sepsis

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DEFINITION

- Sepsis is a broad term used for an incompletely understood process, and **there is no gold standard for its diagnosis**

- ***The term sepsis originates from the ancient Greek word sêpsis ("putrefaction" or "decay of organic matter") and was first used in a medical context in Homer's Iliad, written more than 2700 years ago***

- In the early **1990s** sepsis was clinically defined by a consensus definition generated by a group of key experts.

- ***The Sepsis-1 definition was centered around four systemic inflammatory response syndrome (SIRS) criteria***

TABLE 73.1 Sepsis Definitions

TERM	DEFINITION
1991 Consensus Conference[1]	
SIRS	At least two of the following: • Temperature >38°C or <36°C • Heart rate >90 beats/min • Respiratory rate >20 breaths/min or arterial CO_2 <32 mm Hg • White blood cell count >12 × 10^3/L or <4 × 10^3/L or >10% immature forms
Sepsis	Infection[a] + SIRS
Severe sepsis	Sepsis + acute organ dysfunction
Septic shock	Sepsis + persistent hypotension after fluid resuscitation

- **Sepsis-1** was defined as :(documented or suspected) infection leading to the onset of SIRS as reflected by the presence of two or more SIRS criteria.

- **Severe sepsis** was defined as: sepsis complicated by organ dysfunction

- **septic shock** defined as :“sepsis-induced hypotension persisting despite adequate fluid resuscitation

- The Sepsis-2 definition expanded the list of diagnostic criteria, encompassing a set of 24 general, inflammatory, hemodynamic, organ dysfunction, or tissue perfusion parameters.
- In the Sepsis-2 definition the criteria for severe sepsis remained similar, whereas septic shock was defined more explicitly as refractory hypotension (systolic blood pressure <90 mm Hg or mean arterial blood pressure <70 mm Hg) despite adequate fluid resuscitation

2001 International Sepsis Definitions Conference[2]

No significant changes from 1991 definitions, with the addition that signs and symptoms of sepsis are more varied than captured by 1991 definitions; this resulted in the presentation of a list of these signs and symptoms for the diagnosis of sepsis

- *Sepsis-3 definition, published in 2016, seeks to confine important limitations of Sepsis-1 and Sepsis-2, which include a disproportionate emphasis on inflammation, poor specificity and sensitivity of the SIRS criteria,* and the incorrect concept that sepsis follows a continuum through severe sepsis to shock .

- The new definition abandoned the use of SIRS criteria in the diagnosis of sepsis.
- In addition, in the new definition the presence of organ dysfunction is a requirement for a sepsis diagnosis, and therefore the term *severe sepsis* was eliminated in Sepsis-3

2015 Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)[3]

Sepsis[b]	• Life-threatening organ dysfunction caused by dysregulated host response to infection • Organ dysfunction can be identified as acute change in total SOFA score ≥2 points
Septic shock	• Sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality • Clinically defined as sepsis with persisting hypotension requiring vasopressors to maintain mean arterial pressure ≥65 mm Hg and with serum lactate >2 mmol/L

- **Sepsis-3 definition, sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection**
- In the clinic, organ dysfunction can be represented by an increase in the **Sequential [Sepsisrelated] Organ Failure Assessment (SOFA) score of 2 points or more** ; the baseline SOFA score should be presumed zero unless the patient is known to have preexisting organ dysfunction before the onset of infection

- Septic shock is now defined as a subset of sepsis in which strong circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone;
- these patients can be clinically identified by a **vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia**.

TABLE 73.2 SOFA Score

ORGAN SYSTEM	SCORE
Respiration	
Pao_2/Fio_2, mm Hg (kPa)	
<400 (53.3)	1
<300 (40)	2
<200 (26.7) with respiratory support	3
<100 (13.3) with respiratory support	4
Central nervous system	
GCS score	
13–14	1
10–12	2
6–9	3
<6	4
Cardiovascular	
MAP or use vasopressors (μg/kg/min)	
MAP <70 mm Hg	1
Dopamine <5 or dobutamine (any dose)[a]	2
Dopamine 5.1–15 or epinephrine ≤0.1 or norepinephrine ≤0.1	3
Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1	4
Liver	
Bilirubin, mg/dL (μmol/L)	
1.2–1.9 (20–32)	1
2.0–5.9 (33–101)	2
6.0–11.9 (102–204)	3
>12.0 (204)	4
Coagulation	
Platelets, × 10^3/μL	
<150	1
<100	2
<50	3
<20	4
Renal	
Creatinine, mg/dL (μmol/L) or urine output, mL/day	
1.2–1.9 (110–170)	1
2.0–3.4 (171–299)	2
3.5–4.9 (300–440) or <500	3
>5.0 (440) or <200	4

- The 2016 Task Force also introduced the quick SOFA, or qSOFA, score, composed of three components that are easy to measure at the bedside:
- respiratory rate of 22 breaths/min or greater,
- altered mentation,
- and systolic blood pressure of 100 mm Hg or less.

- Evidence indicated that in out-of-hospital, emergency department, and general hospital ward settings, adult patients with suspected infection and a higher risk for poor outcomes typical of sepsis can be rapidly identified by the presence of at least two qSOFA criteria.

- Moreover, failure to meet two or more SOFA or qSOFA criteria should not lead to a delay of treatment of infection or any other intervention deemed necessary by physicians

- As well as SIRS criteria, the criteria of qSOFA may be present in a patient without infection, due to other acute conditions such as hypovolemia, severe heart failure, or massive pulmonary thromboembolism. Thus, these scales are tools designed to help improve patient care and as such should never replace clinical judgment

comments against them

- Failure to use SIRS criteria may result in failure to recognize the onset of a continuum of sepsis until the patient has progressed to dysfunction of organs. Thus the CFCA states that this could lead to a failure to recognize the signs of potentially lethal infections until it is too late

CLINICAL SIGNS AND SYMPTOMS

- **Correctly recognizing a septic patient can be challenging, as clinical signs and symptoms at presentation can be variable and nonspecific.**
- The manifestations of sepsis depend on:
- the source of infection,
- The causative pathogen,
- the type and extent of organ dysfunction,
- drug use
- and comorbidity of the patient,
- and the delay before consulting a physician or before start of treatment

- The most common underlying comorbidities of patients admitted for sepsis include :

- chronic obstructive pulmonary disease,
- neoplasm,
- human immunodeficiency virus (HIV) infection,
- chronic liver disease,
- chronic renal disease,
- diabetes,
- peripheral vascular disease,
- autoimmune disease.

- ***General variables include:***

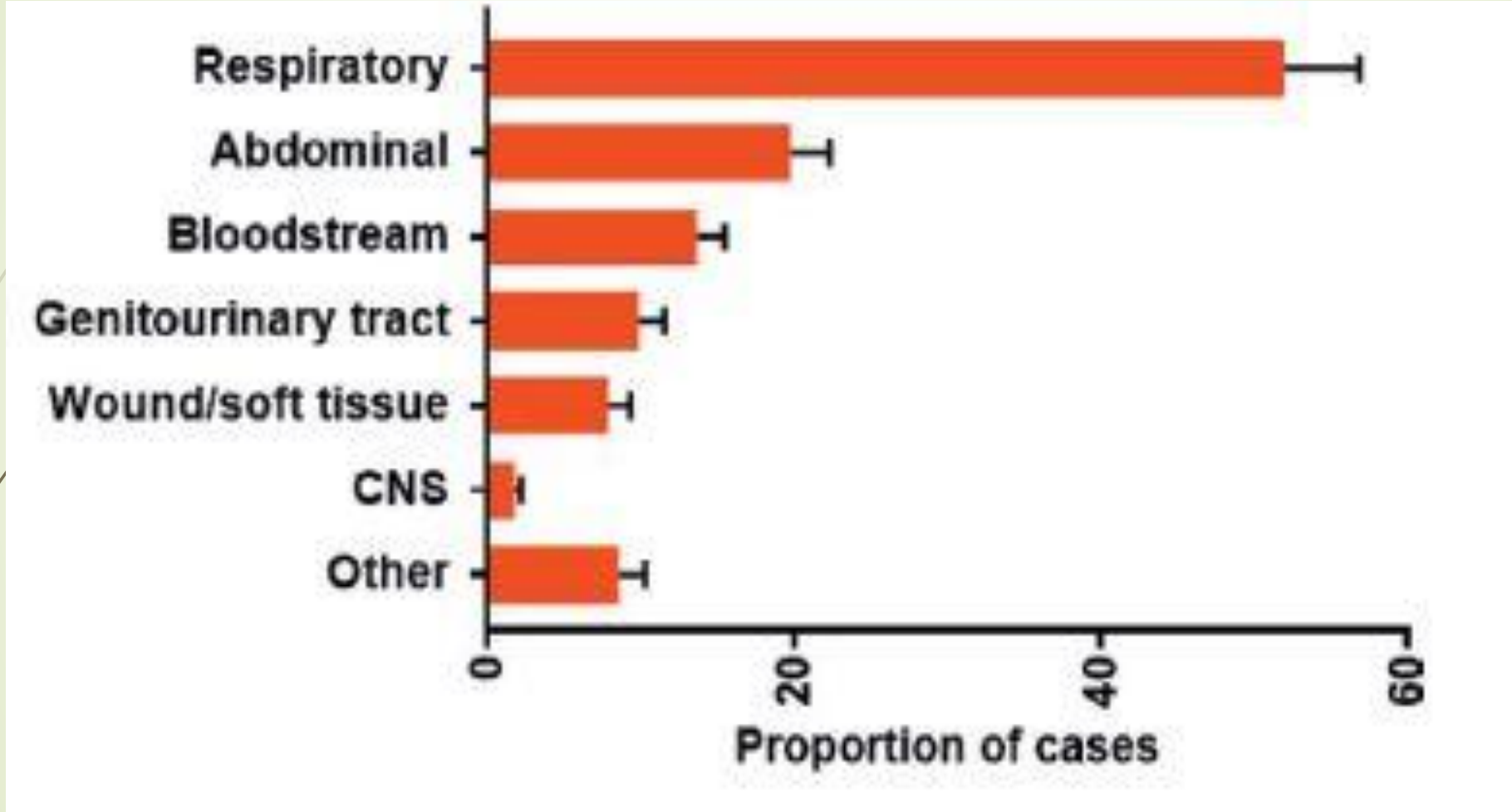
- **fever,tachycardia, tachypnea, altered mental status, significant edema, or positive fluid balance (>20 mL/kg over 24 hours). Hypothermia is observed in 9% to 35% of patients with sepsis and is associated with adverse outcomes**

Source of Sepsis

- **Pneumonia is the most common source of sepsis in adults,**
- **followed by abdominal,**
- **urinary tract,**
- **and skin/soft tissue infections**

These preferred sites account for 80% to 90% of all adult sepsis cases,

- the remainder being caused by bone/joint infections, ear-nose-throat infections, and others. More than one source is found in approximately 6% of episodes.


Respiratory
Abdominal
Bloodstream
Genitourinary tract
Wound/soft tissue
CNS
Other
0
20
40
60
Proportion of cases

EPIDEMIOLOGY

- There is substantial variability in the reported incidence and mortality of sepsis depending on the case definitions and diagnosis codes used to identify patients
- The current global estimates of 31.5 million episodes of sepsis per year comes from a systematic review that extrapolated data from selected highincome countries (United States, Germany, Australia, Taiwan, Norway, Spain, and Sweden)
- incidence rate of hospitalization among emergency medical services encounters is greater for sepsis than for acute myocardial infarction or stroke.

- Median ICU length of stay was 5 days (range, 2–6 days). Median hospital length of stay was 10 days (range, 8–12 days). The cost of treating sepsis in US hospitals was estimated to be $24 billion in 2013, making it the most expensive condition treated in US hospitals in that year
- Sepsis is estimated to account for more than 5.3 million deaths around the world each year
- In the United States, sepsis contributes to one in every two to three in-hospital deaths and represents the most frequent cause of death in noncoronary ICUs

- US data from 2014 show that of all patients admitted for sepsis, 15.0% died in the hospital, and 6.2% were discharged to a hospice.
- Data from Australia and New Zealand show hospital fatality rates for sepsis and septic shock of 14% and 22%
- in Brazil identified 794 patients with sepsis, in whom mortality was observed in more than 50%

Trends in Time: Incidence and Mortality

- numerous studies have suggested that the incidence of sepsis is increasing over time, while mortality is decreasing
- Key factors that contribute to the overall rise in the worldwide incidence of sepsis include :
- the aging of the population,
- the emergence of antimicrobial resistance,
- the growing use of immunosuppressive drugs and therapies,
- and the increased number of patients who are at risk for developing sepsis

Risk Factors

- People at the highest risk of developing sepsis include infants and elderly adults as well as patients with chronic or serious illnesses such as diabetes and cancer and patients with an impaired immune system

TABLE 73.3 Risk Factors for Sepsis

Demographic Factors

Older age (>65 years old)
Male sex
Black race
Nutrition
Vaccination status
Genetic polymorphisms

Environmental Factors

Poor socioeconomic status
Seasonal variation and contacts
Disease outbreaks
Travel

Comorbidities

Diabetes
Chronic obstructive pulmonary disease
Cancer
Chronic renal disease
Chronic liver disease
Human immunodeficiency virus
Use of immunosuppressive agents

Hospital Factors

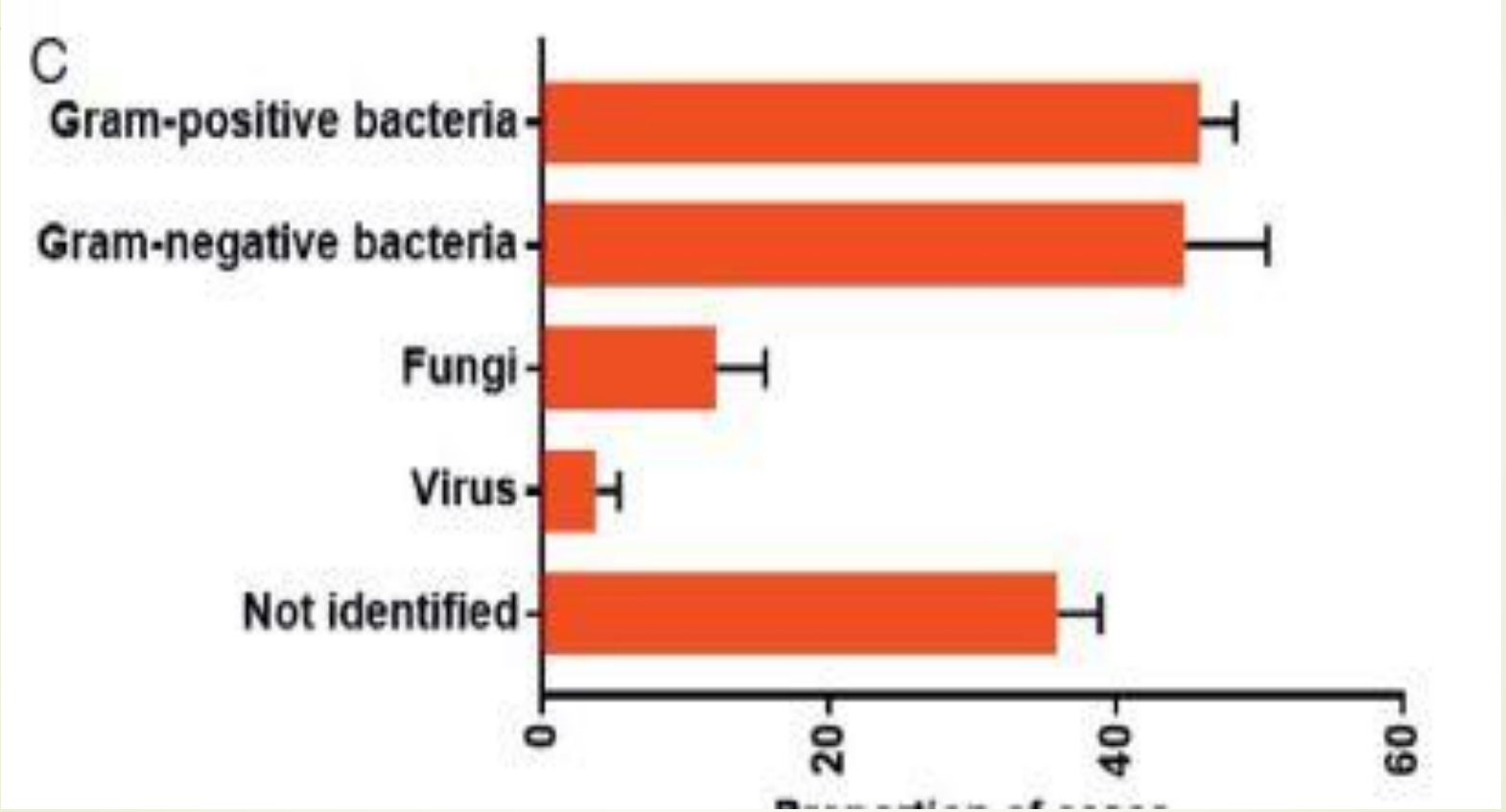
Duration of hospitalization
Antibiotic resistance
Catheters (e.g., urine catheters, intravenous lines)
Complications of surgery (wound infection, emergency vs. elective surgery)

MICROBIOLOGY

- Most cases today occur in patients with previous morbidities and are caused by opportunists from the patient's own microbiome.
- It is important to determine the exact cause of sepsis, i**nvestigate microbial resistance both in a given patient and in the population**

Main Causative Agents

- Blood cultures are positive in approximately one-third of patients
- An epidemiologic study of sepsis that during the period 1979–2000, the incidence of sepsis caused by gram-positive microorganisms steadily increased
- The most common isolated gram-positive bacterial pathogens are *Staphylococcus aureus, Streptococcus pneumoniae*, and *Enterococcus* spp.;
- the most common gram-negative pathogens are *Escherichia coli, Klebsiella* spp., *Pseudomonas* spp., and *Acinetobacter* spp


C
Gram-positive bacteria
Gram-negative bacteria
Fungi
Virus
Not identified
0
20
40
60

- The increase of fungal infections over the last 2 decades could not be prevented by the introduction of new antifungals.
- This is worrisome, as fungal sepsis is associated with a high mortality.
- *Candida* spp. Are the most prominent of all the fungi that can cause sepsis.
- Reported ICU mortality is more than 1.5 times higher in patients with *Candida* bloodstream infections compared with bacterial bloodstream infections.
- Important risk factors for candidemia include:
- **immunosuppressed or neutropenic state, prior intense antibiotic therapy, indwelling vascular catheters, prolonged ICU stay, and colonization in multiple sites**

TABLE 73.4 Distribution in Percentages of Identified Organisms in Culture-Positive Infected Patients Included in the EPIC II Study According to Geographic Region

ORGANISM	WESTERN EUROPE	EASTERN EUROPE	CENTRAL/SOUTH AMERICA	NORTH AMERICA	OCEANIA	AFRICA	ASIA
Gram-Positive							
Staphylococcus aureus	20%	22%	19%	27%	28%	30%	16%
Staphylococcus epidermidis	11%	12%	9%	12%	8%	15%	9%
Streptococcus pneumoniae	5%	5%	3%	4%	3%	6%	2%
Enterococcus spp.	13%	15%	4%	10%	9%	0%	6%
Other	7%	4%	4%	11%	9%	7%	4%
Gram-Negative							
Escherichia coli	17%	15%	14%	14%	13%	11%	17%
Enterobacter	7%	8%	9%	8%	3%	7%	5%
Klebsiella spp.	10%	21%	16%	9%	12%	19%	21%
Pseudomonas spp.	17%	29%	26%	13%	15%	15%	30%
Acinetobacter spp.	6%	17%	14%	4%	4%	15%	19%
Other	18%	15%	17%	11%	21%	20%	15%
Anaerobes	5%	3%	1%	8%	3%	2%	3%
Fungi							
Candida	19%	19%	13%	19%	13%	11%	16%
Aspergillus	2%	1%	1%	3%	2%	0%	1%

ONLINE SPECIAL ARTICLE

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

Table of Current Recommendations and Changes From Previous 2016 Recommendations

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
1. For hospitals and health systems, we recommend using a performance improvement program for sepsis, including sepsis screening for acutely ill, high-risk patients and standard operating procedures for treatment.	***Strong,*** *moderate-quality evidence (for screening)* ***Strong,*** *very low-quality evidence (for standard operating procedures)*	**Changed from *Best practice statement*** "We **recommend** that hospitals and hospital systems have a performance improvement program for sepsis including sepsis screening for acutely ill, high-risk patients."
2. We recommend against using qSOFA compared with SIRS, NEWS, or MEWS as a single-screening tool for sepsis or septic shock.	***Strong***, *moderate-quality evidence*	***NEW***
3. For adults suspected of having sepsis, we suggest measuring blood lactate.	***Weak,*** *low quality of evidence*	

- Studies have shown that **qSOFA is more specific but less sensitive** than **having two of four SIRS criteria** for early identification of infection induced organ dysfunction
- Neither SIRS nor qSOFA are ideal screening tools for sepsis and the bedside clinician needs to understand the limitations of each
- It has been suggested that lactate can also be used to screen for the presence of sepsis among undifferentiated adult patients with clinically suspected (but not confirmed) sepsis.
- The lactate cutoffs determining an elevated level ranged from 1.6−2.5 mmol/L

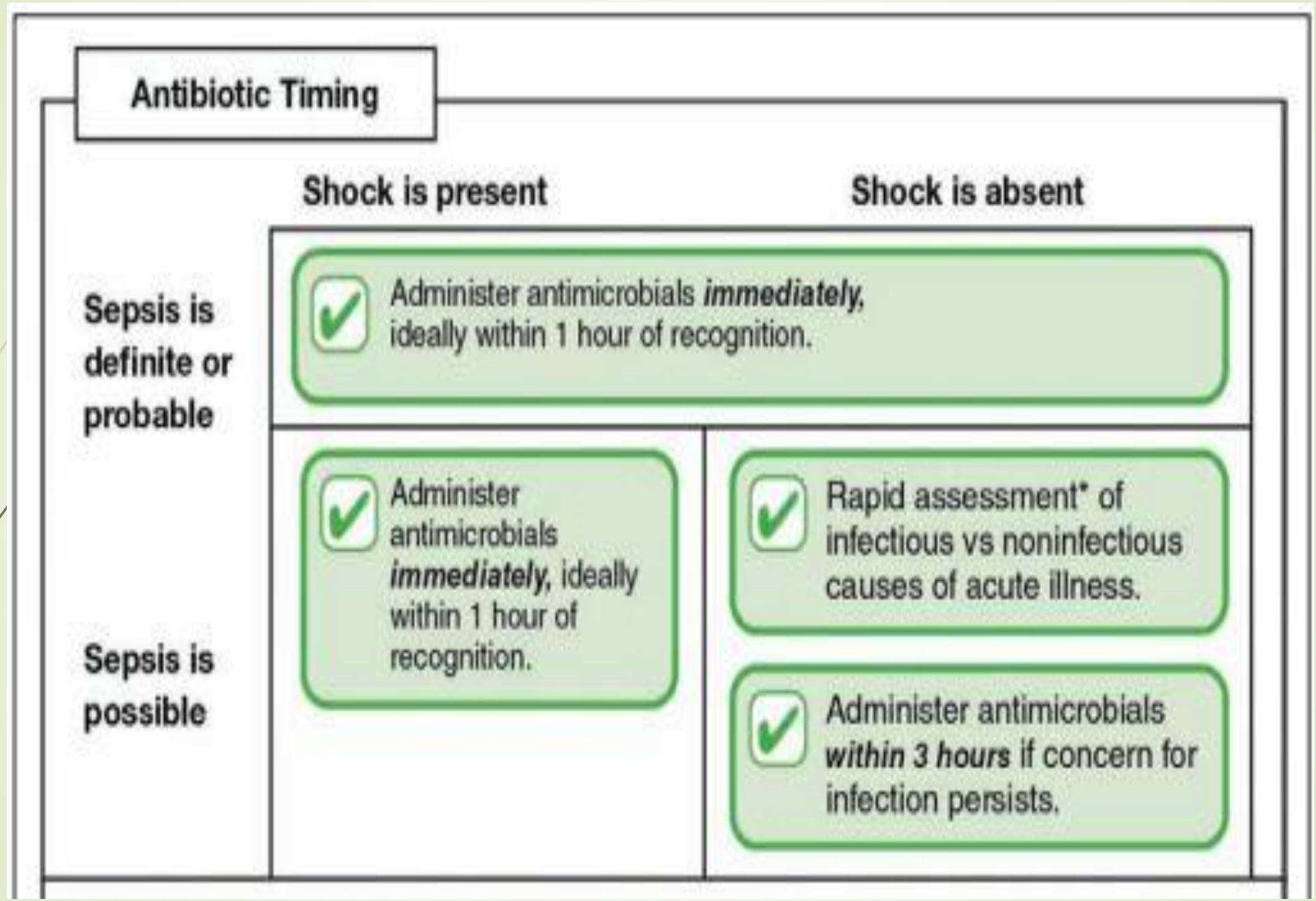
INITIAL RESUSCITATION		
4. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately.	***Best practice statement***	
5. For patients with sepsis induced hypoperfusion or septic shock we suggest that at least 30 mL/kg of IV crystalloid fluid should be given within the first 3 hr of resuscitation.	**Weak**, *low quality of evidence*	**DOWNGRADE** from ***Strong***, low quality of evidence "We **recommend** that in the initial resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hr"
6. For adults with sepsis or septic shock, we suggest using dynamic measures to guide fluid resuscitation, over physical examination, or static parameters alone.	***Weak,*** *very low quality of evidence*	
7. For adults with sepsis or septic shock, we suggest guiding resuscitation to decrease serum lactate in patients with elevated lactate level, over not using serum lactate.	***Weak,*** *low quality of evidence*	
8. For adults with septic shock, we suggest using capillary refill time to guide resuscitation as an adjunct to other measures of perfusion.	***Weak,*** *low quality of evidence*	***NEW***
MEAN ARTERIAL PRESSURE		
9. For adults with septic shock on vasopressors, we recommend an initial target mean arterial pressure (MAP) of 65 mm Hg over higher MAP targets	***Strong,*** *moderate-quality evidence*	

- To avoid over- and under-resuscitation, fluid administration beyond the initial resuscitation should be guided by careful assessment of intravascular volume status and organ perfusion. Heart rate, central venous pressure (CVP) and systolic blood pressure alone are poor indicators of fluid status.
- **Dynamic measures** have demonstrated better diagnostic accuracy at predicting fluid responsiveness compared with static techniques**. Dynamic measures include passive leg raising combined with cardiac output (CO) measurement, fluid challenges against stroke volume (SV), systolic pressure or pulse pressure, and increases of SV in response to changes in intrathoracic pressure.**

- regions where measurement of CO or SV may not be possible, **a >15% increase in pulse pressure could indicate that the patient is fluid responsive utilizing a passive leg-raise test for 60–90 seconds**
- When advanced hemodynamic monitoring is not available, alternative measures of organ perfusion may be used to evaluate the effectiveness and safety of volume administration. **Temperature of the extremities, skin mottling and capillary refill time (CRT**) have been validated and shown to be reproducible signs of tissue perfusion

INFECTION		
11. For adults with suspected sepsis or septic shock but unconfirmed infection, we recommend continuously re-evaluating and searching for alternative diagnoses and discontinuing empiric antimicrobials if an alternative cause of illness is demonstrated or strongly suspected.	***Best practice statement***	
12. For adults with possible septic shock or a high likelihood for sepsis, we recommend administering antimicrobials immediately, ideally within 1 hr of recognition.	***Strong,*** *low quality of evidence (Septic shock)* ***Strong,*** *very low quality of evidence (Sepsis without shock)*	**CHANGED from previous:** "We recommend that administration of intravenous antimicrobials should be initiated as soon as possible after recognition and within one hour for both a) septic shock and b) sepsis without shock" ***strong recommendation,*** *moderate quality of evidence*
13. For adults with possible sepsis without shock, we recommend rapid assessment of the likelihood of infectious versus noninfectious causes of acute illness.	***Best practice statement***	

14. For adults with possible sepsis without shock, we suggest a time-limited course of rapid investigation and if concern for infection persists, the administration of antimicrobials within 3 hr from the time when sepsis was first recognized.	***Weak,*** *very low quality of evidence*	**NEW from previous:** "We recommend that administration of IV antimicrobials should be initiated as soon as possible after recognition and within 1 hr for both a) septic shock and b) sepsis without shock" ***strong recommendation,*** *moderate quality of evidence*
15. For adults with a low likelihood of infection and without shock, we suggest deferring antimicrobials while continuing to closely monitor the patient.	***Weak,*** *very low quality of evidence*	**NEW from previous:** "We recommend that administration of IV antimicrobials should be initiated as soon as possible after recognition and within 1 hr for both a) septic shock and b) sepsis without shock" ***strong recommendation,*** *moderate quality of evidence*
16. For adults with suspected sepsis or septic shock, we suggest against using procalcitonin plus clinical evaluation to decide when to start antimicrobials, as compared to clinical evaluation alone.	***Weak,*** *very low quality of evidence*	

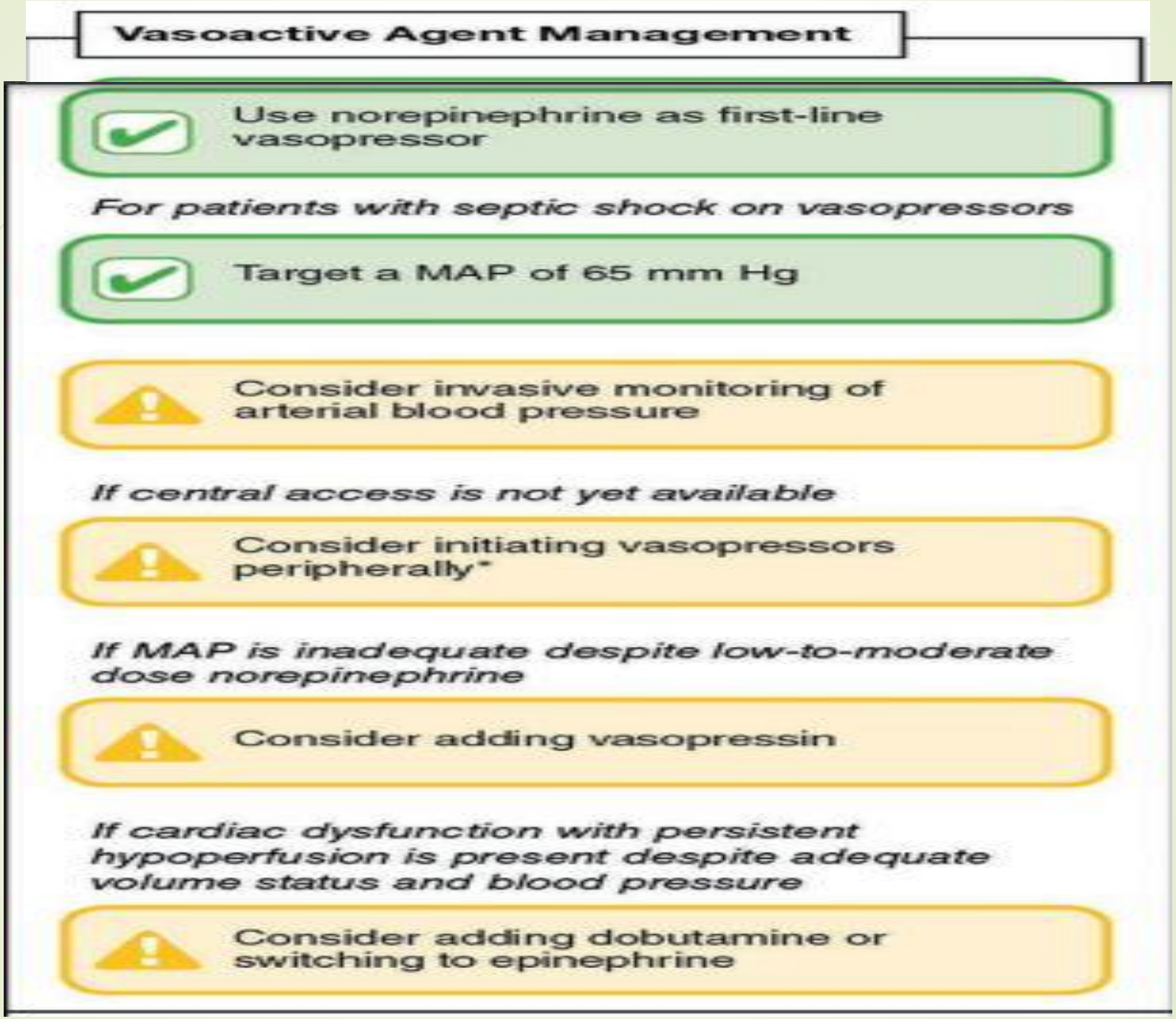

Antibiotic Timing
Shock is present
Shock is absent
Sepsis is definite or probable
Administer antimicrobials *immediately*, ideally within 1 hour of recognition.
Sepsis is possible
Administer antimicrobials *immediately*, ideally within 1 hour of recognition.
Rapid assessment* of infectious vs noninfectious causes of acute illness.
Administer antimicrobials *within 3 hours* if concern for infection persists.

HEMODYNAMIC MANAGEMENT		
32. For adults with sepsis or septic shock, we recommend using crystalloids as first-line fluid for resuscitation.	***Strong,*** *moderate-quality evidence*	
33. For adults with sepsis or septic shock, we suggest using balanced crystalloids instead of normal saline for resuscitation.	***Weak,*** *low quality of evidence*	**CHANGED from *weak recommendation***, *low quality of evidence.* "We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock"
34. For adults with sepsis or septic shock, we suggest using albumin in patients who received large volumes of crystalloids.	***Weak,*** *moderate-quality evidence*	
35. For adults with sepsis or septic shock, we recommend against using starches for resuscitation.	***Strong,*** *high-quality evidence*	

37. For adults with septic shock, we recommend using norepinephrine as the first-line agent over other vasopressors.	***Strong*** Dopamine. *High-quality evidence* Vasopressin. *Moderate-quality evidence* Epinephrine. *Low quality of evidence* Selepressin. *Low quality of evidence* Angiotensin II. *Very low-quality evidence*
38. For adults with septic shock on norepinephrine with inadequate mean arterial pressure levels, we suggest adding vasopressin instead of escalating the dose of norepinephrine.	***Weak,*** *moderate quality evidence*
39. For adults with septic shock and inadequate mean arterial pressure levels despite norepinephrine and vasopressin, we suggest adding epinephrine.	***Weak,*** *low quality of evidence*

41. For adults with septic shock and cardiac dysfunction with persistent hypoperfusion despite adequate volume status and arterial blood pressure, we suggest either adding dobutamine to norepinephrine or using epinephrine alone.	**Weak,** *low quality of evidence*	
42. For adults with septic shock and cardiac dysfunction with persistent hypoperfusion despite adequate volume status and arterial blood pressure, we suggest against using levosimendan.	**Weak,** *low quality of evidence*	**NEW**
43. For adults with septic shock, we suggest invasive monitoring of arterial blood pressure over noninvasive monitoring, as soon as practical and if resources are available.	**Weak,** *very low quality of evidence*	
44. For adults with septic shock, we suggest starting vasopressors peripherally to restore mean arterial pressure rather than delaying initiation until a central venous access is secured.	**Weak,** *very low quality of evidence*	**NEW**

45. There is insufficient evidence to make a recommendation on the use of restrictive versus liberal fluid strategies in the first 24 hr of resuscitation in patients with sepsis and septic shock who still have signs of hypoperfusion and volume depletion after the initial resuscitation.	***No recommendation***	**NEW** "We suggest using either balanced crystalloids or saline for fluid resuscitation of patients with sepsis or septic shock" ***Weak recommendation***, *low quality of evidence* "We suggest using crystalloids over gelatins when resuscitating patients with sepsis or septic shock." ***Weak recommendation***, *low quality of evidence*


Vasoactive Agent Management
Use norepinephrine as first-line vasopressor
For patients with septic shock on vasopressors
Target a MAP of 65 mm Hg
Consider invasive monitoring of arterial blood pressure
If central access is not yet available
Consider initiating vasopressors peripherally*
If MAP is inadequate despite low-to-moderate dose norepinephrine
Consider adding vasopressin
If cardiac dysfunction with persistent hypoperfusion is present despite adequate volume status and blood pressure
Consider adding dobutamine or switching to epinephrine

ADDITIONAL THERAPIES		
58. For adults with septic shock and an ongoing requirement for vasopressor therapy we suggest using IV corticosteroids.	***Weak,*** *moderate-quality evidence*	**UPGRADE from *Weak recommendation,*** *low quality of evidence* "We suggest against using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). If this is not achievable, we suggest IV hydrocortisone at a dose of 200 mg/day."
59. For adults with sepsis or septic shock we suggest against using polymyxin B hemoperfusion.	***Weak,*** *low quality of evidence*	**NEW from previous:** "We make no recommendation regarding the use of blood purification techniques"
60. There is insufficient evidence to make a recommendation on the use of other blood purification techniques.	***No recommendation***	
61. For adults with sepsis or septic shock we recommend using a restrictive (over liberal) transfusion strategy.	***Strong,*** *moderate-quality evidence*	

62. For adults with sepsis or septic shock we suggest against using IV immunoglobulins.	***Weak,*** *low quality of evidence*
63. For adults with sepsis or septic shock, and who have risk factors for gastrointestinal (GI) bleeding, we suggest using stress ulcer prophylaxis.	***Weak,*** *moderate-quality evidence*
64. For adults with sepsis or septic shock, we recommend using pharmacologic venous thromboembolism (VTE) prophylaxis unless a contraindication to such therapy exists.	***Strong,*** *moderate-quality evidence*
65. For adults with sepsis or septic shock, we recommend using low molecular weight heparin over unfractionated heparin for VTE prophylaxis	***Strong,*** *moderate-quality evidence*
66. For adults with sepsis or septic shock, we suggest against using mechanical VTE prophylaxis, in addition to pharmacological prophylaxis, over pharmacologic prophylaxis alone.	***Weak,*** *low quality of evidence*

70. For adults with sepsis or septic shock we suggest against using IV vitamin C.	***Weak,*** *low quality of evidence*	***NEW***
71. For adults with septic shock and hypoperfusion-induced lactic acidemia, we suggest against using sodium bicarbonate therapy to improve hemodynamics or to reduce vasopressor requirements.	***Weak,*** *low quality of evidence*	
72. For adults with septic shock and severe metabolic acidemia (pH ≤ 7.2) and acute kidney injury (AKIN score 2 or 3), we suggest using sodium bicarbonate therapy	***Weak,*** *low quality of evidence*	
73. For adult patients with sepsis or septic shock who can be fed enterally, we suggest early (within 72 hr) initiation of enteral nutrition.	***Weak,*** *very low quality of evidence*	

Thanks your attention