Bloodstream infections in solid-organ transplant recipients

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Bacterial infections now constitute the most frequent complication among solid organ transplant recipient, having overtaken classical opportunistic infections

Bloodstream infections (BSI) occur in over one-third of SOT recipients and are associated with high rate of mortality, almost reaching 50% when accompanied by septic shock

The management of BSI in SOT recipients is one of the most challenging clinical issues today

ORIGINAL ARTICLE

Changing trends in the aetiology, treatment and outcomes of bloodstream infection occurring in the first year after solid organ transplantation: a single-centre prospective cohort study

Isabel Oriol[1,2], Núria Sabé[1,2], Antonella F. Simonetti[1,2], Laura Lladó[3], Anna Manonelles[4], Jose González[5], Fe Tubau[2,6] & Jordi Carratalà[1,2]

Transplant International 2017; 30: 903–913

Table 3. Causative organisms of all episodes of bloodstream infection (BSI) occurring during the first year of solid organ transplant compared by 2-year periods.

Aetiology	All episodes of BSI	2007–2008 (*N* = 42)	2009–2010 (*N* = 24)	2011–2012 (*N* = 60)	2013–2014 (*N* = 43)	2015–2016 (*N* = 49)
Gram-positive bacteria (*n*, %)	42 (19.3)	15 (40.5)	7 (35.0)	11 (22.4)	8 (20.5)	1 (2.2)
Streptococci (*n*, %)	3 (1.4)	1 (2.4)	0	0	1 (2.3)	1 (2.0)
Staphylococcus aureus (*n*, %)	11 (5.0)	3 (7.1)	6 (25.0)	1 (1.7)	1 (2.3)	0
Enterococcus faecalis (*n*, %)	8 (3.7)	4 (9.5)	1 (4.2)	2 (3.3)	1 (2.3)	0
Enterococcus faecium (*n*, %)	3 (1.4)	0	0	2 (3.3)	1 (2.3)	0
CNS (*n*, %)	16 (7.3)	7 (16.7)	0	6 (10.0)	3 (7.0)	0
Gram-negative bacilli (*n*, %)	138 (63.3)	20 (54.1)	12 (60.0)	33 (67.3)	31 (79.5)	42 (93.3)
Multidrug-resistant GNB (*n*, %)	57 (26.1)	2 (4.8)	5 (20.8)	15 (25.0)	16 (37.2)	19 (38.8)
Enterobacteriaceae (*n*, %)	105 (48.2)	19 (45.2)	8 (33.3)	23 (38.3)	23 (53.5)	32 (65.3)
Klebsiella pneumoniae (*n*, %)	33 (15.1)	3 (7.1)	2 (8.3)	7 (11.7)	8 (18.6)	13 (26.5)
Escherichia coli (*n*, %)	52 (23.9)	9 (21.4)	4 (16.7)	15 (25.0)	11 (25.6)	13 (26.5)
ESBL-producing *Enterobacteriaceae* (*n*, %)	44 (20.2)	3 (7.1)	2 (8.3)	10 (16.7)	12 (27.9)	17 (34.7)
ESBL-producing *K. pneumoniae* (*n*, %)	24 (11.0)	0	0	5 (8.3)	7 (16.3)	12 (24.5)
ESBL-producing *E. coli* (*n*, %)	11 (5.0)	2 (4.7)	0	3 (5.0)	3 (6.9)	3 (6.1)
Other Enterobacteriaceae (*n*, %)	20 (9.2)	7 (16.7)	2 (8.3)	1 (1.7)	4 (9.3)	6 (12.2)
Nonfermenting GNB (*n*, %)	32 (14.7)	1 (2.4)	4 (16.7)	10 (16.7)	7 (16.3)	10 (20.4)
Pseudomonas aeruginosa (*n*, %)	29 (13.3)	1 (2.4)	3 (12.5)	8 (13.3)	7 (16.3)	10 (20.4)
MDR *P. aeruginosa* (*n*, %)	16 (7.3)	1 (2.4)	3 (12.5)	4 (6.7)	5 (11.6)	3 (6.1)
Nonfermenting GNB other than *P. aeruginosa* (*n*, %)	3 (1.4)	0	1 (4.2)	2 (3.3)	0	0
Candida spp. (*n*, %)	7 (3.2)	2 (5.4)	1 (5.0)	3 (6.1)	0	1 (2.2)
Anaerobes (*n*, %)	3 (1.4)	0	0	2 (4.1)	0	1 (2.2)
Polymicrobial (*n*, %)	28 (12.8)	5 (11.9)	4 (16.7)	11 (18.3)	4 (9.3)	4 (8.2)

CNS, Coagulase-negative staphylococci; MDR, multidrug-resistant; ESBL, extended-spectrum β-lactamase.

Table 2. Trends of clinical characteristics of all episodes at the onset of bloodstream infection compared by 2-year periods.

Variable	All episodes of BSI	2007–2008 (*N* = 42)	2009–2010 (*N* = 24)	2011–2012 (*N* = 60)	2013–2014 (*N* = 43)	2015–2016 (*N* = 49)
Source of BSI						
Primary source (*n*, %)	28 (13.1)	7 (16.7)	7 (29.2)	5 (8.3)	4 (9.3)	5 (10.4)
Catheter-related BSI (*n*, %)	30 (13.6)	9 (21.4)	5 (20.8)	12 (20.0)	4 (9.3)	0
Pneumonia (*n*, %)	6 (2.8)	0	1 (4.2)	1 (1.7)	3 (7.0)	1 (2.1)
Urinary tract infection (*n*, %)	97 (44.9)	18 (42.9)	8 (33.3)	19 (31.7)	19 (44.2)	33 (68.8)
Abdominal (*n*, %)	43 (19.6)	5 (11.9)	2 (8.3)	18 (30.0)	10 (23.3)	8 (16.7)
Other (*n*, %)	13 (6.1)	3 (7.1)	1 (4.2)	5 (8.3)	3 (7.0)	1 (2.1)
Prior antibiotic therapy* (*n*, %)	151 (69.6)	40 (95.2)	13 (54.2)	47 (78.3)	26 (61.9)	25 (51.0)
Prior use of carbapenem (*n*, %)	45 (20.6)	5 (11.9)	3 (12.5)	16 (26.7)	8 (18.6)	13 (26.5)
Prior use of cephalosporin (*n*, %)	16 (7.5)	3 (7.1)	3 (12.5)	5 (8.3)	1 (2.3)	4 (8.2)
Prior use of quinolone (*n*, %)	11 (5.0)	2 (4.8)	0	6 (10.0)	2 (4.7)	1 (2.0)
Prior use of β-lactam/β-lactamase inhibitors (*n*, %)	46 (21.5)	21 (50.0)	1 (4.2)	14 (23.3)	6 (14.0)	4 (8.2)
Use of urinary catheter (*n*, %)	109 (50.0)	21 (50.0)	15 (62.5)	29 (48.3)	20 (46.5)	24 (49.0)
Use of venous catheter (*n*, %)	134 (61.2)	27 (64.3)	17 (70.8)	41 (68.3)	25 (58.1)	24 (49.0)
Septic shock at presentation† (*n*, %)	38 (17.8)	2 (4.9)	4 (16.7)	17 (28.3)	5 (11.6)	10 (20.8)
Nosocomial acquisition (*n*, %)	167 (76.6)	38 (90.5)	20 (83.3)	50 (83.3)	25 (58.1)	34 (69.4)
Days since transplantation (median, IQR)	39 (12–133)	32 (13–143)	32 (11–94)	35 (15–92)	68 (11–132)	54 (11–205)
Days since hospital stay (median, IQR)	10 (0–28)	13 (0–27)	11 (2–31)	16 (3–35)	5 (0–14)	4 (0–12)

*Prior antibiotic therapy was defined as the administration of any systemic antibiotic in the preceding month.

†Septic shock was defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation.

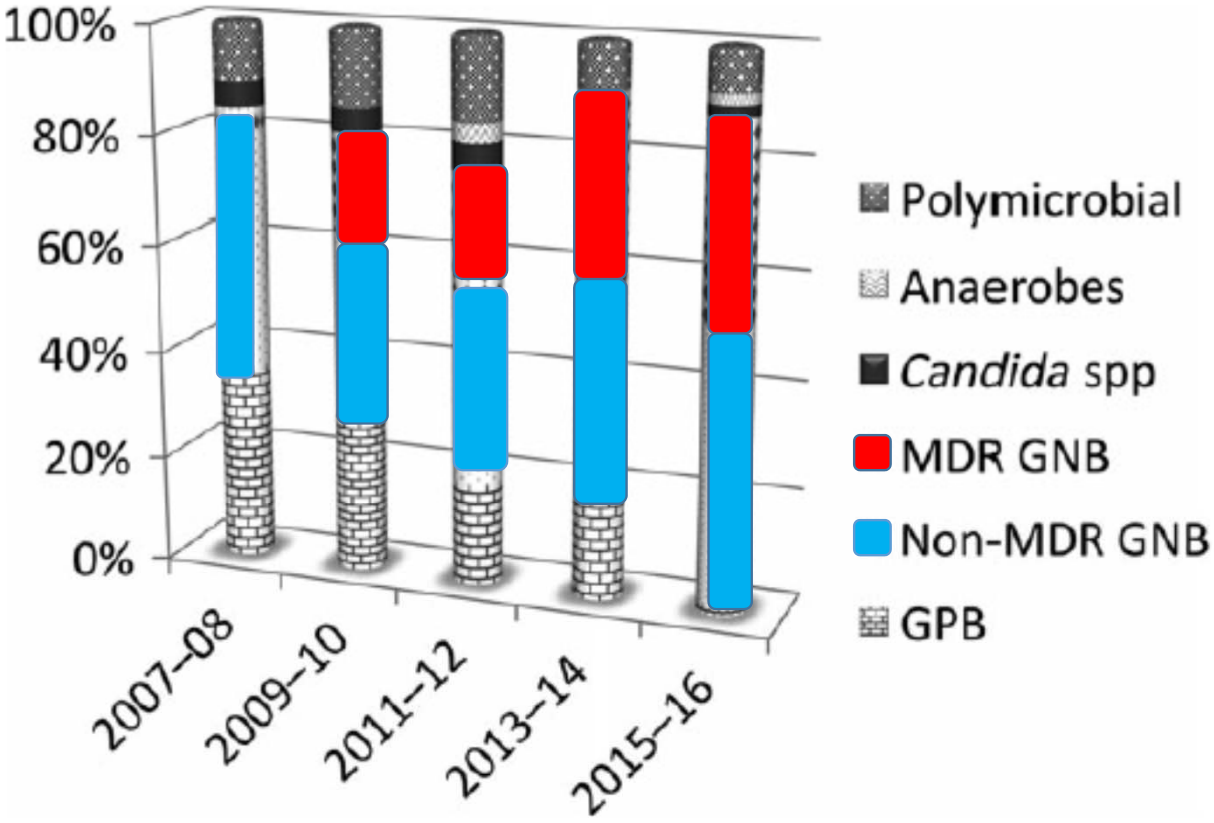

Figure 1 Changes in the aetiology of bloodstream infection by 2-year periods.

Steady increase in Gram negative bacilli (GNB) BSI (54% -93%, p<0.001), mainly due to *Pseudomonas aeruginosa* (2.4%-20%) and *Enterobacteriaceae* strain. *Klebsiella pneumoniae* (with increase from 7% to 26.5%) was the causative agent of almost a quarter of the episodes of BSI in the last 2 year period.

Transpl Int. 2017 Sep;30(9):903-913. doi: 10.1111/tri.12984

Acquisition of Carbapenemase-Producing *Enterobacteriaceae* in Solid Organ Transplantation Recipients

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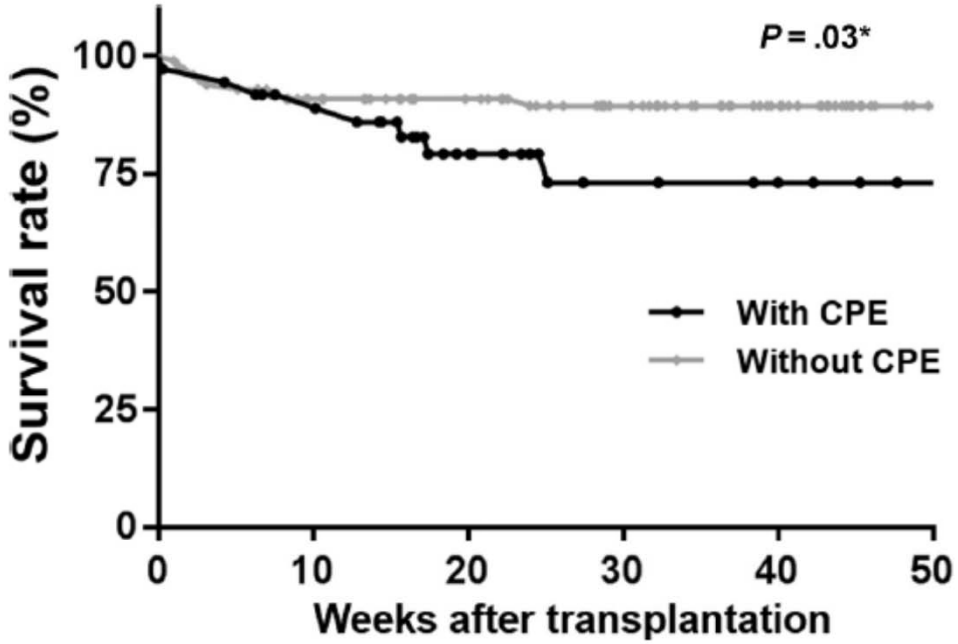
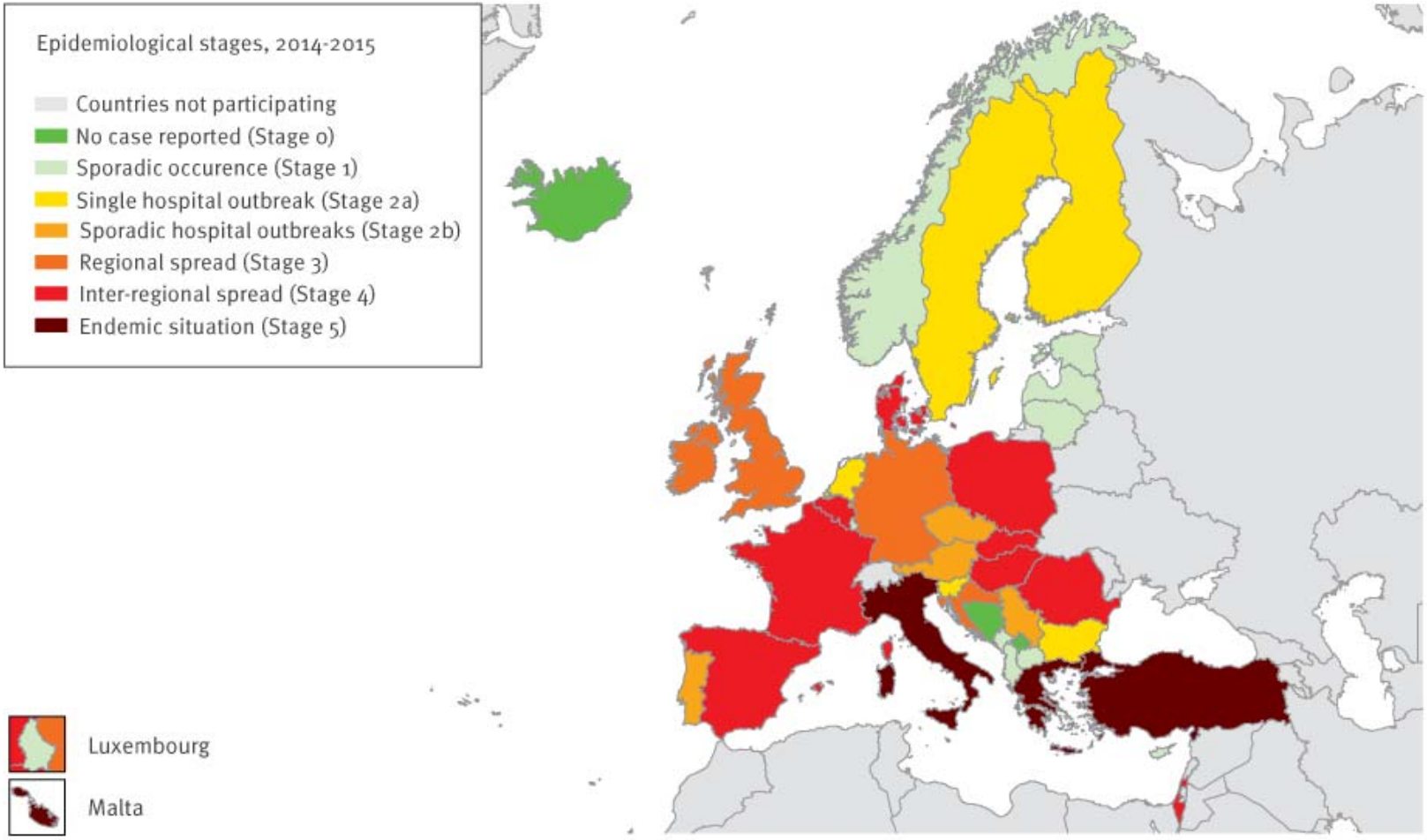
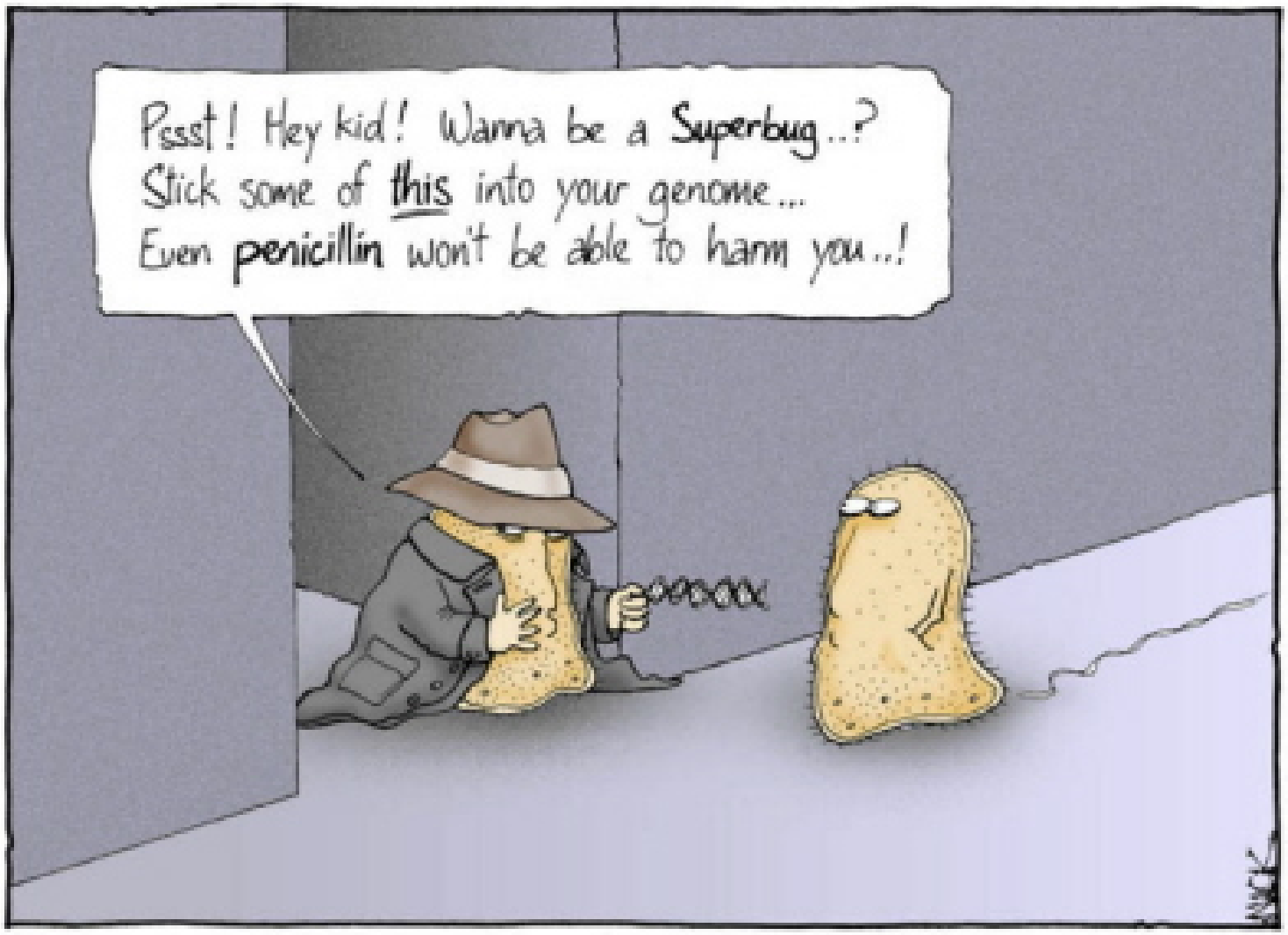


Fig 2. Kaplan–Meier survival curve for solid organ transplantation recipients with or without acquisition of carbapenemase-producing *Enterobacteriaceae*. *Log-rank test. Abbreviations: CPE, carbapenemase-producing *Enterobacteriaceae*.

Carbapenemase-producing Enterobacteriaceae in Europe:
assessment by national experts from 38 countries, May 2015



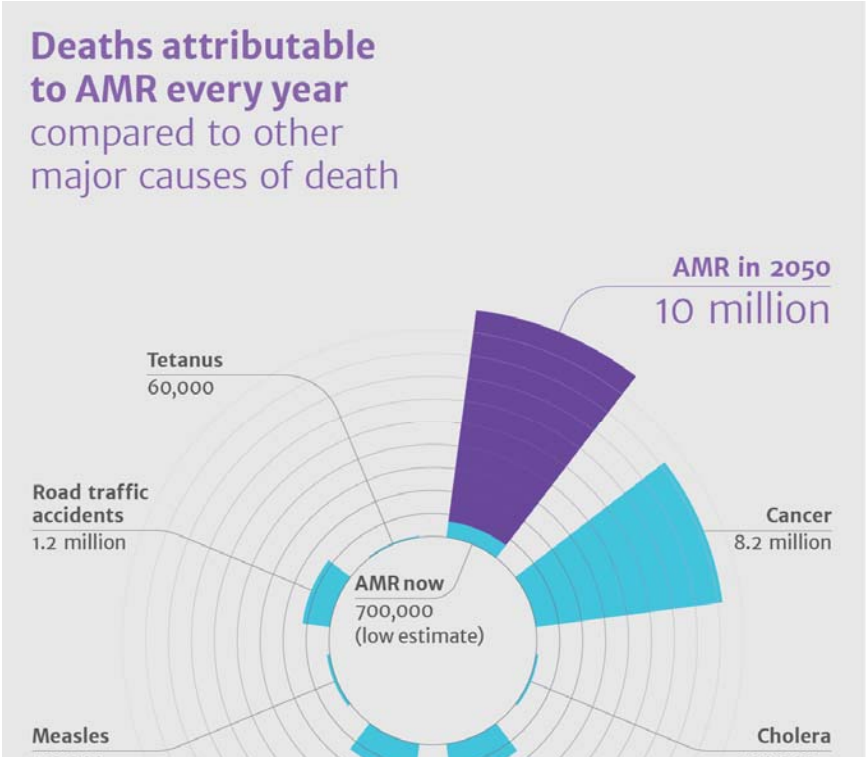
Eurosurveillance 2015



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Review on Antimicrobial Resistance

Tackling drug-resistant infections globally

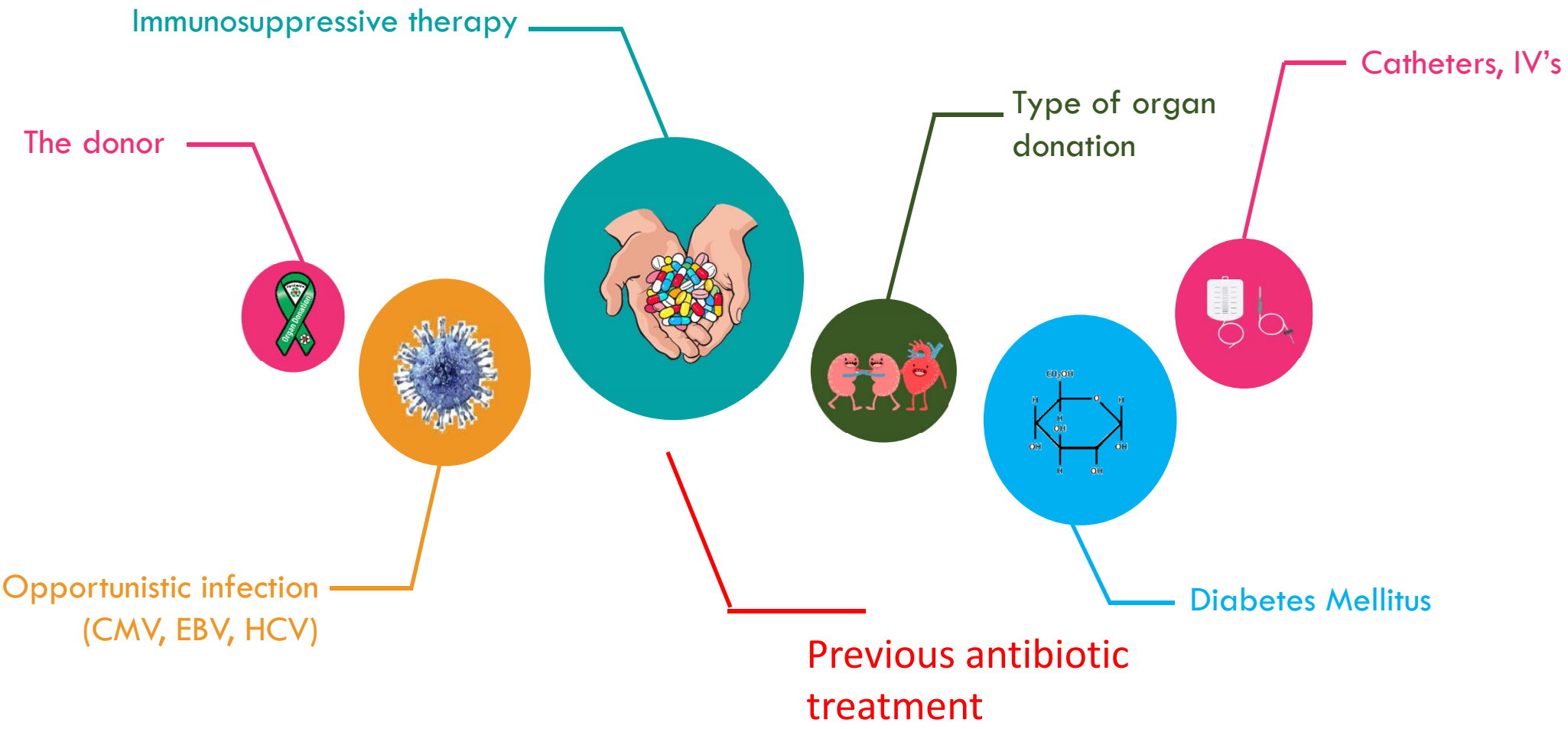


The secondary health effects of AMR: a return to the *dark age* of medicine?

Sources

Diabetes	www.who.int/mediacentre/factsheets/fs312/en/	Measles	www.sciencedirect.com/science/article/pii/S0140673612617280
Cancer	www.who.int/mediacentre/factsheets/fs297/en/	Road traffic accidents	www.who.int/mediacentre/factsheets/fs358/en/
Cholera	www.who.int/mediacentre/factsheets/fs107/en/	Tetanus	www.sciencedirect.com/science/article/pii/S0140673612617280
Diarrhoeal disease	www.sciencedirect.com/science/article/pii/S0140673612617280		

Risk factors in SOT



RESEARCH ARTICLE

Incidence of Carbapenem-Resistant Gram Negatives in Italian Transplant Recipients: A Nationwide Surveillance Study

Simone Lanini[1]*, Alessandro Nanni Costa[2], Vincenzo Puro[1], Francesco Procaccio[2], Paolo Antonio Grossi[3], Francesca Vespasiano[2], Andrea Ricci[2], Sergio Vesconi[4], Michael G. Ison[5], Yehuda Carmeli[6], Giuseppe Ippolito[1], Donor-Recipient Infection (DRIn) Collaborative Study Group[¶]

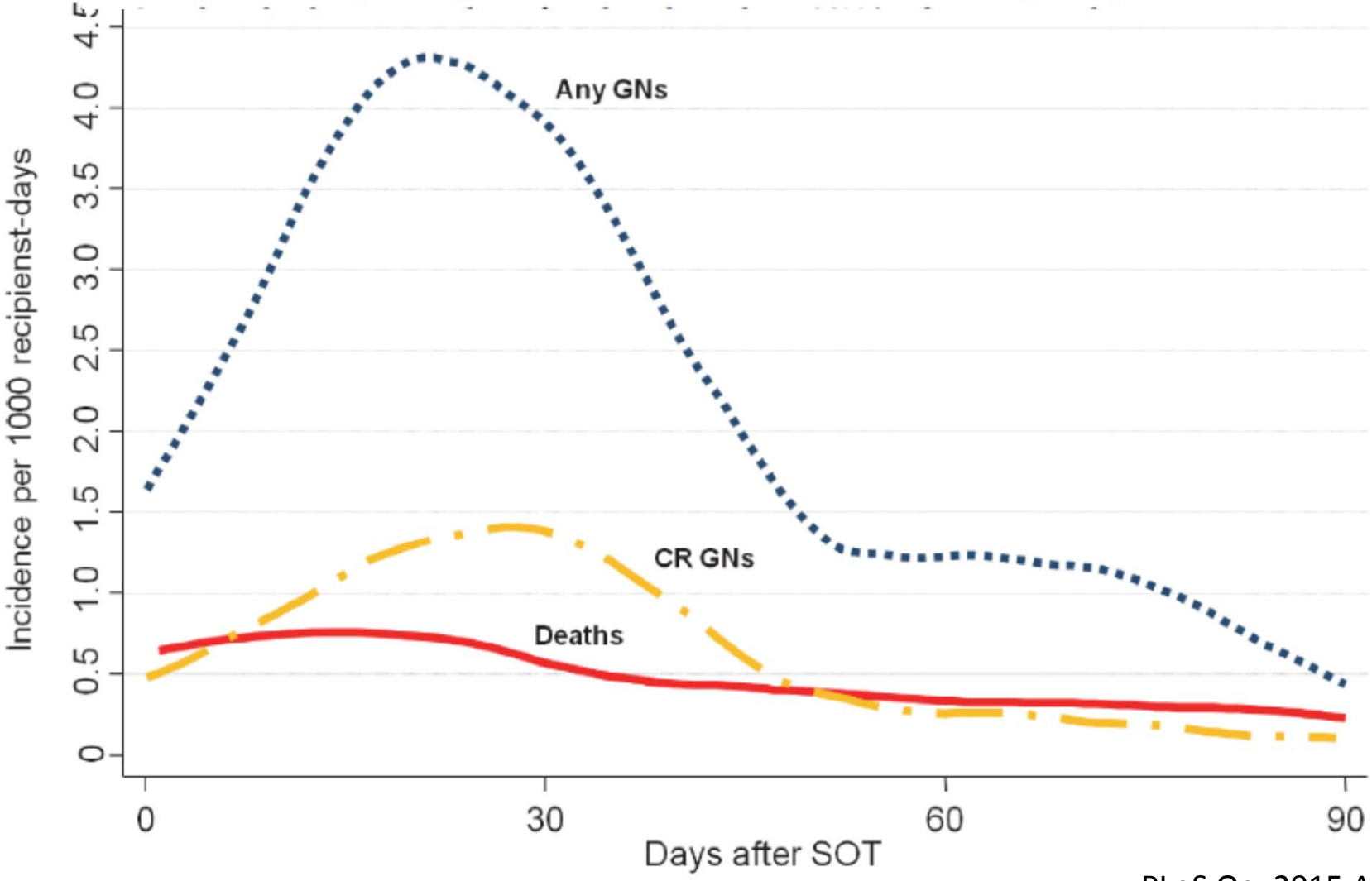
16.5% TESTED POSITIVE TO GNB
AT LEAST ONCE
OF THESE, 26% WERE CR GNB

Table 1. Events of infection according the etiology (left columns) and the anatomical site (right columns).

Bacteria	Carbapenem phenotype			*Anatomical site of isolation* [A]			
	Susceptible	*Resistant*	*All*	*Blood*	*R. tract*	*U. tract*	*other* [B]
Klebsiella spp.	27	26 (49.1%)	53	9	7	32	12
A. baumannii	5	4 (44.4%)	9	2	5	0	2
P. aeruginosa	20	9 (31.0%)	29	3	15	7	7
E. coli	52	1 (1.9%)	53	5	7	48	6
Other enterobacteriacea	18	2(10.0%)	20	2	3	12	6
Other GN	14	7(33.3%)	21	1	8	7	3
Total	136	49(26.5%)	185	22	45	106	36

PLoS One. 2015 Apr 2;10(4):e0123706.

The median time to the first GNs clinical isolate was 26 days (IQR 16–33; Table 2). As reported in Fig 2, GNs occurred most frequently in the early post-SOT. Incidence rates were 4.33, 1.67 and 1.14 per 1,000 recipient-days at 0–30, 31–60, and 61–90 days after SOT, respectively.



PLoS Oe. 2015 Apr 2;10(4):e0123706.

Higher incidence of CR-GNs clinical isolates:

- lung recipients,
- admitted to hospital for more than 48h before SOT and
- longer hospital stay after SOT.

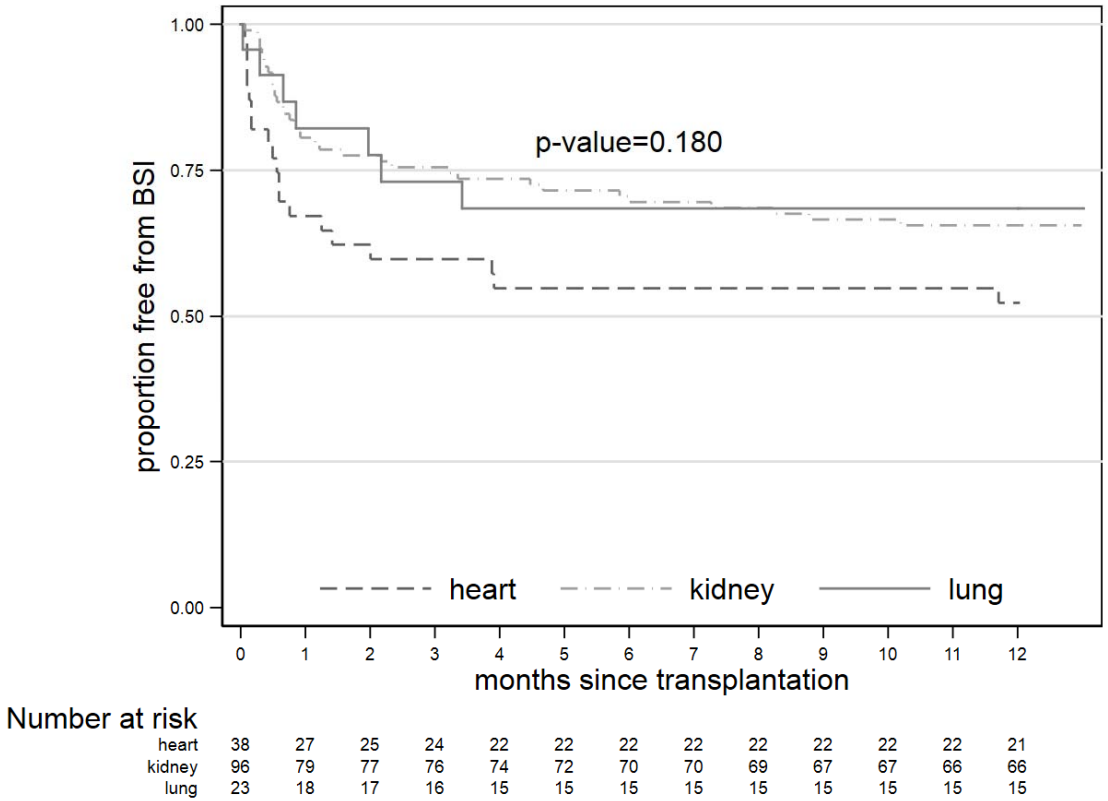
Mortality was more than 10 times higher in recipients who had culture(s) positive to CR-GNs after SOT than in those who did not.

No evidence was found that having received organ(s) from a donor who tested positive to GNs or CR-GNs the donation day was associated to an increased risk of death

Donation day test	no GN	649	32	56,740	0.56(0.40–0.80)	base	-	base	-
	CS GN	205	9	17,707	0.51(0.26–0.98)	0.88(0.41–1.87)	0.734	1.00(0.46–2.19)	0.995
	CR GN	33	3	2,813	1.07(0.34–3.31)	1.89(0.57–6.33)	0.301	1.37(0.39–4.81)	0.627

PLoS One. 2015 Apr 2;10(4):e0123706.

Bloodstream infections within the first year after solid organ transplant (Pavia experience)



Microbiological Data

72.7%

Gram- negatives

K. pneumoniae:

- *ESBL*: 30.4%
- *KPC*: 10.8%

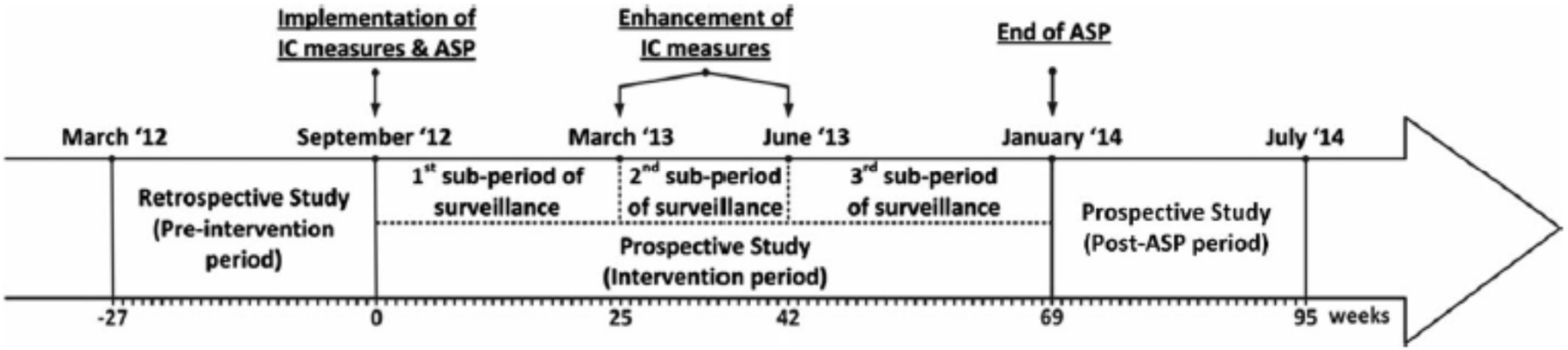
22.7%

Gram- positives

- *E. faecalis*: 50%
- MRSA*:* 14.3%

Rectal carriers show an increased risk of developping a BSI in the follow up

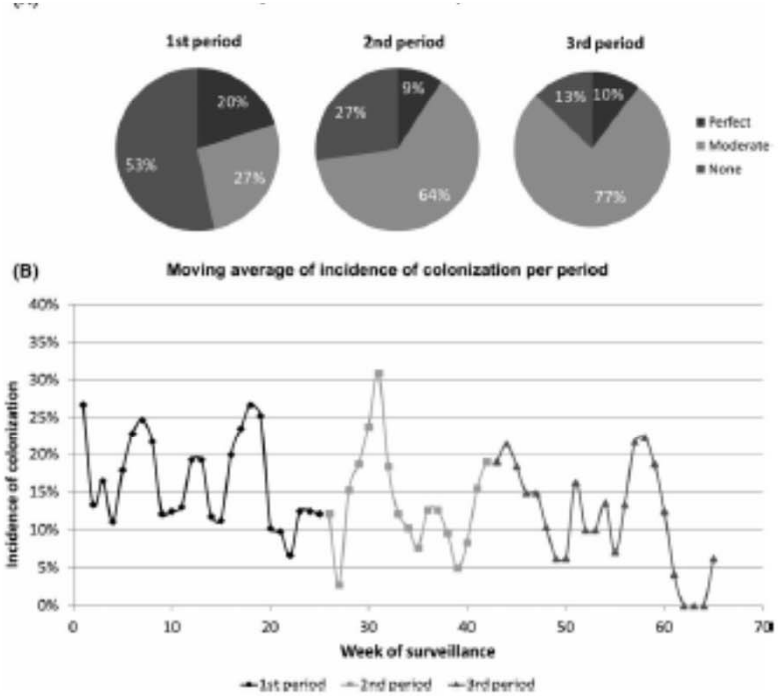
Epidemiological surveillance of multidrug-resistant gram-negative bacteria in a solid organ transplantation department

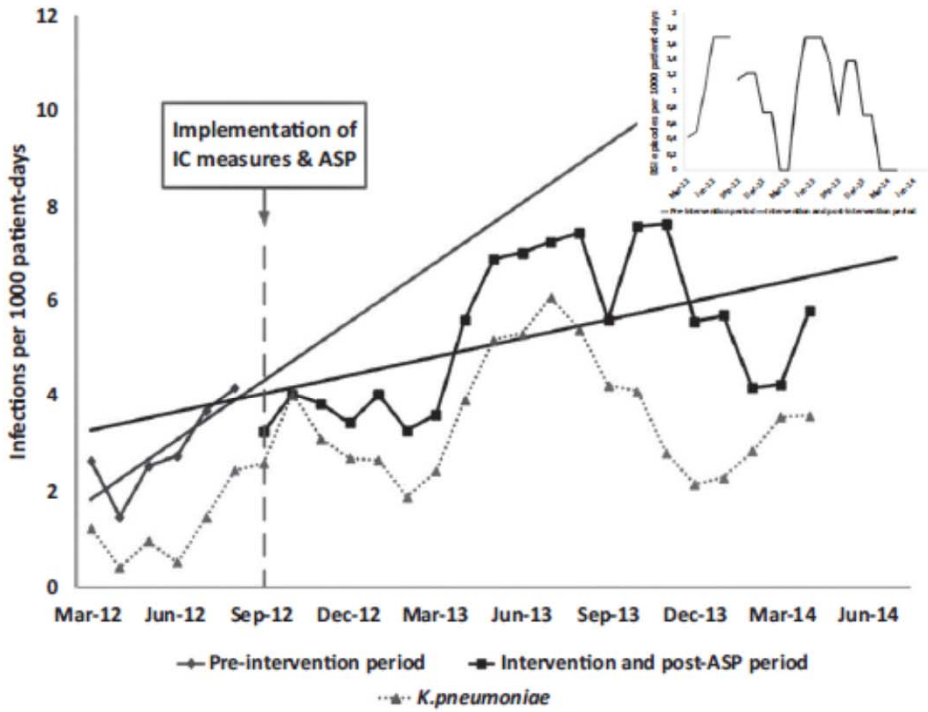


Rectal suveillance swabs (weekly)
Contact precautions
Enviromnental cleaning
Education
Hand hygiene

Transpl Infect Dis. 2017;19:e12686.
https://doi.org/10.1111/tid.12686

Epidemiological surveillance of multidrug-resistant gram-negative bacteria in a solid organ transplantation department





The time between detection of colonization and infection was 10 ±9.6 days.

Transpl Infect Dis. 2017;19:e12686.
https://doi.org/10.1111/tid.12686

Risk factors for carbapenem-resistant *Klebsiella pneumoniae* bloodstream infection among rectal carriers: a prospective observational multicentre study

M. Giannella[1], E. M. Trecarichi[2], F. G. De Rosa[3], V. Del Bono[4], M. Bassetti[5], R. E. Lewis[1], A. R. Losito[2], S. Corcione[3], C. Saffioti[4], M. Bartoletti[1], G. Maiuro[2], C. S. Cardellino[3], S. Tedeschi[1], R. Cauda[2], C. Viscoli[4], P. Viale[1] and M. Tumbarello[2]

TABLE 2. Logistic regression analysis of risk factors for CR-KP BSI development in rectal carriers

	OR (95% CI)	P-value	Risk score point
Admission to ICU	1.65 (1.05–2.59)	0.03	2
Invasive abdominal procedures	1.87 (1.16–3.04)	0.01	3
Chemotherapy/radiation therapy	3.07 (1.78–5.29)	<0.0001	4
Colonization at site besides stool (risk per each additional site)	3.37 (2.56–4.43)	<0.0001	5 per site

ICU, intensive care unit; OR, odds ratio.

Clin Microbiol Infect. 2014 Dec;20(12):1357-62.

Effect of appropriate combination therapy on mortality of patients with bloodstream infections due to carbapenemase-producing Enterobacteriaceae (INCREMENT): a retrospective cohort study

Belén Gutiérrez-Gutiérrez, Elena Salamanca*, Marina de Cueto, Po-Ren Hsueh, Pierluigi Viale, José Ramón Paño-Pardo, Mario Venditti, Mario Tumbarello, George Daikos, Rafael Cantón, Yohei Doi, Felipe Francisco Tuon, Ilias Karaiskos, Elena Pérez-Nadales, Mitchell J Schwaber, Özlem Kurt Azap, Maria Souli, Emmanuel Roilides, Spyros Pournaras, Murat Akova, Federico Pérez, Joaquín Bermejo, Antonio Oliver, Manel Almela, Warren Lowman, Benito Almirante, Robert A Bonomo, Yehuda Carmeli, David L Paterson, Alvaro Pascual, Jesús Rodríguez-Baño, and the REIPI/ESGBIS/INCREMENT Investigators†*

- The score includes
- severe sepsis or shock at presentation (five points),
- a Pitt bacteraemia score of at least 6 (four points),
- a Charlson comorbidity index score of at least 2 (three points),
- a source of BSI other than urinary or biliary tract (three points)

Risks of Infection and Mortality Among Patients Colonized With *Klebsiella pneumoniae* Carbapenemase–Producing *K. pneumoniae*: Validation of Scores and Proposal for Management

Angela Cano,[1,a,b] Belén Gutiérrez-Gutiérrez,[2,a,b] Isabel Machuca,[1] Irene Gracia-Ahufinger,[3,b] Elena Pérez-Nadales,[4,b] Manuel Causse,[3,b] Juan José Castón,[1,b] Julia Guzman-Puche,[3] Julian Torre-Giménez,[1] Lara Kindelán,[1] Luis Martínez-Martinez,[3,b] Jesús Rodriguez-Baño,[2,b] and Julian Torre-Cisneros[1,b]

The risk of developing an active infection in colonized patients is controversial, especially regarding severe infections such as bacteremia.

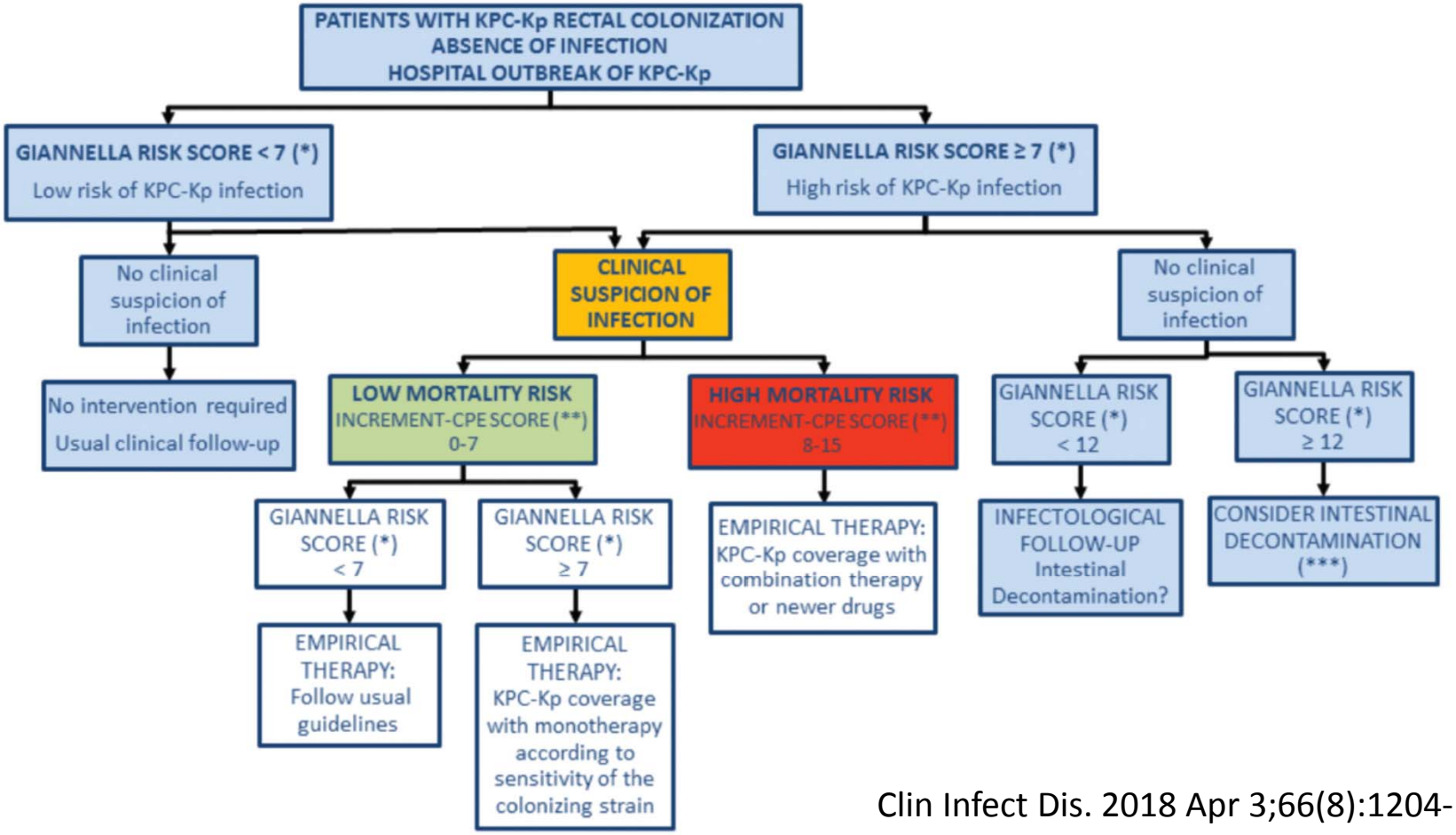
Empiric treatment is frequently inadequate, and adequate treatment is initiated after the susceptibility test is available.

This delay in initiating appropriate treatment may have a negative impact on mortality.

Table 3. Characteristics of 94 Patients Colonized With *Klebsiella pneumoniae* Carbapenemase–Producing *K. pneumoniae* in the Giannella Score <7 and ≥7 Groups

Characteristic	GRS 0–6 (n = 48)	GRS ≥7 (n = 46)	*P* Value
Age, y, median (IQR)	66.5 (56.5–76.2)	60 (49.0–67.0)	.007[a]
Male sex	16 (33.3)	19 (41.3)	.42
Surgery in the previous 3 mo	17 (35.4)	32 (69.6)	<.001
Antimicrobial therapy in the previous month (for ≥2 d)	36 (75.0)	35 (76.1)	.90
Clinical unit before infection			<.001
Medical	24 (50.0)	6 (13.0)	
Surgical	11 (22.9)	12 (26.1)	
Intensive care unit	13 (27.1)	28 (60.9)	
Neutropenia	6 (12.5)	11 (23.9)	.15
Chronic kidney disease	13 (27.1)	8 (17.4)	.26
Solid organ transplantation	10 (20.8)	4 (8.7)	.10
Charlson comorbidity index, median (IQR)	4 (3–6)	2.5 (1–4)	.01[a]
Immunosuppression	26 (54.2)	23 (50.0)	.69
No infection	16 (33.3)	2 (4.3)	<.001
Non–KPC-Kp infection	29 (60.4)	5 (10.9)	<.001
KPC-Kp infection	3 (6.2)	39 (84.8)	<.001
Non–KPC-Kp bacteremia	4 (8.3)	3 (6.5)	.74[b]
KPC-Kp bacteremia	1 (2.1)	21 (45.7)	<.001
ICS, median (IQR)[c]	3 (3–3)	10 (6–11)	<.001[a]
High risk of mortality according to ICS	1 (2.1)	27 (58.7)	<.001[a]
Died during follow-up	13 (27.1)	24 (52.2)	.01

Clin Infect Dis. 2018 Apr 3;66(8):1204-1210.



Clin Infect Dis. 2018 Apr 3;66(8):1204-1210.

Management of multidrug resistant Gram-negative bacilli infections in solid organ transplant recipients: SET/GESITRA-SEIMC/REIPI recommendations☆

Can a patient colonized with CPE be accepted for transplantation?

There are no data to contraindicate the transplantation of patients colonized with CPE. Nonetheless these recipients have an increased risk of graft infection and death

Rectal swabs samples should be obtained at transplant as a screening measure for CPE intestinal colonization. Repeated surveillance swabs should be performed based on the local epidemiological setting

CPE colonization is not necessarily to be considered a contraindication for organ donation unless colonization regards the organ to be transplanted


Antimicrobial Stewardship Program
Stopping Bugs
Saving Drugs


Thank you for the attention