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National disparities in the relationship between antimicrobial resistance and antimicrobial consumption in Europe: an observational study in 29 countries.

Short title: Antimicrobial resistance and consumption in Europe

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Abstract

Background Antimicrobial resistance in invasive infections is driven mainly by human antimicrobial consumption. Limited cross-national comparative evidence exists about variation in antimicrobial consumption and effect on resistance.

Methods and Findings We examined the relationship between national community antimicrobial consumption rates (2013) and national hospital antimicrobial resistance rates (2014) across 29 countries in the European Economic Area (EEA). Consumption rates were obtained from European Surveillance of Antimicrobial Consumption Network (ESAC-Net). Resistance data were obtained from European Antimicrobial Resistance Surveillance Network (EARS-Net), based on 196,480 invasive isolates in 2014. Data availability and consistency were good. Some countries did not report figures for each strain of resistant bacteria. National antimicrobial consumption rates (2013) varied from <13DDD (Estonia, Netherlands, and Sweden) to ≥30 DDD (France, Greece, Romania) per 1000 population/day. National antimicrobial resistance rates (hospital isolates, 15 species) also varied from <6.1% (Finland, Iceland, Sweden) to >37.2% (Bulgaria, Greece, Romania, Slovakia). National antimicrobial consumption rates (2013) showed strong to moderate correlation with national hospital antimicrobial resistance rates (2014) in 19 strains of bacteria (r=0.84 to r=0.39). Some countries defied the trend with high consumption and low resistance (France, Belgium, Luxembourg) or low consumption and high resistance (Bulgaria, Hungary, Latvia).

Conclusions We found associations between national community antimicrobial consumption and national hospital antimicrobial resistance across a wide range of bacteria. These associations were not uniform. Different mechanisms may drive resistance in hospital-based invasive infections. Future research on international variations in

antimicrobial resistance should consider environmental factors, agricultural use, vaccination policies and prescribing quality.

Introduction

Antimicrobial resistance is a serious global threat to public health. Increasing human antimicrobial consumption is widely considered to be highly influential, with agricultural use, environmental pollution, clonal and horizontal spread and long-term persistence also contributory.[1,2] Recent evidence comes from meta-analyses that report positive associations between antimicrobial consumption and the development of resistance at both population and individual levels.[3,4]

Across Europe, there is wide variation at national level in both antimicrobial resistance and consumption. In general, lower rates of antimicrobial resistance are found in northern European countries and higher rates of resistance found in southern European countries.[5] Previous studies have found strong correlations between specific antimicrobial consumption and resistances but have only studied a limited number of resistant strains of bacteria, mainly *Streptococcus*, *Staphylococcus* and *Escherichia coli.*[4-6] A systematic review and meta-analysis of 243 studies examined both population and individual level data, mainly in Europe.[4] It confirmed a positive relationship between antimicrobial consumption and resistance (pooled effect size (odds ratio) of 2.3 (95% CI 2.2 – 2.5)), although this was only observed for enteric bacteria and *Streptococcus*. The authors were not able to identify factors consistently predictive of this relationship.[4]

The aim of this study was to evaluate the relationship between antimicrobial consumption and resistance across Europe, with focus on a wide range of resistant bacteria.

Methods

Study Design

This was a cross-sectional study of routinely collected data comparing national community level antimicrobial consumption rates and national hospital antimicrobial resistance rates across 29 countries in the European Economic Area (EEA).

Data sources, measures and procedures

We compared antimicrobial consumption rates in 2013 with antimicrobial resistance rates in 2014 in order to reflect a 1-year time lag between antimicrobial use and the subsequent development of resistance, in accordance with previous studies.[5,7] We used national data for antimicrobial consumption from ESAC-Net, an interactive online database which provides European reference data on antimicrobial consumption from hospital and community settings.[8] The reports from the database are published by the European Surveillance System (TESSy).[9] In 2013, antimicrobial consumption data were available for 30 European countries in the EEA. Most countries based their antimicrobial consumption data on community or primary care data (i.e. outside of hospital). Cyprus, Iceland and Romania provided combined community and hospital antimicrobial consumption data only. Approximately 90% of national antimicrobial consumption is based in the community so the figures provided for these three countries may overestimate community consumption. [10] Data were obtained for the years 2009-2013 to allow annual fluctuations in antimicrobial consumption to be observed. Data were provided in the form of DDD per 1000 inhabitants per day. DDD, as defined by the WHO, is the assumed average treatment dose per day for a drug prescribed for its main indication in adults.[11] Drugs that have been assigned a code in the Anatomical Therapeutic Chemical (ATC) classification system were assigned a DDD. The national antimicrobial consumption figures refer to ATC group J01 (antibacterials for systemic use). Data sources included either sales or reimbursement figures or both and varied by country. Sales data include sales of antimicrobials obtained without a prescription. Full details of data sources can be found on the ECDC website.[8]

The main outcome measures were antimicrobial resistance levels in 2014. We obtained these data from the EARS-Net interactive database, also provided through TESSy.[12] Antimicrobial resistance data in the EARS-Net database were exclusively based on invasive isolates from blood or CSF and were collected through a voluntary network of national surveillance systems in each participating country from 900 laboratories serving 1400 hospitals. National data were uploaded directly by the national data manager to TESSy on a yearly basis. [13] Isolates have been reported consistently to EARS-Net by most countries since 2003. Specific resistance levels were only reported if at least 10 isolates per country for the bacterial species in question were tested. We looked at data on all antimicrobial resistant strains that were collected by TESSy (26 strains in total: see Table 2), including resistant strains of *Enterococcus faecalis*, *Enterococcus faecium, Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pneumoniae*.

We developed a value for resistance and consumption for each country. The resistance 'value' was the mean rate of hospital antimicrobial resistance per country for 2014. This value included the 15 resistant strains of bacteria which showed a positive correlation (r=>0.3) with overall antimicrobial consumption that were available for every country (Table 1: included strains in bold). The consumption 'value' was the overall national consumption rate (ATC J01 group) reported by the ECDC for 2013 (DDD per 1000 inhabitants per day)

(Supplementary Table 1, available online). We then developed a ratio of mean antimicrobial resistance to overall antimicrobial consumption per country to describe the pattern of the association between high antimicrobial consumption and high resistance, and to identify outliers in this association.

Statistical methods

We assessed the correlation (Pearson's r) between overall antimicrobial consumption and antimicrobial resistance for 29 European countries. Firstly, we assessed correlation between overall antimicrobial consumption and resistance rates for each organism (n=26). We then assessed correlation between antimicrobial consumption values for the antibiotic class specific to the resistant strain and the rates of resistance in that strain. Finally, we compared the national mean resistance rates to overall antimicrobial consumption as described above.

Results

Antimicrobial consumption data were available for 30 countries for 2013. The Netherlands, Estonia, and Sweden had the lowest rates of overall antimicrobial consumption in 2013 (≤13 DDD per 1000 inhabitants per day). France, Romania and Greece had the highest (≥30 DDD per 1000 inhabitants per day). The ranges of consumption rates were wide. Year to year variation was small except for Romania between 2009 and 2011. The overall national consumption of antimicrobials between 2009 and 2013 is shown in Supplementary Table 1 (available online). The types of antimicrobials used and their rates of use in each EEA country in 2013 are shown in Supplementary Figure 1 (available online).

Resistance data were available for 29 EEA countries for 2014. Data were not available for Poland. Resistance rates were based on 196,480 invasive isolates in 2014, a mean of 6549 isolates per country (Table 2). Seven countries reported less than 1000 isolates: Bulgaria (847), Cyprus (540), Estonia (967), Iceland (299), Latvia (670), Luxembourg (716), and Malta (299). Swedish data for *E. coli* resistant to aminopenicillins were missing in 2014 (2013 data were used in their place), and Greek data for *S. pneumoniae* resistant to macrolides were missing for 2013 and 2014.

Figure 1 shows the relationship across 29 countries between overall antimicrobial consumption for 2013 and resistance rates for 2014 in three common pathogenic strains of bacteria: *E. coli* resistant to aminopenicillins; MRSA; and *S. pneumoniae* resistant to macrolides. This figure demonstrates the overall trend of lower antimicrobial resistance associated with lower antimicrobial consumption. Of the three strains, *E. coli* resistant to aminopenicillins represented the highest rate of antimicrobial resistance across all countries.

Figure 1

The correlation scores between overall and specific antimicrobial consumption and resistance rates of each of the 26 resistant strains of bacteria for all countries studied are shown in Table 1. Strong or moderate correlations were observed between 19 of the resistant strains and overall antimicrobial consumption. Strong or moderate correlations were observed between 12 resistant strains and specific antimicrobial consumption including the 3 pathogenic strains in Figure 1. Of note is the strong correlation between the consumption of fluoroquinolones and rates of resistance of *E. coli* to fluoroquinolones (r=0.84, p = <0.001).

Table 1

Table 2 shows the ratios of mean national antimicrobial resistance to overall national antimicrobial consumption. Mean national antimicrobial resistance rates were highest in Romania (45.9%) followed by Slovakia (40.3%) and Greece (37.8%). Iceland, Finland and Sweden had the lowest mean antimicrobial resistance rates (5.3%, 5.9% and 6.7%, respectively). France, Belgium and Luxembourg, each with high rates of consumption, had low rates of mean antimicrobial resistance. Latvia, Bulgaria and Hungary, each with low rates of consumption had high rates of antimicrobial resistance. Total antimicrobial consumption (all countries) was moderately correlated with mean resistance (all countries) (r= 0.54, p = 0.003) (see Figure 2). The inclusion of all resistant strains available for each country in the analysis, regardless of whether there was a positive correlation with overall consumption, did not alter the results.

Table 2

Figure 2

Discussion

We found moderate to strong correlations between rates of overall community antimicrobial consumption and hospital antimicrobial resistance rates across 29 European countries, with respect to 19 strains of resistant bacteria; significant correlation was not found for the remaining 7 resistant strains included in our study. We also found moderate to strong correlations between specific community antimicrobial consumption and resistance rates with respect to 12 out of 23 strains of resistant bacteria for which we could access data. In addition, we discovered significant disparities across Europe when comparing national ratios of mean resistance (incorporating 15 strains of resistant bacteria) to overall antimicrobial consumption.

Our study confirms the relationship between community antimicrobial consumption and serious resistant infections in patients in hospital. It is striking that the antibiotics were prescribed (and most likely consumed) in the community but the bacterial resistance reported was found in invasive hospital specimens from blood or CSF. Our study was unable to determine whether the infections were acquired in hospital or the community. Resistant strains often emerge within hospital due to the frequent use of broad-spectrum antibiotics as well as the proximity of patients to each other and healthcare workers.

Our findings emphasise the importance of reducing antibiotic consumption in the community at national level to limit resistance in serious hospital infections. The strongest correlations were seen between total national antimicrobial consumption and MRSA, carbapenem resistant *K. pneumoniae,* and macrolide resistant *S. pneumoniae*. Regarding correlations between specific antibiotic consumption and species resistance (i.e. a specific antibiotic and an organism resistant to that antibiotic) strongest correlations were seen for fluoroquinolone resistant *E coli*, aminoglycoside resistant *P.aeruginosa,* and *E. coli* resistant to third generation cephalosporins. Many of these associations accord with earlier studies. [5,6] We found no correlation between consumption of beta lactams and *S. pneumoniae* resistant to penicillins in contrast to previous studies (Goossens *et al*: 2000-1 data, Spearman's rho = 0.84 (0.62-0.94), 19 countries [5]; Van de Sande Bruisma *et al*: 2003-4 data, Pearson's r = 0.78 (0.48-0.92), 17 countries [6]). Both studies looked at a smaller number of countries than the present study, and during an earlier time-frame.

Our study found striking exceptions to the previously reported international pattern of associations between low antibiotic consumption and low resistance, and high antibiotic consumption and high resistance. At the time of our analysis, those countries with high rates of antimicrobial consumption and low rates of resistance (France, Luxembourg and Belgium) were all high prescribers of beta-lactam antimicrobials (a class of antibiotics which includes penicillins, amoxicillin, flucloxacillin, cephalosporins and carbapenems), the most commonly prescribed antibiotics in Europe.[10] In the early 2000's, European campaigns to reduce overall antimicrobial use [14-16] achieved substantial reductions in prescribing and were associated with subsequent reductions in antimicrobial resistance, particularly in penicillin-non-susceptible *S. pneumoniae* (PNSP). [16,17] These campaigns coincided with the introduction of the Heptavalent Pneumococcal Conjugate Vaccine (PCV7) into the vaccination schedule in France. [17,18] The subsequent widespread use of PCV immunisation across Europe is considered to have influenced the decrease in penicillin resistance-levels by eliminating infections with common 'classic' resistant serotypes. [13,18] This may explain why we found no correlation between beta lactams and *S. pneumoniae* resistant to penicillin in our 2013/14 data. Penicillin resistant streptococci have remained low since 2010.[12] PCVs are part of the vaccination schedule for the majority of European countries but there are variations in routine systems for monitoring PCV coverage[19]. It is possible that in countries where the uptake of vaccination is poor, herd immunity is insufficient to keep population levels of resistant *S. pneumoniae* low. Variations in reporting practices of *S. pneumoniae* resistance also decrease our ability to draw meaningful conclusions about the relationship between consumption and resistance with regards to *S. pneumoniae* and beta lactam consumption.[13]

Antimicrobial prescribing 'quality' may also contribute to the between country discrepancies observed in the relationship between resistance and consumption rates at national level.[20] Quality indicators include factors such as total amount of specific antimicrobials consumed, ratio between consumption volumes of broad and narrow spectrum antimicrobials, and seasonal variation of total antimicrobial use and quinolone use.[20-22] High rates of resistance despite low volumes of antimicrobial prescribing were identified in Latvia, Bulgaria and Hungary. Possible reasons for this discrepancy include high seasonal variation (Hungary), [22] and high use of fluoroquinolones (Hungary and Bulgaria). [21,22] Neither of these factors appear to apply in Latvia, which reported moderate seasonal variation in antimicrobial consumption. However, high levels of antimicrobial prescribing for upper respiratory tract infections (usually caused by viruses) and a trend towards using broader spectrum antimicrobials such as quinolones for uncomplicated urinary tract infection have been reported from Latvia. [23] Controlling high rates of antimicrobial resistance in countries with low volumes of consumption may require greater adherence to prescribing guidelines and formularies.

The major strength of our study is its size. Using routinely collected data we compared 29 different countries regarding 26 different strains of resistant bacteria. We believe this to be the most comprehensive investigation so far reported in Europe. Our use of a unique mean resistance score offered a novel method for analysing broader national trends, which allowed us to highlight international discrepancies not previously reported in the literature. We also believe that using data from invasive samples (blood and CSF) to determine resistance is an important strength of our study, contributing to greater consistency of reporting.[13] National variations in the number of invasive samples included may reflect differences between countries in the frequency of use of blood cultures.

The limitations of our study were mainly related to data availability and comprehensiveness. Not all countries reported figures for community antimicrobial consumption or for each strain of resistant bacteria, for every year, although data consistency has improved greatly.[13]

In summary, this study has highlighted the strength of association between total and specific community consumption rates of antibiotics and resistance rates in up to 20 strains of resistant bacteria across 29 European countries. The community basis of the observed antimicrobial consumption rates emphasises the important influence of choice of antibiotic prescription in the community on the risk of resistance in serious hospital infections. The discrepancies we identified in this association imply that antimicrobial prescribing quality contributes to patterns of resistance as well as the volume of consumption. Future work on international variations in antimicrobial resistance could address the role of environmental factors, socio-economic status and overcrowding, agricultural antimicrobial practices, as well as vaccination policies and the quality of prescribing.

Funding

This study was carried out as part of our routine work within the department.

Transparency declarations

We declare no competing interests.

Contributors

LMcD collected, collated, analysed and interpreted the data, and wrote the final manuscript. LMcD, DA, MA, AD, and PW conceived the study. DA, MA, AD, UM and PW contributed to the data analysis and interpretation, and revised the final manuscript. PW is guarantor for the study.

Ethical approval

Ethical approval was not required as the data used in this study are in the public domain.

References

1. Laxminarayan R, Duse A, Wattal C*, et al.* Antibiotic resistance—the need for global solutions. *The Lancet Infectious Diseases* 2013;**13**:1057-98.
2. Holmes AH, Moore LS, Sundsfjord A*, et al.* Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet* 2016;**387**:176-87.
3. Costelloe C, Metcalfe C, Lovering A*, et al.* Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ* 2010;**340**:c2096.
4. Bell BG, Schellevis F, Stobberingh E*, et al.* A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. *BMC Infect Dis* 2014;**14**:13.
5. Goossens H, Ferech M, Vander Stichele R*, et al.* Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet.* 2005;**365**:579-87.
6. van de Sande-Bruinsma N, Grundmann H, Verloo D*, et al.* Antimicrobial Drug Use and Resistance in Europe. *Emerging Infectious Diseases* 2008;**14**:1722-30.
7. Bergman M, Huikko S, Pihlajamaki M*, et al.* Effect of macrolide consumption on erythromycin resistance in Streptococcus pyogenes in Finland in 1997-2001. *Clin Infect Dis* 2004;**38**:1251-6.

8. European Centre for Disease Prevention and Control 2016 *Antimicrobial consumption interactive database (ESAC-Net)* http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/esac-net-database/Pages/database.aspx

9. European Centre for Disease Prevention and Control 2016 *Indicator-based surveillance* http://ecdc.europa.eu/en/activities/surveillance/Pages/index.aspx

10. European Centre for Disease Prevention and Control 2014 *Summary of the latest data on antibiotic consumption in the European Union* http://ecdc.europa.eu/en/eaad/antibiotics-get-informed/antibiotics-resistance-consumption/Documents/antibiotics-consumption-EU-data-2014.pdf

11. WHO Collaboration Centre for Drug Statistics Methodology 2016 *Definition and general considerations* http://www.whocc.no/ddd/definition_and_general_considera/

12. European Centre for Disease Prevention and Control 2016 *Antimicrobial resistance interactive database (EARS-Net)* http://atlas.ecdc.europa.eu/public/index.aspx?Instance=GeneralAtlas

13. European Centre for Disease Prevention and Control 2015 *Antimicrobial resistance surveillance in Europe 2014* http://ecdc.europa.eu/en/publications/publications/antimicrobial-resistance-europe-2014.pdf

14. Sabuncu E, David J, Bernede-Bauduin C*, et al.* Significant reduction of antibiotic use in the community after a nationwide campaign in France, 2002-2007. *PLoS Med* 2009;**6**:e1000084.

15. Goossens H, Coenen S, Costers M*, et al.* Achievements of the Belgian Antibiotic Policy Coordination Committee (BAPCOC). *Euro Surveill* 2008;**13**.

16. Huttner B, Goossens H, Verheij T*, et al.* Characteristics and outcomes of public campaigns aimed at improving the use of antibiotics in outpatients in high-income countries. *Lancet Infect Dis* 2010;**10**:17-31.

17. Cohen R, Levy C, de La Rocque F*, et al.* Impact of pneumococcal conjugate vaccine and of reduction of antibiotic use on nasopharyngeal carriage of nonsusceptible pneumococci in children with acute otitis media. *Pediatr Infect Dis J* 2006;**25**:1001-7.

18. Cohen R, Biscardi S, Levy C. The multifaceted impact of pneumococcal conjugate vaccine implementation in children in France between 2001 to 2014. *Hum Vaccin Immunother* 2016;**12**:277-84.

19. Castiglia P. Recommendations for pneumococcal immunization outside routine childhood immunization programs in Western Europe. *Adv Ther* 2014;**31**:1011-44.

20. Coenen S, Ferech M, Haaijer-Ruskamp FM*, et al.* European Surveillance of Antimicrobial Consumption (ESAC): quality indicators for outpatient antibiotic use in Europe. *Qual Saf Health Care* 2007;**16**:440-5.

21. Adriaenssens N, Coenen S, Versporten A*, et al.* European Surveillance of Antimicrobial Consumption (ESAC): outpatient quinolone use in Europe (1997-2009). *J Antimicrob Chemother* 2011;**66 Suppl 6**:vi47-56.

22. European Centre for Disease Prevention and Control 2016 *Quality indicators for antibiotic consumption in the community* http://ecdc.europa.eu/en/healthtopics/antimicrobial-resistance-and-consumption/antimicrobial-consumption/esac-net-database/Pages/quality-indicators-primary-care.aspx

23. Dumpis U, Dimina E, Akermanis M*, et al.* Assessment of antibiotic prescribing in Latvian general practitioners. *BMC Fam Pract* 2013;**14**:9.

Table 1. Correlation between overall and specific antimicrobial consumption (2013) and resistance (2014) across 29 European countries
(descending order of correlation strength)

Resistant species of bacteria[1] (2014) (ATC[2] code of specific antibiotic studied)	**Correlation with overall[3] (specific[4]) consumption (2013) all countries** (Pearson's r)
MRSA (J01C)	0.64** (0.53**)
K. pneumoniae resistant to carbapenems (J01DD)	0.58** (ns)
S. pneumoniae resistant to macrolides (J011FA)	0.56** (0.49**)
***E. coli* resistant to fluoroquinolones** (J01MA)	0.56** (0.84**)
***E. coli* resistant to aminopenicillins** (J01C)	0.53** (0.52**)
***E. coli* resistant to carbapenems** (J01DH)	0.52** (ns)
P. aeruginosa resistant to amikacin (J01GB06)	0.51** (n/a)
***P. aeruginosa* resistant to aminoglycosides** (J01G)	0.49** (0.67**)
***K. pneumoniae* resistant to fluoroquinolones** (J01MA)	0.48** (0.52**)
***E. faecalis* resistant to vancomycin** (J01X)	0.48** (ns)
***E. coli* resistant to 3rd Generation cephalosporins** (J01DD)	0.46* (0.55**)
***K. pneumoniae* resistant to 3rd generation cephalosporins** (J01DD)	0.44* (0.39*)
Multidrug resistant *K. pneumoniae*	0.43* (n/a)
***P. aeruginosa* resistant to carbapenems** (J01DH)	0.42* (ns)
***P. aeruginosa* resistant to fluoroquinolones** (J01MA)	0.42* (0.47**)
***E. faecium* resistant to vancomycin** (J01X)	0.41* (0.49**)
S. aureus resistant to rifampicin (J04AB02)	0.40* (n/a)
***K. pneumoniae* resistant to aminoglycosides** (J01G)	0.39* (0.5**)
***E. coli* resistant to aminoglycosides** (J01G)	0.38* (ns)
P. aeruginosa resistant to piperacillin (J01CA)	ns (ns)
P. aeruginosa resistant to ceftazidime (J01DD)	ns (ns)
S. pneumoniae resistant to penicillins (J01C)	ns (ns)
E. faecalis resistant to high level gentamicin (J01GB)	ns (0.56**)
E. faecalis resistant to aminopenicillins (J01C)	ns (ns)
E. faecium resistant to aminopenicillins (J01C)	ns (ns)
E. faecium resistant to high level gentamicin (J01GB)	ns (ns)

ns = result not significant, n/a= data not available

**p<0.05, **p <0.01*

[1] The numbers of invasive isolates for each species were: S pneumoniae (11,516), S Aureus (43,794), E coli (86,580), enterococci (22,291), K pneumoniae (20,068), P. Aeruginosa (11,973). Species in bold are included in mean resistance score

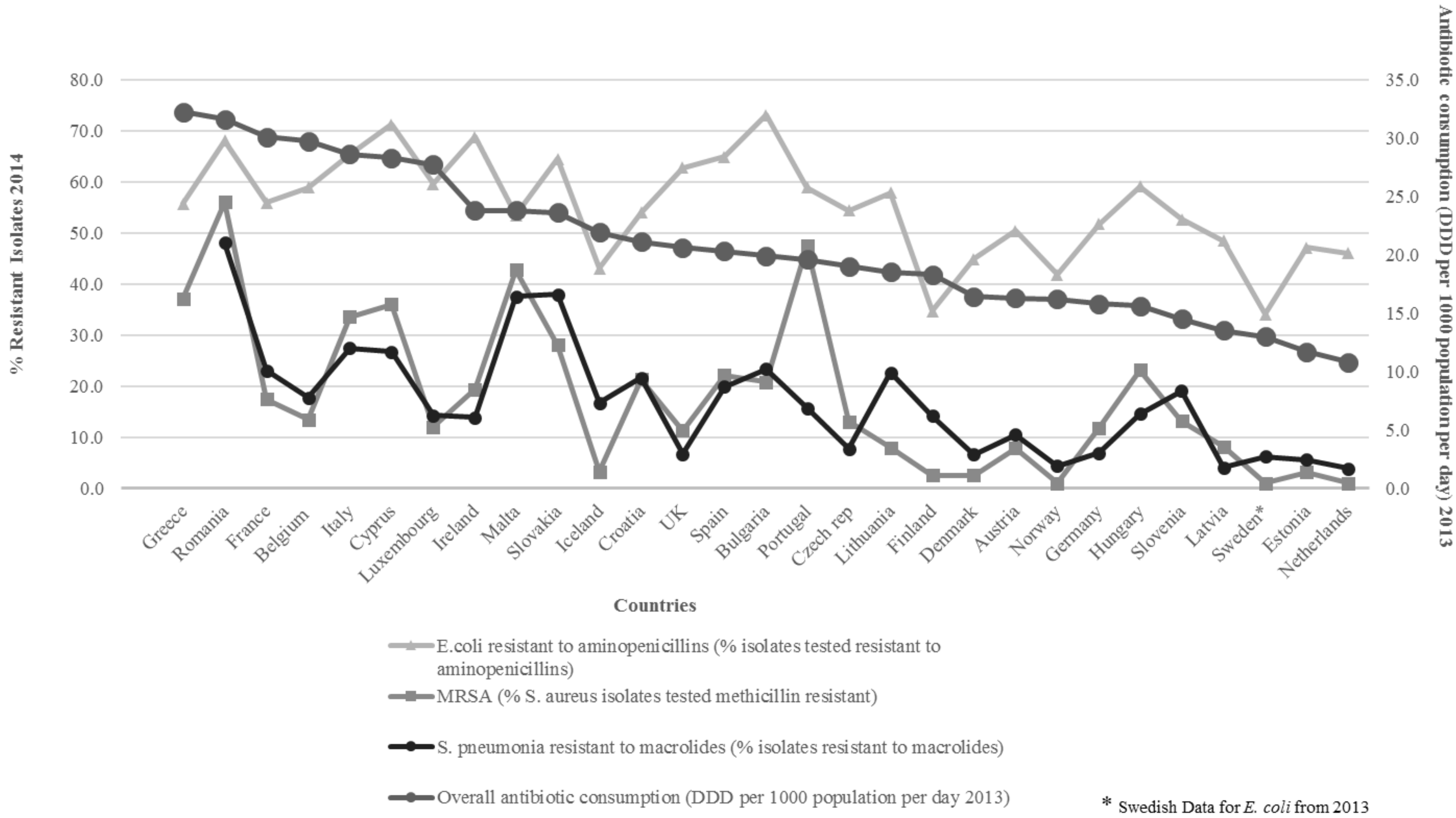
[2] ATC = anatomical therapeutic classification

[3] All antimicrobial consumption (ATC J01 codes only)

[4] *Specific consumption refers to the consumption of the antibiotic to which the organism is resistant.*

Figure 1 The relationship between consumption and resistance in 3 pathogenic strains of bacteria

The relationship across Europe between total antimicrobial consumption for 2013 and resistance rates for 2014 in 3 pathogenic strains of bacteria: *E coli, MRSA*, and *S. pneumoniae*



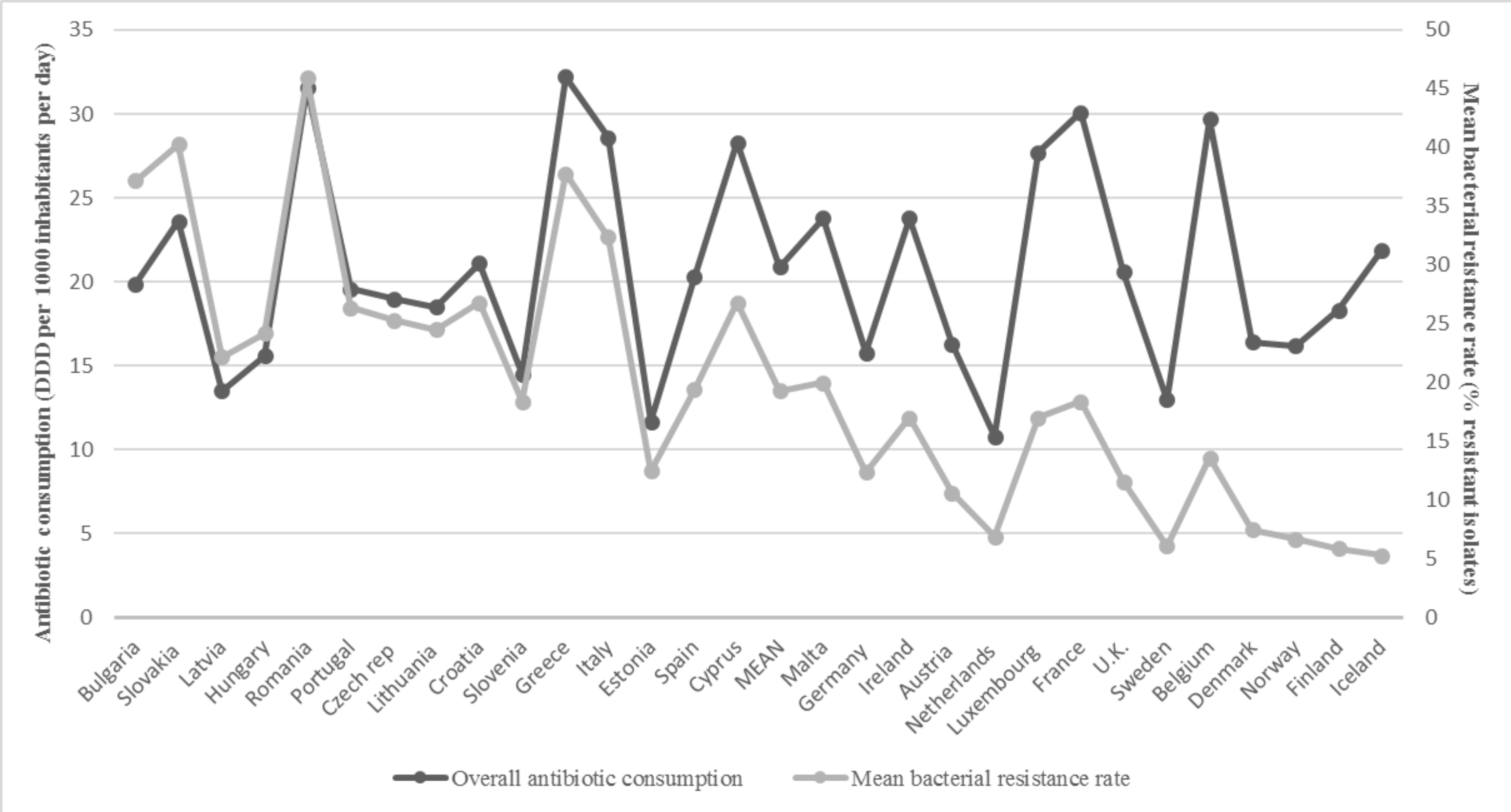
% Resistant Isolates 2014
Antibiotic consumption (DDD per 1000 population per day) 2013
Countries
Greece
Romania
France
Belgium
Italy
Cyprus
Luxembourg
Ireland
Malta
Slovakia
Iceland
Croatia
UK
Spain
Bulgaria
Portugal
Czech rep
Lithuania
Finland
Denmark
Austria
Norway
Germany
Hungary
Slovenia
Latvia
Sweden*
Estonia
Netherlands
E.coli resistant to aminopenicillins (% isolates tested resistant to aminopenicillins)
MRSA (% S. aureus isolates tested methicillin resistant)
S. pneumonia resistant to macrolides (% isolates resistant to macrolides)
Overall antibiotic consumption (DDD per 1000 population per day 2013)
* Swedish Data for E. coli from 2013

Table 2. National antimicrobial consumption rates (2013) and mean national antimicrobial resistance rates (2014) per European Country

Country *(n= number of isolates reported)*	National antimicrobial consumption rate[1] (2013) *(DDD per 1000 inhabitants per day)*	National mean antimicrobial resistance rate[2] (2014) *(%)*	Ratio of resistance to consumption[3]
Bulgaria (847)	19.9	37.2	1.9*
Slovakia (2,742)	23.6	40.3	1.7
Latvia (670)	13.5	22.2	1.6*
Hungary (5,303)	15.6	24.2	1.6*
Romania[4] (1,268)	31.6	45.9	1.5
Portugal (12,871)	19.6	26.4	1.3*
Czech rep (7,556)	19.0	25.3	1.3*
Lithuania (1,351)	18.5	24.5	1.3*
Croatia (2,480)	21.1	26.8	1.3
Slovenia (2,591)	14.5	18.4	1.3
Greece (4,216)	32.2	37.8	1.2
Italy (9,886)	28.6	32.4	1.1
Estonia (967)	11.7	12.5	1.1
Spain (12,042)	20.3	19.4	1.0*
Cyprus[1] (540)	28.3	26.8	0.9
MEAN (6,549)	**20.9**	**19.30**	**0.9**
Malta (550)	23.8	20.0	0.8
Germany (13,856)	15.8	12.4	0.8
Ireland (5339)	23.8	17.0	0.7**
Austria (10,603)	16.3	10.6	0.6
Netherlands (13,237)	10.8	6.9	0.6
Luxembourg (716)	27.7	17.0	0.6**
France (23,182)	30.1	18.4	0.6**
U.K. (15,040)	20.6	11.6	0.6
Sweden (13,638)	13.0	6.1	0.5
Belgium (6,531)	29.7	13.6	0.5**
Denmark (9,718)	16.4	7.5	0.5
Norway (7,271)	16.2	6.7	0.4
Finland (8,137)	18.3	5.9	0.3
Iceland[4,a] (299)	21.9	5.3	0.2

[1] ATC Code J01 group (antibacterials for systemic use)
[2] Mean percentage isolate resistance rate, based on 15 species of resistant bacteria (see Table 1)
[3] higher ratio values indicate high rates of resistance for a given volume of antibiotic consumption
[4] Consumption figures based on combined hospital and community data which may overestimate consumption
** – country demonstrates lower than average consumption but higher than average resistance*
*** – country demonstrates higher than average consumption but lower than average resistance*
[a] Iceland not highlighted as demonstrating higher than average consumption with lower than average resistance as total care data were used

Figure 2. Total antimicrobial consumption and mean antimicrobial resistance for 29 European Countries (ordered by ratio of resistance to consumption)



Overall correlation between consumption and resistance r = 0.54, *p* =0.003; number = 29

Closed circles – overall antibiotic consumption, filled squares – mean bacterial resistance