Top Ten Infecciones en adultos

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Disclosures

Speaker, Scientific advisory:

Astellas, MSD, Angellini, Pfizer

Research grants:

Instituto de Salud Carlos III, Ministry of Economy, Spain

COMBACTE-MAGNET, Innovative Medicines Initiative, EU

- CAP (1)
- Listeriosis (1)
- Necrotizing fasciitis (1)
- Timing of surgical prophylaxis (1)
- CP Enterobacteriaceae (1)
- *Clostridium difficile* (1)
- Room disinfection (1)
- Emergent pathogens (2)
- Micafungin and ICU-acquired sepsis (1)

Review period: May 2016 – May 2017

JAMA 2, LANCET 4, CID 3, NEJM 1

Original Investigation | LESS IS MORE

Duration of Antibiotic Treatment in Community-Acquired Pneumonia

A Multicenter Randomized Clinical Trial

Ane Uranga, MD; Pedro P. España, MD; Amaia Bilbao, MSc, PhD; Jose María Quintana, MD, PhD; Ignacio Arriaga, MD; Maider Intxausti, MD; Jose Luis Lobo, MD, PhD; Laura Tomás, MD; Jesus Camino, MD; Juan Nuñez, MD; Alberto Capelastegui, MD, PhD

Uranga A. JAMA Intern Med 2016; 176: 1257-1265

Objective: To validate IDSA/ATS guidelines for duration of antibiotic treatment in hospitalized patients with CAP.

Design and Setting: Multicenter, noninferiority, RCT. Four teaching hospitals in Spain (January 1, 2012 – August 31, 2013).

Intervention: A total of 312 patients were randomized at day 5 to an intervention (ATBs for a minimum of 5 days) or control group (duration of ATBs determined by physicians).

Primary outcome: Clinical success rate at days 10 and 30 after admission and CAP-related symptoms at days 5 and 10 (18-item CAP symptom questionnaire score range, 0-90).

Uranga A. JAMA Intern Med 2016

Duration of antibiotic treatment in CAP
A multicenter randomized clinical trial

Outcome Intent-to-treat analysis	Control n= 150	Intervention n= 162	P value
Clinical success, n (%)			
At day 10	71 (49)	90 (56)	0.18
At day 30	132 (89)	147 (92)	0.33
CAP symptom questionnaire score, mean (SD)			
At day 5	24.7 (11)	27.2 (12)	0.10
At day 10	18.6 (9.0)	17.9 (8)	0.69

Uranga A. JAMA Intern Med 2016

The new antibiotic mantra "Shorter is Better"

Infections for which short-course therapy has been shown to be equivalent in efficacy to longer therapy

	Treatment, Days	
Disease	**Short**	**Long**
Community-acquired pneumonia[1-3]	3-5	7-10
Nosocomial pneumonia[6,7]	≤8	10-15
Pyelonephritis[10]	5-7	10-14
Intraabdominal infection[11]	4	10
Acute exacerbation of chronic bronchitis and COPD[12]	≤5	≥7
Acute bacterial sinusitis[13]	5	10
Cellulitis[14]	5-6	10
Chronic osteomyelitis[15]	42	84

Spellberg B. JAMA Intern Med 2016

Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study

Caroline Charlier, Élodie Perrodeau, Alexandre Leclercq, Benoît Cazenave, Benoît Pilmis, Benoît Henry, Amanda Lopes, Mylène M Maury, Alexandra Moura, François Goffinet, Hélène Bracq Dieye, Pierre Thouvenot, Marie-Noëlle Ungeheuer, Mathieu Tourdjman, Véronique Goulet, Henriette de Valk, Olivier Lortholary, Philippe Ravaud, Marc Lecuit, on behalf of the MONALISA study group

Charlier C. Lancet Infect Dis 2017; 17: 510-519

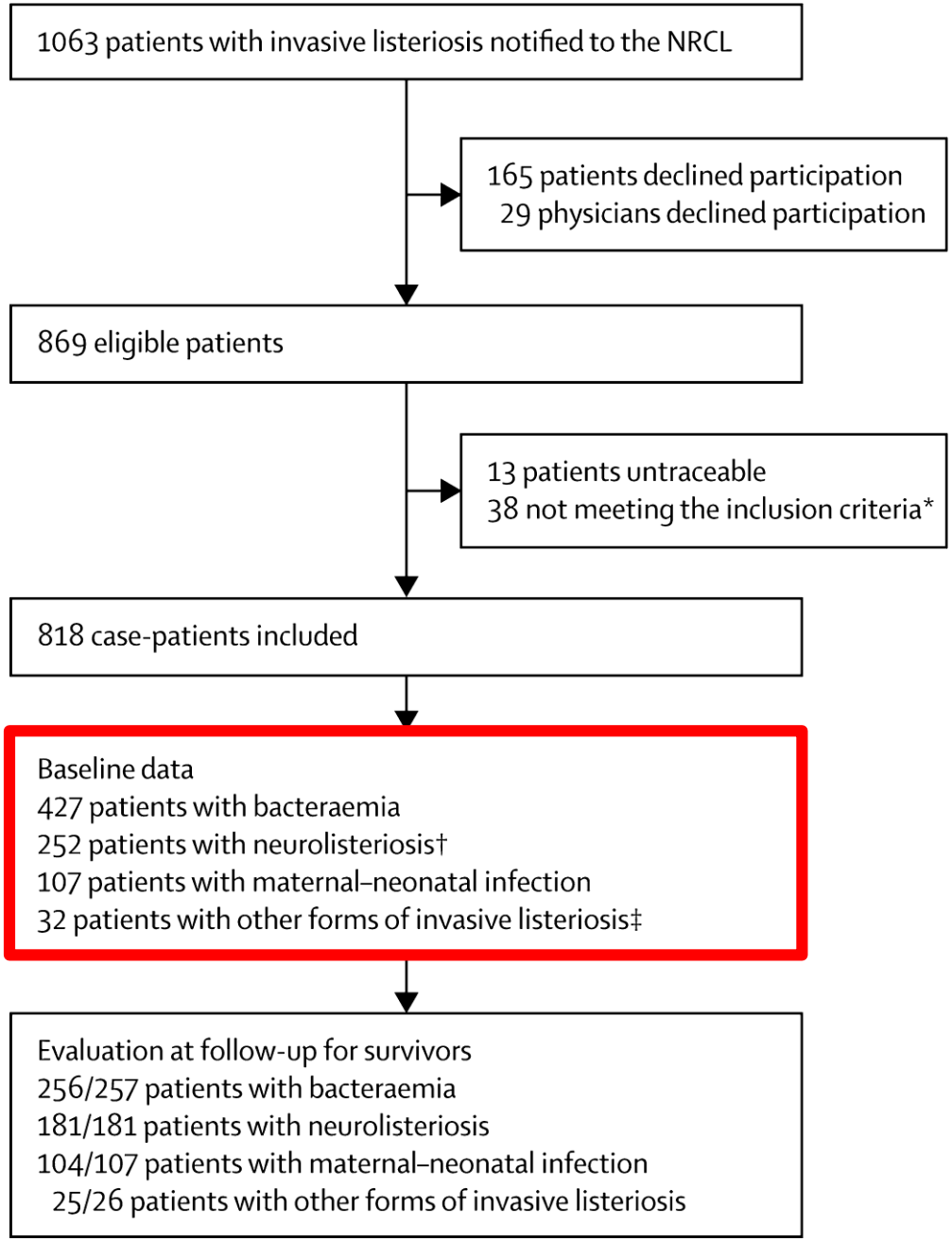
Objective: To characterize clinical features and prognostic factors of listeriosis.

Design and Setting: Nationwide prospective observational study in France (MONALISA). Microbiologically proven cases declared to the National Center for *Listeria* (Nov 2009 – July 2013).

Patients: 818 cases from 372 centers.

Measurements: Clinical features, characterization of isolates, and determination of predictors of 3-month mortality or persisting impairment using logistic regression.

Charlier C. Lancet Infect Dis 2017


1063 patients with invasive listeriosis notified to the NRCL
165 patients declined participation
29 physicians declined participation
869 eligible patients
13 patients untraceable
38 not meeting the inclusion criteria*
818 case-patients included
Baseline data
427 patients with bacteraemia
252 patients with neurolisteriosis†
107 patients with maternal–neonatal infection
32 patients with other forms of invasive listeriosis‡
Evaluation at follow-up for survivors
256/257 patients with bacteraemia
181/181 patients with neurolisteriosis
104/107 patients with maternal–neonatal infection
25/26 patients with other forms of invasive listeriosis

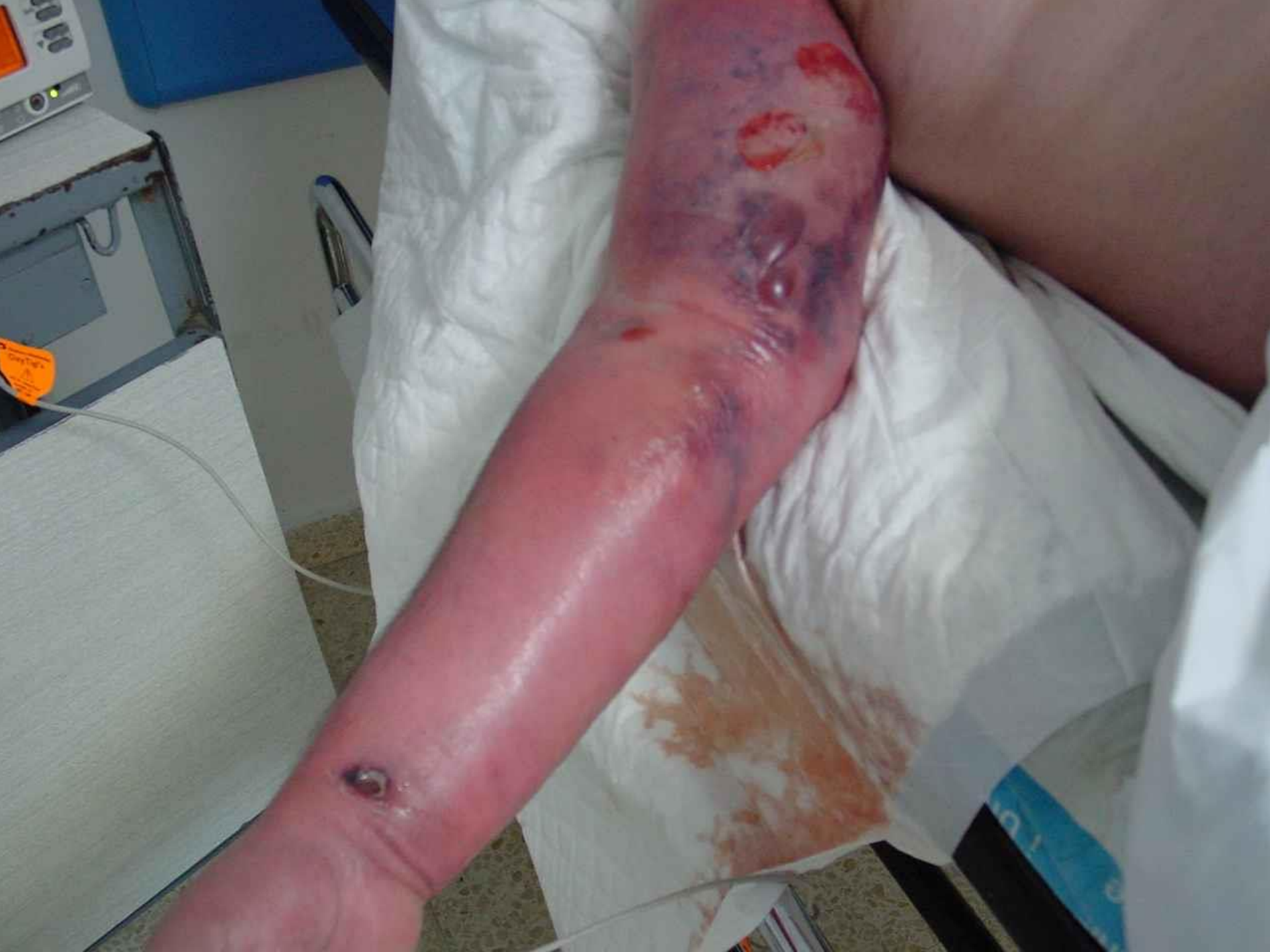
Neonatal Bacteremia Neurolisteriosis

Outcomes			
Intensive care unit management	2/107 (2%)	89/427 (21%)	152/252 (60%)
Median hospital stay (days)	6 (4–11)	15 (7–24)	23 (15–33)
Mechanical ventilation	0	43/427 (10%)	83/252 (33%)
Multi-organ failure	0	75/427 (18%)	49/252 (19%)
Aggravation of any pre-existing organ dysfunction	0	182/427 (43%)	58/252 (23%)
3-month mortality	0	194/427 (45%)	75/252 (30%)
Median interval from diagnosis to 3-month mortality (days)	..	10 (3–23)	14 (5–30)
3-month in-hospital mortality§	0	170/427 (40%)	69/252 (27%)
Median interval from diagnosis to 3-month in-hospital mortality (days)	..	7 (2–19)	11 (5–24)
Post-hospitalisation follow-up	104/107 (97%)	256/257 (99%)	181/181 (100%)
Median post-hospitalisation follow-up (months)	5 (3–9)	5 (3–11)	5 (3–13)
3-month post-hospitalisation mortality	..	24/257 (9%)	6/181 (3%)
Median interval from diagnosis to 3-month post-hospitalisation mortality (days)	..	54 (24–68)	62 (58–68)
New infection during post-hospitalisation period¶	0	19/255 (7%)	7/181 (4%)
Recurrence of listeriosis‖	0	2/255 (1%)	1/179 (1%)

Multivariate logistic regression analyses

	Odds ratio (95% CI)*	p value
3-month mortality for bacteraemia and neurolisteriosis (n=679)†		
Female sex	1·60 (1·04–2·46)	0·034
Age (years)	1·03 (1·01–1·05)	0·001
At least one immunosuppressing comorbidity	0·43 (0·15–1·22)	0·113
Ongoing organ neoplasia	5·19 (3·01–8·95)	<0·0001
Recent weight loss >5 kg	1·74 (1·05–2·87)	0·031
Intensive care unit management	1·48 (0·90–2·41)	0·120
Multi-organ failure	7·98 (4·32–14·72)	<0·0001
Aggravation of any pre-existing organ dysfunction	4·35 (2·79–6·81)	<0·0001
Diarrhoea	0·58 (0·33–1·01)	0·053
Influenza-like symptoms	0·47 (0·27–0·80)	0·006
Monocytopenia <200 cells per µL	3·70 (1·82–7·49)	0·0003
Neutrophils (cells per µL)	1·05 (1·01–1·08)	0·006
Co-trimoxazole therapy	0·49 (0·26–0·92)	0·027
Aminoglycoside therapy	0·60 (0·38–0·94)	0·024
Active beta-lactam therapy‡	0·10 (0·04–0·26)	<0·0001

3-month mortality for neurolisteriosis (n=252)		
Female sex	2·68 (1·24–5·83)	0·013
Age (years)	1·35 (0·99–1·85)	0·058
Ongoing organ neoplasia	4·58 (1·53–13·73)	0·007
Recent major weight loss	2·65 (1·08–6·55)	0·034
Multi-organ failure	3·08 (1·25–7·58)	0·014
Aggravation of any pre-existing organ dysfunction	2·75 (1·23–6·16)	0·014
Influenza-like symptoms	0·47 (0·20–1·12)	0·087
Mechanical ventilation	2·89 (1·31–6·37)	0·009
Monocytopenia <200 cells per µL	3·57 (1·24–10·23)	0·018
Positive blood cultures	3·67 (1·60–8·40)	0·002
Protein concentration in the CSF	1·18 (0·99–1·41)	0·062
Adjunctive dexamethasone for meningitis	4·58 (1·50–13·98)	0·008
Neurological impairment in neurolisteriosis (n=181)§		
Age (years)	0·98 (0·96–1·00)	0·048
Encephalitis symptoms¶	21·65 (2·58–181·59)	0·005
Number of neurological symptoms	1·37 (1·11–1·69)	0·004
Glasgow Coma Scale score	1·08 (0·98–1·20)	0·102



Impact of Intravenous Immunoglobulin on Survival in Necrotizing Fasciitis With Vasopressor-Dependent Shock: A Propensity Score–Matched Analysis From 130 US Hospitals

Sameer S. Kadri,[1,2] Bruce J. Swihart,[3] Stephanie L. Bonne,[4] Samuel F. Hohmann,[5,6] Laura V. Hennessy,[7] Peter Louras,[7] Heather L. Evans,[7] Chanu Rhee,[8] Anthony F. Suffredini,[1] David C. Hooper,[2] Dean A. Follmann,[3] Eileen M. Bulger,[7] and Robert L. Danner[1]

Kadri SS. Clin Infect Dis 2017; 64: 877 - 885

Background: IVIG is sometimes administered for presumptive TSS, but its frequency of use and efficacy are unclear.

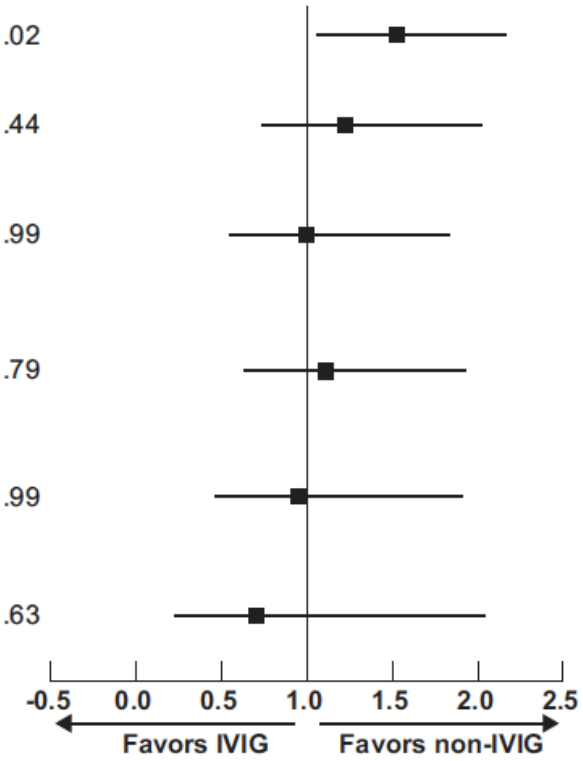
Methods: Adult patients with NF and vasopressor-dependent shock undergoing surgical debridement (2010-2014) were identified at 130 US hospitals. IVIG cases were propensity-matched and risk-adjusted.

Outcome: The primary outcome was in-hospital mortality and the secondary outcome was median LOS.

Kadri SS.Clin inefct Dis 2017

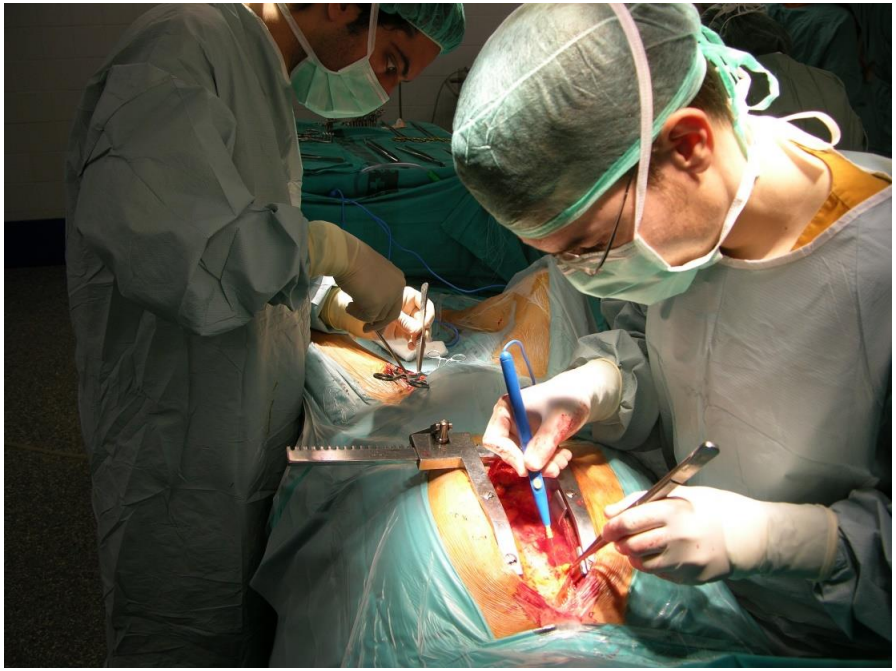
Of 4127 cases of debrided NF with shock , 164 (4%) received IVIG

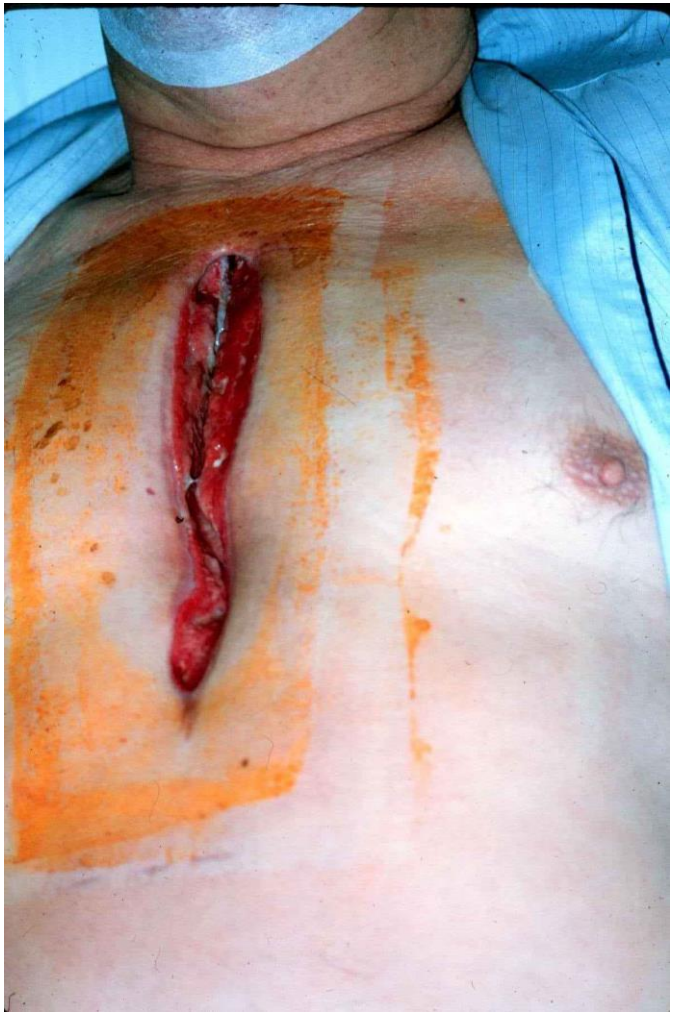
Comparison of NF shock cases	IVIG Cases No.	IVIG Cases Mortality (%)	Non-IVIG Cases No.	Non-IVIG Cases Mortality (%)	*P* Value
All cases; unadjusted	164	26.8	3963	19.4	.02
Matched pairs, unadjusted	161	27.3	161	23.6	.44
Matched pairs adjusted by multivariable logistic regression*	161	27.3	161	23.6	.99
Matched pairs, treated with clindamycin†	153	26.3	153	25	.79
Matched pairs receiving IVIG within 2 days†	90	28.9	90	30	.99
Matched pairs coded for TSS, GAS, and/or SA†	56	16.1	56	21.4	.63



In-hospital mortality did not differ between matched IVIG and non-IVIG groups (27.3% vs 23.6%; adjusted OR, 1.00; 95% CI, 0.55 – 1.83)

Median LOS was similar between groups (26 vs 26; p= 0.84)





Timing of surgical antimicrobial prophylaxis: a phase 3 randomised controlled trial

Walter P Weber, Edin Mujagic*, Marcel Zwahlen, Marcel Bundi, Henry Hoffmann, Savas D Soysal, Marko Kraljević, Tarik Delko, Marco von Strauss, Lukas Iselin, Richard X Sousa Da Silva, Jasmin Zeindler, Rachel Rosenthal, Heidi Misteli, Christoph Kindler, Peter Müller, Ramon Saccilotto, Andrea Kopp Lugli, Mark Kaufmann, Lorenz Gürke, Daniel Oertli, Evelin Bucheli-Laffer, Julia Landin, Andreas F Widmer, Christoph A Fux, Walter R Marti*

Weber WP. Lancet Infect Dis 2017; 17: 605 – 614.

Background: The precise optimum timing for the administration of SAP for the prevention of SSI is unknown.

Design and Setting: Phase 3, randomized, controlled superiority trial. General surgery adult inpatients at two Swiss hospitals (2013 - 2015).

Intervention: 5580 pts were randomly assigned to receive SAP early or late; 1.5 g IV cefuroxime (plus 500 mg metronidazole in colorectal surgery).

Primary outcome: SSI within 30 days of surgery.

Weber WP. Lancet Infect Dis 2017

Median administration time was 42 min before incision in the early group (IQR 30 – 55) and 16 min before incision in the late group (IQR 10 – 25)

	SAP in anaesthesia room, early administration (n=2296)*	SAP in operating room, late administration (n=2300)*	Odds ratio (95% CI)	p value†
Primary outcome				
Surgical site infection	113 (5%)	121 (5%)	0·93 (0·72–1·21)	0·601
Superficial incisional infection	48 (2%)	55 (2%)	0·87 (0·59–1·29)	0·491
Deep incisional infection	23 (1%)	20 (1%)	1·15 (0·63–2·11)	0·642
Organ space infection	42 (2%)	46 (2%)	0·91 (0·60–1·39)	0·673
Secondary outcomes				
All-cause 30-day mortality	29 (1%)	24 (1%)	1·21 (0·70–2·09)	0·485
Median length of hospital stay, days	5·1 (3–9)	5·0 (3–10)	NA	0·375

Weber WP. Lancet Infect Dis 2017

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†*

Gutierrez-Gutierrez B. Lancet Infect Dis 2017; April 22 (Epub ahead of print)

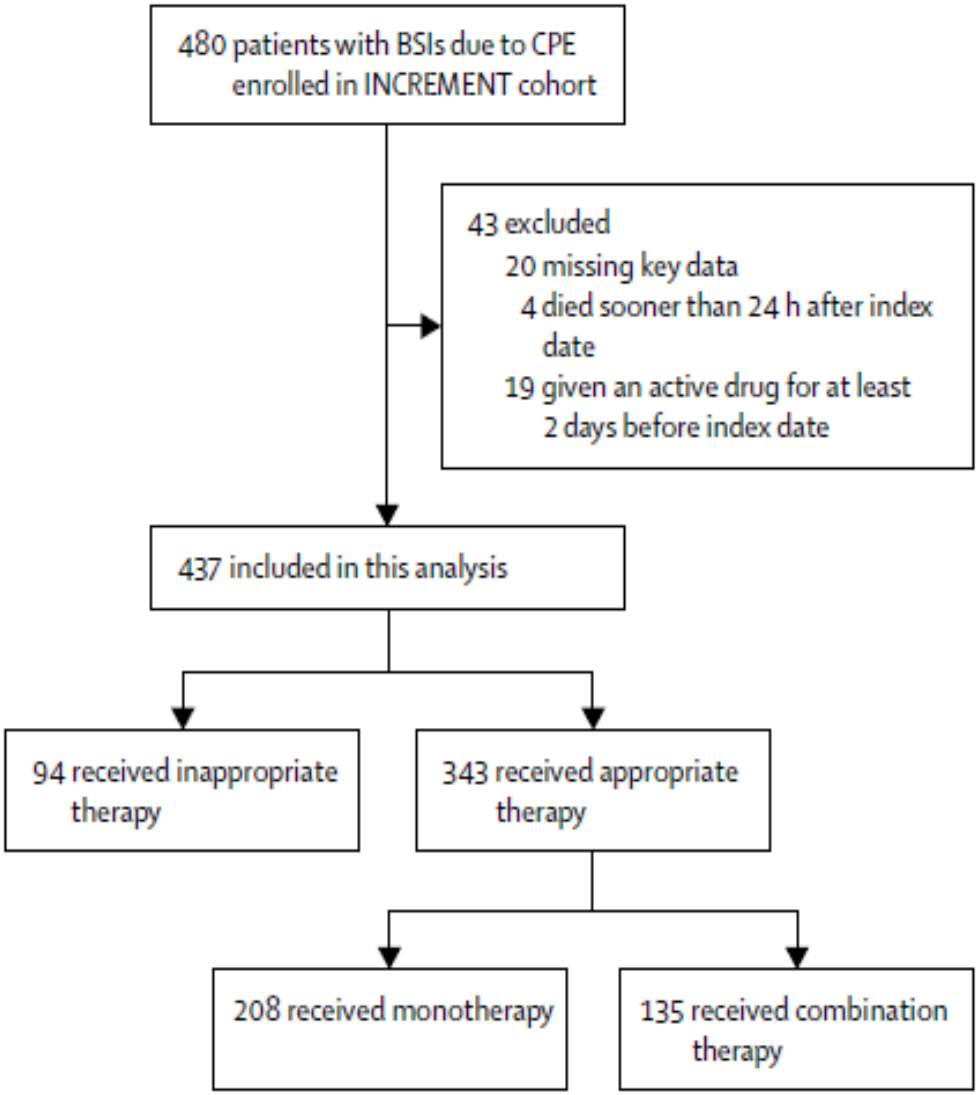
Objective: To investigate the effect of appropriate therapy and appropriate combination therapy on mortality of patients with BSI due to CPE.

Design: Retrospective cohort study of patients with clinically significant monomicrobial BSIs due to CPE from the INCREMENT cohort (01/2004 – 12/2103).

Setting: 26 tertiary hospitals in ten countries.

Primary outcome: 30 day all-cause mortality.

Gutierrez-Gutierrez B. Lancet Infect Dis 2017



	Appropriate therapy (n=343)	Inappropriate therapy (n=94)	p value
Age (years)	66 (55·5–76·0)	66 (50–77)	0·76
Male sex	197 (57%)	58 (62%)	0·46
Enterobacteriaceae	..	..	0·27
Klebsiella pneumoniae	291 (85%)	84 (89%)	..
Other	52 (15%)	10 (11%)	..
Enterobacter cloacae	24 (7%)	4 (4%)	..
Escherichia coli	14 (4%)	3 (3%)	..
Enterobacter aerogenes	10 (3%)	3 (3%)	..
Citrobacter spp	3 (1%)	0	..
Serratia marcescens	1 (<1%)	0	..
Type of carbapenemase	..	..	0·64
OXA-48	57 (17%)	12 (13%)	..
KPC	253 (74%)	76 (81%)	..
Metallo-β-lactamases	33 (10%)	6 (6%)	..
VIM	30 (9%)	6 (6%)	..
Other	3 (1%)	0	..
Nosocomial acquisition	298 (87%)	87 (93%)	0·13
Source other than urinary or biliary tract	272 (79%)	76 (81%)	0·74
ICU admission	123 (36%)	36 (38%)	0·66
Charlson comorbidity index score	2 (1–4)	2 (2–4)	0·74
Pitt bacteraemia score	2 (1–5)	3 (0–5)	0·50
Severe sepsis or septic shock	172 (50%)	57 (61%)	0·07
30 day mortality	132 (38%)	57 (61%)	0·0001

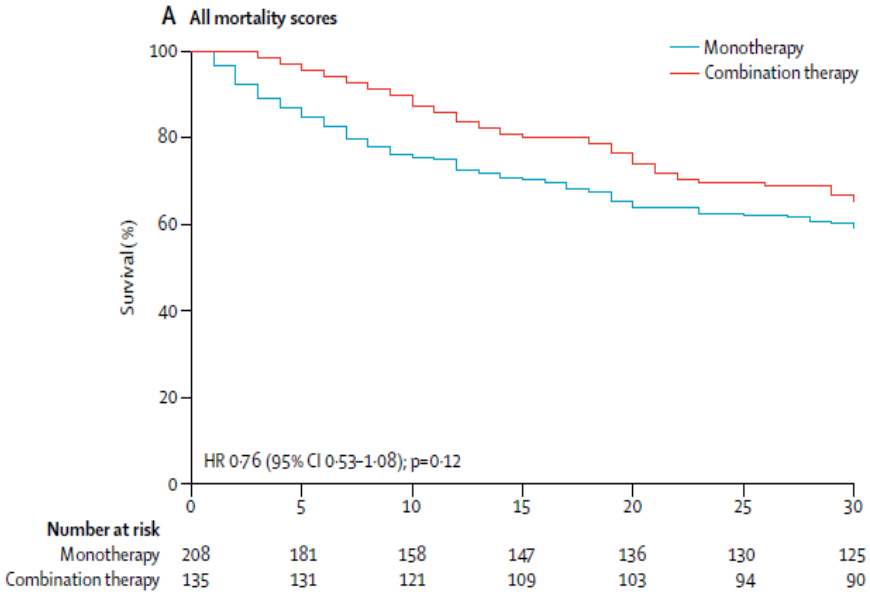
Gutierrez-Gutierrez B. Lancet Infect Dis 2017

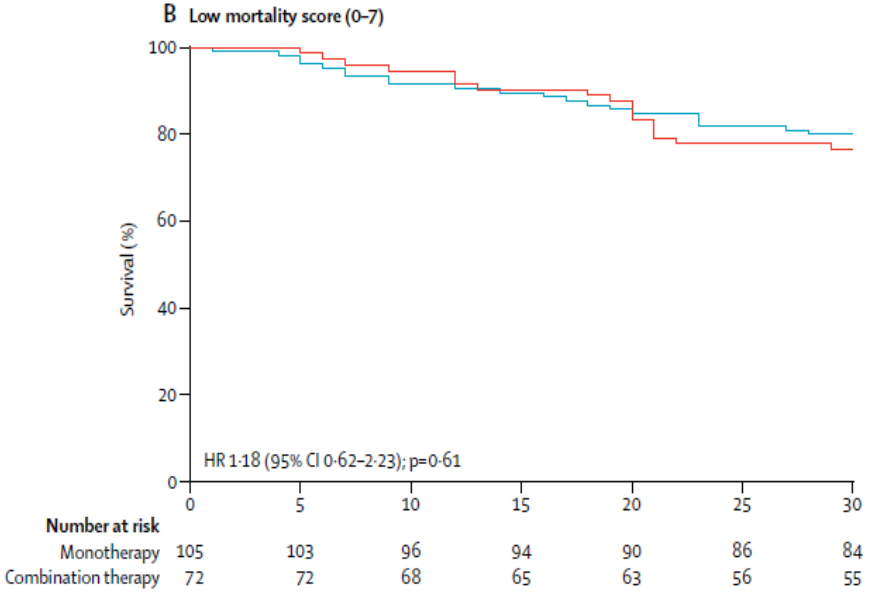
	Crude analysis		Adjusted analysis*	
	HR (95% CI)	p value	HR (95% CI)	p value
Age (per year)	1·00 (1·00–1·01)	0·32	..	..
Male sex	0·93 (0·70–1·24)	0·62	..	..
Klebsiella pneumoniae	1·29 (0·83–2·02)	0·25	..	..
OXA-type carbapenemase	1·43 (1·00- 2·05)	0·05	..	..
Nosocomial acquisition	1·83 (1·06- 3·16)	0·03	..	..
Source other than urinary or biliary tracts†	2·12 (1·37- 3·29)	0·0009	1·72 (1·09–2·72)	0·02
ICU admission	1·55 (1·16–2·08)	0·003	..	..
Charlson comorbidity index score (per unit)	1·10 (1·05–1·16)	<0·0001	1·13 (1·07–1·20)	<0·0001
Mechanical ventilation	1·76 (1·32–2·34)	<0·0001	..	..
Mental status: not alert	2·45 (1·82–3·29)	<0·0001	..	..
Chronic kidney disease	1·33 (0·97–1·84)	0·08	..	..
Chronic liver disease	1·58 (1·08–2·31)	0·02	..	..
Leukaemia or metastatic cancer	1·61 (1·12–2·31)	0·009	..	..
Pitt bacteraemia score (per unit)	1·17 (1·13–1·22)	<0·0001	1·09 (1·04–1·15)	0·0003
Severe sepsis or septic shock	3·87 (2·78–5·39)	<0·0001	3·11 (2·14–4·51)	<0·0001
Early appropriate therapy (started in ≤2 days after infection)	0·84 (0·59–1·21)	0·35	..	..
Appropriate therapy (started in ≤5 days after infection)	0·44 (0·33–0·61)	<0·0001	0·45 (0·33–0·62)	<0·0001
High-mortality-risk centre	2·25 (1·69–2·99)	<0·0001	2·37 (1·74–3·22)	<0·0001
Study period 2004–11 (reference 2012–13)	1·52 (1·09–2·13)	0·01	1·43 (1·02–2·01)	0·04

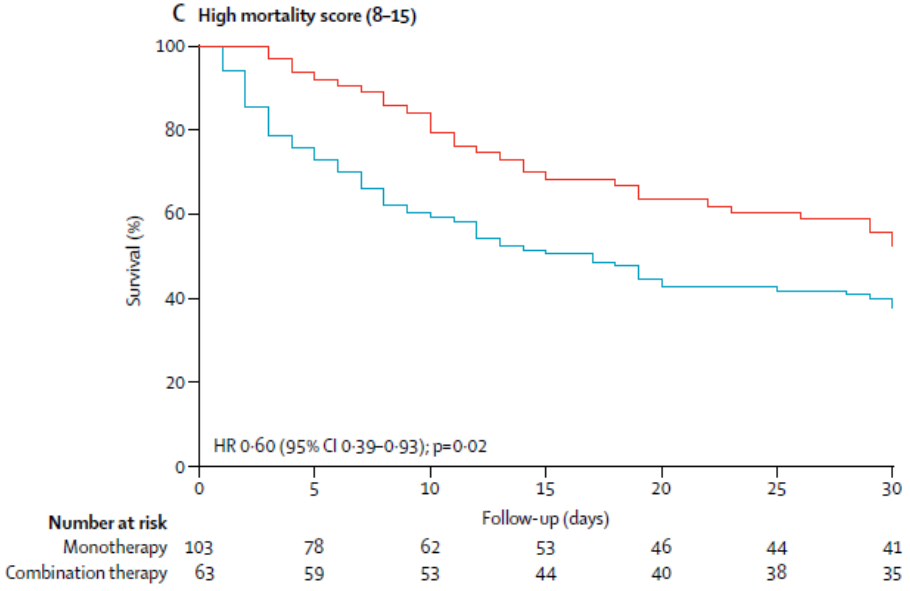
HR=hazard ratio. OXA=oxacillinase. ICU=intensive care unit. *All variance inflation factor values of the variables included in the final multivariate model were less than 1·4. We included variables with a univariate p value of 0·2 or less for mortality in the initial model. †Biliary tract infections included cholecystitis and cholangitis.

***Table 2:* Univariate and multivariate Cox regression analyses for mortality of patients with bacteraemia due to carbapenemase-producing Enterobacteriaceae**

Gutierrez-Gutierrez B. Lancet Infect Dis 2017







	OR or HR (95% CI)	p value
Low mortality score (0–7)*†		
Combination therapy	1·21 (0·56–2·56)	0·62
High-mortality-risk centre	2·95 (1·37–6·32)	0·005
Study period 2004–11 (reference 2012–13)	1·62 (0·73–3·85)	0·25
Propensity score	0·86 (0·20–3·38)	0·84
High mortality score (8–15)‡		
Combination therapy	0·56 (0·34–0·91)	0·02
High-mortality-risk centre	1·94 (1·27–2·96)	0·002
Study period 2004–11 (reference 2012–13)	1·61 (1·00–2·61)	0·05
Propensity score	1·98 (0·85–4·62)	0·11

OR=odds ratio. HR=hazard ratio. *Proportional hazards assumptions not fulfilled for low mortality score, so we used logistic regression. †ORs presented. ‡HRs presented.

Table 4: **Multivariate analysis of mortality-associated variables according to INCREMENT-CPE mortality score strata**

Bezlotoxumab for Prevention of Recurrent *Clostridium difficile* Infection

M.H. Wilcox, D.N. Gerding, I.R. Poxton, C. Kelly, R. Nathan, T. Birch, O.A. Cornely, G. Rahav, E. Bouza, C. Lee, G. Jenkin, W. Jensen, Y.-S. Kim, J. Yoshida, L. Gabryelski, A. Pedley, K. Eves, R. Tipping, D. Guris, N. Kartsonis, and M.-B. Dorr, for the MODIFY I and MODIFY II Investigators*

Wilcox MH. New Engl J Med 2017; 376: 305 - 317

Rationale: Actoxumab and bezlotoxumab are monoclonal antibodies against CD toxins A and B, respectively.

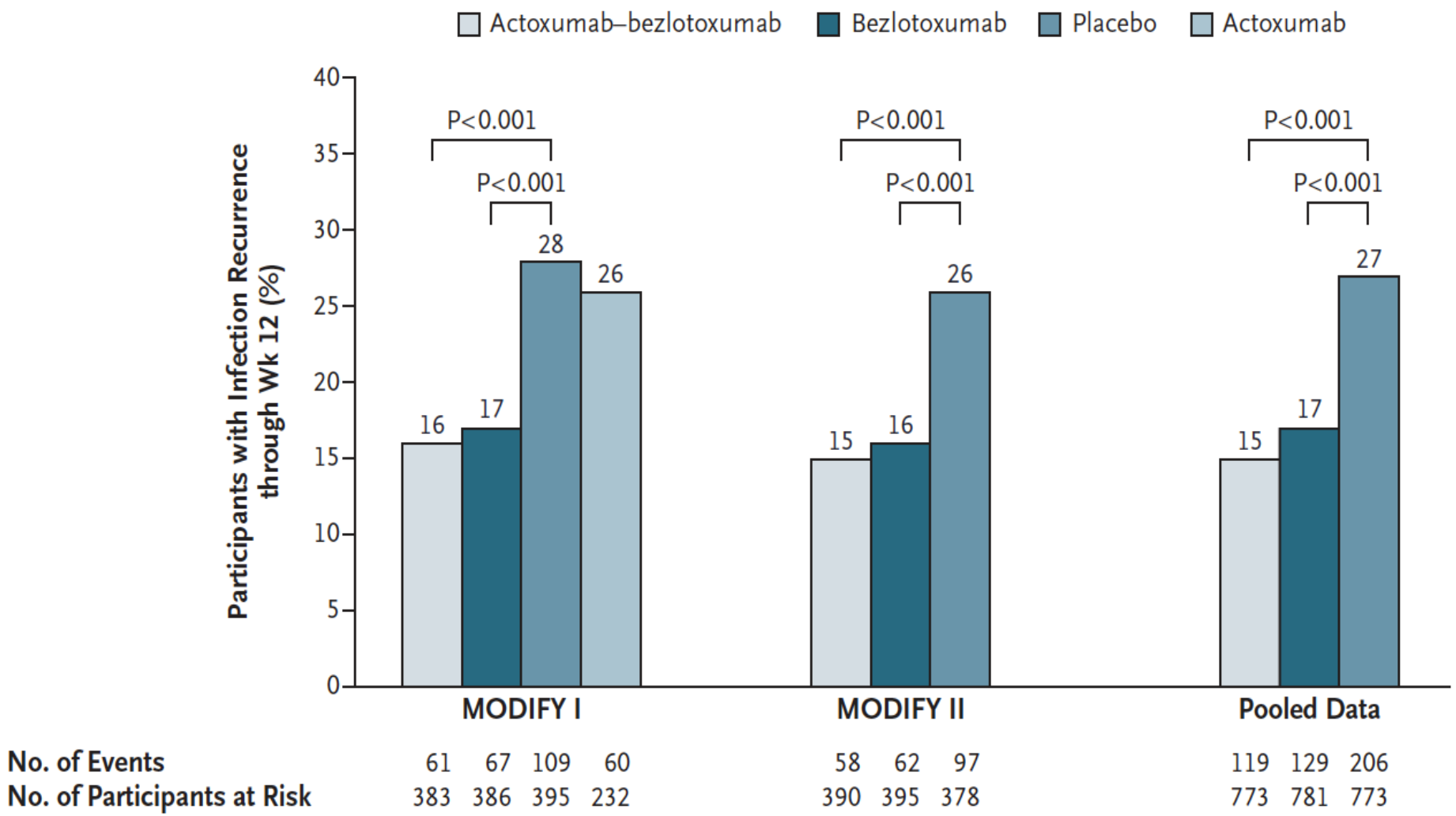
Design: Two double-blind, randomized, placebo-controlled, phase 3 trials (MODIFY I and MODIFY II); 322 sites in 30 countries (2011-15).

Patients: 2655 adults received an infusion of bezlotoxumab (10 mg/Kg), actoxumab plus bezlotoxumab (10 mg/Kg each), or placebo.

Primary end point: Recurrent infection within 12 weeks (MIT).

Wilcox MH. New Engl J Med 2017

Participants with recurrent CDI during the 12 week follow-up period



Rate of recurrent CDI for patients randomized to three treatment arms, using pooled data from two randomized trial (MODIFY I and MODIFY II)

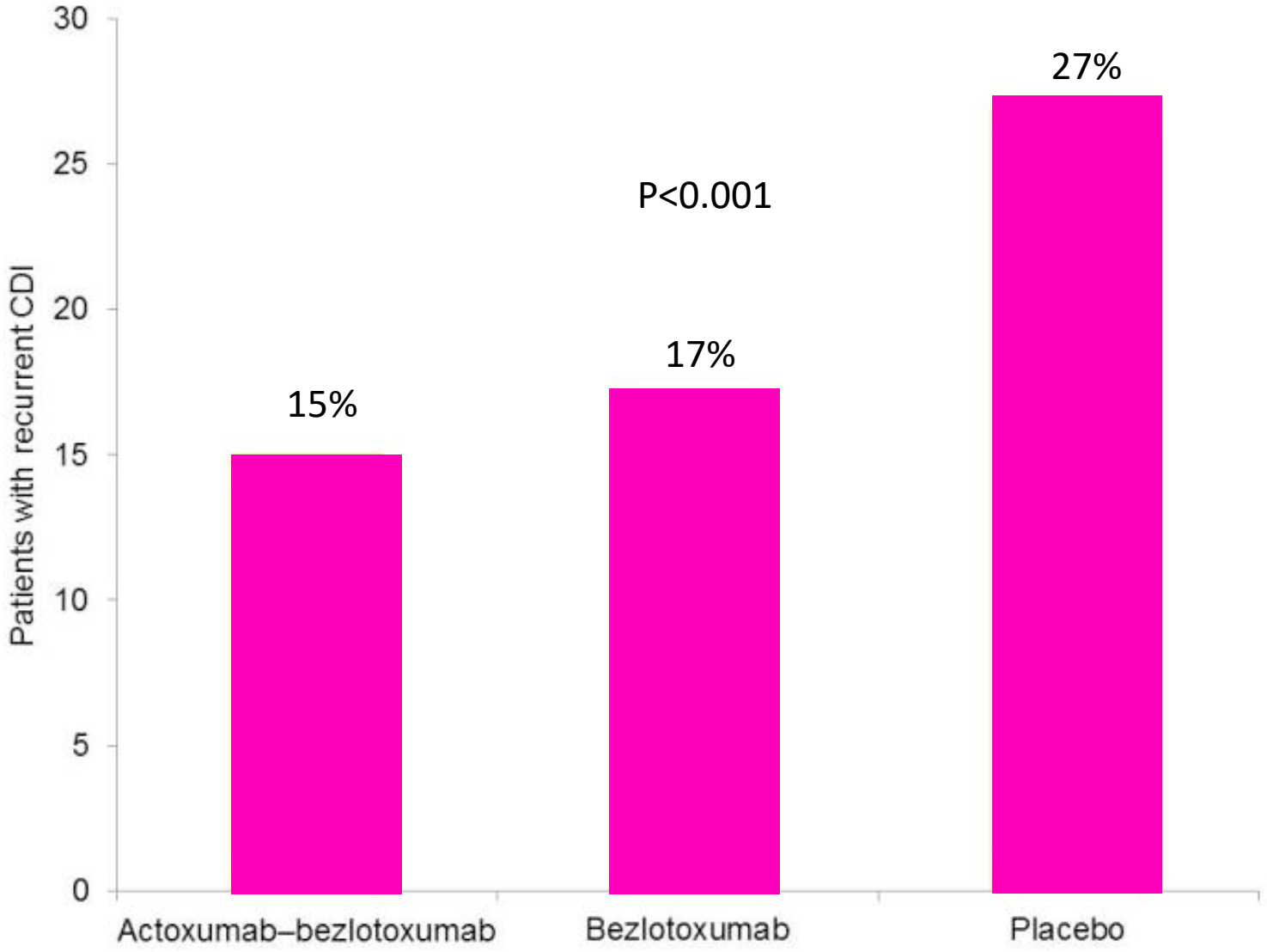


Table 2. Clinical Adverse Events in the As-Treated Population in Both Trials.

Time Period and Event	Actoxumab plus Bezlotoxumab (N=777)	Bezlotoxumab (N=786)	Actoxumab (N=235)	Placebo (N=781)
		number of participants (percent)		
During the 24 hours after infusion				
Infusion-specific reaction*	62 (8.0)	81 (10.3)	26 (11.1)	59 (7.6)
Treatment stopped because of an adverse event	0	1 (0.1)	1 (0.4)	0
During the 4 weeks after infusion				
One or more adverse events	455 (58.6)	485 (61.7)	158 (67.2)	478 (61.2)
Serious adverse event	123 (15.8)	156 (19.8)	65 (27.7)	167 (21.4)
Death	28 (3.6)	32 (4.1)	14 (6.0)	32 (4.1)
Drug-related adverse event†	50 (6.4)	59 (7.5)	17 (7.2)	46 (5.9)
Serious drug-related adverse event‡	5 (0.6)	4 (0.5)	3 (1.3)	2 (0.3)
Most common adverse events§				
Abdominal pain	32 (4.1)	34 (4.3)	15 (6.4)	34 (4.4)
Diarrhea	46 (5.9)	47 (6.0)	13 (5.5)	45 (5.8)
Nausea	47 (6.0)	52 (6.6)	28 (11.9)	39 (5.0)
Vomiting	24 (3.1)	31 (3.9)	10 (4.3)	21 (2.7)
Fatigue	21 (2.7)	18 (2.3)	11 (4.7)	12 (1.5)
Pyrexia	31 (4.0)	36 (4.6)	11 (4.7)	27 (3.5)
C. difficile infection¶	27 (3.5)	23 (2.9)	20 (8.5)	48 (6.1)
Urinary tract infection	24 (3.1)	32 (4.1)	13 (5.5)	35 (4.5)
Headache	33 (4.2)	35 (4.5)	14 (6.0)	24 (3.1)
During the 12 weeks after infusion				
Serious adverse event‖	212 (27.3)	231 (29.4)	104 (44.3)	255 (32.7)
Death	51 (6.6)	56 (7.1)	27 (11.5)	59 (7.6)

Enhanced terminal room disinfection and acquisition and infection caused by multidrug-resistant organisms and *Clostridium difficile* (the Benefits of Enhanced Terminal Room Disinfection study): a cluster-randomised, multicentre, crossover study

Deverick J Anderson, Luke F Chen, David J Weber, Rebekah W Moehring, Sarah S Lewis, Patricia F Triplett, Michael Blocker, Paul Becherer, J Conrad Schwab, Lauren P Knelson, Yuliya Lokhnygina, William A Rutala, Hajime Kanamori, Maria F Gergen, Daniel J Sexton; for the CDC Prevention Epicenters Program

Anderson DJ. Lancet 2017; 389: 805-814

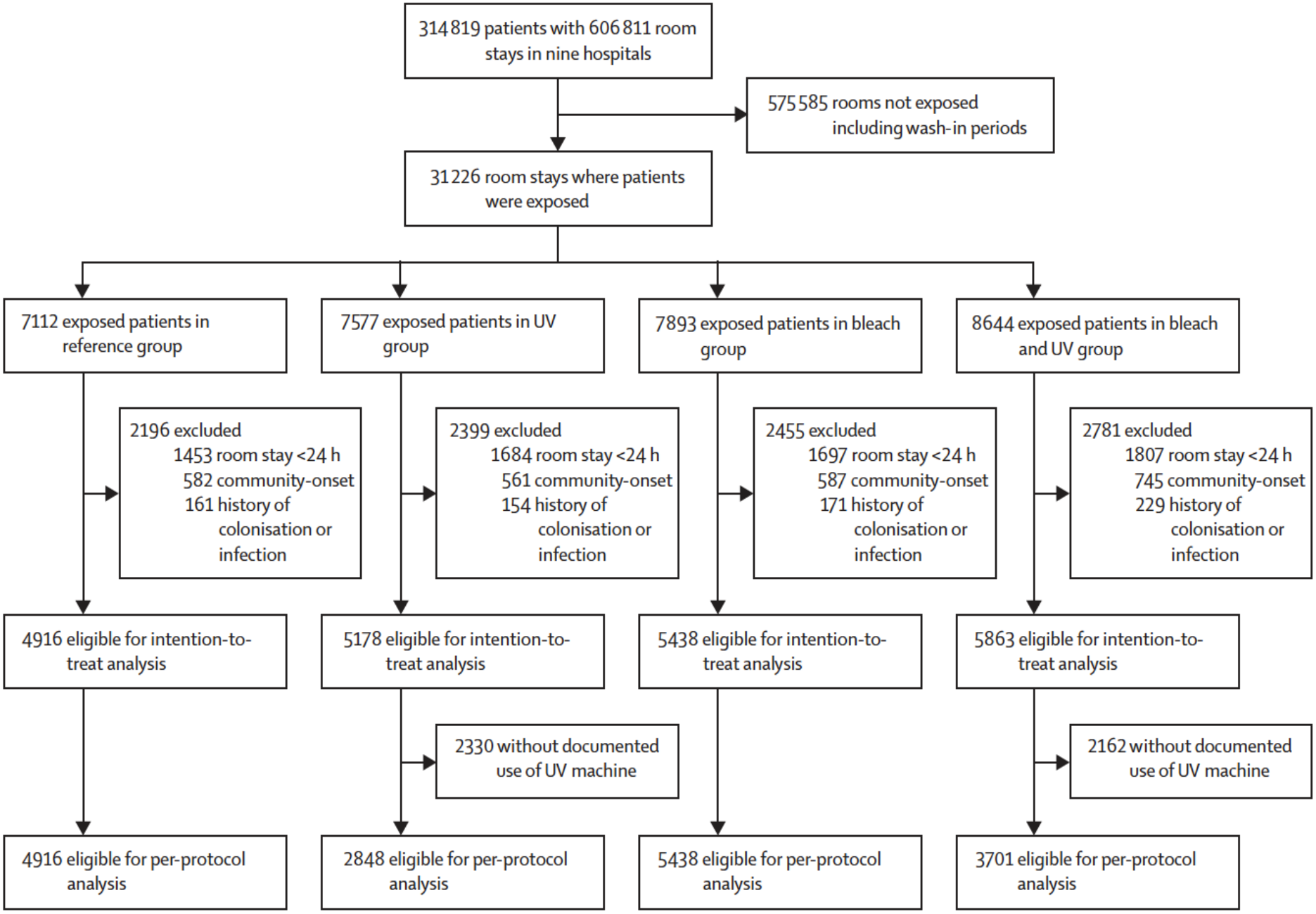
Objective: To determine the effect of three enhanced strategies for terminal room disinfection (disinfection of a room between occupying patients) on acquisition and infection due to MRSA, VRE, *C. difficile*, and MDR *Acinetobacter*.

Design and Setting: Pragmatic, cluster-randomized, crossover trial at nine hospitals in the USA.

Interventions: Reference (quaternary ammonium), UV (quaternary ammonium and UV light), Bleach, and Bleach and UV light.

Primary outcome: incidence of infection or colonization with all targeted organisms among exposed patients.

Anderson DJ. Lancet 2017


314 819 patients with 606 811 room stays in nine hospitals
575 585 rooms not exposed including wash-in periods
31 226 room stays where patients were exposed
7112 exposed patients in reference group
7577 exposed patients in UV group
7893 exposed patients in bleach group
8644 exposed patients in bleach and UV group
2196 excluded
1453 room stay <24 h
582 community-onset
161 history of colonisation or infection
2399 excluded
1684 room stay <24 h
561 community-onset
154 history of colonisation or infection
2455 excluded
1697 room stay <24 h
587 community-onset
171 history of colonisation or infection
2781 excluded
1807 room stay <24 h
745 community-onset
229 history of colonisation or infection
4916 eligible for intention-to-treat analysis
5178 eligible for intention-to-treat analysis
5438 eligible for intention-to-treat analysis
5863 eligible for intention-to-treat analysis
2330 without documented use of UV machine
2162 without documented use of UV machine
4916 eligible for per-protocol analysis
2848 eligible for per-protocol analysis
5438 eligible for per-protocol analysis
3701 eligible for per-protocol analysis

Intention-to-treat analysis (RR/ 95% CI)

Organisms	Reference	UV	Bleach	Bleach and UV
All targeted organisms	Reference	0.70 (0.50-0.98)	0.85 (0.69-1.04)	0.91 (0.76-1.09)
C. difficile	-	-	Reference	1.00 (0.57-1.75)
MRSA	Reference	0.78 (0.58-1.05)	1.00 (0.82-1.21)	0.97 (0.78-1.22)
VRE	Reference	0.41 (0.15-1.13)	0.43 (0.19-1.00)	0.36 (0.18-0.70)

Patients admitted to rooms previously occupied by pts harboring target organism were 10-30 % less likely to acquire the same organism if the room was terminally disinfected using and enhanced strategy.

The largest reduction occurred when UV light device was added to the standard disinfectant strategy.

Anderson DJ. Lancet 2017

Insidious Risk of Severe *Mycobacterium chimaera* Infection in Cardiac Surgery Patients

Meera Chand,[1,2,3,a] Theresa Lamagni,[1,a] Katharina Kranzer,[1] Jessica Hedge,[4] Ginny Moore,[1] Simon Parks,[1] Samuel Collins,[1] Carlos del Ojo Elias,[4] Nada Ahmed,[1] Tim Brown,[1] E. Grace Smith,[1,3] Peter Hoffman,[1] Peter Kirwan,[1] Brendan Mason,[5] Alison Smith-Palmer,[6] Philip Veal,[7] Maeve K. Lalor,[1] Allan Bennett,[1] James Walker,[1] Alicia Yeap,[1] Antonio Isidro Carrion Martin,[1,8] Gayle Dolan,[1,9] Sonia Bhatt,[1] Andrew Skingsley,[1] André Charlett,[1] David Pearce,[1] Katherine Russell,[1] Simon Kendall,[10,11] Andrew A. Klein,[12,13] Stephen Robins,[14] Silke Schelenz,[15] William Newsholme,[2] Stephanie Thomas,[16] Tim Collyns,[17] Eleri Davies,[5,18] Jim McMenamin,[6] Lorraine Doherty,[7] Tim E. A. Peto,[4] Derrick Crook,[1,4] Maria Zambon,[1,3] and Nick Phin[1]

Chand M. Clin Infect Dis 2017; 64: 335 - 342

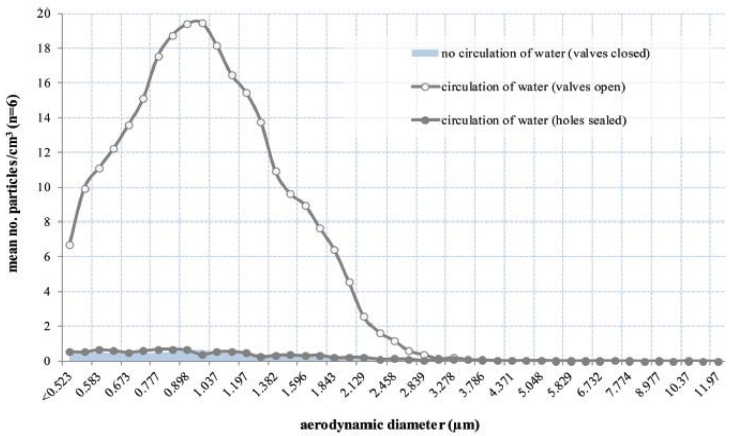
UK investigation to assess risk of invasive *M. chimaera* infection in cardiothoracic surgery and a possible association with cardiopulmonary bypass heater-cooler units following alerts in Switzerland and the Netherlands.

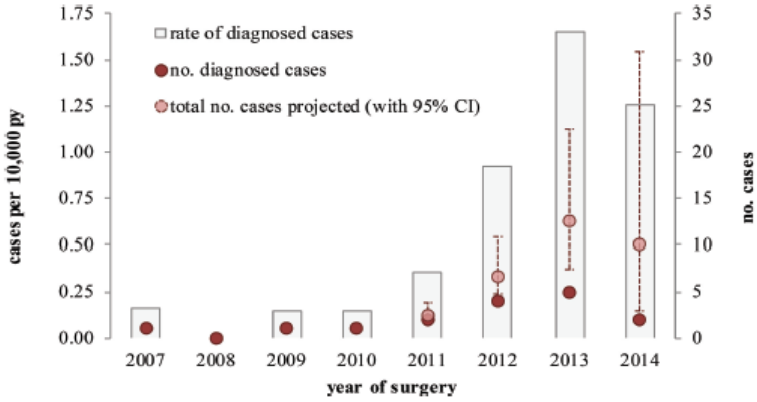
- Identification of cardiovascular by-pass associated *M. chimaera* infection through national laboratory and hospital admission data linkage.
- Cohort study to assess patient risk
- Microbiological and aerobiological investigations of heater-coolers *in situ* and under controlled laboratory conditions
- Whole-genome sequencing of clinical and environmental isolates.

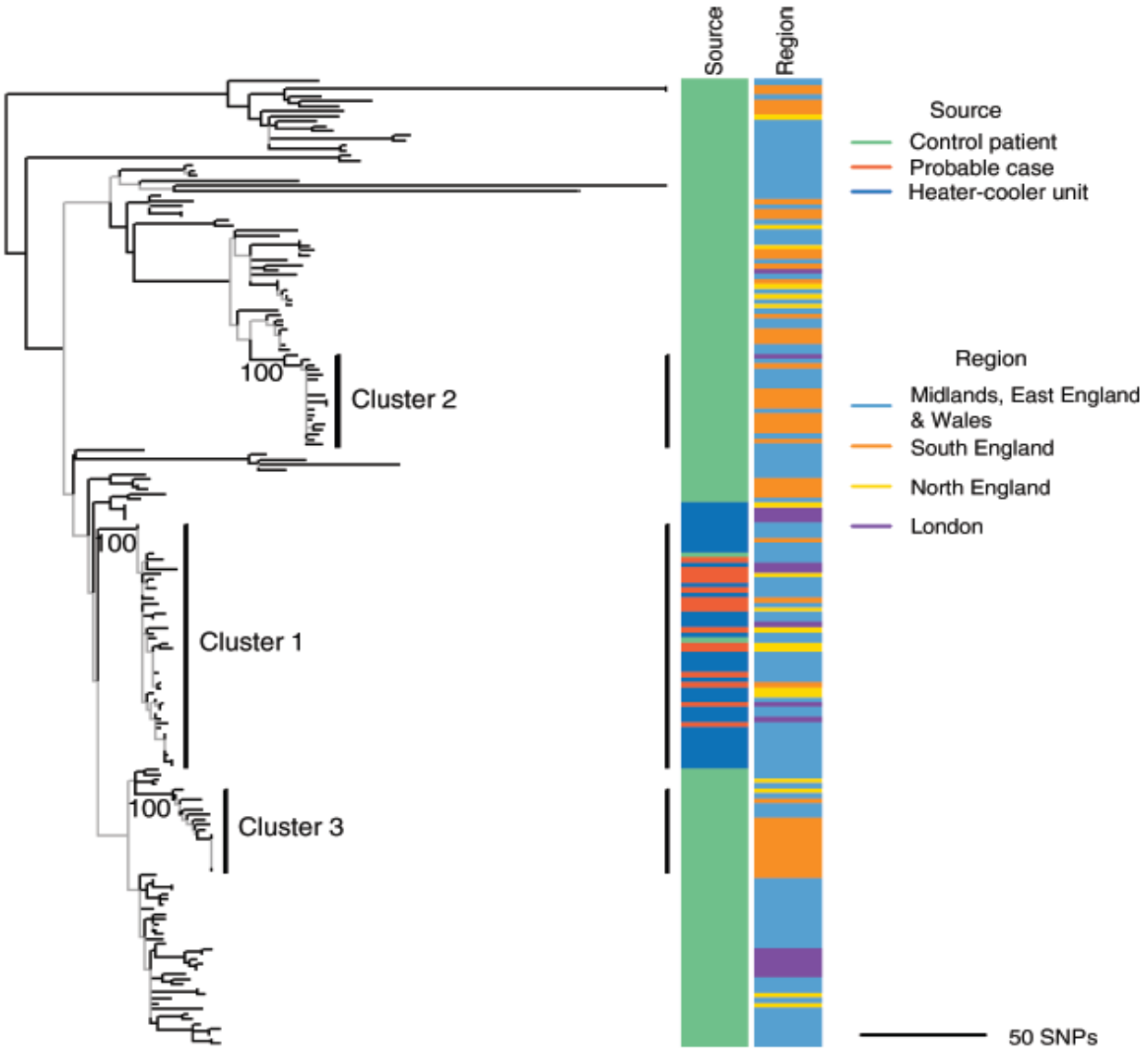
Chand M. Clin Infect Dis 2017

Table 1. Clinical Characteristics of Probable Cases of Severe *Mycobacterium chimaera* Infection Associated With Cardiopulmonary Bypass Surgery, United Kingdom

Characteristic	All Cases (N = 18)
Female sex, No. (%)	5 (28)
Median age (range), y	63 (7–81)
Type of surgery, No. (%)	
Aortic valve replacement	14 (77)
Mitral valve replacement	3 (17)
Aortic valve replacement and homograft to pulmonary valve (redo)	1 (6)
Site of infection, No. (%)	
Sternal osteomyelitis	2 (11)
Anterior mediastinal abscess	1 (6)
Spinal osteomyelitis and discitis	1 (6)
Endocarditis	5 (28)
Endocarditis, aortic root abscess	3 (17)
Endocarditis, disseminated infection	3 (17)
Disseminated infection	3 (17)
Median time between surgery and presentation (range), y	1.15 (0.25–5.1)
Median time between presentation and first mycobacterial culture (range), d	85 (6–457)
Outcome, No. (%)	
Death	9 (50)
Recovered	2 (11)
Remains unwell and on treatment	7 (38)
Median time between culture and death (range), d	71 (14–567)

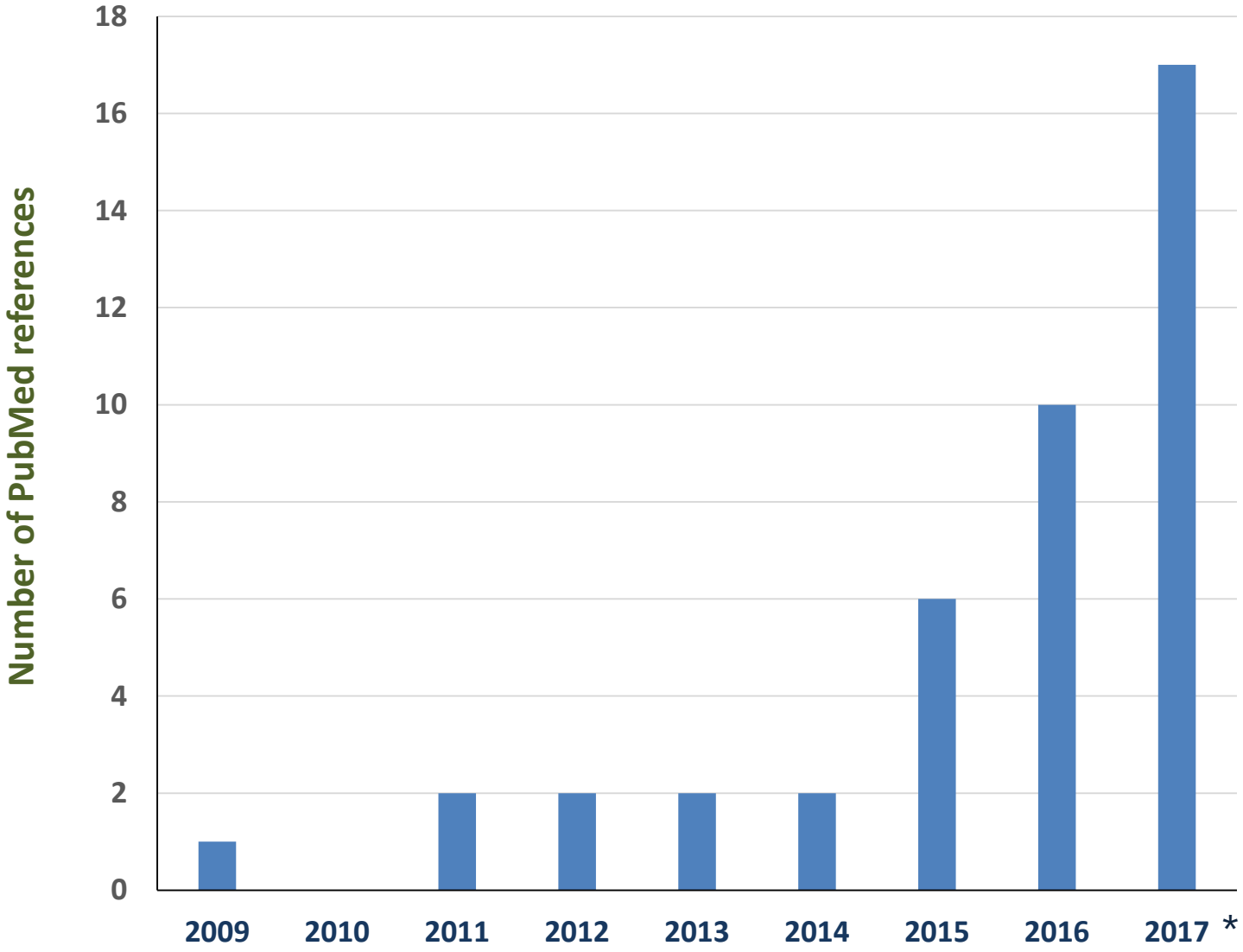






Chand M. Clin Infect Dis 2017

2017: The year of Candida auris



*As per 16 April 2017

Microbiol Immunol. 2009;53:41-4. *Emerg Infect Dis* 2013;19:1670-3. *Emerg Infect Dis* 2015;21:1091-2. *Antimicrob Resist Infect Control* 2016;5:35.

J Clin Microbiol 2011;49:3139-42. *Emerg Infect Dis* 2014;20:1250-1. *J Infect* 2016;73:369-74. *MMWR Morb Mortal Wkly Rep* 2016;65:1234-7

Simultaneous Emergence of Multidrug-Resistant *Candida auris* on 3 Continents Confirmed by Whole-Genome Sequencing and Epidemiological Analyses

Shawn R. Lockhart,[1] Kizee A. Etienne,[1] Snigdha Vallabhaneni,[1] Joveria Farooqi,[4] Anuradha Chowdhary,[6] Nelesh P. Govender,[7] Arnaldo Lopes Colombo,[8] Belinda Calvo,[9] Christina A. Cuomo,[2] Christopher A. Desjardins,[2] Elizabeth L. Berkow,[1] Mariana Castanheira,[3] Rindidzani E. Magobo,[7] Kauser Jabeen,[4] Rana J. Asghar,[5] Jacques F. Meis,[10,11] Brendan Jackson,[1] Tom Chiller,[1] and Anastasia P. Litvintseva[1]

Lockhart SR. Clin Infect Dis 2017; 64: 134 - 140

54 patients with *Candida auris* infection

- Pakistan, India, South Africa, and Venezuela
- Period: 2012 to 2015
- Median age: 54 years (7% of neonates)
- Predisposing conditions:

  DM (41%), recent surgery (51%), CVC (73%)
- Receiving systemic antifungals when *C. auris* was isolated: 41%
- The median time from admission to infection: 19 days
- Bloodstream infection: 61%
- All-cause in-hospital mortality: 59%

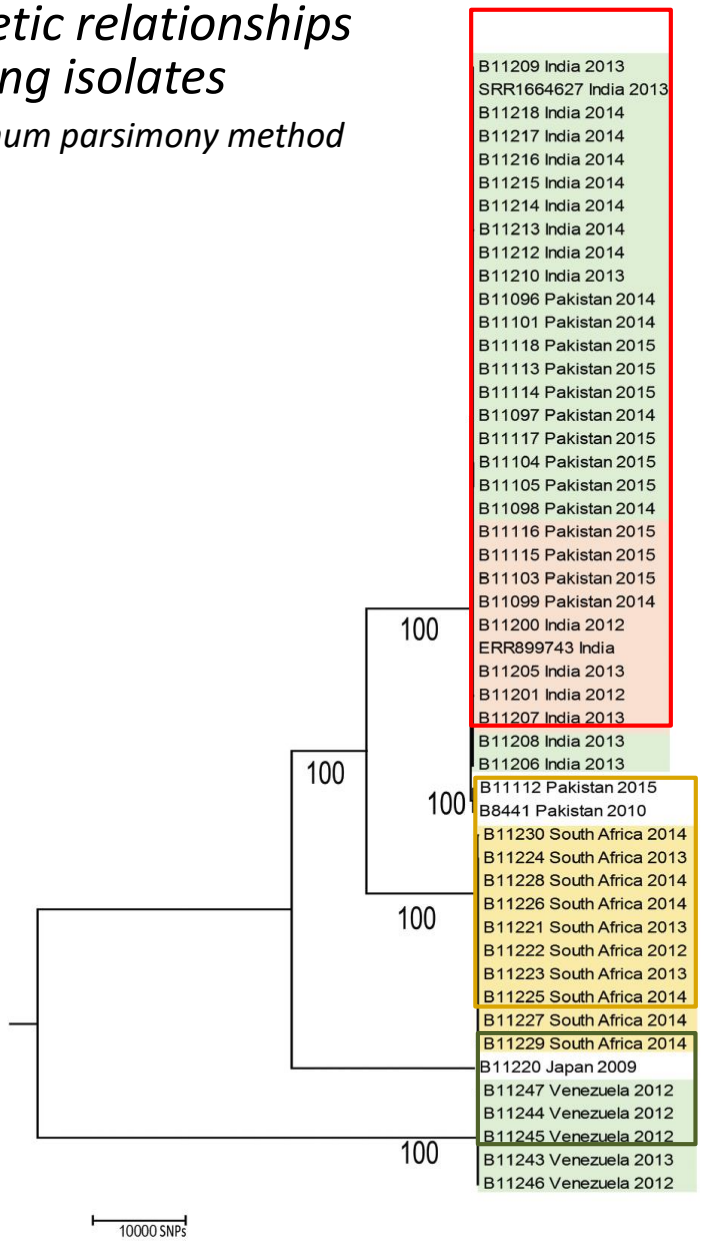
Lockart SR. Clin Infect Dis 2017

Antifungal	MIC Range, µg/mL	MIC_{50}, µg/mL	MIC_{90}, µg/mL
Fluconazole	4–256	128	256
Voriconazole	0.03–16	2	8
Itraconazole	0.125–2	0.5	1
Posaconazole	0.06–1	0.5	1
Caspofungin	0.03–16	0.25	1
Anidulafungin*	0.125–16	0.5	1
Micafungin	0.06–4	0.25	2
Flucytosine	0.125–128	0.125	0.5
Amphotericin B	0.38–4	1	2

Resistance to FLUCONAZOLE*	93% of isolates
Resistance to VORICONAZOLE	54% of isolates
Resistance to AMPHOTERICIN B	54% of isolates
Resistance to ECHINOCANDINS	7% of isolates
Resistance to ≥2 CLASSES	**41% of isolates**

Genetic relationships among isolates

maximum parsimony method



India-Pakistan

South Africa

East Asia

Venezuela

Known mutations in *ERG11* hot spot

- Y132F
- K143R
- F126T

Four distinct clades representing each geographical region

Low genetic diversity among isolates ***within*** each clade

Lockart SR. Clin Infect Dis 2017

Empirical Micafungin Treatment and Survival Without Invasive Fungal Infection in Adults With ICU-Acquired Sepsis, *Candida* Colonization, and Multiple Organ Failure

The EMPIRICUS Randomized Clinical Trial

Jean-Francois Timsit, MD, PhD; Elie Azoulay, MD, PhD; Carole Schwebel, MD, PhD; Pierre Emmanuel Charles, MD, PhD; Muriel Cornet, PhamD; Bertrand Souweine, MD, PhD; Kada Klouche, MD, PhD; Samir Jaber, MD, PhD; Jean-Louis Trouillet, MD, PhD; Fabrice Bruneel, MD; Laurent Argaud, MD, PhD; Joel Cousson, MD; Ferhat Meziani, MD, PhD; Didier Gruson, MD, PhD; Adeline Paris, PharmD; Michael Darmon, MD, PhD; Maité Garrouste-Orgeas, MD, PhD; Jean-Christophe Navellou, MD; Arnaud Foucrier, MD; Bernard Allaouchiche, MD, PhD; Vincent Das, MD; Jean-Pierre Gangneux, PharmD, PhD; Stéphane Ruckly, MSc; Daniele Maubon, MD, PhD; Vincent Jullien, PharmD; Michel Wolff, MD, PhD; for the EMPIRICUS Trial Group

Timsit JF. JAMA 2016; 316: 1555 - 1564

Objective: To determine whether empirical micafungin reduces IFI-free survival at day 28.

Design and Setting: Randomized, double-blind placebo controlled trial, of 260 critically ill patients with ICU-acquired sepsis, multiple Candida colonization, multiple organ failure, and exposed to broad-spectrum antibacterial agents in 19 French ICUs (2012 – 2015).

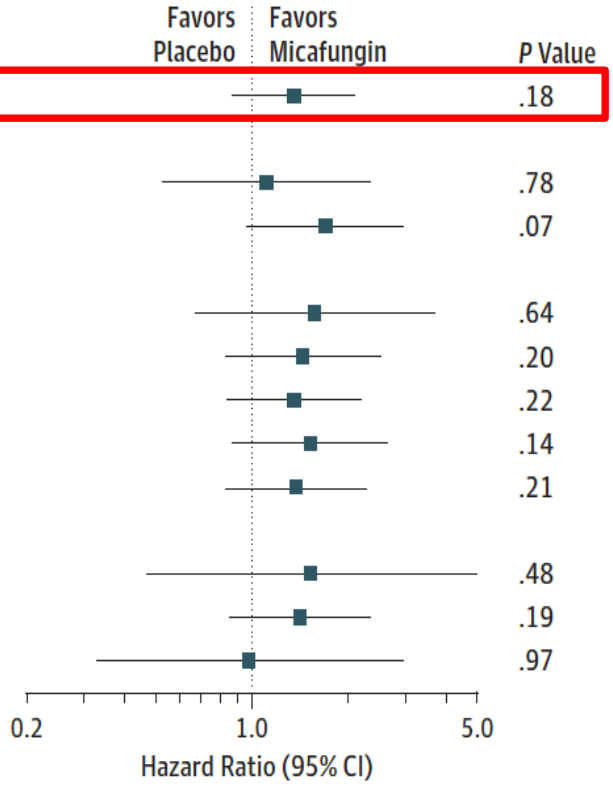
Interventions: Empirical treatment with micafungin (100 mg once daily, for 14 days) vs placebo.

Primary outcomes: Survival without proven IFI at 28 days.

Timsit JF. JAMA 2016

Comparison of IFI-free survival at day 28

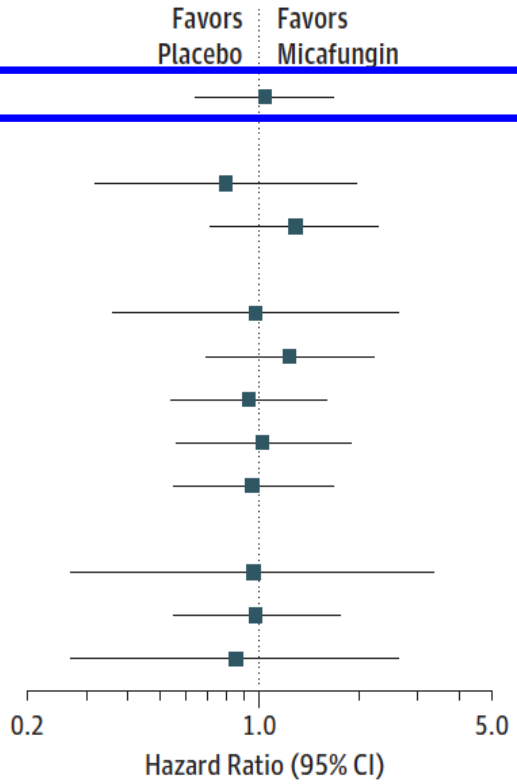
	Micafungin		Placebo			
	Survived at Day 28, No.	Total No.	Survived at Day 28, No.	Total No.	Hazard Ratio (95% CI)	*P* Value
All patients	87	128	74	123	1.35 (0.87-2.08)	.18
SOFA score						
≤8	51	66	52	68	1.11 (0.53-2.33)	.78
>8	36	62	22	55	1.69 (0.96-2.94)	.07
Admission category						
Surgical	22	34	16	31	1.56 (0.67-3.70)	.64
Medical	65	94	58	92	1.43 (0.83-2.50)	.20
Colonization index ≥0.5[a]	68	101	58	99	1.35 (0.84-2.17)	.22
Corrected colonization index ≥0.4[b]	52	76	45	80	1.52 (0.87-2.63)	.14
Candida score ≥3	64	96	47	85	1.37 (0.83-2.27)	.21
(1-3)-ß-D-glucan, pg/mL[c]						
>250	14	21	14	25	1.52 (0.47-5.00)	.48
>80	58	91	47	84	1.41 (0.85-2.33)	.19
≤80	29	37	27	39	0.98 (0.30-2.94)	.97



Timsit JF. JAMA 2016

Comparison of survival at day 28

	Micafungin		Placebo				
	Survived at Day 28, No.	Total No.	Survived at Day 28, No.	Total No.	Hazard Ratio (95% CI)	Favors Placebo / Favors Micafungin	*P* Value
All patients	90	128	86	123	1.04 (0.64-1.67)		.88
SOFA score							
≤8	53	66	58	68	0.79 (0.32-1.96)		.62
>8	37	62	28	55	1.28 (0.71-2.27)		.42
Admission category							
Surgical	23	34	23	31	0.97 (0.36-2.63)		.96
Medical	67	94	63	92	1.23 (0.69-2.22)		.48
Colonization index ≥0.5[a]	70	101	70	99	0.93 (0.54-1.59)		.78
Corrected colonization index ≥0.4[b]	54	76	56	80	1.02 (0.56-1.89)		.94
Candida score ≥3	66	96	58	85	0.95 (0.55-1.67)		.87
(1-3)-ß-D-glucan, pg/mL[c]							
>250	14	21	17	25	0.96 (0.27-3.33)		.95
>80	61	91	58	84	0.98 (0.55-1.75)		.96
≤80	29	37	28	39	0.85 (0.27-2.63)		.78



Timsit JF. JAMA 2016


Muchas gracias por su atención!
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