

CONVEGNO  
ECM

# Antimicrobico-resistenza: cure e ambiente #6

## L'ecllettismo dell'antibiotico-resistenza

7 giugno 2023

ORE 9.15-17.20

Auditorium di Sant'Apollonia  
via S. Gallo, 25a - Firenze

ANTIBIOTICORESISTENZA E MOVIMENTI DELLE POPOLAZIONI

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Regione Toscana



Servizio  
Sanitario  
della  
Toscana

# Human Mobility

Le modalità e le ragioni della mobilità umana sono varie e possono essere caratterizzate in termini di fattori politici, economici e sociali.

Il termine “**migrante**” comprende: rifugiati, richiedenti asilo e sfollati interni. Queste categorie differiscono dai migranti economici che lasciano il loro paese di origine per lavoro, istruzione o ricongiungimento familiare.

Circa il 3,5% della popolazione mondiale (circa 272 milioni di persone) sono considerati migranti internazionali con alcuni che lasciano la propria casa per motivi economici e altri cacciati dalle loro case a causa di conflitti, disastri umanitari e gli effetti locali del cambiamento climatico.

Nel 2019, 50,8 milioni di persone erano sfollate a causa di conflitti, violenze e altri disastri.

La migrazione è influenzata da fattori sociali, economici, politici e ambientali sia come motore di viaggio che nel Paese di destinazione.

Oltre il 50% degli attuali rifugiati sono stati sfollati con la forza dalle proprie case, in particolare da Siria, Afghanistan e Somalia, Paesi in cui sono presenti conflitti prolungati.



# Capturing the evidence on access to essential antibiotics in refugee and migrant populations

## Definizioni

**Asylum seeker.** An individual who is seeking international protection. In countries with individualized procedures, an asylum seeker is someone whose claim has not yet been finally decided by the country in which he or she has submitted it. Not every asylum seeker will ultimately be recognized as a refugee, but every recognized refugee is initially an asylum seeker (10).

**Migrant.** There is no universally accepted definition of migrant. For the purpose of collecting data on migration, the United Nations Department of Economic and Social Affairs defines an international migrant as “any person who changes his or her country of usual residence” (11). It includes anyone who is moving or has moved across an international border or has spent a substantial duration of stay abroad or causes for migration. The International Organization for Migration (IOM) considers the migration forms of movement within and outside a State. It includes “a person who moves away from his or her country of usual residence, whether within a country or across an international border, permanently, and for a variety of reasons” (12).

- **documented migrant:** a migrant who is in the country in accordance with his or her legal status
- **migrant in an irregular situation:** a person who has crossed an international border while not in accordance with the law of that State or the law of the State which that State is a party.

**Refugee.** According to the United Nations Convention relating to the Status of Refugees (Art. 1A(2)) (12), a refugee is:



a person who, owing to a well-founded fear of persecution for reasons of race, religion, nationality, membership of a particular social group or political opinions, is outside the country of his nationality and is unable or, owing to such fear, is unwilling to avail himself of the protection of that country.

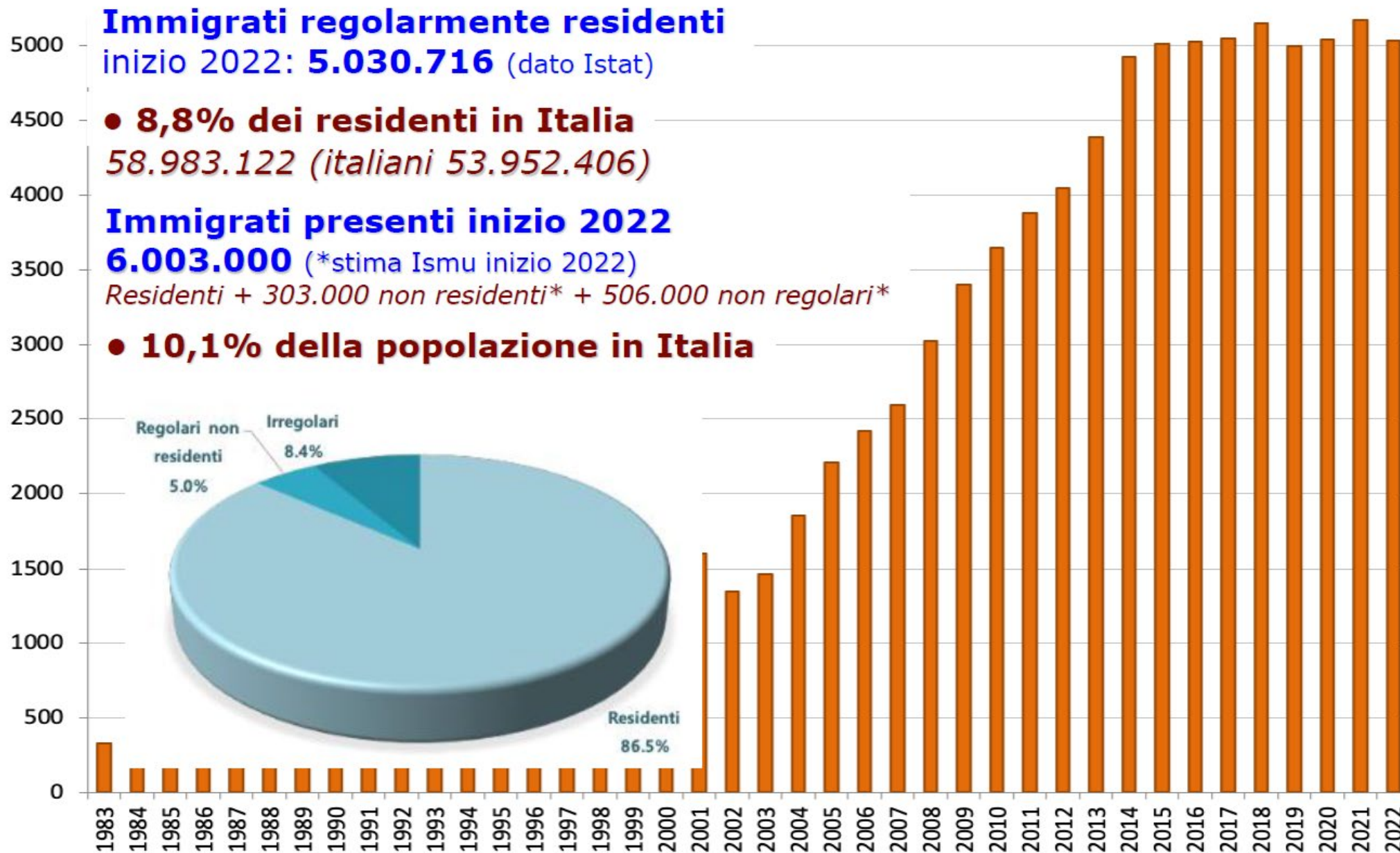
For State Parties to the African Union Convention governing the specific aspects of refugee problems in Africa (Art. 1(2)) (13), the term refugee also applies to:



every person who, owing to external aggression, occupation, foreign domination or events seriously disturbing public order in either part or the whole of his country of origin or nationality, is compelled to leave his place of habitual residence in order to seek refuge in another place outside his country of origin or nationality.



# Immigrazione in Italia: numero totale e trend all'inizio del 2022



# Immigrazione in Italia: dati di contesto

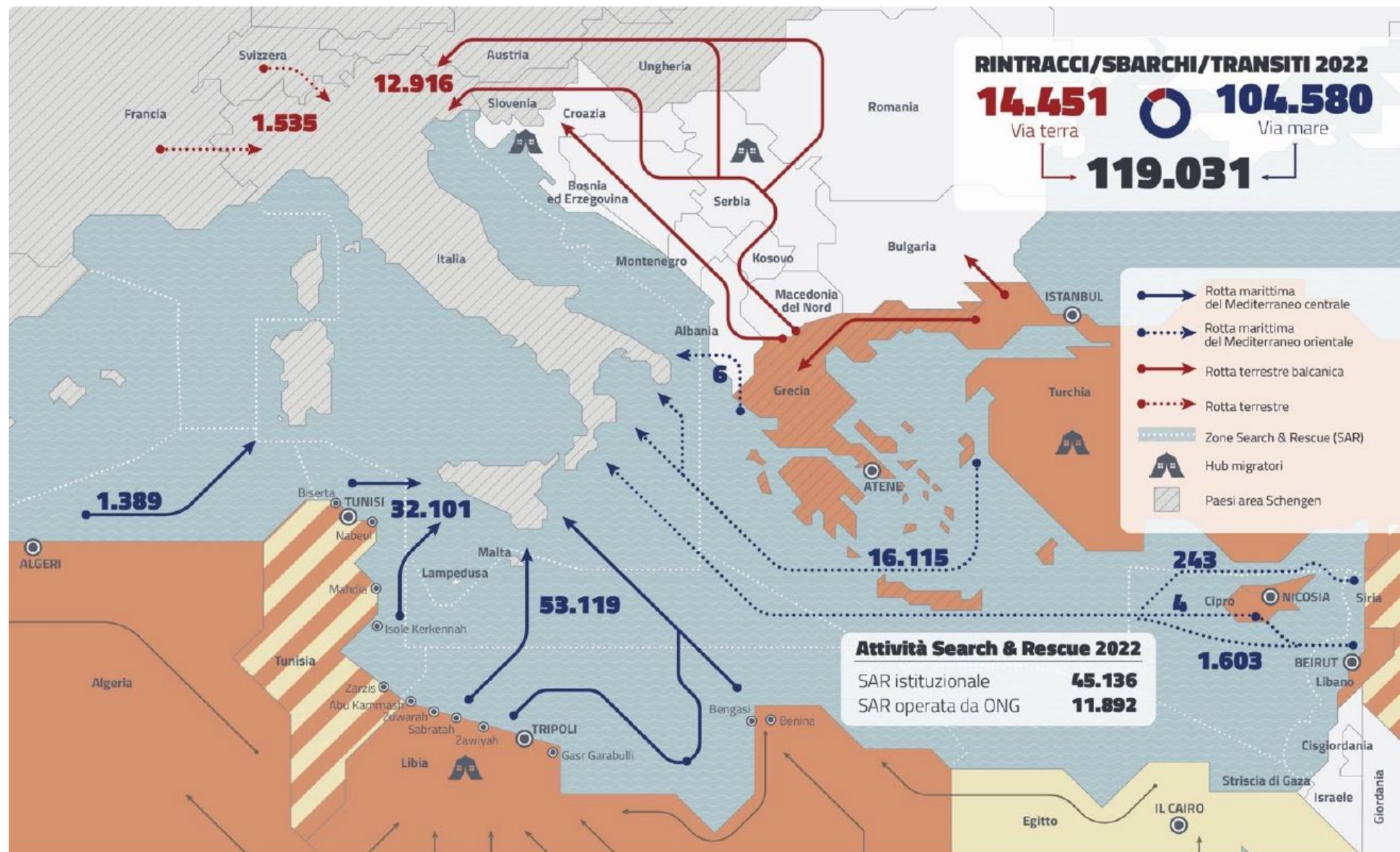


Nazionalità	Presenza (quota sul totale)	% femmine
Romania	20,7%	57,6%
Albania	8,3%	48,8%
Marocco	8,3%	46,2%
Cina	6,4%	49,6%
Ucraina	4,5%	77,6%
<b>Totale Nazionale</b>	<b>5.193.669</b>	<b>51%</b>

Regioni* con più cittadini stranieri residenti			Province* con più cittadini stranieri residenti		
Regione	Totale	% su pop. tot. resid.	Provincia	Totale	% su pop. tot. resid.
Lombardia	1.206.023	11,9%	Roma	555.453	12,8%
Lazio	682.968	11,6%	Milano	488.432	14,9%
Emilia Romagna	559.586	12,5%	Torino	222.173	9,9%
Veneto	505.955	10,3%	Brescia	157.958	12,5%
Piemonte	429.375	9,9%	Napoli	135.594	4,4%



# Immigrazione irregolare: Rintracci/Sbarchi/Transiti 2022



ANTIBIOTIC RESISTANCE  
POSES A **BIG** THREAT TO  
**GLOBAL HEALTH**



World Health  
Organization



## IMPLEMENTATION OF THE GLOBAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE



### Global database for antimicrobial resistance country self-assessment



The 70<sup>th</sup> World Health Assembly also marked an exciting development in the field of antimicrobial resistance (AMR). A database has been launched based on [the first global assessment](#) of how countries perceive their progress on AMR. This important step, taken by WHO, FAO and OIE, provides a clearer picture of existing initiatives, processes and activities around AMR. It also highlights any gaps and empowers countries to reach out for guidance and support. Encouragingly, more than 90% of people in the world (6.5 billion) live in a country that has developed, or is developing, a multisectoral national action plan on AMR. However, there is still a lot of work to be done: the international community must rally around low-income countries, burdened with higher rates of infectious disease and weaker health systems, to help them implement impactful and achievable plans.

### New WHO Director-General highlights antimicrobial resistance as perfect example of complex challenges the world faces

The Member States of WHO have elected Dr Tedros Adhanom Ghebreyesus as the new Director-General of WHO: he will begin his five-year term on 1 July 2017. As Director-General, Dr Tedros intends to focus on five key areas, of which strengthening the capacity of national authorities and local communities to detect, prevent and manage health emergencies, including antimicrobial resistance (AMR), is one. In his statement to the Assembly Dr Tedros highlighted AMR as “the perfect example of the complex, multisectoral, multi-stakeholder challenges we will increasingly face in the future, requiring a more agile, strategic, innovative, collaborative leadership”. Other priorities for the new Director-General include advancing universal health coverage; putting the well-being of women, children and adolescents at the centre of global health and development; supporting national health authorities to better understand and address the effects of climate and environmental change on health; and building WHO into a more effective, transparent and accountable agency. Dr Tedros has stated that he will address AMR as a global health priority, championing the ‘One Health approach’ and working with agencies such as FAO and OIE, to advance a public health approach to monitoring and mitigating its impact.



### AMR at the World Health Assembly

In Committee meetings, there was active discussion and support for the ongoing progress in addressing AMR. 60 Member States made interventions with 11 interventions from civil society and organizations in relations with WHO. The importance of intersectoral action was reiterated with support for WHO action in collaboration with FAO and OIE. Ongoing support to countries that have not yet developed a national action plan was requested. The report on “Improving the prevention, diagnosis and clinical management of sepsis” was well received and it is anticipated that a resolution on the same will be adopted during the Assembly. The importance of developing the framework on stewardship and development was reiterated. Delegates welcomed the establishment of the Interagency Coordination Group on AMR and look forward to receiving updates. There was active discussion about the role of the Joint External Evaluation in validating the self-assessment questionnaire. The AMR Secretariat clarified that, as with the entire JEE process, countries’ participation in these processes is voluntary.

*“..there is still a lot of work to be done: the international community must rally around low-income countries, burdened with higher rates of infectious disease and weaker health systems, to help them implement impactful and achievable plans.”*



# Antibiotici nei Paesi a basso e medio reddito

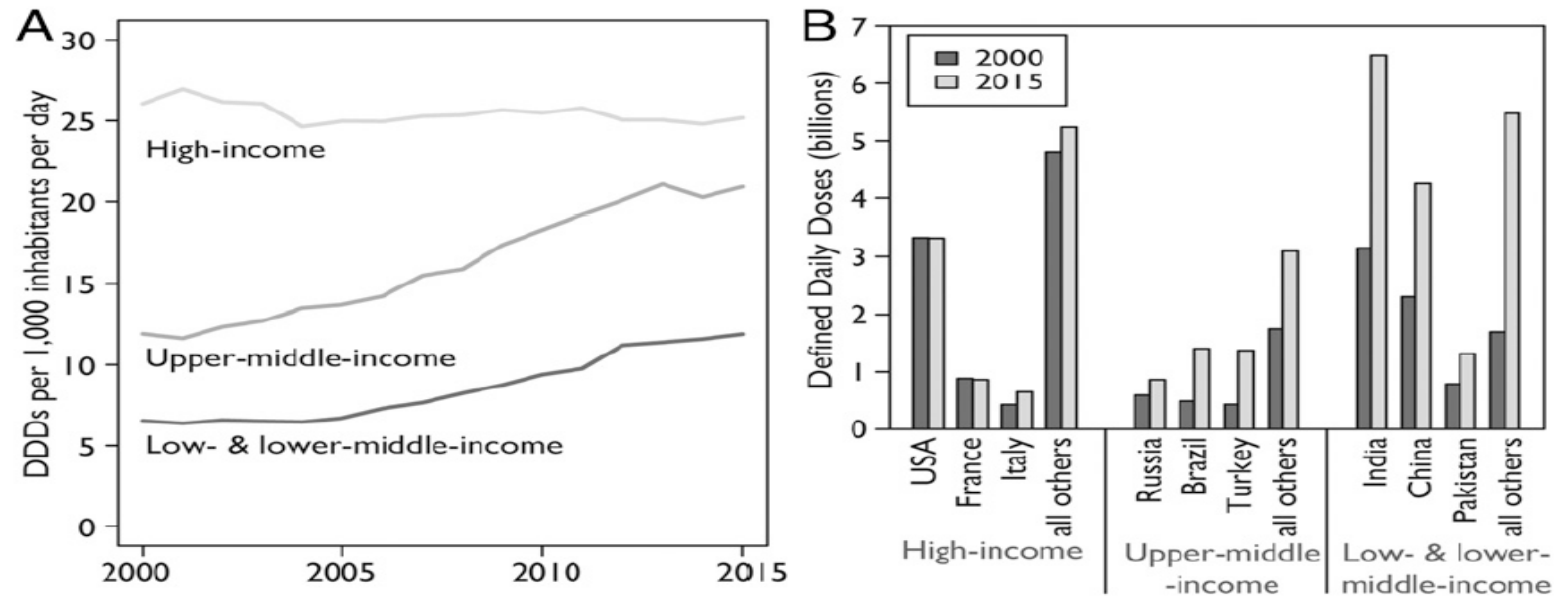
“Considerando che gli antibiotici giocano un ruolo fondamentale nel ridurre mortalità e morbosità dovute alle infezioni batteriche, la resistenza agli antibiotici è un problema grave nei paesi a risorse limitate dove l'incidenza delle malattie infettive è molto elevata, i tassi di resistenza sono più alti che nei paesi industrializzati, e le opzioni terapeutiche non sono frequentemente disponibili o sono troppo costosi”.

# Global increase and geographic convergence in antibiotic consumption between 2000 and 2015

Eili Y. Klein<sup>a,b,c,1</sup>, Thomas P. Van Boeckel<sup>d</sup>, Elena M. Martinez<sup>a</sup>, Suraj Pant<sup>a</sup>, Sumanth Gandra<sup>a</sup>, Simon A. Levin<sup>e,f,g,1</sup>, Herman Goossens<sup>h</sup>, and Ramanan Laxminarayan<sup>a,f,i</sup>

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[www.pnas.org/cgi/doi/10.1073/pnas.1717295115](http://www.pnas.org/cgi/doi/10.1073/pnas.1717295115)



**Fig. 2.** Global antibiotic consumption by country income classification: 2000–2015. (A) Graph showing how the antibiotic consumption rate in DDDs per 1,000 inhabitants per day has rapidly increased for LMICs, while remaining nearly constant for HICs. However, as shown in B, the larger population sizes in many LMICs result in greater total antibiotic consumption (DDD) in LMICs even though their consumption rate (and thus per capita use) is lower. In B, each bar reflects total consumption in the specified year for that country or group of countries. Data source: IQVIA MIDAS, 2000–2015, IQVIA Inc. All rights reserved (<https://www.iqvia.com/solutions/commercialization/geographies/midas>).



## Relentless increase of resistance to fluoroquinolones and expanded-spectrum cephalosporins in *Escherichia coli*: 20 years of surveillance in resource-limited settings from Latin America

A. Bartoloni<sup>1,2</sup>, L. Pallecchi<sup>3</sup>, E. Riccobono<sup>3</sup>, A. Mantella<sup>1</sup>, D. Magnelli<sup>1</sup>, T. Di Maggio<sup>3</sup>, A. L. Villagran<sup>4</sup>, Y. Lara<sup>5</sup>, C. Saavedra<sup>6</sup>, M. Strohmeyer<sup>1</sup>, F. Bartalesi<sup>2</sup>, C. Trigoso<sup>7</sup> and G. M. Rossolini<sup>3,8</sup>

1) Dipartimento Area Critica Medico Chirurgica, Clinica Malattie Infettive, Università Di Firenze, Florence, Italy, 2) Malattie Infettive e Tropicali, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy, 3) Dipartimento di Biotecnologie, Sezione di Microbiologia, Università di Siena, Siena, Italy, 4) Hospital Basico Villa Montes, Villa Montes, Bolivia, 5) Hospital San Antonio de los Sauces, Monteagudo, Bolivia, 6) Hospital Dermatologico, Monteagudo, Bolivia, 7) Facultad de Medicina, Enfermería, Nutrición y Tecnología Médica, Universidad Mayor de San Andrés, La Paz, Bolivia and 8) Dipartimento di Emergenza, Urgenza e dei Servizi Diagnostici, UO Microbiologia e Virologia, Azienda Ospedaliera-Universitaria Senese, Siena, Italy

**TABLE 1.** Antibiotic resistance rates in commensal *Escherichia coli* from healthy children in the Bolivian Chaco over the past two decades

Year	No. of studied children	Urban areas (no. of children) <sup>a</sup>	Antibiotic resistance rates (%) <sup>b</sup>						Reference	
			AMP	TET	SXT	CHL	NAL	CIP		ESC
1992	296	C (296)	97	92	94	69	4	0	0	[7]
2002	1594	C (794), VM (790)	97	94	96	70	36	16	0.1	[5]
2005	1600	C (800), VM (800)	97	92	94	67	51	26	1.9	[6]
2011	482	C (160), VM (156), M (166)	98	95	94	78	76	44 <sup>c</sup>	12 <sup>d</sup>	This study

<sup>a</sup>C, Camiri; VM, Villa Montes; M, Monteagudo.

<sup>b</sup>AMP, ampicillin; TET, tetracycline; SXT, trimethoprim-sulphamethoxazole; CHL, chloramphenicol; NAL, nalidixic acid; CIP, ciprofloxacin; ESC, expanded-spectrum cephalosporins (ceftriaxone and/or ceftazidime).

<sup>c</sup>Camiri 39%, Villa Montes 40%, Monteagudo 51%.

<sup>d</sup>Camiri 9%, Villa Montes 17%, Monteagudo 11%.



# Antibióticos, solamente con receta del profesional de salud



HOLA DOÑA ROSA ME CONTARON QUE TU HIJITA CHARO ESTÁ MUY ENFERMITA

SI DOÑA NANCY, MI CHARITO ESTÁ CON FIEBRE, SU PECHITO SE HUNDE Y SE JALA ENTRE SUS COSTILLAS, Y TAMBIÉN ESTÁ POSHEQUITA.

LE VOY A DAR LA MEDICINA QUE COMPRE EN LA FARMACIA POR RECOMENDACION DE MI VECINA

¡QUE!

¡AY DOÑA NANCY!, LA SEÑORITA DE LA FARMACIA DICE QUE LE VA A SANAR RAPIDITO.

Y PARA QUE NO SIGA POSHECA, LE VOY A CONVIDAR BASTANTE CHICHA DE MAÍZ BIEN COCINADO CON CUATRO HACHAS OXIDADAS QUEMADAS EN CARBÓN AL ROJO VIVO, Y CON ESO MI HIJITA VA HACERSE BIEN CHAPOSA.

3

Proyecto "ANTRES"

DISCULPE, ESCUCHE LA CONVERSACION DE LAS DOS Y NINGUNA TIENE RAZON! NO HAY QUE USAR ASI NOMAS LAS MEDICINAS, PUEDEN HACERLE DAÑO A CHARITO. LLEVELO RAPIDAMENTE AL HOSPITAL Y EL PROFESIONAL DE SALUD SABRA INDICAR LO CORRECTO.

OYE CHABELA, SI SARA NO HUBIERA ESTADO AQUI, HABRIAMOS COMETIDO UNA BURRADA.

¡CARITOS ES LLEVADO AL CENTRO DE SALUD!

MUY BIEN CHARITITO, VAS A TOMAR ANTIBIOTICOS POR 7 DIAS, CADA 8 HORAS

8

Proyecto "ANTRES"

DOÑA SARA, MI HIJITO YA ESTA TOMANDO LOS ANTIBIOTICOS QUE LE RECOMENDÓ EL PROFESIONAL DE SALUD, DESDE HACE TRES DIAS Y ESTA MEJOR, PERO SI SIGO DÁNDOLE SE VA HACER POSHECA, DICEN QUE MATA LA SANGRE.

NO DOÑA CHABELA! CUMPLE CON LOS DIAS INDICADOS, SI NO SE COMBATE LA BACTERIA SE HACE MAS FUERTE LA ENFERMEDAD Y PUEDE VOLVER CON MAS COMPLICACIONES!

ENTONCES, SEGUIRE DÁNDOLE SU REMEDIO PARA QUE SE SANE COMPLETAMENTE.

CLARO DOÑA CHABELA! RECUERDA "SI A TU LULLLITO QUIERES SANAR EL TRATAMIENTO COMPLETO DEBERÁS USAR"

GRACIAS POR RECORDARMELO, ASI LO HARE

9

Proyecto "ANTRES"

FIN





# LOS ANTIBIÓTICOS Y SU USO

## BUEN USO

## MAL USO



## ¿Qué ganas si usas bien los Antibióticos?

**MENOS GASTOS Y MENOS COMPLICACIONES  
EN LA VIDA POR PROBLEMAS DE SALUD**

Comité de Apoyo al





**Si a tu llullito quieres sanar**



**"Antibióticos, solamente con receta del profesional de salud"**

**el tratamiento COMPLETO debes usar**



**Los antibióticos son adecuados**



**"Antibióticos, solamente con receta del profesional de salud"**

**cuando el profesional de salud te los ha recetado**



## Citrobacter braakii carrying plasmid-borne *mcr-1* colistin resistance gene from ready-to-eat food from a market in the Chaco region of Bolivia

Samanta Sennati<sup>1</sup>, Vincenzo Di Pilato<sup>2</sup>,  
Eleonora Riccobono<sup>3</sup>, Tiziana Di Maggio<sup>1</sup>,  
Ana Liz Villagran<sup>4</sup>, Lucia Pallecchi<sup>1</sup>,  
Alessandro Bartoloni<sup>3,5</sup>, Gian Maria Rossolini<sup>3,6</sup> and  
Tommaso Giani<sup>1\*</sup>

<sup>1</sup>Department of Medical Biotechnologies, University of Siena, Siena, Italy; <sup>2</sup>Department of Surgery and Translational Medicine, University of Florence, Florence, Italy; <sup>3</sup>Department of Experimental and Clinical Medicine, University of Florence, Careggi University Hospital, Florence, Italy; <sup>4</sup>Hospital Básico Villa Montes, Villa Montes, Plurinational State of Bolivia; <sup>5</sup>Infectious and Tropical Diseases Unit, Florence Careggi University Hospital, Florence, Italy; <sup>6</sup>Clinical Microbiology and Virology Unit, Florence Careggi University Hospital, Florence, Italy



## Epidemiological Alert

Enterobacteriaceae with plasmid-mediated transferable colistin resistance, public health implications in the Americas

10 June 2016

Due to the detection in several countries in the Region of the Americas of plasmid-mediated colistin resistance mechanism encoded by the *mcr-1* gene, isolated from animals and humans, the Pan American Health Organization / World Health Organization (PAHO / WHO) urges Member States to implement and maintain the capability to detect, prevent and control transmission of colistin resistance *mcr-1* microorganisms. PAHO / WHO also calls on Member States to take measures leading to prohibiting the use of these antimicrobials for prophylaxis and as growth promoters in animals destined for human consumption.

### Situation summary

In November 2015, the detection of a plasmid-mediated colistin resistance mechanism, related to the *mcr-1* (**M**obile **C**olistin **R**esistance) gene that produces an enzyme responsible for bacterial resistance to this antibiotic treatment, was reported. Colistin is a last line antibiotic used for treatment of multidrug-resistant infections. This *mcr-1* gene is in a plasmid, allowing bacteria to easily spread the resistance to other bacteria.<sup>1</sup>

Until this discovery, it had been known that resistance to polymyxin, in which colistin is included, occurred by chromosomal mutations and the horizontal transfer of genes conferring resistance has not been reported.

The identification of this gene occurred through a retrospective study of prevalence *mcr-1* gene in *E. coli* and *K. pneumoniae* strains collected between April 2011 and November 2014 in China. The study identified *mcr-1* carriage in *E. coli* isolates collected from 78 (15%) out of 523 samples of raw meat; 166 (21%) out of 804 animal samples; and 16 (1%) out of 1,322 samples from inpatients with infection.

Other countries later reported similar retrospective findings. The *mcr-1* gene was detected in databases and collections of bacterial strains from all continents. Samples of bacteria such as *E. coli* and *Salmonella*, with plasmid mediated colistin resistance, were isolated from various sources: humans (isolates from the community), pigs, and poultry meat.<sup>2, 3, 4</sup>

### Colistin Resistance (or polymyxin $\beta$ )

Colistin belongs to the polymyxin family, broad spectrum antibiotic discovered in the 1940s to treat gram-negative infections. After several years of clinical use, its popularity declined because of its nephrotoxicity and neurotoxicity.

In recent years, the antibiotic has reemerged as a last line treatment option for organisms resistant to multiple antibiotics, including carbapenems, such as *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* responsible for high morbidity and mortality health care associated infections.

Until a few years ago colistin resistance had been rare and mostly chromosomally mediated, and involved mutations in genes leading to modification in the lipopolysaccharide, the colistin site of action.<sup>2, 3</sup>



# High prevalence of carriage of *mcr-1*-positive enteric bacteria among healthy children from rural communities in the Chaco region, Bolivia, September to October 2016

Tommaso Gianì<sup>1,2</sup>, Samanta Sennati<sup>1</sup>, Alberto Antonelli<sup>2</sup>, Vincenzo Di Pilato<sup>2</sup>, Tiziana di Maggio<sup>1</sup>, Antonia Mantella<sup>2</sup>, Claudia Niccolai<sup>2</sup>, Michele Spinicci<sup>2</sup>, Joaquín Monasterio<sup>3</sup>, Paul Castellanos<sup>4</sup>, Mirtha Martínez<sup>5</sup>, Fausto Contreras<sup>5</sup>, Dorian Balderrama Villaroel<sup>6</sup>, Esther Damiani<sup>6</sup>, Sdenka Maury<sup>7</sup>, Rodolfo Rocabado<sup>8</sup>, Lucía Pallecchi<sup>1</sup>, Alessandro Bartoloni<sup>1,9</sup>, Gian Maria Rossolini<sup>1,10</sup>

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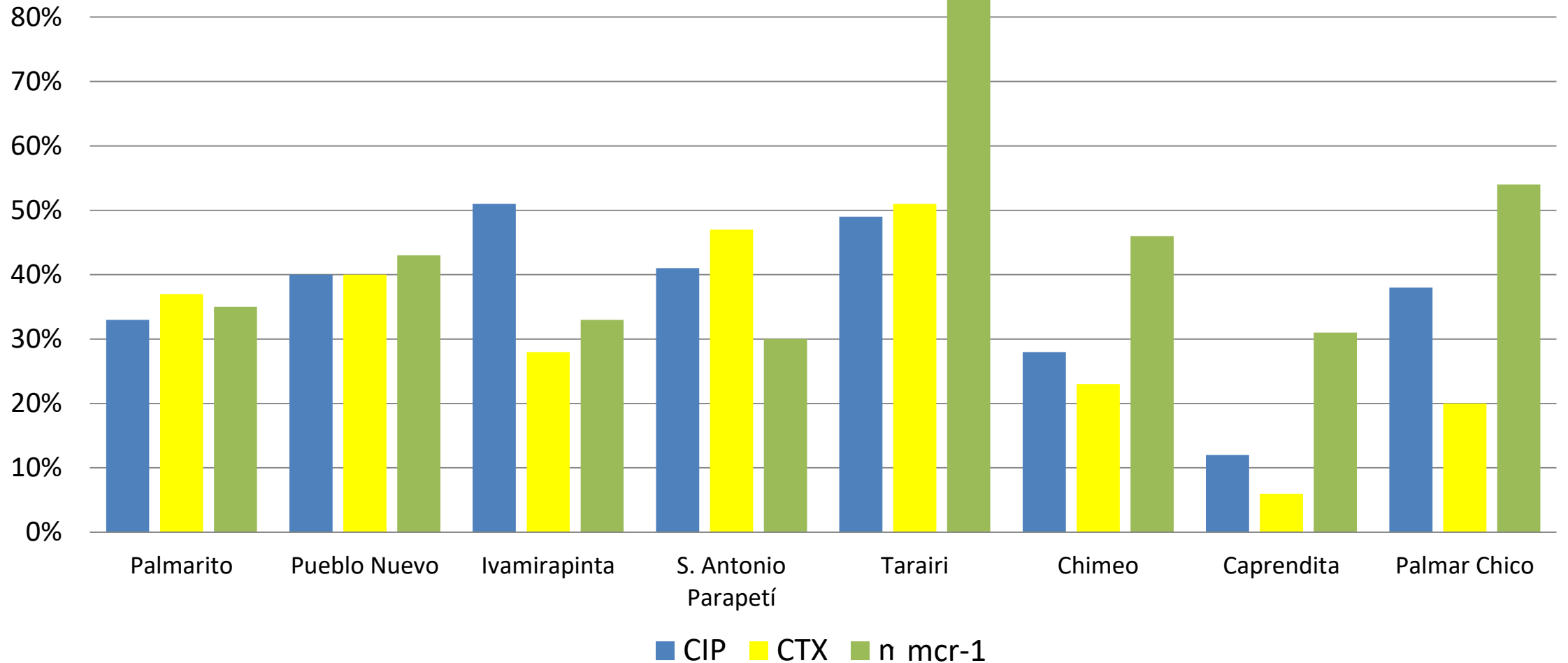
<sup>8</sup>. Servicios Generales de Salud, Ministerio de Salud, La Paz, Bolivia

<sup>9</sup>. Infectious and Tropical Diseases Unit, Careggi University Hospital, Florence, Italy

<sup>10</sup>. Clinical Microbiology and Virology Unit, Careggi University Hospital, Florence, Italy

## Fecal carriage of resistant enterobacteria in school children living in the Bolivian Chaco 2016

Euro Surveill. 2018;





Ministerio de  
Desarrollo Rural y Tierras

SERVICIO NACIONAL DE SANIDAD AGROPECUARIA  
E INOCUIDAD ALIMENTARIA  
REGISTRO DE EMPADRONAMIENTO DE PRODUCTOS

Todos los productos de la unidad \*\* Principio Activo: colistina \*\*\* Clase:  
Farmacológicos \*\*\*\* Tipo: Antibiótico



Registro	Nombre comercial	Ingrediente activo	Laboratorio producción	Pais(es) de origen	Clase	Tipo	Fecha Registro
004627/11	AGROFLORMICIN	ERITROMICINA, COLISTINA	AGROSERVET S.R.L.	Bolivia	Farmacológico	Antibióticos	
002506/08	AMOXICOL PS	AMOXICILINA TRIHIDRATO Y COLISTINA BASE	LABORATORIOS FAEVE S.A.	Argentina	Farmacológico	Antibióticos	31/07/1
000883/05	COLIALPLUCINA	COLISTINA (SULFATO) JOSAMICINA	VIRBAC S.A. DE C.V.	México	Farmacológico	Antibióticos	01/07/1
003839/09	COLIMICIN PREMIX	COLISTINA Sulfato 80 g, Carbonato de Calcio 1000 g	PLUS COMAGRO S.R.L.	Bolivia	Farmacológico	Antibióticos	07/11/1
004354/10	COLIMIX	COLISTINA 40 G., C.S.P.	PERUVIAN PHARMACEUTIC S.A.C.	Perú	Farmacológico	Antibióticos	15/11/1
005077/12	COLIMIX 8	COLISTINA 40 G., BROMHEXINA HCl 0.5 g.	PERUVIAN PHARMACEUTIC S.A.C.	Perú	Farmacológico	Antibióticos	02/07/1
006061/14	COLISEPT AVG	LEVOFLOXACINO 20 g., COLISTINA Sulfato (como Colistina Base) 10.0 g.	MONTANA S.A.	Perú	Farmacológico	Antibióticos	22/06/1
007082/16	COLISPRO	COLISTINA Sulfato (como Colistina Base) 10.0 g.	PLUS COMAGRO S.R.L.	Bolivia	Farmacológico	Antibióticos	09/08/1
007460/16	COLISTIN PLUS-8	Sulfato de Colistina 80 gr	PLUS COMAGRO S.R.L.	Bolivia	Farmacológico	Antibióticos	21/08/1
000744/05	COLISTINA 20% POLVO ORAL	COLISTINA BASE (como Sulfato)	VETERQUIMICA S.A.	Chile	Farmacológico	Antibióticos	30/11/1
001756/07	COLISTINA SOLUBLE	Sulfato de Colistina	COMERCIO E INDUSTRIA UNIQUMICA	Brasil	Farmacológico	Antibióticos	24/12/1
007133/16	COLISTINA Sulfato 10% BIOFARMA	COLISTINA (como Sulfato) 10.00 G, Afrechillo de Trigo	BIOFARMA S.A.	Argentina	Farmacológico	Antibióticos	



**RESOLUCIÓN ADMINISTRATIVA - SENASAG N° 0158/2019.**

Santísima Trinidad, 14 de Agosto del 2019

El Director General Ejecutivo a.i. del Servicio Nacional de Sanidad Agropecuaria e Inocuidad Alimentaria "SENASAG", Dr. Jorge Antonio Berrios Arévalo, **JEFE NACIONAL DE SANIDAD ANIMAL**, designado mediante **Resolución Administrativa N°156/2019**, con la facultad conferida por el artículo 10, del Decreto Supremo N° 25729.

**RESUELVE:**

**ARTÍCULO PRIMERO (OBJETO).**- **PROHÍBASE** en todo el territorio nacional, el registro, importación, fabricación, comercialización y uso de productos de uso veterinario que contengan el ingrediente activo "COLISTINA" (POLIMIXINA E), y sus sales, como parte de su formulación como promotores de crecimiento animal destinados al consumo humano.



# Antimicrobial resistance among migrants in Europe: a systematic review and meta-analysis

Laura B Nellums\*, Hayley Thompson\*, Alison Holmes, Enrique Castro-Sánchez, Jonathan A Otter, Marie Norredam, Jon S Friedland, Sally Hargreaves

	All migrants	Refugees and asylum seekers	Other migrants	High-migrant community setting	Hospital
Any detected antimicrobial resistance carriage or infection	25.4% (19.1–31.8)	33.0% (18.3–47.6)	6.6% (1.8–11.3)	33.1% (11.1–55.1)	24.3% (16.1–32.6)
Meticillin-resistant <i>Staphylococcus aureus</i>	7.8% (4.8–10.7)	8.2% (5.0–11.3)	6.0% (1.3–10.7)	9.8% (0.0–20.3)	7.4% (4.2–10.6)
Drug-resistant Gram-negative bacteria	27.2% (17.6–36.8)	27.2% (17.2–37.1)	27.3% (6.0–6.1)	32.1% (19.9–44.4)	24.9% (10.9–39.0)

Data are pooled prevalence (95% CI).

Table 2: Antibiotic resistance across migrant groups and settings

# Tubercolosi

- ❑ L'incidenza della TB resistente ai farmaci è aumentata costantemente negli ultimi anni, minacciando l'obiettivo di porre fine alla sua diffusione pandemica
- ❑ Secondo il rapporto OMS, a livello globale, nel 2021 si sono verificati circa 450.000 nuovi casi (IC 95% 399.000–501.000) di TB resistente ai farmaci (MDR-TB) che rappresentano circa il 4% dei casi totali
- ❑ Rifugiati e migranti sono tra le categorie più a rischio di sviluppare la TB a causa delle loro condizioni di vita e del sovraffollamento negli insediamenti che ne aumentano potenzialmente il rischio
- ❑ L'impatto della migrazione sull'epidemiologia della TB è elevato e la diffusione globale della MDR-TB è stata strettamente collegata alla migrazione umana
- ❑ I numeri di nuovi casi di TB notificati restano comunque relativamente bassi nelle nazioni del Nord America e dell'Europa occidentale e in genere variano al di sotto di 25 per 100.000 persone
- ❑ Precedenti trattamenti con farmaci anti-tubercolari e lo stato di nato all'estero sono i maggiori fattori di rischio per MDR-TB
- ❑ I frequenti trasferimenti e le barriere linguistiche e culturali acquiscono le difficoltà per il tracciamento dei contatti nelle popolazioni migranti per cui si rendono necessarie strategie specifiche per il controllo della TB nei Paesi di accoglienza



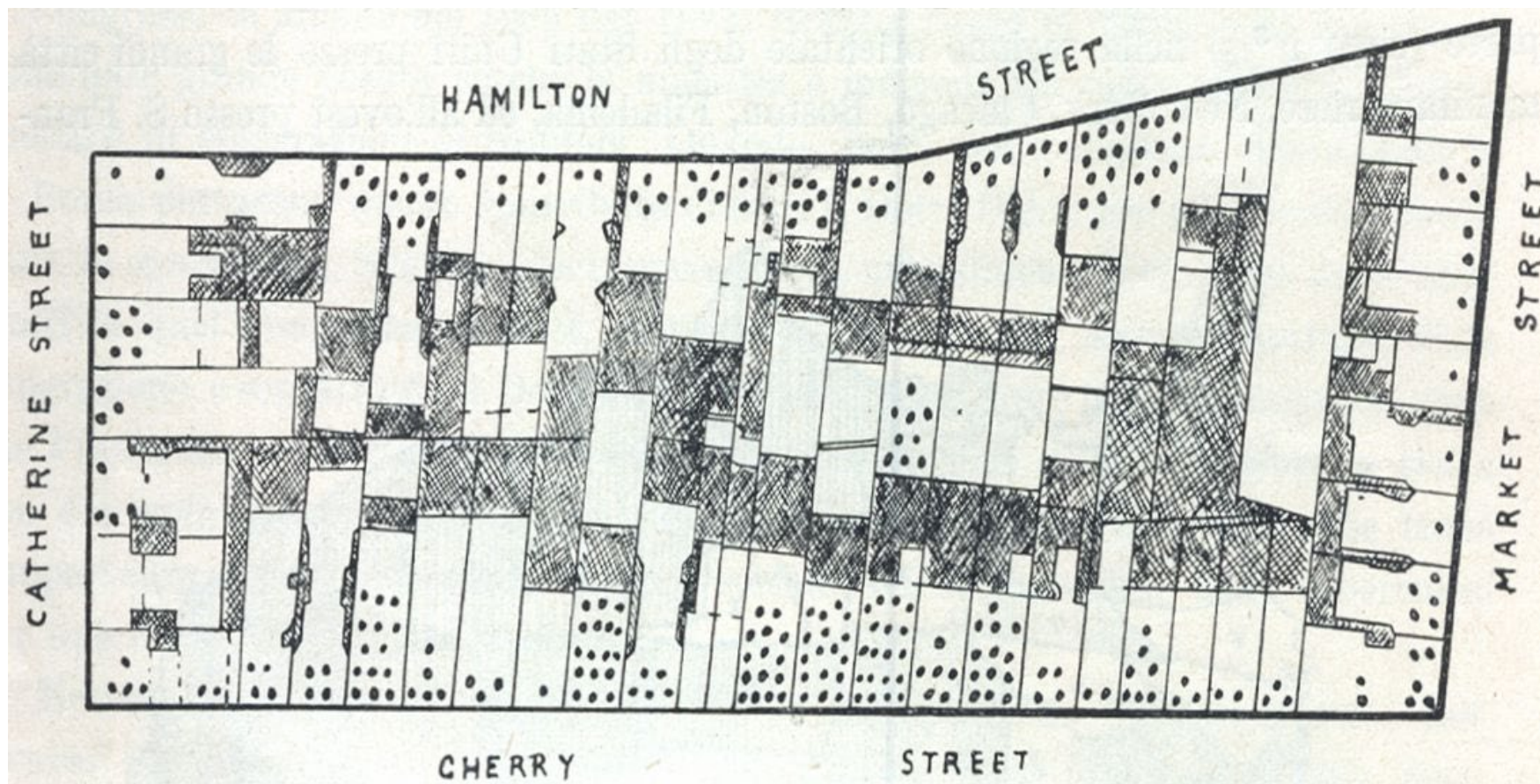


Fig. 9. — Pianta del « Lung's Block » di New York, abitato quasi esclusivamente da italiani.

(da STELLA).

Le zone *tratteggiate* rappresentano l'area scoperta delle abitazioni ed i *punti* il numero dei casi di tubercolosi polmonare negli anni dal 1894 al 1903.



Tenendo conto che la nostra emigrazione è formata con gente nel fiore dell'età, selezionata e volontariamente e perchè così vogliono i paesi immigratori, occorre pensare che il germe specifico trovi terreno adatto al suo sviluppo per diminuita resistenza organica del nostro lavoratore e per facilitato contagio in individui originariamente immuni.

Le influenze dannose sull'organismo possono essere riconosciute nel clima e nel lavoro mettendo in confronto l'emigrazione al Sud con quella diretta al Nord. Nel primo caso sono prevalentemente agricoltori dell'Italia settentrionale, i quali lavorano nei vasti campi dell'Argentina e, sia pure, nelle *fazendas* del Brasile, che vivono in ambienti rustici sì, ma costruiti in mezzo alle *pampas* o a foreste semi-vergini ove l'aria si rinnova più spesso ed è più pura (se non c'è malaria). Nelle città sopra-popolate, però, le tristi condizioni d'abitabilità si fanno risentire anche in queste regioni.

Nel secondo caso, prevalgono i contadini dell'Italia meridionale e delle isole, che trasformandosi in operai di qualsiasi mestiere, dopo aver vissuto tutto il giorno in ambienti polverosi o delle cave, o dei lavori ferroviari o delle officine vanno poi a terminare la giornata ed a passare la notte nelle strette straducole e nelle buie casette dei quartieri italiani delle grandi metropoli nord-americane, « non perchè piaccia loro di vivervi, ma perchè la loro povertà ve li obbliga » (STELLA).



# AMR e conflitti











- ❖ Lo sviluppo e la diffusione dell'AMR sono favoriti da condizioni di vita e sanitarie che si associano inevitabilmente allo scoppio e al perdurare di conflitti armati
- ❖ Sovraffollamento, strutture sanitarie danneggiate, carenza di farmaci, risorse insufficienti, mancanza di personale qualificato, malnutrizione, scarsi tassi di vaccinazione e sorveglianza inadeguata del consumo di antimicrobici e della diffusione di resistenze batteriche agli antibiotici costituiscono i presupposti ideali per lo sviluppo dell'AMR
- ❖ Ferite da esplosivi o ustioni possono essere facilmente contaminate da batteri con il personale sanitario che, durante tali emergenze, finisce per occuparsi esclusivamente della stabilizzazione della condizione acuta e non della cura a lungo termine.
- ❖ Diagnosi inadeguate e utilizzo di farmaci scaduti o obsoleti, contribuiscono all'aumento dei tassi di AMR nelle aree oggetto di conflitto armato

# AMR e conflitti: guerra in Siria

Review

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## Antimicrobial resistance in the protracted Syrian conflict: halting a war in the war

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& Monzer Hamze<sup>1</sup>



The Syrian conflict has led to a devastating humanitarian crisis creating one of the largest global refugee crises in modern history. According to the current estimations of the United Nations High Commissioner for Refugees, there are 6.6 million internally displaced persons in Syria and 5.6 million refugees abroad. The majority of Syrian refugees are hosted in neighboring countries such as Turkey (3.6 million), Lebanon (1 million) and Jordan (0.66 million) though there are larger numbers of unregistered refugees [6,7].

Emerging evidence from several conflict-affected countries shows that conflict provides ideal conditions for AMR to develop and spread, and the protracted 9-year armed conflict in Syria is not an exception to this rule [8].

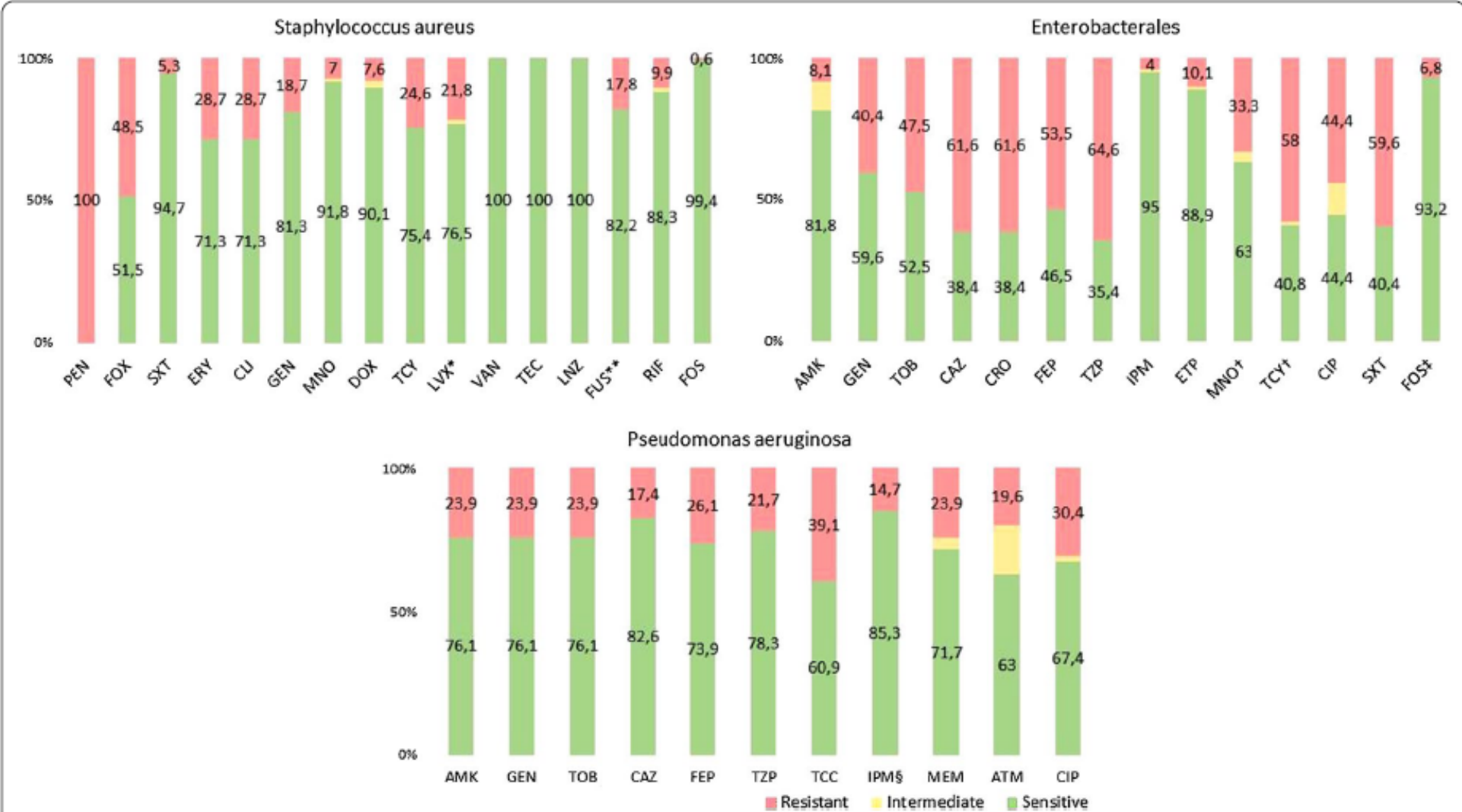


**Table 1. Spotlight on antimicrobial resistance levels inside Syria before and after the Syrian crisis.**

Location	Year	Study description	Sample	Key findings	Ref.
<b>Antimicrobial resistance data in Syria before the onset of the crisis</b>					
Syria	2003	A nationwide surveillance	-	8% of new TB cases were RIF resistant/MDR-TB	[23]
Misiyf	2004	Prospective culture analysis of urine samples from all outpatients in the community	127 positive samples	68.6% of isolates were Enterobacteriaceae and 30.6% were Gram-positive mainly <i>Staphylococcus aureus</i> Resistance was for AMP (69%), TMP-SMX (55%), AMC (37%), OFX (35%)	[24]
Damascus	September 2003–May 2004	Susceptibility testing of <i>Streptococcus pneumoniae</i> from meningitis children	25 isolates	64% were resistant to PEN, 48% to TMP-SMX, 16% to ERY and 16% to TET No resistance to 3GC and AMC	[25]
NR	1995–2005	Susceptibility testing of <i>Brucella melitensis</i> isolates from animals in Syria	Five Syrian isolates	100% of isolates were susceptible to tetracycline, streptomycin, gentamicin, ciprofloxacin, norfloxacin and levofloxacin	[26]
Damascus	2010	Prospective isolation of aerobic bacteria from diabetic foot ulcers and their susceptibility to antibiotics	128 isolates of 100 specimens	61% of <i>S. aureus</i> were MRSA	[27]
Damascus	2012	Isolation of aerobic bacteria from conjunctivitis along with antibiotic susceptibilities	51 patients	High susceptibility to first and second-line agents reported	[27]
Damascus	2012	Susceptibility testing of aerobic bacteria isolated from tonsillitis of children with recurrent tonsillitis	80 patients	25% of <i>Klebsiella pneumoniae</i> isolates were carbapenem resistant and 15% of <i>Escherichia coli</i> were IMP resistant	[28]
Aleppo	January 2008–June 2011	Review of <i>Acinetobacter baumannii</i> isolates from outpatients	260 nonrepetitive isolates	65% of isolates were IMP resistant and 7% were CST resistant Resistance was: 87% for TZP, 80–95% 3GC, 85% 4GC, 81% CP, 78% AMK, 74% TMP-SMX, 7% CST	[29]
Aleppo	October 2010 and June 2011	Prevalence of PMQR genes ( <i>qnrA</i> , <i>qnrB</i> , <i>qnrS</i> , <i>qepA</i> and <i>aac[6']-Ib-cr</i> ) among ESBL-producing isolates obtained from three university hospitals	123 nonrepetitive isolates (99 <i>E. coli</i> and 24 <i>K. pneumoniae</i> )	66% of the ESBL-producing isolates were CP-resistant 84% had one of the five PMQR genes with <i>aac[6']-Ib-cr</i> variant (75.6%) being the most common PMQR genes followed by <i>qnrB</i> (24.4%) and <i>qnrS</i> (16.3%); No <i>qnrA</i> or <i>qepA</i> genes were identified	[30]
NR	2008–2011	Epidemiology of all Finnish CPE isolates found until the end of 2011	One patient	The first OXA-48 producing <i>E. coli</i> reported in Finland was imported from Syria in 2009	[31]
NR	2008	Molecular analysis of CPE isolates recovered in Germany between 2008 and 2010	One patient	Sporadic report of OXA-48 producing <i>E. coli</i> from a patient previously hospitalized in Syria	[32]
NR	January 2010–April 2011	Molecular analysis of OXA-48 producing CPE recovered at nine Belgian hospitals during the study period	One patient	Sporadic report of OXA-48 producing <i>E. coli</i> from a patient previously hospitalized in Syria (before 2010)	[33]

3GC: Third-generation cephalosporin; 4GC: Fourth-generation cephalosporin; AMC: Amoxicillin/clavulanate; AMK: Amikacin; AMP: Ampicillin; CP: Ciprofloxacin; CPE: Carbapenemase-producing *E. coli*; CST: Colistin; EMB: Ethambutol; ERY: Erythromycin; ESBL: Extended spectrum  $\beta$ -lactamases; GM: Gentamicin; IMP: Imipenem; INH: Isoniazid; LVX: Levofloxacin; MDR: Multidrug resistant; MRSA: Methicillin-resistant *Staphylococcus aureus*; NIF: Nitrofurantoin; NR: Not reported; OFX: Ofloxacin; PEN: Penicillin; PMQR: Plasmid-mediated quinolone resistance; RIF: Rifampicin; RRDR: Rifampicin drug resistance region; STR: Streptomycin; TB: Tuberculosis; TET: Tetracycline; TMP-SMX: Trimethoprim-sulfamethoxazole; TZP: Piperacillin-tazobactam; VRSA: Vancomycin-resistant *S. aureus*.

Valutazione retrospettiva degli antibiogrammi di tutti gli isolati consecutivi non duplicati dai campioni prelevati da pazienti ricoverati al Weapon Traumatology Training Center of the International Committee of the Red Cross in Tripoli tra il 2016 e il 2019 da campioni di cute e tessuti molli e biopsie ossee



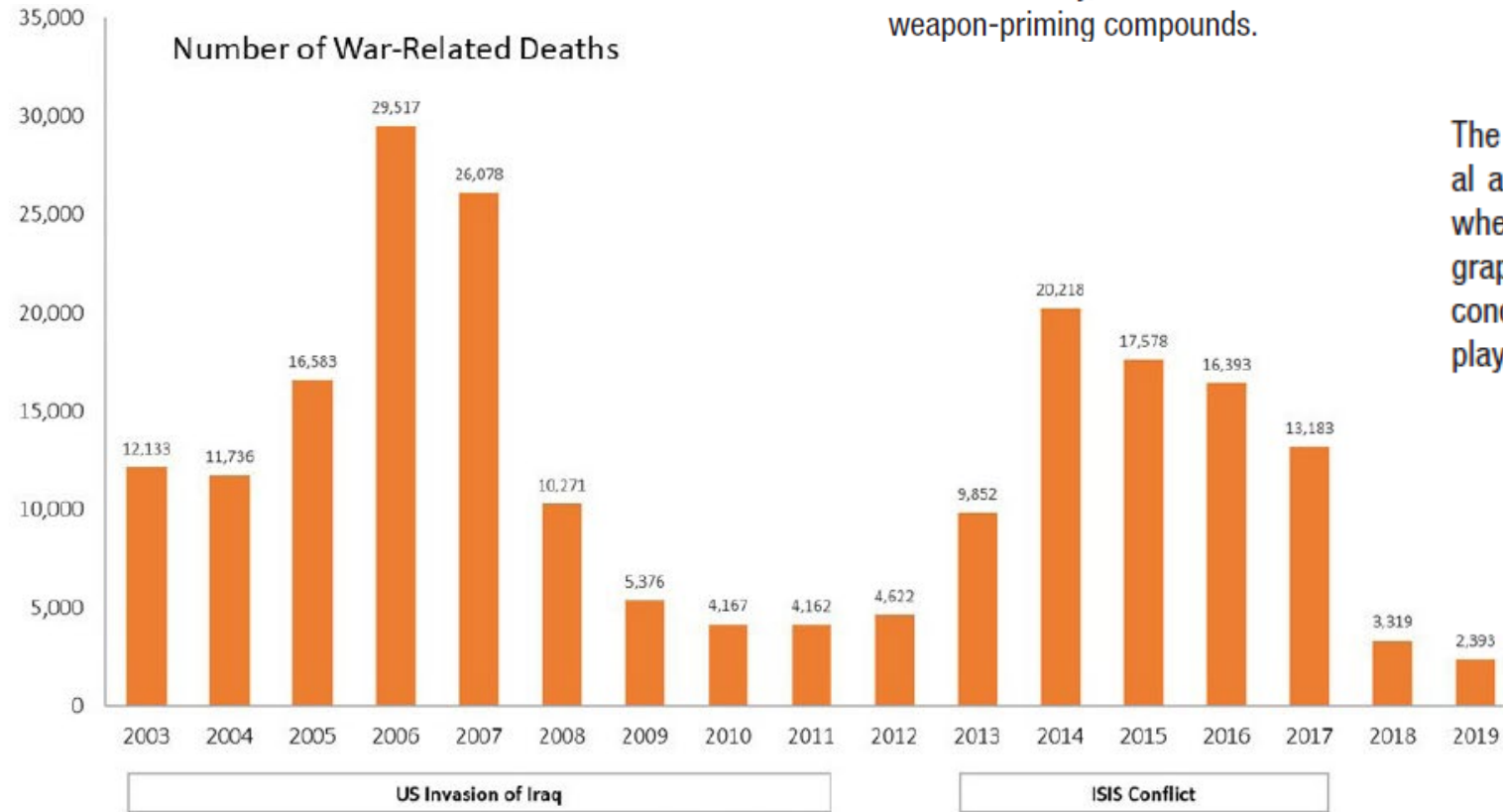
**Fig. 1** Antibiotic resistance profiles of *Staphylococcus aureus* (n = 171), Enterobacterales (n = 99), and *Pseudomonas aeruginosa* isolates (n = 46). \*n = 119, \*\*n = 157, †n = 81, ‡n = 74, §n = 34. AMK Amikacin, ATM Aztreonam, CAZ Ceftazidime, CIP Ciprofloxacin, CLI Clindamycin, CRO Ceftriaxone, DOX Doxycycline, ERY Erythromycin, ETP Ertapenem, FEP Cefepime, FOS Fosfomycin, FOX Cefoxitin, FUS Fusidic acid, GEN Gentamicin, IPM Imipenem, LNZ: Linezolid, LVX Levofloxacin, MEM Meropenem, MNO Minocycline, PEN Penicillin, SXT Trimethoprim-sulfamethoxazole, TCC Ticarcillin-clavulanic acid, TCY Tetracycline, TEC Teicoplanin, TOB Tobramycin, TZP Piperacillin-tazobactam, VAN Vancomycin



# AMR e conflitti: guerra in Iraq

AMR co-selection from heavy metals is becoming more strongly implicated due to conflict-driven environmental contamination, as with lead, mercury, chromium, copper, lead nickel and zinc used to coat bullets, missiles, gun barrels and military vehicles, while antimony, barium and boron are used as weapon-priming compounds.

Iraq experienced a sequence of conflicts since the 1980s, and reports point to a progressive deterioration of Iraq's national healthcare system, lack or limitation in trained staff, infection prevention and control, access to antibiotics as well as sanitation control and debridement of highly contaminated wounds from explosives or burns, as well as inappropriate diagnoses and drug regimens, all potential contributors to the rising rates of AMR in Iraq.



The rise of AMR in Iraq, with indications of regional and global spread, remains direly understudied, where clinical, microbiological, historical, ethnographic and environmental research is needed to conclusively establish the roles that war and conflict play in the rise of multidrug-resistant organisms.

Understanding the link between AMR and conflict is essential for a global response to AMR, especially with little indication that global conflict will abate in years to come.

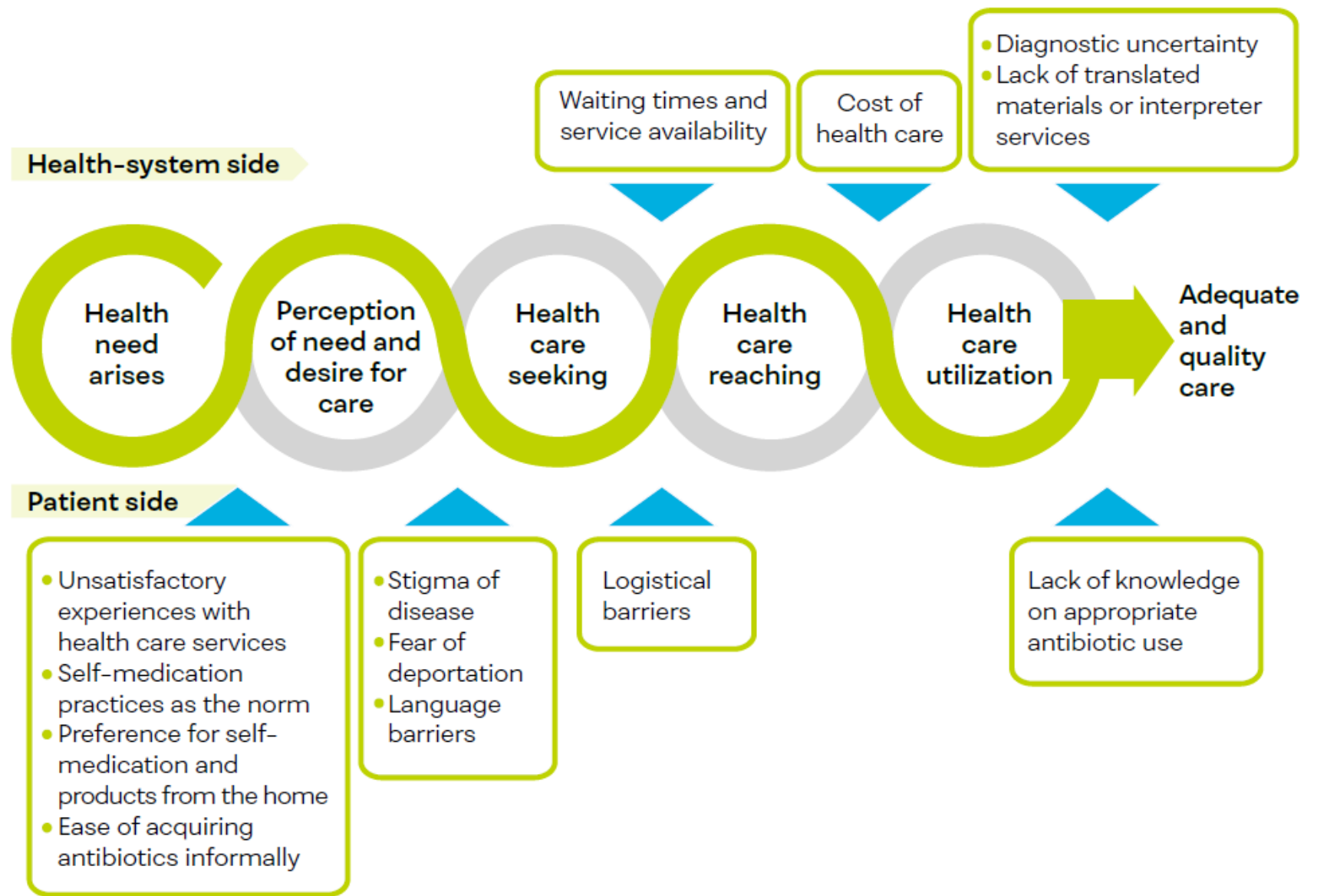
Frequency of war and conflict-related deaths in Iraq (2003–2019). ISIS, Islamic State of Iraq and Syria.

# Fattori associati a disuguaglianze di salute

Factor commonly known to be associated with health inequalities (HI factor), n (%)	Number of papers that included HI factor in research, N= 58	Number of papers that associated HI factor and antibiotic use, N= 58	Summary of results
<b>Protected characteristics</b>			
Age	43 (74)	17 (29)	Older age groups, especially those in residential care, were prescribed more antibiotics than younger age groups. <sup>21-31</sup>
Pregnancy and maternity	2 (3)	2 (3)	Younger pregnant women used more antibiotics than older pregnant women, <sup>24,32</sup> and white more than non-white pregnancy women. <sup>24</sup>
Race/ethnicity	32 (55)	22 (38)	There was an association between race/ethnicity and antibiotic use, particularly in acne and dental infections. <sup>23-26,33-46</sup>
Sex	34 (59)	9 (16)	Females had higher antibiotic use than males. <sup>23,26,27,29,30,34</sup>
Sexual orientation	2 (3)	1 (2)	MSM received recommended treatment for <i>N. gonorrhoeae</i> more often than other men. <sup>39</sup>
<b>Socioeconomic characteristics</b>			
Income	12 (21)	7 (12)	High income resulted in both increased and decreased antibiotic use depending on the healthcare setting and country. <sup>26,29,34,47-49</sup>
Insurance	14 (24)	7 (12)	Patients with no insurance were less likely to be prescribed antibiotics compared with other insurance types. <sup>33,46,50,51</sup>
Employment status	6 (10)	2 (3)	Unemployment was not found to affect antibiotic use across both healthcare settings. <sup>27,52</sup>
Deprivation	10 (17)	8 (14)	Areas of high deprivation had higher antibiotic use compared with areas of no or low deprivation. <sup>30,37,43,44,53,54</sup>
Education	9 (16)	6 (10)	Higher education resulted in improved awareness regarding antibiotics and more rational use. <sup>45,47</sup>
<b>Geography</b>			
Urban versus rural setting	8 (14)	6 (10)	Area of living affected antibiotic use, dependent on care sector and type of infection. <sup>22,26,28,46,55</sup>
Region	13 (22)	7 (12)	The UK and USA found geographical variation in antibiotic use. <sup>34,37,53,56-59</sup>
<b>Vulnerable groups</b> Migration status	6 (10)	6 (10)	There were differences in accessibility to antibiotics across countries; patients who faced barriers to obtaining antibiotics were more likely to seek alternative routes of supply. <sup>60-63</sup>

Harvey EJ, De Brún C, Casale E, Finistrella V, Ashiru-Oredope D. Influence of factors commonly known to be associated with health inequalities on antibiotic use in high-income countries: a systematic scoping review. *J Antimicrob Chemother.* 2023 Apr 3;78(4):861-870

# Ostacoli all'accesso agli antibiotici e uso appropriato lungo il continuum di cura





ORIGINAL ARTICLE


**Differences in antibiotic treatment and utilization of diagnostic tests in Dutch primary care between natives and non-western immigrants**

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*Results:* First generation non-western immigrants were more likely to undergo diagnostic tests and received more antibiotics than native Dutch (respectively OR: 2.08; 95% CI: 1.64–2.63; and OR: 1.31; 95% CI: 1.04–1.65). No differences were found for the second generation immigrants. The results found were independent of potential confounders. *Conclusions:* The highest rates of antibiotic prescription and diagnostic tests concern first generation non-western immigrants. In order to promote a rational and restricted use of antibiotics in outpatients first generation immigrants should be a prioritized target group.

## Prescription of antibiotics in the medical care of newly arrived refugees and migrants

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Christine Happle<sup>4</sup> | Frank Müller<sup>1</sup> | Anne Simmenroth<sup>5</sup>

**Results:** Nineteen percent of all patients in our study received systemic antibiotics during the observation period, with children below the age of 10 years receiving antibiotics most frequently (24%). The most commonly prescribed antibiotics were penicillins (65%), macrolides (12%), and cephalosporins (7%). The most frequent diagnoses associated with antibiotic prescription were acute tonsillitis (26%), bronchitis (21%), infections of the upper respiratory tract (14%), and urinary tract infections (10%). In case of acute bronchitis 74% of the antibiotic prescriptions were probably not indicated. In addition, we found a significant number of inappropriate prescriptions such as amoxicillin for tonsillitis (67%), and ciprofloxacin and cotrimoxazol for urinary tract infections (49%).

**Conclusion:** Regarding inappropriate prescription of antibiotics in refugee healthcare, this study shows a rate ranging from 8% for upper respiratory tract infections to 75% for acute bronchitis. Unnecessary use of antibiotics is a global problem contributing to gratuitous costs, side effects, and antimicrobial resistance. This research contributes to the development of stringent antibiotic stewardship regimens in the particularly vulnerable population of migrants and refugees.



Research article

Open Access

## **Why do paediatricians prescribe antibiotics? Results of an Italian regional project**

Maria Luisa Moro<sup>\*†1</sup>, Massimiliano Marchi<sup>†1</sup>, Carlo Gagliotti<sup>†1</sup>, Simona Di Mario<sup>†2</sup>, Davide Resi<sup>†1</sup> and the "Progetto Bambini a Antibiotici [ProBA]" Regional Group

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I bambini con genitori nati all'estero avevano maggiori possibilità di ricevere prescrizioni di antibiotici per condizioni che era improbabile che fossero di origine batterica



Task Force 10  
Migration

Policy brief

# VACCINATIONS FOR MIGRANTS AND REFUGEES DURING AND AFTER COVID-19

SEPTEMBER 2021

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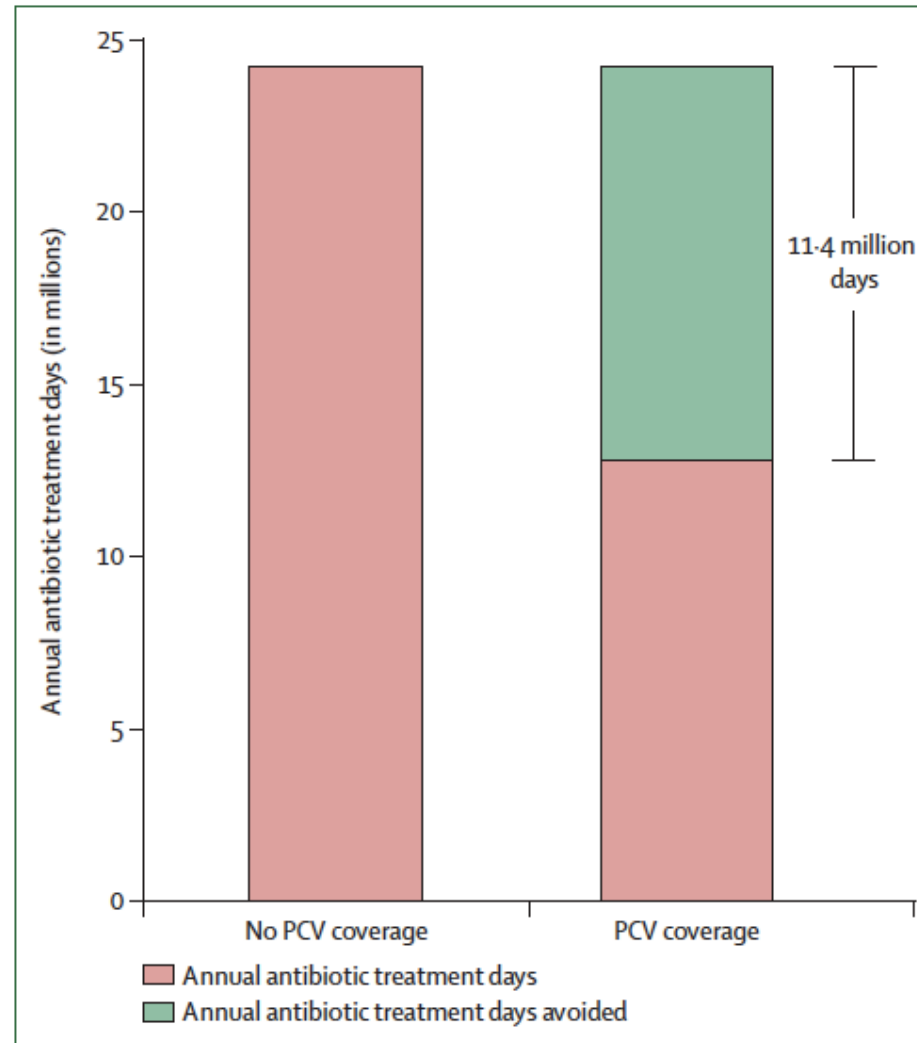


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Ramanan Laxminarayan, Precious Matsoso, Suraj Pant, Charles Brower, John-Arne Røttingen, Keith Klugman, Sally Davies



**Figure 3: Days on antibiotics for suspected pneumonia, averted by provision of pneumococcal conjugate vaccine (PCV)**  
Bar represents antibiotic days avoided with PCV coverage.

# Conclusioni

- ❖ Le popolazioni migranti sono vulnerabili all'AMR e evidenziano la necessità di:
  - migliorare le condizioni di vita
  - garantire l'accesso all'assistenza sanitaria
  - promuovere le iniziative per facilitare l'individuazione e il trattamento appropriato delle infezioni sostenute da germi resistenti agli antibiotici durante il percorso migratorio e nei Paesi ospitanti
- ❖ Programmi di prevenzione e controllo delle infezioni e di sorveglianza dell'AMR dovrebbero essere integrate in tutti gli aspetti dell'assistenza sanitaria e dovrebbero essere accessibili per tutti i gruppi di migranti
- ❖ L'implementazione di programmi di vaccinazione costituisce un approccio efficace per la riduzione dell'uso di antibiotici e di conseguenza della pressione selettiva per lo sviluppo di AMR, per cui le popolazioni di rifugiati e migranti dovrebbero essere incluse nei programmi vaccinali utilizzando strategie adeguate alla condizione di popolazioni fragili da raggiungere



Grazie per  
l'attenzione

