



Zakaj bolniki s sepso umirajo?

Prof. dr. Matjaž Jereb, dr. med.

Klinika za infekcijske bolezni in vročinska stanja, UKCL

Katedra za infektologijo in epidemiologijo, MF, UL



WORLD SEPSIS DAY INFOGRAPHICS



A GLOBAL HEALTH CRISIS



47 000 000 - 50 000 000
cases per year



At least 11 000 000 die
- 1 death every 2.8 seconds



Survivors may face
lifelong consequences



1 in every 5 deaths worldwide
is associated with sepsis



Global
Sepsis
Alliance

www.worldsepsisday.org
www.global-sepsis-alliance.org

September | World
13 | Sepsis
2020 | Day

WORLD SEPSIS DAY INFOGRAPHICS



POST-SEPSIS SYMPTOMS

Sepsis Does Not End at Hospital Discharge



Sadness



Difficulty Swallowing



Muscle Weakness



Clouded Thinking



Difficulty Sleeping



Poor Memory



Difficulty Concentrating



Fatigue



Anxiety



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Sepsa - zdravljenje



Protimikrobno zdravljenje

Bolezen	Smrtnost pred antibiotiki (%)	Smrtnost v dobi antibiotikov (%)	Razlike v preživetju(%)
Doma pridobljena pljučnica	~35	~10	~25
Bolnišnična pljučnica	~60	~30	~30
Infekcijski endokarditis	~100	~25	~75
Okužbe kože in mehkih tkiv	~11	~0,5	~10

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021

Critical Care Medicine



Initial Resuscitation

Recommendations

4. Sepsis and septic shock are medical emergencies, and we **recommend** that treatment and resuscitation begin immediately.

Best practice statement.

5. For patients with sepsis induced hypoperfusion or septic shock we **suggest** that at least 30 mL/kg of IV crystalloid fluid should be given within the first 3 hours of resuscitation.

Weak recommendation, low-quality evidence.

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021



Vasoactive Agents

Recommendations

37. For adults with septic shock, we **recommend** using norepinephrine as the first-line agent over other vaso-pressors. *Strong recommendation*
38. For adults with septic shock on norepinephrine with inadequate MAP levels, we **suggest** adding vasopressin instead of escalating the dose of norepinephrine. *Weak recommendation, moderate-quality evidence.*
39. For adults with septic shock and inadequate MAP levels despite norepinephrine and vasopressin, we **suggest** adding epinephrine. *Weak recommendation, low-quality evidence.*

Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021

Critical Care Medicine



Time to Antibiotics

Recommendations

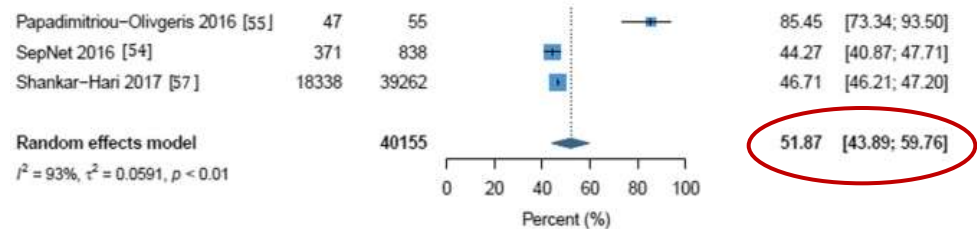
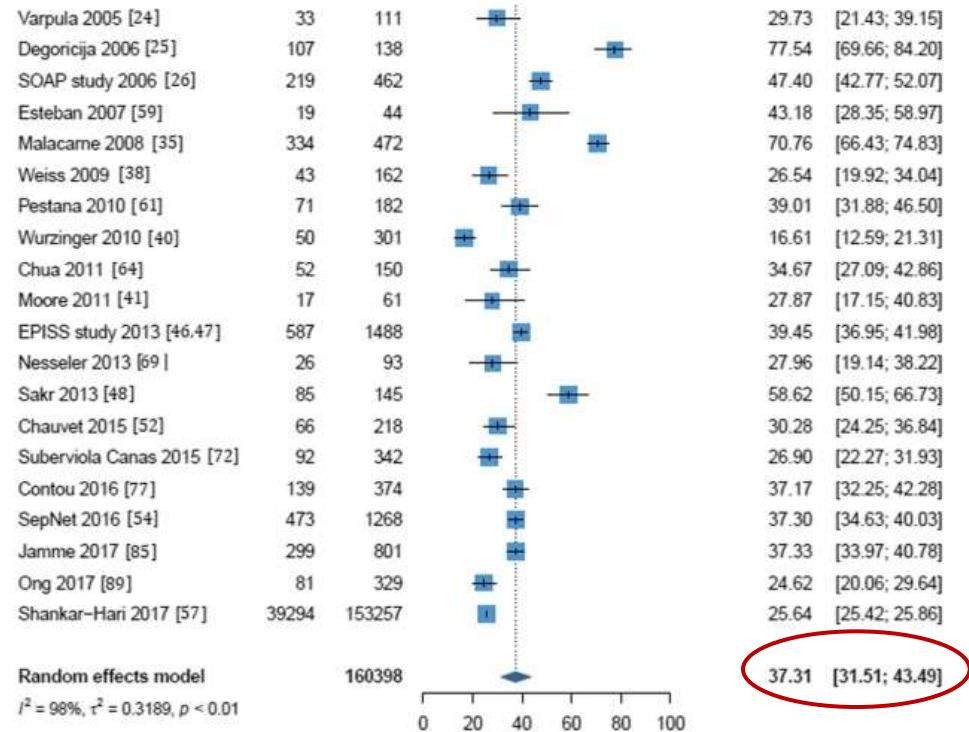
12. For adults with possible septic shock or a high likelihood for sepsis, we **recommend** administering antimicrobials immediately, ideally within one hour of recognition.

Strong recommendation, low quality of evidence (septic shock)

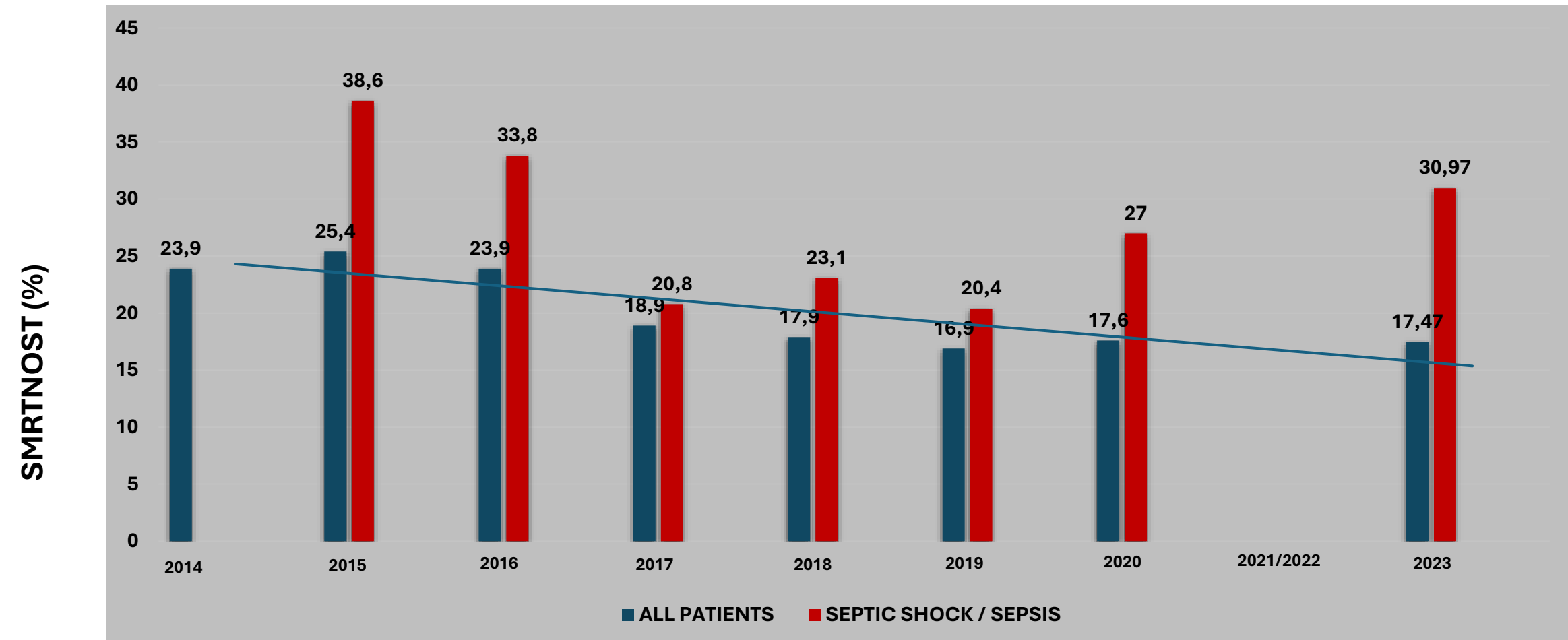
Strong recommendation, very low quality of evidence (sepsis without shock)



Septični šok in smrtnost



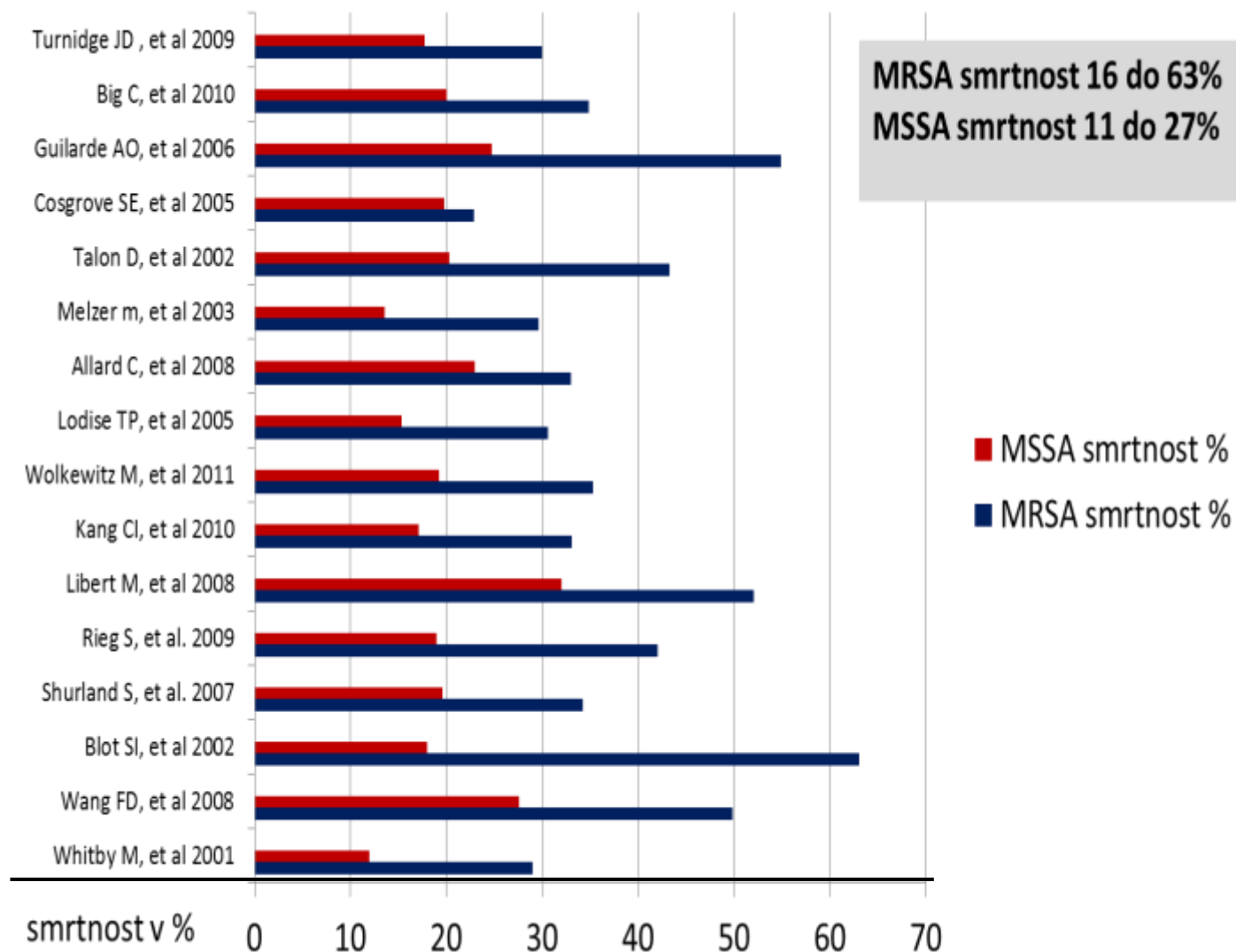
Septični šok / sepsa in smrtnost – EIT KIBVS



Sepsa in antibiotik

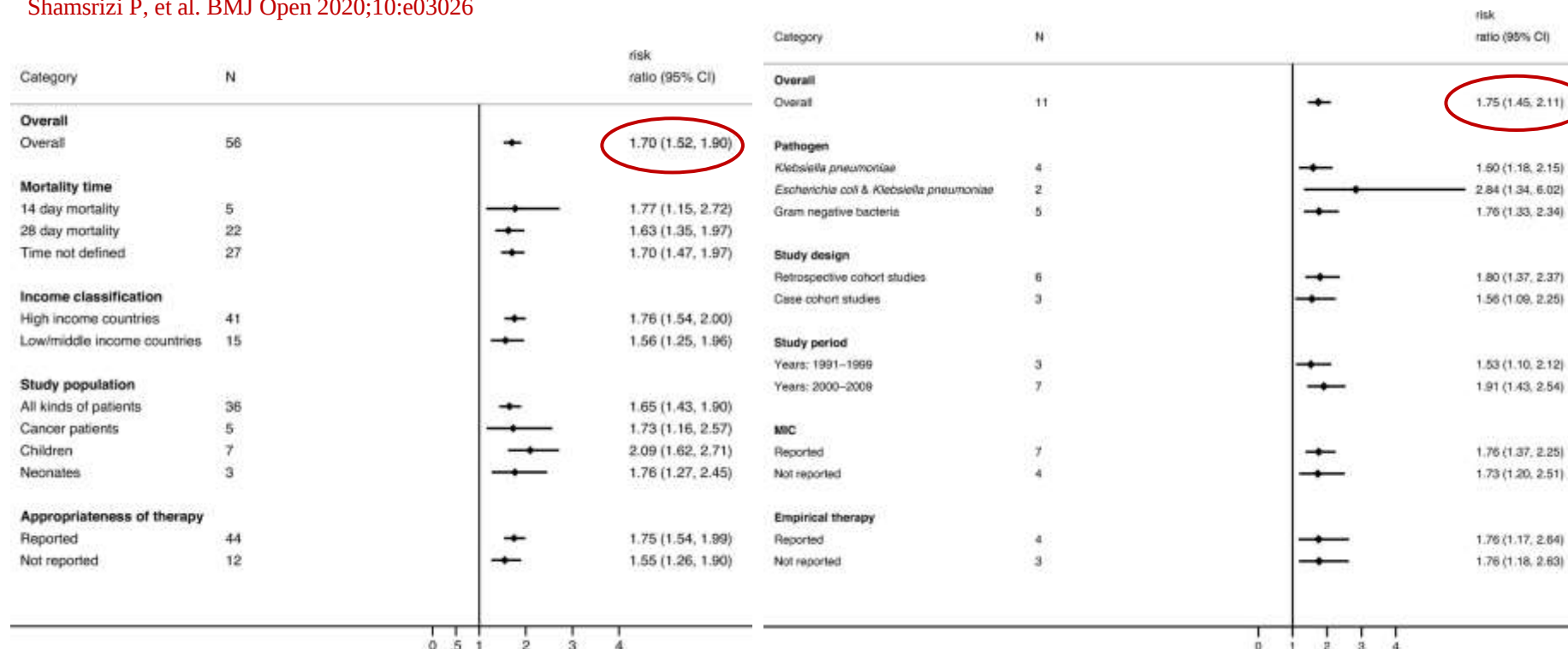
Avtor	N	Mesto raziskave	Čas do atb v h (mediana)	Razmerje obetov za smrt
Gaieski CCM 2010; 38;1045-53	261	urgenca, ZDA (šok)	119	0.30 (v 1h: po 1h)
Daniels Emerg Med J 2010; doi:10.1136	567	bolnica, Anglija	121	0.62 (v 1h: po 1h)
Kumar CCM 2006; 34(6): 1589-1596	2154	urgenca, Kanada (šok)	360	0.59 (v 1h: po 3h)
Appelboam CCM 2010; 14(Suppl 1):50	375	bolnica, Anglija	240	0.74 (v 1h: po 3h)
Levy CCM 2010; 38(2): 1-8	15022	multi-centrična		0.86 (v 1h: po 3h)

Po Gramu poz. sepsa



ESBL enterobakterije in smrtnost

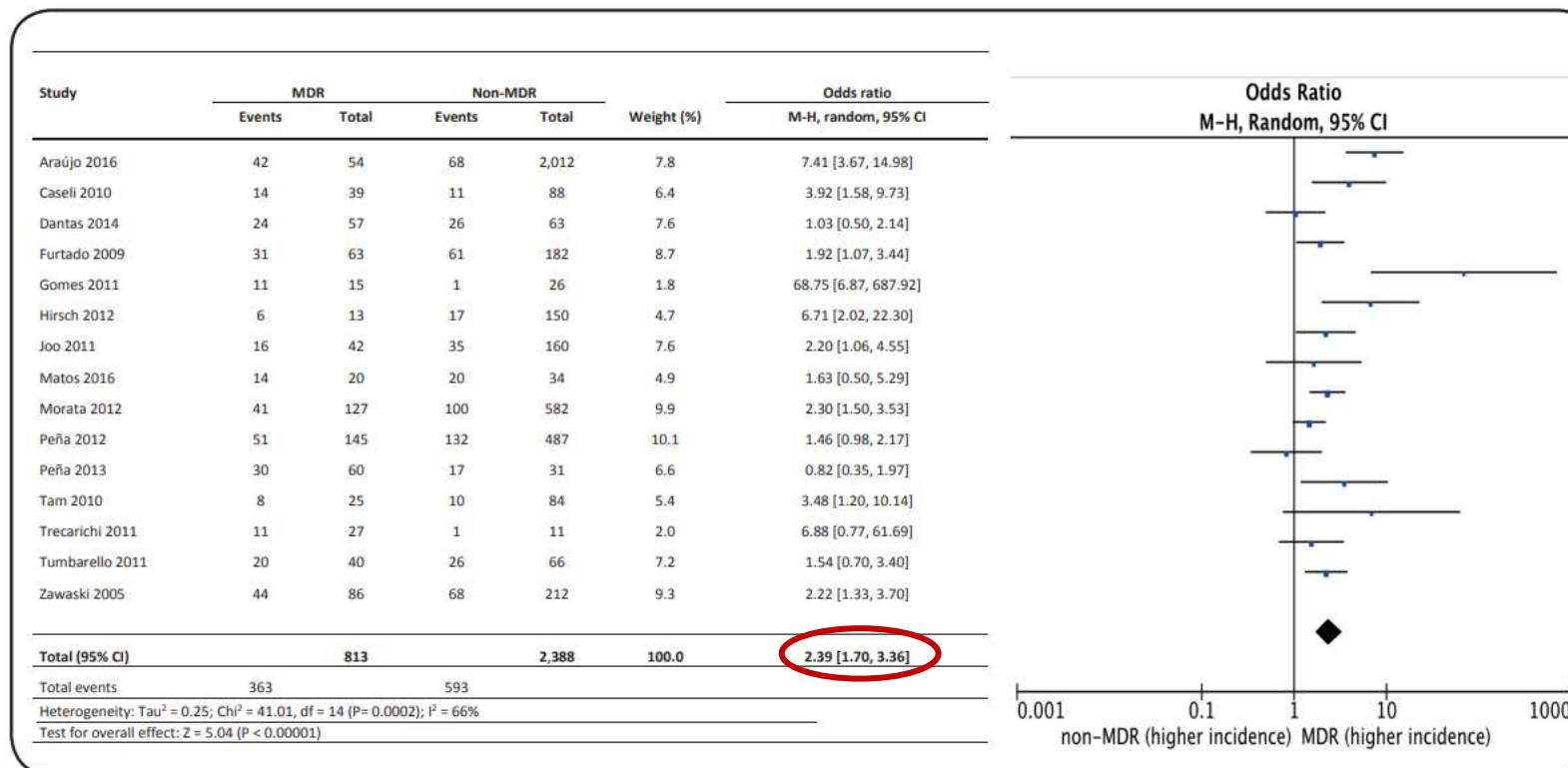
Shamsrizi P, et al. BMJ Open 2020;10:e03026



Smrtnost ESBL : non
ESBL

Atributivna smrtnost ESBL : non ESBL

Večkratno odporni *Ps. aeruginosa* in smrtnost



deMatos EC, et al. Rev Soc Bras Med Trop. 2018; 51:415-20.

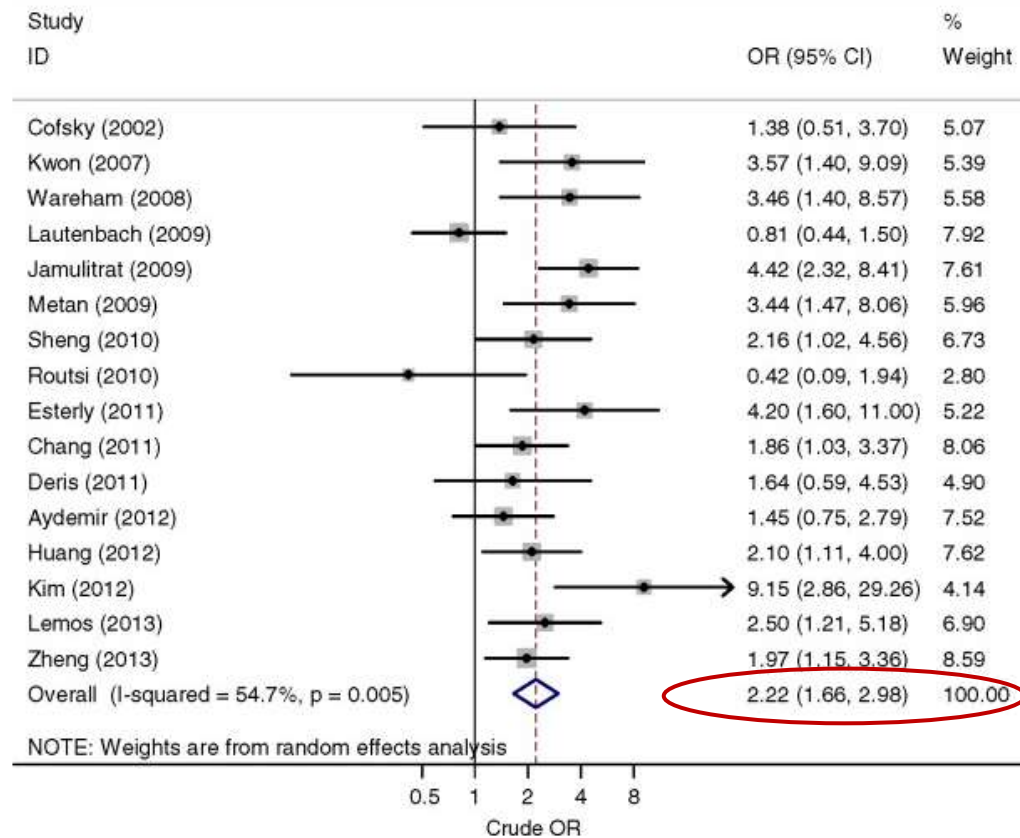


Original Article

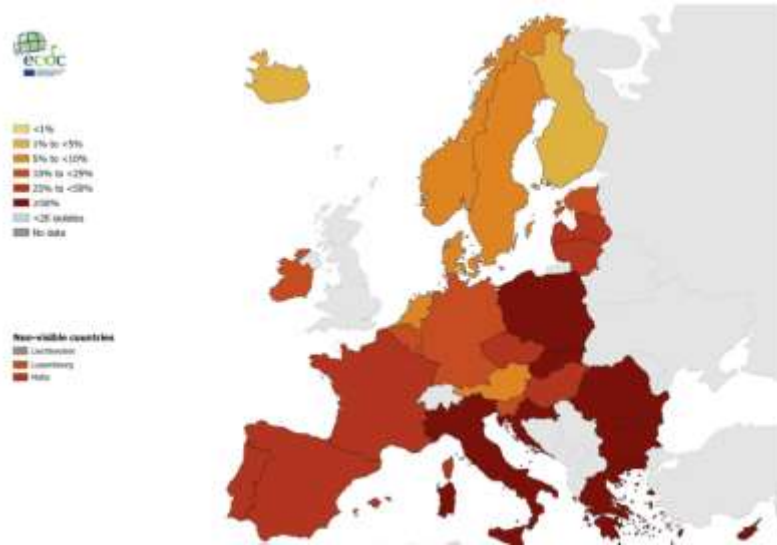
Bacteriology

Carbapenem resistance and mortality in patients with *Acinetobacter baumannii* infection: systematic review and meta-analysis

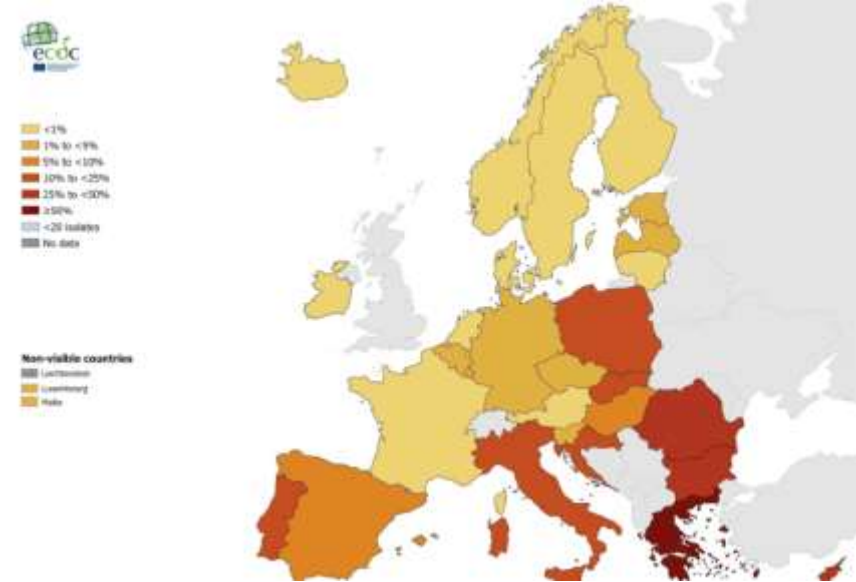
E.V. Lemos ^{a,*}, F.P. de la Hoz ^b, T.R. Einarson ^d, W.F. McGhan ^a, E. Quevedo ^e, C. Castañeda ^{b,c}, K. Kawai ^a



Večkratno odporne po Gramu neg. bakterije



K. pneumoniae –
CEF III R

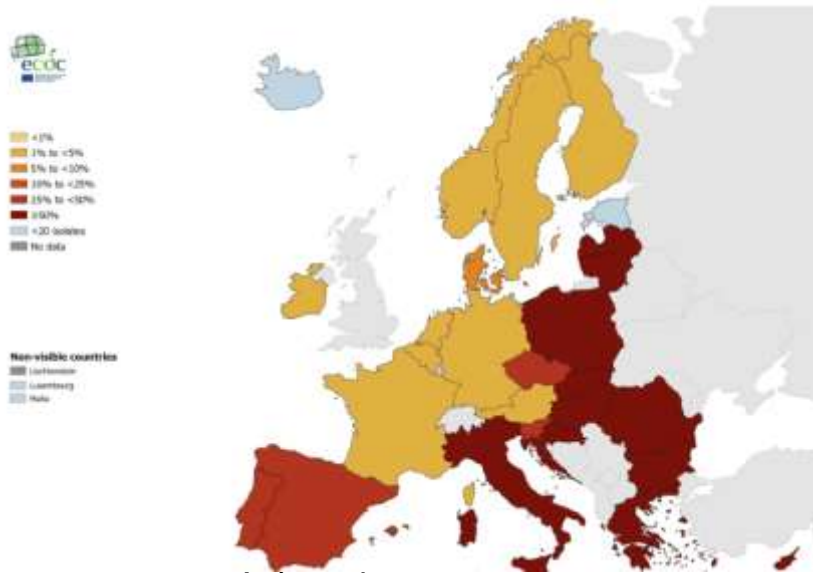


K. pneumoniae –
Carbapenems R

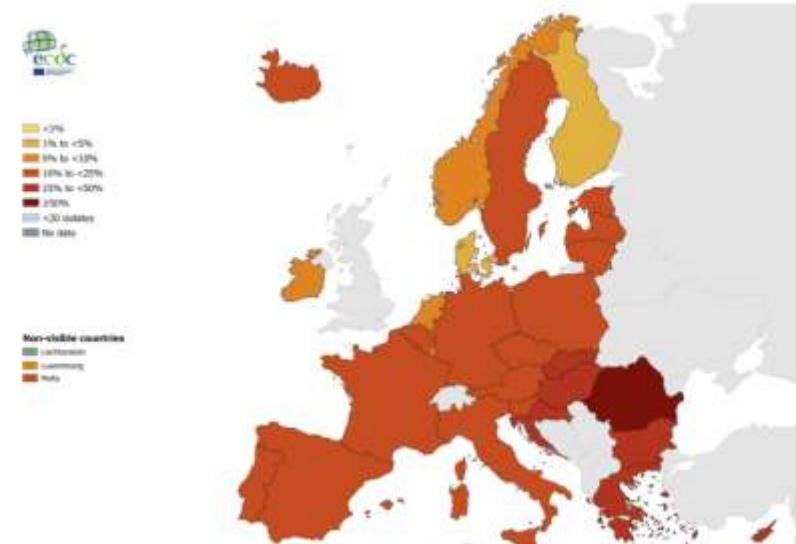
K. pneumoniae cef III R = 32,7% / v SLO = 20.7%
K. pneumoniae carbapenem R = 10,9% / v SLO = 1.9%
E.coli cef III R = 14.3% / v SLO 9.3%

Večkratno odporne po Gramu neg. bakterije

EARS - net 2022



Acinetobacter spp.
- Carbapenems R



Ps. aeruginosa –
Carbapenems R

Acinetobacter spp. – carbapenem R
=36,3% / v SLO = 43,3%
MDR (fluoroquinolones ,
aminoglycosides , carbapenems) =
31.8% / v SLO = 41,7%

Ps. aeruginosa - carbapenem R = 18. 6%
/ v SLO =14,5%,
MDR (pip/ tazo, ceftazidim,
fluoroquinolones , aminoglycosides ,
carbapenems) = 13,4% / v SLO = 8.3%

Septični šok in čas do smrti

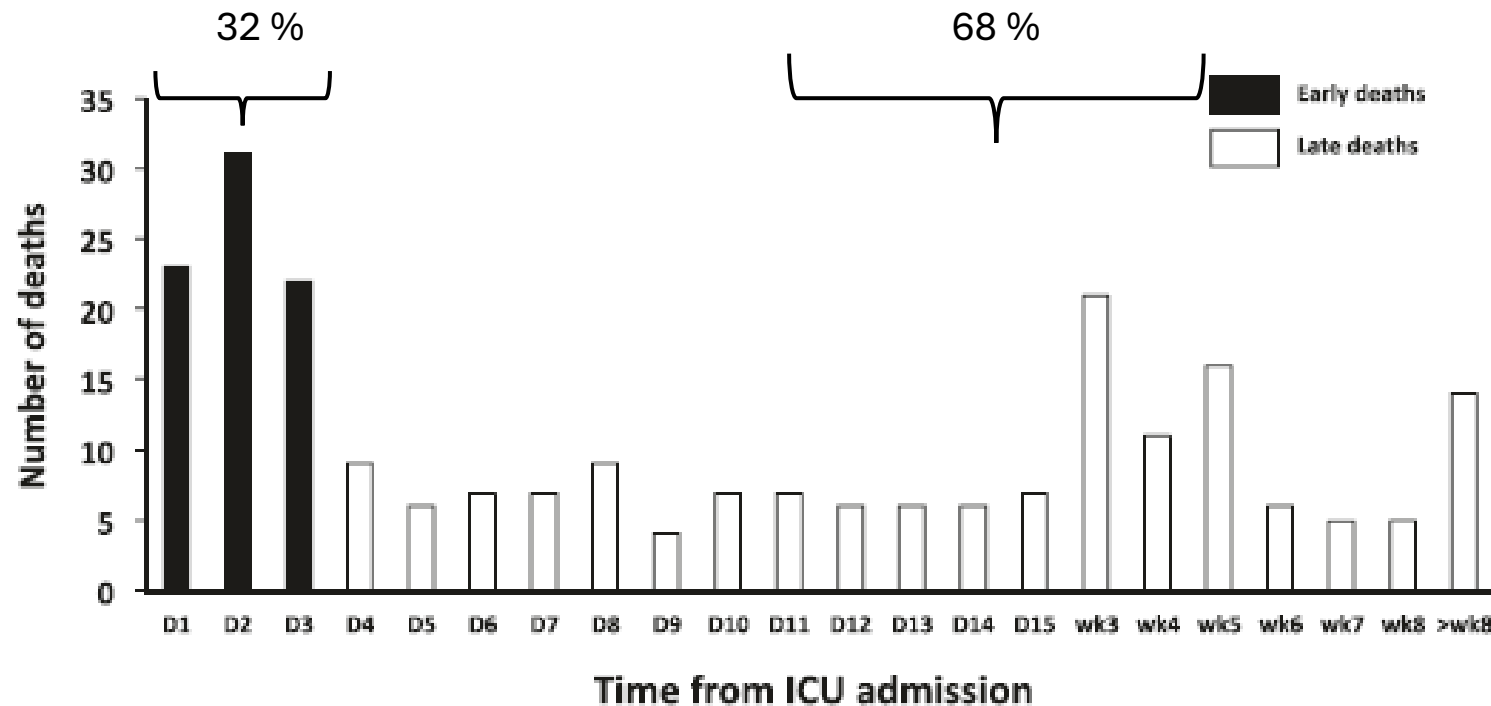
Daviaud et al. *Annals of Intensive Care* (2015) 5:16
DOI 10.1186/s13613-015-0058-8

Annals of Intensive Care
a SpringerOpen Journal

RESEARCH

Open Access

Timing and causes of death in septic shock 



Septični šok in čas do smrti

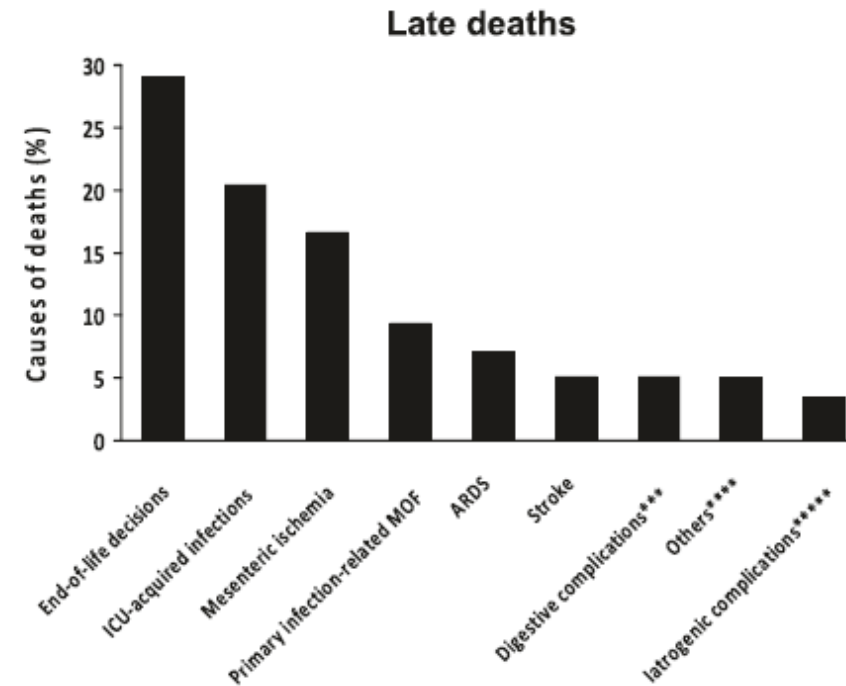
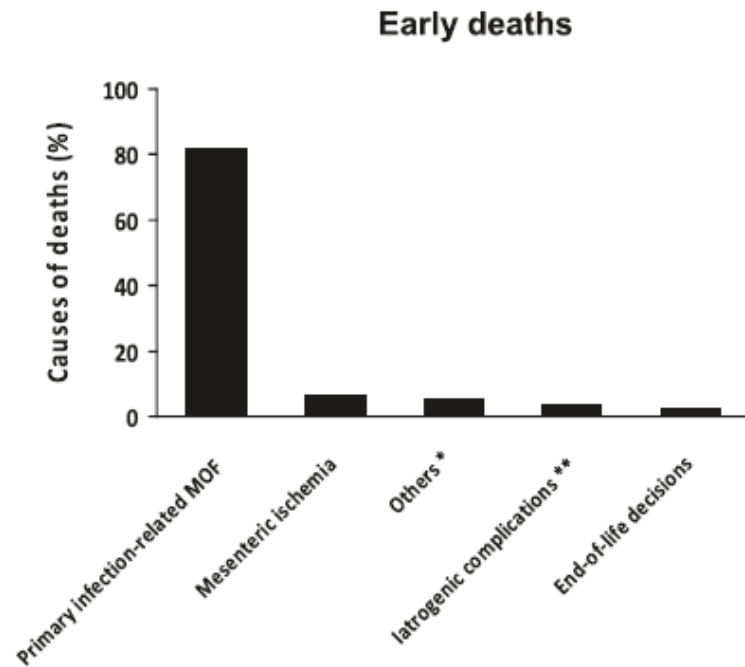
Daviaud et al. *Annals of Intensive Care* (2015) 5:16
DOI 10.1186/s13613-015-0058-8

Annals of Intensive Care
a SpringerOpen Journal

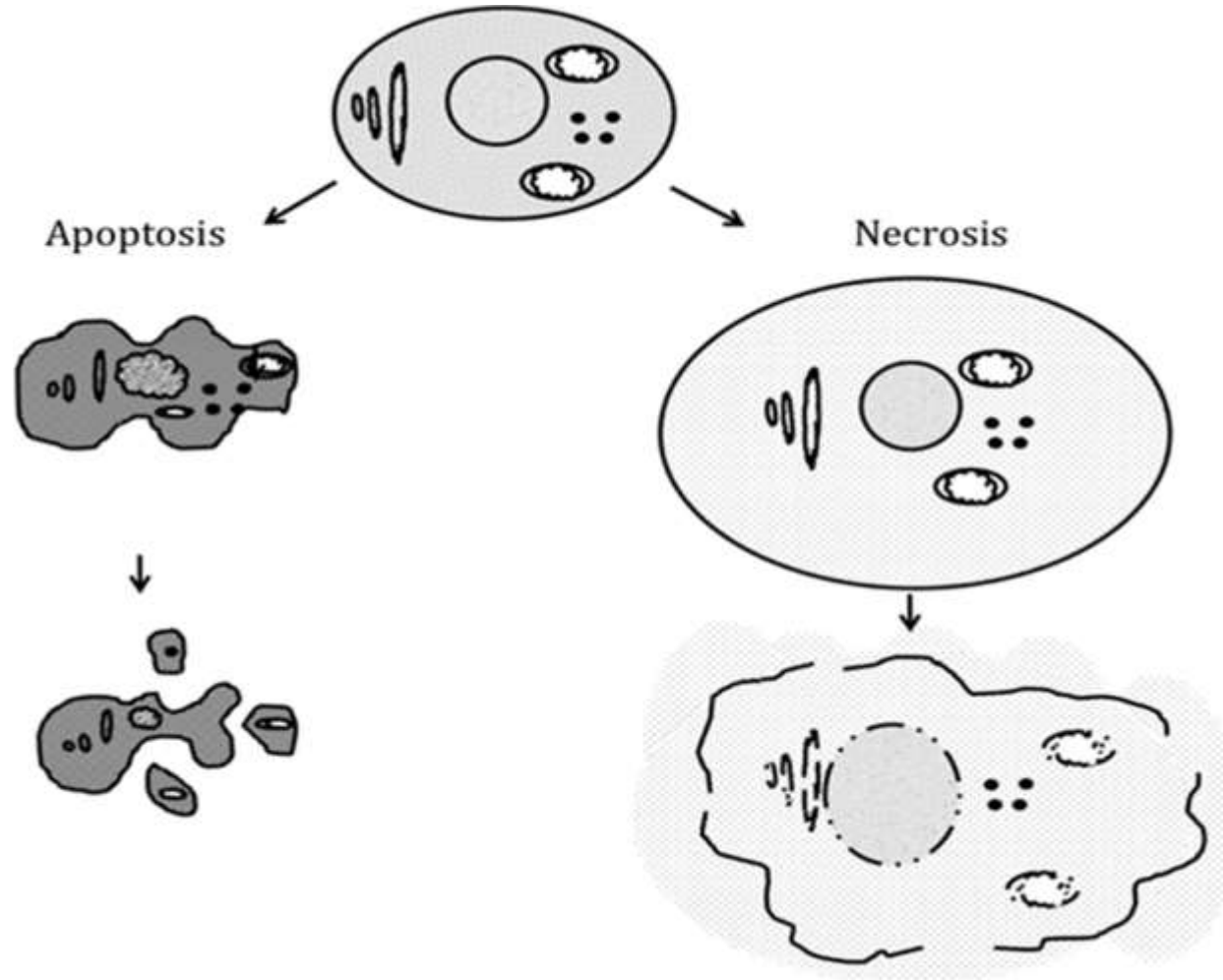
RESEARCH

Open Access

Timing and causes of death in septic shock

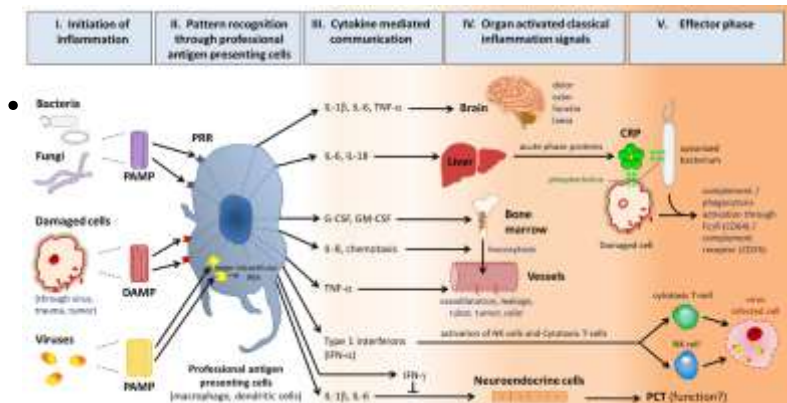


Celična smrt = odpoved organa = smrt organizma



Okvara organov pri sepsi

- Moteno delovanje mikrocirkulacije – okvara endotelija. Izguba avtoregulacije, dušikov oksid...
- Okvara mikrocirkulacije vpliva na prekrvavitev tkiv, hipoksija tkiv, celična smrt, odpoved organa, smrt bolnika
- Posledica vnetnega dogajanja, označevalci vnetja...



Okvara organov pri sepsi

- Okvarjena cirkulacija = zmanjšan transport kisika / okvarjena regulacija pretoka
- Celična hipoksija
- Moten celični metabolizem
- Okvara mitohondrijev
- Okvara membranskih pump
- Povečana prepustnost celične membrane
- Motena regulacija znotrajceličnega pH

Septični šok in SOFA

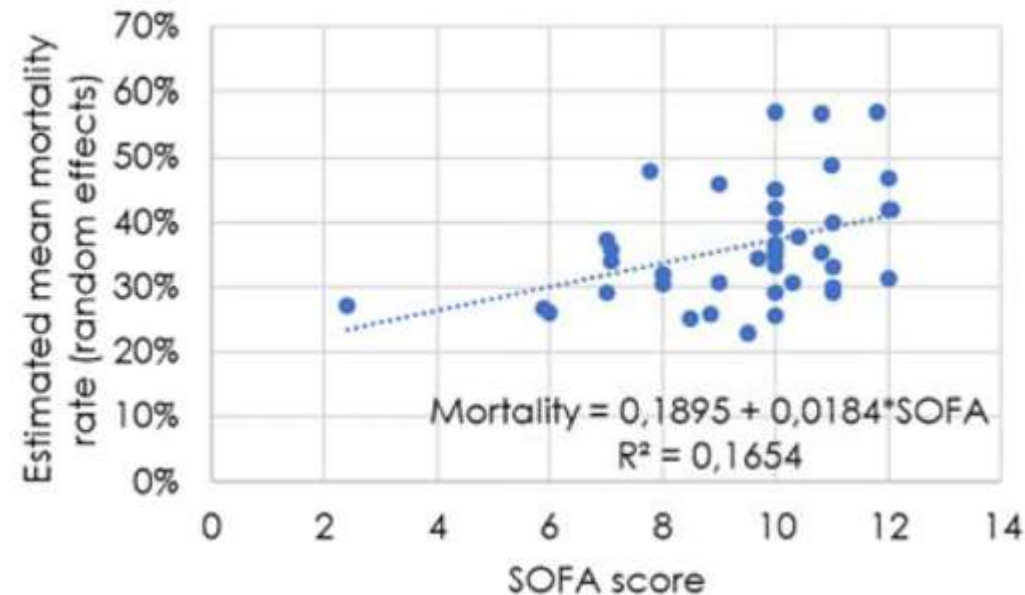
Bauer et al. Critical Care (2020) 24:239
<https://doi.org/10.1186/s13054-020-02950-2>

Critical Care

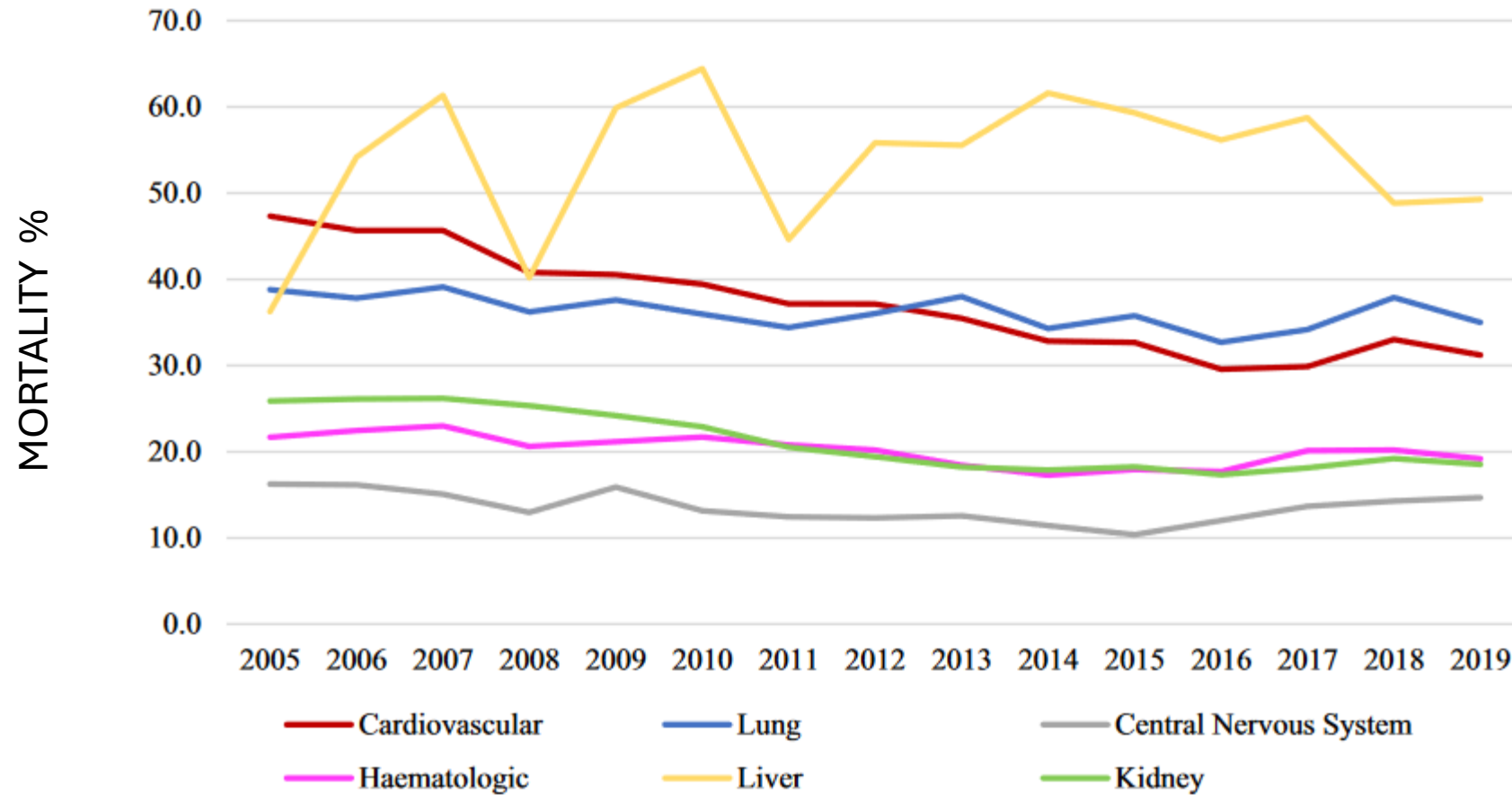
RESEARCH

Open Access

Mortality in sepsis and septic shock in Europe, North America and Australia between 2009 and 2019— results from a systematic review and meta-analysis



Smrtnost bolnikov s sepsa in okvara organov



Smrtnost bolnikov s sepsa in okvara organov

Number of organ failure	n	Mortality	HR (95% CI) unadjusted	HR (95% CI) adjusted
1	1141	8.9	1	1
2	1582	17.8	1.7 (1.4–1.9)**	1.6 (1.4–1.8)**
3	1077	23.5	2.1 (1.8–2.4)**	2.0 (1.7–2.3)**
≥4	396	38.9	2.8 (2.4–3.3)**	2.7 (2.2–3.2)**

HR = Hazard ratio; *P < 0.05; **P < 0.01

Organ dysfunction	n	Mortality	HR (95% CI) unadjusted	HR (95% CI) adjusted
Respiratory	2914	23.0	1.8 (1.6–2.0)**	1.6 (1.4–1.8)**
Cardiovascular	3065	19.5	1.1 (1.0–1.2)	1.1 (1.0–1.2)
Renal	1636	26.4	1.6 (1.5–1.8)**	1.6 (1.5–1.8)**
Hepatic	59	32.2	1.7 (1.3–2.4)**	2.0 (1.4–2.7)**
Hematologic	1242	22.8	1.2 (1.1–1.3)**	1.2 (1.0–1.3)**
Neurologic	171	20.5	1.0 (0.8–1.3)	1.0 (0.8–1.3)

HR = Hazard ratio; *P < 0.05; **P < 0.01

INFECTION



INFLAMMATION



Pro-inflammatory cytokines
oxidative stress



Endothelial cells
smooth muscle cells
erythrocytes, leukocytes, platelets



MICROCIRCULATION
DYSFUNCTION



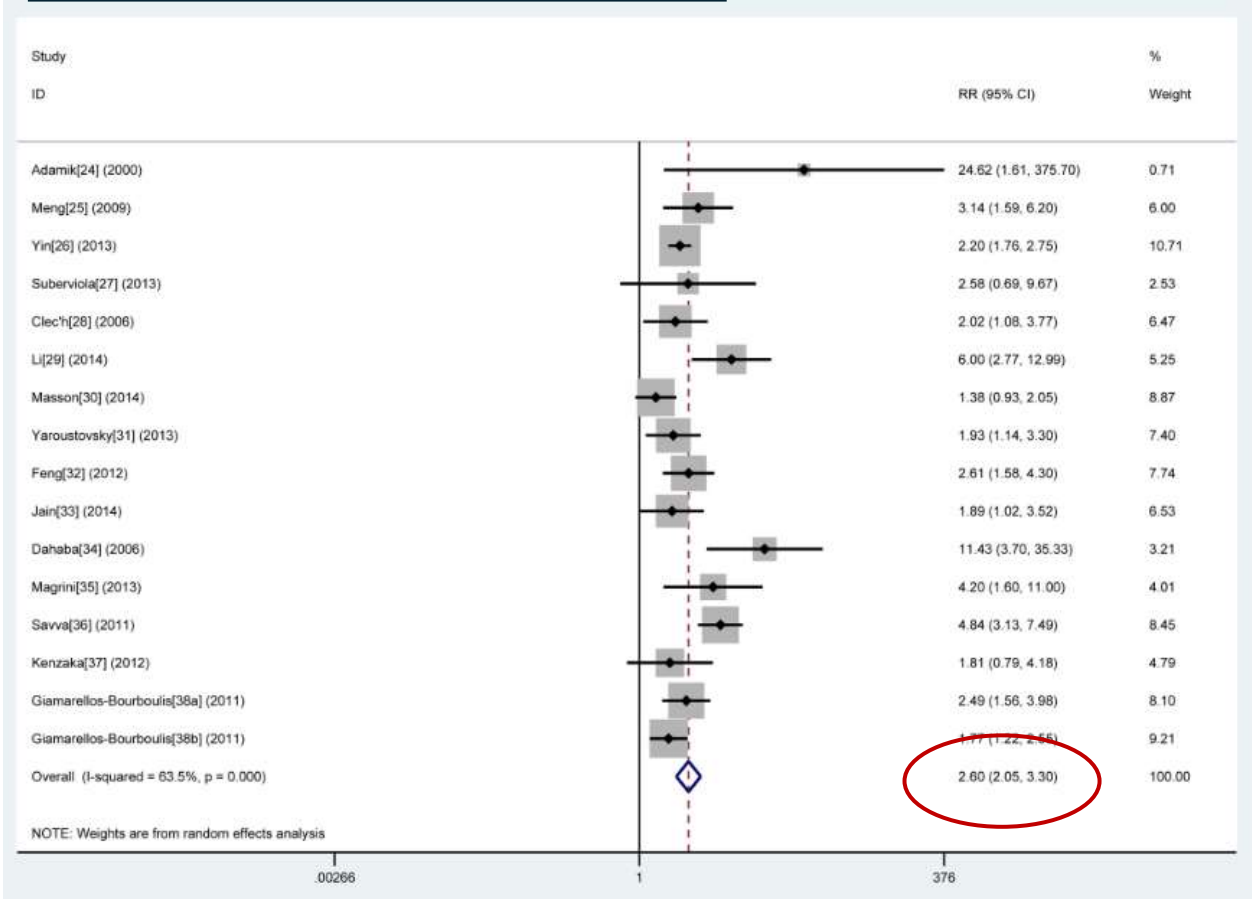
TISSUE HYPOPERFUSION
Mitochondrial damage,
metabolic reprogramming (warburg effect)



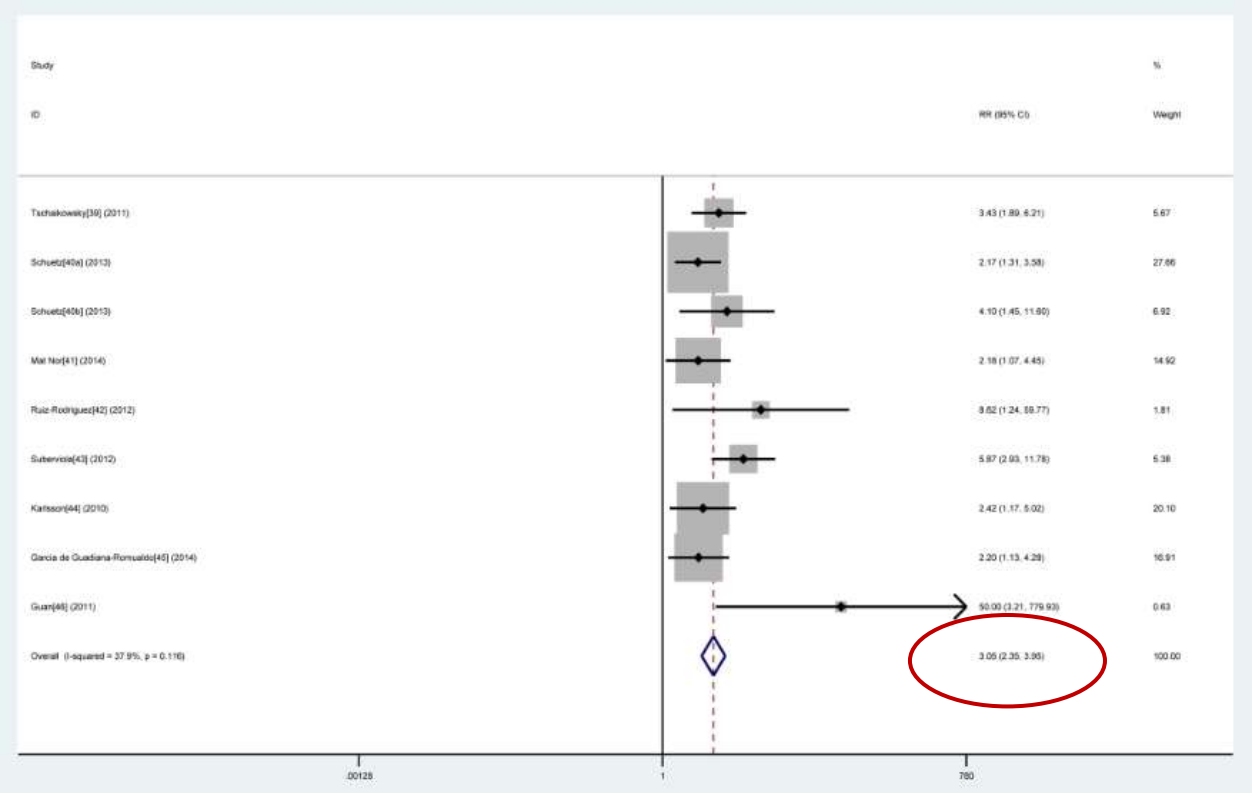
ORGAN DYSFUNCTION

Prognostic Value of Procalcitonin in Adult Patients with Sepsis: A Systematic Review and Meta-Analysis

PCT ob sprejemu



PCT tekom zdravljenja



Usefulness of presepsin as diagnostic and prognostic marker of sepsis in daily clinical practice

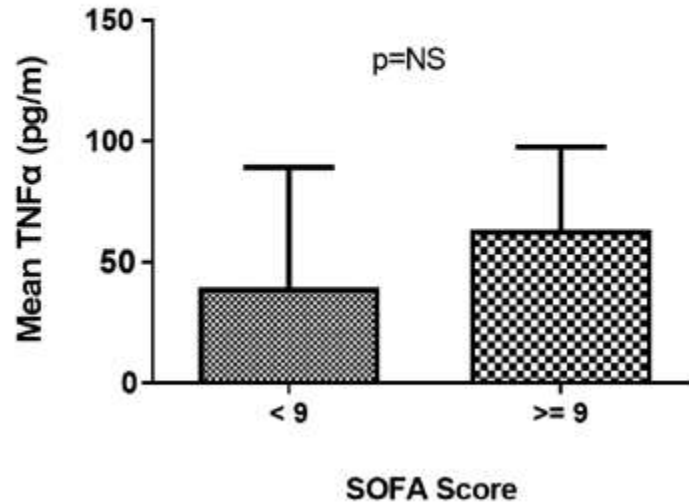
Matjaz Jereb¹, Matej Mavric¹, Miha Skvarc², Alja Drobic¹, Spela Dolenc¹, Natalija Planinc Strunjas¹, Boris Luksic³, Nina Grasselli Kmet¹

		PRES		APACHE II		PCT		CRP	
		Median	range	Median	range	Median	range	Median	range
Diagnosis	Sepsis (n = 9)	771	286-5565	14	6-26	1,0	0-31	180	72-432
	Shock (n = 45)	1914	342-20000	26	13-43	19,0	0-499	246	37-457
	p-value	0,014		< 0,001		0,002		0,628	
Outcome	Died (n = 21)	3154	625-20000	29	15-43	19	2-499	233	37-457
	Survived (n = 33)	1208	286-12096	21	6-39	15	0-238	246	50-453
	p-value	0,009		0,002		0,136		0,382	
Aetiology	None (n = 19)	1941	342-20000	26	13-43	13,6	0-157	178	37-457
	G-pos. (n = 25)	1314	297-13332	23	12-37	19	0-499	292	75-457
	G-neg. (n = 10)	2906	286-11359	31	6-40	17,5	0-238	215	102-453
	p-value	0,381		0,224		0,969		0,863	

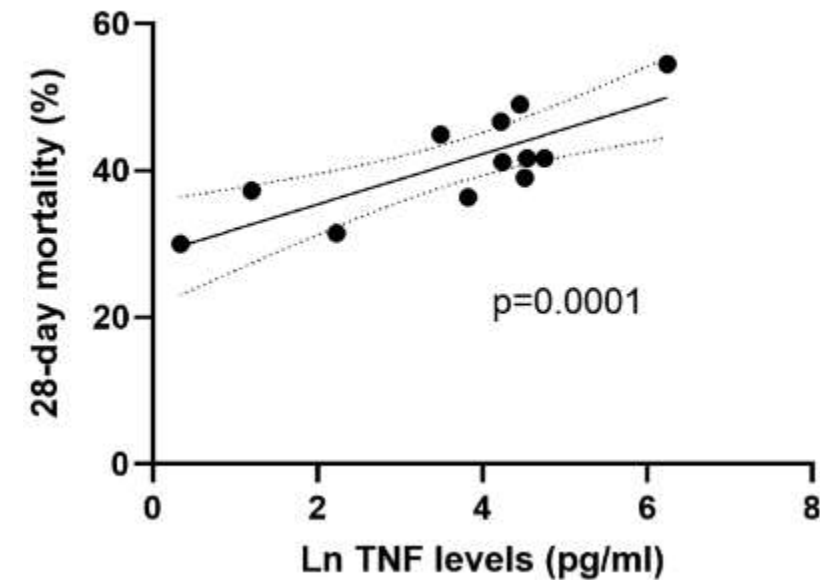
PRES: presepsin concentration (pg/mL); PCT: procalcitonin concentration (mcg/mL); CRP: C-reactive protein concentration (mg/L); G-pos.: Gram-positive sepsis/septic shock; G-neg.: Gram-negative sepsis/septic shock.

Proinflammatory cytokines levels in sepsis and healthy volunteers, and tumor necrosis factor-alpha associated sepsis mortality: A systematic review and meta-analysis

TNF α levels in sepsis according to SOFA score

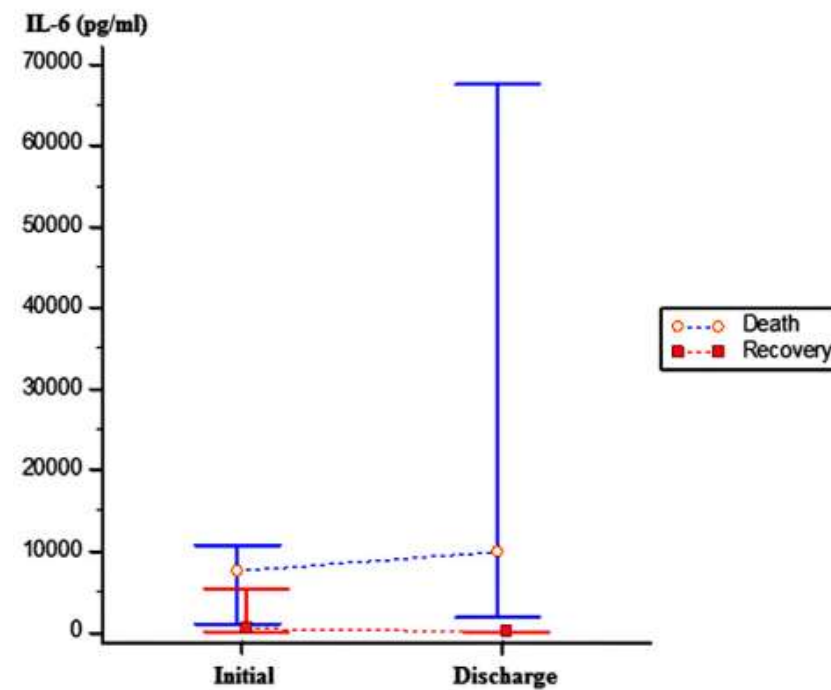
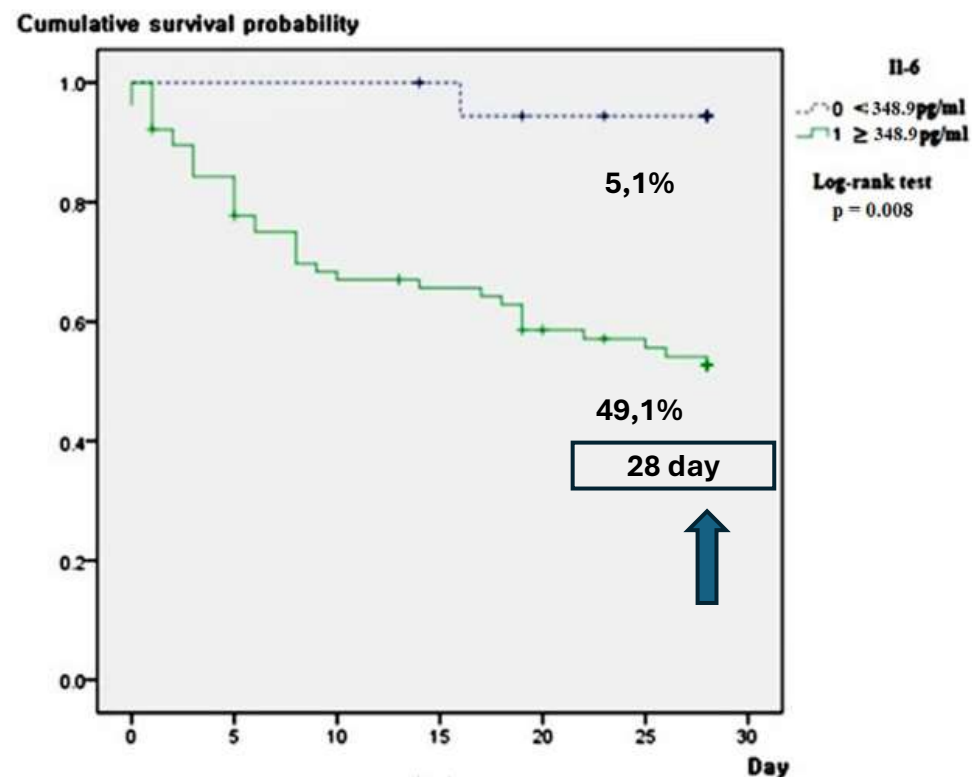
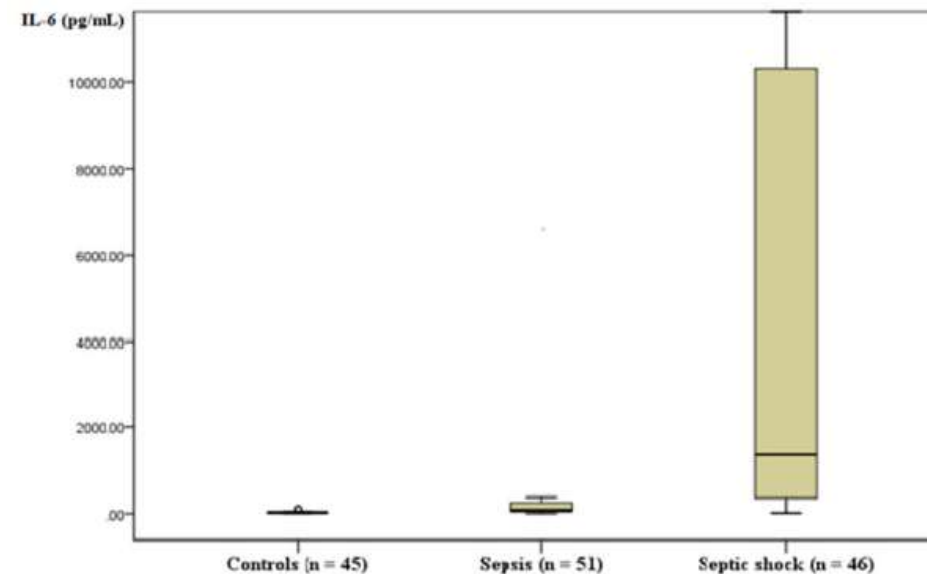


TNF α levels and sepsis mortality



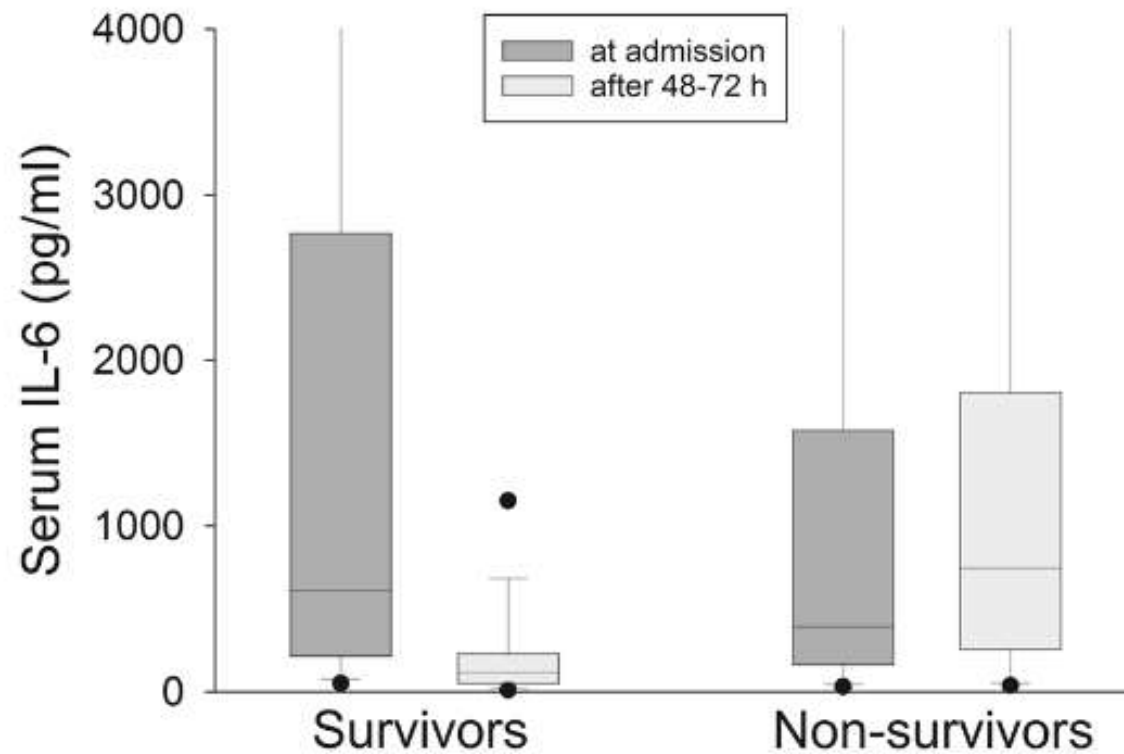


Diagnostic and prognostic value of interleukin-6, pentraxin 3, and procalcitonin levels among sepsis and septic shock patients: a prospective controlled study according to the Sepsis-3 definitions





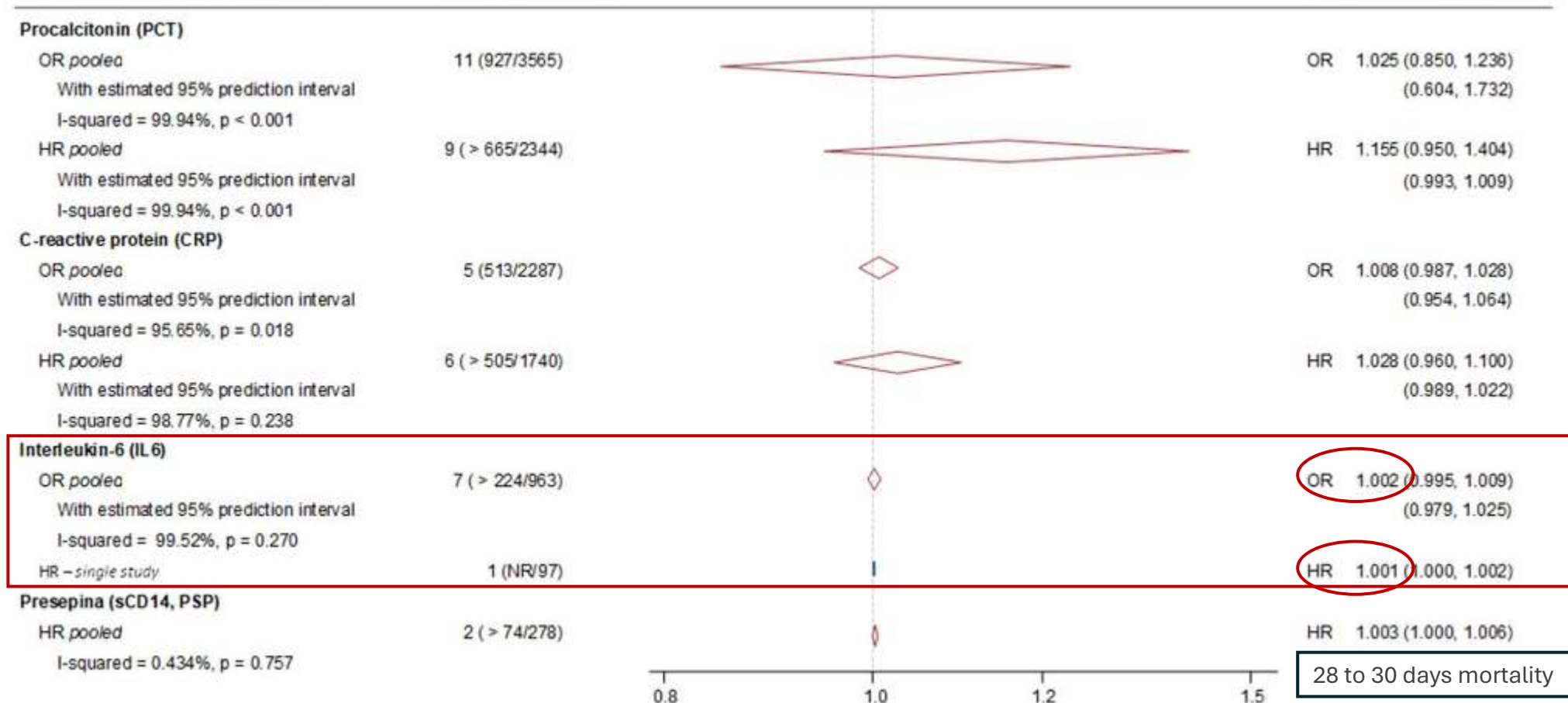
Is Interleukin-6 a better predictor of successful antibiotic therapy than procalcitonin and C-reactive protein? A single center study in critically ill adults





Basal procalcitonin, C-reactive protein, interleukin-6, and presepsin for prediction of mortality in critically ill septic patients: a systematic review and meta-analysis

Franco DM, et al. Diag Prog Res 2023;7:15.



Kaj lahko naredimo?

- Izboljšamo diagnostiko
 - orodja za prepoznavo bolnikov (qSOFA, MEWS, LIP score,.....)
 - novi biomarkerji
 - izboljšamo lahko triažo bolnikov
- Skrajšamo čas do ustreznega antibiotika
 - nove mikrobiološke metode (MALDITOF, SeptiFast...)
 - inkubacija HK že na oddelku
- Optimizacija antibiotične terapije
 - polnilni odmerki, merjenje koncentracije atb...
- Odstranitev vira okužbe
 - boljše sodelovanje med različnimi strokami
- Izboljšamo lahko zdravljenje na EIT
 - multimodal vasopresorna terapija (NE+vasopressin+AT-II)

Kaj lahko naredimo?

- Uporaba novih orodij
 - „Sepsis ImmunoScore“ / algoritem za hitro diagnostiko in napoved sepse
 - mezenhimske matične celice
 - membrane za odstranjevanje posrednikov vnetja

Zaključki

- Sepsa je kompleksna bolezen z visoko smrtnostjo, ki je posledica odpovedi organov.
- Odpoved vsakega organa prispeva k neugodni prognozi.
- Ključna je okvara endotelija na nivoju mikrocirkulacije.
- Hitro ukrepanje rešuje življenja bolnikov s sepsa ali septičnim šokom.
- Personaliziran pristop je prihodnost obravnave bolnikov s sepsa.