TMT CONGRESS & EVENTS

STEWARDSHIP ANTIMICROBICA IN DIFFERENTI SETTING OSPEDALIERI E TERRITORIALI

21 Ottobre 2024 – Ore 16.00-19.00 VIRTUAL EDITION

Residenze per anziani: monitoraggio terapie antibiotiche e infection control

M. Tinelli

Former Director, Division of Infectious and Tropical Diseases, Hospital of Lodi-South Milan
Consultant of the National Health Council, Ministry of Health, Rome
Executive Committee Member of the Italian Society of Infectious and Tropical Diseases
Executive Committee Member of EUCIC/ESGIE (European Society of Microbiology and Infectious Diseases- ESCMID)

Dati demografici - Italia 2024

Popolazione Italia:

Totale popolazione: **59 ML** abitanti

Totale over 65: 18,68 ML - 24,1 %

Anni 65- 80: **14.18 ML –popolazione**

Anni over 80: **4,5 ML**

Aspettativa di vita (2023):

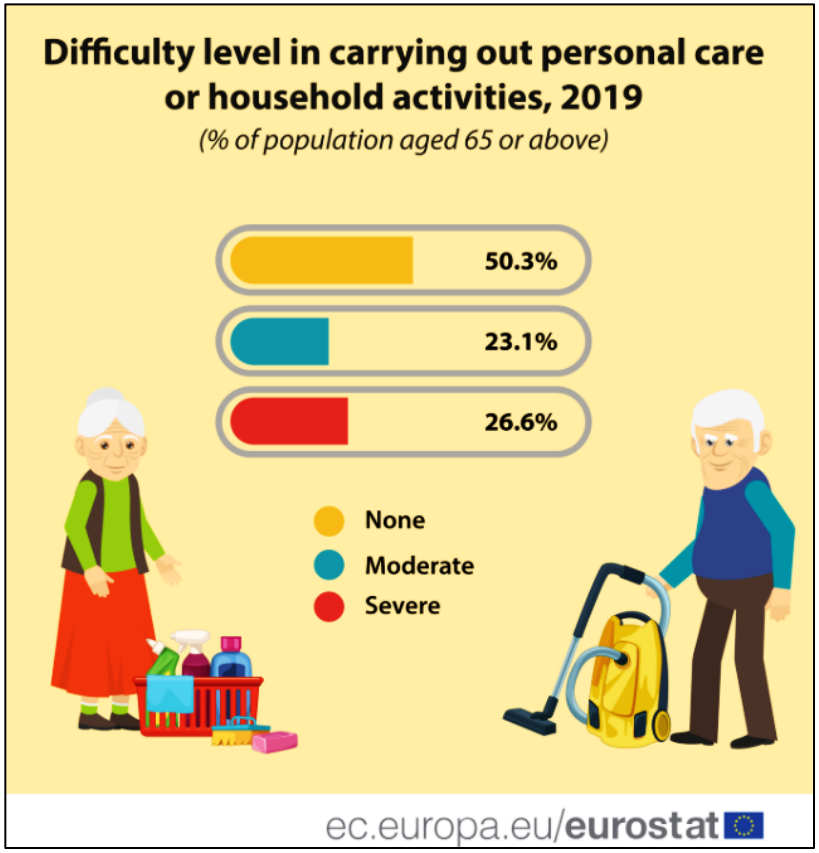
83,1 anni media

85,2 anni donne - 81,1 anni uomini

Nel **2030** la percentuale della popolazione italiana di **65 anni** si assesterebbe intorno al **30%** della popolazione totale;

• Si assisterà ad un **aumento del numero complessivo delle famiglie senza nuclei (persone sole),** con un incremento del 20,5%, da 9 a circa 11 milioni nel periodo 2021-2041 (**41,4% delle famiglie totali**),

Dati ISTAT, CENSIS,SDA Bocconi 2024



Gli anziani **di 65 anni e più** si trovano in condizione di **multicronicità e gravi limitazioni funzionali (3.981.990), in peggioramento rispetto a quanto osservato nel 2021**. Essi sono affetti da almeno una patologia grave:

carcinoma, ictus, Alzheimer, patologie cardiovascolari, diabete, Parkinson, malattie respiratorie croniche

Over65 con limitazioni funzionali per fascia di età, stima 2021

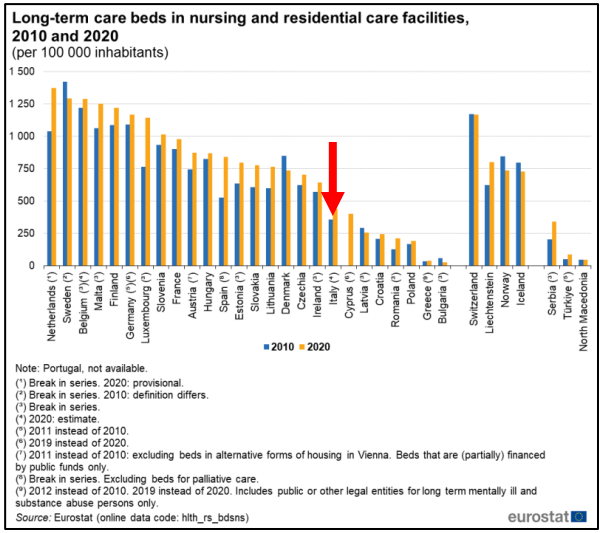
Fascia di età	Prevalenza da Istat (2021)	Popolazione di riferimento (1.1.2021)	Stima
65-74	14,60%	6.915.504	1.009.664
75-84	32,50%	4.825.173	1.568.181
85 e più	63,80%	2.200.854	1.404.145

Dati EUROSTAT e ISTAT 2022

3.981.990

LTCFs in Europe, 2022

In 2020, there were approximately **3.4 million long-term care beds in nursing and residential care facilities** in the 26 EU Member States for which data are available (no data available for Portugal; 2019 data for Germany, Greece and Cyprus).



RSA in Italia

Dal **2017 al 2022** In Italia siamo passati dalle **220 mila** persone con oltre 65 anni residenti in RSA alle **327 mila**, con un boom proprio negli ultimi due anni post pandemia. Nel 2022 il **2,5% degli anziani** con almeno 65 anni e il **4,6% degli over 75** ha avuto almeno **un ricovero in RSA**

Dati ISTAT e Italia Longeva, 2022

Capacità produttiva per tipo di servizio erogato

2019	Residenziale	296.050	14.836
	Semiresidenziale	17.507	n.d.
	Domiciliare (ADI e SAD)	15.789.122*	n.d.
2020	Residenziale	295.836	11.171
	Semiresidenziale	16.781	n.d.
	Domiciliare (ADI e SAD)	13.202.896*	n.d.
2021	Residenziale	211.673	n.d.
	Semiresidenziale	14.782	n.d.
	Domiciliare (ADI e SAD)	14.064.480	n.d.

* ore erogate

Fonte: Ministero della Salute (più anni), *Annuario Statistico del Servizio Sanitario Nazionale*; Dati I.Stat (più anni), *Presidi residenziali socio-assistenziali e socio-sanitari*

- In Italia continua la **diminuzione di offerta di posti in servizi semi-residenziali socio-sanitari**, che dopo il -4% tra 2019 e 2020 segna un ulteriore **-12% tra 2020 e 2021**;
- le ore di **assistenza domiciliare integrata (ADI)** erogate sono **aumentate del 6,5%.**

Dati ISTAT 2024

Main aspects inherent to high heterogeneity of nursing homes in Europe

Aspect	Current issues
Typology of LTCF	There are different type of LTCFs in European countries. In 2017, the ECDC classified European LTCFs in: - **General nursing homes**: residents need medical or skilled nursing and supervision 24h a day. These facilities provide principally care to seniors with severe illnesses or injuries; - **Residential homes**: residents are unable to live independently, require supervision and assistance for the activities of daily living. These facilities usually include personal care, housekeeping and three meals a day; - **Specialised LTCFs**: specialised in one specific type of care for e.g. physical impairment, chronic diseases such as multiple sclerosis, dementia, psychiatric illnesses, rehabilitation care, palliative care, intensive care; - **Mixed LTCFs**: these facilities provide different types of care in the same facility (a mix of the above mentioned LTCF types); - **Other facilities**: not classifiable among the above mentioned LTCF types
LTCF providers by organizational status and regulatory processes	- Most European countries face issues relating to **access to and financing of LTCF systems**: this is problematic, also regarding the quality of LTCF - There is a clear **trend towards privatization** of LTCFs: 57.8% of LTCFs in Europe are private - High incidence and expansion of **informal care** (family members, personnel often unpaid, absence of quality control) -
Standards of care and quality monitoring	- Low quality monitoring in European LTCFs: few countries systematically measure whether LTC is safe, effective, and centred around the needs of care recipients. - **Lack of standardized assessment tools** used by providers to monitor quality
Epidemiology of MDRO infections	- The crude prevalence of residents with at least one healthcare associated infections in LTCFs ranges from 0.4% to 7.1% (HALT-2 project). - Transfer from a LTCF represent the strongest risk factor for bacteremia due to **MDR Gram-negative bacilli** in hospital setting - Lack of reports about the **local epidemiology** of MDRO infections in LTCFs - Colonization of patients by MDRO favors the spread of resistant strains
Infection control	Strategies for infection control can greatly vary among LTCFs: - **Poor compliance** with infection control practices - Adherence to hand hygiene, management of urinary catheters and enteral feeding could great vary among LTCFs - LTCFs face difficulties in implementing all the core components for infection control programmes with **the limited resources available**
Antimicrobial stewardship programs	- Great variability in antibiotic consumption among LTCFs - Different AS programs - Different outcome measures for AS programs

LTCFs: long-term care facilities; MDRO: multidrug-resistant organisms

Institutional risk factors of infections inLTCFs

- **Structural factors related to facilities**
- **Low-technology**
- **Collective living**
- **Increase movement of patients and between hospital wards**
- **Understaffing and overcrowding**
- **Difficult to coordinate**
- **Patient tranfer between departments and healthcare institutions**
- **Previous antibiotic therapy**

Tinelli M, Tiseo G, Falcone M; ESCMID Study Group for Infections in the Elderly. Prevention of the spread of multidrug-resistant organisms in nursing homes. Aging Clin Exp Res. 2021 Mar;33(3):679-687

Microrganisms are spreading in the healthcare settings

The burden of infections with antibiotic-resistant bacteria is increasing in elderly population with multiple chronic diseases and disabilities

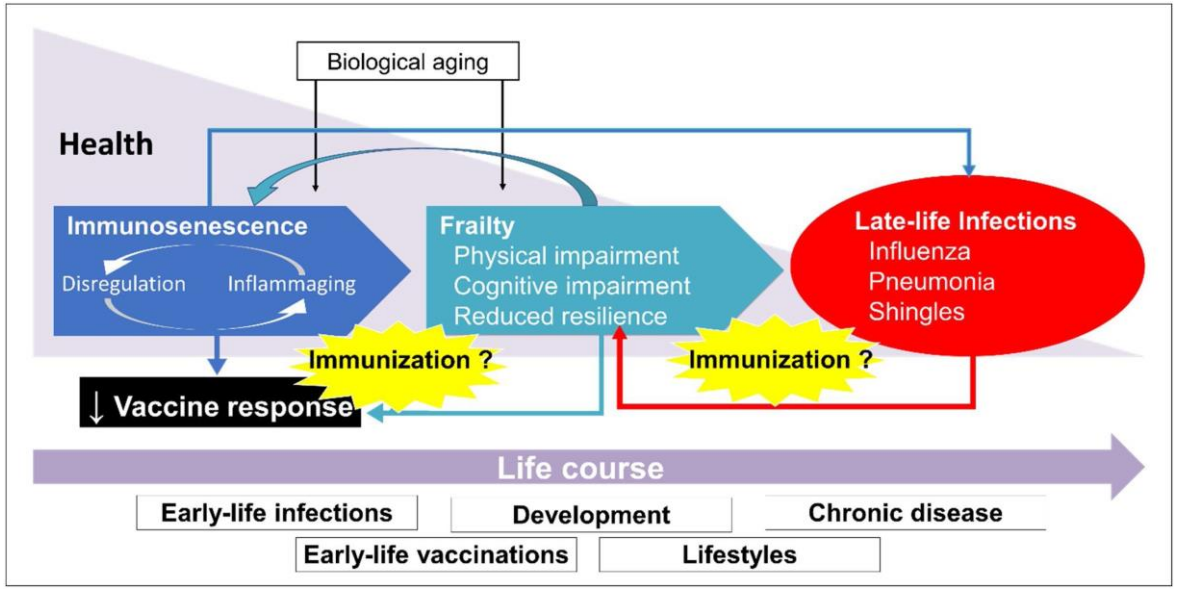
and environment

Contents lists available at ScienceDirect
2021
Ageing Research Reviews
journal homepage: www.elsevier.com/locate/arr

Review

Fostering healthy aging: The interdependency of infections, immunity and frailty

Davide L. Vetrano [a,b,*], Federico Triolo [a], Stefania Maggi [c], Richard Malley [d], Thomas A. Jackson [e,f], Andrea Poscia [g], Roberto Bernabei [b], Luigi Ferrucci [h], Laura Fratiglioni [a,i]



L'evidenza attuale suggerisce che **infezioni e fragilità incrociano ripetutamente percorsi fisiopatologici e accelerano il processo di invecchiamento in un circolo vizioso**. Tali prove aprono a diverse considerazioni.

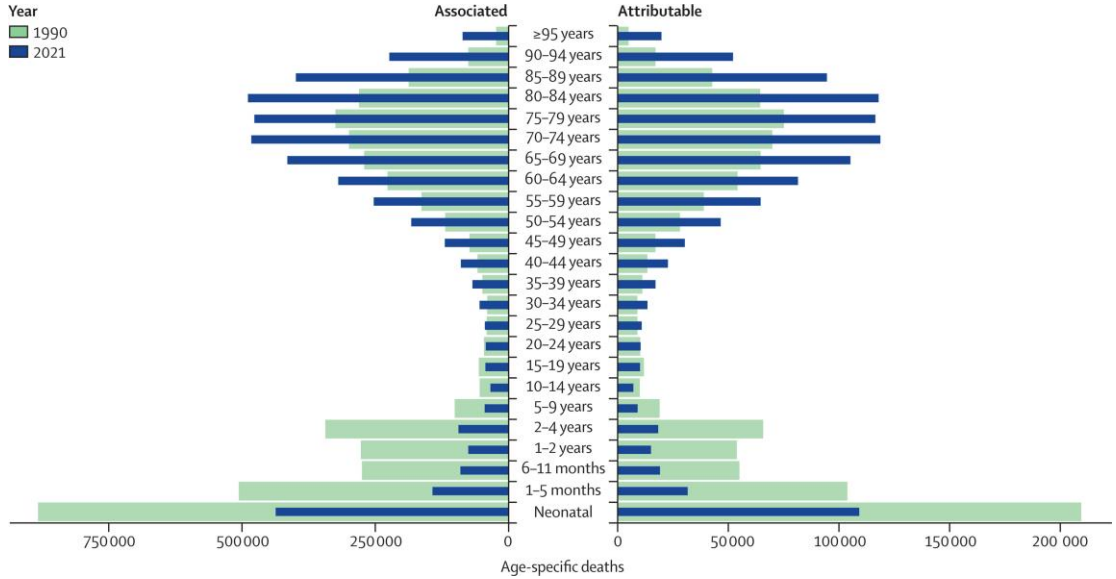
In primo luogo, la **prevenzione di entrambe** le condizioni passa attraverso un approccio basato sull'intero arco della vita, che comprende diversi aspetti individuali e sociali.

In secondo luogo, il **mantenimento di un sistema immunitario ben funzionante** può essere ottenuto prevenendo la fragilità e viceversa.

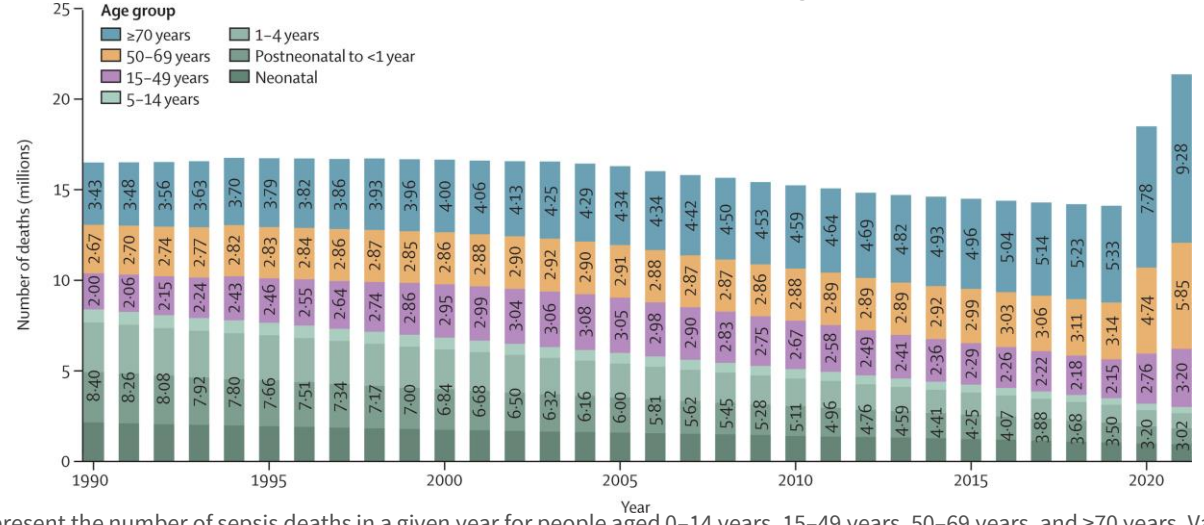
In terzo luogo, aumentare **l'aderenza alla vaccinazione** può ritardare l'insorgenza della fragilità e mantenere l'omeostasi del sistema immunitario, oltre a prevenire le infezioni.

Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. Lancet, September 16, 2024

Deaths attributable and associated with antimicrobial resistance, by detailed age group, for 1990 and 2021

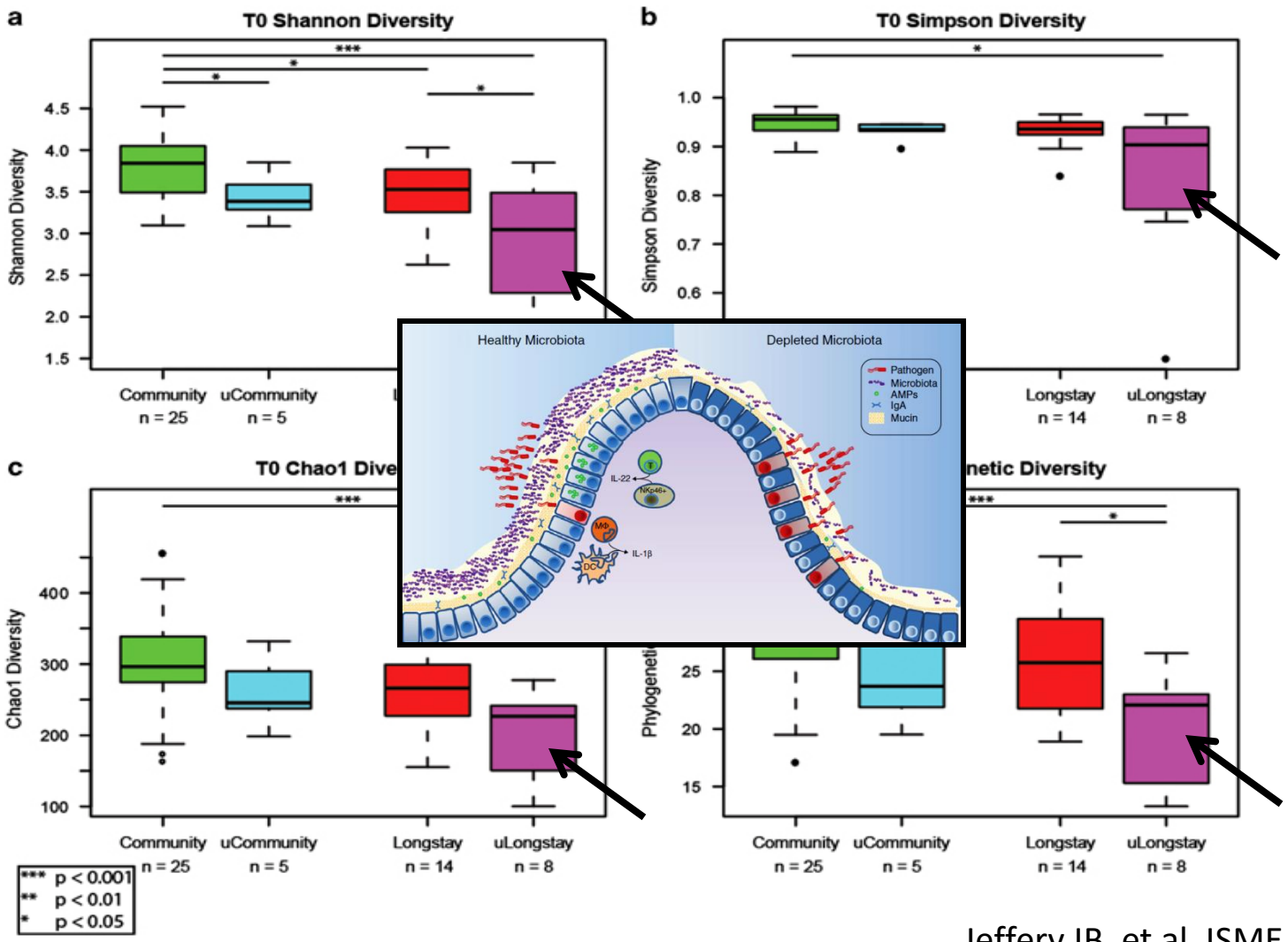


Global time trend of sepsis, by age, 1990–2021



Bar labels represent the number of sepsis deaths in a given year for people aged 0–14 years, 15–49 years, 50–69 years, and ≥70 years. Values for the age group of 0–14 years represent the sum of sepsis deaths among neonates, postneonates to <1 year, 1–4 years, and 5–14 years.

Living in a LTCF is associated to a less different and not stable microbioma



Jeffery IB, et al. ISME J 2016

Main risks factor of Infection/Colonization with MDR bacteria in elderly population

- contact with the healthcare system
- the environment
- animals, or the food chain
- exposure to antibiotics
- breach in host barrier functions e.g. chemotherapy or surgery

J Antimicrob Chemother 2012; **67**: 2982–2987
doi:10.1093/jac/dks300 Advance Access publication 3 August 2012
Journal of Antimicrobial Chemotherapy

Epidemiology and genetic characteristics of extended-spectrum β-lactamase-producing Gram-negative bacteria causing urinary tract infections in long-term care facilities

Marco Tinelli[1], Maria Adriana Cataldo[2]*, Elisabetta Mantengoli[3], Chiara Cadeddu[4], Ettore Cunietti[5], Francesco Luzzaro[6], Gian Maria Rossolini[3,7] and Evelina Tacconelli[8]

Indipendent risk for UTI acquisition

Previous antibiotic therapy (**OR 4**, 95% CI 1.2-10.9; p= 0.02)

presence of urinary catheter (**OR 15**, 95% CI 6.9-30.5; p<0.01)

Highest risk for UTI development:

Exposure, whitin 30 days, to >7 days of **quinolones and cephalosporins** (**OR 7**, 95% CI 1.2-40; p= 0.02)

antibiotics **2022, 11, 953** MDPI

Article

Antibiotic Exposure during the Preceding Six Months Is Related to Intestinal ESBL-Producing Enterobacteriaceae Carriage in the Elderly

Man Zhang [1,2,3,†], Xiaohua Qin [1,2,†], Baixing Ding [1,2], Zhen Shen [1,2,4], Zike Sheng [1,2,5], Shi Wu [1,2], Yang Yang [1,2], Xiaogang Xu [1,2], Fupin Hu [1,2], Xiaoqin Wang [6], Yu Zhang [3] and Minggui Wang [1,2,*]

Prior use of second generation cephalosporins (p = 0.001), third generation cephalosporins (p < 0.001), fluoroquinolones (p < 0.001), and macrolides (p = 0.013) **increased the risk of intestinal ESBL-PE carriage**

Open Forum Infectious Diseases **2020**

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

Epidemiology of Vancomycin-Resistant *Enterococcus faecium* and *Enterococcus faecalis* Colonization in Nursing Facilities

Elyse Davis,[1] Liam Hicks,[1] Ihsan Ali,[1,2] Elizabeth Salzman,[1] Joyce Wang,[2] Evan Snitkin,[3,4] Kristen Gibson,[4] Marco Cassone,[4] Lona Mody,[4,5] and Betsy Foxman[1,6]

Such as increased virulence or **exposure to specific antibiotic classes**—also contribute should be considered in future studies.

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents
Vol 59. Issue 6, Jun 2022,
journal homepage: www.elsevier.com/locate/ijantimicag

Dynamics of carbapenemase-producing Enterobacterales intestinal colonisation in the elderly population after hospital discharge, Italy, 2018–2020

Marco Tinelli[a,b], Angelo Rossini[c], Luigia Scudeller[d], Dorjan Zabzuni[b], Giulia Errico[e], Elena Fogato[f], Roberto D'Angelo[f], Flaminia Gentiloni Silverj[g], Elisabetta Cesana[b], Luigi Cesare Bergamaschini[h], Francesca Pasi[i], Monica Monaco[e], Marina Cerquetti[e], Annalisa Pantosti[e], Maria Giufrè[e,*]

CPE-positive samples obtained from patients in LTCF or at home at the follow-up times.

Place of residence		Time of sampling T4 N=65	T8 N=42	T12 N=28
LTCF	N. patients	44	30	13
	N. CPE carriers	23 (52.3*)	13 (43.3)	2 (15.4)
Home	N. patients	21	12	15
	N. CPE carriers	5 (23.8*)	3 (25.0)	3 (20.0)

137 patients enrolled:

- 73 in Rome
- 64 in Milan

➢In **60% of patients** KPC **colonization is not detectable at 4th month**

Distruption of the normal microbiota is considered a breach to colonization resistance, favoring the acquisition of exogenous microorganism such as *Clostridium difficile* or CPE from other patients or the environment.

In this view, it could be hypothesized that the **lower percentage of colonized patients staying at home than in LTCF** may reflect the **easier reconstitution of a normal microbiota at home, in a "normal"environment.**

Tinelli et al. Int J Antimicrob Agents. Vol 59. Issu

Sequence types (ST)s and carbapenemase genes distribution among *K. pneumoniae* and *E. coli* isolates, from patients with persistent or non-persistent carriage at T4

K. pneumoniae						*E. coli*		
Non-persistent carriers (N=34)			Persistent carriers (N=25)			Non-persistent carriers (N=3)		Persistent carrier (N=2)
ST	n	%	ST	n	%	ST	n	ST
307	15	44.1	307	8	32.0	12	1	410
512	9	26.5	512	8	32.0	410	1	648
101	4	11.8	101	7	28.0	1288	1	
15	1	2.9	258	1	4.0			
35	1	2.9	915	1	4.0			
395	1	2.9						
405	1	2.9						
441	1	2.9						
449	1	2.9						
Carbapenemase			**Carbapenemase**			**Carbapenemase**		**Carbapenemase**
	n	%		n	%		n	
KPC-3	27	79.4	KPC-3	20	80.0	KPC-2	1	KPC-2
KPC-2	6	17.6	KPC-2	5	20.0	OXA-181	1	OXA-181
nd	1	2.9				NDM-5	1	

The majority of ***K. pneumoniae*** **clones colonizing the elderly population** in Italy **belonged to the same high-risk clones** previously identified in invasive infections.

ST307
ST101
ST512

CP-KP obtained from colonized elderly patients belonged to the **high-risk clones ST512, ST307 and ST101, the most common in Italy.**

More than 40% of the investigated patients were **persistent carriers at 4-month follow-up.**

Tinelli et al. Int J Antimicrob Agents. Vol 59. Issue 6, Jun 2022, 106594

microorganisms September 2022, *10*(8), 1561 MDPI

Article

Whole Genome Sequencing and Molecular Analysis of Carbapenemase-Producing *Escherichia coli* from Intestinal Carriage in Elderly Inpatients

Maria Giufrè [1,*], Giulia Errico [1], Monica Monaco [1], Maria Del Grosso [1], Michela Sabbatucci [1,2], Annalisa Pantosti [1], Marina Cerquetti [1], Michela Pagnotta [1], Manuela Marra [3], Maria Carollo [3], Angelo Rossini [4], Elena Fogato [5], Elisabetta Cesana [6], Flaminia Gentiloni Silverj [7], Dorjan Zabzuni [6] and Marco Tinelli [6,8]

***Escherichia coli* resistant to Carbapenems**

antibiotics 3 August 2023, 12, 1282

Article

Whole-Genome Sequencing and Molecular Analysis of Ceftazidime–Avibactam-Resistant KPC-Producing *Klebsiella pneumoniae* from Intestinal Colonization in Elderly Patients

Giulia Errico [1], Maria Del Grosso [1], Michela Pagnotta [1], Manuela Marra [2], Maria Carollo [2], Marina Cerquetti [1], Elena Fogato [3], Elisabetta Cesana [4], Flaminia Gentiloni Silverj [5], Dorjan Zabzuni [4], Angelo Rossini [6], Annalisa Pantosti [1], Marco Tinelli [4], Monica Monaco [1] and Maria Giufrè [1,*]

***Klebsiella pneumoniae* resistant to Ceftazidime-avibactam**

The evolution of MDR resistance in the elderly patients

Acinetobacter resistant to Cefiderocol

JOURNAL ARTICLE CORRECTED PROOF

Evolution and Transmission of Cefiderocol–Resistant *Acinetobacter baumannii* During an Outbreak in the Burn Intensive Care Unit

Steven M Smoke ✉, Alison Brophy, Samuel Reveron, Alina Iovleva, Ellen G Kline, Michael Marano, Lincoln P Miller, Ryan K Shields

Clinical Infectious Diseases, ciac647, https://doi.org/10.1093/cid/ciac647 **17 August 2022**

Clinical success was achieved in 36% and complicated by treatment-emergent resistance and interpatient transmission of cefiderocol-resistant

antibiotics **2022, 11, 723** MDPI

Review

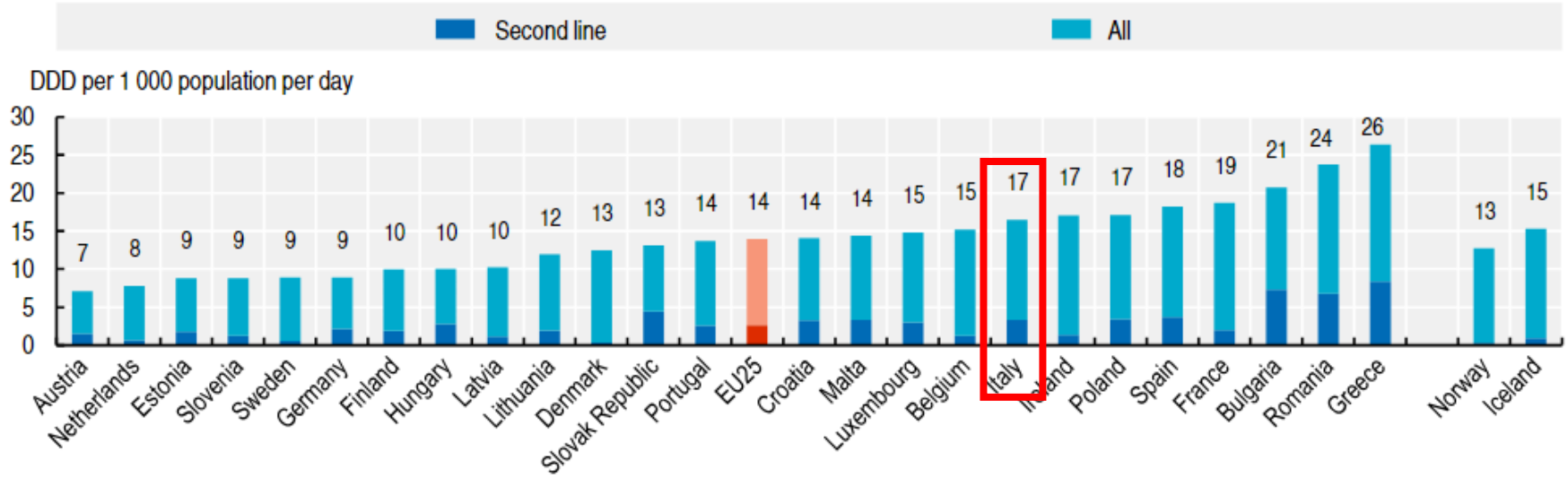
Cefiderocol: Systematic Review of Mechanisms of Resistance, Heteroresistance and In Vivo Emergence of Resistance

Stamatis Karakonstantis [1,2,*], Maria Rousaki [2] and Evangelos I. Kritsotakis [3]

The evolution of MDR resistance in the elderly patients

A variety of mechanisms, typically acting in concert, have been reported to confer resistance to cefiderocol: **β-lactamases** (especially NDM, KPC and AmpC variants conferring resistance to ceftazidime/avibactam, OXA-427, and PER- and SHV-type ESBLs), **porin mutations, and mutations affecting siderophore receptors, efflux pumps, and target (PBP-3) modifications.**

Overall volume of antibiotics prescribed, 2020



Note: The EU average is unweighted. Data only include antibiotics prescribed in primary care (outside hospital).
Source: European Centre for Disease Prevention and Control.

StatLink https://stat.link/3xs9k2

75% of antibiotics is prescrived in population over 65

PRESCRIZIONE ANTIBIOTICI NELLA POPOLAZIONE GERIATRICA RESIDENTE IN COMUNITA' IN ITALIA

Le associazioni di **penicilline, inclusi gli inibitori delle beta-lattamasi,** sono la categoria terapeutica **maggiormente utilizzata nella popolazione over 65**

Nel dettaglio l'associazione **amoxicillina/acido clavulanico** rappresenta la totalità dei consumi dell'intera categoria (6,1 DDD/1000 abitanti die), in calo di quasi il 20% rispetto al 2019

Seguono i **macrolidi e i fluorochinoloni** rispettivamente con 3,9 e 3,5 DDD/1000 abitanti die.

Anche in questo caso le molecole che coprono la quasi totalità dei consumi dei macrolidi sono **la claritromicina, con 2 DDD, e l'azitromicina con 1,8 DDD**

Osservatorio Nazionale sull'impiego dei Medicinali. L'uso degli antibiotici in Italia. Rapporto Nazionale 2020. Roma: Agenzia Italiana del Farmaco, 2023

Nelle RSA non sempre sono disponibili tutte le classi di antibiotici come in ospedale

- Costi elevati
- Rimborsi differenti rispetto al sistema ospedaliero
- Difficoltà di somministrazione di farmaci per via parenterale

Le beta lattamine, i fluorochinoloni, i macrolidi, le cefalosporine di terza generazione e gli aminoglicosidi
sono gli antibiotici più usati nelle RSA sia in monoterapia che in combinazione.

M.Tinelli, Convegno Antibiotico-terapia, Milano , Giugno 2017

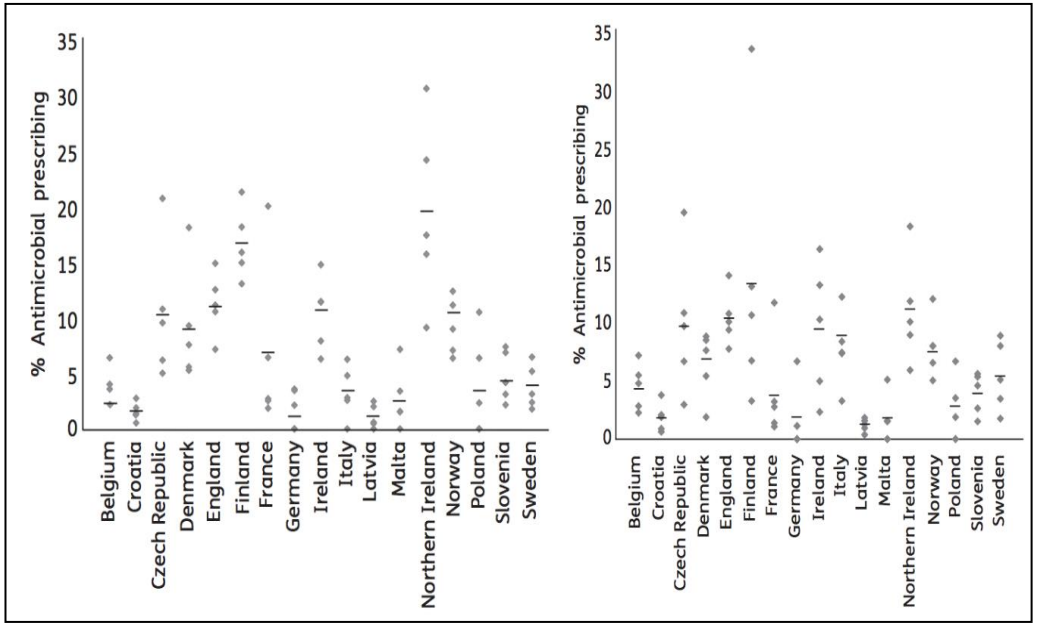
Antimicrobial consumption and impact of Antimicrobial Stewardship programmes in long-term care facilities

Falcone M,Paul M,Yahav D,Orlando G, Tiseo G, Prendki V, Güerri-Fernández R,Gavazzi G, Mutters NT, Cookson B, Tinelli M;

Study Group for Infections in the Elderly (ESGIE). Clin Microbiol Infect. 2018 Aug 1.

Author	Country	Design	Setting	Type of LTCF*	Study period	Variable	Results
Blix HS, 2007 [28]	Norway	PPS	133 LTCFs	Type A	2003	Mean use of antibiotics	14.8 DDDs/100 bed-day
Blix HS, 2010 [29]	Norway	PPS	44 LTCFs	Type A	2006	Median prevalence of antibiotic prescription	3%
Rummukainen ML, 2013 [30]	Finland	ESAC PPS	9 LTCFs	Type A	2009-2010	Prevalence of antimicrobial prescription	5-30%
Roche FM, 2016 [26]	Ireland	PPS	24 LTCFs	Type B	2013	Median prevalence of antibiotic prescription	7.5%
McClean P, 2012 [24]	Ireland	PPS	30 LTCFs	Type C	2010-2011	Median prevalence of antibiotic prescription	9.2%
Stuart RL, 2012 [39]	Australia	PPS	5 LTCFs	Type C	2011	Prevalence of antibiotic prescription	9%
van Buul LW, 2015 [13]	Netherlands	Prospective study.	10 LTCFs	Type D	2012	Prevalence of antibiotic prescription in Registered Infection Consultations	88%
Andersen BA, 2000 [27]	Norway	PPS	65-70 LTCFs	Types A, C	1997-1999	Median prevalence of antibiotic prescription	7%
Sundvall PD, 2015 [31]	UK	Retrospective longitudinal cohort study	Number not specified	Types A, C	2011	Percentage of individuals prescribed antibiotics	49% (82% with urinary catheter)
Gillespie D, 2015 [32]	UK	Prospective cohort study	10 LTCFs	Types A, C, D	2010-2012	Incidence of antibiotic prescription	2.16 prescriptions per resident year (95% CI: 1.90–2.46)
Burns K, 2015 [25]	Ireland	HALT-1/HALT-2-PPS	69/190 LTCFs	Types A, C, D	2010/2013	Median prevalence of antibiotic prescription	11.0%/ 9.7%
Roukens M, 2017 [33]	Netherlands	Retrospective study	96 LTCFs	All types	2012-2014	Mean total use of systemic antimicrobials	73 DDDs/1000 residents-day
Daneman N, 2011 [34]	Canada	PPS	363 LTCFs	All types	2009	Prevalence of antibiotic use	5.9%
Daneman N, 2013 [35]	Canada	Retrospective study	630 LTCFs	All types	2010	Prevalence of incident antibiotic treatment course	77.8%
Daneman N, 2017 [36]	Canada	Retrospective cohort study	600 LTCFs	All types	2014	Median prevalence of antibiotic prescription	44.9%

Legend. DDD: defined daily dose; ESAC: European Surveillance of Antimicrobial Consumption; LTCFs: long-term care facilities; PPS: point-prevalence survey; UK: United Kingdom;



Variation in prescribing of antimicrobials in nursing homes between **and within European countries**

Great variability in LTCFs across and 43 within countries. Difficult to analyze, because of the differences in 44 the types of LTCFs, **their organization and the population cared-for in the different LTCFs. Educational interventions are effective in reducing unnecessary antibiotic prescriptions**

Clinical Microbiology and Infection 24 (2018) 72–77

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

Predictors of mortality in nursing-home residents with pneumonia: a multicentre study

M. Falcone [1,*], A. Russo [1], F. Gentiloni Silverj [2], D. Marzorati [2], R. Bagarolo [3], M. Monti [4], R. Velleca [4], R. D'Angelo [5], A. Frustaglia [6], G.C. Zuccarelli [6], R. Prina [6], M. Vignati [7], M.G. Marnati [8], M. Venditti [1], M. Tinelli [9]

Antibiotic regimens administered to patients in nursing-home acquired pneumonia	446 patients	
	No.	**%**
Monotherapy	**249**	**55.8**
ß-lactam/ß-lactamase inhibitor	**71**	**28.5**
Quinolone	**48**	**19.2**
Macrolide	**33**	13.3
Cephalosporin	87	35
Anti-pseudomonal beta-lactam	10	4
Combination therapy	**197**	**44.2**
ß-lactam/ß-lactamase inhibitor plus a quinolone or a macrolide	**23**	**11.7**
Aminoglycosides plus a ß-lactam/ß-lactamase inhibitor	**46**	**23.3**
Cephalosporin plus a macrolide	**65**	**33**
Cephalosporin plus a quinolone	21	10.6
Anti-pseudomonal ß-lactam plus a quinolone or a macrolide	30	15.3
Anti-pseudomonal ß-lactam plus an anti-MRSA agent	7	3.5
Anti-pseudomonal ß-lactam plus a macrolide plus an anti-MRSA agent	3	1.6
Anti-pseudomonal ß-lactam plus a quinolone plus an anti-MRSA agent	2	1

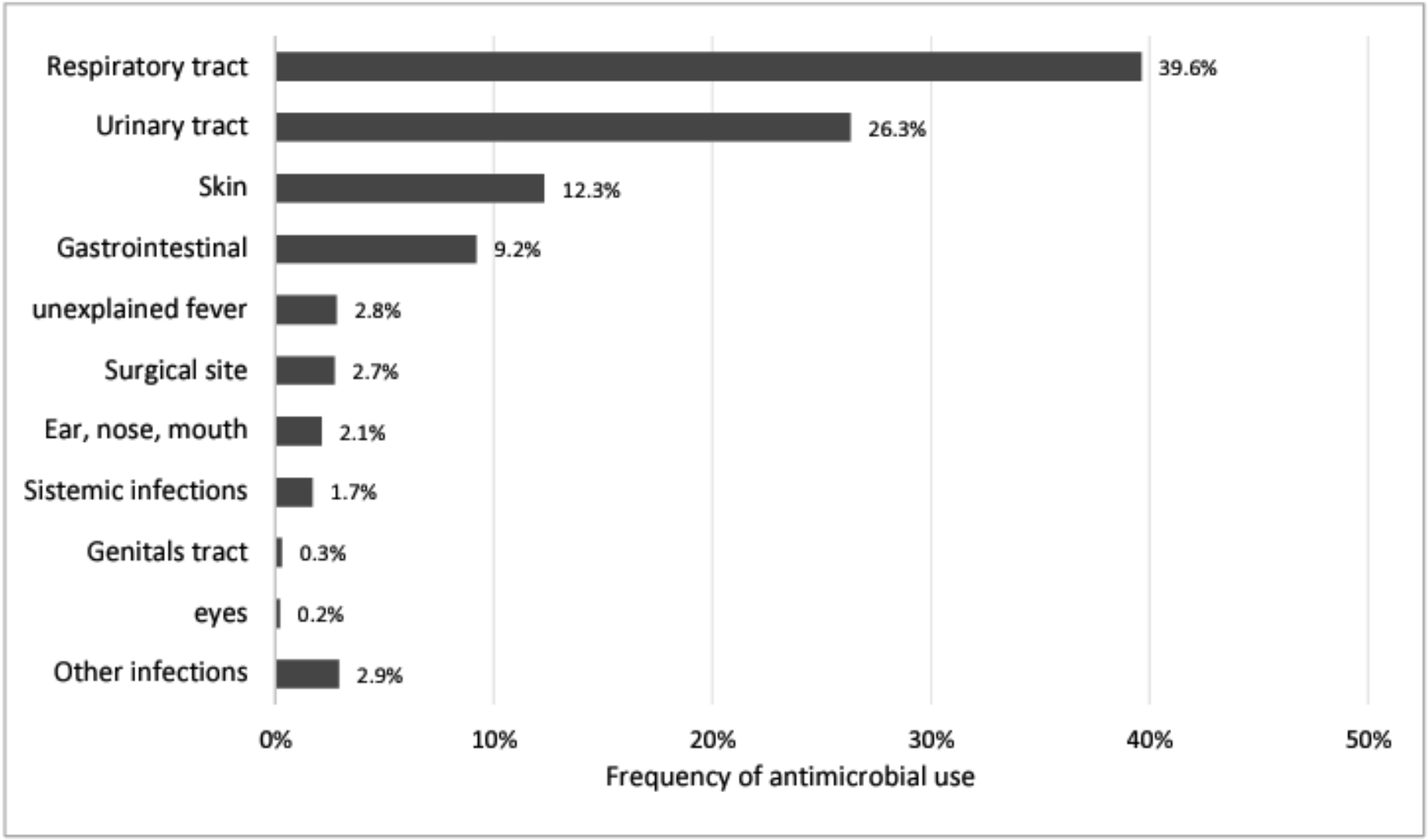
Personal characteristics, risk factors and antibacterial therapy in residents of long-term care facilities – data of the HALT Studies (health care associated infection in long-term care facilities) in Europe

	Europe		
	HALT	HALT-2	HALT-3
	28 countries	19 countries	26 countries
Year	2010	2013	2016–2017
Months	May–Sept.	April–May	April 2016–Nov. 2017
Long-term care facilities (n)	649	1,051	1,788
Residents (n)	65,426	77,264	102301
85 Y (%)	44.8	46.5 (0–100)	48.6(19.1–61.5)
Male %	29.4	30.7 (0–100)	32.3 (24.1–46.0)
Urinary catheter (%)	7.2	8.8 (0–86.7)	8.4 (3.1–18.2)
Vascular catheter (%)	0.8	1.4 (0–66.7)	1.5 (0–10.9)
Antibacterials, thereof	**4.3**	**4.4 (0–50.0)**	**4.9 (0.7–10.5)**
Tetracyclines (J01A)		2.9	2.0 (0–8.9)
Beta-lactams. penicillins (J01C)		29.3	12 (0–60.0)
other beta-lactams (J01D)		12.5	7.6 (0–32.8)
Sulfonamides and trimetoprim (J01E)		11.9	27.4 (0–60.1)
Macrolides. lincosamides etc(J01F)		6.4	6.8 (0–50)
Aminoglycoside (J01G)		1.2	0.1 (0–0.4)
Quinolones (J01M)		16	4.8 (0–56.0)
combinations of antibacterials (J01R)		0	0.2 (0–0.7)
other antibacterials (J01X)		19.8	39.3 (0–87.5)

Heudorf U, Stalla K. Use of antibiotics in long-term care facilities for the elderly in Germany - point prevalence as a possible first step for data-based antibiotic stewardship. GMS **Hyg Infect Control. 2024 Apr 17;19:**

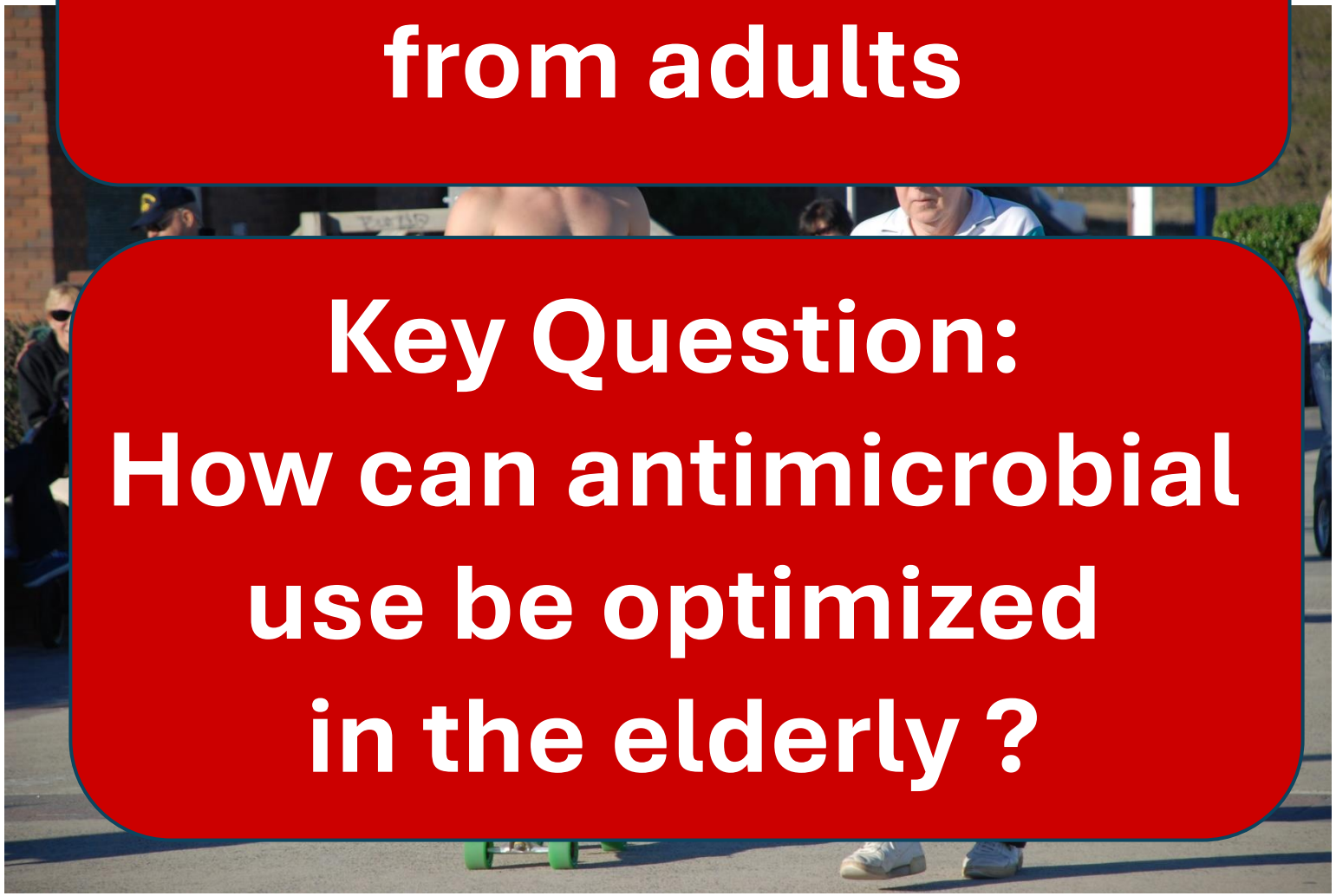
Healthcare-Associated Infection in Long-Term Care Facilities (HALT3 - 2017) in Italy

Anatomical site of treatment: prevalence rate calculated on the total number of prescribed antimicrobial agents.



Antibiotic treatment is the same

It is quite different from adults



Key Question: How can antimicrobial use be optimized in the elderly ?

Photo from: «**Emotions from the world**», M. Tinelli, Ed. February 2019, Copyright

Appropriate antibiotic treatment

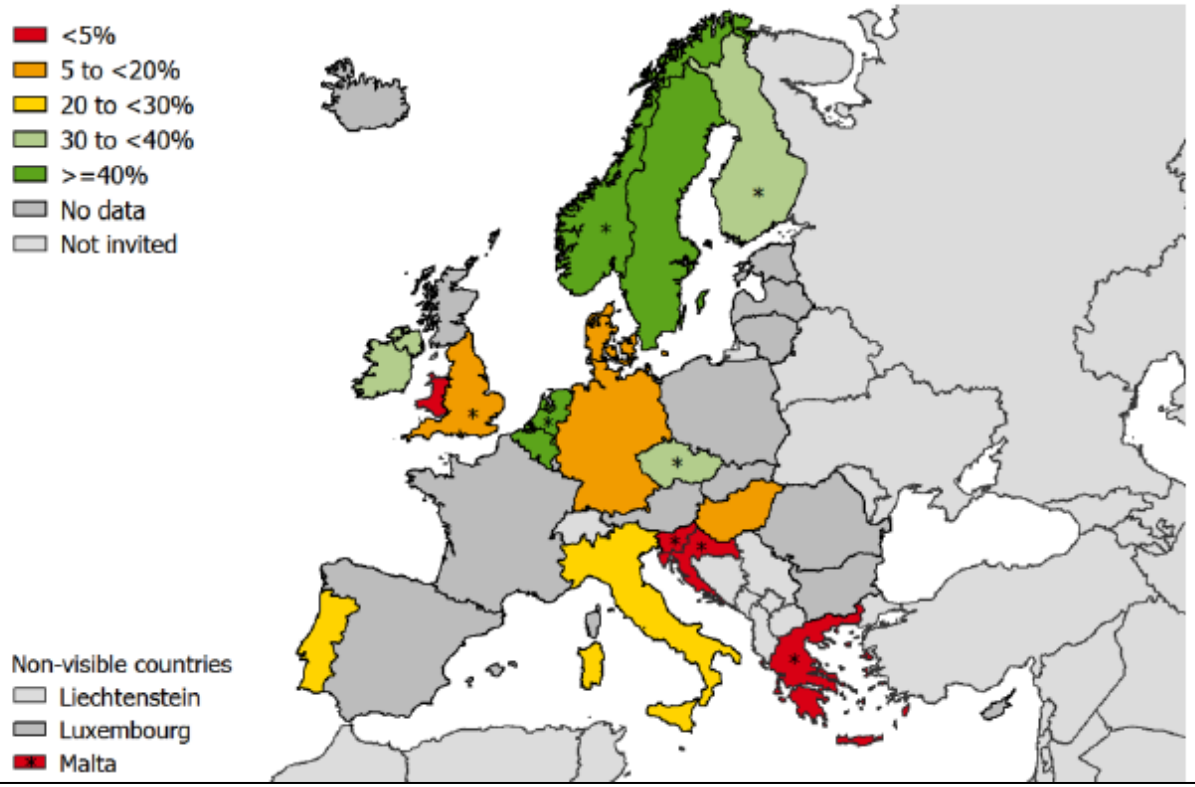
Right Dose

De-escalation

Right Duration of Therapy

Tailor the antibiotic treatment

Figure 19. Percentage of the included LTCFs with written therapeutic guidelines for UTIs, RTIs and wound and soft tissue infections,



HALT-2,4 ECDC, 2013, 2017

- **No specific guidelines for rational prescribing in 50% of European LTCFs**
- **Restricted antibiotic formulary:16%**
- **Minimal education programs**

Considerations for the optimal management of antibiotic therapy in elderly patients

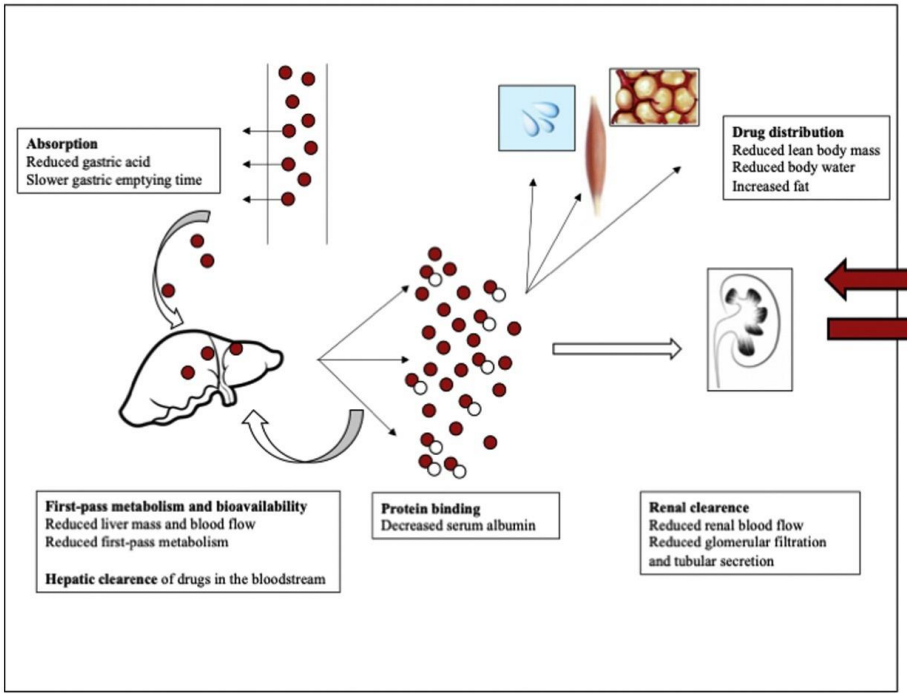
Journal of Global Antimicrobial Resistance 22 (2020) 325–333

Marco Falcone[a,*], Mical Paul[b], Giusy Tiseo[a], Dafna Yahav[c], Virginie Prendki[d], Lena E. Friberg[e], Roberto Guerri[f], Gaetan Gavazzi[g], Cristina Mussini[h], Marco Tinelli[i], for the ESCMID Study Group for Infections in the Elderly (ESGIE)

- **Decreased absorption**
- **Decreased distribution**
- **Decreased metabolism**
- **Decreased renal elimination**

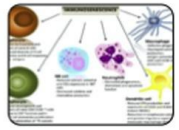
Pharmacokinetics

(concentration and elimination of antibiotics)



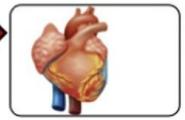
Pharmacodynamics

(relationship between the concentration of antibiotics and the clinical effect)

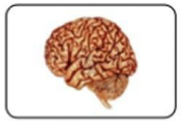


IMMUNOSENESCENCE
Inability to functional adaptations
Up-regulation of pro-infammatory cytokines
Altered function of immune cells (macrophages, neutrophils, lymphocytes)
Altered sensitivity of receptors

PHYSICAL ABILITY TO DEAL WITH INFECTIONS
Reduced muscle mass (reduced coughing during pneumonia)
Inability to take drugs (reduced compliance)
Inability to adequate hydration (dehydration favors UTI)



REDUCED CARDIOVASCULAR COMPENSATORY CAPACITY
Reduced ability to deal with infections
Reduced organ perfusion
Reduced ability to deal with septic syndromes



VULNERABILITY OF THE CENTRAL NERVOUS SYSTEM AND NEUROENDOCRINE SYSTEM
Cognitive impairment and less reactivity to stress
Reduced capacity to deal with oxidative stress
Altered responsiveness of adrenergic receptors

DECREASED HEMATOPOIETIC RESERVE
Increased risk for experiencing hematologic toxicities

ALTERED SAFETY
ALTERED EFFICACY

Absorption

Pharmacokinetics and drug metabolism in the elderly

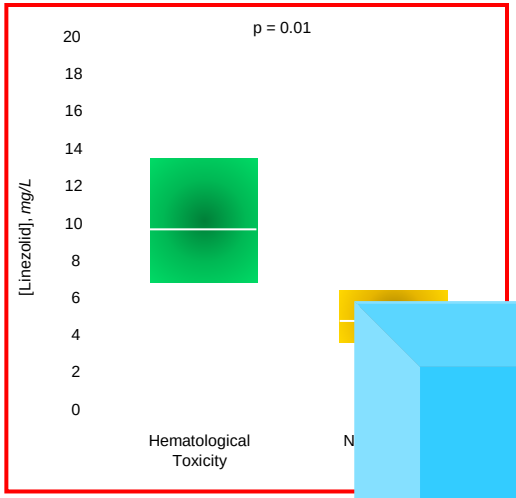
Table 1. Age-related physiological changes and their pharmacokinetic consequences.

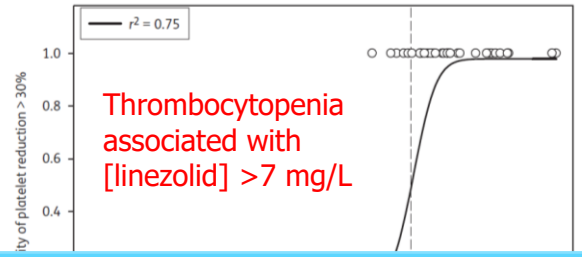
Physiological changes in the elderly	Pharmacokinetic consequences
Increased gastric pH	Slightly decreased absorption (rarely clinically significant)
Delayed gastric emptying	
Reduced splanchnic blood flow	
Decreased absorption surface	
Decreased gastrointestinal motility	

Medications containing metals, such as antacids with aluminum additives and iron supplements, can reduce the absorption of tetracyclines and fluoroquinolones.

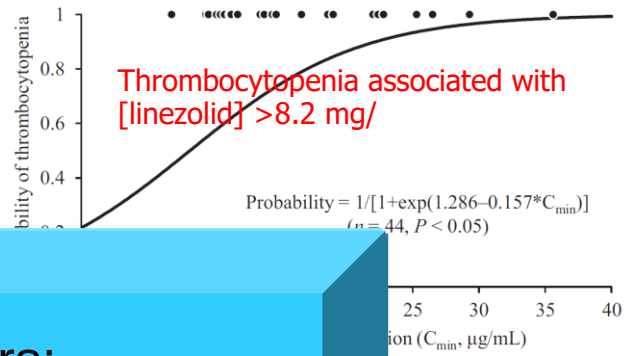
- Klotz, Drug Metab Rev 2009 -

The issue of drug overexposure: the case of linezolid…





Thrombocytopenia associated with [linezolid] >7 mg/L

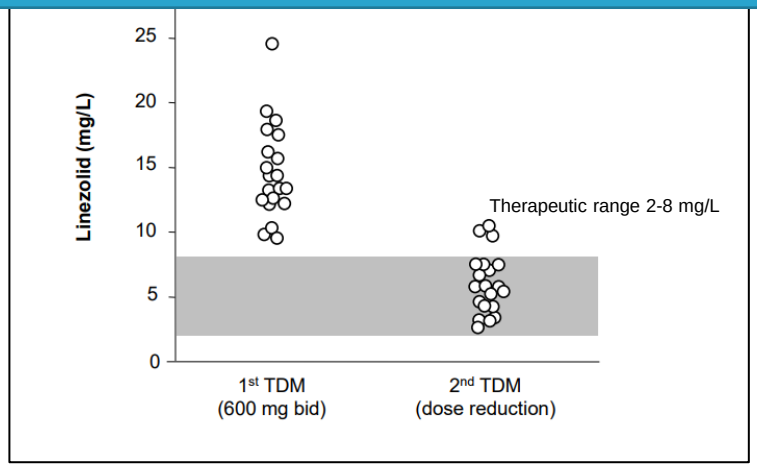


Thrombocytopenia associated with [linezolid] >8.2 mg/

In patients over 75 yrs:

- **loading dose: 600 mg x 2 for 3 days**
- **manteinance therapy: 300 mg x 2**

can be a strategy to avoid drug toxicity

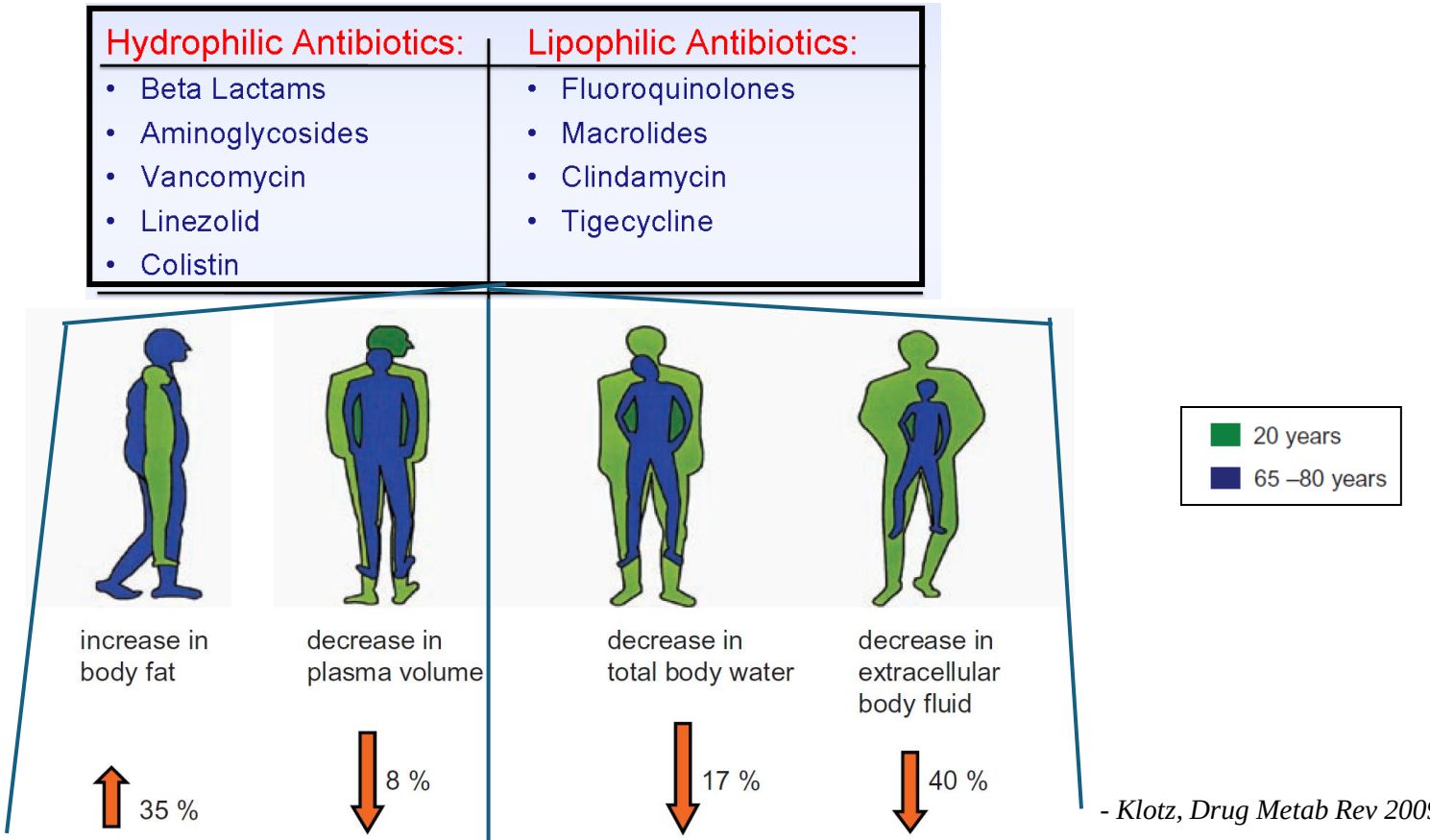


Age quartiles	$[Linezolid]_{trough}$
≤ 40 yrs	4.6 ± 4.9 mg/L
40 – 60 yrs	6.1 ± 4.5 mg/L
60 – 80 yrs	10.0 ± 7.0 mg/L**
> 80 yrs	12.6 ± 9.3 mg/L**

**p<0.01 vs group I (<40 yrs)

Distribution → Tissue penetration

Physiologic change	Result	PK parameter	PK effect
Reduced muscle mass and total water	Accumulation of hydrophilic drugs	Volume of distribution	**Increase of drug plasma concentrations**
Increased body fat	Accumulation of lipophilic drugs	Volume of distribution	**Increase of drug half-life**

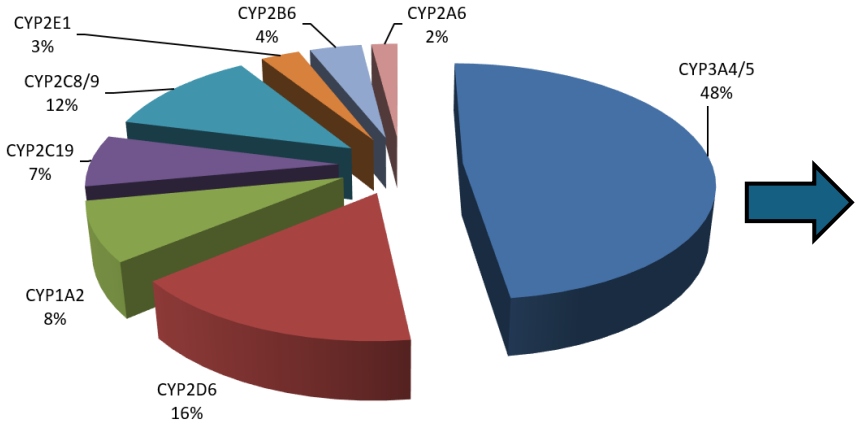


- Klotz, Drug Metab Rev 2009

Metabolism

Pharmacokinetics and drug metabolism in the elderly

Physiological changes in the elderly	Pharmacokinetic consequences
Decreased hepatic blood flow	First-pass metabolism can be less effective.
Decreased hepatic mass	Phase I metabolism of some drugs might be slightly impaired.



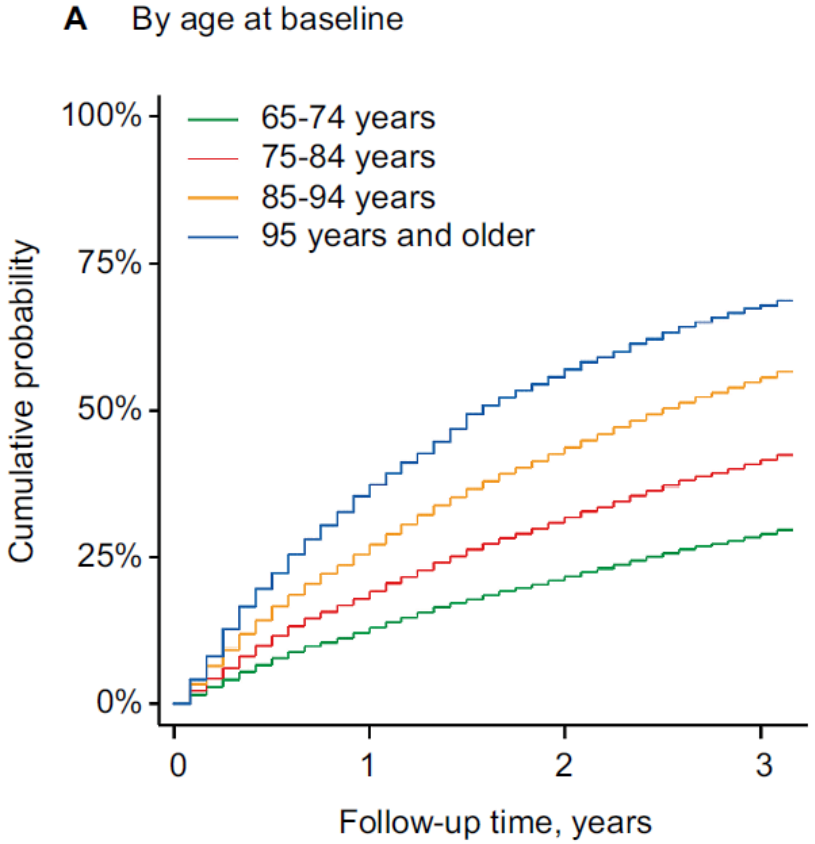
Antibiotic interactions with concomitant medications very common in the elderly

Clinical significance

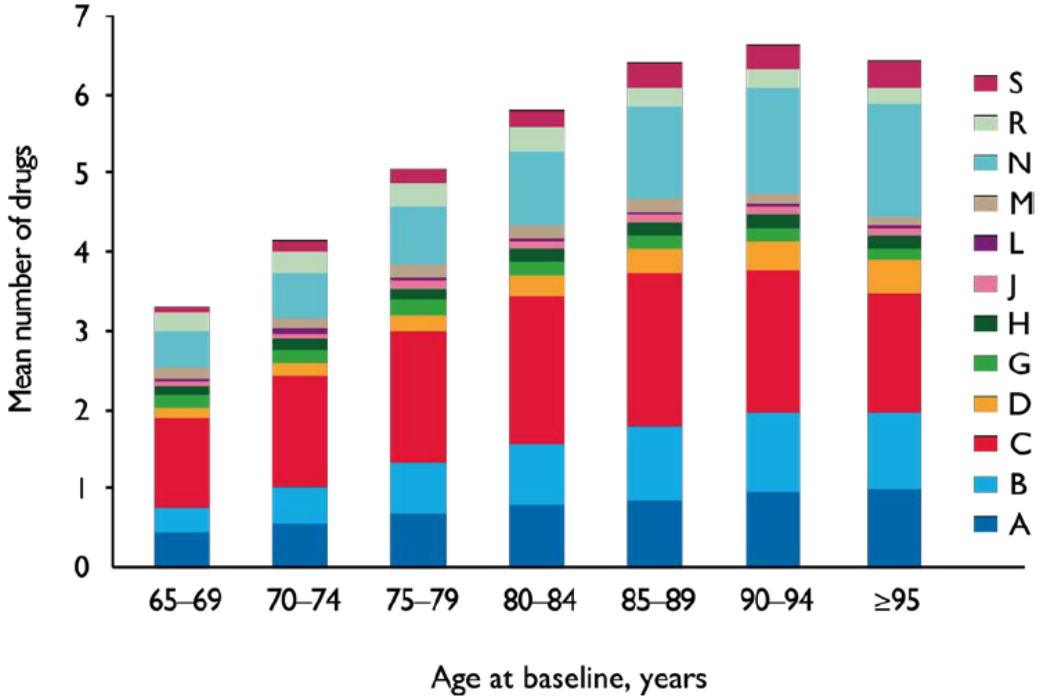
< rate of biotransformation of some drugs

- Klotz, Drug Metab Rev 2009 -

Cumulative incidence of polypharmacy increased with age



Mean number of drugs at from different therapeutic groups baseline, by age



In this nationwide, longitudinal study of **1.7 million people**, we found that nearly **half of older adults were exposed to polypharmacy at baseline** and that about **20% of the remaining half experienced polypharmacy during the first year of follow-up.**

The epidemiology of polypharmacy in older adults: register-based prospective cohort study. Morin L. et al., Clinical Epidemiology 2018:10 289–298

Excretion

- ✓ Even in the absence of kidney disease, **renal clearance may be reduced by 35-50% in healthy elderly** vs healthy younger men
- ✓ Reduced **renal clearance of active metabolites may enhance therapeutic effect or increase risk of toxicity**

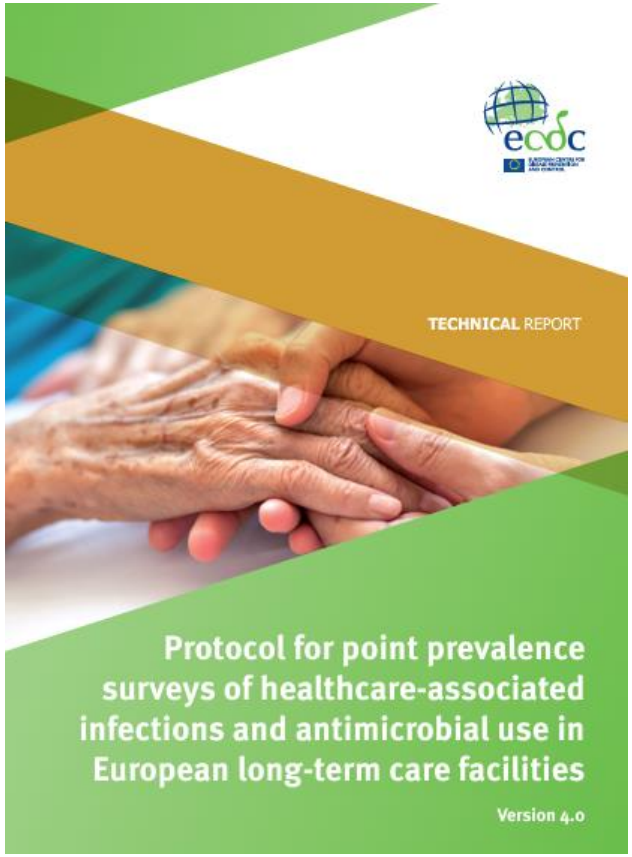
% del farmaco escreto immodificato nelle urine	Clearance della creatinina (ml/min)	
	70 anni (Cl: 60 ml/min)	20 anni (Cl 120 ml/min)
10	1,1	1,0
20	1,1	1,0
30	1,2	1,0
40	1,3	1,0
50	1,3	1,0
60	1,4	1,0
80	1,7	1,0
90	1,8	1,0
100	2,0	1,0

- ✓ Need to reduce dose and/or increase dosing intervals
- ✓ Drug dosing decision must **take into account pharmacodynamic as well as pharmacokinetic considerations**

New and incoming antibiotics: dosage adjustment in the elderly

Antibiotic	Dosage adjustment	Main side effects
Ceftolozane/tazobactam	CrCl more than 50 mL/minute: no dosage adjustment	Nausea , diarrhea / headache
Ceftazidime/avibactam	CrCl more than 50 mL/minute: no dosage adjustment	Nausea , diarrhea / headache
Meropenem/vaborbactam	CrCl more than 50 mL/minute: no dosage adjustment	Diarrhea, anemia, phlebitis/infusion
Imipenem/relebactam	CrCL ≤60 (serum Cr<1.2 mg/dL) **need dosage adjustment**	Diarrhea, nausea, and vomiting
Aztreonam/avibactam	CrCL ≤60 (serum Cr<1.2 mg/dL) **need dosage adjustment**	Diarrhea, nausea, and vomiting, rash, phlebitis/infusion, slight liver enzyme elevations
Cefiderocol	No dosage adjustment	Nausea, maculopapular rash, or urticaria
Eravacycline	No dosage adjustment	Phlebitis/infusion, colitis, maculopapular rash, urticaria
Tedizolid	No dose adjustments are required for severe hepatic or renal impairment	Headache, dizziness, diarrhea, nausea, and vomiting, pruritus
Dalvabancin	CrCl ≤ 30 mL/min 2-dose regimen 750 mg followed 1 week later by 375 mg	Nausea, headache, diarrhea, and elevations in liver enzyme tests.

Are all nursing homes ready for modern infection control and the burn of MDROs ?



European Centre for Disease Prevention and Control. Protocol for point prevalence surveys of healthcare-associated infections and antimicrobial use in European long-term care facilities – version 4.0. Stockholm: ECDC; 2023.

Antimicrobial policy

Variable	Description/definition
Antimicrobial stewardship	The facility has the following mechanisms in place: • An antimicrobial committee; • Regular annual training on appropriate antimicrobial prescribing; • Written guidelines for appropriate antimicrobial use (good practice) in the facility; • Data available on annual antimicrobial consumption by antimicrobial class; • A system to remind healthcare workers of the importance of microbiological samples to inform the best antimicrobial choice; • Local (i.e. for that region/locality) or national (if the country is small) antimicrobial resistance profile summaries available in the LTCF or in the local general practitioner surgeries; • A system that requires permission from a designated person(s) for prescribing restricted antimicrobials, not included in local formulary; • Advice from a pharmacist for antimicrobials, not included in the formulary; • A therapeutic formulary, comprising a list of antimicrobials; • Feedback to the local general practitioner on antimicrobial consumption in the facility; • None of the above. Antimicrobial committee: This committee is in charge of the development of local guidelines and protocols for antibiotic use in the LTCF. The team should comprise (at least) healthcare providers prescribing antimicrobial agents to LTCF residents, a pharmacist, a co-ordinating physician (if present), an infection prevention and control practitioner, and (if possible) a microbiologist. Written guidelines for appropriate antimicrobial use: Recommendations for empirical and targeted treatment of the most frequent infections, including dosage of antimicrobial agents, administration route and duration of treatment. Commonly a first and second therapy choice is proposed. Annual antimicrobial consumption data: A report on the quantity of antimicrobial agents prescribed/received during the previous year, classified by group. Antimicrobial resistance profiles: These profiles are used to monitor antimicrobial resistance patterns for key micro-organisms in order to guide the choice of antimicrobial agents for treatment. Data are obtained by the surveillance of antimicrobial susceptibility testing results provided by clinical microbiology laboratories. Therapeutic formulary: A list of eligible pharmaceutical agents by indication, intended as a manual for prescribers to guide their prescriptions. The therapeutic formulary should include a specific chapter on antimicrobial therapy.
Written therapeutic guidelines	Written therapeutic guidelines for respiratory tract infections, urinary tract infections and/or wound and soft tissue infections.
Surveillance programme for antimicrobial consumption	Is there a programme in place for the surveillance of antimicrobial consumption in the facility?
Surveillance programme for antimicrobial-resistant microorganisms	This could be, for e.g. annual summary reports for MRSA, *Clostridioides (Clostridium) difficile*, carbapenem-resistant *Klebsiella pneumoniae*, etc.

Disponible en ligne sur ScienceDirect www.sciencedirect.com
Elsevier Masson France EM|consulte www.em-consulte.com
Médecine et maladies infectieuses
Médecine et maladies infectieuses 45 (2015) 286–292

Original article

Information concerning multidrug-resistant bacterial colonization or infection in the medical transfer letter☆

Evolution of information relative to multidrug bacteria in the medical transfer letter of patients hospitalized in our hospital from 2009 to 2012.
Évolution de présence de l'information relative à la bactérie multirésistante dans le courrier de transfert des patients hospitalisés dans notre établissement entre 2009 et 2012.

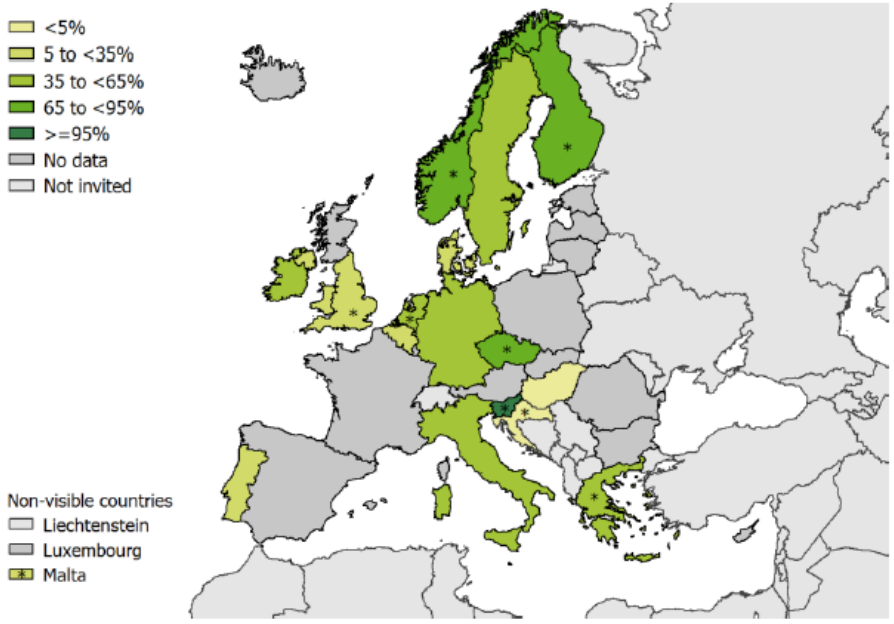
	Presence of information: *n* (%)				Logistic regression
	2009 (*n* = 57)	2010 (*n* = 73)	2011 (*n* = 89)	2012 (*n* = 95)	Coefficient (*P*)
Presence of the discharge letter	57 (100.00%)	68 (93.15%)	86 (96.63%)	90 (94.74%)	–0.27 (*P* = 0.324)
Entire name of the MDR bacterium (genus and specie)	37 (64.91%)	38 (52.05%)	63 (70.79%)	68 (71.58%)	0.20 (*P* = 0.074)
MDR bacterium information	26 (45.61%)	34 (46.58%)	46 (51.69%)	57 (60%)	0.20 (*P* = 0.052)
Mention of isolation precautions	5 (8.77%)	15 (20.55%)	29 (32.58%)	31 (32.63%)	0.45 (*P* = 0.001)
Mention of MDR bacterium or isolation precaution	28 (49.12%)	38 (52.05%)	52 (58.43%)	61 (64.21%)	0.20 (*P* = 0.042)
Mention of the 3 elements	3 (5.26%)	11 (15.07%)	22 (24.72%)	28 (29.47%)	0.55 (*P* < 0.001)

Information (mention of MDR bacterium or isolation precaution) was **present in 57% of records.**

Full information (genus and species, concept of MDR bacterium and mention of isolation precaution) was **found in 20%** .

European Countries written protocols

Figure 14. Percentage of included LTCFs with written protocols for all five selected infection prevention and control protocols, HALT-2, 2013**



** Poor or very poor national representativeness of LTCF sample*
*** Protocols for management of MRSA and/or other multidrug-resistant microorganisms, urinary catheters, enteral feeding, venous catheters/lines, and hand hygiene.*

Hand hygiene: 95.9%
MRSA and MDRO: 76.9%
Urinary catheters: 84.0%
Venous catheters 50.0%
Enteral feeding 76.8%

HALT 4 ECDC, 2017

Countries like **Germany, the Netherlands, Sweden, and France have specific regulations and frameworks that guide these protocols**, often influenced by national health policies and quality standards. ECDC 2024

Residents in LTCF cannot be "isolated" or "raised barries" like patients in acute care

Acute Care

Single room

Contact Precautions

- Gloves for walking into room
- Gowns for touching patient or environment

Restricted to room except for medically necessary activities

Long-term Care

Few single rooms; **difficult to move patients**

Residents are **encouraged to interact with one another**, eat in common areas and share other activities

Universal screening at admission in LTCFs/NHs is controversial

Becker and Diel *Journal of Occupational Medicine and Toxicology* (2017) 12:3
DOI 10.1186/s12995-017-0149-6

Journal of Occupational Medicine and Toxicology

RESEARCH Open Access

Screening for Methicillin-resistant *Staphylococcus aureus* in a residence home for elderly in Germany

Jürgen Becker[1*] and Roland Diel[2]

Screening tests are **promising tools** as part of potential new strategies.

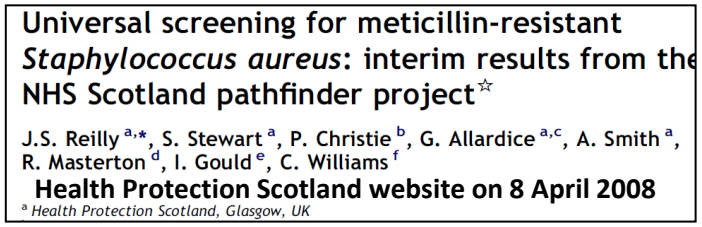
INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY APRIL 2015, VOL. 36, NO. 4

ORIGINAL ARTICLE

Universal Screening and Decolonization for Control of MRSA in Nursing Homes: A Cluster Randomized Controlled Study

Cristina Bellini, MD;[1] Christiane Petignat, MD;[1,2] Eric Masserey, MD;[2] Christophe Büla, MD;[3] Bernard Burnand, MD;[4] Valentin Rousson, PhD;[4] Dominique S. Blanc, PhD;[1] Giorgio Zanetti, MD[1,2]

Universal screening **did not significantly reduce the prevalence** of the MRSA carriage



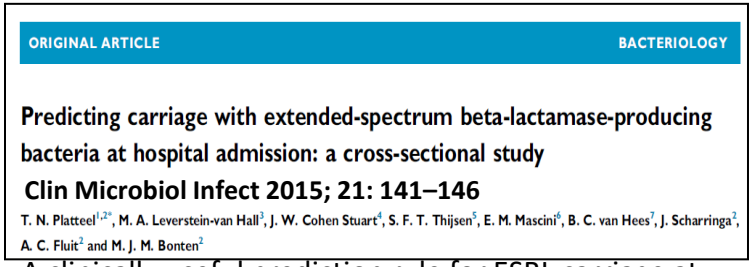
Universal screening for meticillin-resistant *Staphylococcus aureus*: interim results from the NHS Scotland pathfinder project☆

J.S. Reilly [a,*], S. Stewart [a], P. Christie [b], G. Allardice [a,c], A. Smith [a], R. Masterton [d], I. Gould [e], C. Williams [f]

Health Protection Scotland website on 8 April 2008

[a] *Health Protection Scotland, Glasgow, UK*

Relatively **low effectiveness**



ORIGINAL ARTICLE BACTERIOLOGY

Predicting carriage with extended-spectrum beta-lactamase-producing bacteria at hospital admission: a cross-sectional study

Clin Microbiol Infect 2015; 21: 141–146

T. N. Platteel[1,2*], M. A. Leverstein-van Hall[3], J. W. Cohen Stuart[4], S. F. T. Thijsen[5], E. M. Mascini[6], B. C. van Hees[7], J. Scharringa[2], A. C. Fluit[2] and M. J. M. Bonten[2]

A clinically useful prediction rule for ESBL carriage at admission **could not be developed**.

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY SEPTEMBER 2011, VOL. 32, NO. 9

ORIGINAL ARTICLE

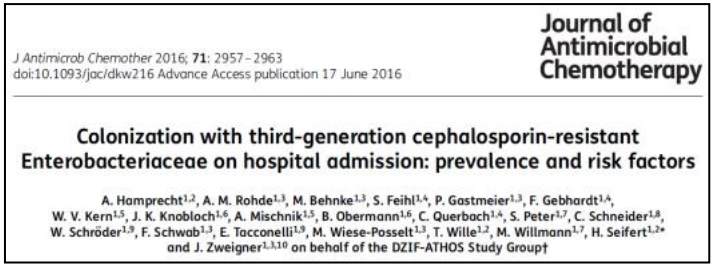
Carbapenem-Resistant *Klebsiella pneumoniae* in Post-Acute-Care Facilities in Israel

Debby Ben-David, MD;[1] Samira Masarwa, MA;[1] Shiri Navon-Venezia, PhD;[1] Hagit Mishali, MA;[1] Ilan Fridental, MD;[1] Bina Rubinovitch, MD;[1] Gill Smollan, MD;[1] Yehuda Carmeli, MD;[1] Mitchell J. Schwaber, MD[1]; Israel PACF CRKP (Post-Acute-Care Facility Carbapenem-Resistant *Klebsiella pneumoniae*) Working Group[1]

A policy of **screening for carriage on admission was protective** (OR, 0.41; P = .03).

Chapter 3
Section 3.06
Infection Prevention and Control at Long-term-care Homes
Ontario,Canada,2009

Screening in **residents admitted with symptoms is effective**



J Antimicrob Chemother 2016; **71**: 2957–2963
doi:10.1093/jac/dkw216 Advance Access publication 17 June 2016

Journal of Antimicrobial Chemotherapy

Colonization with third-generation cephalosporin-resistant Enterobacteriaceae on hospital admission: prevalence and risk factors

A. Hamprecht[1,2], A. M. Rohde[1,3], M. Behnke[1,3], S. Feihl[1,4], P. Gastmeier[1,3], F. Gebhardt[1,4], W. V. Kern[1,5], J. K. Knobloch[1,6], A. Mischnik[1,5], B. Obermann[1,6], C. Querbach[1,4], S. Peter[1,7], C. Schneider[1,8], W. Schröder[1,9], F. Schwab[1,3], E. Tacconelli[1,9], M. Wiese-Posselt[1,3], T. Wille[1,2], M. Willmann[1,7], H. Seifert[1,2*] and J. Zweigner[1,3,10] on behalf of the DZIF-ATHOS Study Group†

Unlikely to be effective for the prevention of 3GCREB transmission.

Systematic review on screening policies for MDR-GN in Hospitals and LTCFs

Lit. Search from 2010 – 2022

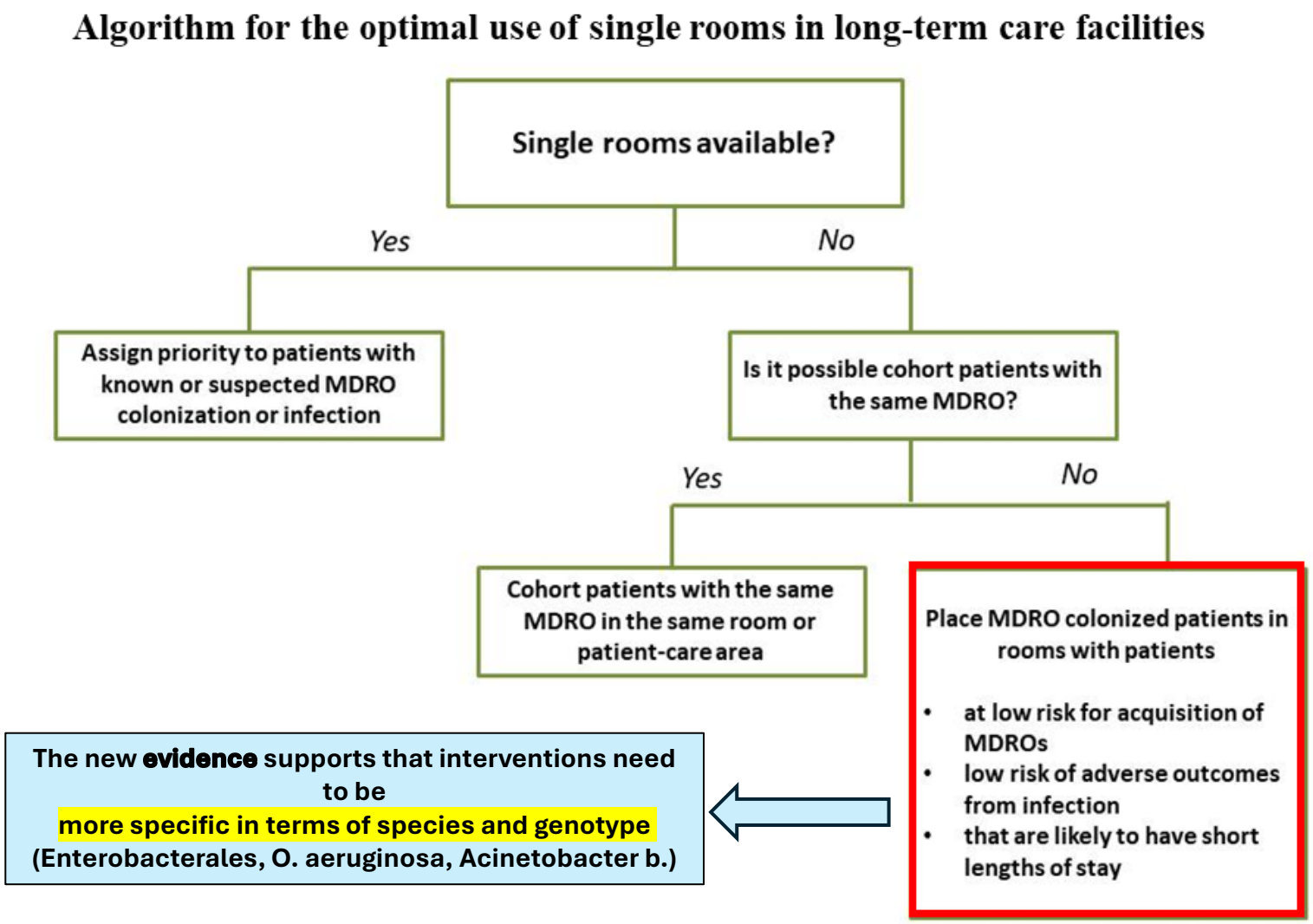
- **~12.000 articles**
- **100 studies included**

- **50%** used screening of **high-risk areas**
  - 14% used screening of high-risk patients only in high-risk areas
- **11%** used screening of **high-risk patients**
- **10%** used **complete admission screening** for all patients

Arzilli,G et al.. Screening for Antimicrobial-ResistantGram-negative. JHI 2022 84;119-130

Algorithm for the optimal use of single rooms in long-term care facilities in MDRO colonized patients .

Tinelli M, Tiseo G, Falcone M; ESCMID Study Group for Infections in the Elderly. Prevention of the spread of multidrug-resistant organisms in nursing homes. Aging Clin Exp Res. 2021 Mar;33(3):679-687

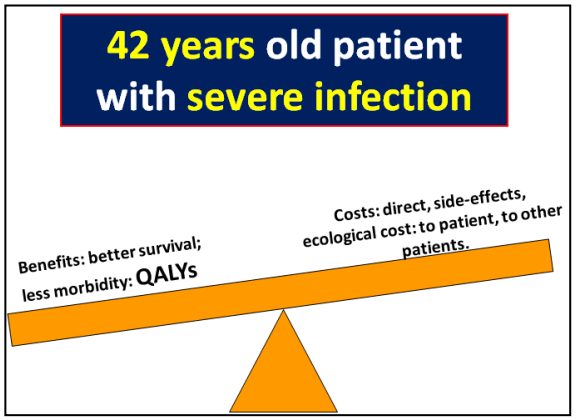


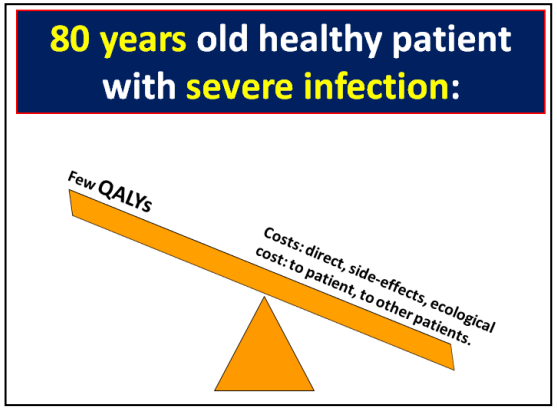
Forever young ?

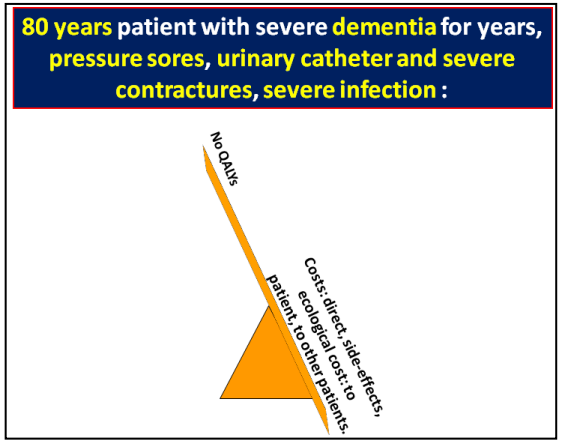
Handcrafted by Ceramica Artistica Lodigiana “Vecchia Lodi” - Copyright by M.Tinelli

Ethical dilemmas

- Can we decide that in a given situation patients have such a **limited life expectancy** that antibiotic treatment can be given up?
- Can we decide that in a given situation patients have such a **low quality of life** that antibiotic treatment can be given up?
- Can we decide that in patients with **extreme dementia** antibiotic treatment won't be offered?







Prevenire la fragilità, prevenire e gestire al meglio le infezioni nell'anziano è anche preservare la dignità della persona che caratterizza il grado di civiltà di un popolo