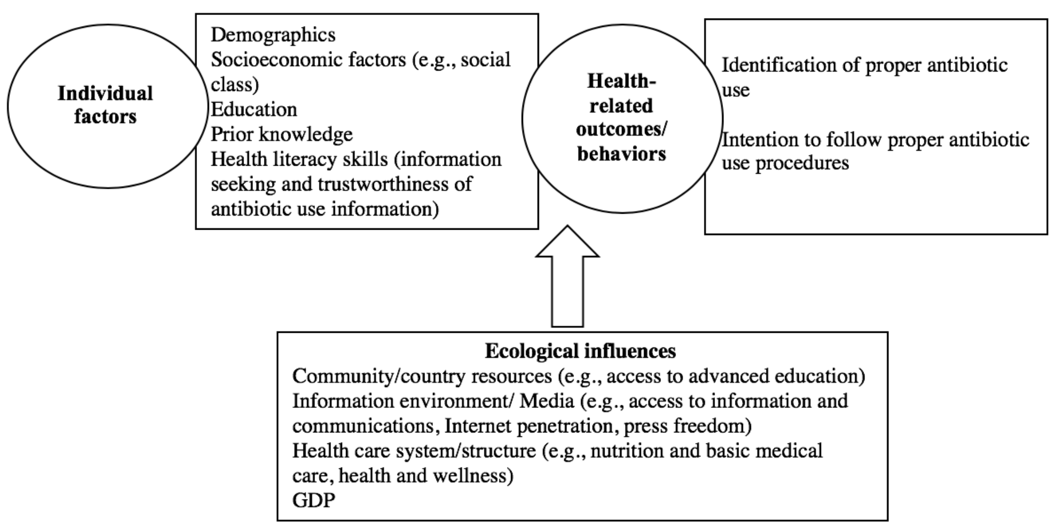

Figure 1. A theoretical framework of health literacy and health information seeking.

Individual-Level Communication Factors in the Combined Framework

The HLS framework conceptualizes communication and information-seeking skills as a form of health literacy (Squiers et al., 2012), which can be defined as "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions" (U.S. Department of Health and Human Services, 2000, para. 1). Low health literacy consistently predicts low health knowledge, poor health outcomes (e.g., health status, mortality rates), and poor healthcare utilization (e.g., medical adherence, hospitalization, screening, and vaccination; Berkman, Sheridan, Donahue, Halpern, & Crotty, 2011; DeWalt & Hink, 2009). Of particular importance to antibiotic resistance is how individuals seek and navigate misleading information about antibiotic use. HISB differentiates health information seeking into active processes (e.g., accessing and using information to make decisions) and passive processes (e.g., receiving information from personal interactions, traditional media, and new media; Longo, 2005; Longo et al., 2010).

Communication sources and trust in them influence how individuals manage their health (Anker, Reinhart, & Freeley, 2011; Hesse et al., 2005; Lambert & Loiselle, 2007; Niederdeppe et al., 2007). Incorporating these variables into the analysis adds new dimensions to HISB; they have been found to increase positive outcomes at the cognitive (e.g., knowledge) and behavior change levels (e.g., lifestyle; Kalichman, Benotsch, Weinhardt, Austin, & Luke, 2002; Shim, Kelly, & Hornik, 2006; van der Molen, 1999). Of all the communication sources, medical professionals are consistently rated as important and trustworthy (Dutta-Bergman, 2003; Hesse et al., 2005). Mass media sources tend to play only a supplemental role (Cutilli, 2010).

Other Individual Factors in the Combined Framework

This combined framework of HLS and HISB includes traditional individual-level factors that influence health literacy and information-seeking skills. For example, individuals' sociodemographic characteristics (e.g., age, gender, education level, and socioeconomic status) consistently predict health outcomes in multiple nations (Dubrovina, Siwiec, & Ornowski, 2012; Lantz et al., 1998). Prior knowledge is another individual factor that facilitates health literacy and subsequent outcomes (Baker, 2006). Other factors include community characteristics (e.g., general community social capital, percentage of sample on public insurance, the percentage of primary care and specialist physicians per 100,000) that have been associated with access to healthcare and health status (Hendryx, Ahern, Lovrich, & McCurdy, 2002; Kondo et al., 2009).

Structural Factors in the Combined Framework

Health literacy involves a dynamic, interactive process between individuals and systems (Longo, 2005; Squiers et al., 2012). The combined framework identifies determinants closely aligned with prior research on the interplays between distal and proximal determinants on health outcomes. The most widely used factors are perhaps the national socioeconomic status or GDP per capita, and healthcare system and expenditures. Their association with health outcomes is well documented (World Bank, 1993). Data from developing and industrialized countries show predictive power of GDP and healthcare expenditures (Macinko et al., 2003; Nixon & Ulmann, 2006; Or, 2000). Healthcare expenditures are less powerful than mortality in predicting life expectancies and chronic conditions (Bradley, Elkins, Herrin, & Elbel, 2011; Nixon & Ulmann, 2006), demonstrating how economic factors are only a small piece of the puzzle.

There is a need to explore other relevant determinants across the social, education, and political spectrums. For example, Nutrition & Basic Medical Care is an alternative indicator of the effectiveness of a healthcare system, which includes undernourishment, depth of food deficit, maternal mortality, child mortality, and deaths from infectious diseases. This composite measure is instrumental because of the close association among mortality, decreases in infectious diseases, and antibiotic use (Keenan et al., 2018). Similarly, mortality-based measures, including life expectancy, have been used extensively to evaluate the health of populations across the world (Mathers, Sadana, Salomon, Murray, & Lopez, 2001). This composite measure is instrumental because of the close association among mortality, decreases in infectious diseases, and antibiotic use (Keenan et al., 2018). This index takes into the account the interrelations among submeasures (e.g., malnutrition and childhood mortality; Pelletier, 1994), thereby offering a more nuanced interpretation of results. Similarly, Health & Wellness assesses the performance of healthcare systems. It encompasses healthcare access, healthcare quality, and crucial indicators of quality of life. These structural determinants could influence individuals' ability to seek and engage with healthcare systems (Levesque, Harris, & Russell, 2013) and may indirectly impact the ways in which individuals receive antibiotic treatment information and options.

Finally, the combined framework places a strong emphasis on information environment (e.g., Access to Information & Communications). The infrastructure, along with healthcare spending, influences health information technology adoption and dissemination that ultimately trickles down to health literacy through how accessible health information is for citizens (Anderson, Rainey, & Eysenbach, 2003; Brodie et al., 2000; Edejer, 2000; Hesse et al., 2005). Using this framework can shed light on key predictors of future behavior (Ajzen, 2011; Webb & Sheeran, 2006) at the global level.

The goal of this study, therefore, is to explore how the individual and structural variables are associated with (1) EU citizens' identification of proper antibiotic use and (2) their plan to follow proper treatment procedures. Acknowledging the gap in the literature, we propose the following hypotheses and research questions:

H1: *Individuals' knowledge of antibiotic use, sources of information, perceived trustworthiness of information, social class, and type of community will be positively associated with their identification of proper antibiotic use.*

RQ1: *What will be the effects of GDP, Nutrition & Medical Care, Access to Information & Communications, Health & Wellness, and Access to Advanced Education on the associations between individual-level factors and identification of proper antibiotic use?*

H2: *Individuals' knowledge of antibiotic use, sources of information, trustworthiness of information, social class, and type of community will be positively associated with their intention to follow proper treatment procedures.*

RQ2: What will be the effects of GDP, Nutrition & Medical Care, Access to Information & Communications, Health & Wellness, and Access to Advanced Education on the associations between individual-level factors and intention to follow proper treatment procedures?

Method

This study analyzed data from the 2016 European Commission's Eurobarometer survey (GESIS, n.d.), which assesses public opinions among 28 EU members and candidate countries. The survey is a face-to-face home interview using a multistage probability sample of EU citizens 15 years of age and older (see Table 1). The structural variables were gathered from the World Bank and Social Progress Index (SPI).

Table 1. Measures for the Individual Variables.

Measures	Question	Answer Categories
Identification of proper antibiotic use	What was the reason for last taking the antibiotics that you used?	Pneumonia Bronchitis Rhinopharyngitis Flu Cold Sore throat Cough Fever Headache Diarrhea Urinary tract infection Skin or wound infection Other DK
Intention to follow proper antibiotic use procedures	How do you now plan to use antibiotics?	You will always consult a doctor You will no longer self-medicate with antibiotics You will no longer take antibiotics without a prescription You will no longer keep leftover antibiotics for next time you are ill You will use antibiotics against the flu You will give leftover antibiotics to your relatives or friends when they are ill Other None DK

Knowledge of antibiotic use and treatment	Please tell me whether you think the following statement is true or false	Antibiotics kill viruses Antibiotics are effective against colds and flu Unnecessary use of antibiotics makes them become ineffective Taking antibiotics often has side effects such as diarrhea
Sources of general antibiotic use information	How did you first get this information about not taking any antibiotics unnecessarily?	You saw it on a TV, Internet, newspaper, TV news, radio A doctor talked to you about it, a pharmacist, another health professional family or friends
Trustworthiness of antibiotic use information	Which of the following sources of information would you use to get trustworthy information on antibiotics?	You saw it on a TV, Internet, newspaper, TV news, radio A doctor talked to you about it, a pharmacist, another health professional family or friends
Social class		The working class of the society, the lower middle class of society, the middle class of the society, the upper middle class of the society, the higher class of the society
Type of community		A rural area or a village, a small or medium-sized town, or a large town/city, with an option of "don't know."

Dependent Variables

Measures at individual and structural levels and their labels are described next. We referenced resources from governments and relevant research to code the data into proper use and proper plan to use antibiotics (European Commission, 2017; Hedrick, 2012).

Proper antibiotic use: The question, "What was the reason for last taking the antibiotics that you used?" assessed individuals' ability to identify proper antibiotic use. Of the choices, correct answers included "pneumonia," "urinary tract infection," and "skin or wound infection." They were added together (M = 0.25, SD = 0.44, range: 0–3).

Intention to follow proper antibiotic use procedures: The question, "How do you now plan to use antibiotics?" measured intention to follow proper antibiotic treatment procedures. Correct responses included, "You will always consult a doctor," "You will no longer self-medicate with antibiotics," "You will no longer take antibiotics without a prescription," and "You will no longer keep leftover antibiotics for next time you are ill." These responses were added to create the intention to follow proper antibiotic use. "Other" and "none" were coded as "missing" (*M* = 1.4, *SD* = 0.91, range = 0–4).

Independent Variables (Individual Level)

Demographics: Gender was assessed with two options (male = 0 and female = 1). Social class was measured by asking respondents whether they belong to the working, lower middle, middle, upper middle, or higher class. Type of community was measured by asking participants if they lived in a rural area or a village (1), a small or medium-sized town (2), or a large town/city (3).

Prior antibiotic use record was a follow-up question for those who already confirmed their antibiotic use in the last 12 months.

Knowledge of antibiotic use and treatment was measured by asking, "Please tell me whether you think the following statement is true or false," with two options: "when you feel better (false = 0)" and "when you take all of the antibiotics as directed (true = 1)."

Sources of general antibiotic use information was based on the question, "How did you first get this information about not taking any antibiotics unnecessarily?" Options were coded into three source categories: mass media (you saw it on a TV, Internet, newspaper, TV news, radio), medical professionals (a doctor, a pharmacist, or another health professional), and interpersonal (family or friends).

Trustworthiness of antibiotic use information was measured by asking, "Which of the following sources of information would you use to get trustworthy information on antibiotics?" Identical to the previous variable, options were coded into three categories: mass media (you saw it on a TV, Internet, newspaper, TV news, radio), medical professionals (talked with a doctor, a pharmacist, or another health professional), and interpersonal (family or friends).

Independent Variables (Structural Level)

Structural variables were selected to represent different aspects of the socioeconomic situations (GDP per capita), healthcare systems (Nutrition & Basic Medical Care, Health & Wellness), information environment (Access to Information & Communications, Internet penetration), and education (Access to Advanced Education). Higher scores mean stronger socioeconomic development, healthcare services, information environment, and education systems (see Table 2). GDP per capita (*M* = $26,626; *SD* = 16,691) was retrieved from the World Bank (2016). Of the countries, Luxembourg had the highest average income per person ($101,909), and Bulgaria had the lowest ($6,993.5).

The rest of the structural variables were from the SPIs (Porter, Stern, & Green, 2015). Nutrition & Basic Medical Care measures several aspects, including undernourishment, depth of food deficit, maternal mortality, child mortality, and deaths from infectious diseases. In Europe, Romania scored the lowest (98.04), and Finland scored the highest (99.63). Health & Wellness assesses a few aspects of foundations of well-being for citizens, including life expectancy, premature deaths from noncommunicable diseases, obesity rate, outdoor air pollution attributable deaths, and suicide rate. Lithuania was ranked the lowest among the countries in this sample (48.71); Italy scored the highest (78.19). Access to Advanced Education was an indicator of opportunity. It was constructed based on numbers of years of tertiary schooling, women's average years in school, inequality in school, and globally ranked universities. Portugal was ranked the lowest (0.39), and Ireland scored the highest (1.68). Access to Information & Communications ranks countries based on three criteria: mobile telephone subscription per 100 people, Internet penetration, and press freedom. Of the countries, Denmark was ranked the highest (95.8), and Hungary had the lowest score (51.7).

Table 2. Structural Variables for the 28 Countries Analyzed.

Country	GDP per capita ($)	Nutrition & Basic Medical Care	Access to Info & Comms	Health & Wellness	Access to Advanced Education	Sample size
Austria	43,665	99.46	90.97	71.19	0.56	59
Belgium	40,356	99.18	91.55	67.28	1.17	70
Bulgaria	6,993	98.43	75.96	57.84	0.85	76
Croatia	11,579	99.32	81.91	62.42	0.72	51
Cyprus Republic	23,075	99.45	84.5	75.7	1.32	34
Czech Republic	17,556	99.29	90.35	63.9	0.54	61
Denmark	53,014	99.23	95.80	68.82	0.95	24
Estonia	17,074	99.38	91.67	59.94	1.1	47
Finland	42,405	99.63	95.16	68.14	0.95	49
France	36,526	99.22	87.69	71.5	0.88	56
Germany	41,176	99.30	92.05	70.16	0.76	62
Greece	18,007	99.22	78.66	75.36	1.28	45

Hungary	12,365	99	83.32	51.7	0.77	70
Ireland	60,664	99.59	94.17	69.99	1.68	81
Italy	30,049	99.42	79.52	78.19	0.45	46
Latvia	13,666	98.67	86.85	52.27	0.78	46
Lithuania	14,252	99.06	85.64	48.71	1.05	111
Luxembourg	101,909	99.45	93.38	70.43	1.05	12
Malta	23,819	98.97	83.84	70.24	0.6	34
Netherlands	44,292	99.24	94.7	74.39	0.98	25
Poland	12,566	99.18	86.59	59.29	0.77	49
Portugal	19,220	99.05	84.38	70.48	0.39	50
Romania	8,958	98.04	78.69	59.4	0.44	74
Slovakia	16,089	98.79	90.4	61.02	0.63	86
Slovenia	20,729	99.45	84.83	65.82	0.79	64
Spain	25,683	99.31	86.23	76.16	0.96	54
Sweden	50,585	99.43	94.44	72.33	0.94	30
United Kingdom	43,929	99.14	90.14	71.47	0.96	42
M	26,626	99.12	87.20	64.97	0.865	
SD	16,661	.364	5.73	8.25	.304	

Analysis Strategy

To test H1, which examined factors associated with identification of proper antibiotic use, we used simple linear regression. In this exploratory stage, respondents' gender, type of community, and social class were entered as control variables. The survey was conducted in multiple countries with vast differences in terms of income; therefore, self-reported social class could be used as an alternative.

To explore RQ1, we performed analyses of variance (ANOVAs) to detect whether there were differences between the 28 countries in the means of the two outcome variables. We then used multilevel analysis to test the effects of individual and structural-level factors. To avoid multicollinearity, we assessed the tolerance and variance of inflation factors (VIF) on all variables at both levels, using simple linear regression. Internet penetration displayed a high VIF value of 6.82. Bivariate Pearson's correlation tests confirmed significant associations between the variable and GDP per capita (r = 0.65, p < 0.001), as well as Access to Information & Communications (r = 0.90, p < 0.001). It was excluded from our analysis. Further checks indicated that none of the variables had a tolerance value below 0.90 or a VIF value above 4.0 (Hair, Black, Babin, & Anderson, 2010).

To test H2, which assumed associations between individual health literacy factors and intention to follow proper antibiotic use, we used simple linear regression with individual-level variables as independent, controlling for gender, type of community, and social class. To explore RQ2, the multilevel analysis allows for capturing the variation of variables nested in country groups.

Results

The survey included responses from 27,525 Europeans (see Table 2). We only used responses from those who chose to answer the questions (dependent variables) on their use and knowledge of antibiotics. Of the 1,508 respondents, 560 were male (37.1%). Nearly half were middle class (47.9%), followed by working class (25.2%) and the lower middle class (18.9%). Only small proportions of respondents identified themselves as upper middle class (6.9%) or higher class in the society (1.2%). Most respondents (43.9%) lived in small or medium-sized towns; fewer than one third (28.1%) lived in a rural area or a village, and the rest (28%) were city dwellers.

H1 Testing (Linear Regression)

H1 examined the relationships between respondents' identification of proper antibiotic use and individual-level factors. Results showed that only respondents' knowledge was positively associated with their identification of *proper use* (β = .08, p <.01), suggesting that the more knowledgeable people are, the more likely they are to properly identify correct use of antibiotics. H1 is partially supported. See Table 3.

Table 3. Hierarchical Linear Regression Results on Associations Between Individual Factors and Identification of Proper (H1) and Intention to Follow Proper Treatment Plan (H2).

Independent Variable	Identification of proper antibiotic use		Intention to follow proper treatment plan	
	Model 1	Model 2	Model 1	Model 2
Block 1				
Gender	.05	.04	-.018	-.031
Type of Community	.02	.03	.016	.017
Social Class	.01	.00	.006	-.005
Block 2				
Interpersonal Communication		.01		-.098***
Medical Professionals		.06		.064*
Mass Media		.05		.125***
Trust in Interpersonal Comms		.02		.003
Trust in Medical Professionals		.01		.17***
Trust in Mass Media		.01		.095**
Knowledge of Antibiotic Use		.08**		.039
R^2	.003**	.013**	.001	.058***

* *p* < .05. ** *p* < .01. *** *p* < .001.

RQ1 Testing (Multilevel Modeling)

We first ran an ANOVA to show whether there is a need to conduct multilevel modeling. Results from our ANOVA showed statistically significant differences between the 28 countries in terms of scores for proper antibiotic use, $F(27,1480) = 2.882$, $p < 0.001$, indicating the need for multilevel analyses.

The goals of multilevel testing were to examine the effects of structural variables on the variance of the model when individual-level variables are nested in country groups. First, individual-level variables were entered as fixed effects. Next, structural variables were entered as fixed effects. Last, individual-level factors were entered as fixed effects and these country-level variables as random effects in one model. The first and second columns in Table 4 present the values of fixed effects for the individual and structural levels, respectively. The third column includes both values for fixed effects for the individual-level variables and values for random effects for the structural variables. For multilevel modeling, we reported unstandardized coefficients (*b*).

For RQ1, four individual-level variables were significantly associated with proper antibiotic use in terms of fixed effects (see model 1 in Table 4 under the "identification of proper use" variable). They included medical professional sources (*b* = 0.039, *p* < .05), mass media sources (*b* = 0.030, *p* < .05), and antibiotic use knowledge (*b* = 0.032, *p* < .01). This means that those who had received information on antibiotic use from medical professional and mass media sources, and those who were knowledgeable were more likely to use antibiotics properly.

Regarding random effects on proper antibiotic use, the country-level variables explained a small amount of variance for the model, showing some limited influence on the outcome variable. Among the structural variables, only Access to Advanced Education had a statistically significant relationship with the identification of proper antibiotic use (*b* = -0.21, *p* < .001) (see model 2 in Table 4 under the "identification of proper use" variable).

Table 4. Multilevel Models for Both Outcome Variables.

Independent variables	Identification of proper use			Intention to follow proper treatment procedures		
	Model 1 (Fixed Effects)	Model 2 (Fixed Effects)	Model 3 (Fixed & Random)	Model 1 (Fixed Effects)	Model 2 (Fixed Effects)	Model 3 (Fixed & Random)
Individual level						
Gender	0.045		0.056*	-0.044		-0.030
Social Class	0.016		0.018	0.020		0.051
Type of Community	0.002		-0.001	-0.018		-0.018
Interpersonal Communication	0.010		0.013	0.225***		0.218***
Medical Professionals	0.039*		0.038*	0.036		0.050
Mass Media	0.030*		0.025*	0.133***		0.127***
Trust in Interpersonal Communications	0.054		0.058	0.041		0.071
Trust in Medical Professionals	-0.001		-0.004	0.177***		0.125**
Trust in Mass Media	0.001		-0.007	0.129**		0.172***

Knowledge of Antibiotic Use	0.032**		0.029**	0.032		0.038
Wald Z	24.90**			132.14***		
Residual variance	0.190			0.780		
Intercept						
Structural level			*Random Effects*			
GDP per capita		0.002	0.0004		-0.005	0.0002
Nutrition & Basic Medical Care		0.045	0.0005		-0.44***	0.0002
Health & Wellness		0.002	0.0001		0.024***	0.0004
Access to Information & Communications		0.005	0.0005		0.017**	0.0008
Access to Advanced Education		-0.21***	0.0002		-0.053	0.0165
Intraclass correlation			0.003			0.030
Residual variance		0.188	0.184		0.80	0.736

* $p < .05$. ** $p < .01$. *** $p < .001$.

H2 Testing (Linear Regression)

In the exploratory step, again, we used hierarchical linear regression with all individual factors while controlling for demographics. For the intention to follow proper treatment procedures (H2), there was a mixture of protective factors within individuals' health literacy skills, including using sources from medical professionals (β = .06, $p < .05$) and from mass media (β = .13, $p < .001$), as well as their trust toward medical professionals (β = .17, $p < .001$) and toward mass media (β = .10, $p < .01$). Using interpersonal communication sources (β = -.10, $p < .001$), however, was negatively associated with behavioral intention;

this suggests that these health literacy factors are both a protective factor and a risk factor, thereby making the implementation of antibiotic-related education and policy more challenging. H2 received mixed support.

RQ2 (Multilevel Modeling)

To answer RQ2, we first performed ANOVAs on the outcome variables. Test results showed that *proper use plan* was significantly different between country groups, $F(27, 1480) = 3.947$, $p < 0.001$. To conduct multilevel modeling, again, we entered all the individual variables as fixed effects in the first stage. In the second stage, only country-level variables were included. Third individual-level variables were entered as fixed effects and structural variables as random effects.

For the intention to follow proper treatment procedures, several statistically significant individual-level health literacy predictors were found (see model 1 in Table 4 under the "intention to follow proper treatment procedures" variable). They included information from interpersonal communication ($b = 0.225$, $p < .001$) and mass media ($b = 0.133$, $p < .001$), as well as the two variables on trust: trust in medical professionals ($b = 0.177$, $p < .001$) and trust in mass media sources ($b = 0.129$, $p < .01$). This demonstrates that those who communicate with family and friends, receive information from mass media sources, and have higher trust in the media and health professionals were more likely to follow proper treatment.

Regarding random effects, the country-level variables explained 74% of variance for the model, showing stronger influence on the outcome variable. Three structural variables included Nutrition & Basic Medical care ($b = -0.44$, $p < .001$), Health & Wellness ($b = 0.024$, $p < .001$), and Access to Information & Communications ($b = 0.017$, $p < .01$) (see model 2 in Table 4 under the "intention to follow proper treatment procedures" variable). This means that citizens from countries with better Access to Information & Communications and stronger Health & Wellness will follow antibiotic use procedures properly. Counterintuitively, Nutrition & Basic Medical Care was negatively associated with following a proper treatment plan.

Discussion

Analyzing how EU citizens' understanding of antibiotic resistance through the lens of the combined health literacy and health-information-seeking model reveals the intricacies among the individual and structural factors that otherwise would have been overlooked. This study found that structural factors play a role with varying degrees of influence in EU citizens' identification and intention.

How Individual Factors Predicted Outcomes

Consistent with prior research (Kalichman et al., 2002; Shim et al., 2006; van der Molen, 1999), knowledge of antibiotics and treatment was associated with identification of proper antibiotic use. Interestingly, knowledge was not associated with behavioral intention, suggesting a gap of translating cognitive-based outcomes to actions.

Other health literacy measures were not associated with identification, but were associated with intention to follow proper treatment. For example, uses of and trust in medical professional and media sources all were significant positive predictors, adding evidence to health literacy theoretical research that posits a connection between health literacy and health-related outcomes (Longo, 2005; Longo et al., 2010; Squiers et al., 2012). While some medical professionals may not have enough time to properly advise patients on antibiotic use (Hart & Kariuki, 1998; Okeke, Lamikanra, & Edelman, 1999; Reardon, 2014), our results nevertheless show the importance of involving mass media and medical communities together in combating the antibiotic resistance crisis.

How Structural Factors Predicted Outcomes

Results from the multilevel models revealed that individual and structural factors both exerted varying degrees of influence. This is in line with the combined theoretical framework that posits a dynamic interplay between health literacy skills and ecological determinants in relation to health outcomes (Longo, 2005; Longo et al., 2010; Squiers et al., 2012). For identification of proper antibiotic use, one structural-level variable and three individual-level variables were significant predictors. Knowledge and medical professional and mass media sources were positively associated with identification. For this outcome variable, structural determinants have relatively limited effects on the model's variance. Moreover, advanced education was inversely related to identification. Future studies should continue to explore these nested influences using data from other non-EU countries in order to provide another layer of evidence to support this finding and beyond.

For intention to follow proper treatment, individuals' health literacy skills, such as using mass media, family, and friends as sources of information, as well as individuals' trust in mass media and media professionals, were significant predictors. This finding echoes prior research that has established a connection among sources of information, perceived trust of health information, and behavioral outcomes (Kalichman et al., 2002; Shim et al., 2006; van der Molen, 1999), specifically how sources of mass media and medical professionals complement each other (Cutilli, 2010; Dutta-Bergman, 2003; Hesse et al., 2005).

Structural variables had comparatively more effects on the model's variance for intention. Undoubtedly, these individual-level health literacy skills correspond to a country's development of access to information and communication, suggesting that continuing to invest in communication technology (i.e., mobile phone and Internet access) may complement any health initiatives while bringing about positive behavioral change in individuals through information sources. This finding may be of particular importance to developing countries fighting antibiotic resistance; research has advocated for the use of mobile phones in healthcare interventions (Kaplan, 2006).

In addition, two structural factors that represent a country's healthcare system and progress produced significant but opposing relationships when entered as fixed effects. Health & Wellness had a positive association with behavioral intention, whereas Nutrition & Basic Medical Care had a negative association with the outcome variable. These seemingly less intuitive findings in fact may reflect the qualitative difference between treatments at the beginning and the end-of-life spectrums, as well as between intervention and prevention approaches in these EU countries' healthcare systems. Our study reveals that

Nutrition & Basic Medical Care, which primarily looked at the beginning-of-life factors, may not capture the preventive care angle as described in Health & Wellness. In other words, increasing life expectancies and reducing the rate of chronic diseases focus on improving quality of life and may have a more relevant and immediate influence on positive behavioral intention outcomes.

When entered as fixed effect, however, Nutrition & Basic Medical Care had a negative association with the outcome variable. However, its random effect indicates that it has a low effect on the model, suggesting minimal variation between countries in the sample. Replicating this study using data from countries with different levels of progress may reveal a clearer picture of the counterintuitive result of Nutrition & Basic Medical Care.

Finally, it is surprising to find that GDP—a consistent predictor of a country's individual- and population-level health outcomes (e.g., mortality and self-reported health) in prior research (Macinko et al., 2003; Nixon & Ulmann, 2006; World Bank, 1993)—was not associated with the two outcomes. This nonsignificant finding echoes the emerging idea that other societal and education factors may better capture the nuances of health behaviors (Bradley et al., 2011; The Social Progress Imperative, 2017). This finding deserves further examination; besides economic developments, these European countries share similarities in many other aspects, and prior work has not incorporated other relevant distal-level dimensions such as those (Health & Wellness and Nutrition & Basic Medical Care) used in our study (Macinko et al., 2003; Nixon & Ulmann, 2006).

Contributions and Implications

This study significantly contributes to the literature of antibiotic resistance research and the combined framework in a number of ways. It applies health literacy and information seeking to antibiotic resistance research and expands the model by combining structural variables. Our theoretical and analytical strategy is consistent with the recent WHO One Health initiative, which calls for analyzing multiple touch points across various levels to combat antibiotic resistance (WHO, 2016). Given that health literacy is a dynamic process and that ecological determinants have a profound impact on health literacy in the area of information seeking and sources of information, our findings show that antibiotic resistance is a structural-related issue, as opposed to a purely individual-based medical problem. Investing in a country's information environment and improving healthcare access and quality while working with the medical communities and mass media in tandem could generate a trickle-down effect on citizens' knowledge and behavioral intention related to antibiotic use.

Limitations

This study is not without limitations. The nature of a secondary data set with predetermined variables prohibits us from distinguishing variations within mass media sources because they are not created equal, and quality of information may vary greatly. Additionally, the way in which behavioral outcome was queried in this secondary data set did not include a specific timeline, which, as suggested by Fishbein and Cappella (2006), may not adequately capture the extent of follow-up. Despite these measurement issues, the individual-level findings are largely consistent with prior literature (Anker et al., 2011; Hesse et al., 2005; Lambert & Loiselle, 2007; Niederdeppe et al., 2007). Finally, EU citizens' antibiotic use behavior was not measured nor included in this data set, thus limiting the analysis to knowledge and behavioral intention. While the results of this EU-based study may not be generalizable to other geographical contexts, they suggest that further development should be extended to other regions.

Conclusion

Antibiotic resistance is not a medical-only issue. Taking the structural variables into account, our multinational study using the 2016 Eurobarometer survey suggests that it should be approached from the societal and policy angle. Preventions and interventions should adjust their efforts, considering the impact of national infrastructure (Access to Information & Communications), and continue to invest in preventive care (Health & Wellness). Investing in these structural resources and involving changes at the national policy level may produce effective and sustainable changes that will ultimately enhance citizens' health literacy skills and their identification and behavioral intention of using antibiotics properly.

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