Identificación del paciente con sospecha de infección por gérmenes multirresistentes

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Medicina Interna/Infecciosas

Hospital Clínico San Carlos

Guión

- Infección en urgencias
- Gérmenes multirresistentes
  - Betalactamasa de expectro extendido (BLEE)
- Infección urinaria
- Infección de piel y partes blandas
- Infección intrabdominal
- Neumonía

La infección en Urgencias

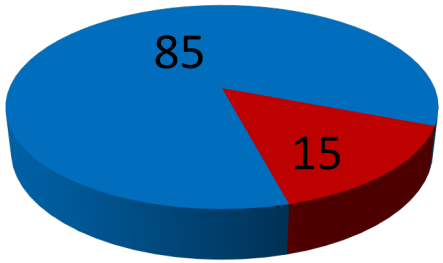
- Problema asistencial relevante
- Incremento en la prevalencia
  - Mayor supervivencia
  - Pacientes crónicos comorbilidades
  - Mayor frecuencia de estados de inmunosupresión
- Incremento en la selección de factores de resistencia a antimicrobianos
- Indicar correctamente el tratamiento antimicrobiano tiene consecuencias

Estudio INFURG-SEMES

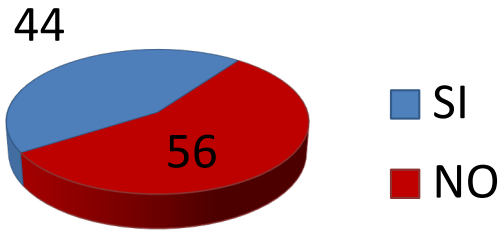
Estudio descriptivo de la infección en 49 hospitales Españoles

n= 79.654 pacientes

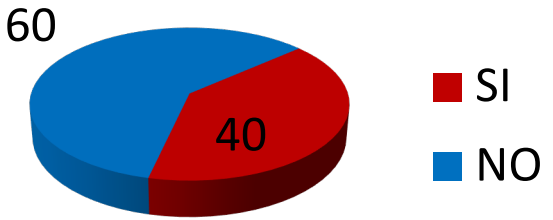
Prevalencia

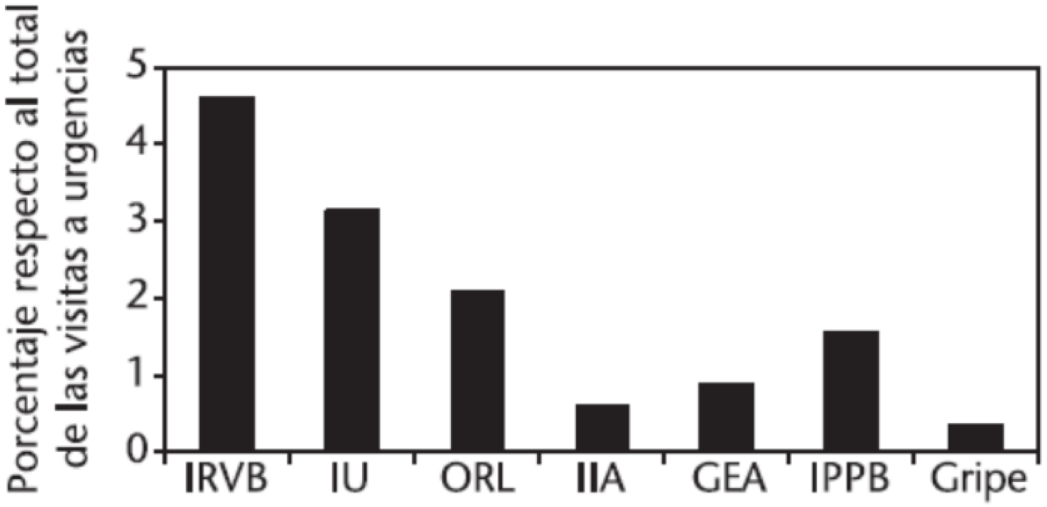


Cultivo



Comorbilidades



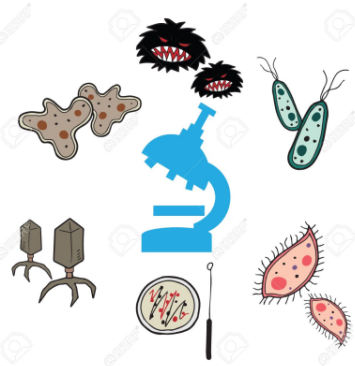


Martínez Ortiz de Zárate M, et al. Emergencias 2013

Criterios para la toma de decisiones en el tratamiento antimicrobiano

1. **Factores del huésped**
   a. Gravedad infección
   b. Localización de la infección
   c. Adquisición
   d. Factores individuales
   e. Epidemiología local
   f. Otros: Comorbilidad/Interacciones/Alergias

2. **Identificación del microorganismo causante de la infección**
   a. Cultivos, gram, técnicas moleculares
   b. Empírico
3. **Determinación de la sensibilidad antimicrobiana de los microorganismos causantes de la infección**
   a. Cultivos
   b. Patrones de sensibilidad locales



Adecuación de las prescripciones antimicrobianas realizadas en el área de urgencias

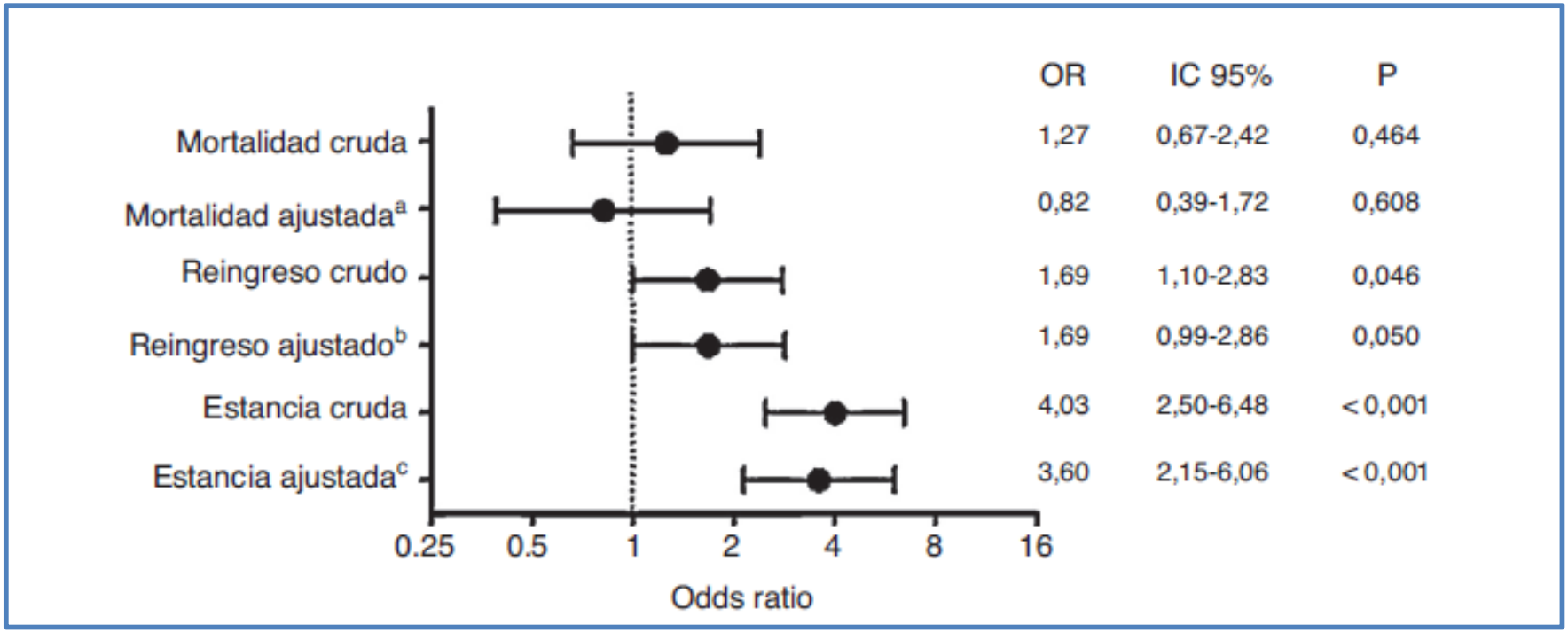
N=676
57% mujeres
Edad 47,2 (DE 21)
Atb indicado 56,8%
- Mayor espectro del necesitado
-Duración inadecuada

LOCALIZACIÓN	PRESCRIPCIONES CORRECTAS
Tracto urinario	36,4% 67/184
Tracto respiratorio superior	6,5% 11/163
Piel y partes blandas	6,7% 7/104
Tracto respiratorio inferior	18,3% 17/93

Prescripción antibiótica correcta: aquella en el que estando indicado el tratamiento antibiótico, se selecciona un antimicrobiano con una pauta y duración recomendadas en guías de tratamiento de referencia.

Yunquera-Romero L, et al Rev Esp Quimiot 2018

Indicar en Urgencias el tratamiento antimicrobiano correcto es trascendente



Gonzalez del Castillo J et al. EIMC 2017

Original

Efecto de la inadecuación de la antibioterapia en Urgencias sobre la eficiencia en la hospitalización

Juan González-del Castillo[a,b,*], Clara Domínguez-Bernal[b], María Cristina Gutiérrez-Martín[b], María José Núñez-Orantos[c], Francisco Javier Candel[d] y Francisco Javier Martín-Sánchez[a,b]

[a] *Servicio de Urgencias, Hospital Clínico San Carlos, Madrid, España*
[b] *Instituto de Investigación Sanitaria del Hospital Clínico San Carlos, Madrid, España*
[c] *Servicio de Medicina Interna, Hospital Clínico San Carlos, Madrid, España*
[d] *Servicio de Microbiología Clínica, Hospital Clínico San Carlos, Madrid, España*

Características de los pacientes agrupados en función de la prescripción apropiada del tratamiento antibiótico

	Total, n (%) (n = 376)	Apropiado, n (%) (n = 334)	Inapropiado, n (%) (n = 42)	p
Datos demográficos				
Edad, media (DE)	71,1 (21)	70,6 (22)	75,2 (16)	0,184
Varón, n (%)	206 (54,8)	190 (56,9)	16 (38,1)	**0,021**
Factores de riesgo				
Sonda vesical	24 (6,4)	17 (5,1)	7 (16,7)	**0,004**
Catéter central	6 (1,6)	6 (1,8)	0 (0)	0,381
Institucionalización	32 (8,5)	25 (7,5)	7 (16,7)	**0,044**
Instrumentación en el último mes	15 (4)	14 (4,2)	1 (2,4)	0,572
Inmunosupresión	30 (8)	27 (8,1)	3 (7,1)	0,832
Corticoterapia crónica	26 (6,9)	22 (6,6)	4 (9,5)	0,480
Antibiótico previo en los últimos 3 meses	152 (40,4)	129 (38,6)	23 (54,8)	**0,045**
Antibiótico previo en el último mes	76 (20,2)	65 (19,5)	11 (26,2)	0,306
Ingreso previo en los últimos 3 meses	128 (34)	109 (32,6)	19 (45,2)	0,104
Al menos un factor de riesgo	145 (38,6)	121 (36,2)	24 (57,1)	**0,009**
Variables de resultado				
Estancia prolongada	165 (46,1)	139 (43,8)	26 (63,4)	**0,018**
Reingreso a 30 días	74 (19,7)	65 (19,5)	9 (21,4)	0,762
Mortalidad a 30 días	44 (11,7)	42 (12,6)	2 (4,8)	0,138

Gonzalez del Castillo J et al. EIMC 2017

A Systematic Review of Antimicrobial Stewardship Interventions in the Emergency Department

Type of Intervention	Number of Included Studies	Outcomes With a Statistically Significant Change From Baseline (n = number of studies)
Guideline or clinical pathway implementation ± education[19-22,28-30,32,37,40,41,43,44]	13	• Increase in appropriate antibiotic prescribing (n = 4)[28,32,40,43] • Decrease in antimicrobial use (n = 3)[21,30,44] • Decrease in ED or hospital length of stay (n = 4)[19,20,28,40] • Decrease in hospital admission or increased discharge from ED (n = 2)[20,28] • ED readmission within 30 days (n = 2)[28,40] • 30-Day mortality (n = 1)[28]
Multifaceted intervention[18,23,24,26,33,35,36,39,45,47,49,52]	12	• Increase in appropriate antibiotic prescribing (n = 4)[35,36,45,52] • Increased adherence to guidelines (n = 4)[26,36,47,49] • Decrease in antimicrobial use (n = 4)[18,24,45,49] • Decrease in ED length of stay (n = 1)[33] • Time to follow-up after ED discharge (n = 1)[18] • Total cost per patient (n = 1)[33]

Losier M, et al. Ann Pharmacother 2017

Gérmenes multirresistentes

Microorganism	Resistance marker
Gram-positive	
Staphylococcus aureus	Methicillin (MRSA)
Enterococcus spp.	Vancomycin (VRE)
Gram-negative	
Enterobacteriaceae	3rd generation cephalosporins (particularly ESBL-producing)
	Carbapenems (particularly carbapenemase-producing)
Pseudomonas aeruginosa	≥ 3 antibiotic classes, including carbapenems[a], cephalosporins[b], piperacillin-tazobactam, flouroquinolones, aminoglycosides[d] and colistin
Acinetobacter baumannii	Carbapenems

[a]Imipenem, meropenem or doripenem; [b]ceftazidime or cefepime; [c]ciprofloxacin or levofloxacin; gentamicin, tobramycin or amikacin.
ESBL: extended spectrum beta-lactamase; MRSA: methicillin-resistant *Staphylococcus aureus;* VRE: vancomycin-resistant enterococcus.

Garnacho Montero et al. Critical Care (2015) 19:114

RESUMEN DEL DÍA Las seis noticias imprescindibles de este martes

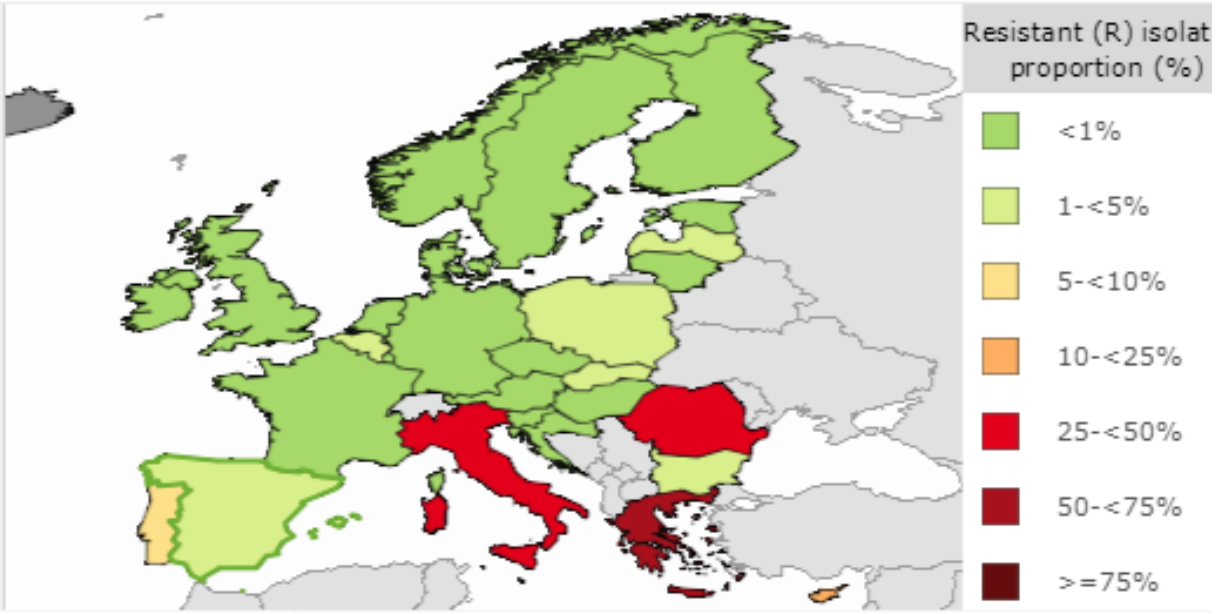
35.000 personas mueren cada año por infecciones causadas por bacterias multirresistentes

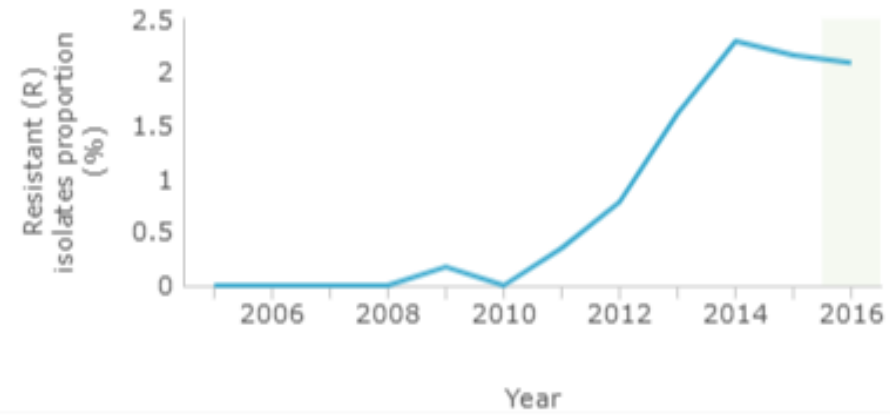
Surveillance Atlas of Infectious Diseases

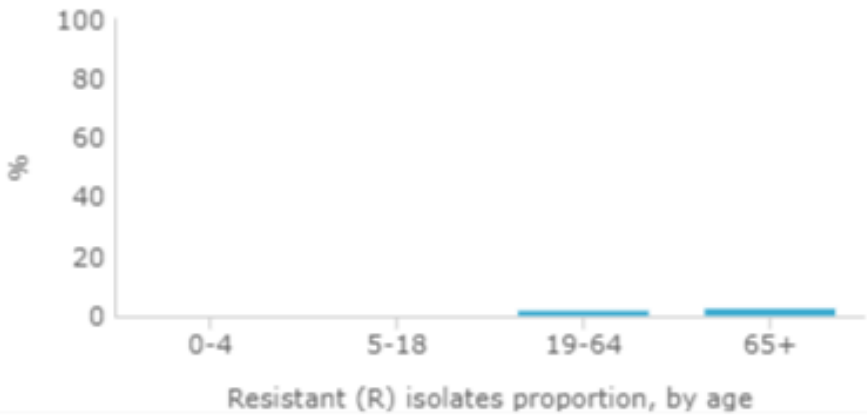
Antimicrobial resistance | Klebsiella pneumoniae | Carbapenems | Resistant (R) isolates proportion

2016

Malta	5.9
Netherlands	0.1
Norway	0.0
Poland	2.1
Portugal	5.2
Romania	31.4
Slovakia	2.5
Slovenia	0.0
Spain	2.1
Sweden	0.1
United Kingdom	0.3

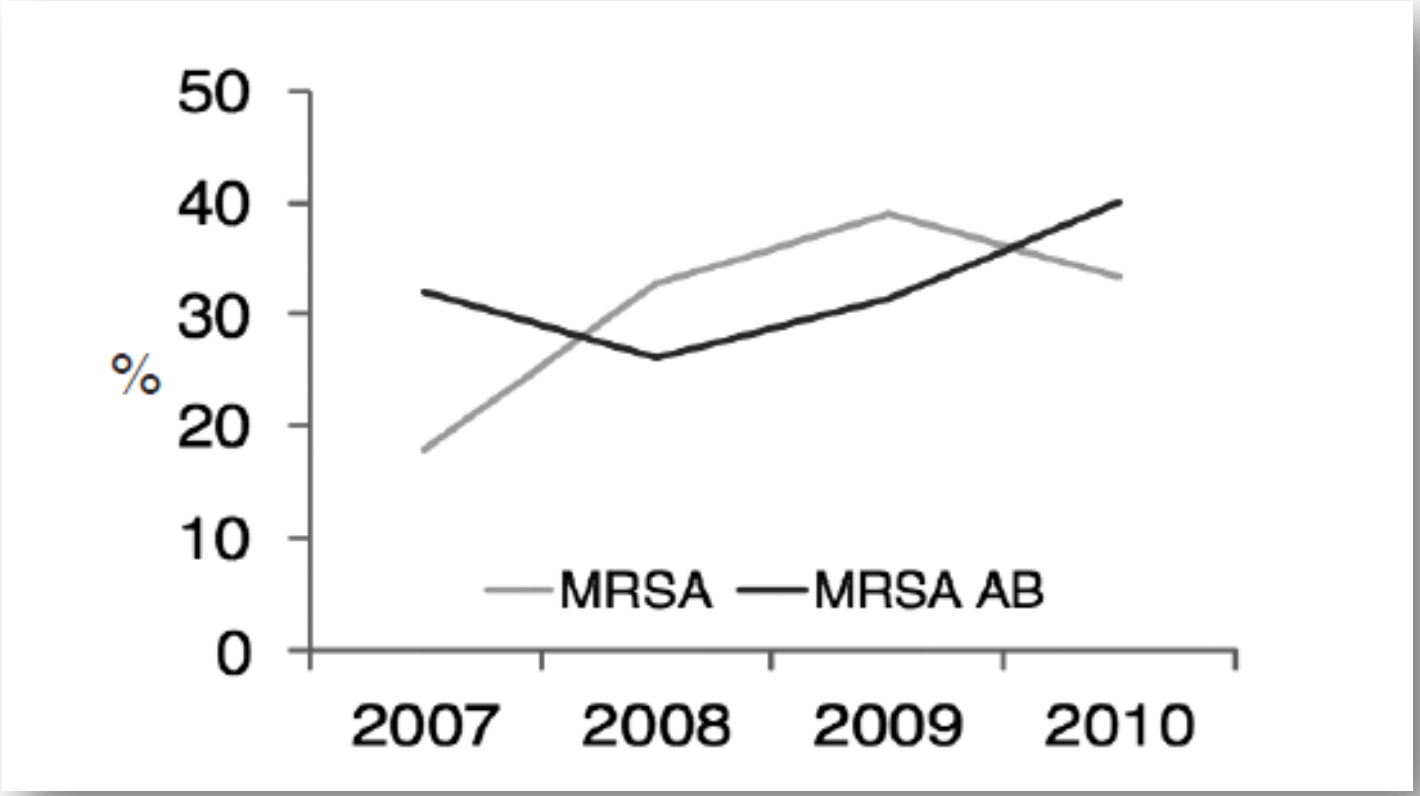






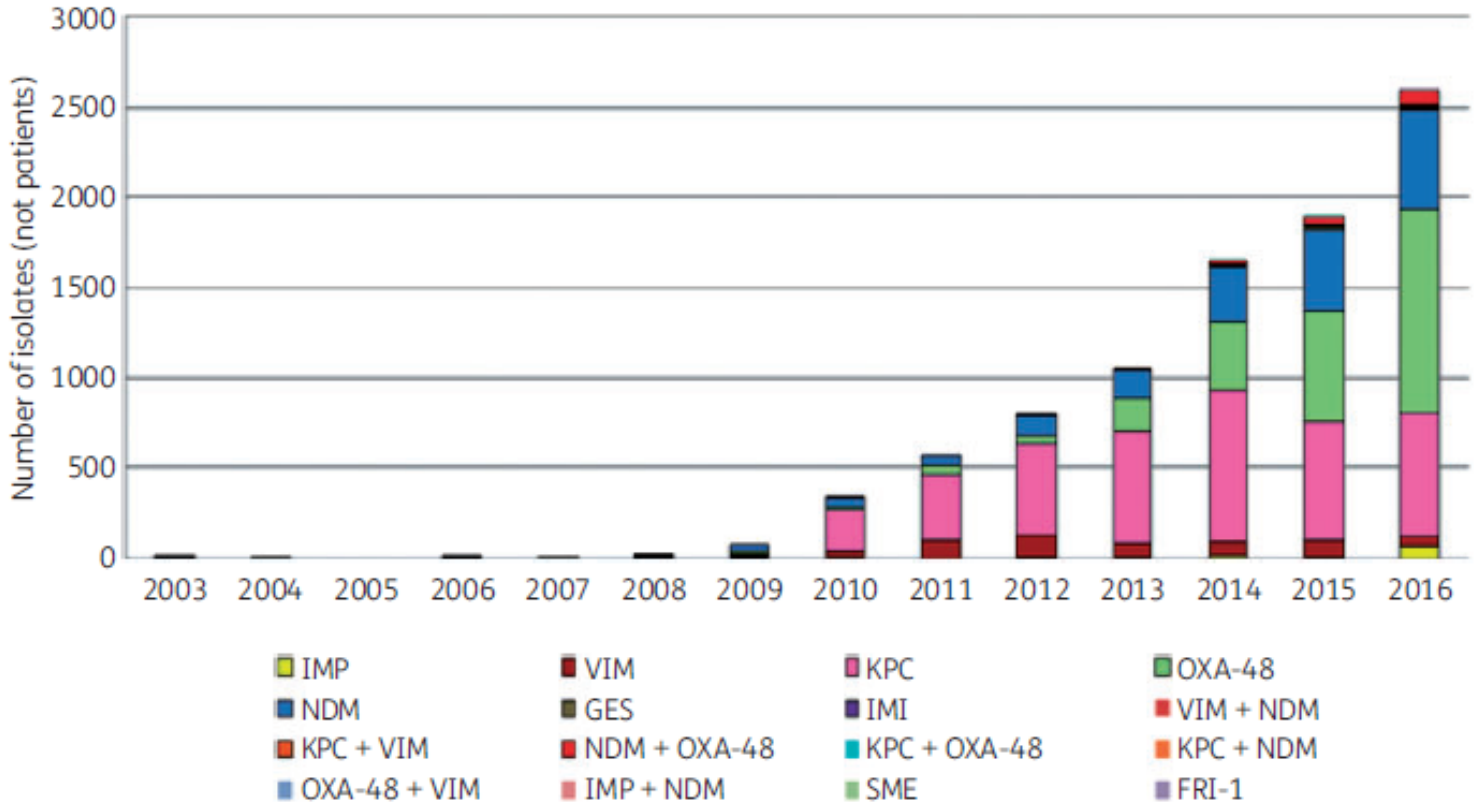
https://www.ecdc.europa.eu/en/antimicrobial-resistance/surveillance-and-disease-data/data-ecdc

MR Staphylococcus aureus infections and factors associated with resistance to methicillin in a hospital emergency department



Gonzalez del Castillo J, et al. Rev Esp Quimiot 2013

Carbapenemase-producing Enterobacteriaceae



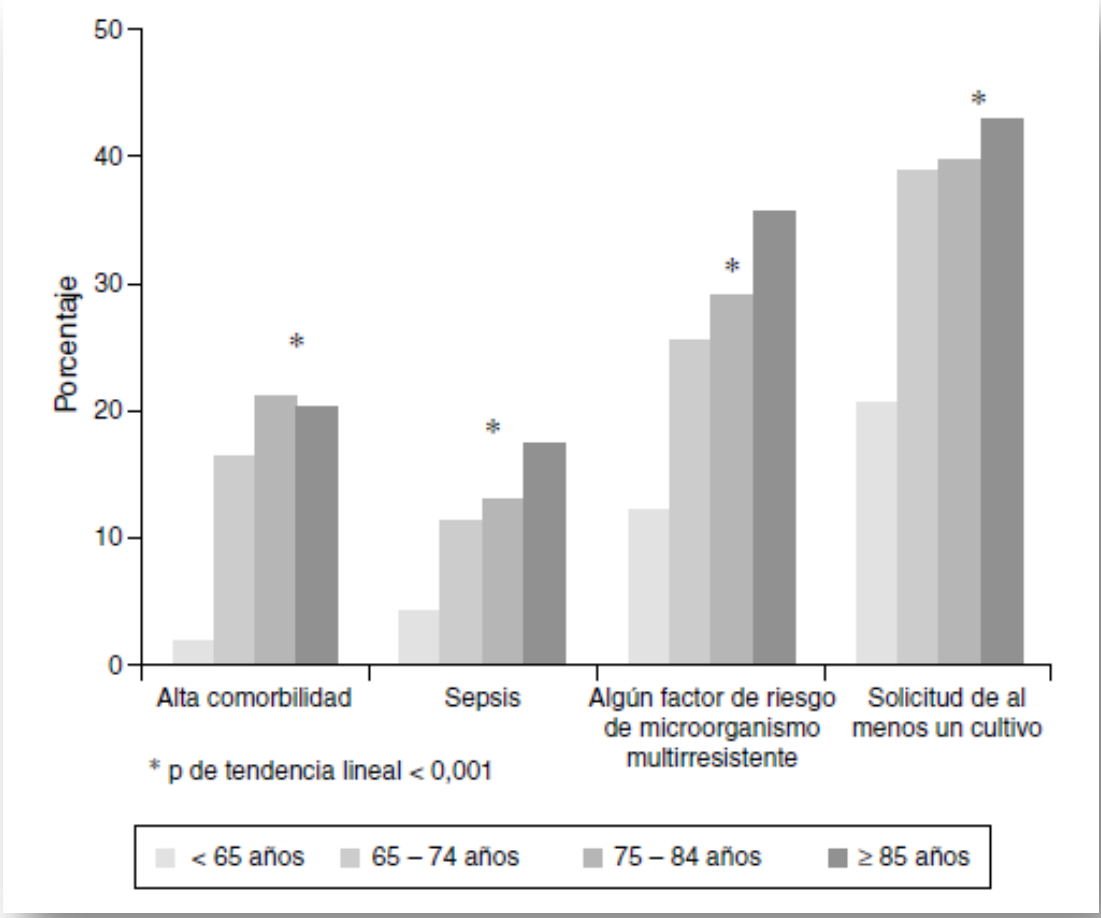
Hawkey T et al, JAC 2018

Colonization of long-term care facility residents in three Italian Provinces by multidrug-resistant bacteria

	% of studied		
	Milan	**Piacenza**	**Bolzano**
All ESβL-positive enterobacteria	60.5	66.1	53.0
All high-level AmpC-positive enterobacteria	5.7	3.3	25.2
All carbapenemase-positive enterobacteria	7.6	0.0	1.6
MRSA (Methycillin-R Staph Aureus)	24.0	5.7	14.8
VRE (Vancomycin-R Enterococcus)	20.2	0.8	0.8

Nucleo et al. Antimicrobial Resistance and Infection Control (2018)

Perfil y manejo inicial de los ancianos atendidos por infección en los servicios de Urgencias hospitalarios



Martin Sanchez FJ et al. Rev Esp Ger Gerontol 2016

Impact on morbidity, mortality and length of stay of hospital acquired infections by resistant microorganisms (Spain)

Type of resistant microorganism	Mortality HR (95%IC)	30-day readmissions OR (95%IC)	30-day Emergency Department visits OR (95%IC)
MRSA	1.79 (1.02-3.14)	2.78 (1.30-5.96)	2.80 (1.65-4.74)
E. coli ESBL	1.18 (0.65-2.10)	2.94 (1.38-6.29)	2.28 (1.32-3.96)
K. pneumoniae ESBL	2.22 (0.95-5.21)	1.35 (0.39-4.67)	1.03 (0.40-3.00)
P. aeruginosa CR	2.14 (1.10-4.17)	1.10 (0.25-4.97)	0.40 (0.11-1.42)
Others MRO	N.A.	N.A.	N.A.

The table shows the Hazard Ratio (mortality) or the Odds Ratio (30-day readmissions and 30-day Emergency Department visits) and its 95% confidence intervals (95%IC) of each multi-resistant organism after the multivariate analysis. SARM = methicillin-resistant *Staphylococcus aureus*; ESBL= extended-spectrum beta-lactamase producing; CR= Carbapenem resistant; MRO= multi-resistant organisms; N.A.= data Not Analyzed due to small sample size

Barrasa JI, et al. CID 2018

Zero resistance program in Intensive Care Units

4. GRAVEDAD DEL PACIENTE

1. HISTORIA SANITARIA DEL PACIENTE

2. USO PREVIO DE ANTIBIÓTICOS

3. CONDICIONES MEDICAS DEL PACIENTE

Table 2 Checklist of risk factors for carriage of multidrug-resistant (MDR) bacteria

Risk factor		
1. Hospital admissionlasting > 5 days, during last 3 months	Yes ☐	NO ☐
2. Institutionalized (prison, healthcare and social centers, geriatric centers, etc.)	Yes ☐	NO ☐
3. Known colonization or infection with MDR pathogens	Yes ☐	NO ☐
4. Antibiotic therapy ≥ 7 days in previous month (particularly 3rd and 4th generation cephalosporins, flouroquinolones and carbapenems)	Yes ☐	NO ☐
5. End-stage renaldisease under chronic hemodialysis or ambulatory peritoneal dialysis.	Yes ☐	NO ☐
6. Comorbidities associated with high incidence of colonization or infection with MDR pathogens: Cystic fibrosis, bronchiectasis, chronic skin ulcers, etc.	Yes ☐	NO ☐

Garnacho Montero et al. Critical Care (2015) 19:114

Beta-lactamasa de espectro extendido BLEE

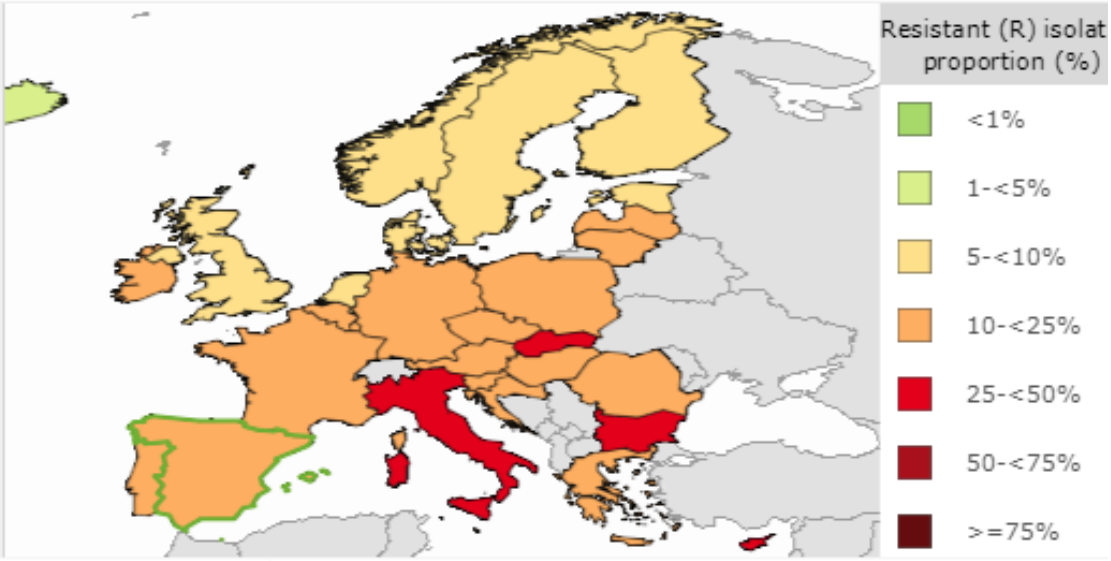
- BLEE: enzimas bacterianas capaces de generar resistencias a traves de su capacidad para hidrolizar las cefalosporinas de tercera generación
- Bacterias gram-negativas, la mayoría enterobacterias, especialmente E. coli.
- Los inhibidores de betalactamasas (clavulánico) no tienen ningún efecto sobre las BLEE, salvo tazobactam o avibactam.
- Suelen requerir Atb de ultimo recurso (Carbapenémicos, Piperacilina/Tazo o Ceftolozano/Tazo)

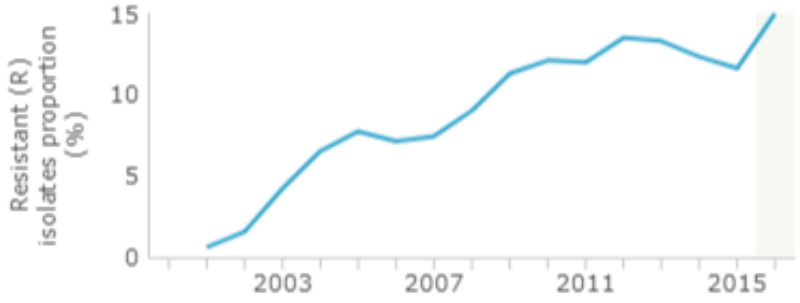
Surveillance Atlas of Infectious Diseases

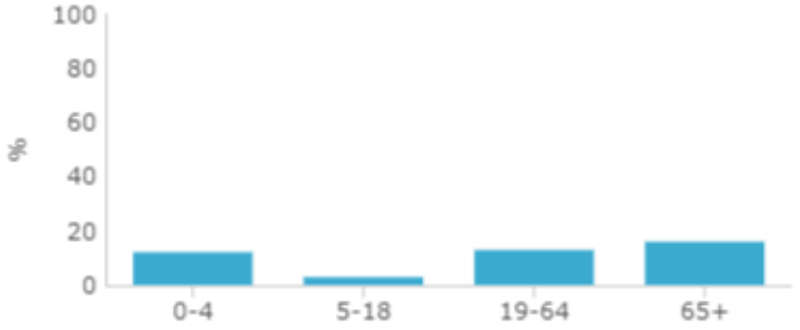
Antimicrobial resistance | Escherichia coli | Third-generation cephalosporins

Resistant (R) isolates proportion | 2016

Malta	14.6
Netherlands	6.4
Norway	5.6
Poland	13.7
Portugal	16.1
Romania	23.4
Slovakia	29.7
Slovenia	12.5
Spain	15.0
Sweden	8.3
United Kingdom	9.2







Factores asociados a la presencia de hemocultivos + para enterobacterias-BLEE (al ingreso)

Parameter	Regression coefficient	*P*	OR (95% CI)	Score
Recent hospitalization[a]	1.73	<0.001	5.69 (2.94–10.99)	3
Admission from another healthcare facility	1.72	0.006	5.61 (1.65–19.08)	3
Charlson comorbidity index ≥ 4	1.33	<0.001	3.80 (1.90–7.59)	2
Previous therapy with β-lactams and/or fluoroquinolones[b]	1.30	<0.001	3.68 (1.96–6.91)	2
History of urinary catheterization[c]	1.25	<0.001	3.52 (1.96–6.91)	2
Age ≥70 years	1.16	<0.001	3.20 (1.79–5.70)	2

[a] During the 12 months preceding index hospitalization.
[b] Includes treatment with β-lactam/β-lactamase inhibitor combinations, oxyiminocephlosporins, and/or fluoroquinolones during the 3 months preceding index admission.
[c] During the 30 days preceding index blood culture.

Tumbarello M et al. JAC 2013

Utility of a Clinical Risk Factor Scoring Model in Predicting Infection with ESBL on Hospital Admission

Attribute	No. of points
Recent antibiotic therapy with β-lactams and/or fluoroquinolones[a]	3
Previous hospitalization[b]	2
Transfer from another healthcare facility	4
Recent history of urinary catheterization[c]	5
Immunosuppression[d]	2

[a] During the 3 months preceding the index hospitalization.

[b] During the 12 months preceding the index hospitalization.

[c] During the 30 days preceding the index admission.

[d] During the 3 months preceding the index admission.

Johnson SW et al. Infect Control Hosp Epidemiol. 2013

Factores de riesgo independientes de bacteriemia por BLEE

1. **Contacto con el sistema sanitario**
   OR 2.1; IC95% 1.2–3.8
2. **Portador de sonda urinaria**
   OR, 3.1; 95% CI, 1.5–6.5
3. **Uso previo de antimicrobianos (3 M)**
   OR 2.7; 95% CI, 1.5–4.9

Rodriguez Baño J, CID 2010

Infección urinaria
Factores de riesgo para BLEE

Edad > de 65 años

Diabetes mellitus

Hospitalización reciente

Tratamiento antibiótico en los 2 meses previos

Infección previa por una enterobacteria con BLEE

Infecciones urinarias de repetición

Gonzalez del Castillo J et al, Rev Esp Quimiot 2016

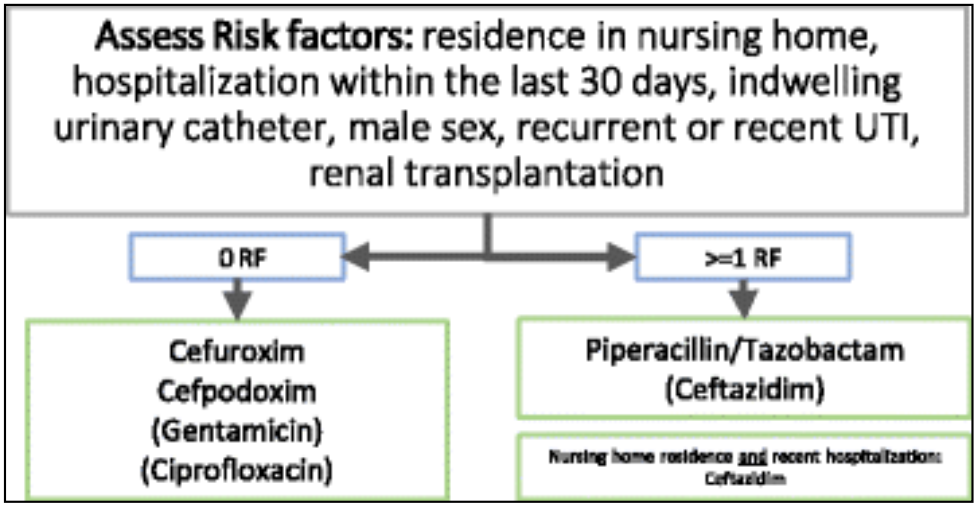
A Clinical Decision Rule Identifies Risk Factors Associated With Antimicrobial-Resistant Urinary Pathogens in the Emergency Department

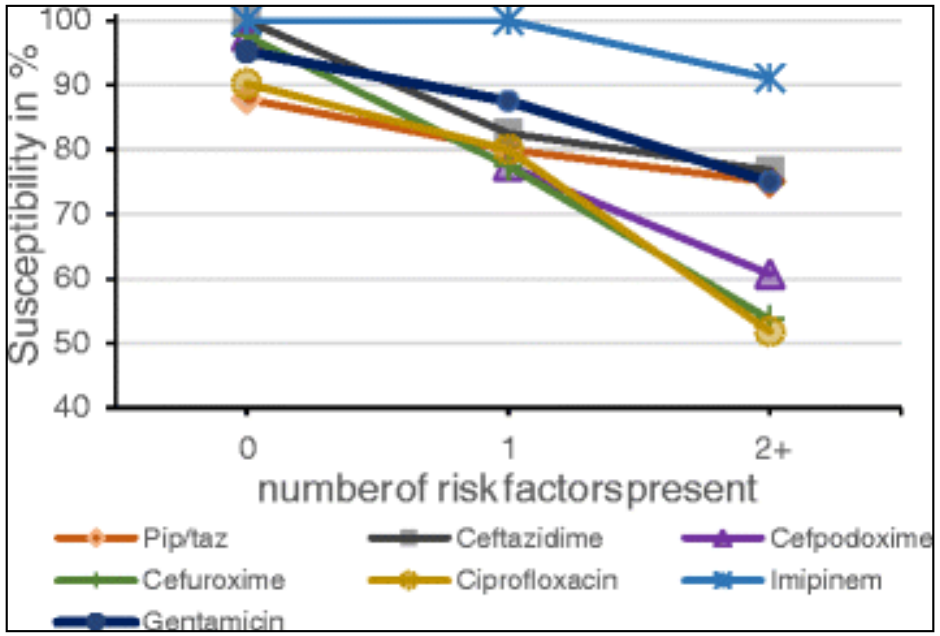
- Retrospective study, Iowa City, USA
- N= 360 patients with UTI
- 6.7% of patients (n = 24) had a multidrug-resistant (MDR) UTI

Patient Characteristic	aOR (95% CI)[a]
Male	8.04 (3.20-20.1)
History of dialysis	
Yes	8.72 (1.95-38.9)
Nursing home resident	
Yes	4.17 (1.13-15.3)

Faine BA, et al. Ann Pharmacother 2015

Empiric antibiotic therapy in urinary tract infection in patients with risk factors for antibiotic resistance in a German emergency department



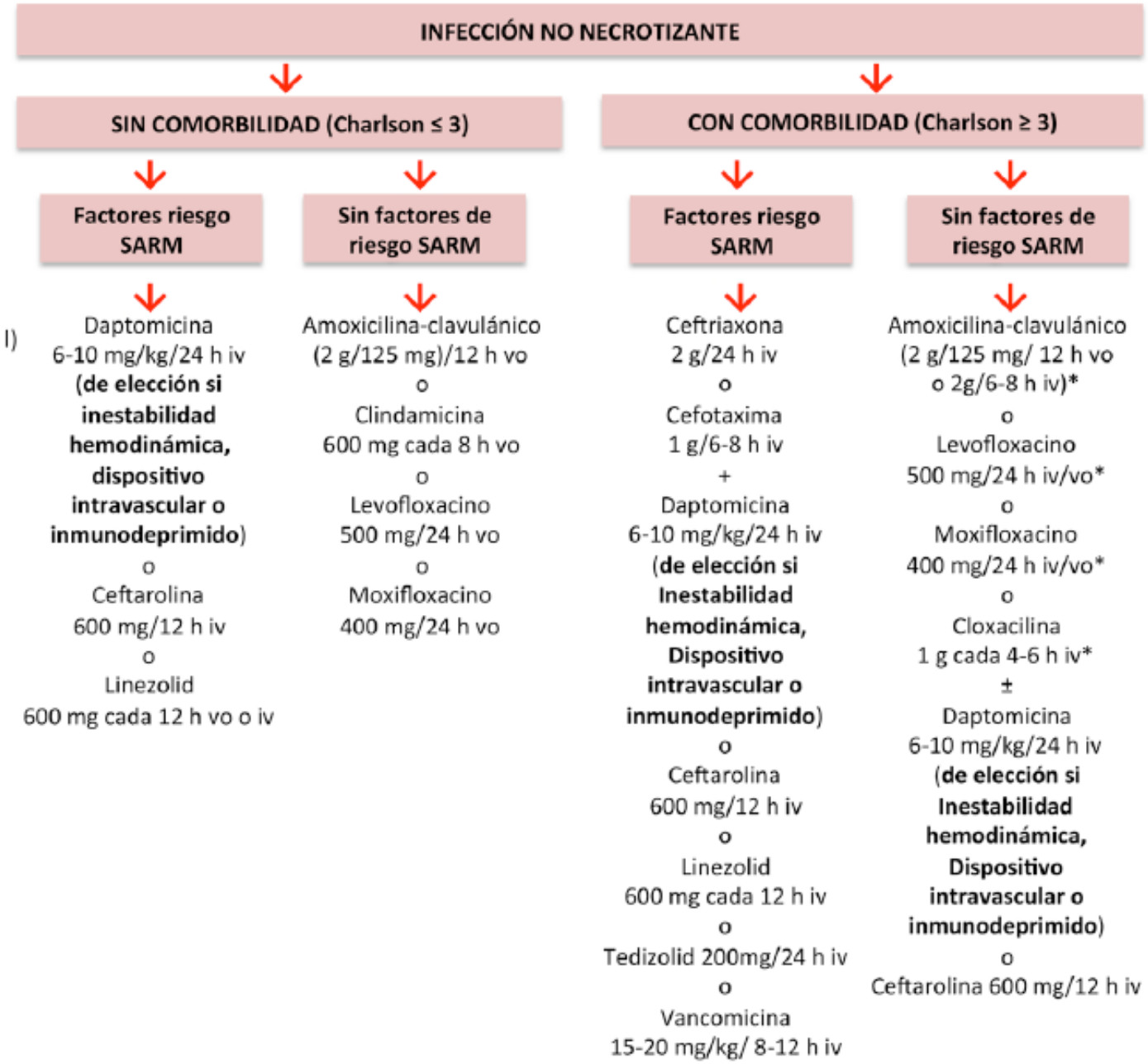


Bischoff F, et al. BMC Infect Dis 2017

Infección de piel y partes blandas
Factores de riesgo para SARM

Infección o colonización previa por SARM
Hospitalización prolongada reciente (> 14 días)
Tratamiento antimicrobiano en los 3 meses previos
Procedente de centro sociosanitario en un área con prevalencia > 20% de SAMR
Úlceras de larga evolución o gran tamaño
Insuficiencia renal crónica en programa de diálisis
Procedimiento quirúrgico reciente

Gonzalez del Castillo J et al, Rev Esp Quimiot 2016



Gonzalez del Castillo J et al, Rev Esp Quimiot 2016

Epidemiology and Risk Factors for Isolation of Multi-Drug–Resistant Organisms in Patients with Complicated Intra-Abdominal Infections

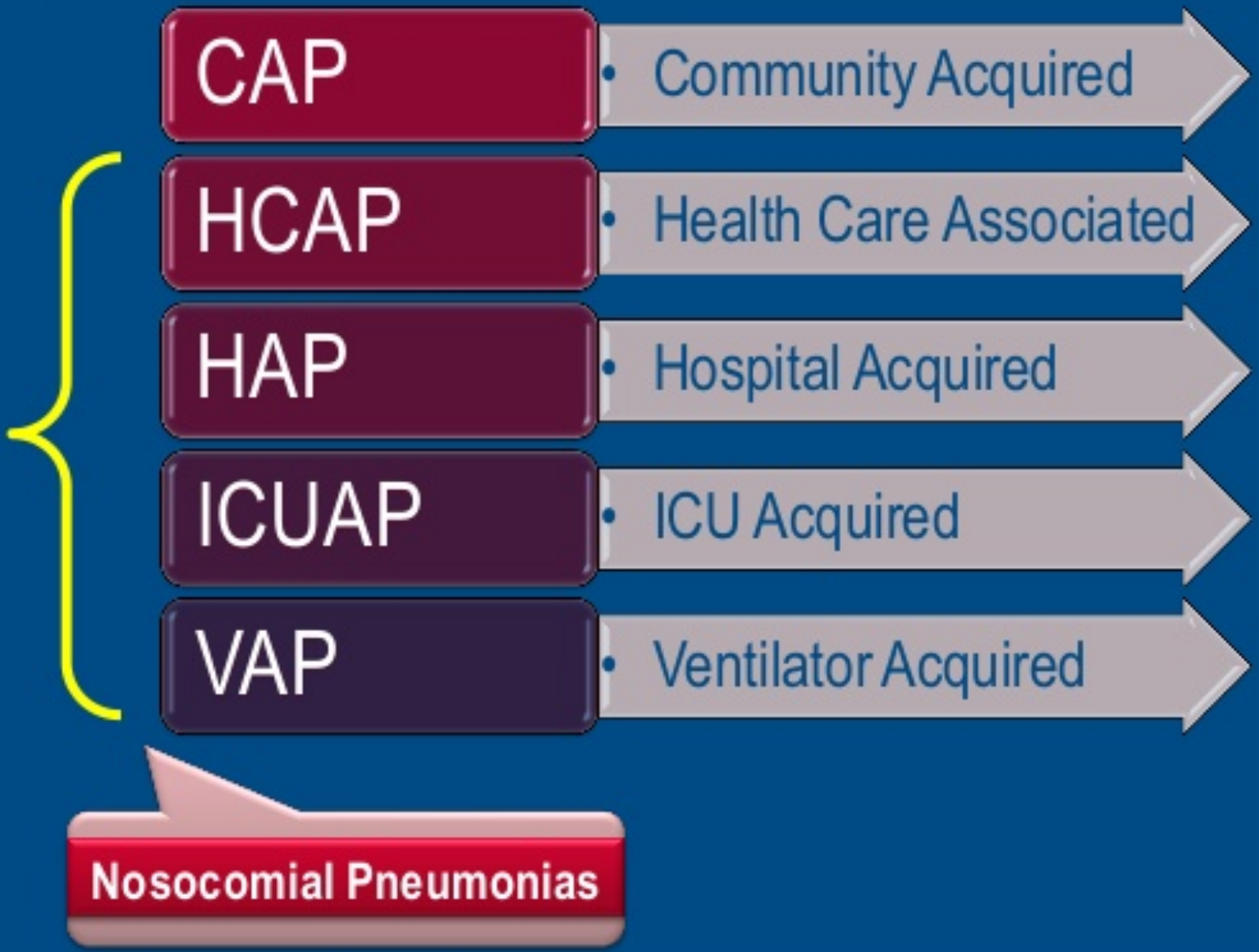
- N= 1986 patients
- 3534 micro-organisms were isolated from intraperitoneal fluid samples
- 46.5% of cultures, two or more pathogens were identified.
- MDROs represented 9.8% of the total of isolated micro-organisms.
- The overall incidence rate of MDROs was 13.9%.

Variables	*OR*	*95% CI*	*p*
Antimicrobial therapy in the previous 7 days	2.08	1.56–2.79	<0.001
Severe cardiovascular disease	1.46	1.07–2.00	<0.05
Leukocytosis or leukopenia	1.93	1.39–2.68	<0.001
HA-cIAI	2.38	1.78–3.19	<0.001
Inadequate source control	1.67	1.14–2.45	<0.05

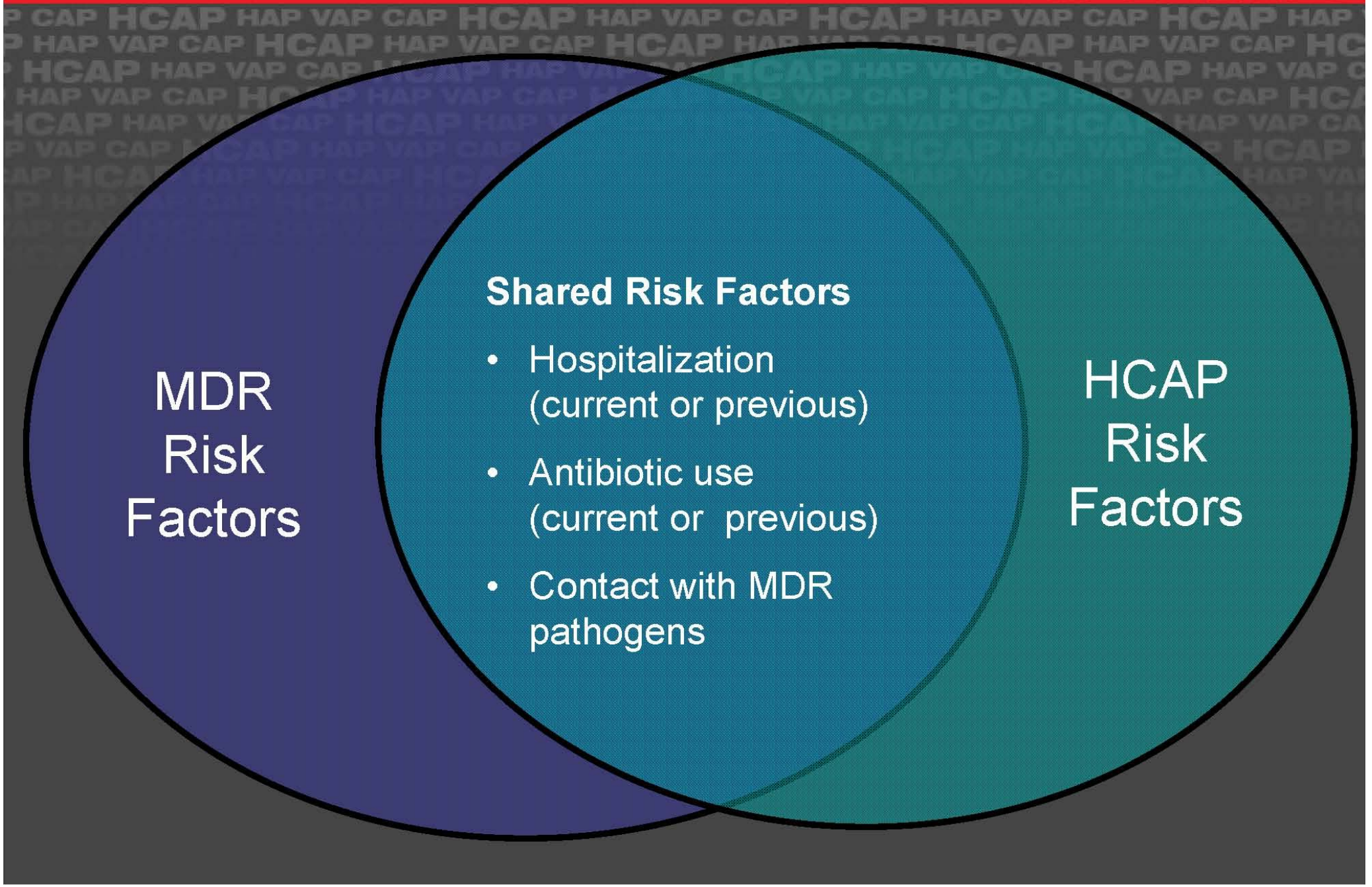
OR = odds ratio; CI = confidence interval; HA-cIAI = health-care–associated complicated intra-abdominal infection.

Labricciosa FM, et al. Surg Inf 2018

Pneumonias – Classification



Strong Overlap Between HCAP and MDR Risk Factors



Predictores en Urgencias de patógenos resistentes en las neumonías procedentes de la comunidad

- N= 139 pacientes
- Edad media de 75 años (DE: 15,3)
- 63,3% varones
- Hospital de la Santa Creu i Sant Pau de Barcelona

- ✓ Haber ingresado en los 90 días previos (OR 8,92, [IC 95%: 1,9-41,4])
- ✓ Saturación inicial de oxígeno (OR 0,85 [IC 95%: 0,7-0,9])
  - Valor predictivo positivo 20%
  - Valor predictivo negativo 99,1%

Torres OH, et al. Emergencias 2017

Clinical predictors of methicillin-resistant Staphylococcus aureus in nosocomial and healthcare-associated pneumonia: a multicenter, matched case–control study

1. **Respiratory infection/colonization caused by MRSA in the previous year** [odds ratio (OR) 14.81, 95% confidence interval (CI) 4.13–53.13, p < 0.001]

2. **Hospitalization in the previous 90 days** (OR 2.41, 95% CI 1.21–4.81, p = 0.012)

3. **Age** (OR 1.02, 95% CI 1.001–1.05, p = 0.040)

Positive Predictive Value of 52.5% (95% CI 43.9–61.2)
Negative predictive value of 82.0% (95% CI 75.3–88.8)

Torre Cisneros J, et al. Eur J Clin Microbiol Infect Dis 2017

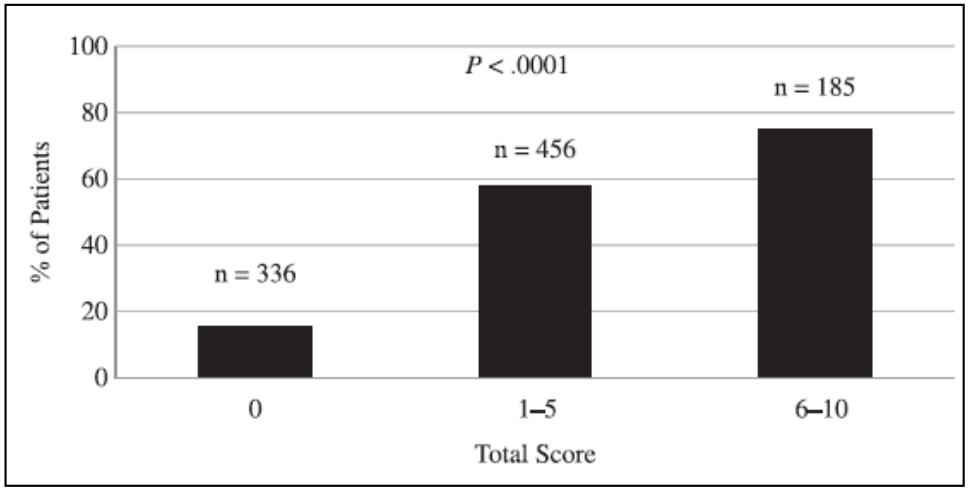
Validation of a Clinical Score for Assessing the Risk of Resistant Pathogens in Patients With Pneumonia Presenting to the Emergency Department

Table 1. Baseline Patient Characteristics

Characteristics	Resistant Organism (n = 456)	No Resistant Organism (n = 521)	*P* Value
Age, mean (SD), years	61.1 (16.2)	60.0 (17.5)	.321
Male	58.8%	53%	.081
Race			
Caucasian	57.9%	54.5%	.320
African-American	41.2%	44.7%	
Other	0.9%	0.8%	
Severity of illness			
ICU admission	62.5%	44.9%	.001
Mechanical ventilation	52.9%	36.7%	.001
HCAP risk factors			
LTC admission	25.4%	11.1%	.001
HD	10.3%	4.8%	.001
Immunosuppression	37.1%	27.8%	.003
Prior antibiotics	58.6%	31.3%	.001
Recent hospitalization	55.9%	33.4%	.001
HCAP	91.0%	65.6%	.001

Abbreviations: HCAP, healthcare-associated pneumonia; HD, hemodialysis; ICU, intensive care unit; LTC, long-term care; SD, standard deviation.

1. *Recent hospitalization (4 points)*
2. *Nursing home (3 points)*
3. *Chronic hemodialysis (2 points)*
4. *Critically ill (1 point).*



Schorr A, et al. CID 2012

Stratifying Risk Factors for Multidrug-Resistant Pathogens in Hospitalized Patients Coming From the Community With Pneumonia

Table 2. Risk Factors for Multidrug-Resistant Pathogens Among the Study Population

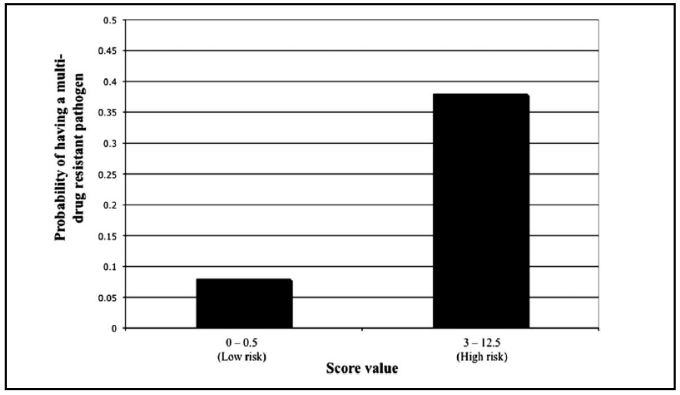
Risk Factor for MDR	Prevalence, No. (%)
Risk factors for HCAP	284 (30)
Hospitalization for ≥2 days in the preceding 90 days	200 (21)
Residency in a nursing home or extended-care facility	66 (7)
Home infusion therapy (including antibiotics)	39 (4)
Home wound care	36 (4)
Chronic dialysis within 30 days	8 (0.9)
Family member with MDR pathogen	0 (0)
Immunosuppression	267 (29)
Severe immunosuppression[a]	135 (15)
Mild-to-moderate immunosuppression[b]	132 (14)
Other	
Antimicrobial therapy in preceding 90 days	155 (17)

IDSA CRITERIA FOR MDR RISK

Table 4. Scoring System to Evaluate the Presence of Multidrug-Resistant Pathogens in Patients With Pneumonia From the Community Who are Hospitalized

Variable	Score
No risk factors for MDR pathogen (including comorbidities)	0
≥1 of the following: cerebrovascular disease, diabetes, COPD, antimicrobial therapy in preceding 90 days, immunosuppression, home wound care, home infusion therapy (including antibiotics)	0.5
Residence in a nursing home or extended-care facility	3
Hospitalization for ≥2 days in the preceding 90 days	4
Chronic renal failure	5

Abbreviations: COPD, chronic obstructive pulmonary disease; MDR, multidrug-resistant.



Aliberti S, et al CID 2015

Individualizing Risk of Multidrug-Resistant Pathogens in Community-Onset Pneumonia

Isolation of MDR strain n = 99 patients		Isolation of non-MDR strain n = 201 patients	
MRSA	42 (42.4%)	*Streptococcus pneumoniae*	69 (34.3%)
Pseudomonas aeruginosa	11 (11.1%)	MSSA	31 (15.4%)
Klebsiella pneumonia	10 (10.1%)	*Mycoplasma pneumoniae*	15 (7.5%)
Serratia marcescens	8 (8.1%)	*Pseudomonas aeruginosa*	15 (7.5%)
Escherichia coli	7 (7.1%)	*Klebsiella pneumoniae*	14 (7%)
MRSA + *P. aeruginosa*	6 (6.1%)	*Haemophilus influenzae*	13 (6.6%)
Acinetobacter baumannii	6 (6.1%)	*Clamydia pneumoniae*	10 (4.9%)
Enterobacter cloacae	4 (4%)	*Mycobacterium spp*	10 (4.9%)
E. cloacae + *S. maltophilia*	2 (2%)	*Legionella pneumophila*	10 (4.9%)
MRSA + *A. baumannii*	2 (2%)	*Enterobacter cloacae*	8 (4%)
Stenotrophomonas maltophilia	1 (1%)	*Escherichia coli*	6 (3%)

Variables	p	OR	95% CI	VIF
Bilateral Pulmonary Infiltration	0.018	1.75	1.09–2.79	1.05
Pleural effusion	<0.001	1.95	1.25–3.07	1.02
At least one of HCAP criteria: Previous hospitalization (3 months), dialysis, i.v. therapy previous 30 days, residence in nursing home or long-term care facility	<0.001	2.52	1.57–4.09	1.07
PaO2/FiO2 ratio < 300	<0.001	4.08	2.55–6.67	1.03

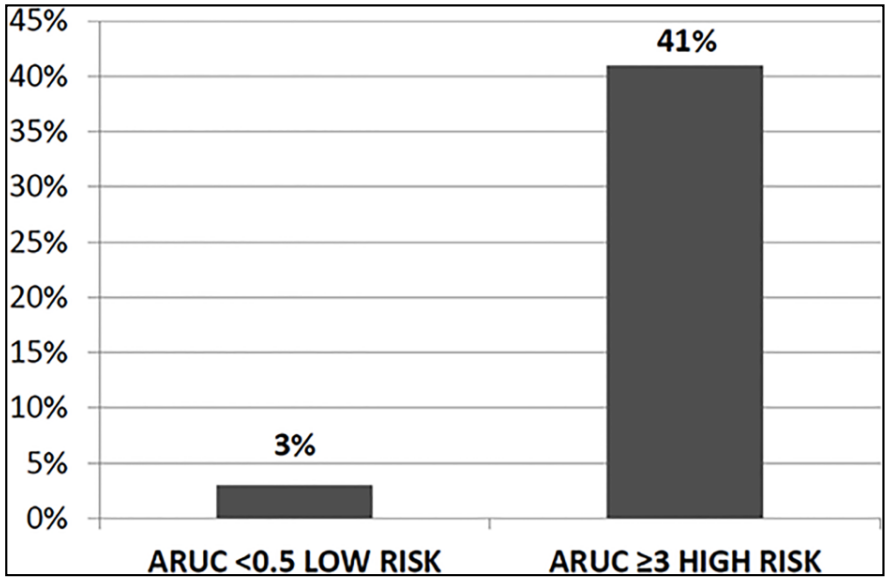
Legend. MDR: multidrug-resistant; HCAP: health-care associated pneumonia.

Falcone M, et al. PlosOne 2015

ARUC score for early identification of patients with MDR-pneumonia

HCAP criteria (at least one of the following): Previous hospitalization (3 months), dialysis, i.v. therapy previous 30 days, residence in nursing home or long-term care facility	**+ 1 pts**
Bilateral Pulmonary Infiltration	**+ 0.5 pts**
Pleural effusion	**+ 0.5 pts**
PaO2/FiO2 < 300	**+ 1.5 pts**

Legend. MDR: multidrug-resistant; HCAP: health-care associated pneumonia; COPD: chronic obstructive pulmonary disease.



Falcone M, et al. PlosOne 2015

Puntos clave

¿Cuando pienso en gérmenes multirresistentes?

1. **Cuando el paciente esta grave**
   - Siempre es posible desescalar la intensidad del antibiótico al ver la evolución clínica/cultivos
2. **Cuando el paciente ha estado en contacto con el sistema sanitario**
   - En el último mes (o 3 meses)
3. **Cuando ha tomado antibióticos previamente**
   - En el último mes (o 3 meses)
4. **Si el paciente presenta condiciones médicas graves**
   - Insuficiencia renal, inmunosuprimido, comorbilidades, historia previa de colonización

3 escenarios concretos

- **Neumonía**
  - Meropenem ó Pip/Tazo
  - Sospecha SARM: + Vancomicina (o Linezolid)
- **Infección urinaria (pielonefritis aguda)**
  - Carbapenémico
- **Infección de piel y partes blandas (no necrotizante)**
  - Sospecha SARM: Daptomicina
  - Sospecha SARM comorbilidad: Dapto+Cefriaxona

Con los antibióticos...
¡PELIGRO!
¡RUTINA!
Tu paciente se merece toda tu atención
Ni menos, ni más ¡Tú decides!

Muchas gracias por
vuestra atención