Bakteriæmiforskning i Region Syd

DSKMs møde om bakteriæmi 31-10-2018

Thøger Gorm Jensen

Områder

- DORIS
  - Bloddyrkninger og bakteriæmier, KMA, OUH 1/1 2000 til 31/12 2008
- Akut kohorten OUH
  - Alle patienter set i akutmodtagelse OUH Odense 1/8 2009 til 31/8 2011
- SydBak
  - Bloddyrkninger og bakteriæmier, Region Syddanmark og Region Sjælland
  - 1/8 2007 til 31/12 2016 (…31/12 2018)
- Anaerobe bakterier & bakteriæmi
- Endocarditis

DORIS

- Bloddyrkninger og bakteriæmier, KMA, OUH 1/1 2000 til 31/12 2008

- Styregruppe
  - Annmarie Lassen FAM, OUH
  - Court Petersen Q , OUH
  - Hans Jørn Kolmos KMA , OUH
  - Thøger Gorm Jensen KMA , OUH

- Tilknyttede
  - Kim Gradel Klinisk Epidemiologisk Afdeling , OUH
  - Stig Lønberg Nielsen Q , OUH
  - Pernille Vinholt KBA , OUH
  - Fredrikke Knutzen Q , OUH
  - Bjarne Magnussen Klinisk Epidemiologisk Afdeling , OUH
  - Jesper Søgaard Christensen Q , OUH

Pneumokok-bakteriæmi

- DORIS: 481 patienter med førstegangs pneumokok-bakteriæmi 2000-2008
- Alder: ≥ 15 år
- Registre: Landspatientregistret, CPR-registret, Manuel journalgennemgang
- 49% mænd, gennemsnitsalder: 65 år
- Fokus
  - pneumoni 79%
  - meningitis 7%
  - knogler, abdomen, øvre luftveje sammenlagt 6%
  - ukendt 34%
- 30-dages mortalitet: 16%

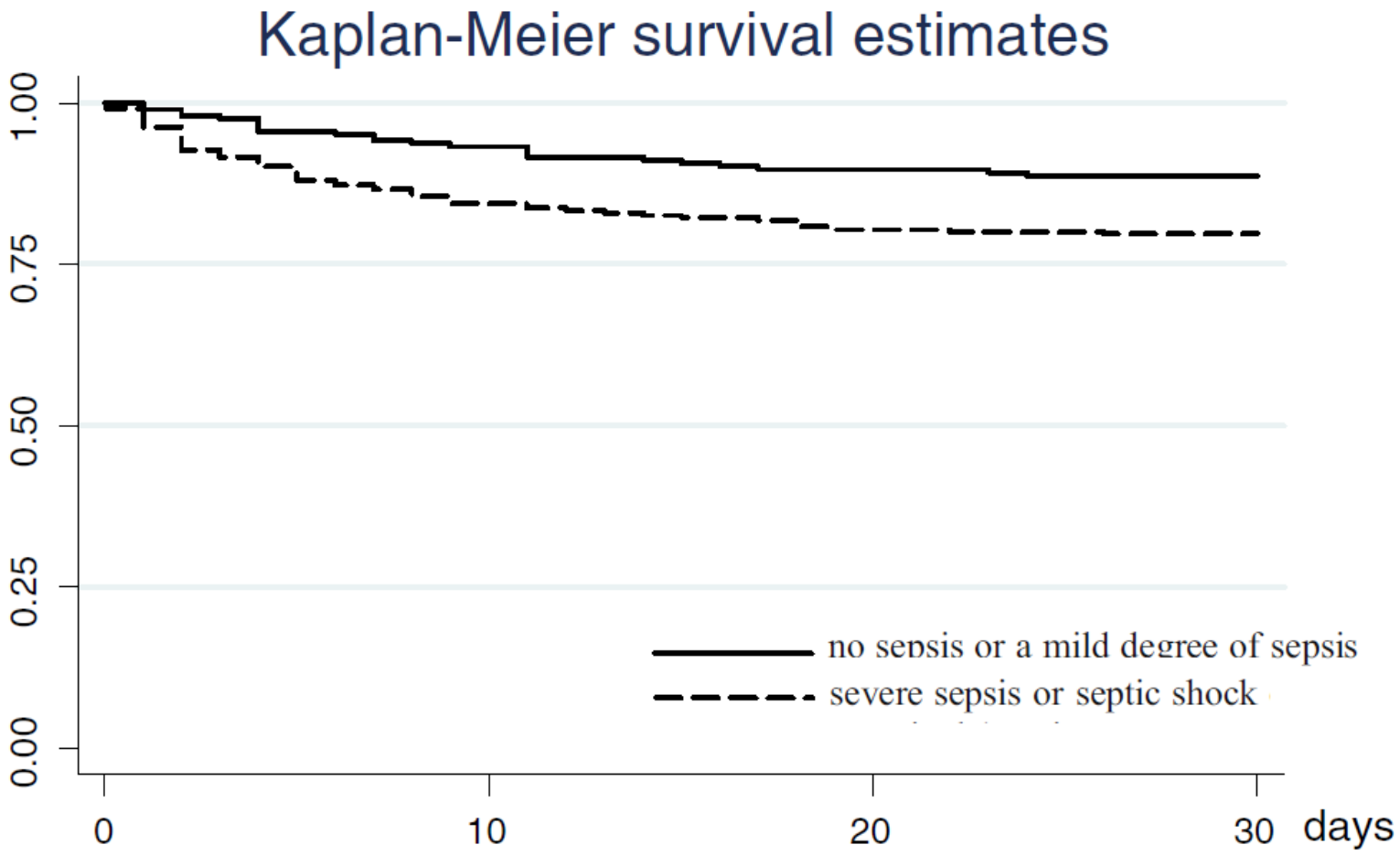
	Multivariat hazard ratio
nosocomiel: 30% , samfundserhvervet 13%	2,0 (1,2-3,2)
mænd: 20%, kvinder: 13%	1,8 (1,1-2,8)
< 60 år: 8%	1
60-79 år: 18%	2,0 (1,0-3,7)
≥ 80 år: 25%	3,7 (1,9-7,5)

- Charlson Comorbidity Index
  - 0-1: 10%
  - ≥ 2: 22%
- Penicillin-følsomhed:
  - følsom: 462 (96%)
  - nedsat følsom: 17 (4%)
  - resistent: 2 (0,4 %)

Bacteremia with Streptococcus pneumoniae: sepsis and other risk factors for 30-day mortality—a hospital-based cohort study
Jesper Søholm Christensen - APMIS 2012

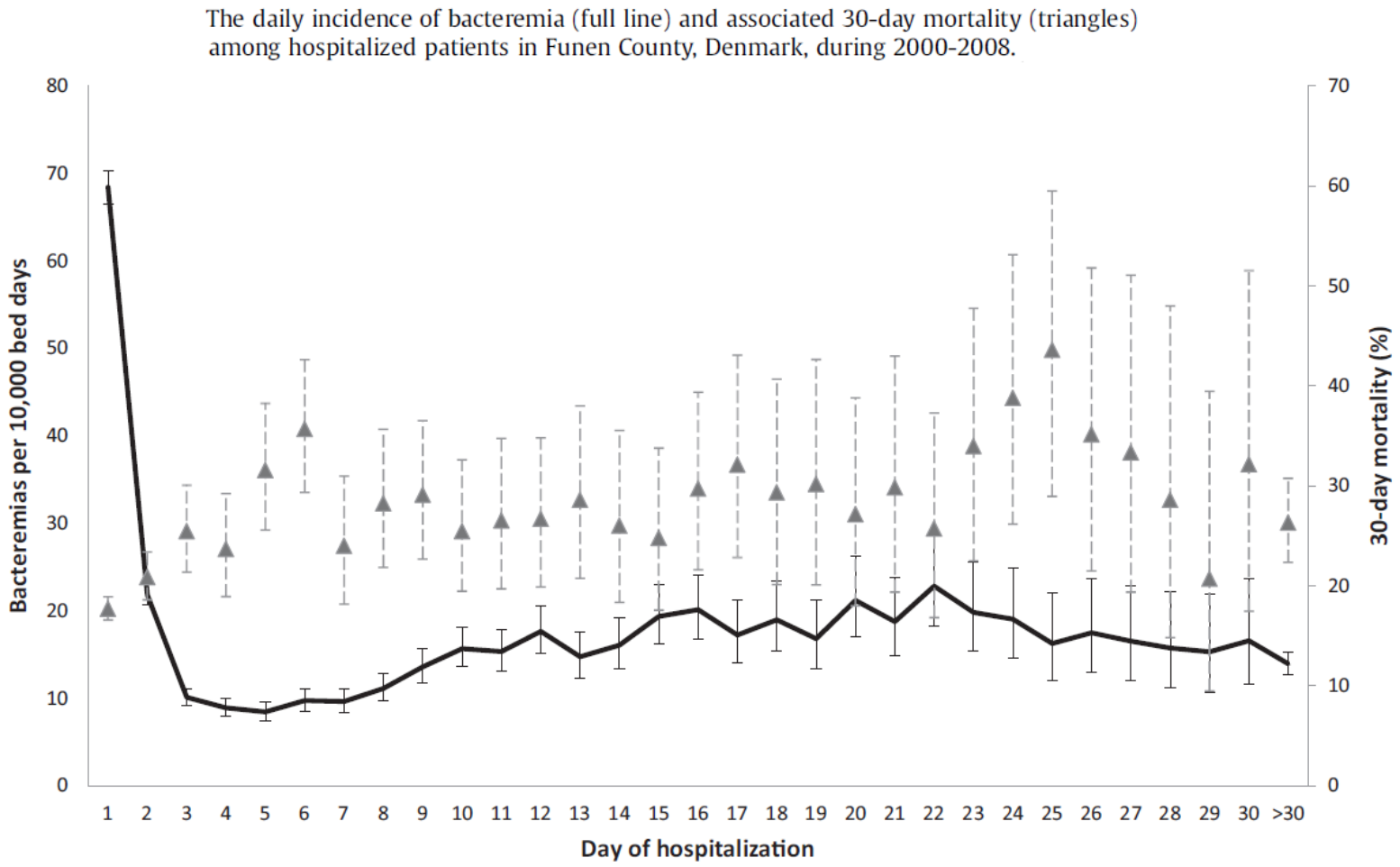
DORIS – Jesper Søholm Christensen

Pneumokok-bakteriæmi



Bacteremia with Streptococcus pneumoniae: sepsis and other risk factors for 30-day mortality—a hospital-based cohort study
Jesper Søholm Christensen - APMIS 2012

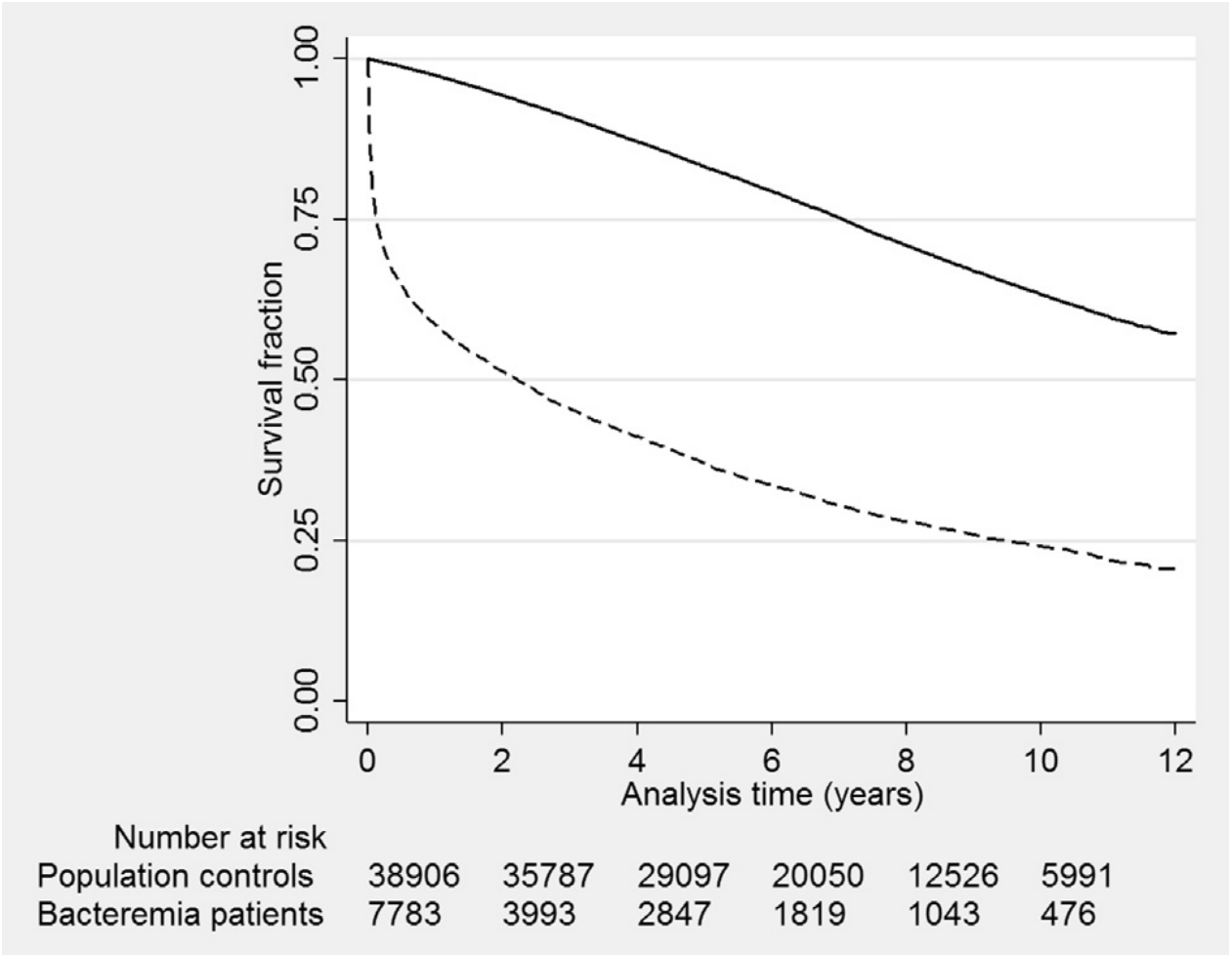
Bakteriæmi og dødelighed under hospitalsindlæggelse



The daily risk of bacteremia during hospitalization and associated 30-day mortality evaluated in relation to the traditional classification of bacteremia

Stig Lønberg Nielsen - American Journal of Infection Control 2015

Bakteriæmi og langtidsdødelighed



Kaplan-Meier survival curves of bacteremia patients (dotted line) and population controls (full line) matched on sex, year of birth, residency, and calendar time during 12 years of follow-up

Bacteremia is associated with excess long-term mortality: A 12-year population-based cohort study
Stig Lønberg Nielsen - Journal of Infection 2014

Bakteriæmi og langtidsdødelighed

- DORIS: 7,783 førstegangsbakteriæmier 2000-2008 og 38,906 populationskontroller
- Alder: ≥ 15 år, bopæl på Fyn
- Registre: Landspatientregistret, CPR-registret, dødsårsagsregistret, cancerregistret, psykiatriregistret og OPED
- Case-control studie (1:5, matchet på køn og årstal for fødsel)
- 54% mænd, medianalder: 72 år (bakteriæmi)
- Dødelig for bakteriæmi-patienter versus populations-kontroller:
  - 30 dage: 22.0% vs. 0.2%
  - 1 år: 41.4% vs. 2.6%
  - 10 år: 75.8% vs. 36.6%
- Hyppigste dødsårsager
  - cancer og cardiovasculær sygdom
- Relativ risiko
  - indenfor 1 år: genitourinary sygdomme og infektionssygdomme
  - efter 1 år: øget for alle større dødsårsager

The daily risk of bacteremia during hospitalization and associated 30-day mortality evaluated in relation to the traditional classification of bacteremia
Stig Lønberg Nielsen - American Journal of Infection Control 2015

DORIS – Kim Gradel

Årstidsvariation af bakteriæmier

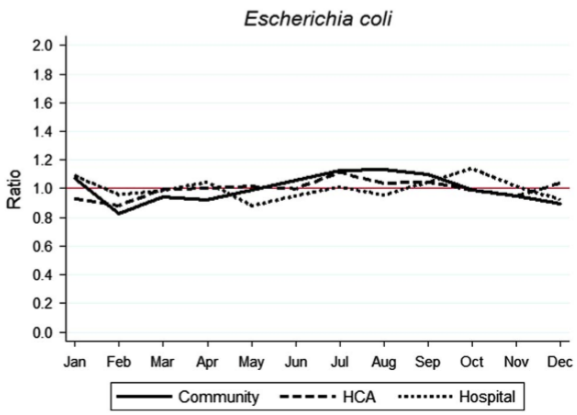


FIGURE 1. Monthly ratios (smoothed number of monthly observations divided by the mean monthly smoothed number) for *Escherichia coli* bacteremia, according to acquisition. HCA, health-care associated.

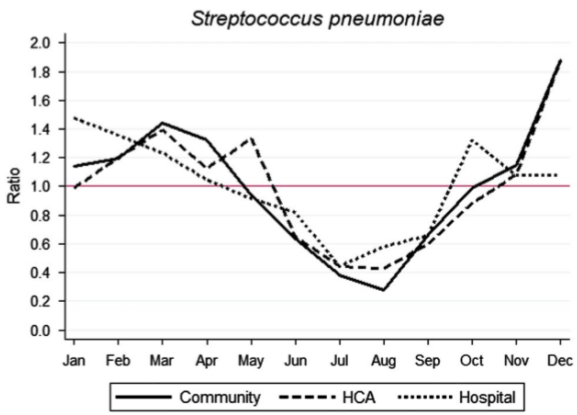


FIGURE 3. Monthly ratios (smoothed number of monthly observations divided by the mean monthly smoothed number) for *Streptococcus pneumoniae* bacteremia, according to acquisition. HCA, health-care associated.

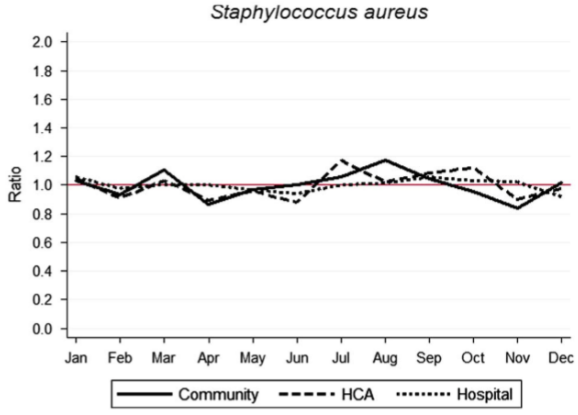


FIGURE 2. Monthly ratios (smoothed number of monthly observations divided by the mean monthly smoothed number) for *Staphylococcus aureus* bacteremia, according to acquisition. HCA, health-care associated.

Seasonal Variation of Escherichia coli, Staphylococcus aureus, and Streptococcus pneumoniae Bacteremia According to Acquisition and Patient Characteristics: A Population-Based Study. Kim Gradel - Infection Control & Hospital Epidemiology 2016

Årstidsvariation af bakteriæmier

- DORIS (2000-2008) og DACOBAN (2000-2011):
  - 16.006 E.coli bacteremia cases
  - 6.924 S.aureus bacteremia cases
  - 4.884 S.pneumoniae bacteremia cases
- Alder: ≥ 15 år
- Registre: MADS OUH, ADBakt Aalborg, Herlev, Hvidovre
- Inddeling:
  - Samfundserhvervet 14.736 (53%)
  - Hospitalsassocieret 6.106 (22%) Indlagt eller ambulatoriebesøg indenfor 1 måned
  - Nosocomiel 6.972 (25%) Bakteriæmi efter 48 timers indlæggelse

- Model: Sinusvariation hen over året. Peak-to-through ratio.

- E. coli: Nogen sæsonvariation (PTT 1,17), stærkest for samfundserhvervede, mindre for Hospitalsassocierede og manglede for nosocomielle. Peak i august/september.
- S. pneumoniae: Kraftig sæsonvariation (PTT 3,42) uafhængig af erhvervelse. Peak i februar
- S. aureus: Ingen sæsonvariation.

Seasonal Variation of Escherichia coli, Staphylococcus aureus, and Streptococcus pneumoniae Bacteremia According to Acquisition and Patient Characteristics: A Population-Based Study. Kim Gradel - Infection Control & Hospital Epidemiology 2016

DORIS – Bjarne Magnussen

Hypoalbumin – Associationen med mortalitet er primært relateret til den akutte tilstand

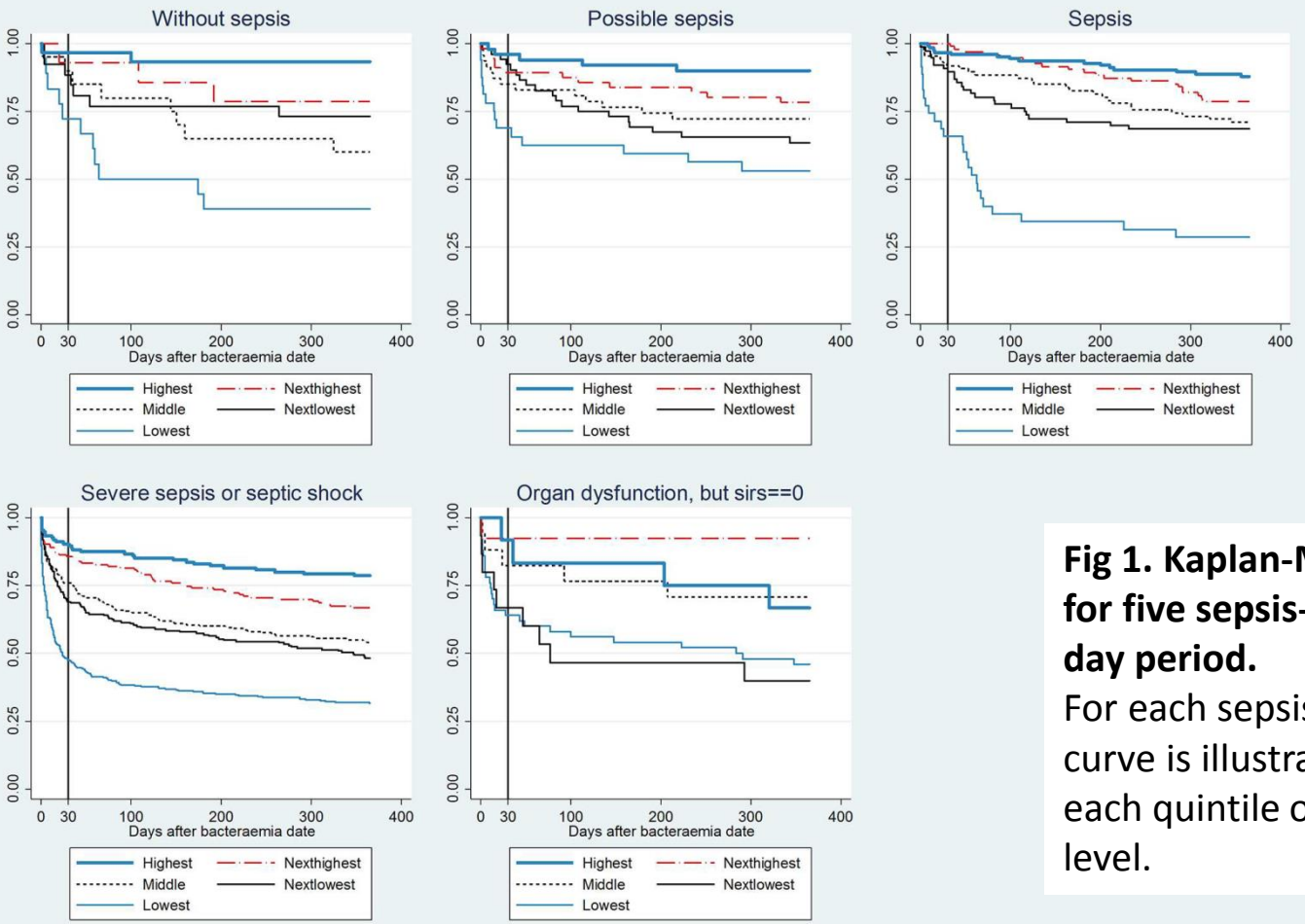
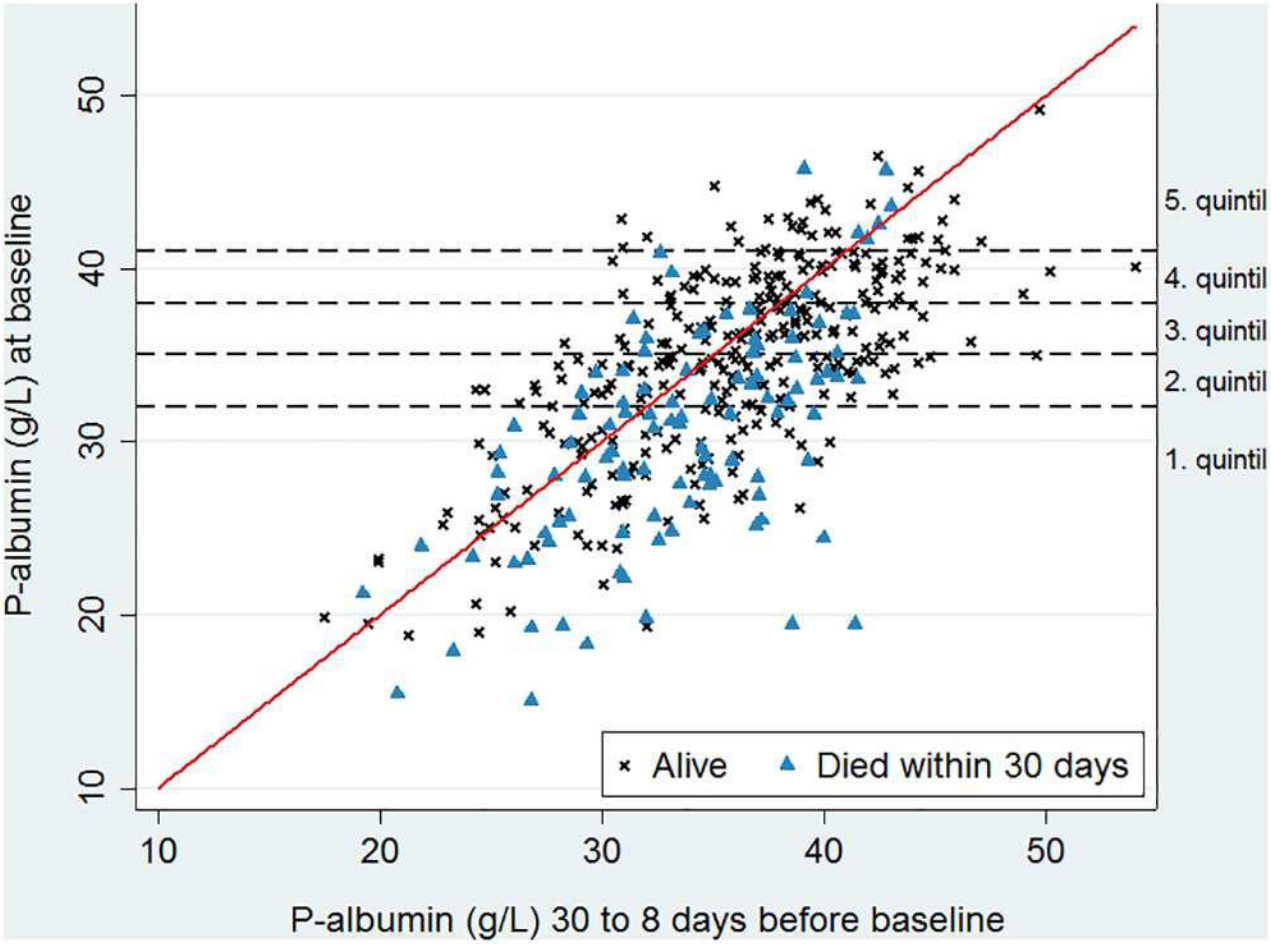


Fig 1. Kaplan-Meier survival curves for five sepsis-groups in the 0–365-day period.
For each sepsis group, a separate curve is illustrated for each quintile of the serumalbumin level.

Association between Hypoalbuminaemia and Mortality in Patients with Community-Acquired Bacteraemia Is Primarily Related to Acute Disorders. Bjarne Magnussen - PLOSone 2016

DORIS – Bjarne Magnussen

Hypoalbumin – Associationen med mortalitet er primært relateret til den akutte tilstand



The x-axis depicts the last measured albumin level in the 8–30-day period and the y-axis depicts the albumin level on the bacteraemia date.

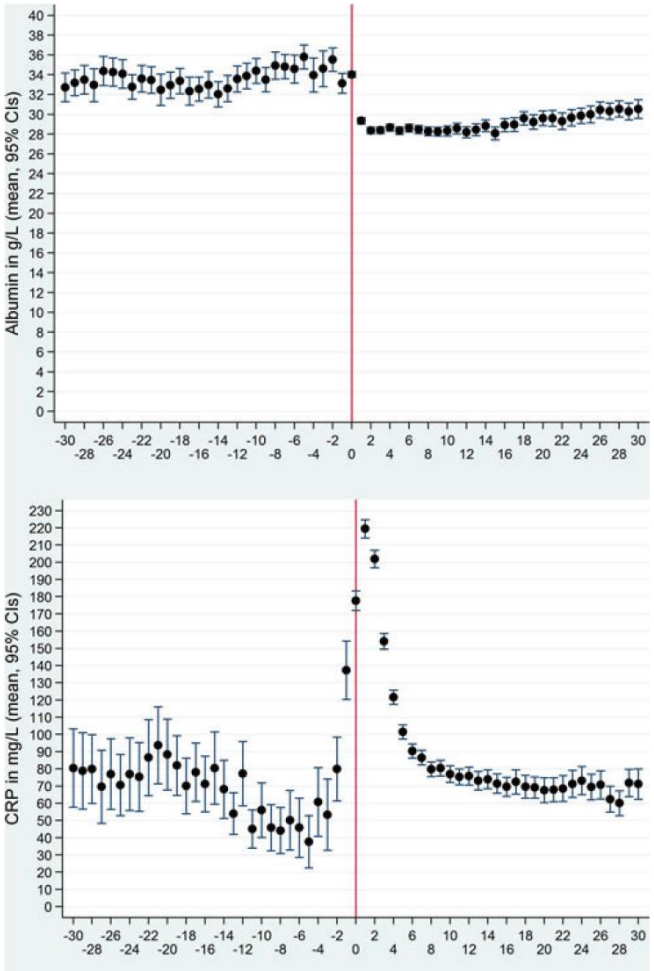
Dots below the diagonal line represent patients with a decline in the albumin level between the last measurement in the 8–30-day period and the measurement on the bacteraemia date, whereas dots above that line represent a corresponding increase in the PA level.

Data for patients, who remained alive 30 days after the bacteraemia date, are represented by crosses, while triangles indicate data for patients who died within 0–30 days after the bacteraemia date.level.

Scatter plot of plasma albumin (PA) levels for 422 patients who had one or more PA measurements in the period from 8–30 days before the bacteraemia date.

Association between Hypoalbuminaemia and Mortality in Patients with Community-Acquired Bacteraemia Is Primarily Related to Acute Disorders. Bjarne Magnussen - PLOSone 2016

Hypoalbumin – akutfase markør for transkapillær lækage



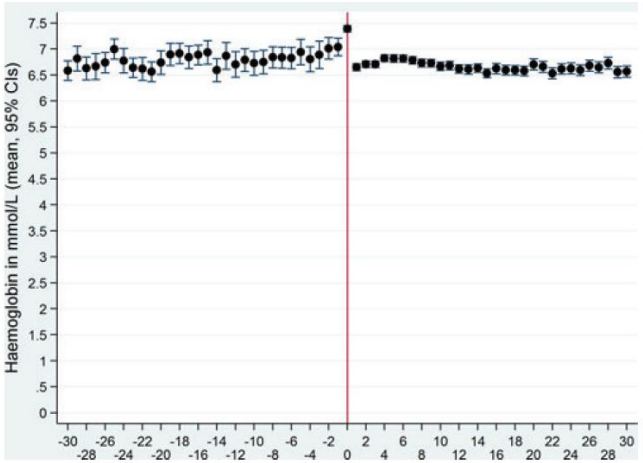


Fig. 2. Mean levels and their 95% confidence intervals of plasma albumin (upper panel), C-reactive protein (middle panel) and haemoglobin (lower panel) from 30 days before through 30 days after the date of bacteraemia (day 0, marked by vertical red line).

Hypoalbuminaemia as a marker of trans-capillary leakage in community-acquired bacteraemia patients. Kim Oren Gradel - Epidemiology and Infection 2018

DORIS

- Bakteriæmi og epidemiologi
  - Bacteremia with Streptococcus pneumoniae: sepsis and other risk factors for 30-day mortality—a hospital-based cohort study. Jesper Søholm Christensen - APMIS 2012
  - The daily risk of bacteremia during hospitalization and associated 30-day mortality evaluated in relation to the traditional classification of bacteremia. Stig Lønberg Nielsen - American Journal of Infection Control 2015
  - The daily risk of bacteremia during hospitalization and associated 30-day mortality evaluated in relation to the traditional classification of bacteremia. Stig Lønberg Nielsen - American Journal of Infection Control 2015
  - Decreasing incidence rates of bacteremia: A 9-year population-based study. Stig Lønberg Nielsen - Journal of Infection 2014

- CRP, S-albumin og bakteriæmi
  - Characteristics of patients with community-acquired bacteremia who have low levels of C-reactive protein (20 mg/L) Fredrikke Christie Knudtzen - Journal of Infection 2014
  - Association between Hypoalbuminaemia and Mortality in Patients with Community-Acquired Bacteraemia Is Primarily Related to Acute Disorders. Bjarne Magnussen - PLOSone 2016
  - Hypoalbuminaemia as a marker of trans-capillary leakage in community-acquired bacteraemia patients. Kim Oren Gradel - Epidemiology and Infection 2018

- DORIS og DACOBAN
  - No Specific Time Window Distinguishes between Community-, Healthcare-, and Hospital-Acquired Bacteremia, but They Are Prognostically Robust Kim Oren Gradel - Infection control and hospital epidemiology 2014
  - Low Completeness of Bacteraemia Registration in the Danish National Patient Registry Kim Oren Grade PLOSone 2015
  - Seasonal Variation of Escherichia coli, Staphylococcus aureus, and Streptococcus pneumoniae Bacteremia According to Acquisition and Patient Characteristics: A Population-Based Study Kim Oren Gradel - Infection control & hospital epidemiology 2016

Akut kohorten og bakteriæmi

- Alle patienter set i akutmodtagelse OUH Odense 1/8 2009 til 31/8 2011

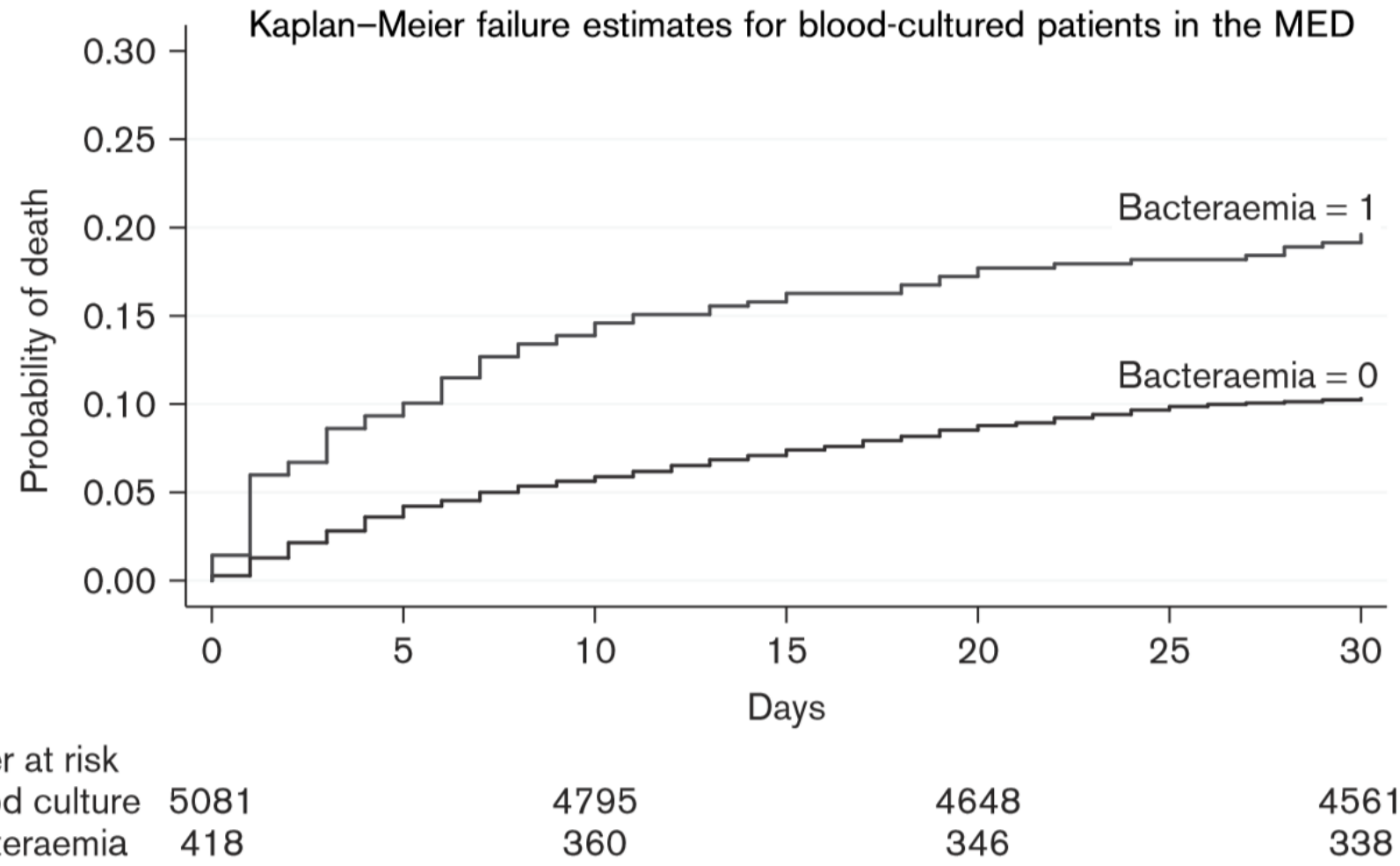
- Bakteriæmi og epidemiologi
  - Mortality and prognostic factors of patients who have blood cultures performed in the emergency department: a cohort study. Katrine P. Lindvig - European Journal of Emergency Medicine 2015

- CRP, S-albumin og bakteriæmi
  - How do bacteraemic patients present to the emergency department and what is the diagnostic validity of the clinical parameters; temperature, C-reactive protein and systemic inflammatory response syndrome? Katrine Prier Lindvig - Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2014

- Sepsis
  - Incidence Rate of Community-Acquired Sepsis Among Hospitalized Acute Medical Patients—A Population-Based Survey. Daniel Pilsgaard Henriksen - Critical Care Medicine 2014
  - Risk Factors for Hospitalization Due to Community-Acquired Sepsis – A Population-Based Case-Control Study. Daniel Pilsgaard Henriksen PLOSone 2014
  - Intermediate-term and long-term mortality among acute medical patients hospitalized with community-acquired sepsis: a population-based study Daniel P. Henriksen - European Journal of Emergency Medicine 2016

Akut kohorte – Katrine P. Lindvig

Mortalitet og prognostiske faktorer



Mortality and prognostic factors of patients who have blood cultures performed in the emergency department: a cohort study
Katrine P. Lindvig - European Journal of Emergency Medicine 2015

Akut kohorte – Katrine P. Lindvig

Mortalitet og prognostiske faktorer

Table 3 Prognostic factors among emergency medical patients with blood cultures

Total	Patients alive within 30 days [*n* (%)]	Patients dead within 30 days [*n* (%)]	Crude hazard ratio (95% CI)	Multivariate COX hazard ratio (95% CI)
Bacteraemia				
No (5081)	4556 (89.7)	525 (10.3)	2.0 (1.6–2.6)	1.0
Yes (418)	336 (80.4)	82 (19.6)		1.4 (1.1–1.8)
Sex				
Female (2868)	2573 (89.7)	295 (10.3)	1.1 (0.9–1.4)	1.0
Male (2631)	2319 (88.1)	312 (11.9)		1.1 (0.9–1.2)
Age				
15–64 (2357)	2263 (96.0)	94 (4.0)	2.2 (2.0–2.5)	1.0
65–79 (1527)	1343 (88.0)	184 (12.0)		2.4 (1.9–3.2)
>80 (1615)	1286 (79.6)	329 (20.4)		4.6 (3.6–6.0)
Charlson comorbidity index				
0 (2258)	2120 (93.9)	138 (6.1)	1.7 (1.5–1.9)	1.0
1 (1226)	1098 (89.6)	128 (10.4)		1.1 (0.9–1.4)
≥2 (2015)	1674 (83.1)	341 (16.9)		1.7 (1.3–2.0)
Immune compromised				
No (4714)	4218 (89.5)	496 (10.5)	1.4 (1.1–1.7)	1.0
Yes (785)	674 (85.9)	111 (14.4)		1.1 (0.9–1.4)
SIRS				
No SIRS (2449)	2254 (92.0)	195 (8.0)	1.8 (1.5–2.1)	1.0
SIRS (3050)	2638 (86.5)	412 (13.5)		1.5 (1.2–1.7)
Organ failure				
0 failure (3013)	2834	179 (5.6)	2.4 (2.1–2.6)	1.0
1 failure (1722)	1512	210 (10.9)		1.6 (1.3–1.9)
≥2 failures (764)	546	218 (22.2)		3.6 (2.9–4.5)
Alcohol use				
No (4954)	4423 (89.3)	531 (10.7)	1.3 (1.0–1.7)	1.0
Yes (531)	458 (86.2)	73 (13.8)		1.7 (1.3–2.3)
Timing of blood cultures				
Day 0 (0–24 h) (4930)	4413 (89.5)	517 (10.5)	1.4 (1.1–1.6)	1.0
Day 1 (24–48 h) (463)	389 (84.0)	74 (16.0)		1.7 (1.3–2.2)
Day 2 (48–72 h) (106)	90 (84.9)	16 (15.1)		1.6 (0.9–2.5)

CI, confidence interval.
Prognostic factors among blood-cultured patients in the Medical Emergency Department, total $n=5499$. Patients alive within 30 days, $n=4892$. Patients dead within 30 days, $n=607$.

Mortality and prognostic factors of patients who have blood cultures performed in the emergency department: a cohort study
Katrine P. Lindvig - European Journal of Emergency Medicine 2015

Anaerobe bakterier og bakteriæmi

- Resistens (i samarbejde med KMA Skejby, KMA i hele DK og ESCMID resp.)
  - Characterisation of a multidrug-resistant Bacteroides fragilis isolate recovered from blood of a patient in Denmark using whole-genome sequencing. Ank N et al Int J Antimicrob Agents. 2015 Jul;46(1):117-20
  - Identification of antimicrobial resistance genes in multidrug-resistant clinical Bacteroides fragilis isolates by whole genome shotgun sequencing. Sydenham TV et al, ESGAI (ESCMID Study Group on Anaerobic Infections). Anaerobe. 2015 Feb;31:59-64.
  - High rates of reduced susceptibility in the Bacteroides fragilis group isolated from blood cultures--the first national survey in Denmark. Justesen US et al. Int J Antimicrob Agents. 2013 Aug;42(2):188-90.

- Kasuistikker og nye species
  - Four cases of bacteremia caused by Oscillibacter ruminantium, a newly described species. Sydenham TV et al Clin Microbiol. 2014 Apr;52(4):1304-7.
  - Two cases of Ruminococcus gnavus bacteremia associated with diverticulitis. Hansen SG et al. J Clin Microbiol. 2013 Apr;51(4):1334-6.
  - Bacteremia with Bacteroides pyogenes after a cat bite. Madsen IR, Justesen US. J Clin Microbiol. 2011 Aug;49(8):3092-3.
  - Solobacterium moorei bacteremia: identification, antimicrobial susceptibility, and clinical characteristics. Pedersen RM et al. J Clin Microbiol. 2011 Jul;49(7):2766-8.
  - Draft Genome Sequences of Sanguibacteroides justesenii, gen. nov., sp. nov., Strains OUH 308042T (= ATCC BAA-2681T) and OUH 334697 (= ATCC BAA-2682), Isolated from Blood Cultures from Two Different Patients. Sydenham TV et al. Genome Announc. 2015 Mar 26;3(2)
  - Draft Genome Sequence of "Terrisporobacter othiniensis" Isolated from a Blood Culture from a Human Patient. Lund LC et al. Genome Announc. 2015 Mar 5;3(2).

Endocarditis

- Region Syddanmark
  - A novel in vitro model for haematogenous spreading of S. aureus device biofilms demonstrating clumping dispersal as an advantageous dissemination mechanism. Grønnemose RB et al. Cell Microbiol. 2017 Dec;19(12).
- Region Syddanmark og Region Sjælland
  - Species identification of Streptococcus bovis group isolates causing bacteremia: a comparison of two MALDI-TOF MS systems. Agergaard CN et al. Diagn Microbiol Infect Dis. 2017 May;88(1):23-25
  - Bacteremia with the bovis group streptococci: species identification and association with infective endocarditis and with gastrointestinal disease. Marmolin ES et al. Diagn Microbiol Infect Dis. 2016 Jun;85(2):239-42
- Nationalt
  - In silico assessment of virulence factors in strains of Streptococcus oralis and Streptococcus mitis isolated from patients with Infective Endocarditis. Rasmussen LH et al. J Med Microbiol. 2017 Sep 6.
  - Whole genome sequencing as a tool for phylogenetic analysis of clinical strains of Mitis group streptococci. Rasmussen LH et al. Eur J Clin Microbiol Infect Dis. 2016 Oct;35(10):1615-25.
  - Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis. Iversen K et al. N Engl J Med. 2018 Aug 28.
  - Whole-genome sequencing of bloodstream Staphylococcus aureus isolates does not distinguish bacteraemia from endocarditis. Lilje B et al. Microb Genom. 2017 Nov;3(11).
  - Prevalence of infective endocarditis in patients with Staphylococcus aureus bacteraemia: the value of screening with echocardiography. Rasmussen RV et al. Eur J Echocardiogr. 2011 Jun;12(6):414-20.

SydBak

- Styregruppe
  - Court Petersen Q
  - Stig Lønberg Nielsen Q
  - Kim Gradel Klinisk, Epidemiologisk Afdeling
  - Ram Dessau KMA Slagelse
  - Jens Kjølseth Møller, KMA SLB
  - Esad Dzajic, KMA SVS
  - Steen Lomborg Andersen, KMA SLB
  - Thøger Gorm Jensen KMA OUH
- Tilknyttede
  - Ulrik Justesen, KMA OUH
  - Anne Marie Rosendahl Madsen, KMA SLB
  - Thilde Fabricius Q
  - Isik Somuncu Johansen Q

SydBak

		Personer	Prøver	Episoder
Grunddata	Undersøgte	321.684	1.153.088	
Fund	Positive kolber	50.669	101.615	
	Ej forurening	40.150	83.963	
	Episoder_species	40.150		53.831
	første_episode	40.150		50.663
	Episoder_speciesuafhængigt	40.150		47.282
	første_episode	40.150		40.150

Hvem bliver førsteforfatter?

Hvordan uddanner vi bedst de kommende forskere?

	Opgørelsesniveau			
Førsteforfatter	**OUH/SDU**	**Tværregionalt**	**Internationalt**	**Hovedtotal**
Studerende	4			4
Yngre læge	7	3		10
ph.d.-studerende	7	2	1	10
Seniorforsker	1	7		8
Hovedtotal	**19**	**12**	**1**	**32**
Yngre forsker	18/19 = 95%			
Seniorforsker		7/12 = 58%		