

Complicated SAB: who we should be worried about and how to evaluate

ECCMID 2014

Barcelona, 12.05.2014



Dr. med. Achim Kaasch

Institut für Medizinische Mikrobiologie, Immunologie und Hygiene

Uniklinik Köln

Clinical Case

- 69 y/o male
- admitted to hospital with chest pain
- diagnosis non-transmural MI
- day 5: coronary angiography, no focal stenosis
- day 7: fever 40°C → presumed pneumonia
- day 8: chest CT unremarkable
- blood cultures positive with *S. aureus*

Basic workup

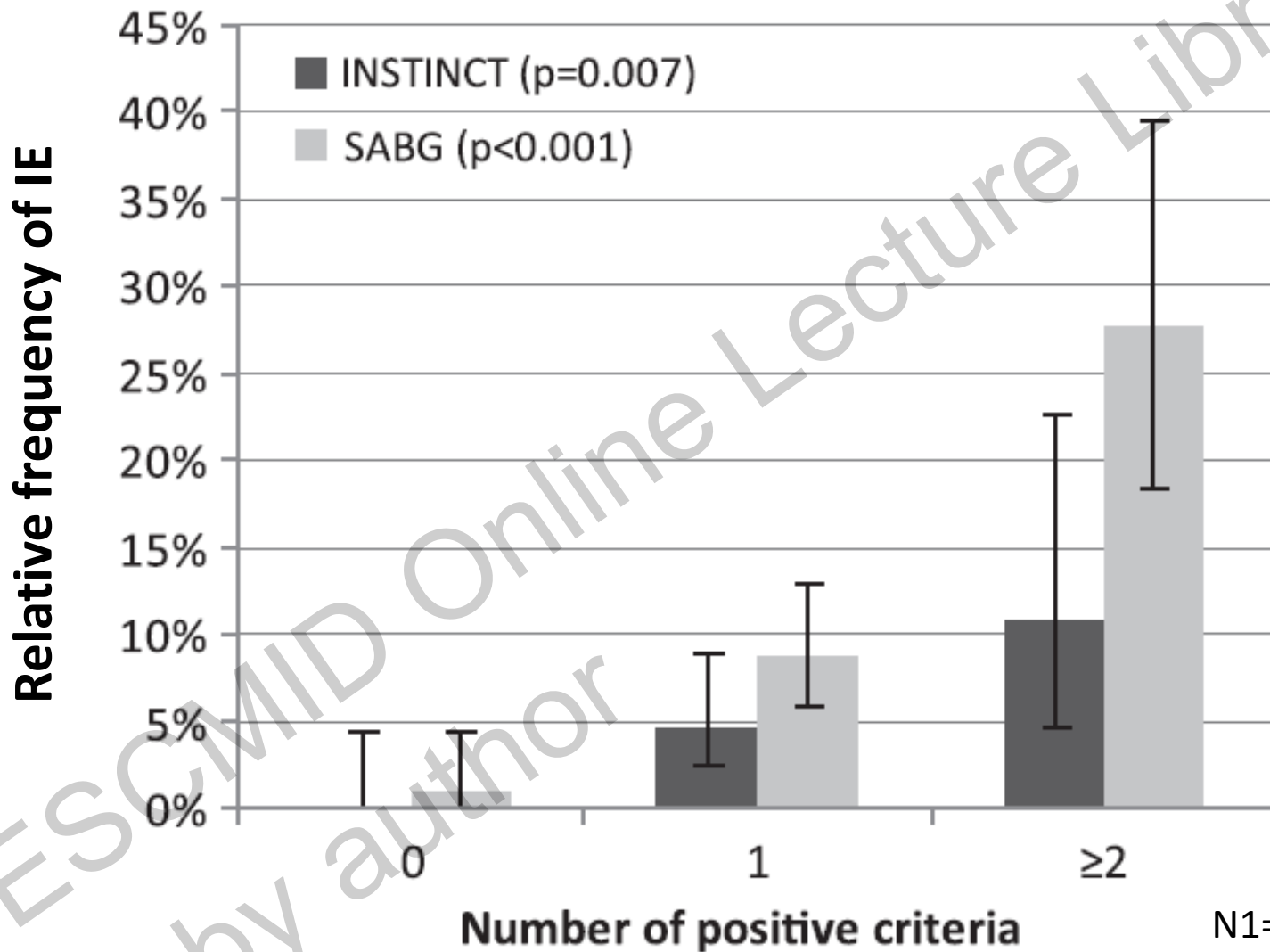
- patient history and clinical examination
- follow-up blood cultures, urine culture
- symptom-guided imaging
- symptom-guided microbiology (swabs, aspirates, biopsies)
- basic lab (CRP, PCT, Creatinine)
- remove catheter
- echocardiography

Question to the audience

Does this patient need echocardiography?

Do all patients need echo?

- community-onset SAB: all patients
- nosocomial
 - no negative BC within 4 days
 - cardiac device
 - hemodialysis
 - spinal infection or osteomyelitis



N1=304

N2=432

Echocardiography

	design	cases	TEE / TTE (% imaged)	IE rate	Recommendation
Holden JAC 2014	prosp.	98	58 / 22 (92%)	13 (16%)	50% of pts with IE did not have intracardiac device, persistent fever, persistent bacteremia; very low FU blood culture rate
Khatib Medicine 2013	post hoc	877	177 / 202 (43%)	64 (7%)	Echo dispensable in uncomplicated SAB
Incani EJCMID 2013	prosp.	144	144 / 0 (100%)	41 (28%)	echo in all patients; since clinical signs of IE in 10% only
Joseph JAC 2013	retro	668	82 / 224 (46%)	31 (10%)	dispensable in line-related bacteremia w/o prosth. valve or CRM device, clinical signs of IE, and responsive to treatment
Rasmussen EJE 2011	prosp. pts w. echo	244 (336 eligible)	244 / 0 (100%)	53 (22%)	all pts should undergo echo
Kaasch CID 2011	post hoc nosocomial SAB	304 432	56/65 119/129	13 (4%) 40 (9%)	TEE not required in subset of patients

Echocardiography

	design	cases	TEE / TTE (% imaged)	IE rate	Recommendation
Holden JAC 2014	prosp.	98	58 / 22 (92%)	13 (16%)	50% of pts with IE did not have intracardiac device, persistent fever, persistent bacteremia; very low FU blood culture rate
Khatib Medicine 2013	post hoc	877	177 / 202 (43%)	64 (7%)	Echo dispensable in uncomplicated SAB
Incani EJCMID 2013	prosp.	144	144 / 0 (100%)	41 (28%)	echo in all patients; since clinical signs of IE in 10% only
Joseph JAC 2013	retro	668	82 / 224 (46%)	31 (10%)	dispensable in line-related bacteremia w/o prosth. valve or CRM device, clinical signs of IE, and responsive to treatment
Rasmussen EJE 2011	prosp. pts w. echo	244 (336 eligible)	244 / 0 (100%)	53 (22%)	all pts should undergo echo
Kaasch CID 2011	post hoc nosocom ial SAB	304 432	56/65 119/129	13 (4%) 40 (9%)	TEE not required in subset of patients

Clinical Case

- 69 y/o male
- diagnosis non-transmural MI
- day 5: coronary angiography
- day 7: fever 40°C
- blood cultures positive with *S. aureus*
- **day 9: Echocardiography unremarkable; pt. is afebrile and leaves hospital on oral antibiotics against medical advice**

Do we have to worry – is this a complicated bacteremia?

Definitions of complicated SAB

	Fowler AIM 2003	Pulcini JI 2009	Price IJM 2010	Neuner DMID 2010	Aguado EID 2011	El Zakhem AM 2014
Skin findings	X					
Community acquisition	X					
Persistent fever	X					X
Persistent bacteremia	X					X
Secondary foci	O	O	O	O	O	O
Retained infected foreign body				X	X	X (any)
Embolic stroke	O					
Relapse	O		O			O
Attributable mortality	O					O

O: complicated outcome

X: risk factors for complicated SAB

„complicated“ means, SAB can not be cured by

- Removal of foreign body
- 14 days antibiotics

but requires

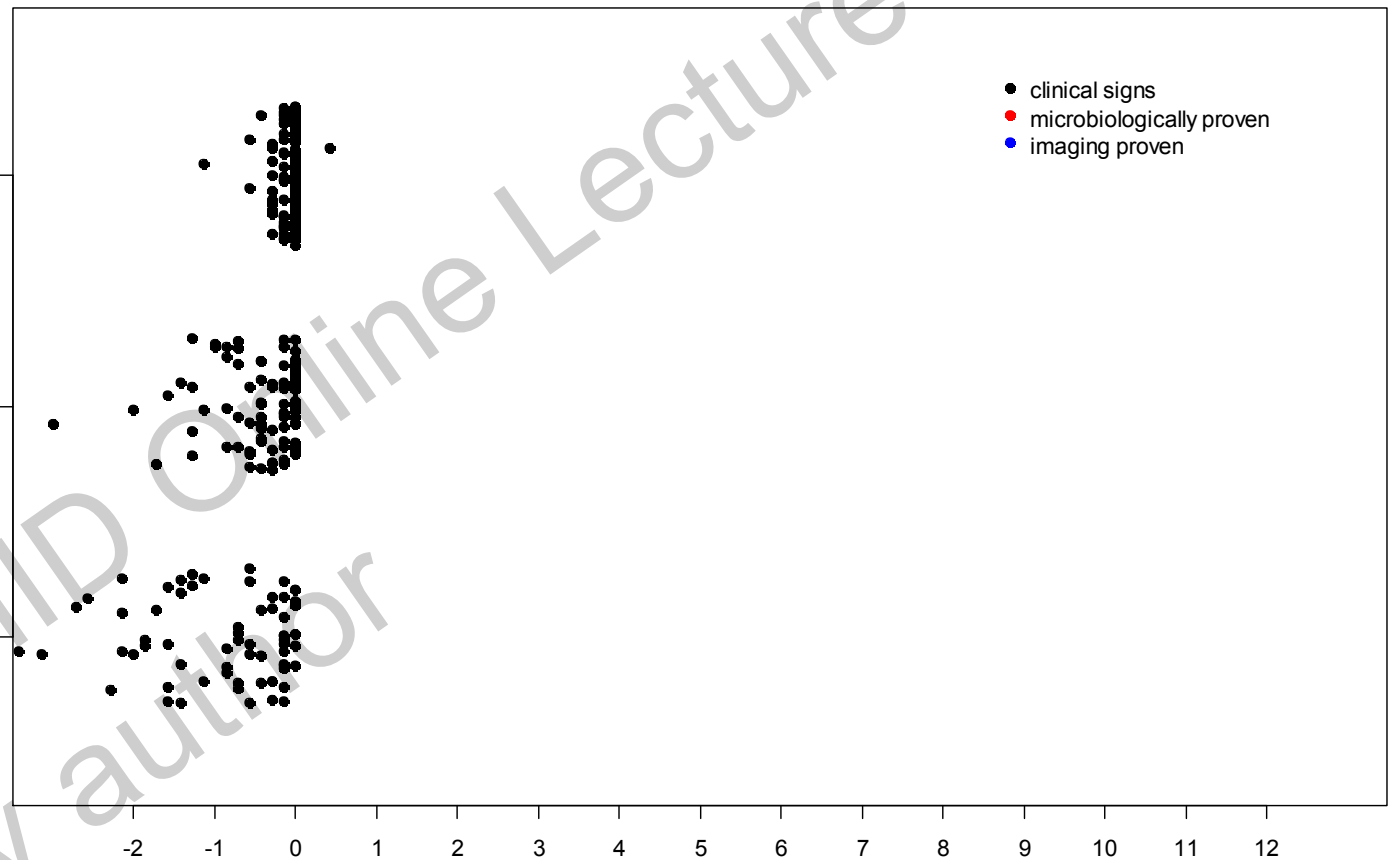
- Further diagnostic workup
- Extended antibiotic therapy
- Interventions

Start of clinical symptoms

Short-term
venous catheter
(n=175)

Endocarditis
(n=104)

Vertebral
osteomyelitis
(n=74)



weeks

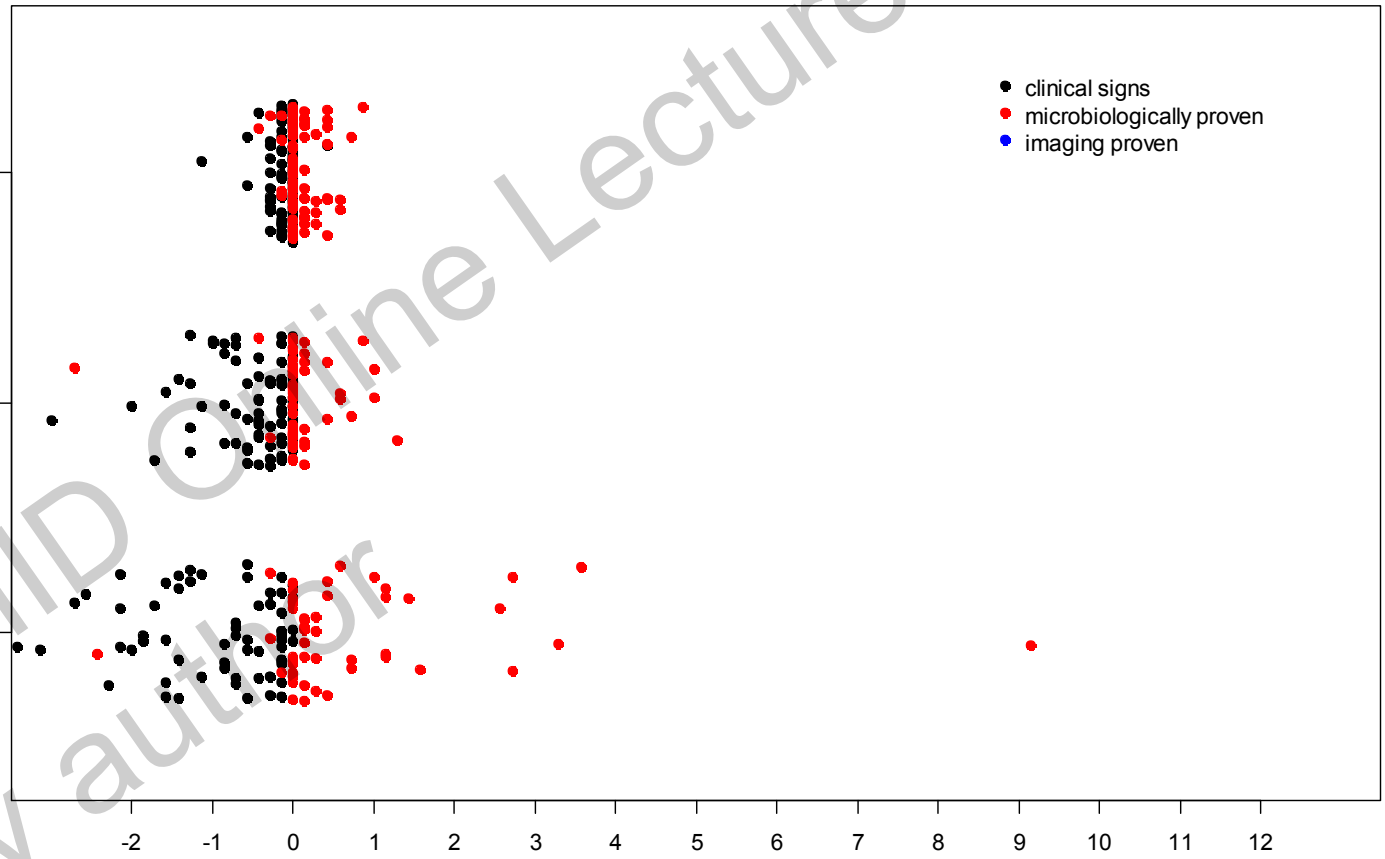
INSTINCT study
N=1056

Microbiological proven

Short-term
venous catheter
(n=175)

Endocarditis
(n=104)

Vertebral
osteomyelitis
(n=74)



weeks

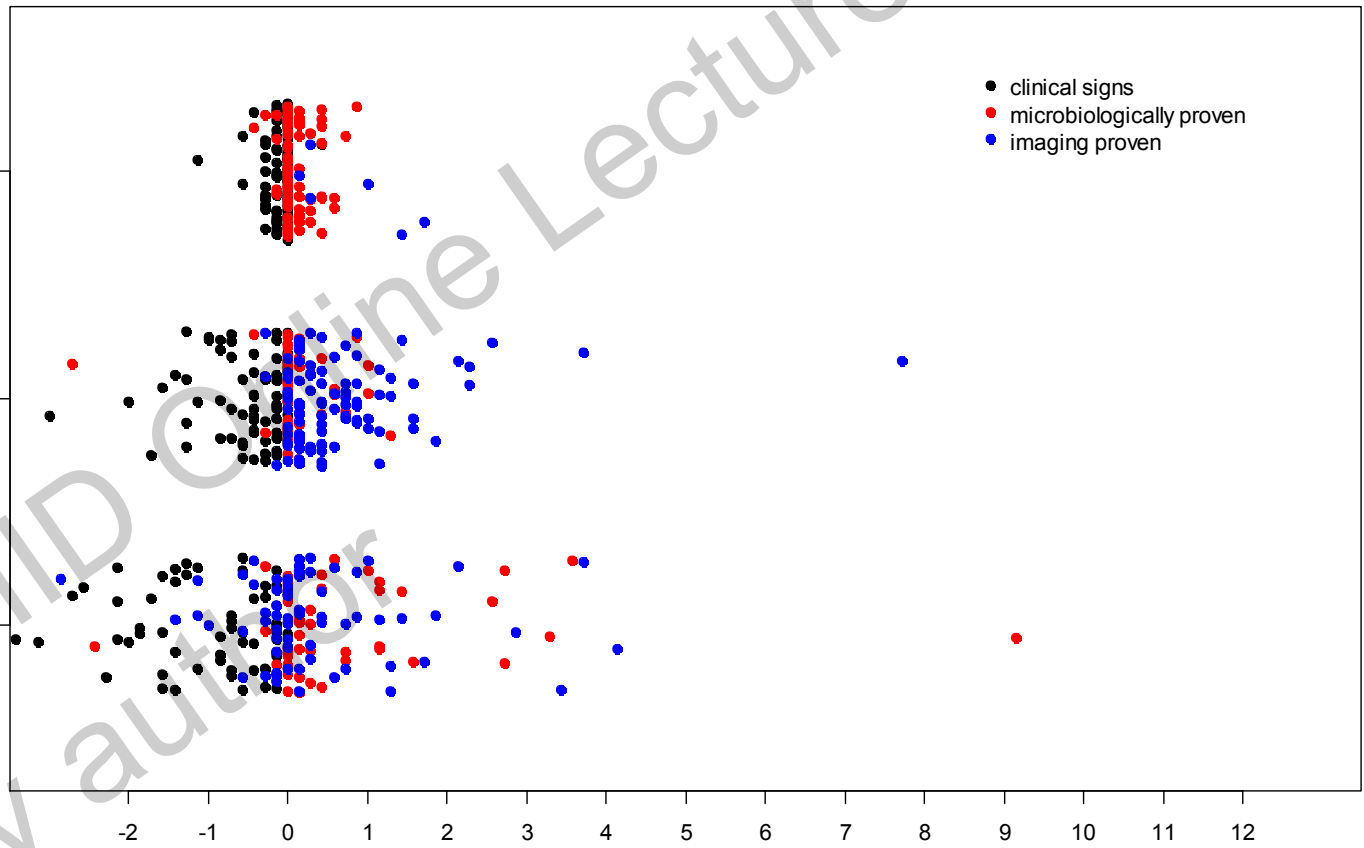
INSTINCT study
N=1056

Imaging proven

Short-term
venous catheter
(n=175)

Endocarditis
(n=104)

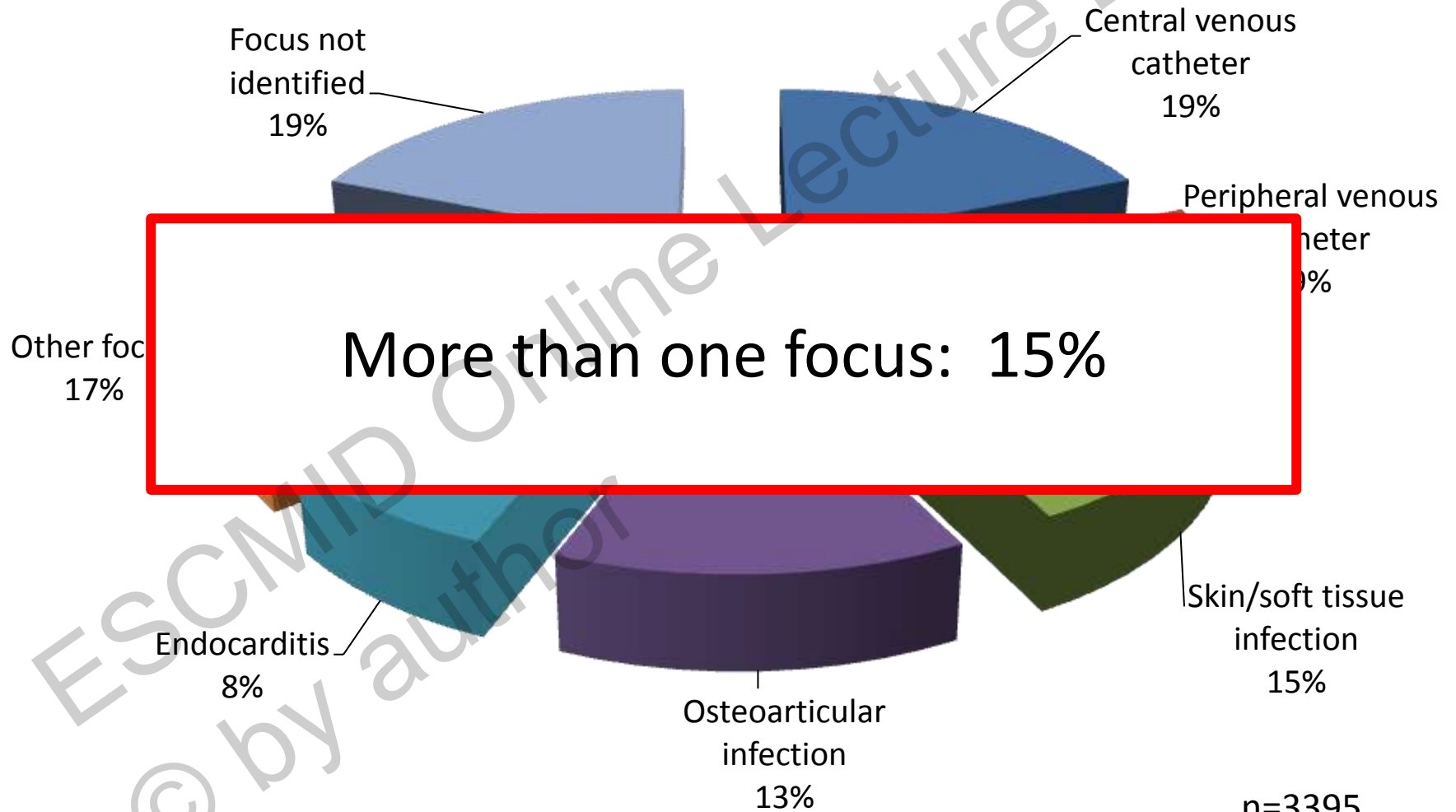
Vertebral
osteomyelitis
(n=74)



weeks

INSTINCT study
N=1056

Dominant infective focus

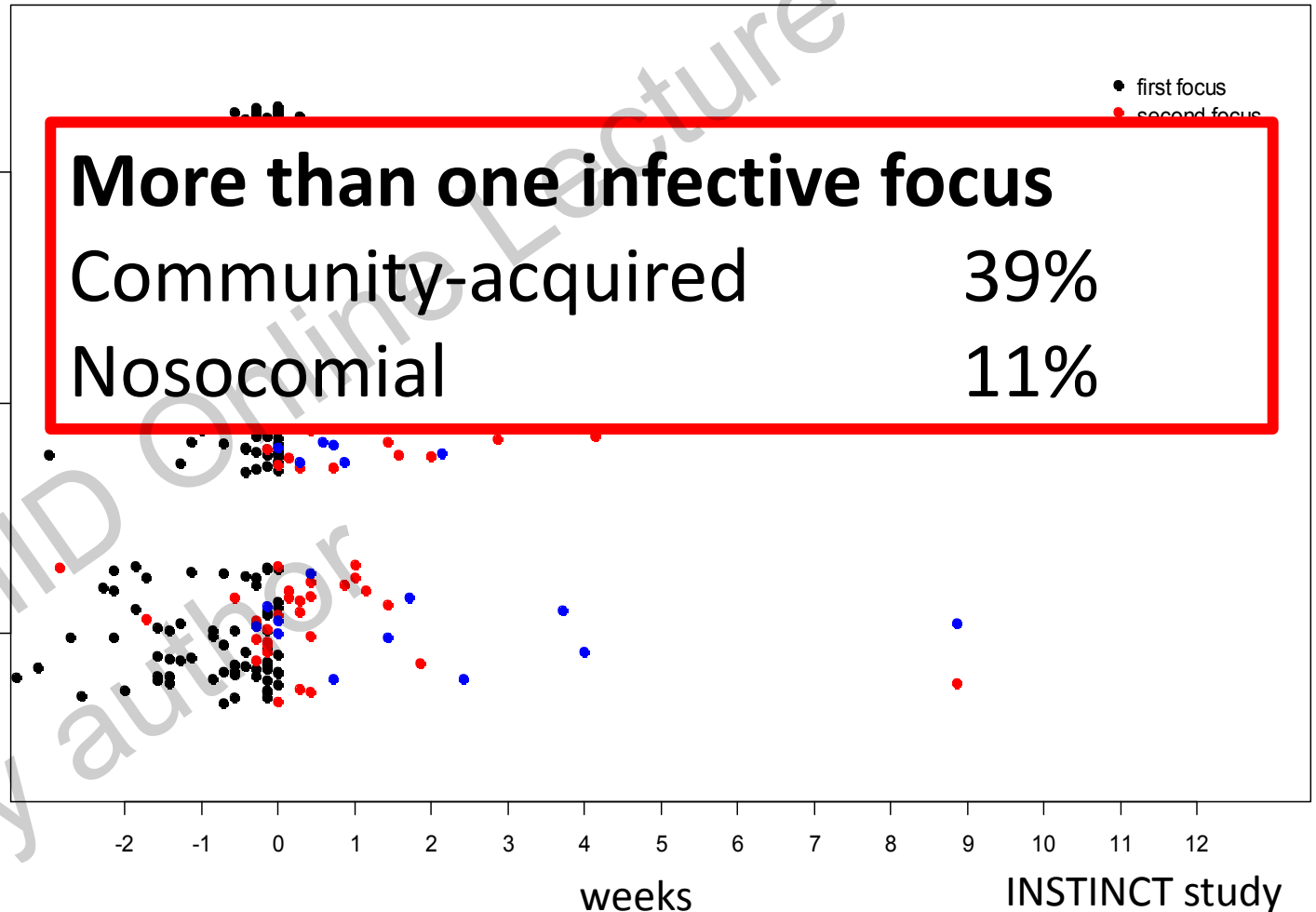


Clinical signs of more than one focus

Short-term
venous catheter
(n=175)

Endocarditis
(n=104)

Vertebral
osteomyelitis
(n=74)



INSTINCT study
N=1056

Clinical Case

- 69 y/o male
- diagnosis non-transmural MI
- day 5: coronary angiography
- day 7: blood cultures positive with *S. aureus*
- day 9: pt. is afebrile and leaves hospital against medical advice
- **day 10: pt. readmitted to other hospital**

prosthetic hip joint since 5 years

Question to the audience

Does the presence of an orthopedic device automatically mean „complicated SAB“ and warrants extended treatment?

Complicated due to risk factors

- Community acquisition
- Presence of foreign bodies
 - orthopedic implant
 - intravascular device (pacemaker, implanted cardiac defibrillator, prosthetic heart valve)
- Hemodialysis
- Injection drug use

Orthopedic device

study	device	prosthetic joint infection
Murdoch CID 2001	any orthopedic device	24/53 (45%)
Lalani SJID 2008	any orthopedic device	12 / 76 (29%)
Sendi JI 2011	prosthetic joint	
INSTINCT unpublished	prosthetic joint	12/70 (17%)

Orthopedic device

study	device	prosthetic joint infection	hematogenous seeding to joint	hematogenous seeding to other devices
Murdoch CID 2001	any orthopedic device	24/53 (45%)	15/44 (34%)	1/15 (7%)
Lalani SJID 2008	any orthopedic device	12 / 76 (29%)	-	16/76 (21%)
Sendi JI 2011	prosthetic joint		12/31 (39%)	-
INSTINCT unpublished	prosthetic joint	12/70 (17%)	9/44 (20%)	

SAB and pacemaker, ICD, and prosthetic valve

	n	Device infection	Comments
Chamis Circ 2001	33	15/33 (45%)	local signs may be minimal
Uslan PACE 2009	62	22/62 (35%)	prosthetic valve as risk factor
Obeid PACE 2012	106	11/30 (36%)	missing data for 63 pts.
INSTINCT unpublished	35	17/35 (49%)	
El Adhab AJM 2005	51	26/51 (51%)	prosthetic valves only

Patients on hemodialysis are at

- higher risk of **infective endocarditis**¹ and **repeat endocarditis**²
- higher risk of **SAB infection**³ and **reinfection**⁴
- higher risk for **hematogenous complications** in catheter-related SAB⁵

¹ Alagna CMI 2013

² Heiro BMCID 2013

³ Laupland JID 2008

⁴ Wiese JI 2013

⁵ Fowler CID 2005

Clinical Case

- 69 y/o male with non-transmural MI
- day 5: coronary angiography
- day 7: blood cultures positive with *S. aureus*
- echo unremarkable, prosthetic joint
- ***Staphylococcus aureus* in urine**

S. aureus bacteriuria as predictor of complicated SAB

	n	complicated SAB	uncomplicated SAB	PPV	NPV
Pulcini JI 2009	106	15/32 (47%)	7/36 (19%)	68%	63%
Perez-Jorge JHM 2010	118	18/48 (38%)	10/60 (17%)	64%	86%
Asgeirsson JI 2012	152*	14/86 (16%)	2/66 (3%)	88%	47%

*UTI origin excluded

Clinical Case

- 69 y/o male with non-transmural MI
- day 5: coronary angiography
- blood cultures positive with *S. aureus*
- echo unremarkable, prosthetic joint
- **follow-up blood culture from day 10 positive**

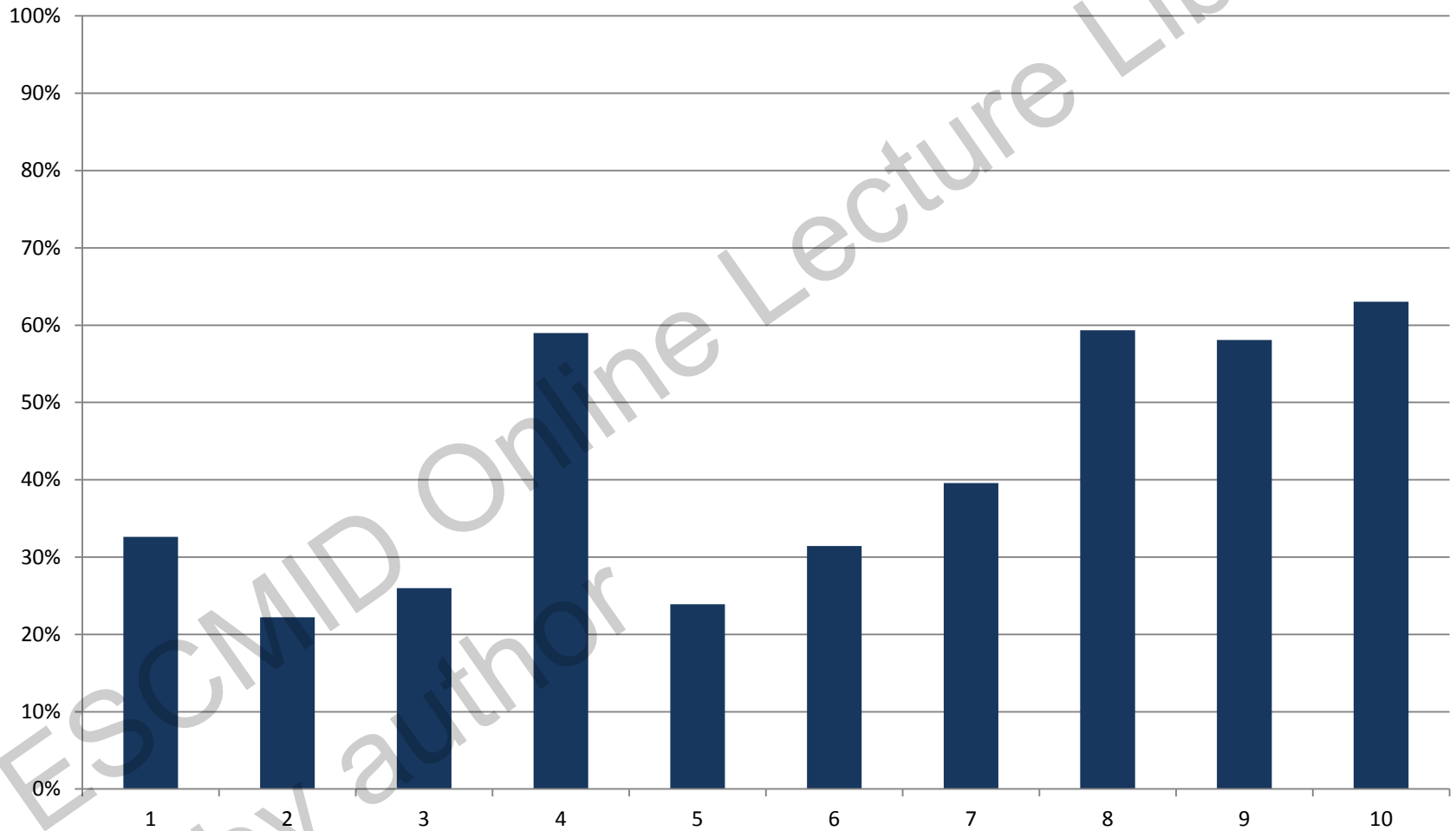
Predictors of complicated course

Table 3. Predictors of Complicated *Staphylococcus aureus* Bacteremia*

Variable	Odds Ratio (95% CI)	P Value
Demographic characteristics		
Surgical hospital service†	1.83 (1.18-2.82)	.006
Community acquired‡	3.08 (1.80-5.28)	<.001
Orthopedic or other prosthetic device	1.77 (1.01-3.11)	.05
Cardiac device	1.70 (0.82-3.51)	.16
Sex	0.84 (0.58-1.22)	.37
HIV positive or injection drug use	1.89 (0.92-3.86)	.09
Age	1.01 (1.00-1.02)	.05
Diabetes mellitus	1.10 (0.74-1.64)	.62
Race	1.15 (0.76-1.72)	.51
Indicators of existing complications		
Skin examination findings suggesting the presence of acute systemic infection	1.80 (1.10-2.95)	.02
New or diastolic murmur	2.46 (1.01-6.02)	.05
Clinical evidence of embolic/autoimmune events	2.05 (0.85-4.95)	.11
Clinical evidence of central nervous system involvement	1.30 (0.74-2.30)	.36
Reported presence of symptoms	1.87 (1.01-3.81)	.06
Septic shock	1.22 (0.77-1.94)	.46
Persistent fever at 72 h	2.00 (1.36-2.92)	<.001
Positive follow-up blood culture result	4.94 (3.37-7.25)	<.001
Treatment-related variables		
Vancomycin therapy	1.16 (0.78-1.74)	.46
Aminoglycoside use	1.42 (0.78-2.59)	.25
Rifampin use	0.87 (0.50-1.50)	.62
Appropriate empiric antibiotic therapy	0.80 (0.44-1.46)	.46
Corticosteroid use	1.63 (0.96-2.77)	.07
Removable source of <i>S aureus</i> bacteremia not removed	1.23 (0.69-2.20)	.49

**Positive follow-up
blood culture
(Persistent fever)**

Follow-up BC within 3 days



N=601

ISAC-01 study, unpublished

Imaging persistent infection

- infective endocarditis
 - echocardiography
- suppurative thrombophlebitis
 - color coded duplex sonography
 - contrast-enhanced CT
- (vertebral) osteomyelitis
 - spinal imaging (MRI)
- retained foreign body (CT)



All imaging negative, what now?

FDG-PET/CT¹



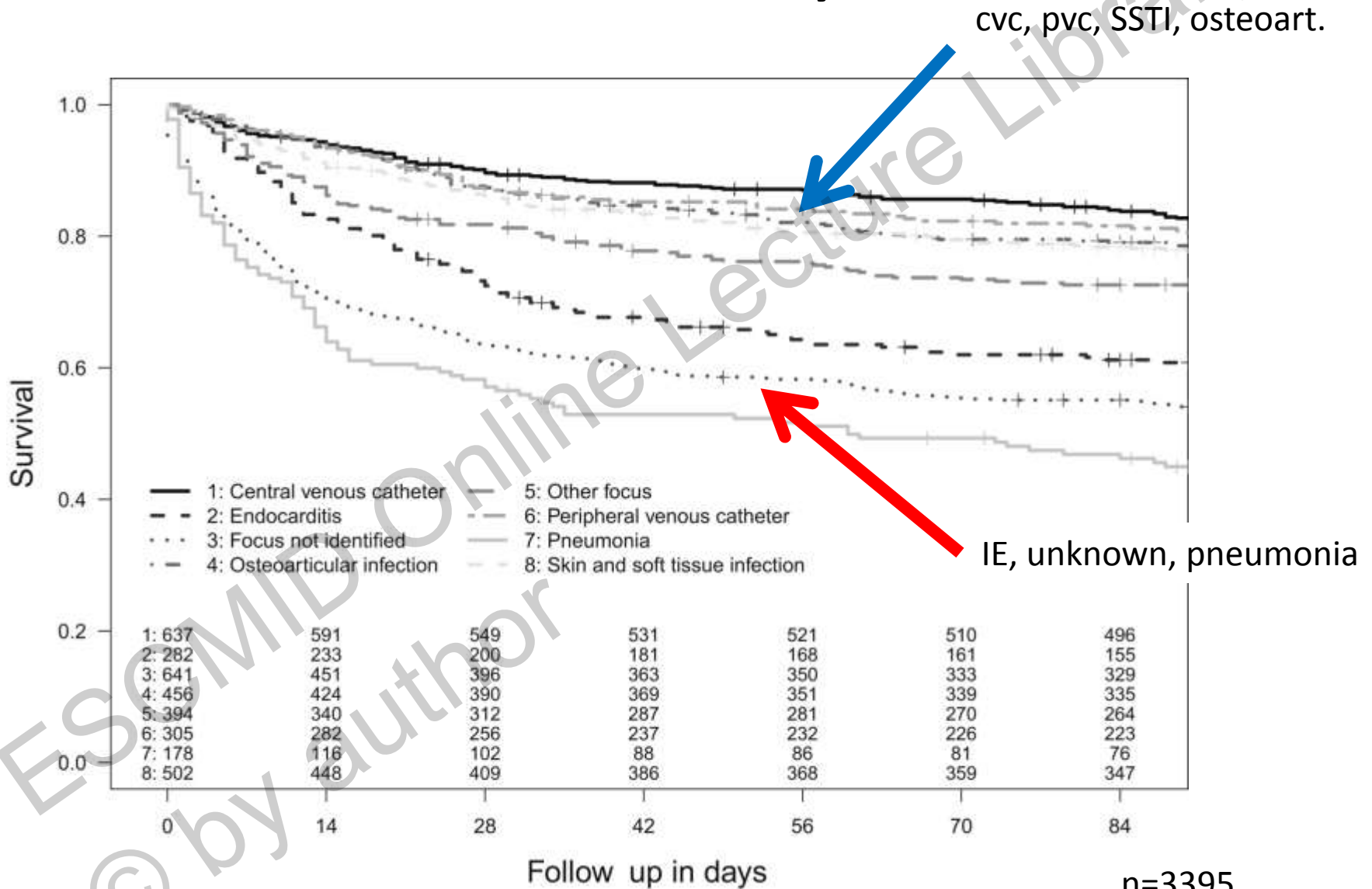
Repeat echocardiography after 7-10 days²

¹ Vos JNM 2010

² Habib EJE 2010

Unidentified focus, what does it mean?

Focus and mortality



n=3395

Kaasch JI 2014

BF 35Hz
12cm

Echokardiographie

S4

2D
63%
K 50
M Aus
Allg



PAT.-T.: 37.0C
TEE-T.: 39.0C

JPEG

92 /min

Diagnosis

Acute infective endocarditis of the aortic valve
with *Staphylococcus aureus* following cardiac
catheterization

Who should we worry about?

- Red flags
 - Persistent bacteremia
 - Retained foreign bodies
 - Deep foci
 - Unidentified focus
- Evaluation
 - Follow-up blood culture
 - Imaging
 - Evaluation by ID team

Acknowledgements

Invasive *Staphylococcus aureus* INfection Cohort (INSTINCT)

Achim J. Kaasch, Harald Seifert, Hanna Birkholz, Katharina Achilles, Andreas Langhorst, Stephan Neumann, Georg Peppinghaus, Nathalie Jazmati, Martin Hellmich, Verena Dlugay (Uniklinik Köln); Siegbert Rieg, Winfried V. Kern, Marc-Fabian Küpper, Gabriele Peyerl-Hoffmann, Christian Theilacker (Freiburg University)

International *S. aureus* collaboration (ISAC)

Alex Soriano, Laura Morata, Josep Mensa, Jose A. Martínez, Manel Almela, Francesc Marco (Hospital Clínic de Barcelona), Jesús Rodríguez-Baño, Luis E. López-Cortés, Juan Gálvez-Acebal, Marina de Cueto, Carmen Velasco, Alvaro Pascual (Hospital Universitario Virgen Macarena, Sevilla), Achim J. Kaasch, Harald Seifert, Hanna Birkholz, Katharina Achilles, Andreas Langhorst, Stephan Neumann, Georg Peppinghaus, Martin Hellmich, Verena Dlugay (Uniklinik Köln); Siegbert Rieg, Winfried V. Kern, Marc-Fabian Küpper, Gabriele Peyerl-Hoffmann, Christian Theilacker (Freiburg University), Vance G. Fowler, Felicia Ruffin, Thomas Rude (Duke University), Cressida Auckland, Stephen Glass, Marina Morgan (Royal Devon and Exeter NHS Foundation Trust); Gavin Barlow, Peter Moss, Tina Burdett (Hull and East Yorkshire Hospitals NHS Trust); Richard Cunningham, Robert Tilley (Plymouth Hospitals NHS Trust); Guy Thwaites, Jonathan Edgeworth, Carolyn Hemsley, John Klein (Guy's and St. Thomas' Hospitals NHS Foundation Trust); Susan Hopkins, Daniel Brudney, Sophie Collier (Royal Free London NHS Foundation Trust); Dakshika Jeyaratnam, Jim Wade, Amanda Fife (King's College Hospital NHS Foundation Trust); Neil Jenkins, Abid Hussein, Melinda Munang (Birmingham Heart of England NHS Foundation Trust); James Price, John Paul, Martin Llewelyn (Brighton and Sussex University Hospitals NHS Trust); Sarah Meisner, Mohammad Abrishami, Rachel Mayer, Susan Murray (Royal United Hospital Bath NHS Trust); Emmanuel Nsutebu, Nicholas Beeching, Jonathan Folb, Chanaka Silva, Andrew Kirby (Royal Liverpool and Broadgreen University Hospitals NHS Trust); Matthew Scarborough, Derrick Crook, Tim Peto, Heather Godwin, Lily O'Connor (Oxford University Hospitals NHS Trust); M. Estée Török, Emma Nickerson, Theodore Gouliouris, Sani Aliyu, Sharon Peacock, (Cambridge University Hospitals NHS Foundation Trust); John Williams (South Tees Hospitals NHS Foundation Trust); Steve Morris-Jones, Philip Gothard, Bruce Macrae, Peter Wilson (University College London Hospitals NHS Foundation Trust); Martin Sheppard (Withybush Hospital, Wales)

ESCMID Online Lecture Library
© by author

Special cases - Immunosuppression

- complicated SAB in central line associated SAB
 - Chemotherapy within 10 days after onset¹ (OR 3.12)
- neutropenia: no difference in mortality²

¹ El Zakhem 2013

² Kang SCC 2012