

# Long term consequences of severe infections

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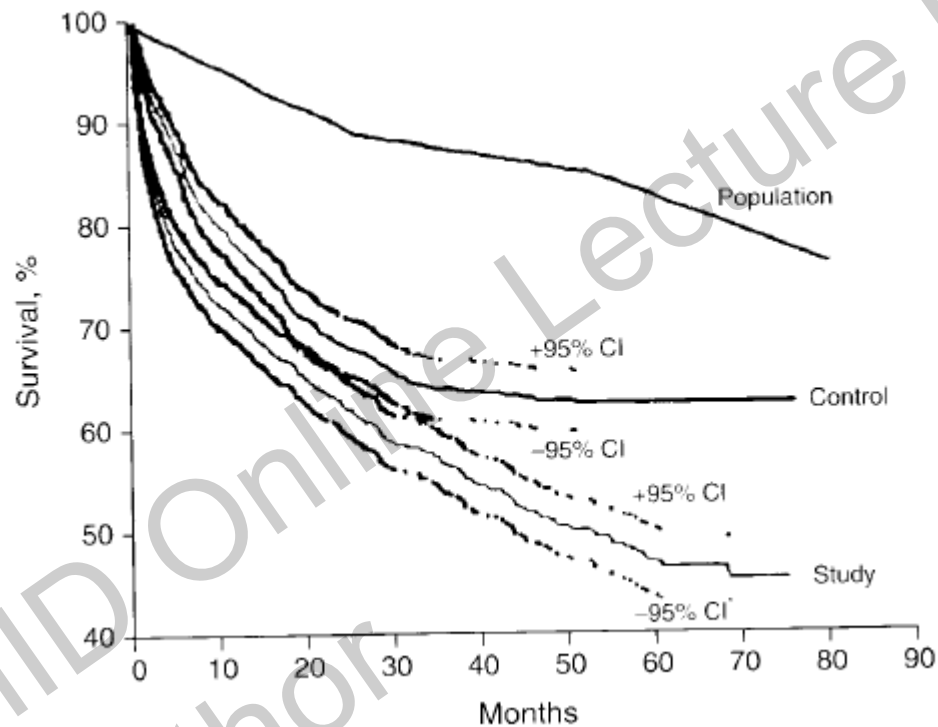
Conflict of interest: Nothing to declare

# Outline:

- Long –term consequences
- Possible explanations
- Implications for research
- Practical implications

# Long-term consequences, survival:

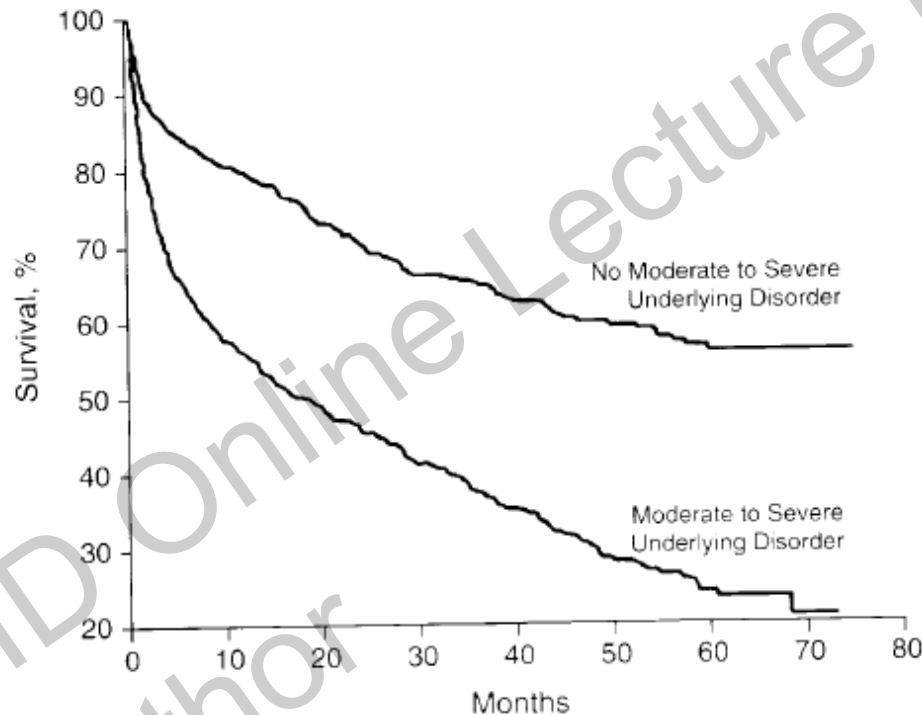
(i) Bacteremia (n=1991), 1-month survivors



Leibovici L et al. JAMA 1995; 274:807-12

# Long-term consequences, survival:

(ii) Bacteremia (n=1991), 1-month survivors



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# Long-term consequences, survival:

(i) Bacteremia (n=1991), 1-month survivors

Table 4.—Variables Significantly Associated With Early Mortality in 1-Month Survivors of Bacteremia on a Multivariable Log Rank Test<sup>a</sup>

Variable	$\chi^2$ Increment	P for Increment
Functional class	131.8	<.001
Malignancy	45.0	<.001
Quartiles of serum albumin	18.0	<.001
Quartiles of age	14.9	<.001
Congestive heart failure	11.7	<.001
Inappropriate empiric antibiotic treatment	11.6	<.001
Atherosclerotic heart disease	7.6	<.001
Quartiles of serum creatinine	4.1	.04
Pathogen	2.8	.09
Shock	2.7	.1
Sex	2.6	.1

<sup>a</sup>The  $\chi^2$  for the whole model = 252 (df=11);  $P<.001$ .

# Long-term consequences, survival:

(iii) Community acquired bacteraemia  
(n=2448)

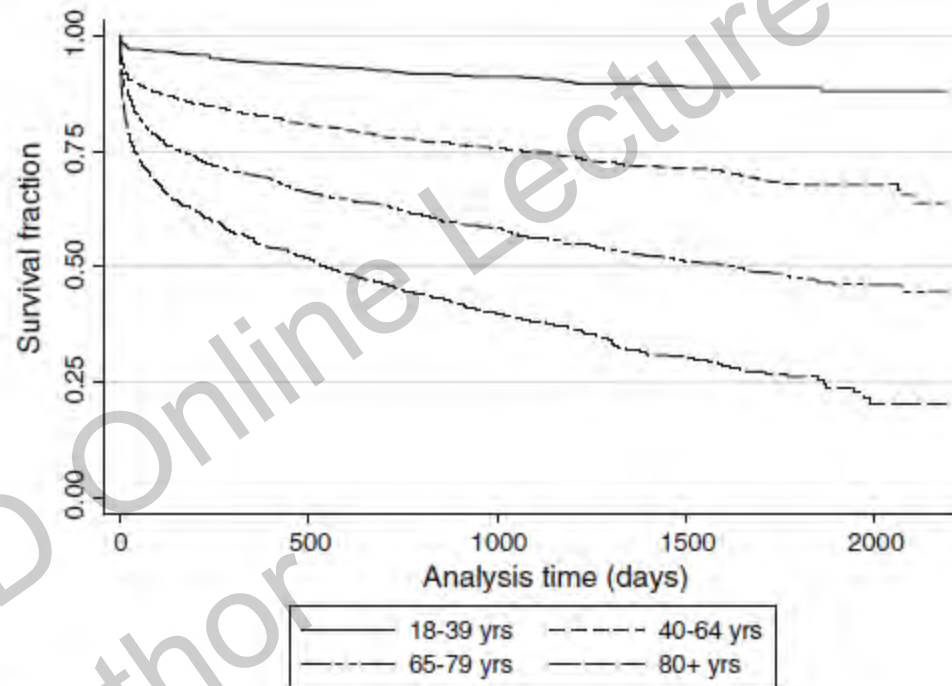
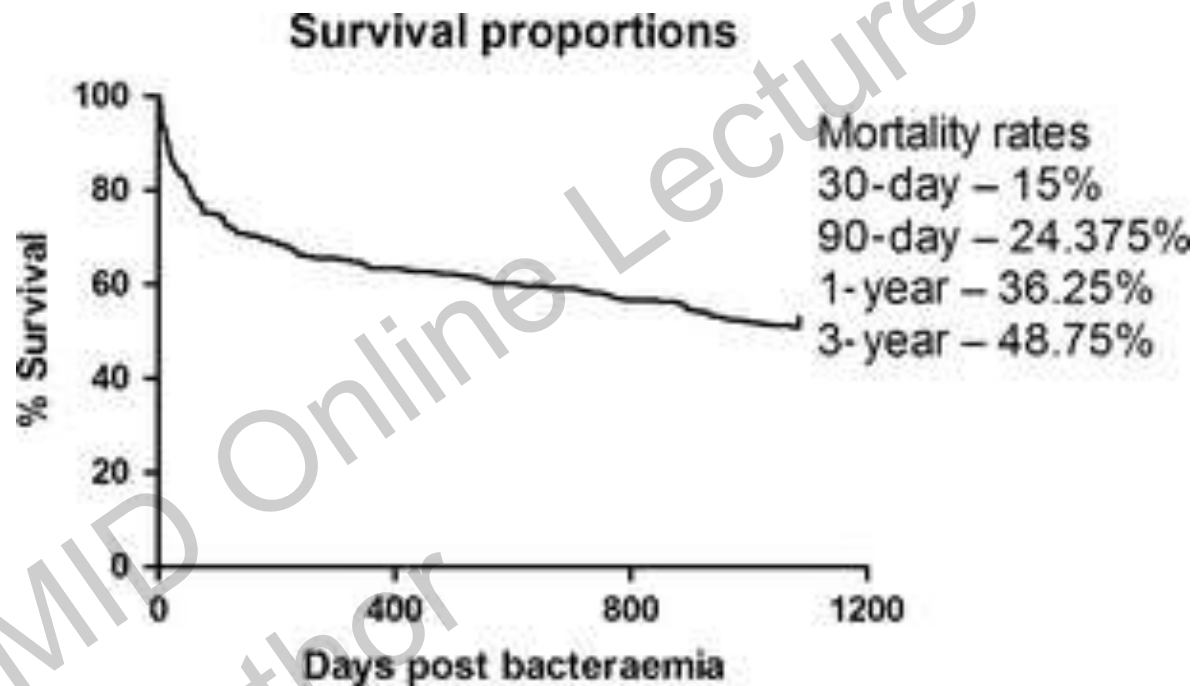
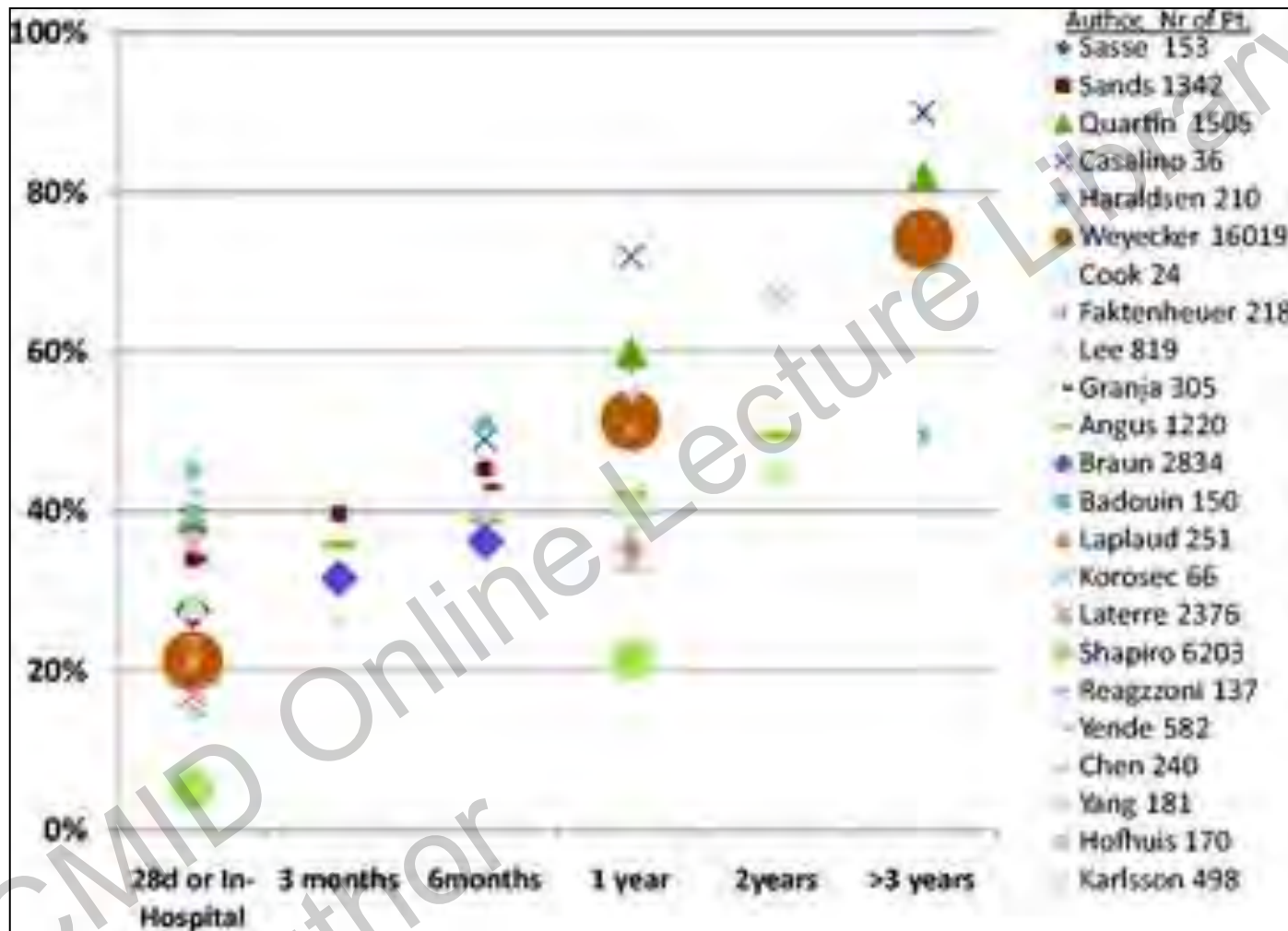


Fig. 1 Long-term survival of patients by age group following community-onset bloodstream infection

## Long-term consequences, survival:

(iv) Bacteraemia (n=322)





Long-term mortality and quality of life in sepsis: A systematic review \*.  
 Winters, Bradford; MD, et al.  
 Critical Care Medicine. 38(5):1276-1283, May 2010.

Figure 2. Total mortality over time for 23 studies providing at least two mortality time points.



# Long –term consequences:

- Long term decrements in sepsis patients' QoL scores compared to population norms (Winters BD et al. Crit Care Med 2010;38:1276-83).
- Lower BMI than controls, or then expected from their own pre-sepsis trajectory (Iwashyna TJ et al. Am J Respir Crit Care Med 2012; 185:835-41).
- Cognitive impairment increased from 6% before the sepsis to 17% after severe sepsis, deterioration higher than in patients hospitalized for other reasons (Iwashyna TJ et al. JAMA 2010;27;304:1787-94).
- Long term significant deterioration in functions of daily living (idem).
- High medical care charges for the years following sepsis (Weycker D et al. Crit Care Med 2003;31:2316-23).

# Three explanations (or a combination of the three):

- Sepsis usually happens in the elderly and sick, and it causes deterioration in life expectancy and functional status as an acute, non-specific event.
- There is an interaction between specific mechanisms of sepsis and underlying disorders.
- The long term consequences are mainly due to long term complications directly related to infection: e.g. metastatic infections; or late infections with resistant pathogens or with fungi; or *Clostridium difficile* infections.

# A few indications that the infection and its management might have influence on long term outcomes:

- Survival curves for patients given appropriate antibiotic treatment continues to diverge from these of patients given inappropriate treatment even after months.
- Idem for different pathogens.
- Long term survival is curtailed even in patients with no moderate to severe underlying disorders.
- Long term survival is influenced by the severity of the original sepsis.
- Cognitive impairment (compared with controls) was observed in children as well as in adults or old people.
- During one year 9% of patients with an episode of bacteraemia had a recurrent episode. Recurrent bacteraemia was associated with a higher risk for 1-year mortality (Jensen US et al. *Clin Microbiol Infect* 2011; 17:1148-54).

# Implications for research: prospective observational studies (i)

- Which sepsis-related factors influence long term outcomes?
  - Severity of sepsis?
  - Specific organ failure?
  - Specific pathogens or sources of infection?
  - interactions with underlying disorders?
- Which management-related factors influence long term outcomes?
  - Antibiotic treatment: appropriate and early empirical treatment; type of antibiotic; duration?
  - Hemodynamic support?
  - Psychoactive drugs or others?
  - Hypo or hyperglycaemia?

# Implications for research: prospective observational studies (ii)

- Which long term consequences of the infection itself might influence long term outcome?
  - Late presentation of metastatic foci of infection?
  - Subsequent fungal infections or infections with resistant pathogens?
  - *Clostridium difficile* colitis or other antibiotic associated diarrhea?

# Implications for research: randomized controlled trials

- The investigation of long term outcomes in trials of treatment modalities for sepsis or severe infections should be encouraged.
- Albeit the added expenses, the true answer whether one treatment is better than another in severe infections or sepsis, especially in elderly people, lies in the people trajectory in the year following the infection, and not only in 4-6 weeks outcome.

# Practical implications:

- Elderly survivors of severe infections should be carefully assessed whether they need intermediate care for recuperation and re-conditioning when leaving the hospital.
- Survivors of sepsis are a large and growing group, and the additional resources demanded to take care of long-term consequences of sepsis should be explicitly taken into account.

# Thank you

