Governance e determinanti socio-economici e loro effetti sulla resistenza antimicrobica

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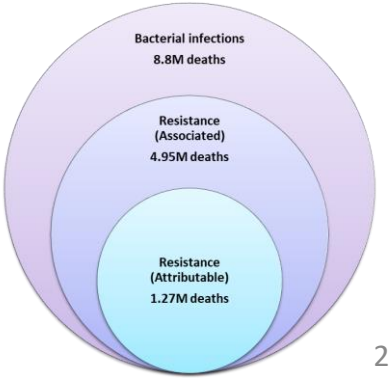
Firenze, 7 giugno 2023

1. **Pathogens with high pandemic potential**

2. **Chemical, biological, radiological and nuclear (CBRN) threats originating from accidental or deliberate release.**

3. **Antimicrobial resistance**, which pose one of the greatest risk to human health, with antibacterial resistance alone causing an annual estimate of 1.27 million deaths globally.



*"**Globally**, between **1.27 million** and **4.95 million** people died because of **bacterial antimicrobial resistance**, …"*

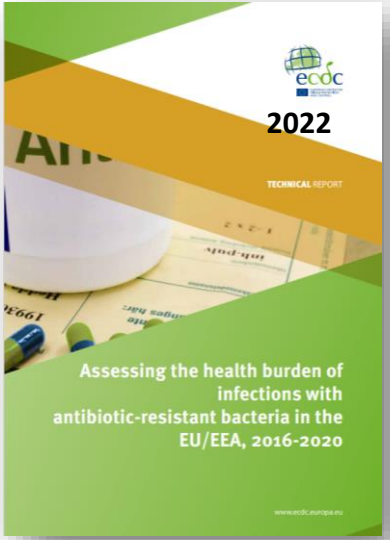
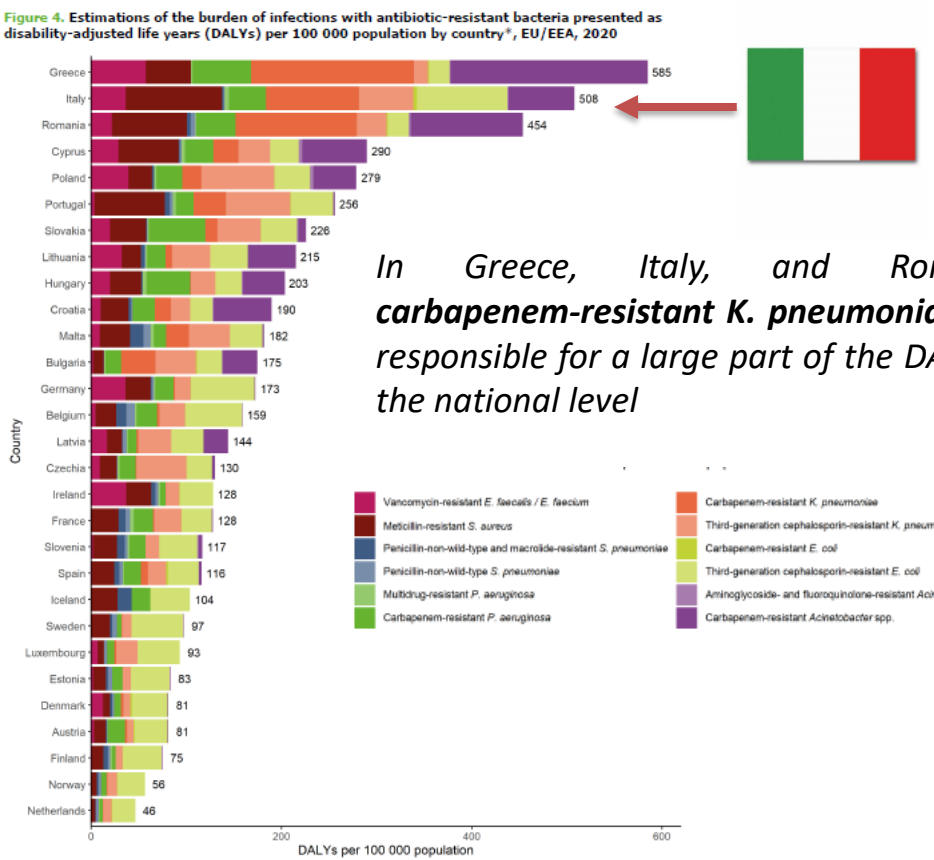
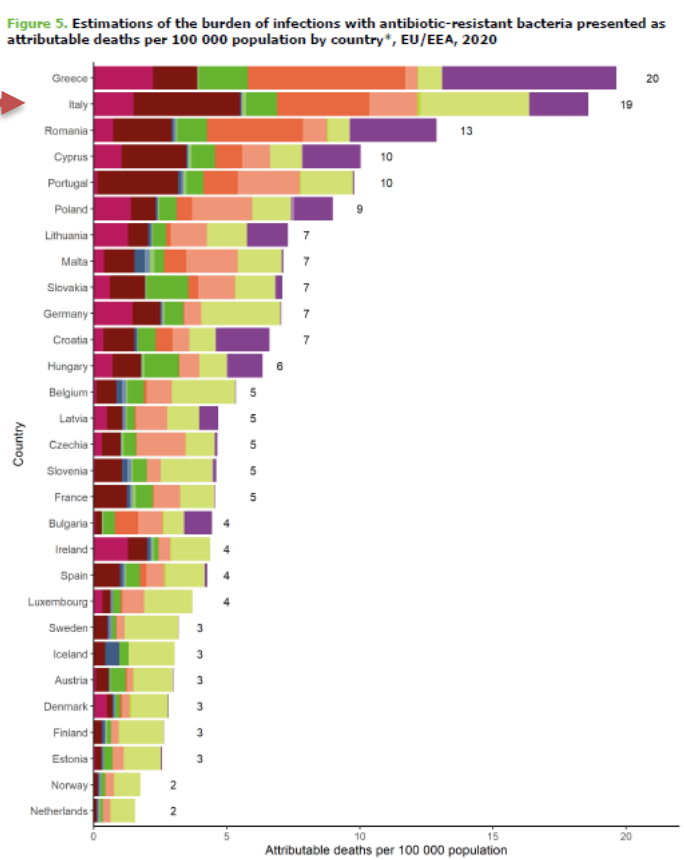


Table 2. Total number of blood isolates of the selected antibiotic-resistant bacteria as reported to EARS-Net, and estimated number of bloodstream infections, number of infections, number of attributable deaths and number of disability-adjusted life years (DALYs), EU/EEA, 2016-2020

	2016	2017	2018	2019	2020
Number of blood isolates as reported to EARS-Net*	39 729	44 306	53 557	54 450	51 798
Estimated number of bloodstream infections after correction for population coverage	107 404	109 556	127 896	134 277	122 070
Estimated median number of infections, all types (95% UI)	685 433 (589 451 - 792 873)	701 816 (603 052 - 811 925)	822 075 (706 070 - 951 816)	865 767 (742 802 - 1 003 591)	801 517 (684 955 - 932 213)
Estimated median number of attributable deaths (95% UI)	30 730 (26 935 - 34 836)	31 178 (27 388 - 35 296)	36 605 (32 227 - 41 352)	38 710 (34 053 - 43 748)	35 813 (31 395 - 40 584)
Estimated median number of DALYs (95% UI)	909 488 (813 858 – 1 013 060)	918 117 (820 200 – 1 024 443)	1 046 858 (940 859 – 1 161 268)	1 101 288 (988 703 – 1 222 498)	1 014 799 (908 022 – 1 129 999)

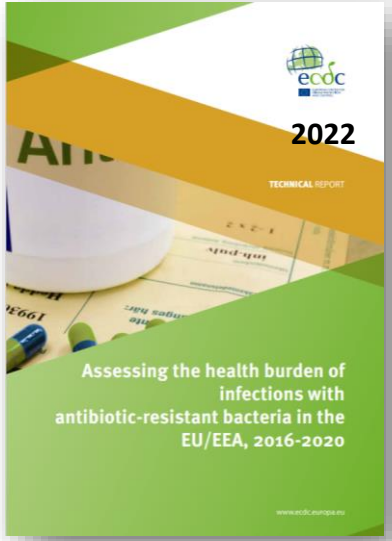
*Changes in annual burden estimates can be affected by **changes in surveillance**, use of different antimicrobial **susceptibility testing** guidelines, as well as potential changes or issues in the **data reporting** at national level as well as **population coverage of the surveillance**. This is especially relevant for 2020 data, with data submission in 2021, when the COVID-19 pandemic placed pressure on all public health services in EU/EEA countries*

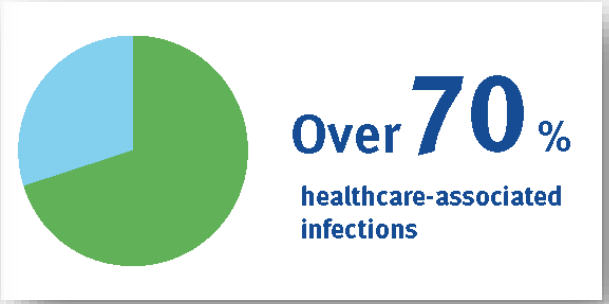




*In Greece, Italy, and Romania, **carbapenem-resistant K. pneumoniae** was responsible for a large part of the DALYs at the national level*

… the overall burden of infections with antibiotic resistant bacteria was estimated to be the highest in Greece, Italy, and Romania, … with the highest individual yearly estimates occurring in Romania in 2018-2019, Greece in 2020 and Italy in 2019-2020





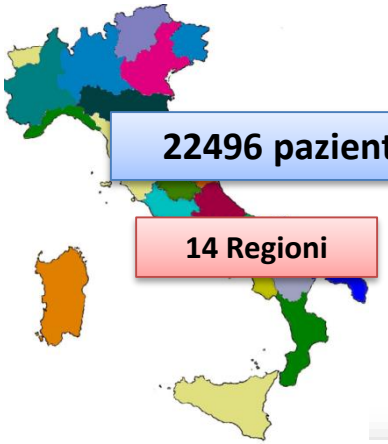
- ✓ **70.9%** dei casi di infezioni associate a batteri resistenti agli antibiotici erano **ICA**
- ✓ 71.4% morti attribuibili
- ✓ 73.0% DALYs

5 May 2023

- ✓ Incidenza di ICA nelle UTI europee nel 2019: **7,4 per 100 pazienti**
- ✓ Variabilità tra i Paesi europei
- ✓ Elevati tassi di resistenza agli antibiotici

“Sorveglianza attiva Prospettica delle Infezioni Nosocomiali nelle Unità di Terapia Intensiva”

SPIN-UTI 2006-2021



22496 pazienti - 109 UTI

14 Regioni

https://spinuti.unict.it/

Ministero della Salute

DIREZIONE GENERALE DELLA PREVENZIONE SANITARIA
Ufficio 05 – Prevenzione delle malattie trasmissibili e profilassi internazionale

0008618-14/03/2023-DGPRE-DGPRE-P

A: Assessorati alla Sanità
Regioni Statuto ordinario e speciale
Province Autonome Trento e Bolzano

Coordinamento Interregionale Prevenzione

Referenti Regionali AMR
Referenti regionali sorveglianza AMR
Referenti Regionali per il controllo delle ICA
Referenti regionali per il contrasto dell’AMR
Referenti regionali per la sorveglianza delle ICA
Referenti regionali per le sorveglianze dedicate all’AMR

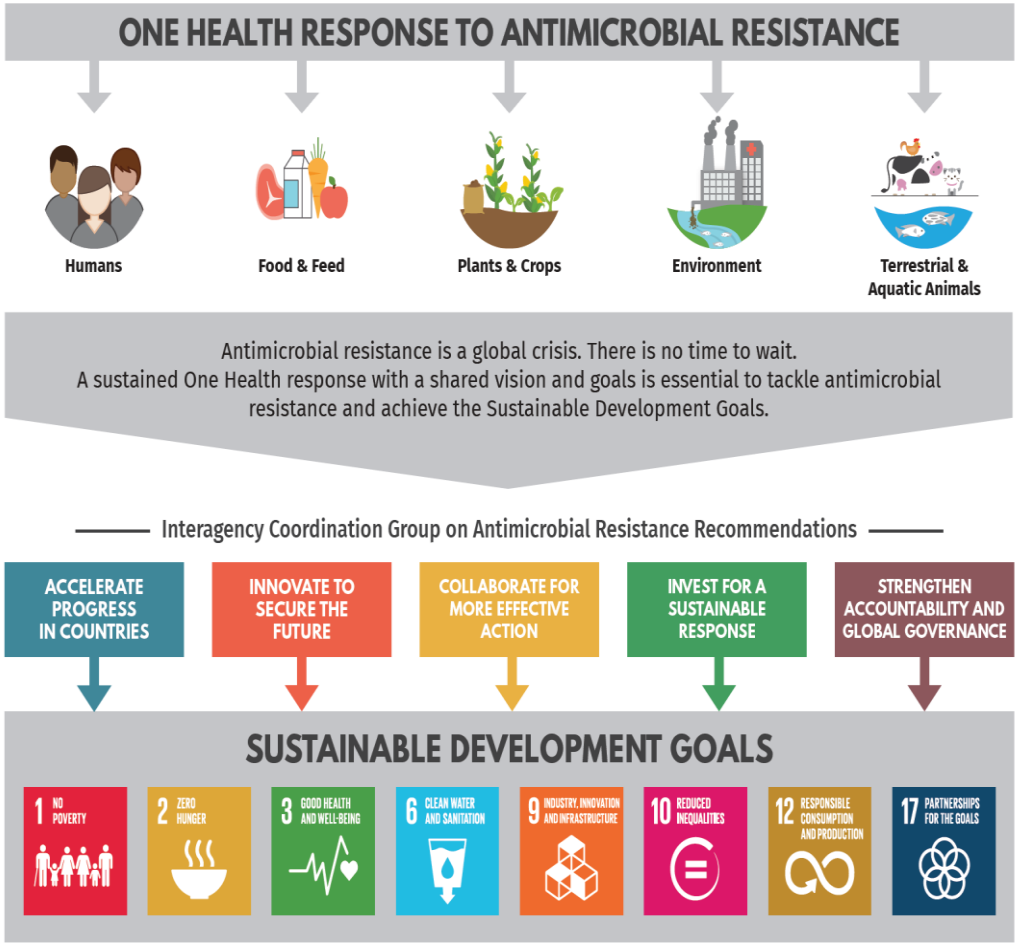
Loro Sedi

e, p.c. Istituto Superiore di Sanità
Dipartimento di Scienze Mediche, Chirurgiche e Tecnologie Avanzate “GF Ingrassia”, Università degli Studi di Catania

OGGETTO: Sorveglianza delle Infezioni Correlate all’Assistenza nelle Unità di Terapia Intensiva: Trasmissione del protocollo “Sorveglianza attiva Prospettica delle Infezioni Nosocomiali nelle Unità di Terapia Intensiva, SPIN-UTI”

… Si auspica la massima collaborazione da parte delle Regioni/PPAA nel promuovere la partecipazione delle strutture presenti sul proprio territorio alla sorveglianza delle ICA nelle UTI, mediante l’adesione ad una delle reti sopra descritte, anche in considerazione delle azioni previste negli ***obiettivi strategici del nuovo Piano Nazionale della Prevenzione (PNP) 2020-2025 e del PNCAR 2022-2025, nei quali si evidenzia la necessità di definire in via prioritaria un programma di sorveglianza e controllo delle ICA****. Si raccomanda, altresì, di considerare la sostenibilità della sorveglianza, avviando un processo di progressiva implementazione sul proprio territorio in base alla capacità delle singole strutture.*

One Health, IACG recommendations and the Sustainable Development Goals



COMMISSIONE EUROPEA

1 June 2023

Bruxelles, 26.4.2023
COM(2023) 191 final

2023/0125 (NLE)

Proposta di

RACCOMANDAZIONE DEL CONSIGLIO

sul potenziamento delle azioni dell'UE per combattere la resistenza antimicrobica con un approccio "One Health"

*… the successful tackling of antimicrobial resistance (AMR) requires the **prudent use of antibiotics** for humans and animals, good **infection prevention and control measures**, and more **research and development** into novel antimicrobials and alternatives to antimicrobials*

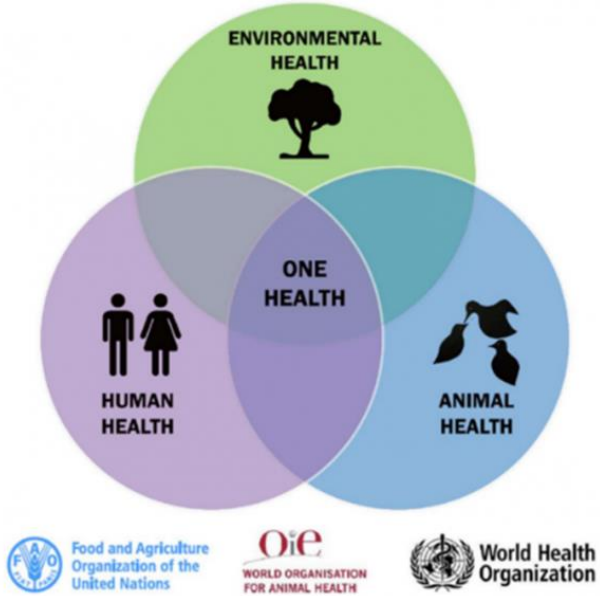


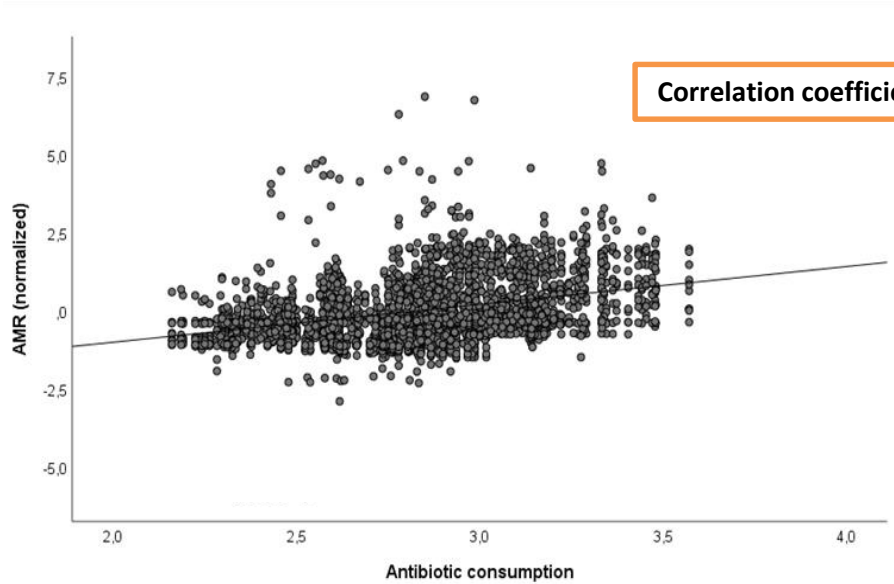
Table 1 The two fundamentals to control antimicrobial resistance

Decrease antimicrobial use and control what is used
Dramatically lower antibiotic volumes currently used (human and non-human)
Restrict broad spectrum and critically important antibiotics in people
Ban the use of critically important antibiotics in food animals
Do not use antibiotics to spray plants
Prevent infections
Do not dump antibiotics into the environment
Stop the presence of antibiotic residues in foods and water
Stop the spread of resistant bacteria and genes and exposure to them
Control spread into the environment
Hygiene
Infection control
Agriculture sector
Aquaculture
No superbugs in foods and water

Collignon Int Med J 2015

*"An analysis of **30 European countries from 2010 to 2019** confirmed that antibiotic use had a significant positive relationship with AMR proportion across ten different pathogen-antibiotic combinations"*

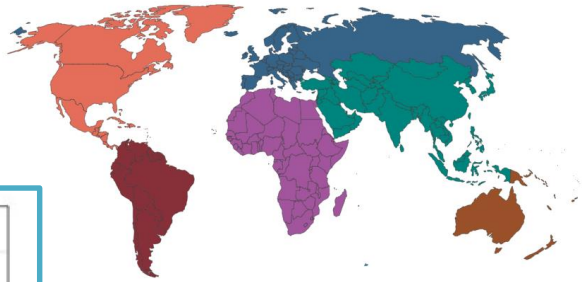
E. coli, K. pneumoniae, S. aureus



Correlation coefficient= 0.3

EARS-Net database

*"Aggregating countries into regional groups shows a pattern where there is **an inverse relationship between AMR and antibiotic use**. These data help confirm that there are other very important factors influencing AMR" (Collignon et al. Antibiotics 2019)*



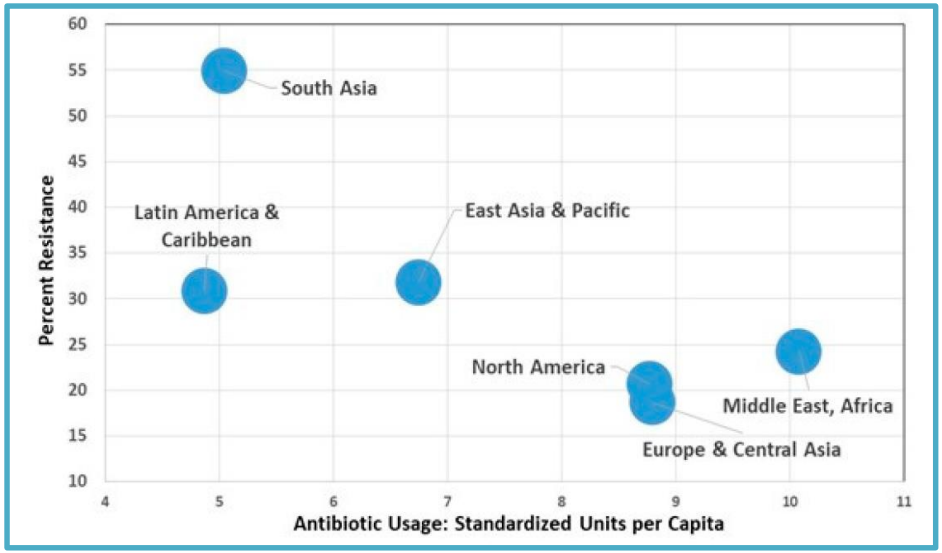
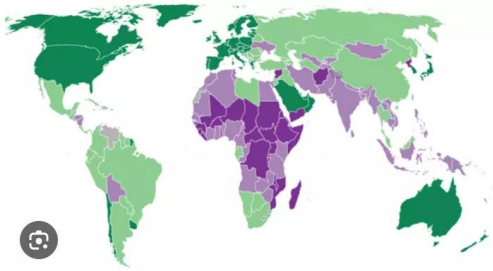


Figure 1. Percent resistance in *E. coli* to third-generation cephalosporins (3GCeph) and fluoroquinolones (FQ). Source Data: Collignon et al. (2018) [15] and figure from Collignon and McEwen [6].

Table 1. Income effects: antibiotic usage and antimicrobial resistance levels.

World Bank Income Group	Antibiotic Usage CDDEP Standardized Units	Percent Resistance *E. coli* to 3GCeph&FQ
High income countries	8.5	18.3
Upper middle-income countries	7.2	31.1
Lower middle-income countries	6.9	42.6
Grand Total	7.9	25.6

Source: Percent resistance *E. coli* to third-generation cephalosporins (3GCeph) and fluoroquinolones (FQ). CDDEP is the Centre for Disease Dynamics, Economics and Policy. Source Data: Collignon et al. (2018) [15].



Antimicrobial Resistance: The Major Contribution of Poor Governance and Corruption to This Growing Problem

Peter Collignon[1,2]*, Prema-chandra Athukorala[3,4], Sanjaya Senanayake[5,6], Fahad Khan[3]

PLOS ONE | DOI:10.1371/journal.pone.0116746 2015

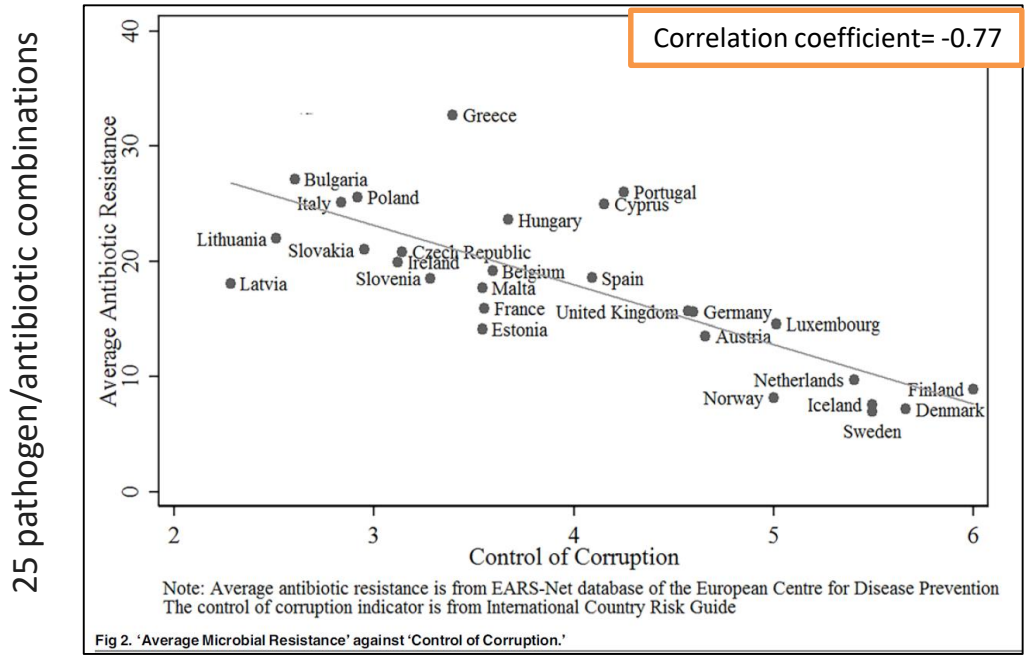


Fig 2. 'Average Microbial Resistance' against 'Control of Corruption.'

Controllo della corruzione ↑ AMR ↓

Lancet Planet Health 2018; 2: e398–405

Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis

Peter Collignon, John J Beggs, Timothy R Walsh, Sumanth Gandra, Ramanan Laxminarayan

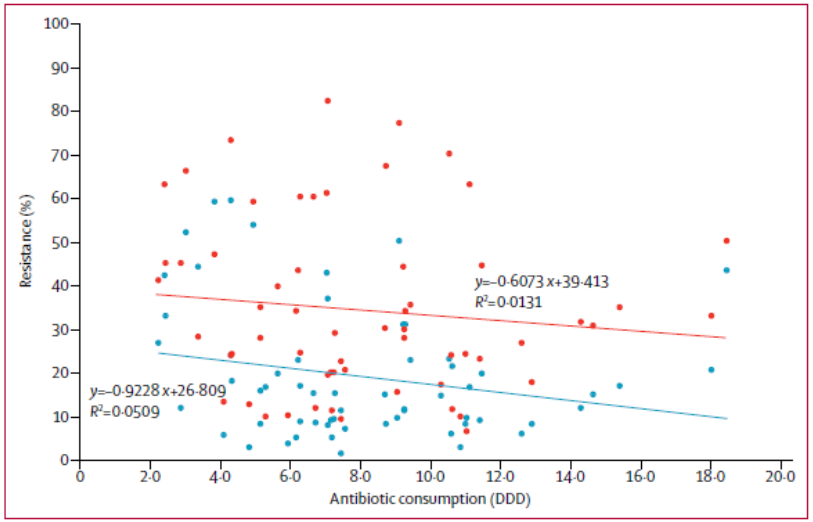


***Figure 2:* *Escherichia coli* resistance levels for fluoroquinolones and third-generation cephalosporins compared with antibiotic consumption**

Figure shows data for percentage of resistance versus defined daily dose (DDD) of antibiotic, plotted only for countries with data for DDD and both measures of resistance. Blue circles indicate *Escherichia coli* resistance to third-generation cephalosporins (%). Red circles indicate *E coli* resistance to fluoroquinolones (%). The blue line shows the linear measure of *E coli* resistance to third-generation cephalosporins. The red line shows the linear measure of *E coli* resistance to third-generation fluoroquinolones. R^2=coefficient of determination.

	Effect on resistance rate of 1 SD increase in each explanatory variable (logit)	p value
Usage (standardised)	2·36	0·070
Governance index	–11·18	<0·0001
Health expenditure index	–6·34	0·0065
GDP per capita index (standardised)	3·36	0·11
Education index	8·59	0·0035
Infrastructure index	–13·24	0·0052
Climate index	–0·25	0·86
R^2	0·75	..

GDP=gross domestic product. R^2=coefficient of determination.

***Table 3:* Effect of changes in indices on the aggregate resistance rate**

Maugeri *et al. Globalization and Health* (2023) 19:12
https://doi.org/10.1186/s12992-023-00913-0

Globalization and Health

RESEARCH Open Access

Socio-economic, governance and health indicators shaping antimicrobial resistance: an ecological analysis of 30 european countries

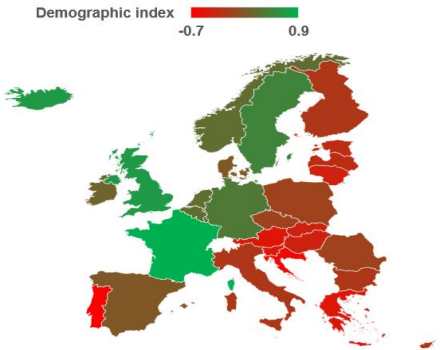
Andrea Maugeri[1], Martina Barchitta[1], Federico Puglisi[2] and Antonella Agodi[1*]

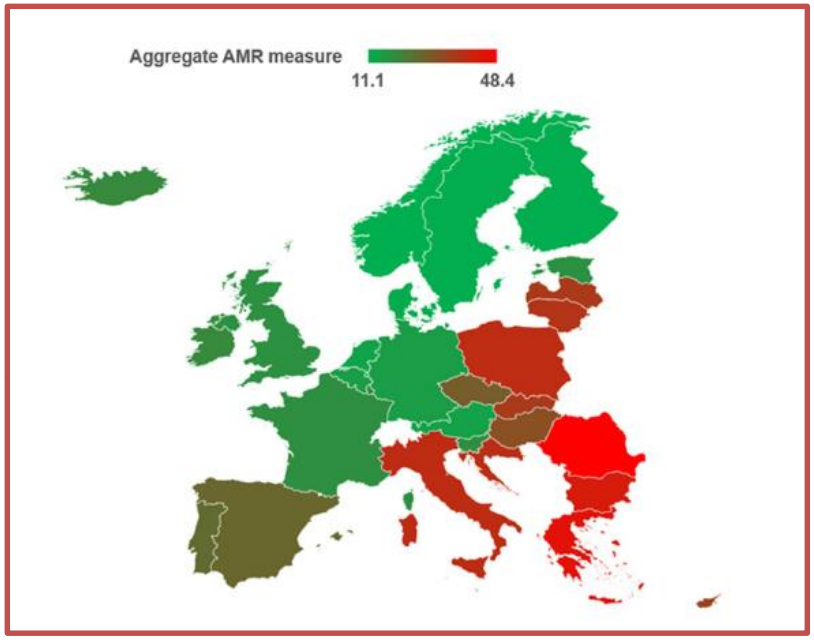
Tre fonti di dati:

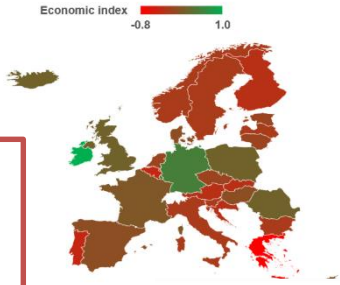
- ECDC Atlas per le **proporzioni di resistenze** per **25 combinazioni tra patogeni e classi di antibiotici**
- ESAC-Net database per i dati sul **consumo di antibiotici a livello comunitario**
- *World Bank* database per **22 indicatori**, convertiti in **5 indici aggregati per i domini demografico, economico, *governance*, salute, «libertà e diritti»**

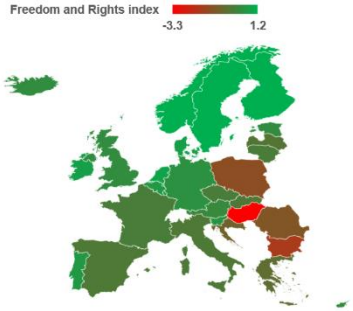
Table 1 Indicators of demographic, health, economic, governance, and freedom domains

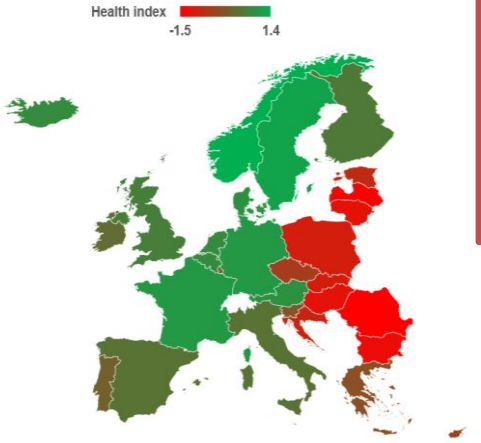
Indicator	Abbreviation	Mean	Standard deviation	Minimum	Maximum	Median	IQR
Demographic indicators							
Total population	D1	17,337,495.0	23,344,767.2	360,563.0	83,092,962.0	7,927,840.5	15,232,512
Land area, km^2	D2	156,916.3	156,509.4	320.0	547,557.0	86,890.0	25,6675.0
Population density, people per km^2	D3	173.5	276.6	3.5	1,514.5	107.1	99.7
Annual population growth	D4	0.7	0.8	0.0	3.9	0.6	0.5
Population aged > 40	D5	0.5	0.0	0.4	0.5	0.5	0.1
Urban population, % of total population	D6	74.9	13.2	53.7	98.0	74.6	20.8
Fertility rate, total births per woman	D7	1.5	0.2	1.1	1.9	1.6	0.3
Health indicators							
Health expenditure, % of total GDP	H1	8.3	1.8	5.3	11.4	8.4	3.3
Health expenditure per capita, US$	H2	3,367.7	2,191.3	687.3	8,239.1	2,744.9	4,074.6
Life expectancy at birth, years	H3	80.3	2.7	74.9	83.5	81.2	4.2
Economic indicators							
GDP, billion US$	E1	629.3	966.6	15.08	3,860.0	250.5	489.5
GDP per capita, US$	E2	37,924.4	23,844.9	9,828.1	114,685.2	29,650.9	31,023.6
5-year average GDP growth	E3	3.2	1.8	0.9	10.1	3.1	2.2
5-year average GDP growth per capita	E4	2.8	1.8	0.7	8.9	2.6	2.7
Governance indicators							
Voice and accountability	G1	1.1	0.4	0.2	1.7	1.1	0.4
Political stability	G2	0.8	0.3	0.3	1.7	0.8	0.5
Government effectiveness	G3	1.1	0.5	0.3	1.9	1.1	0.9
Regulatory quality	G4	1.2	0.4	0.5	1.9	1.2	0.6
Rule of law	G5	1.2	0.6	0.0	2.0	1.1	1.2
Control of corruption	G6	1.1	0.8	0.0	2.2	0.8	1.5
Freedom indicators							
Political rights score	F1	37.2	2.8	26.0	40.0	38.0	3.0
Civil liberties score	F2	54.2	4.3	43.0	60.0	55.0	5.0

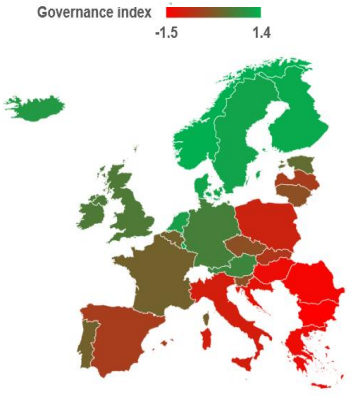

Demographic index
-0.7
0.9


Aggregate AMR measure
11.1
48.4


Economic index
-0.8
1.0


Freedom and Rights index
-3.3
1.2


Health index
-1.5
1.4


Governance index
-1.5
1.4

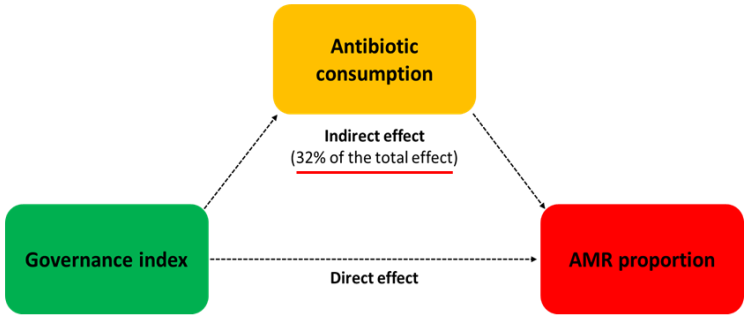
Effects on antibiotic use

Indexes	Beta	Standard Error	p-value
Demographic	3·506	2·792	0·221
Health	1·441	1·824	0·437
Economic	1·873	1·993	0·357
Governance	-8·128	1·923	<0·001
Freedom	3·251	1·652	0·061

Effects on AMR

Indexes	Beta	Standard Error	p-value
Demographic	1·133	2·567	0·663
Health	-5·737	1·645	0·002
Economic	-1·456	1·807	0·429
Governance	-6·803	2·262	0·006
Freedom	0·946	1·585	0·556
Antibiotic use	0·451	0·182	0·021

Mediation analysis



Teoria del contagio: altri fattori possono determinare alti livelli di AMR nei paesi con una *governance* poco efficace

La sola riduzione del consumo di antibiotici non può risolvere il problema della AMR: ulteriori interventi sono necessari per migliorare la *governance* a livello mondiale

appropriatezza nell'uso degli antibiotici, coperture vaccinali, pratiche di IPC, diete ricche in alimenti di origine animale, consumo/appropriatezza dell'uso di antibiotici nel settore animale, smaltimento rifiuti/reflui nell'ambiente

PLOS GLOBAL PUBLIC HEALTH 2023

OPINION

Improving the response to future pandemics requires an improved understanding of the role played by institutions, politics, organization, and governance

Peter Berman[1]*, Maxwell A. Cameron[1], Sarthak Gaurav[2], George Gotsadze[3], Md Zabir Hasan[4], Kristina Jenei[1], Shelly Keidar[1], Yoel Kornreich[5], Chris Lovato[1], David M. Patrick[1,6], Malabika Sarker[7], Paolo Sosa-Villagarcia[8], Veena Sriram[1], Candice Ruck[1]

Scientifc Reports | (2021) 11:22440

OPEN

The role of good governance in the race for global vaccination during the COVID-19 pandemic

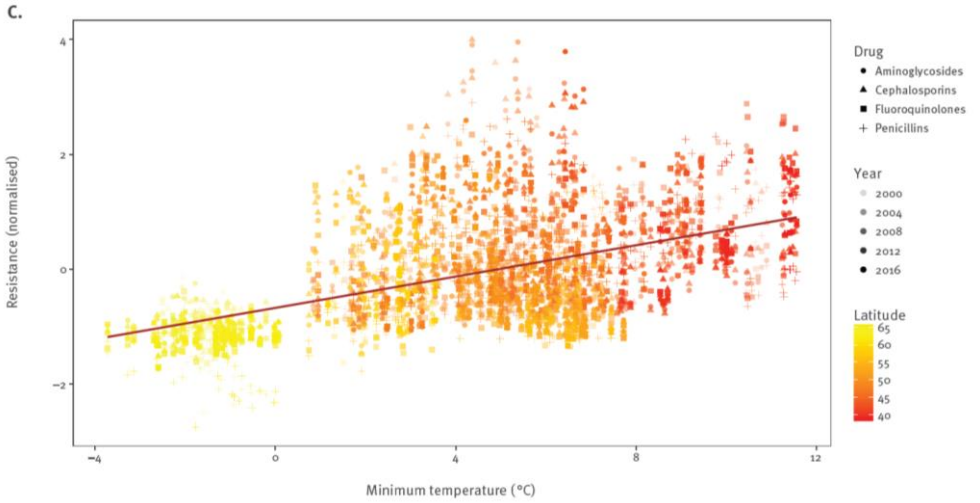
Moosa Tatar[1,2]✉, Mohammad Reza Faraji[3], Jalal Montazeri Shoorekchali[4], José A. Pagán[5] & Fernando A. Wilson[1,2]

Euro Surveill. 2020;25(45):pii=1900414

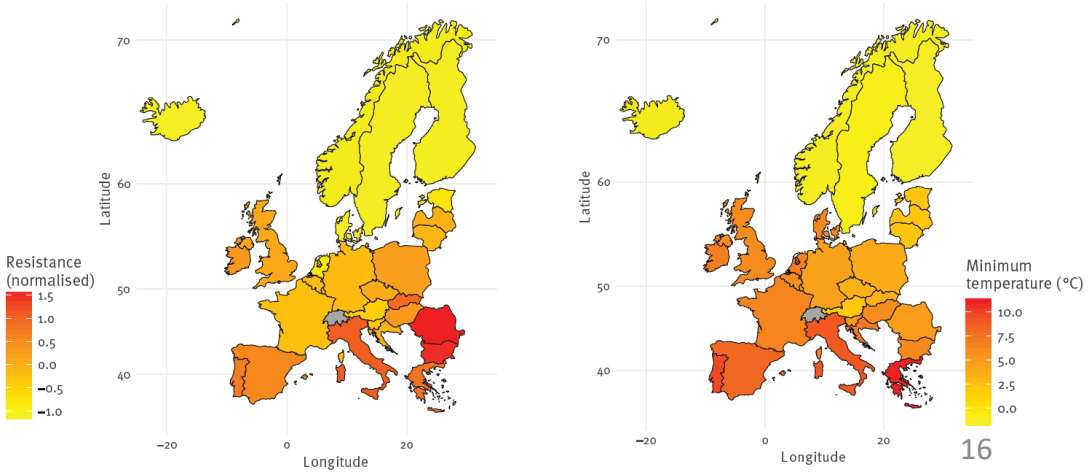
Rates of increase of antibiotic resistance and ambient temperature in Europe: a cross-national analysis of 28 countries between 2000 and 2016

Sarah F McGough[1,2], Derek R MacFadden[1,3], Mohammad W Hattab[4], Kåre Mølbak[5,6], Mauricio Santillana[1,2,7]

Relazione tra il cambiamento climatico e la diffusione di batteri resistenti agli antibiotici: aumento nei tassi di microrganismi resistenti agli antibiotici associato a temperature locali più calde



Nonostante queste evidenze, resta incerto se vi sia una reale relazione tra temperatura e antibiotico-resistenza o se i risultati ottenuti siano esclusivamente dovuti a **gradienti geografici coincidenti e influenzati da altri fattori**



antibiotics 2023 MDPI

Article

Socioeconomic and Governance Factors Disentangle the Relationship between Temperature and Antimicrobial Resistance: A 10-Year Ecological Analysis of European Countries

Andrea Maugeri, Martina Barchitta, Roberta Magnano San Lio and Antonella Agodi *

Analisi ecologica per **valutare l'associazione tra la variazione di temperatura e le proporzioni di microrganismi resistenti agli antibiotici**, tenendo conto anche di importanti fattori predittivi e confondenti

Quattro fonti di dati:

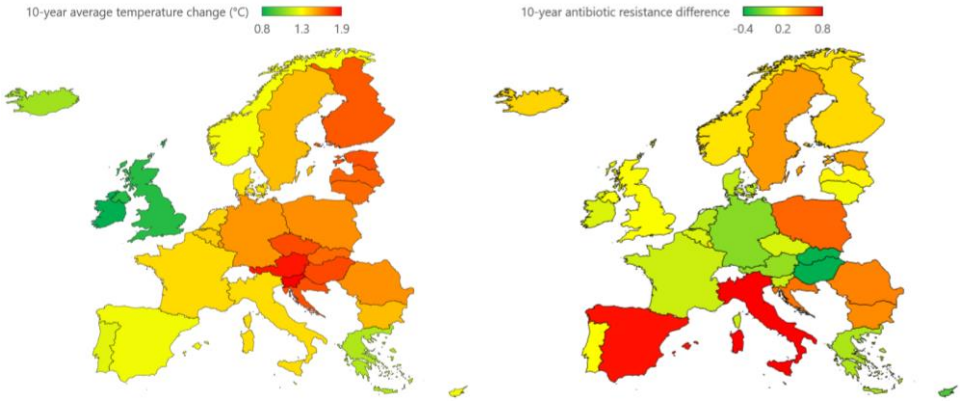
- **variazioni annuali di temperatura** rispetto al periodo di riferimento 1951–1980 (database FAOSTAT)
- **proporzioni di antibiotico-resistenza** per 3 microrganismi - *E. coli, K. pneumoniae, S. aureus* - e 6 classi antibiotici (ECDC Atlas)
- **consumo di antibiotici** per uso sistemico nella comunità (database ESAC-Net)
- **densità di popolazione**, **prodotto interno lordo** (PIL) pro capite e **indicatori di *governance*** (DataBank della World Bank)

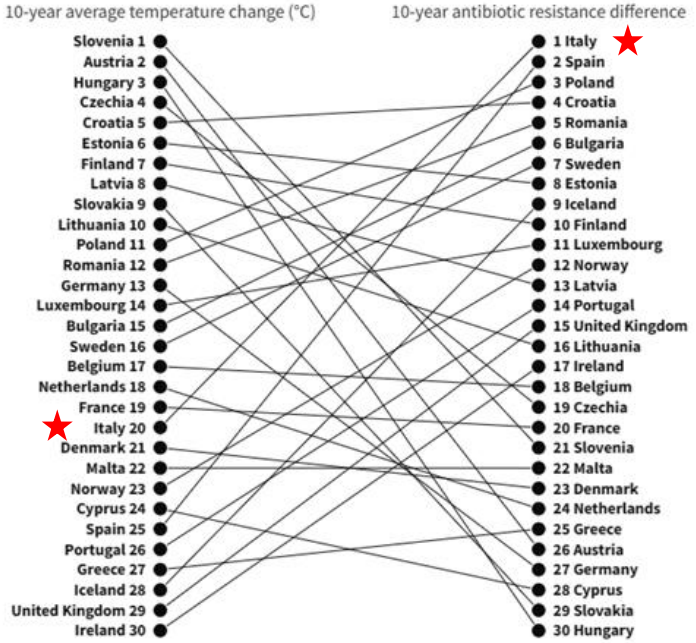
antibiotics 2023 MDPI

Article

Socioeconomic and Governance Factors Disentangle the Relationship between Temperature and Antimicrobial Resistance: A 10-Year Ecological Analysis of European Countries

Andrea Maugeri, Martina Barchitta, Roberta Magnano San Lio and Antonella Agodi *





Multivariable analyses

Model 1 for AMR (adapted from McGough et al.)	
Temperature change	0.140 (0.039; 0.241) ↑
Antibiotic consumption	1.163 (1.044; 1.282) ↑
Population density	0.165 (0.135; 0.196) ↑

Model 2 for AMR	
Temperature change	0.027 (-0.064; 0.118) **n.s.**
Antibiotic consumption	0.506 (0.366; 0.646) ↑
Population density	0.143 (0.116; 0.170) ↑
GDP per capita	0.093 (-0.022; 0.209)
Governance	-1.043 (-1.207; -0.879) ↓

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2022, VOL. 18, NO. 6, e2145069 (5 pages)
https://doi.org/10.1080/21645515.2022.2145069

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COMMENTARY

OPEN ACCESS Check for updates

The approach of World Health Organization to articulate the role and assure impact of vaccines against antimicrobial resistance

Isabel Frost[a,b], Anand Balachandran[c], Sarah Paulin-Deschenaux[c], Hatim Sati[d], and Mateusz Hasso-Agopsowicz[a]

[a]Immunization, Vaccines & Biologicals, UHC/Life Course, World Health Organization, Geneva, Switzerland; [b]Imperial College London, London, UK; [c]Surveillance, Prevention and Control Department, AMR Division, World Health Organization, Geneva, Switzerland; [d]Global Coordination and Partnership Department, AMR Division, World Health Organization, Geneva, Switzerland

*"Effective **infection prevention and control (IPC) has been identified as the cornerstone action to combat AMR** by the World Health Assembly and the Global Action plan on AMR.*

*Similarly, **the Immunization Agenda 2030 highlights vaccines as critical tools to combat AMR**. The action framework describes **a vision for vaccines to contribute fully, sustainably and equitably to the prevention and control of AMR by preventing infections and reducing antimicrobial use**"*


COMMISSIONE EUROPEA

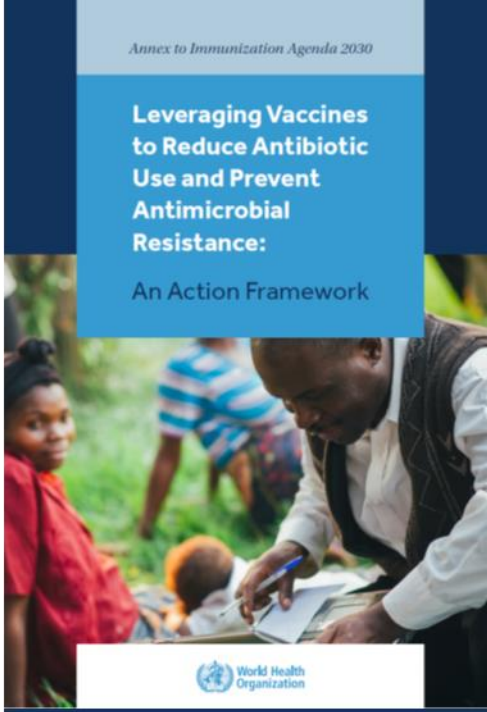
Bruxelles, 26.4.2023
COM(2023) 191 final

2023/0125 (NLE)

Proposta di

RACCOMANDAZIONE DEL CONSIGLIO

sul potenziamento delle azioni dell'UE per combattere la resistenza antimicrobica con un approccio "One Health"



This Action Framework, intended to guide vaccine stakeholders in efforts to maximize the impact of vaccines in preventing and containing AMR, was generated through a consensus-building consultative process

2020

Maugeri et al.
Antimicrobial Resistance & Infection Control (2022) 11:136
https://doi.org/10.1186/s13756-022-01173-0

Antimicrobial Resistance and Infection Control

RESEARCH Open Access

Vaccination coverage in Italian children and antimicrobial resistance: an ecological analysis

Andrea Maugeri[1], Martina Barchitta[1] and Antonella Agodi[1,2*]

vaccines

Vaccines 2022, 10, 554.

MDPI

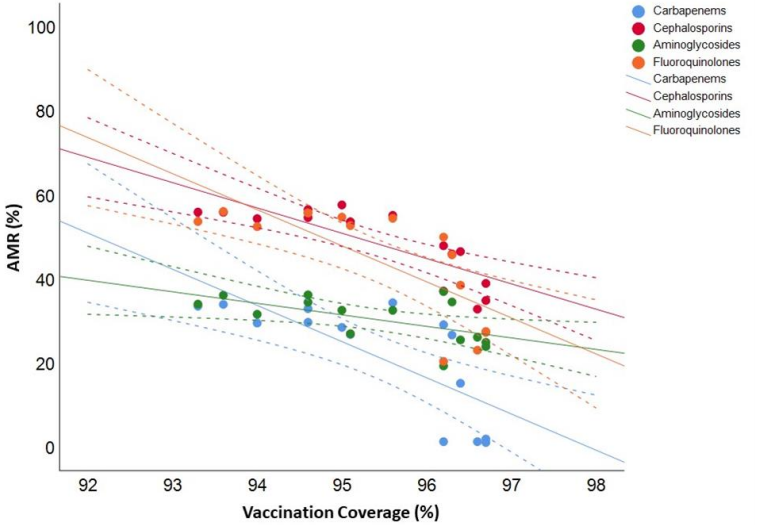
Article

The Inverse Relationship between Influenza Vaccination and Antimicrobial Resistance: An Ecological Analysis of Italian Data

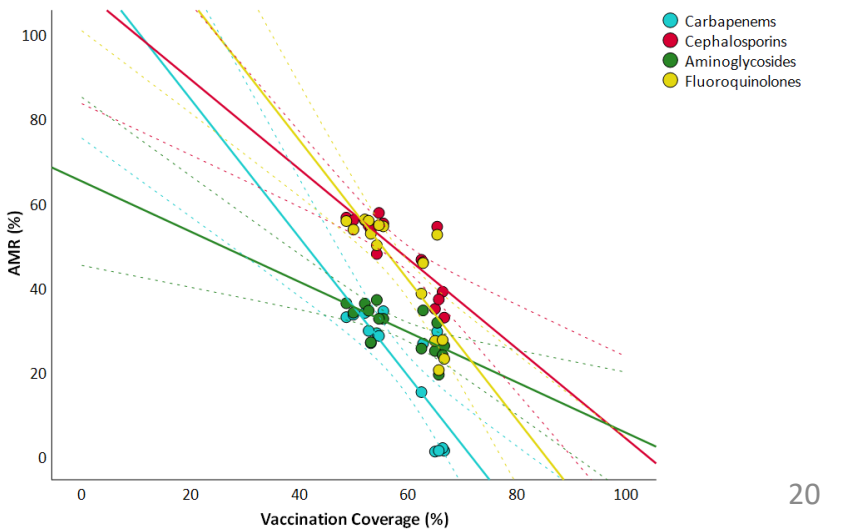
Martina Barchitta, Andrea Maugeri, Rosario Vinci and Antonella Agodi *

Confronto tra le **coperture vaccinali** (EpiCentro, ISS) e **le proporzioni di AMR** (dati AR-ISS ottenuti dal *Surveillance Atlas of Infectious Diseases,* ECDC) **in Italia** dal 2000 al 2020

Relazione tra le coperture vaccinali per difterite-tetano-pertosse e AMR in K. pneumoniae



Coperture vaccinali antinfluenzali nella popolazione sopra I 64 anni e AMR in K. pneumoniae



Transdisciplinary work against antimicrobial resistance

Kamenshchikova A, Wolffs PFG, Hoebe CJPA, Horstman K.

Lancet Infect Dis 2020

"One Health aims to bridge human, animal, and environmental sectors to address shared health concerns. One of the gaps in knowledge articulated by the Global Action Plan is scant understanding of social science and behaviour.

In that context, ***One Health offers a potential for transdisciplinary collaborations, including between social and biomedical disciplines****. […] Study findings substantiate the claim that* ***AMR is not only a biological problem but also a social problem****. Cultures of prescription, sale, and use of antibiotics in human and animal sectors, and practices of antibiotic production and waste management, are essential for understanding drivers of emergence and dissemination of multidrug- resistant bacteria. […]*

If AMR can be considered a biosocial issue, solutions *should neither lie exclusively within the biomedical disciplines nor fall into the social disciplines but* ***should reside on their intersections****."*

Grazie!