SEPSA PRI BOLNIKIH Z IMUNSKO OSLABELOSTJO

~~NATALIJA PLANINC STRUNJAŠ, DR.MED.~~ TOMAŽ VOVKO, DR. MED.

LJUBLJANA, 11.9.25

RAZKRITJA

Klinične raziskave: ARRS in CRP MZ RS, podjetja Pfizer, Melinta Therapeutics,

Posvetovalni odbor/panel: Lenis, Gilead, El Pharma, MSD

Predavanje, svetovanje: MSD, El Pharma, Lenis, Gilead, Krka, Biogen, Pfizer

Nekatere drsnice so zaradi boljšega razumevanja in natančnosti prezentacije v (originalni) angleščini.

SEPSA IN SEPTIČNI ŠOK

- SEPSA: **Življenje ogrožajoče** stanje, kjer pride do **odpovedovanja organskih sistemov (ΔSOFA ≥ 2)** zaradi **neustreznega** odgovora organizma na okužbo („*dysregulated host response to infection*“) .
- SEPTIČNI ŠOK
  - dodatno pomembne cirkulatorne, celične in metabolne spremembe, ki prestavljajo dodatno tveganje za smrtnost
  - klinično = SEPSA + vazoaktivni podpori za MAP ≥ 65 mm Hg IN laktat > 2 mmol/L v odsostnosti hipovolemije
- Bolnišnična smrtnost:
  - Sepsa: >10%
  - Septični šok: >40%

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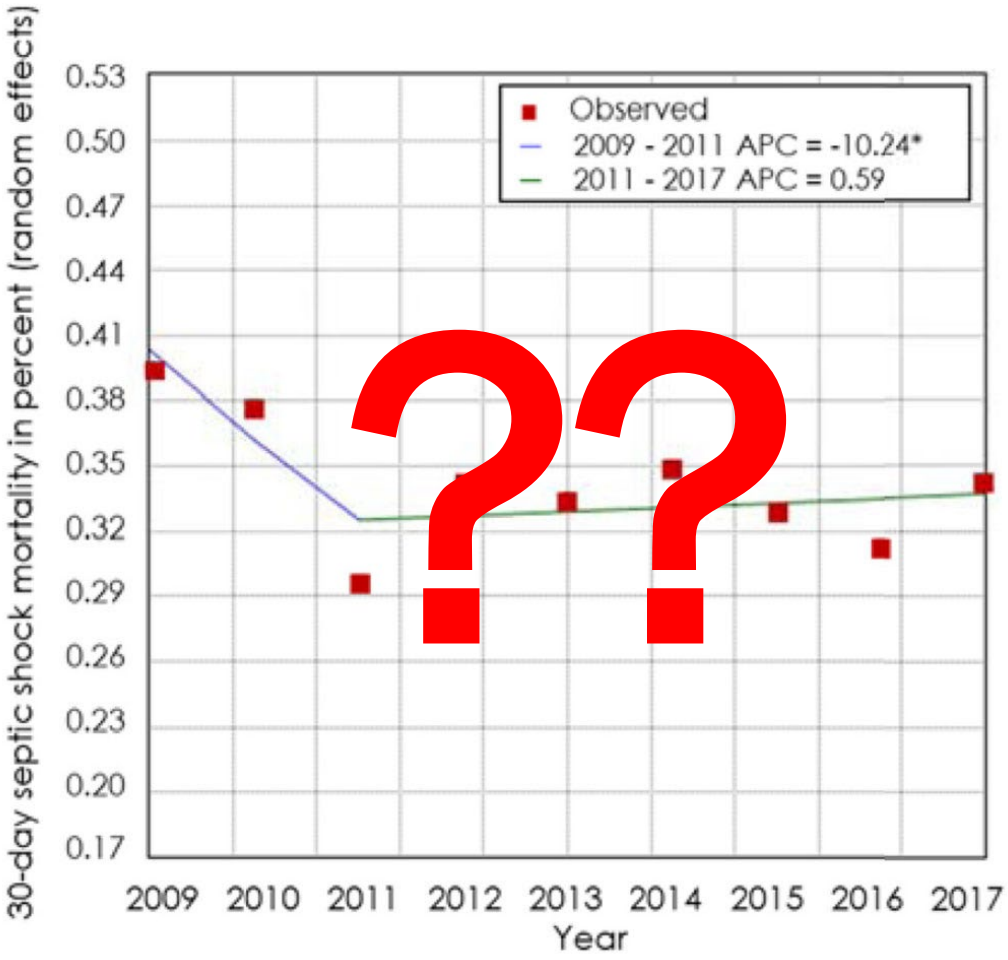


* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.

1. Singer M et al. JAMA. 2016; 315(8): 801-10, 2. Bauer M et al. Crit Care. 2020 May 19;24(1):239

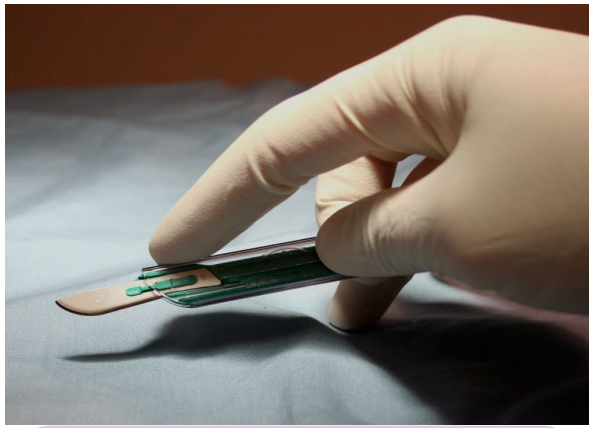
ZDRAVLJENJE SEPSE

Protimikrobno zdravljenje

- pravilna **izbira** protimikrobne terapije
- **čas** uvedbe protimikrobne terapije
- pravilen odmerek in čas infuzije
- antibiotični „stewardship“

Podporno zdravljenje

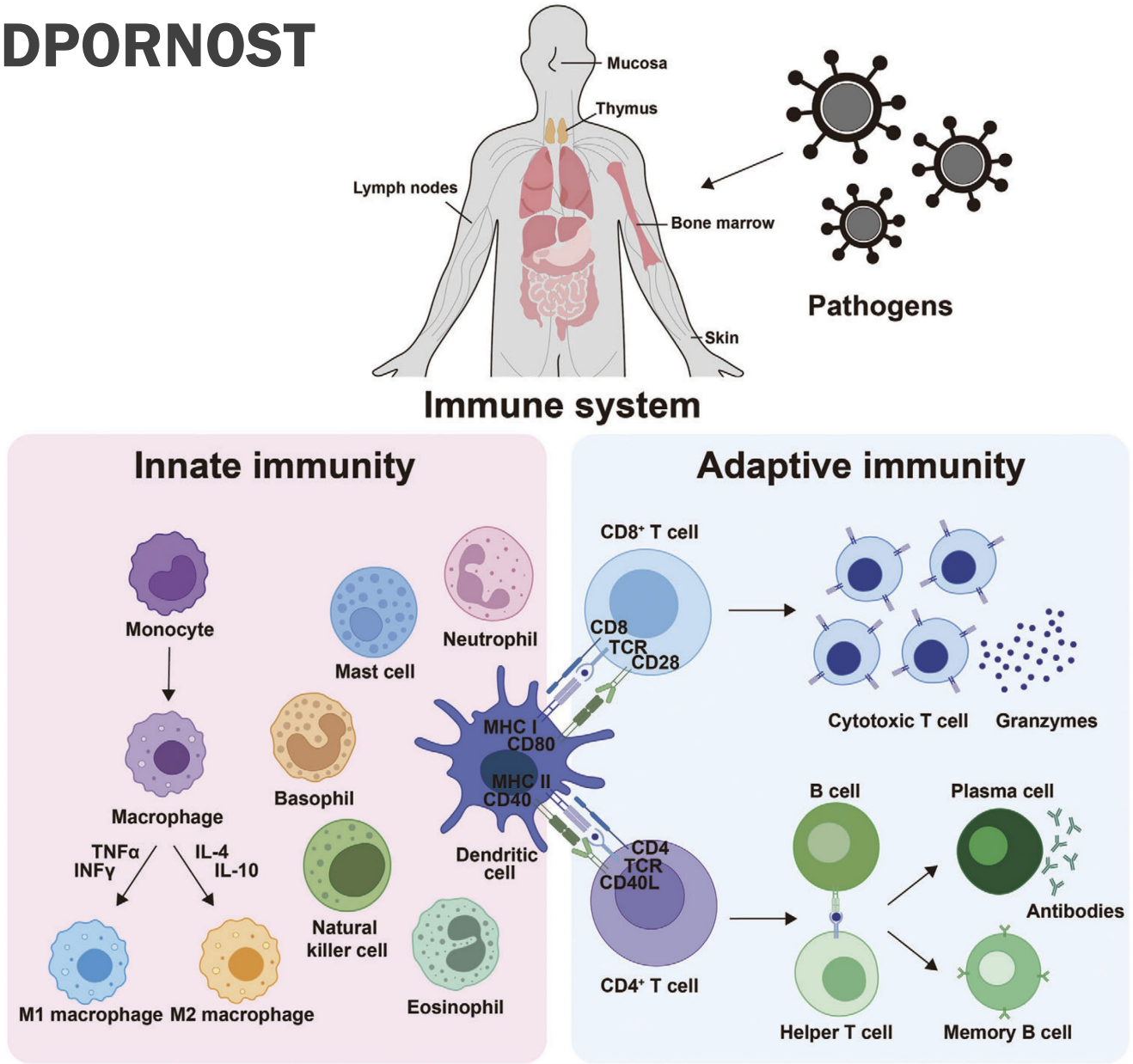
- tekočinsko oživljanje
- nadzor („monitoring“)
- steroidi
- odstranjevanje „toksinov“
- podpora organov



Kontrola izvora (angl. „*source control*“)

- slabe raziskave
- težko kvantificirati
- pogosto izkoriščanje zunanjih virov

IMUNSKI SISTEM: NARAVNA ODPORNOST IN SPECIFIČNA IMUNOST



Park JE et Kim DH. Adv Healthc Mater. 2025 Feb;14(5):e2304496

PRIROJENE MOTNJE IMUNOSTI

Classification and Examples	Clinical Presentation
Disorders of Adaptive Immunity	
Combined immunodeficiencies	
► SCID • T^-, B^+ • γc deficiency • JAK3 deficiency • T^-, B^- • ADA deficiency • RAG 1/2 deficiency	Severe, recurrent, opportunistic infections; failure to thrive; diarrhea; rash
► DiGeorge syndrome	Hypoparathyroidism; seizures; cardiac abnormalities; facial dysmorphism; infection
► Hyper IgE syndrome (*STAT3* LOF)	Chronic dermatitis; recurrent, severe lung infections; skin infections; bone fragility; failure to shed primary teeth
► Wiskott-Aldrich syndrome	Microthrombocytopenia with bleeding and bruising; eczema; recurrent bacterial and viral infections; autoimmune disease
► Ataxia telangiectasia	Chronic sinopulmonary disease; cerebellar ataxia; small, dilated blood vessels of the eyes and skin; malignancy
Predominantly antibody deficiencies ► XLA ► CVID ► Selective IgA deficiency ► Specific antibody deficiency ► IgG subclass deficiency	Recurrent sinopulmonary infections with encapsulated bacteria Autoimmune disease and increased risk of malignancy in CVID
Primary Atopic Disorders	
► CADINS	Severe atopic dermatitis, eosinophilia, cutaneous viral infections, respiratory tract infections
► DOCK8 deficiency	Severe atopic dermatitis, severe allergies, viral infections, autoimmunity
► MALT1 deficiency	Severe dermatitis, elevated IgE levels, poor growth, recurrent skin, respiratory and gastrointestinal tract infections

Disorders of Innate Immunity	
Phagocyte defects	
► Chronic granulomatous disease	Severe infection; abscesses with granuloma formation; colitis
► Leukocyte adhesion deficiency	Recurrent, severe bacterial infections; poor wound healing; delayed separation of the umbilical cord
Complement defects	
► Deficiency in early complement pathway components (C1q, C1r, C2, C4)	SLE–like syndrome; rheumatoid disease; multiple autoimmune diseases; infections
► Deficiency in late complement pathway components (C5, C6, C7, C8, C9)	Neisserial infections; SLE-like syndrome
► C3 and regulatory components	Recurrent infections with encapsulated bacteria
Mendelian susceptibility to mycobacterial disease (MSMD)	
► IL-12/IFN-γ deficiency	Atypical mycobacterial and salmonella infections
Disorders of Immune Dysregulation	
► HLH	Fever, splenomegaly, cytopenia, rash
► ALPS	Splenomegaly; adenopathy; cytopenia
► IPEX	Autoimmune enteritis; early onset diabetes; thyroiditis; cytopenia; eczema
► APECED	Autoimmunity affecting parathyroid, adrenal, other endocrine organs; candidiasis; dental enamel hypoplasia
► CTLA4 haploinsufficiency	Lymphoproliferation, autoimmune cytopenia, hypogammaglobulinemia, recurrent infections, other autoimmunity

ADA, adenosine deaminase; AIRE: autoimmune regulator; ALPS, autoimmune lymphoproliferative syndrome; APECED, autoimmune polyendocrinopathy candidiasis, and ectodermal dystrophy; CADINS, CARD11-associated atopy with dominant interference of NF-κB signaling; CVID, common variable immunodeficiency; HLH, hemophagocytic lymphohistiocytosis; IgA, immunoglobulin A; IgE, immunoglobulin E; IgG, immunoglobulin G; IFNγ, interferon-gamma; IL, interleukin; IPEX, immune dysregulation polyendocrinopathy enteropathy X-linked; JAK3, Janus kinase 3; LOF, loss of function; RAG, recombination activating gene; SCID, severe combined immunodeficiency; SLE, systemic lupus erythematosus; XLA, X-linked agammaglobulinemia

Kim, V.H.D., et al. Allergy Asthma Clin Immunol 20 (Suppl 3), 76 (2024)

PRIDOBLJENE IMUNSKE MOTNJE

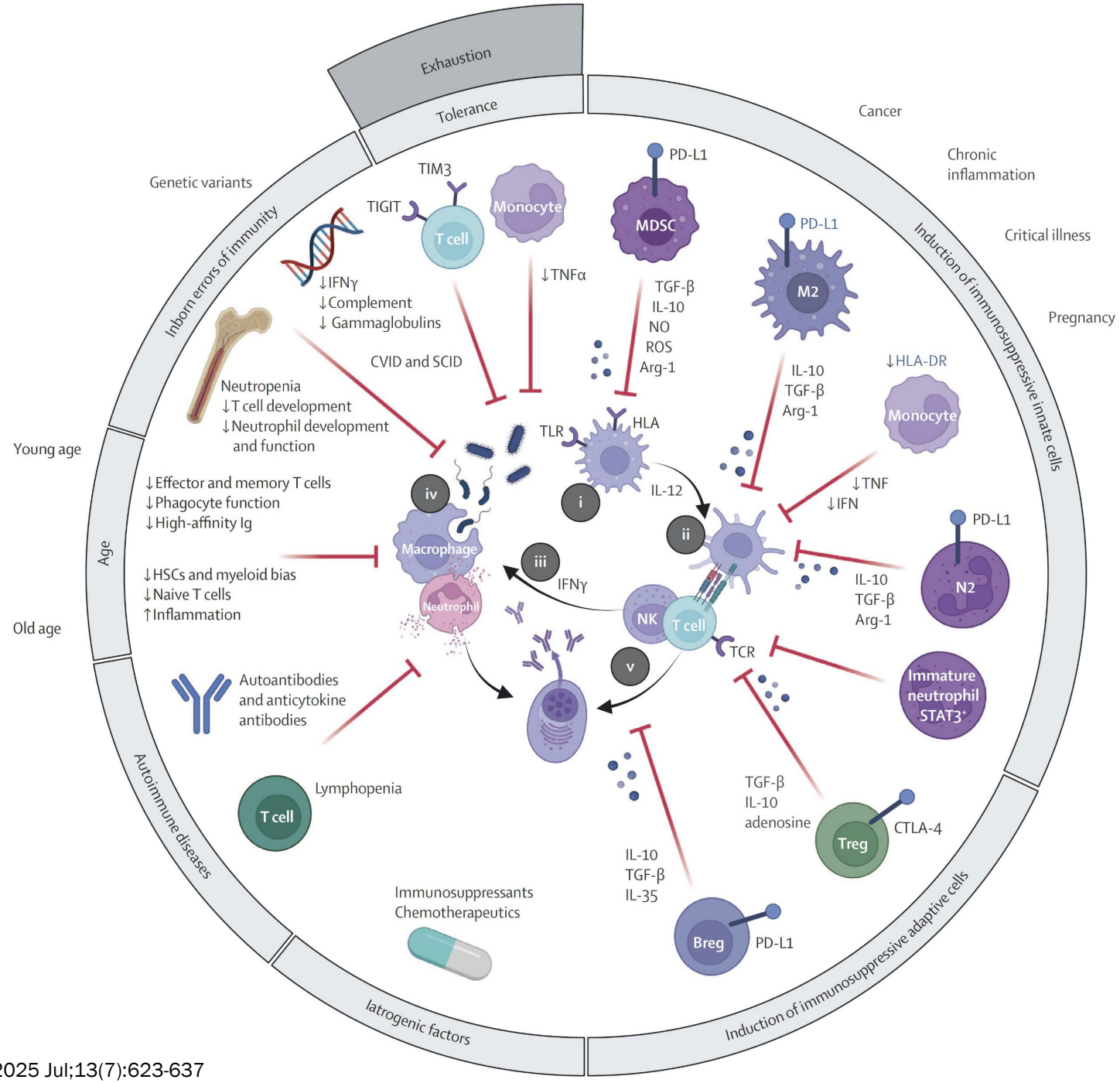
Conditions associated with secondary immunodeficiency

Immunosuppressive therapy
Cytotoxic chemotherapy for malignancy
Treatment of autoimmune disease
Bone marrow ablation prior to transplantation
Treatment or prophylaxis of graft-versus-host disease following bone marrow transplantation
Treatment of rejection following solid organ transplantation
Microbial infection
Viral infection
HIV, AIDS
Measles
Herpes group viruses (HSV-1 or 2, EBV, CMV, VZV)
Bacterial infection (superantigens)
Mycobacterial infection
Parasitic infestation
Malignancy
Hodgkin disease
Chronic lymphocytic leukemia
Multiple myeloma
Solid tumors
Disorders of biochemical homeostasis
Diabetes mellitus
Kidney insufficiency/dialysis
Hepatic insufficiency/cirrhosis
Malnutrition
Autoimmune disease
Systemic lupus erythematosus
Rheumatoid arthritis
Trauma
Burns
Environmental exposure
Radiation
Ionizing
Ultraviolet
Toxic chemicals
Other
Pregnancy
Stress*
Asplenia/hyposplenism
Allogeneic blood transfusion
Aging¶

AIDS: acquired immunodeficiency syndrome; CMV: cytomegalovirus; EBV: Epstein-Barr virus; HIV: human immunodeficiency virus; HSV-1 and 2: herpes simplex viruses 1 and 2; VZV: varicella-zoster virus.

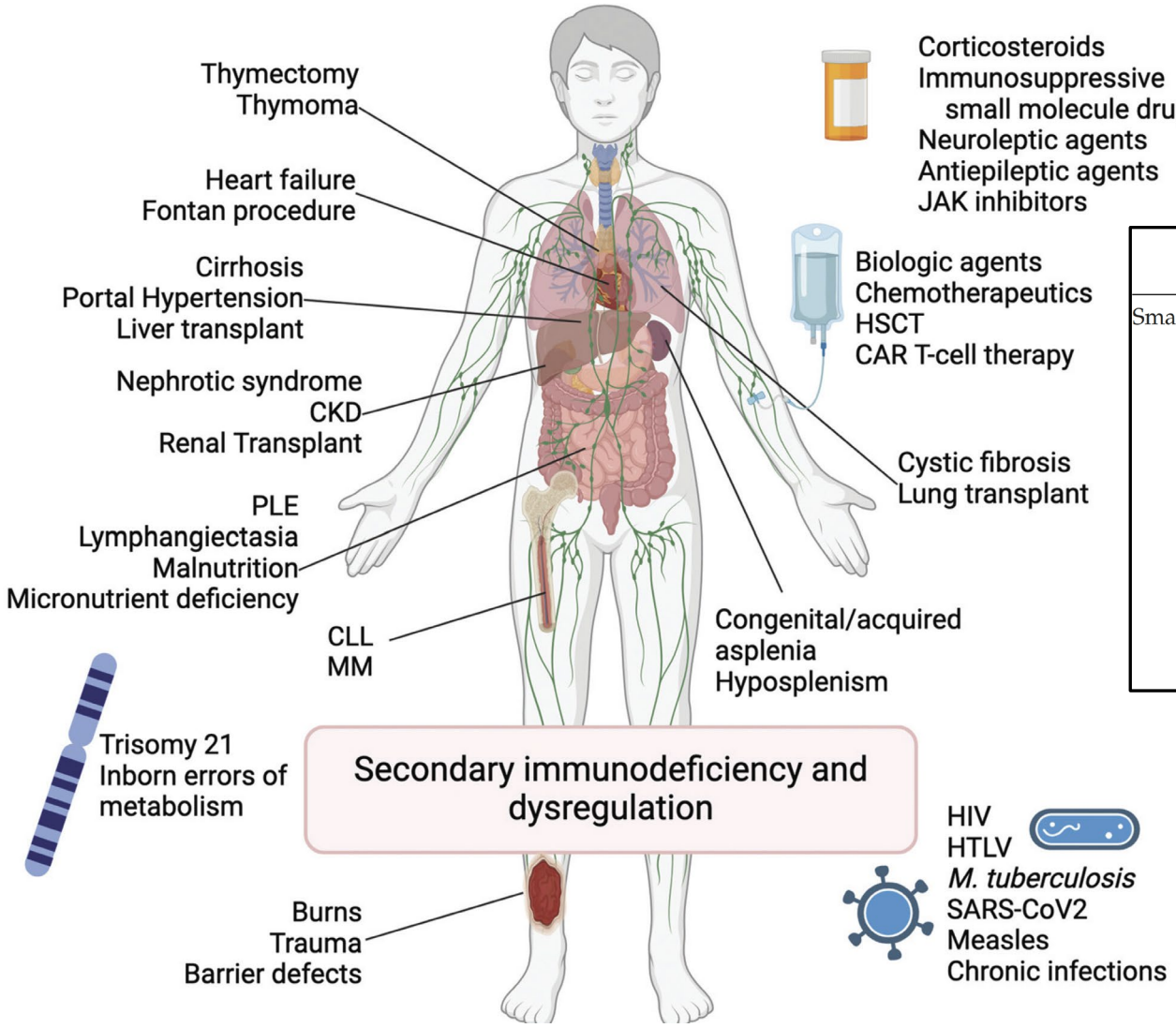
* Stress has been most commonly associated with an increased risk of upper respiratory tract infections and reactivation of herpes viruses, perhaps due to the effects of the endogenous stress cortisol response on the immune system.

¶ Aging has been associated with relative immunodeficiency, with reductions in cellular and humoral adaptive immune responses. Refer to the UpToDate topic on immune function in older adults.



Deinhardt-Emmer S, et al. Lancet Respir Med. 2025 Jul;13(7):623-637

PRIDOBLJENE IMUNSKE MOTNJE



Treatment Class	Drug	Reported Adverse Immunologic Effects
Small molecules	Azathioprine	Reduced IgG and IgM production, lymphopenia
	Corticosteroids	Hypogammaglobulinemia, $CD4^+$ T-cell lymphopenia
	Cyclophosphamide	Hypogammaglobulinemia, neutropenia, lymphopenia
	Cyclosporine	Reduced innate cell activation, reduced T-cell proliferation
	Methotrexate	Hypogammaglobulinemia, reduced response to live vaccines
	Mycophenolic acid	Reduced T- and B-cell proliferation, hypogammaglobulinemia
	Sulfasalazine	Hypogammaglobulinemia, leukopenia, IgA deficiency

Herman KE et Tuttle KL. Allergy Asthma Proc. 2024 Sep 1;45(5):347-354.

BIOLOŠKA ZDRAVILA IN OKUŽBE

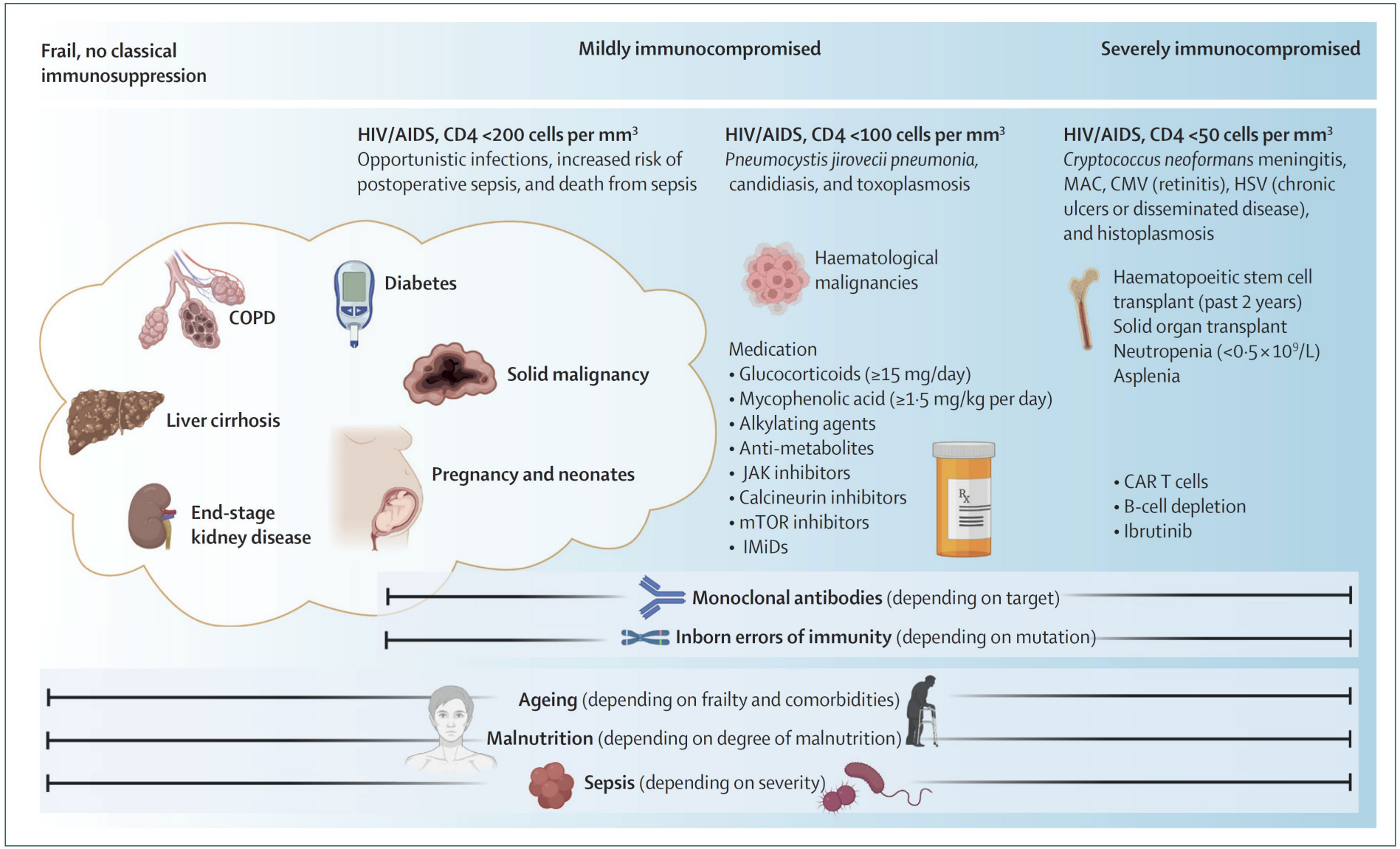
TABLE I. Examples of commonly used biologic treatments and associated secondary immunodeficiency

Molecular target	Example	Licensed indications*	Associated immunologic effects	Associated infection risk†
Anticytokines				
Autoimmune and autoinflammatory diseases				
BAFF (BlyS)	Belimumab	SLE		Not well reported
IL-1	Anakinra Canakinumab Rilonacept	Rheumatoid arthritis sJIA Periodic fever syndromes (CAPS, TRAPS, HIDS/MKD, FMF)	Neutropenia (rare)	Generally well tolerated Moderate increased risk of infections (mild-to-moderate in severity), including RTI
IL-6	Tocilizumab Sarilumab	Rheumatoid arthritis sJIA Polyarticular JIA Giant cell arteritis Cytokine release syndrome Severe COVID-19	Neutropenia	Significant increased risk of infections, including Severe bacterial infections VZV TB/non-TB mycobacteria Hepatitis B reactivation PJP
IL-12 and IL-23 (p40 subunit)	Ustekinumab	Plaque psoriasis Psoriatic arthritis Crohn disease		Generally well tolerated Hepatitis B reactivation TB (theoretic)
IL-17A	Secukinumab Ixekizumab Brodalumab	Plaque psoriasis Psoriatic arthritis Ankylosing spondylitis	Neutropenia	Minor increased risk of infections (mild- moderate in severity), including URTI Candidiasis (mucocutaneous) TB (theoretic)
IFN-γ	Emapalumab	pHLH		Not well reported
TNF-α	Adalimumab Certolizumab pegol Etanercept Golimumab Infliximab	Rheumatoid arthritis JIA Psoriatic arthritis Ankylosing spondylitis Crohn disease Ulcerative colitis Plaque psoriasis Hidradenitis suppurativa Uveitis	Neutropenia	Significant increased risk of infections, including Severe bacterial infections VZV TB/non-TB mycobacteria Other granulomatous infections Hepatitis B and hepatitis C reactivation Invasive fungal infections PJP
Atopic diseases				
TSLP	Tezepelumab	Asthma		Well tolerated Helminth infections (theoreticl)
IL-4 & IL-13 (IL4-receptor α)	Dupilumab	Atopic dermatitis Asthma CRSwNP EoE	Eosinophilia	Well tolerated Helminth infections (theoreticl)
IL-5	Mepolizumab Benralizumab Reslizumab	Asthma EGPA HES		Well tolerated Helminth infections (theoreticl)
IL-13	Tralokinumab	Atopic dermatitis	Eosinophilia	Well tolerated Helminth infections (theoreticl)
Surface molecules				
T cells				
CD25	Basiliximab	Renal transplant rejection		Not well reported
CD52	Alemtuzumab	Multiple sclerosis	Lymphopenia (on-target effect) Neutropenia	Major increased risk of infections, including Severe bacterial infections CMV, EBV HSV, VZV, HPV Hepatitis B and hepatitis C reactivation TB Invasive fungal infection, candidiasis Listeriosis, toxoplasmosis PJP, PML, BKV
B cells				
CD20	Rituximab Obinutuzumab Ocrelizumab Ofatumumab	Rheumatoid arthritis GPA, MPA NHL, CLL Pemphigus vulgaris Multiple sclerosis	B-cell depletion (on-target effect) Late-onset neutropenia Hypogammaglobulinemia Impaired vaccine responses	Significant increased risk of infections, including Severe bacterial infections Hepatitis B and hepatitis C reactivation CMV, VZV Enteroviral infection PJP, PML Severe COVID-19
CD38	Daratumumab	Multiple myeloma	Decreased plasma cells (on-target effect) Hypogammaglobulinemia Lymphopenia Neutropenia	Increased risk of VZV infection
T-cell costimulation				
CD80, CD86	Abatacept Belatacept	Rheumatoid arthritis JIA Renal transplant rejection		Generally well tolerated Associated with PTLD (belatacept only)
Leukocyte movement inhibition				
Integrin α4	Natalizumab	Multiple sclerosis Crohn disease		Major increased risk of PML
Integrin α4β7	Vedolizumab	Crohn disease Ulcerative colitis		No cases of PML reported
Other circulating proteins				
Complement				
C5	Eculizumab	PNH aHUS Myasthenia gravis		Significant increased risk of invasive Neisseria infections
IgE				
IgE	Omalizumab	Asthma Chronic idiopathic urticaria		Well tolerated Helminth infections (theoretic)

aHUS, Atypical hemolytic uremic syndrome; BAFF, B-cell–activating factor; BKV, BK virus; BLys, B lymphocyte stimulator; CAPS, cryopyrin-associated periodic syndrome; CLL, chronic lymphocytic leukemia; CRSwNP, chronic rhinosinusitis with nasal polyposis; EGPA, eosinophilic granulomatosis with polyangiitis; EoE, eosinophilic esophagitis; FMF, familial Mediterranean fever; GPA, granulomatosis with polyangiitis; HES, hypereosinophilic syndrome; HIDS, hyperimmunoglobulin D syndrome; JIA, juvenile idiopathic arthritis; MKD, mevalonate kinase deficiency; MPA, microscopic polyangiitis; NHL, non-Hodgkin lymphoma; pHLH, primary hemophagocytic lymphohistiocytosis; PJP, Pneumocystis jirovecii pneumonia; PML, progressive multifocal leukoencephalopathy; PNH, paroxysmal nocturnal hemoglobinuria; PTLD, posttransplant lymphoproliferative disorder; RTI, respiratory tract infection (including bronchitis, pneumonia); sJIA, systemic-onset juvenile idiopathic arthritis; TRAPS, TNF receptor associated periodic syndrome; TSLP, thymic stromal lymphopoietin;

Labrosse R et Haddad E. J Allergy Clin Immunol. 2023 Mar;151(3):686-690.

STOPNJA IMUNSKE OSLABELOSTI



Deinhardt-Emmer S, et al. Lancet Respir Med. 2025 Jul;13(7):623-637

PROGNOZA?

MAJOR ARTICLE

Is Bacteremic Sepsis Associated With Higher Mortality in Transplant Recipients Than in Nontransplant Patients? A Matched Case-Control Propensity-Adjusted Study

Andre C. Kalil,[1] Ather Syed,[2] Mark E. Rupp,[1] Heather Chambers,[1] Luciano Vargas,[3] Alexander Maskin,[3] Clifford D. Miles,[4] Alan Langnas,[3] and Diana F. Florescu[1,3]

[1]Division of Infectious Diseases, University of Nebraska Medical Center, Omaha; [2]Infectious Diseases, Lakeshore Medical Group, Milwaukee, Wisconsin; Divisions of [3]Transplant Surgery, and [4]Nephrology, University of Nebraska Medical Center, Omaha

Kalil AC, et al. Clin Infect Dis. 2015 Jan 15;60(2):216-22.

Variable	SOT Recipients (n = 123)	Patients Without SOT (n = 246)
Mean age, y	51.4	52.1
Sex, female/male	47.2%/52.8%	47.2%/52.8%
Ethnicity		
White	81.1%	78%
African American	7.4%	15.9%
Hispanic	4.1%	4.9%
Native American	5.7%	1%
Asian	1.6%	0.4%
Mean body mass index, kg/m^2	25.79	29.72
Hospital location		
Wards	81.3%	81.3%
Intensive care unit	18.7%	18.7%
Allograft type		
Liver	34.1%	. . .
Kidney	36.6%	. . .
Kidney/pancreas	13%	. . .
Small bowel	7.3%	. . .
Heart and/or lung	5.7%	. . .
≥3 grafts	3.3%	. . .
Transplant immunosuppression		
Calcineurin inhibitors[a]	90.2%	0
Antiproliferative agents[b]	68.3	0
Steroids	75.6%	5.7%
Induction antibodies[c]	66.7%	0
Fungal prophylaxis	33.3%	0
Cytomegalovirus prophylaxis	54.5%	0
Allograft rejection	8.9%	. . .
Statins administration	28.5%	16.7%
Mean temperature, °C	37.54°	37.53°
Mean WBC count, cells/mL	13 379	11 377
Mean platelet count, cells/mL	124 488	184 363
Blood culture results		
Gram-positive bacteria	63%	76%
Gram-negative bacteria	33%	22%
Candida spp	4.0%	2.0%
Disease severity		
SOFA score	5.81	4.05
Presence of comorbidities	95.1%	82.5%
Septic shock	13.8%	9.8%
Multiorgan failure	21.1%	8.1%

Table 2. Univariable Conditional Logistic Regression

Variable	OR	95% CI	*P* Value
WBC count	.967	.938–.997	.029
Platelets	.994	.991–.997	.000
Respiratory rate	1.022	.993–1.112	.319
Heart rate	1.001	.991–1.012	.826
Temperature	1.010	.851–1.198	.912
Presence of septic shock	1.611	.768–3.380	.207
Presence of multiorgan failure	3.872	1.831–8.186	<.0001
SOFA score	1.199	1.110–1.295	<.0001
Presence of comorbidities	5.634	1.957–16.214	.001
Body mass index	.946	.916–.976	.001
Presence of gram-positive bacteria	.506	.310–.828	.007
Presence of gram-negative bacteria	1.816	1.106–2.982	.018
Presence of *Candida albicans*	3.333	.797–13.948	.099
Presence of non-*albicans Candida*	1.200	.287–5.021	.803
Mono- vs polymicrobial	4.402	.686–2.867	.354
Presence of nosocomial infection	18.579	6.638–52.002	<.0001
Appropriate initial antibiotic regimen	.052	.012–.222	<.0001
Clostridium difficile after sepsis	3.522	1.691–7.337	.001

Kalil AC, et al. Clin Infect Dis. 2015 Jan 15;60(2):216-22.

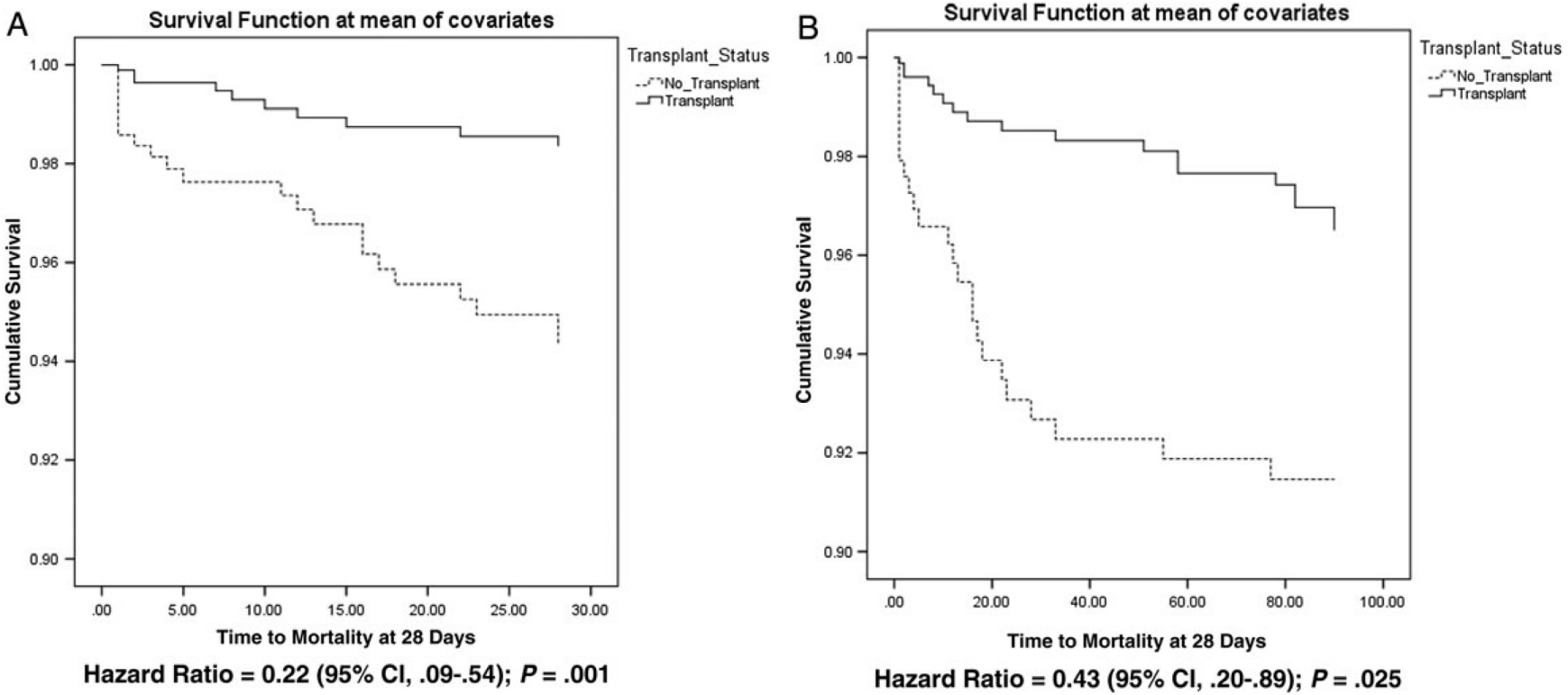


Figure 1. Multivariable Cox proportional hazards survival curves, with the outcome variable of mortality at 28 days (*A*) and 90 days (*B*). Abbreviation: CI, confidence interval.

Table 5. Multivariable Cox Proportional Hazards Regression

Outcome Variable	HR	95% CI	*P* Value
Mortality at 28 d			
Transplant status	.223	.09–.54	.001
Propensity score	5.650	2.90–10.99	<.0001
Mortality at 90 d			
Transplant status	.429	.204–.898	.025
Propensity score	25.953	2.512–7.951	<.0001

Abbreviations: CI, confidence interval; HR, hazard ratio.

SEPTIČNI ŠOK IN IMUNSKA MOTNJA: PACIFIC RAZISKAVA

Table 1 Patients characteristics

Characteristics	Total	Non-exposed (no immunosuppressive treatment)	Exposed (immunosuppressive treatment)	*p* value
	n = 433	n = 330	n = 103	
Age (years)	68 (59–76)	69 (60–77)	67 (58–76)	0.2
Men	277 (64%)	222 (67%)	55 (53%)	0.01
SOFA score at admission	10 (8–12)	10 (8–12)	9 (7–11)	0.01
SAPS II at screening	59 (47–71)	60 (47–71)	56 (48–66)	0.14
Comorbidities				
High blood pressure	230 (53%)	172 (52%)	58 (56%)	0.5
Diabetes	126 (29%)	95 (29%)	31 (30%)	0.8
Chronic heart failure	66 (15%)	50 (15%)	16 (16%)	> 0.9
Chronic respiratory failure	52 (12%)	40 (12%)	12 (12%)	0.9
Chronic renal failure	89 (21%)	48 (15%)	41 (40%)	< 0.001
Infection site				
Lungs	157 (36%)	118 (36%)	39 (38%)	
Abdomen	106 (24%)	85 (26%)	21 (20%)	
Urine	90 (21%)	66 (20%)	24 (23%)	
Skin	26 (6%)	22 (6.7%)	4 (3.9%)	
Central nervous system	9 (2.1%)	8 (2.4%)	1 (1%)	
Joints and bones	12 (2.8%)	6 (1.8%)	6 (5.8%)	
Bacteraemia	33 (7.6%)	25 (7.6%)	8 (7.8%)	
Cause of immunosuppression				
Organ transplantation	–	–	45 (44%)	
Systemic disease	–	–	58 (56%)	
Organ support and outcome				
ICU stay duration (days)	9 (5–15)	9 (5–15)	8 (4–14)	0.2
Number of days with vasopressor support	4 (2–9)	4 (2–10)	3 (1–7)	0.11
Number of mechanically ventilated patients	329 (76%)	259 (78%)	70 (68%)	0.029
Number of days with mechanical ventilation	4 (2–6)	4 (2–6)	4 (2–6)	0.7
Patients with dialysis during hospital stay	133 (31%)	90 (27%)	43 (42%)	0.005
ICU death	108 (25%)	83 (25%)	25 (24%)	0.9
Three-month mortality	126 (29%)	94 (28%)	32 (31%)	0.6

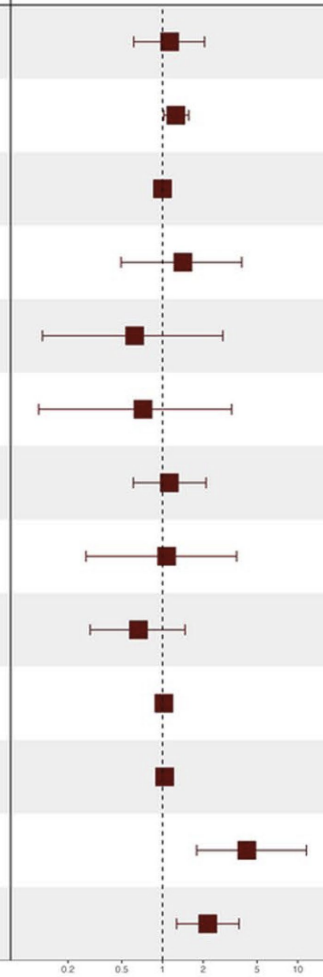
SOFA Sequential Organ Failure Assessment, *ICU* Intensive care unit

Vaidie J, et al. Crit Care. 2023 Sep 2;27(1):340

SEPTIČNI ŠOK IMUNSKO OSLABELIH: PACIFIC RAZISKAVA

A. In intensive care unit

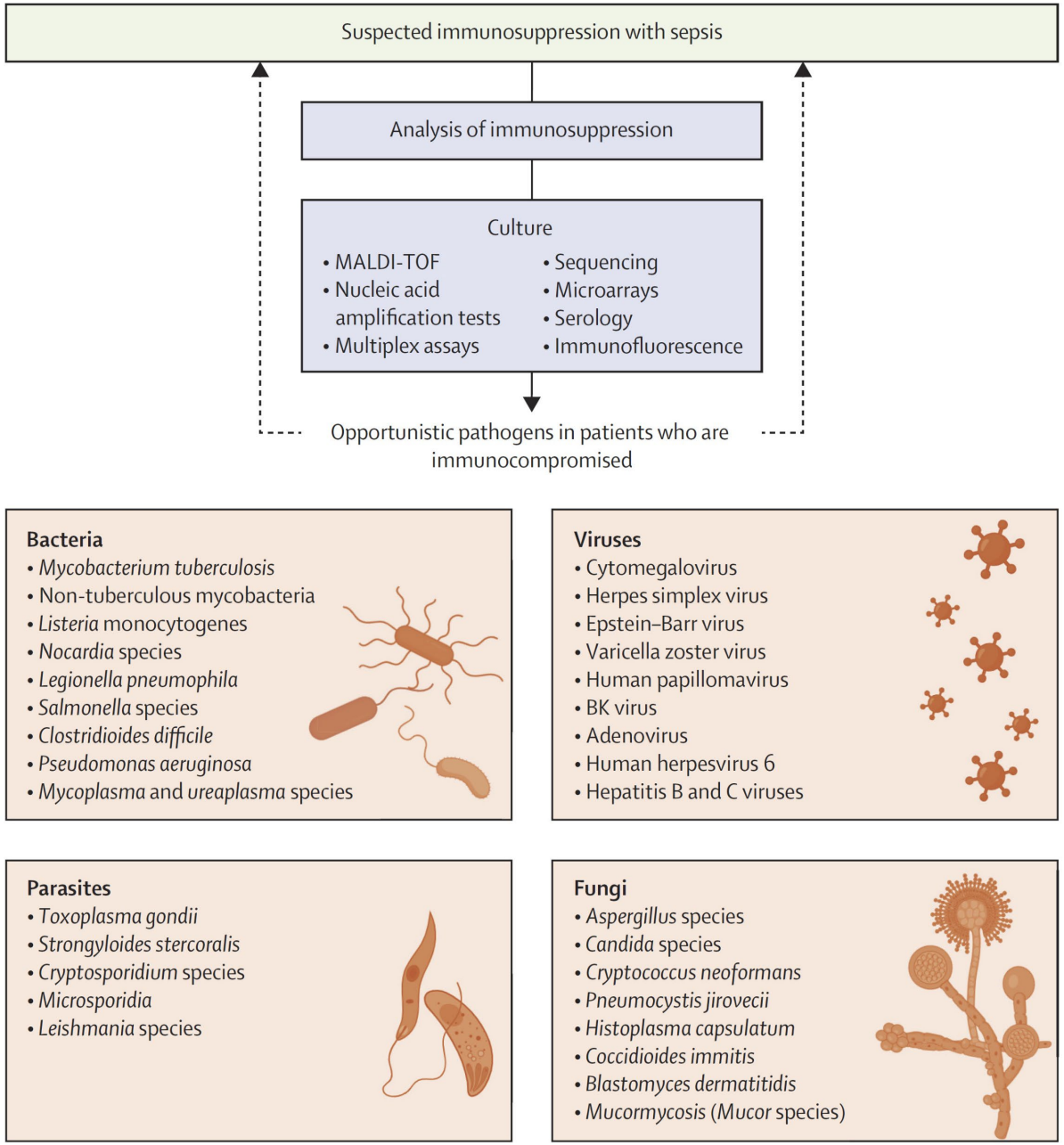
Variable		N	Odds ratio	p
Immunosuppressive treatment		433	1.13 (0.61, 2.05)	0.690
Age (per 10 yrs)		433	1.26 (1.02, 1.56)	0.035
Source of infection	Abdomen	106	Reference	
	Bacteremia	33	1.41 (0.49, 3.86)	0.505
	Central nervous system	9	0.62 (0.13, 2.80)	0.537
	Joints and bones	12	0.72 (0.12, 3.24)	0.686
	Lungs	157	1.12 (0.61, 2.10)	0.711
	Skin	26	1.07 (0.27, 3.53)	0.912
	Urine	90	0.66 (0.29, 1.47)	0.319
SOFA score (per additional point)		433	1.02 (0.94, 1.12)	0.591
SAPS II (per additional point)		433	1.04 (1.02, 1.06)	<0.001
Mechanical Ventilation		433	4.20 (1.79, 11.59)	0.002
Renal Replacement Therapy		433	2.16 (1.27, 3.68)	0.004



Vaidie J, et al. Crit Care. 2023 Sep 2;27(1):340

DIAGNOSTIKA IN ZDRAVLJENJE

"Običajna diagnostika & povzročitelji" +



Deinhardt-Emmer S, et al. Lancet Respir Med. 2025 Jul;13(7):623-637

FEBRILNA NEVTROPENIJA

Patients with chemotherapy-induced neutropenic fever who are at high risk for serious complications

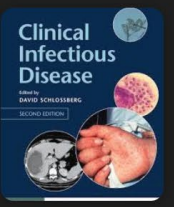
Patients with **any** of the following characteristics are considered to be at high risk for serious complications during episodes of neutropenic fever:
Receipt of cytotoxic therapy sufficiently myelosuppressive to result in anticipated severe neutropenia (ANC <500 cells/mcL) for >7 days*
MASCC risk index score <21[Δ]
CISNE score of ≥3[Δ] (in patients with solid tumors)
Presence of any active uncontrolled comorbid medical problems, including, but not limited to: ▪ Signs of severe sepsis or septic shock (eg, hemodynamic instability, mental status changes of new onset, respiratory dysfunction, oliguria) ▪ Oral or gastrointestinal mucositis that interferes with swallowing or causes severe diarrhea ▪ Gastrointestinal symptoms, including abdominal pain, nausea and vomiting, or diarrhea ▪ Intravascular catheter infection, especially catheter tunnel infection ▪ New pulmonary infiltrate or hypoxemia ▪ Underlying chronic lung disease ▪ Complex infection at the time of presentation
Alemtuzumab or CAR-T cell use within the past two months
Uncontrolled or progressive cancer[¶]
Evidence of hepatic insufficiency (defined as aminotransferase levels >5 times normal values) or renal insufficiency (defined as a creatinine clearance of <30 mL/minute)

Range of pathogens encountered in febrile neutropenic patients

Commonly cultured organisms	Less commonly cultured organisms	Additional organisms
Gram-negative bacteria	**Gram-negative bacteria**	**Fungi**
Escherichia coli	*Proteus* spp	*Cryptococcus* spp
Klebsiella spp	*Haemophilus* spp	*Histoplasma capsulatum*
Enterobacter spp	*Serratia* spp	*Coccidioides* spp
Pseudomonas aeruginosa	*Neisseria meningitidis*	*Blastomyces*
Citrobacter spp	*Capnocytophaga canimorsus*	*Pneumocystis jirovecii* (formerly *P. carinii*)
Acinetobacter spp	*Legionella* spp	**Viruses**
Stenotrophomonas maltophilia	*Bordetella* spp	Herpes simplex virus 1,2
Gram-positive bacteria	**Gram-positive bacteria**	Varicella-zoster virus
Coagulase-negative staphylococci	*Bacillus* spp	Cytomegalovirus
Staphylococcus aureus	*Listeria monocytogenes*	Epstein-Barr virus
Enterococcus spp	*Stomatococcus* spp	Human herpesvirus 6
Viridans group streptococci	*Corynebacterium jeikeium*	Enteroviruses
Streptococcus pneumoniae		Respiratory syncytial virus
Streptococcus pyogenes		Influenza virus
Other bacteria		Parainfluenza virus
Clostridioides difficile		**Other**
Anaerobes		*Babesia* spp
Mycobacteria		*Plasmodium* spp (the cause of malaria)
Fungi		*Toxoplasma* spp
Aspergillus spp		*Strongyloides stercoralis*
Candida spp		*Nocardia* spp

Betalaktam z delanjem na P. aeruginosa
(± vankomicin*
± protiglivno zdravilo**
± ....***)

Adapted from: Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guidelines for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis 2011; 52:e56.



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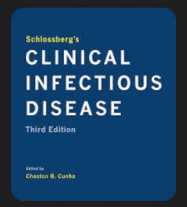

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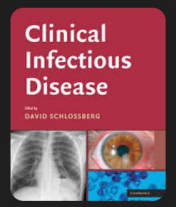

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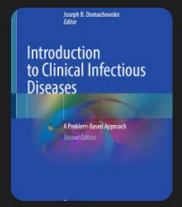

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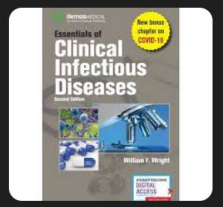

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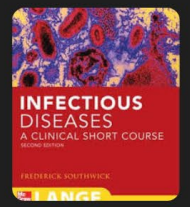

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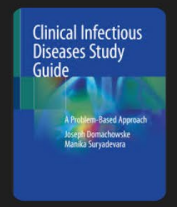

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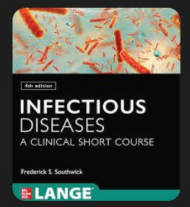

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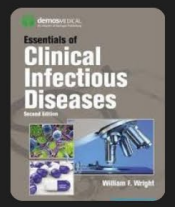

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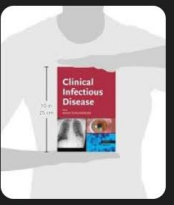

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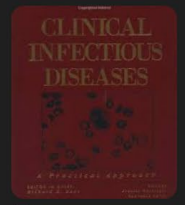

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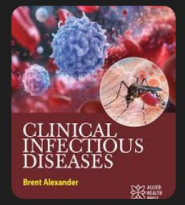

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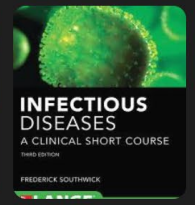

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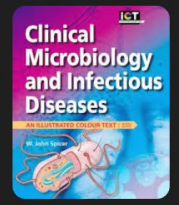

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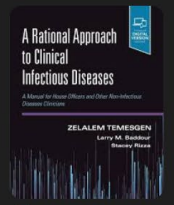

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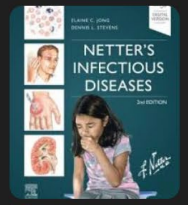

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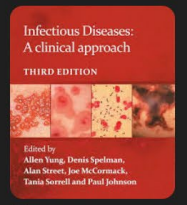

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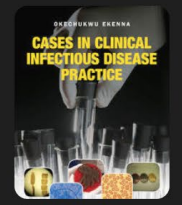

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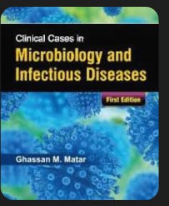

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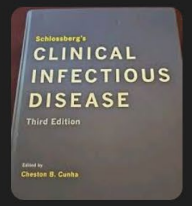

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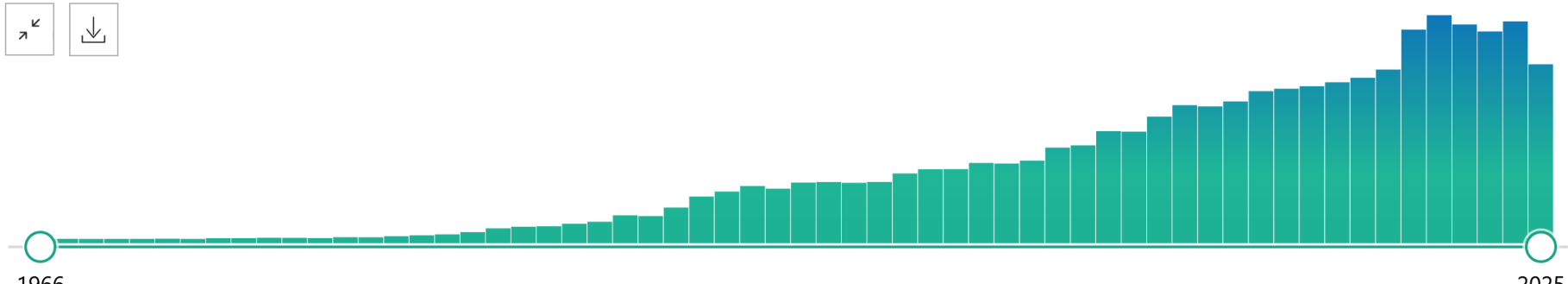
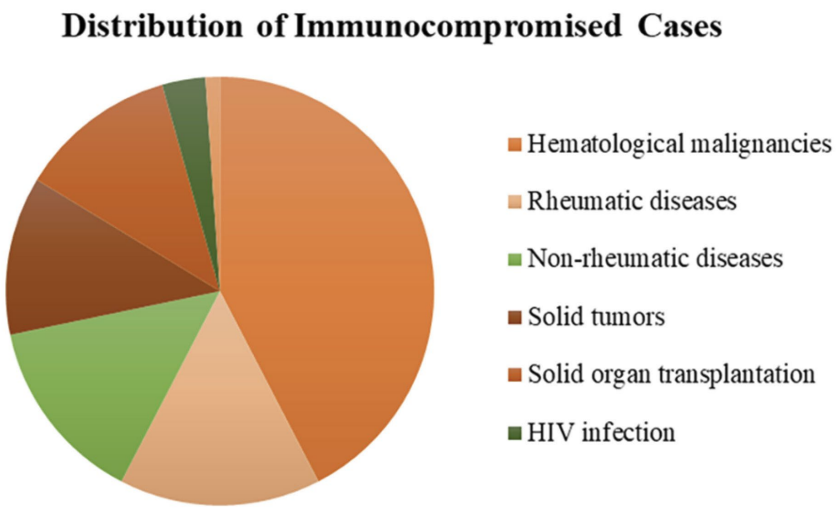


VPLIV METAGENOMSKEGA "NEXT GENERATION SEQUENCING" PR IK

	Immunocompromised group (n = 92)	Control group (n = 216)	P-value
Men (%)	54 (58.69%)	141 (65.28%)	0.273
Age (year)	55 (48-66)	62.5 (49-71)	0.010
Clinical indicators			
SOFA score	5.00 (3.00-8.75)	6.00 (3.00-10.00)	0.226
APACHII score	14.00 (10.00-22.00)	16.00 (11.00-21.00)	0.497
Length of stay (day)	28.00 (19.00-39.00)	24.00 (14.00-37.00)	0.058
Admission to ICU (%)	35 (38.04%)	117 (54.17%)	0.010
Length of ICU stay (day)	13.00 (7.00-23.00)	17.00 (11.50-28.00)	0.083
Treatments			
Mechanical ventilation (%)	29 (31.52%)	105 (48.61%)	0.006
Duration of mechanical ventilation (day)	11 (4.5-20)	14 (8-22)	0.132
Renal replacement therapy (%)	15 (16.30%)	40 (18.52%)	0.642
Duration of renal replacement therapy (hour)	114.50 (39.50-262.75)	70.38 (41.25-167.75)	0.427
Vasoactive medications (%)	36 (39.13%)	108 (50.00%)	0.080
Glucocorticoids (%)	82 (89.13%)	127 (58.80%)	0.000
Blood products (%)	79 (85.87%)	155 (71.76%)	0.008
Case fatality rate (%)	28 (30.43%)	62 (28.70%)	0.760



Li X, et al. Front Cell Infect Microbiol. 2023 Apr 24;13:1170687

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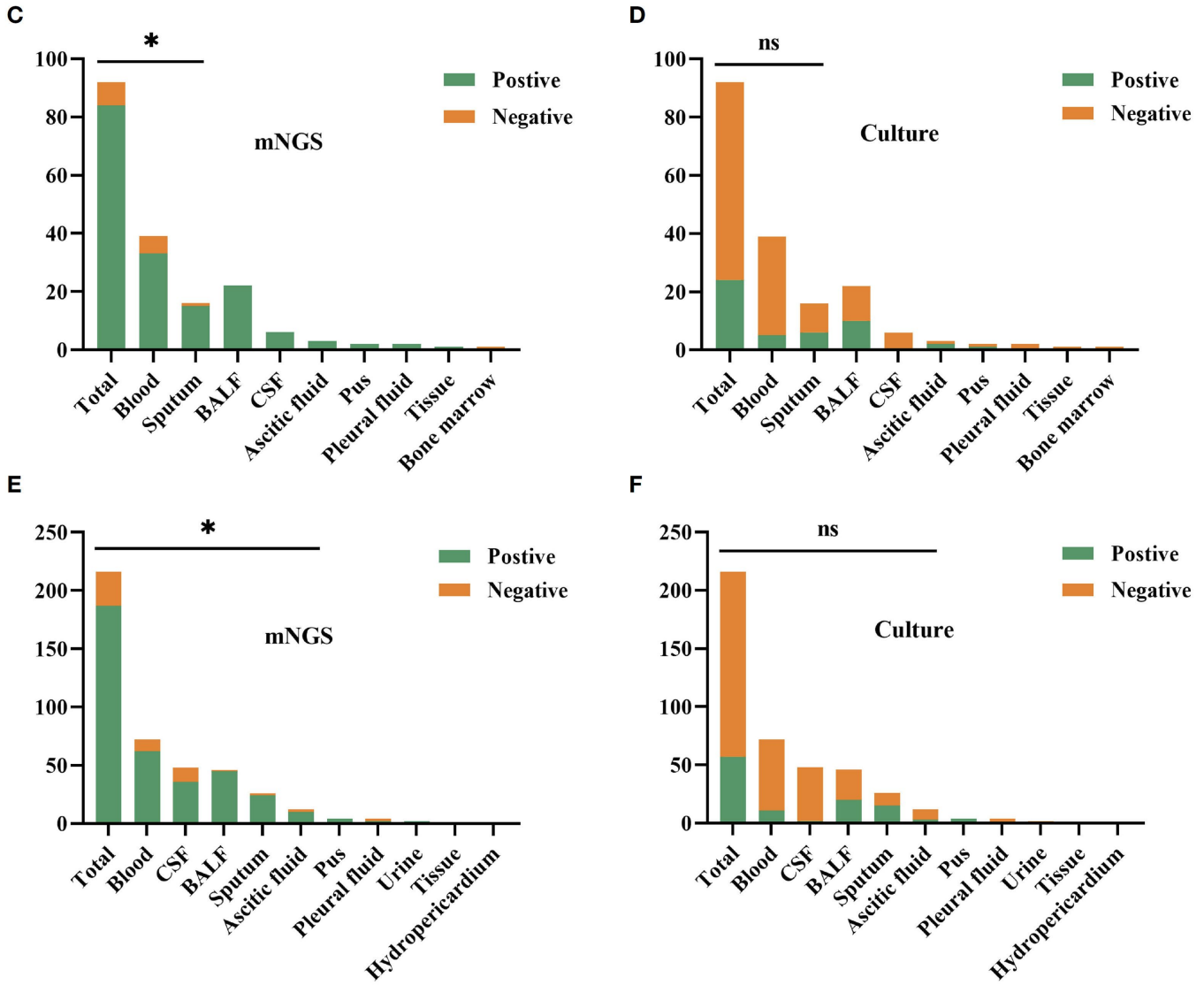

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VPLIV METAGENOMSKEGA "NEXT GENERATION SEQUENCING" PR IK

Clinical effect	Role of mNGS result	Treatment changes owing to mNGS
Positive effect (n=235; 76.3%)	Contributed to definitive diagnosis (n=235; 76.3%)	Treatment adjusted without de-escalation (n =124; 40.3%)
		Antibiotic de-escalated (n = 61; 19.8%)
		Empirical treatment continued (n=50; 16.2%)
Negative effect (n =7; 2.3%)	False-positive result led to incorrect diagnosis (n=7; 2.3%)	Incorrect antibiotic treatment
No effect (n=66; 21.4%)	No additional pathogen detected (n=37; 12.0%)	No changes
	Results deemed false or insignificant (n=29; 9.4%)	

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ZAKLJUČKI

- Ob “napredku” medicine se povečuje število oseb s prirojenimi in pridobljenimi imunskimi motnjami
- Okužbe so pri tej skupini pogostejše, vendar ni nujno, da so povezane z večjim deležem seps in povečano umrljivostjo
- Poznavanje posameznih imunskih motenj je pomembno za iskanje možnih povzročiteljev
- V prihodnosti pričakujemo dodatne diagnostične možnosti, v bližnji prihodnosti poleg “klasične molekularne diagnostike” tudi metagenomsko “next generation sequencing”

HVALA ZA POZORNOST, VPRAŠANJA ☺?