

**Ασθενής με υποψία λοίμωξης στο ΤΕΠ:  
πώς θα σκεφτώ; Τι θα κάνω;**



***Ευτυχία Πολυζωγοπούλου***

***Επίκουρη Καθηγήτρια Επείγουσας Ιατρικής ΕΚΠΑ***

***Πανεπιστημιακή Κλινική Επειγόντων Περιστατικών ΠΓΝ ΑΤΤΙΚΟΝ***







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EMERGENCY



M. Twoby 9-16

"You're on the waiting list  
to start waiting."

**EMERGENCY**



**TRIAGE NURSE**  
*Being the worst  
makes you first.*









## Manifesto for emergency medicine in Europe

COUNCIL OF THE EUROPEAN SOCIETY FOR EMERGENCY MEDICINE

Emergency medical care of a high standard should be available to every person in need in all situations and at all times. This requires a *dedicated system* which provides care for all acutely ill or injured people in an appropriate form.

Good practice in Emergency Medicine will maximize the likelihood of a favourable outcome for the patient. Therapy should be consistent with



# EM Thinker



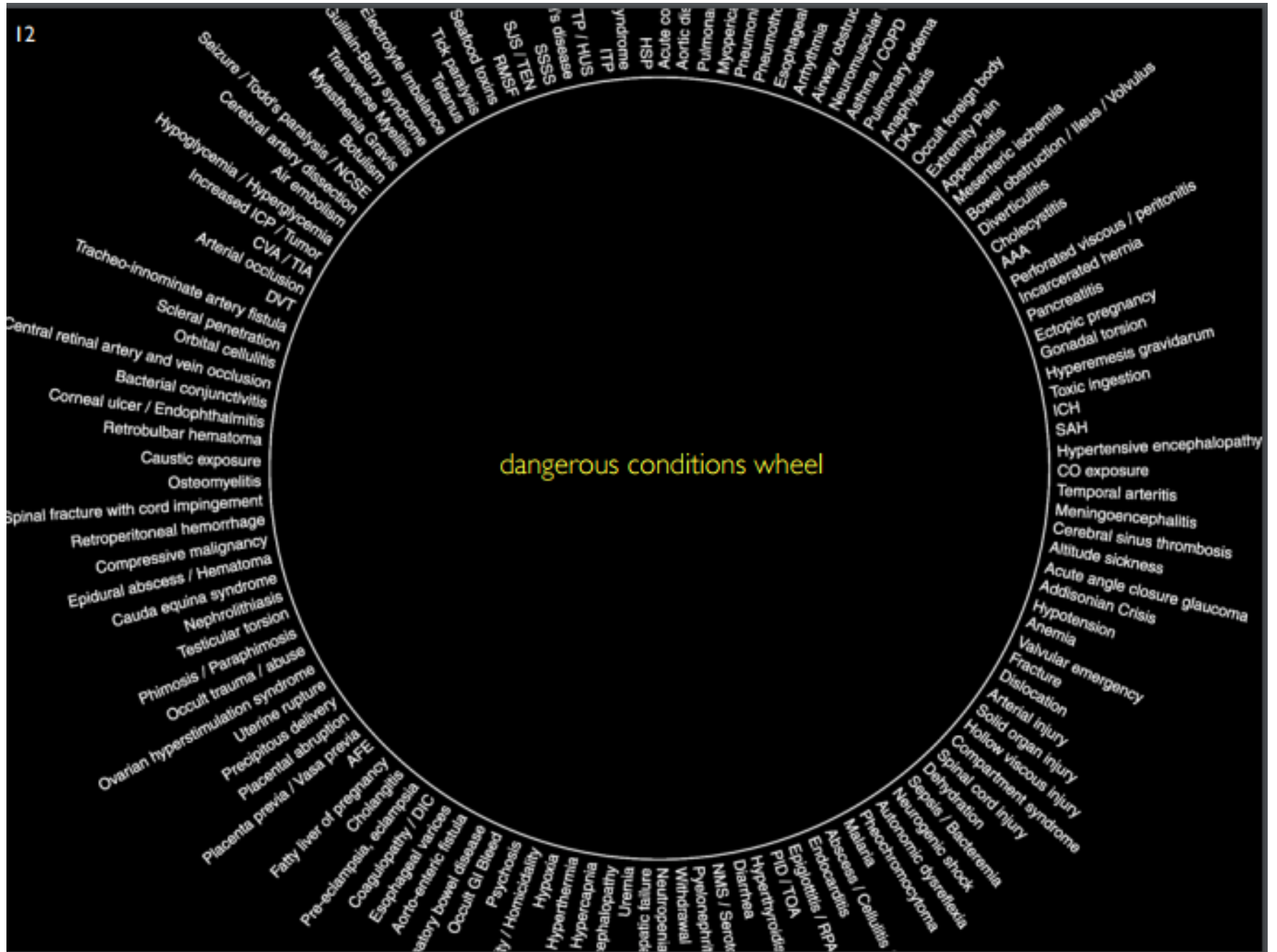
**Think of diagnoses that can kill**

**In minutes**

**In hours**

**In days**

## dangerous conditions wheel







**MISSION**

**Fill the deadly box**

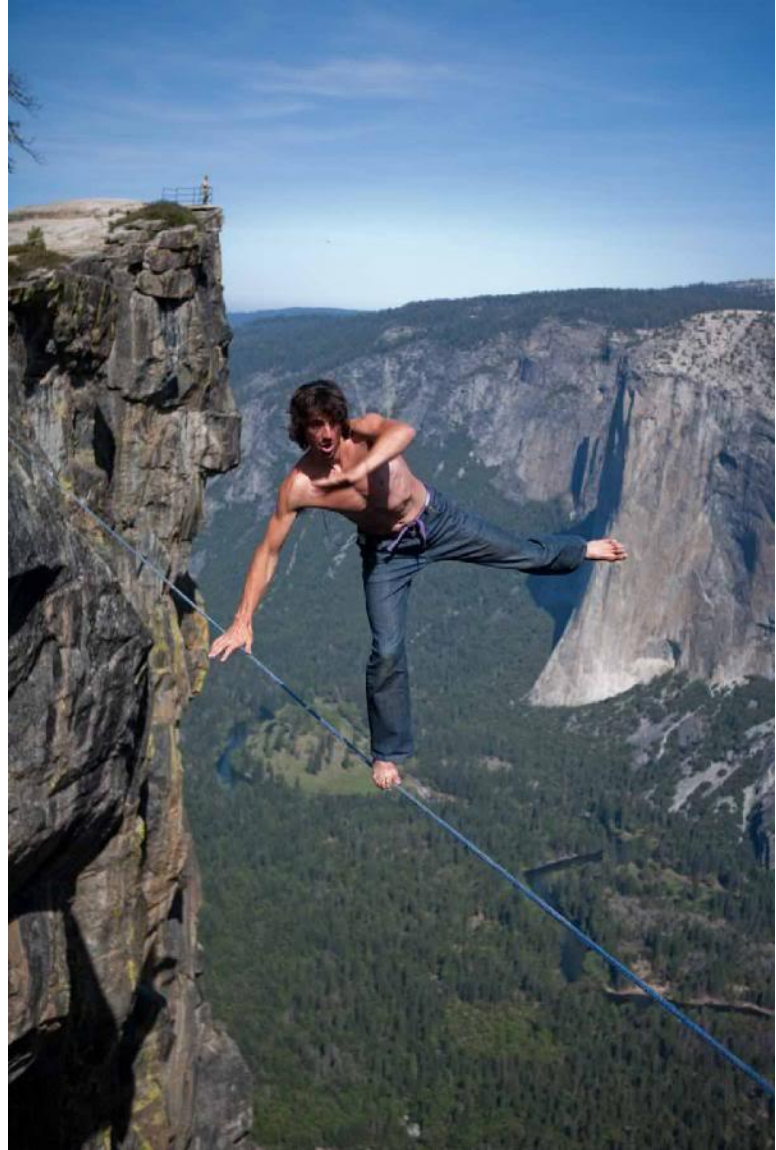
# Time-based approach

how quickly it could kill the patient

**AND**

how quickly I can treat it

**CHALLENGE**







Infection is most often suspected when patients present with fever

Infection is the most common cause of fever

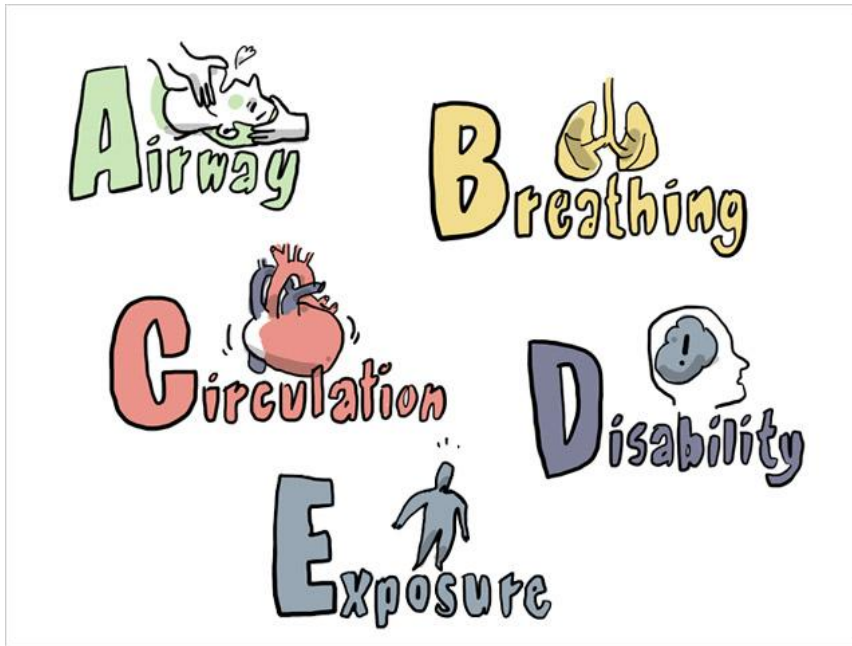
Infections are likely to be most rapidly progressive and acutely life-threatening  
must be the physician's first concern

# **key clinical question**

deciding whether infection is likely enough to warrant antimicrobial administration



# Step 1-The basics



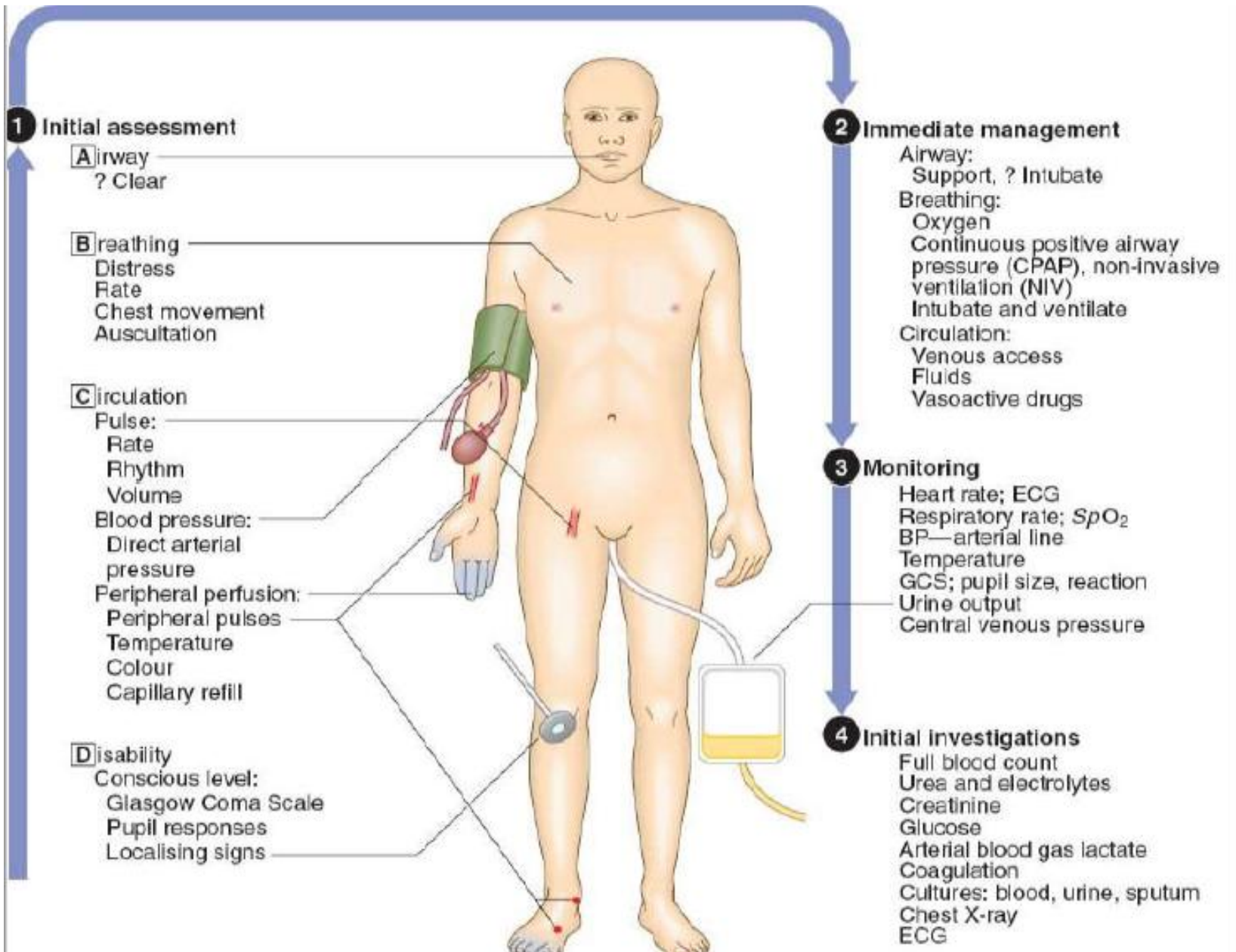
**M**onitor

**O**xygen

**V**ital Signs

**I**v

**E**xposure/draping/lighting



# Next steps

**Step 2**- focused history

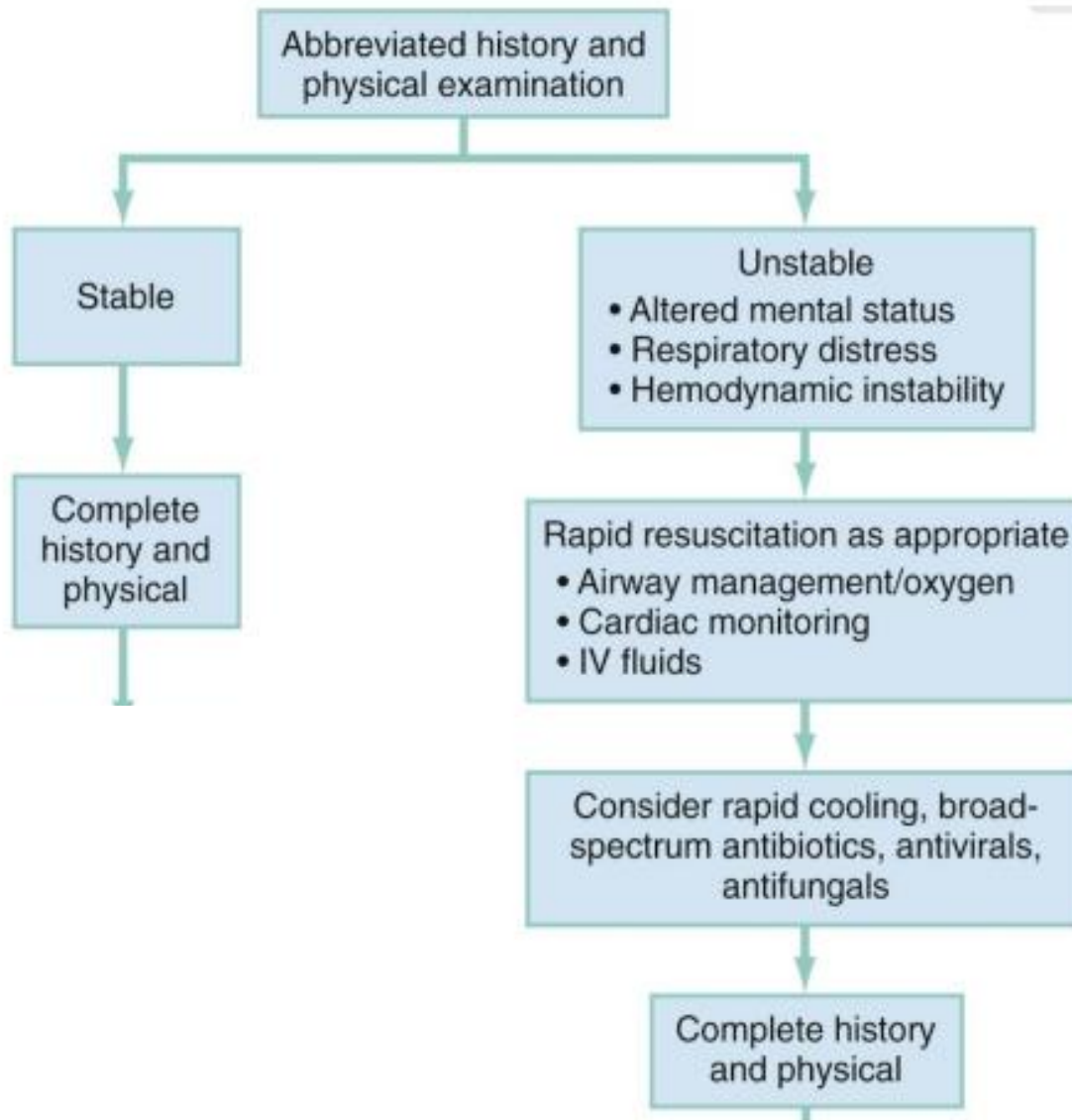
**Step 3**- focused physical examination

**Step 4**-focused labs

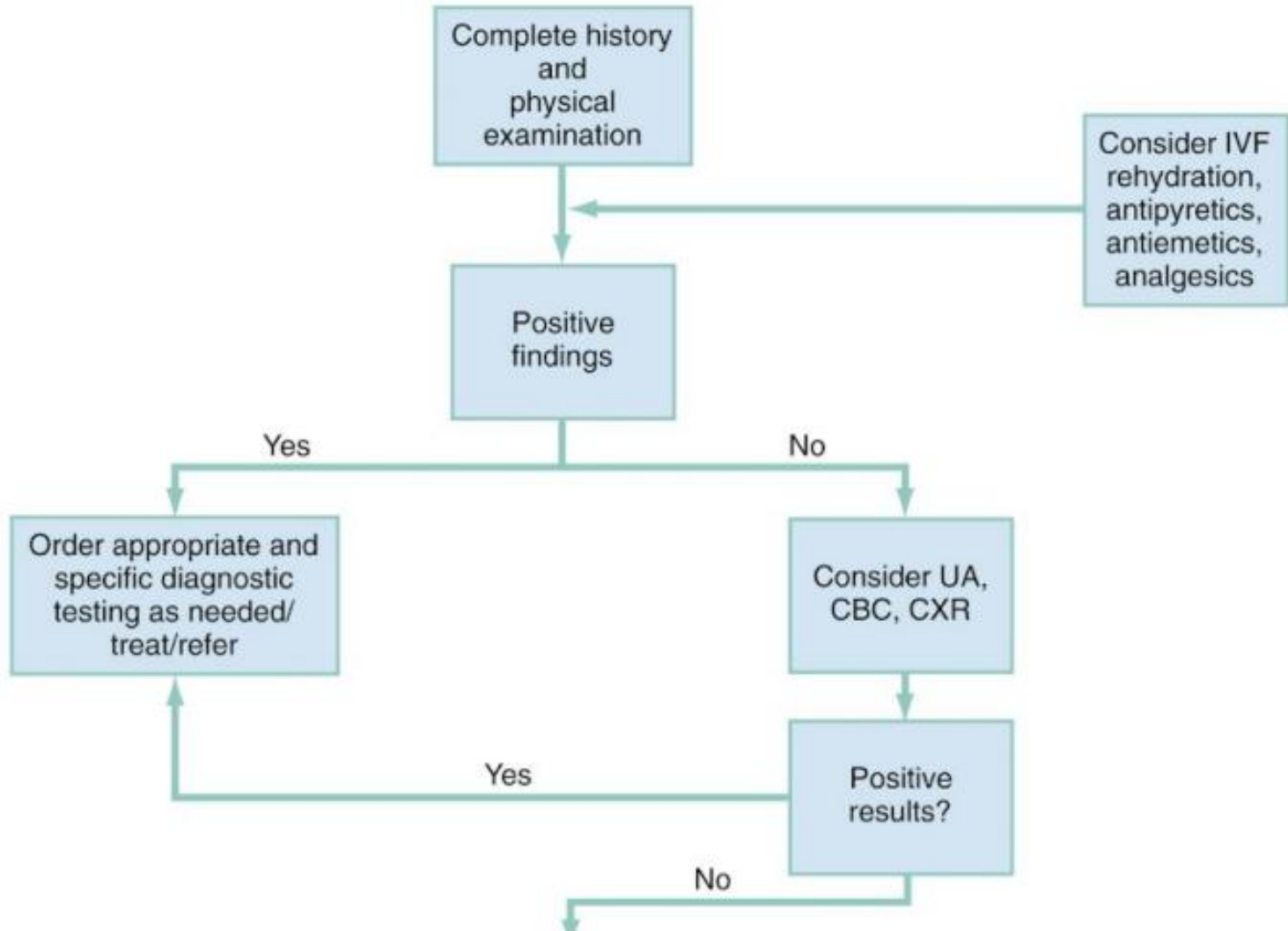
**Step 5**- re-evaluation



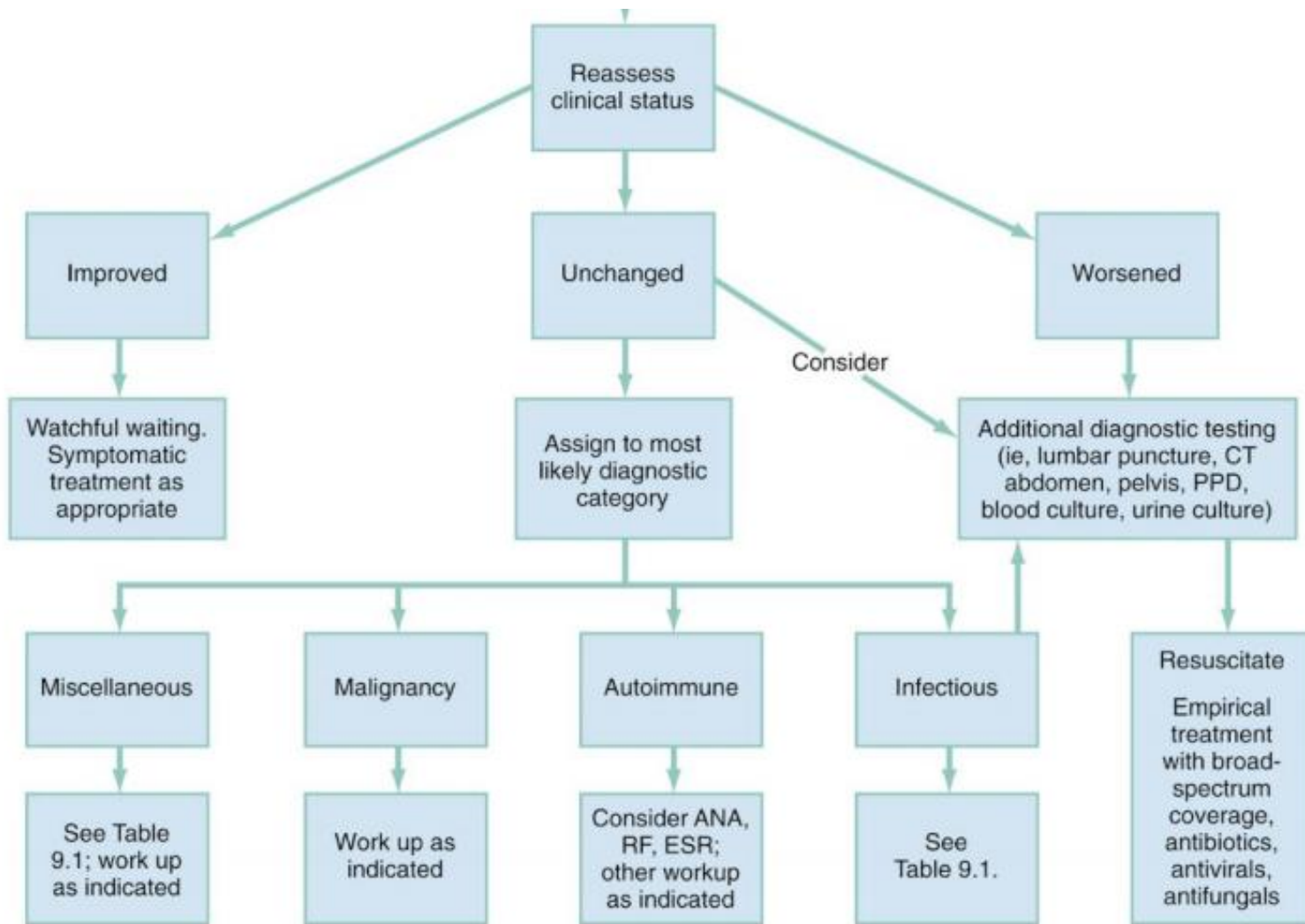
# APPROACH (1)



# APPROACH (2)



# APPROACH (3)



**Table 12-1** Differential Diagnoses—Infectious Causes

ORGAN SYSTEM	CRITICAL DIAGNOSES	EMERGENT DIAGNOSES	NONEMERGENT DIAGNOSES
Respiratory	Bacterial pneumonia with respiratory failure	Bacterial pneumonia, peritonsillar abscess, retropharyngeal abscess, epiglottitis	Otitis media, sinusitis, pharyngitis, bronchitis, influenza, tuberculosis
Cardiovascular		Endocarditis, pericarditis	
Gastrointestinal	Peritonitis	Appendicitis, cholecystitis, diverticulitis, intra-abdominal abscess	Colitis or enteritis
Genitourinary		Pyelonephritis, tubo-ovarian abscess, pelvic inflammatory disease	Cystitis, epididymitis, prostatitis
Neurologic	Meningitis, cavernous sinus, thrombosis	Encephalitis, brain abscess	
Skin and soft tissue		Cellulitis, infected decubitus ulcer, soft tissue abscess	
Systemic	Sepsis or septic shock, meningococcemia		



## Differential Diagnosis - Noninfectious Causes of Fever

Critical Diagnoses	Emergent Diagnoses	Non-emergent Diagnoses
<ul style="list-style-type: none"><li>● Acute myocardial infarction</li><li>● Pulmonary embolism or infarction</li><li>● Intracranial hemorrhage</li><li>● CVA</li><li>● NMS</li><li>● Thyroid Storm</li><li>● Acute Adrenal Insufficiency</li><li>● Transfusion reaction</li><li>● Pulmonary Edema</li></ul>	<ul style="list-style-type: none"><li>● CHF</li><li>● Dehydration</li><li>● Recent seizure</li><li>● Sickle cell disease</li><li>● Transplant rejection</li><li>● Pancreatitis</li><li>● DVT</li></ul>	<ul style="list-style-type: none"><li>● Drug fever</li><li>● Malignancy</li><li>● Gout</li><li>● Sarcoidosis</li><li>● Crohn Disease</li><li>● Postcardiotomy syndrome</li></ul>



TIPS &  
TRICKS

**If the patient look sick  
start early broad-spectrum  
antibiotics to cover  
suspected source**



## Afebrile pts

- Advanced Age
- Immunosuppression
- Malnutrition
- Chronic Disease

- Blood sugar <80 mg/dl
- Sodium <120 or >150 Meq/l
- Potassium <2.5 or > 6 Meq/l
- pH <7.2
- Spo2 <90%
- Bicarbonate <18 mmol/l
- Lactate >4 mmol/l

# The association of body temperature with antibiotic therapy and mortality in patients attending the emergency department with suspected infection

Romy Schuttevaer<sup>a</sup>, Anniek Brink<sup>a</sup>, Jelmer Alsmas<sup>a</sup>,  
Jurriaan E.M. de Steenwinkel<sup>b</sup>, Annelies Verbon<sup>b</sup>,  
Stephanie C.E. Schuit<sup>a</sup> and Hester F. Lingsma<sup>c</sup>

**Background and importance** Previous studies found that septic patients with normothermia have higher mortality than patients with fever. We hypothesize that antibiotic therapy is less frequently initiated if infectious patients present with normothermia to the emergency department (ED).

**Objectives** To examine the association of body temperature with the initiation of antibiotic therapy in patients attending the ED with suspected and proven infection. Additionally, the association of temperature with 30-day mortality was assessed.

**Design, settings and participants** We conducted a retrospective cohort study between 2012 and 2016 at a tertiary university hospital. Adult patients attending the ED with a blood culture taken (i.e. suspected infection) and a positive blood culture (i.e. proven bacteremia) were included.

**Main results** Of 5997 patients with a suspected infection, 45.8% had normothermia, 44.6% hyperthermia and 5.6% hypothermia. Patients with hyperthermia received more often antibiotic therapy (53.5%) compared to normothermic patients (27.6%, adjusted odds ratio [95% confidence interval], 2.59 [2.27–2.95]). Patients with hyperthermia had lower mortality (4.7%) than those with normothermia (7.4%, adjusted odds ratio [95% confidence interval], 0.50 [0.39–0.64]). Sensitivity analyses in patients with proven bacteremia ( $n = 934$ ) showed similar results.

**Conclusion** Normothermia in patients presenting with infection was associated with receiving less antibiotic therapy in the ED compared to presentations with hyperthermia. Moreover, normothermia was associated with a higher mortality risk than hyperthermia. *European Journal of Emergency Medicine* 28: 440–447 Copyright © 2021 The Author(s). Published by Wolters Kluwer Health, Inc.







SIRS criteria (two or more)	qSOFA criteria (two or more)
36 > Temperature > 38	Systolic blood pressure < 100 mmHg
Respiratory rate > 22/min	Respiratory rate > 20/min
Heart rate > 90 bpm	Glasgow Coma Scale ≤ 14
4000 > White cell count > 12,000	

### MEWS

Modified Early Warning Score (MEWS)

Score	3	2	1	0	1	2	3
Respiratory rate		< 9		9 - 14	15 - 20	21 - 30	> 30
Saturation rate (with therapy)	< 90						
Heart frequency		< 40	40 - 50	51 - 100	101 - 110	111 - 130	> 130
Systolic blood pressure	< 70	70 - 80	81 - 100	101 - 200			
Temperature		< 35.1	35.1 - 36.5	36.5 - 37.5	> 37.5		
Consciousness				A	V	P	U
Urine production	< 75mL in the last 4 hours						
Nurse being worried	1 point						

A = Alert    V = Response to verbal stimulation    P = Response to painful stimulation    U = Unresponsive

#### RIT protocol

1. Determine MEWS → MEWS ≥ 3 contact clinician on duty
2. Clinician on duty assess patient < 30 min and draft a plan for treatment
3. Effect of treatment is analyzed < 60 min
4. If no effect of treatment → clinician on duty contracts RIT
5. If not complied with 2,3,4 → clinician on duty or nurse contacts RIT
6. Document aberrant parameters in the patient' charts

Chart 1: The NEWS scoring system

Physiological parameter	Score						
	3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9-11	12-20		21-24	≥25
SpO <sub>2</sub> Scale 1 (%)	≤91	92-93	94-95	≥96			
SpO <sub>2</sub> Scale 2 (%)	≤83	84-85	86-87	88-92 ≥93 on air	93-94 on oxygen	95-96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91-100	101-110	111-219			≥220
Pulse (per minute)	≤40		41-50	51-90	91-110	111-130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1-36.0	36.1-38.0	38.1-39.0	≥39.1	

the severity of the infected patient may change over time, and so the scores should be calculated not only at the patients' admission but also throughout their stay in the ED to evaluate a possible deterioration in the clinical situation

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

**TABLE 1.**

**Table of Current Recommendations and Changes From Previous 2016 Recommendations**

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
<p>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.</p>	<p><b>Strong</b>, moderate-quality evidence (for screening)</p> <p><b>Strong</b>, very low-quality evidence (for standard operating procedures)</p>	<p>Changed from <b>Best practice statement</b></p> <p>"We <b>recommend</b> that hospitals and hospital systems have a performance improvement program for sepsis including sepsis screening for acutely ill, high-risk patients."</p>
<p>2. We recommend against using qSOFA compared with SIRS, NEWS, or MEWS as a single-screening tool for sepsis or septic shock.</p>	<p><b>Strong</b>, moderate-quality evidence</p>	<p><b>NEW</b></p>

Box 1: The relationship of lactate level in sepsis to mortality

Lactate	Mortality
<2	15%
2-4	25%
>4	38%

From: Trzeciak S, Dellinger RP, Chansky ME, Arnold RC, Schorr C, Milcarek B, *et al. Intensive Care Med* 2007, 33(6):970-7





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## Prognosis of emergency department patients with suspected infection and intermediate lactate levels: A systematic review



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### ARTICLE INFO

**Keywords:**

Infection  
Lactate  
Prognosis  
Review

### ABSTRACT

**Purpose:** Previous studies have shown a correlation between blood lactate greater than 4.0 mmol/L and mortality in patients with suspected infection in the emergency department (ED), but data are more limited regarding the prognosis of intermediate blood lactate (2.0–3.9 mmol/L), particularly in the absence of hemodynamic instability. We sought to quantify the prognostic significance of intermediate blood lactate levels in ED patients with suspected infection, emphasizing patients without hypotension.

**Methods:** A systematic review of 4 databases was conducted to identify studies using a comprehensive search strategy. All studies performed on adult ED patients with suspected infection and available data on hemodynamics, intermediate lactate levels, and mortality rates were included.

**Results:** We identified 20 potential publications, 8 of which were included. Intermediate lactate elevation was found in 11062 patients with suspected or confirmed infection, 1672 (15.1%) of whom died. Subgroup analysis of normotensive patients demonstrated a mortality of 1561 (14.9%) of 10 442, with rates from individual studies between 3.2% and 16.4%.

**Conclusion:** This systematic review found that among ED patients with suspected infection, intermediate lactate elevation is associated with a moderate to high risk of mortality, even among patients without hypotension. Physicians should consider close monitoring and aggressive treatment for such patients.

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

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<p>2. We recommend against using qSOFA compared with SIRS, NEWS, or MEWS as a single-screening tool for sepsis or septic shock.</p>	<p><b>Strong</b>, moderate-quality evidence</p>	<p><b>NEW</b></p>
<p>3. For adults suspected of having sepsis, we suggest measuring blood lactate.</p>	<p><b>Weak</b>, low quality of evidence</p>	

# Take home message

the presence of an elevated or normal lactate level significantly increases or decreases, respectively, the likelihood of a final diagnosis of sepsis in patients with suspected sepsis.

However, **lactate alone is neither sensitive nor specific** enough to rule-in or rule-out the diagnosis on its own

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

## Biomarkers to Start Antibiotics

### Recommendation

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 recommendation, very low quality of evidence.*




## Prognostic Role of Soluble Urokinase Plasminogen Activator Receptor at the Emergency Department: A Position Paper by the Hellenic Sepsis Study Group

Dimitrios Velissaris · George Dimopoulos · John Parissis · Zoi Alexiou · Nikolaos Antonakos ·

Dimitrios Babalis · Styliani Gerakari · Vassileios Kaldis · Pantelis Koutoukas · Malvina Lada ·

Konstantinos Leventogiannis · Ioannis Pantazopoulos · Antonios Papadopoulos ·

Eftihia Polyzogopoulou · Charalambos Gogos · Apostolos Armaganidis · Evangelos J. Giamarellos-Bourboulis 

### Key Summary Points

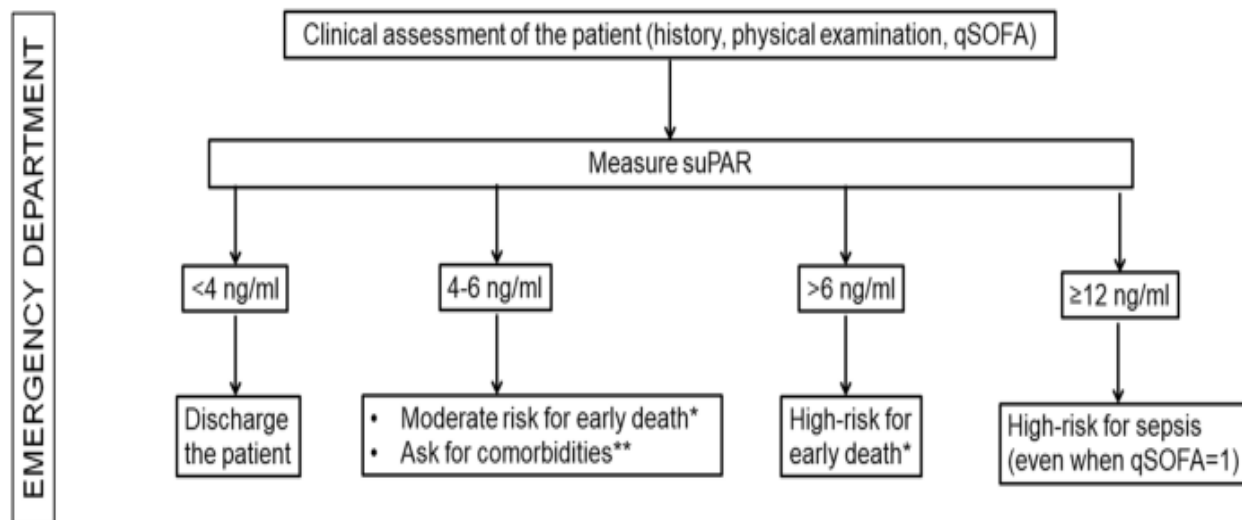
suPAR is a non-specific marker associated with a high negative predictive value for unfavourable outcome.

Levels < 4 ng/ml allow discharge of the patient admitted to the ED after thorough clinical evaluation.

Levels > 6 ng/ml are an alarming sign of risk for unfavourable outcome but need to be interpreted in light of the patient's history.

Levels between 4 and 6 ng/ml need to be interpreted in light of the patient's history of comorbidities, which may increase them, such as rheumatoid arthritis, solid tumour malignancy and chronic renal disease.

Levels > 12 ng/ml in critically ill patients are prognostic of 28-day mortality ranging between 17 and 50% depending on the APACHE II score.





ORIGINAL RESEARCH

Open Access



# Soluble urokinase plasminogen activator receptor and lactate as prognostic biomarkers in patients presenting with non-specific chief complaints in the pre-hospital setting – the PRIUS-study

## Abstract

**Background:** Emergency Medical Services (EMS) are faced daily with patients presenting with non-specific chief complaints (NSC). Patients presenting with NSCs often have normal vital signs. It has previously been established that NSCs may have a serious underlying condition that has yet to be identified. The aim of the current study was to determine if soluble urokinase plasminogen activator receptor (suPAR) and lactate could be used to identify serious conditions among patients presenting with NSCs to the EMS. The secondary aim was to describe the prognostic value for mortality in the group.

**Method:** A blinded prospective observational cohort study was conducted of patients brought to the ED by ambulance after calling the national emergency number 112 and who were assessed as having NSC by the EMS. Biomarkers were measured during index EMS assessment before transportation to the ED. Patients were followed via EMS and hospital electronic health records. Descriptive and logistic regression analyses were used.

**Results:** A total of 414 patients were included, with a median age of 82 years. A serious condition was present in 15.2% of the patients. Elevated suPAR above 3 ng/ml had a positive likelihood ratio (LR+) of 1.17 and a positive predictive value (PPV) of 17.3% as being predictive of a prevalent serious condition. Elevated suPAR above 9 ng/ml had LR+ 4.67 and a PPV of 16.7% as being predictive of 30-day mortality. Lactate was not significantly predictive.

**Conclusion:** Pre-hospital suPAR and lactate cannot differentiate serious conditions in need of urgent treatment and assessment in the ED among patients presenting with non-specific chief complaints. suPAR has shown to be predictive of 30-day mortality, which could add some value to the clinical assessment.

ORIGINAL RESEARCH

Open Access



# Pre-hospital suPAR, lactate and CRP measurements for decision-making: a prospective, observational study of patients presenting non-specific complaints

## Abstract

**Background:** In the pre-hospital setting, non-urgent patients with non-specific chief complaints pose assessment challenges for the emergency medical systems (EMS). Severely ill patients should be identified among these patients, and unnecessary transport to the emergency department (ED) should be avoided. Unnecessary admissions burden EDs, deplete EMS resources and can even be harmful to patients, especially elderly patients. Therefore, tools for facilitating pre-hospital decision-making are needed. They could be based on vital signs or point-of-care laboratory biomarkers. In this study, we examined whether the biomarker soluble urokinase plasminogen activator receptor (suPAR), either alone or combined with C-reactive protein (CRP) and/or lactate, could predict discharge from the ED and act as a pre-hospital support tool for non-conveyance decision-making.

**Methods:** This was a prospective, observational study of adult patients with normal or near-normal vital signs transported by an EMS to an ED with a code referring to deteriorated general condition. The levels of suPAR, CRP and lactate in the patients' pre-hospital blood samples were analysed. The values of hospitalized patients were compared to those of discharged patients to determine whether these biomarkers could predict direct discharge from the ED.

**Results:** A total of 109 patients (median age: 81 years) were included in the study. Of those, 52% were hospitalized and 48% were discharged from the ED. No statistically significant association was found between suPAR and the ED discharge vs hospitalization outcome (OR: 1.04, 95% CI 0.97–1.13, AUROC: 0.58, 95% CI 0.47–0.69). Adding CRP (AUROC: 0.64, 95% CI 0.54–0.75) or lactate (AUROC: 0.60, 95% CI 0.49–0.71) to the regression models did not improve their diagnostic accuracy. None of the patients with a suPAR value of less than 2 ng/ml were admitted to hospital, while 64% of the patients with a suPAR value of more than 6 ng/ml were hospitalized.

**Conclusion:** Pre-hospital suPAR measurements alone or combined with CRP and/or lactate measurements could not predict the ED discharge or hospital admission of 109 non-urgent EMS patients with non-specific chief complaints and normal or near-normal vital signs.

RESEARCH

Open Access



# The early identification of disease progression in patients with suspected infection presenting to the emergency department: a multi-centre derivation and validation study

## Abstract

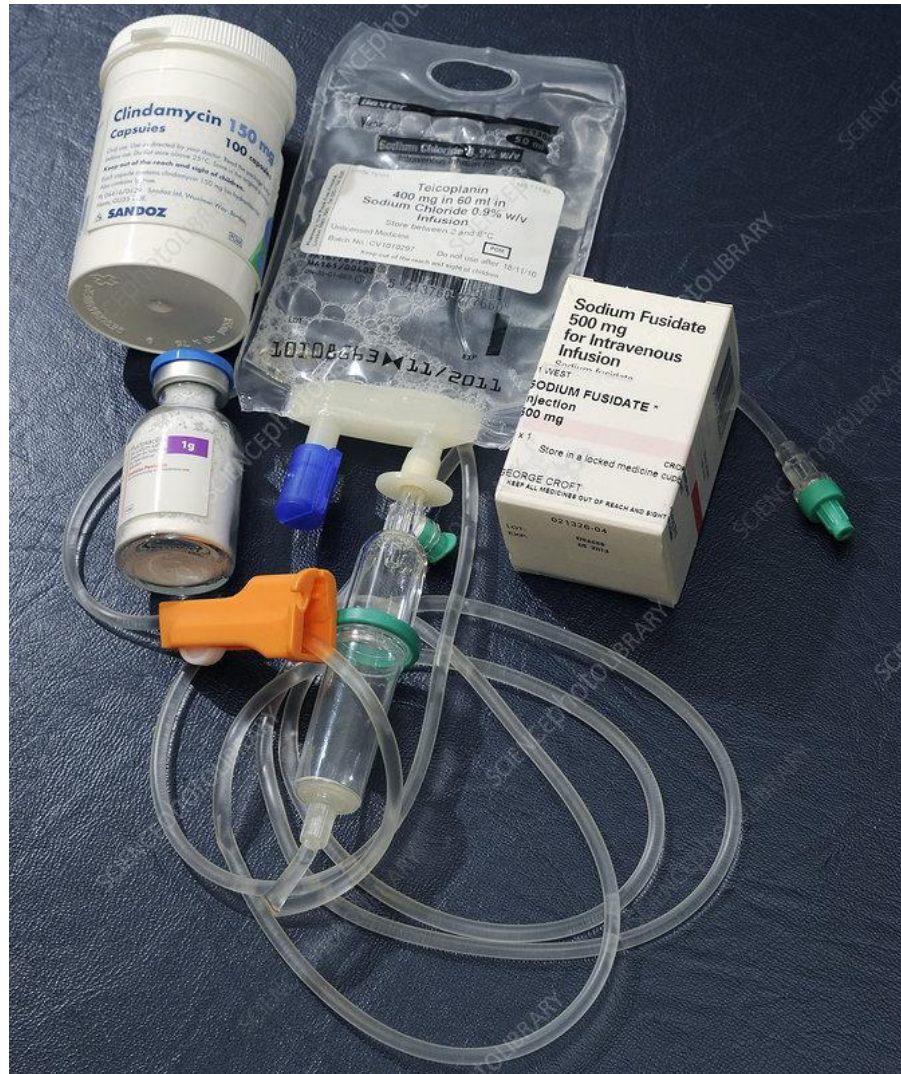
**Background:** There is a lack of validated tools to assess potential disease progression and hospitalisation decisions in patients presenting to the emergency department (ED) with a suspected infection. This study aimed to identify suitable blood biomarkers (MR-proADM, PCT, lactate and CRP) or clinical scores (SIRS, SOFA, qSOFA, NEWS and CRB-65) to fulfil this unmet clinical need.

**Methods:** An observational derivation patient cohort validated by an independent secondary analysis across nine EDs. Logistic and Cox regression, area under the receiver operating characteristic (AUROC) and Kaplan-Meier curves were used to assess performance. Disease progression was identified using a composite endpoint of 28-day mortality, ICU admission and hospitalisation > 10 days.

**Results:** One thousand one hundred seventy-five derivation and 896 validation patients were analysed with respective 28-day mortality rates of 7.1% and 5.0%, and hospitalisation rates of 77.9% and 76.2%. MR-proADM showed greatest accuracy in predicting 28-day mortality and hospitalisation requirement across both cohorts. Patient subgroups with high MR-proADM concentrations ( $\geq 1.54$  nmol/L) and low biomarker (PCT < 0.25 ng/mL, lactate < 2.0 mmol/L or CRP < 67 mg/L) or clinical score (SOFA < 2 points, qSOFA < 2 points, NEWS < 4 points or CRB-65 < 2 points) values were characterised by a significantly longer length of hospitalisation ( $p < 0.001$ ), rate of ICU admission ( $p < 0.001$ ), elevated mortality risk (e.g. SOFA, qSOFA and NEWS HR [95%CI], 45.5 [10.0–207.6], 23.4 [1.1–49.3] and 32.6 [9.4–113.6], respectively) and a greater number of disease progression events ( $p < 0.001$ ), compared to similar subgroups with low MR-proADM concentrations (< 1.54 nmol/L). Increased out-patient treatment across both cohorts could be facilitated using a derivation-derived MR-proADM cut-off of < 0.87 nmol/L (15.0% and 16.6%), with decreased readmission rates and no mortalities.

**Conclusions:** In patients presenting to the ED with a suspected infection, the blood biomarker MR-proADM could most accurately identify the likelihood of further disease progression. Incorporation into an early sepsis management protocol may therefore aid rapid decision-making in order to either initiate, escalate or intensify early treatment strategies, or identify patients suitable for safe out-patient treatment.





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

Recommendations 2021	Recommendation Strength and Quality of Evidence	Changes From 2016 Recommendations
<b>INFECTION</b>		
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.	<b>Best practice statement</b>	
12. For adults with possible septic shock or a high likelihood for sepsis, we recommend administering antimicrobials immediately, ideally within 1 hr of recognition.	<b>Strong, low quality of evidence (Septic shock)</b> <b>Strong, very low quality of evidence (Sepsis without shock)</b>	<b>CHANGED from previous:</b> “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”  <b>strong recommendation, moderate quality of evidence</b>
13. For adults with possible sepsis without shock, we recommend rapid assessment of the likelihood of infectious versus noninfectious causes of acute illness.	<b>Best practice statement</b>	
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.	<b>Weak, very low quality of evidence</b>	<b>NEW from previous:</b> “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”  <b>strong recommendation, moderate quality of evidence</b>
15. For adults with a low likelihood of infection and without shock, we suggest deferring antimicrobials while continuing to closely monitor the patient.	<b>Weak, very low quality of evidence</b>	<b>NEW from previous:</b> “We recommend that administration of IV antimicrobials should be initiated as soon as possible after recognition and within 1 hr for both a) septic



# USUAL CARE



# BEST CARE



Evaluate



Diagnose



POCUS

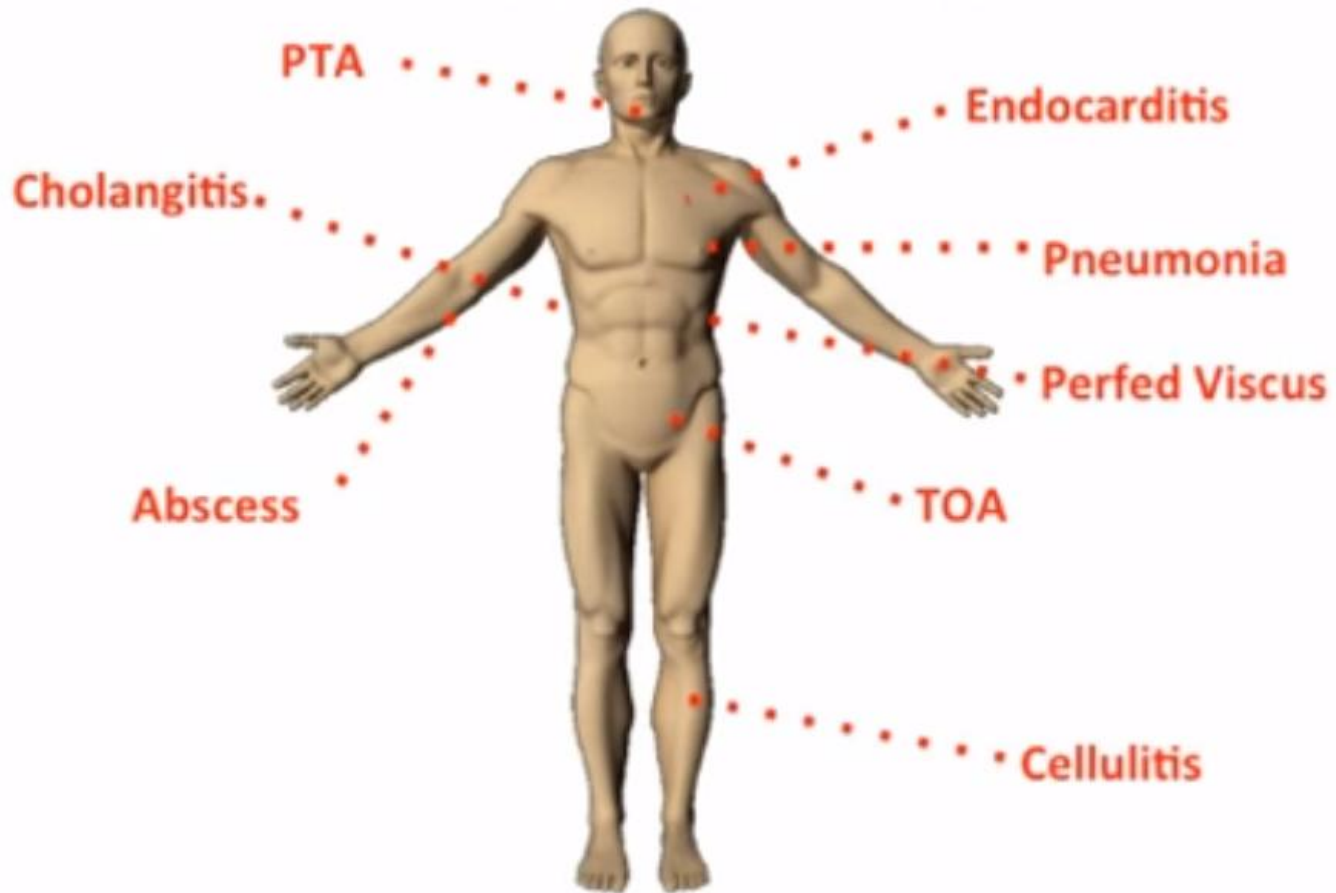


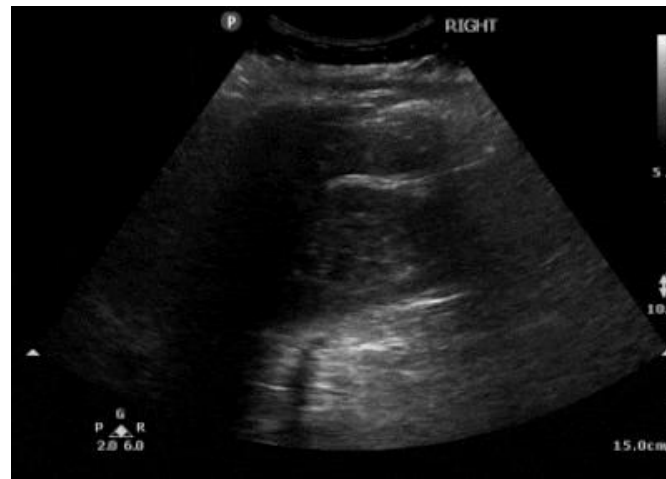
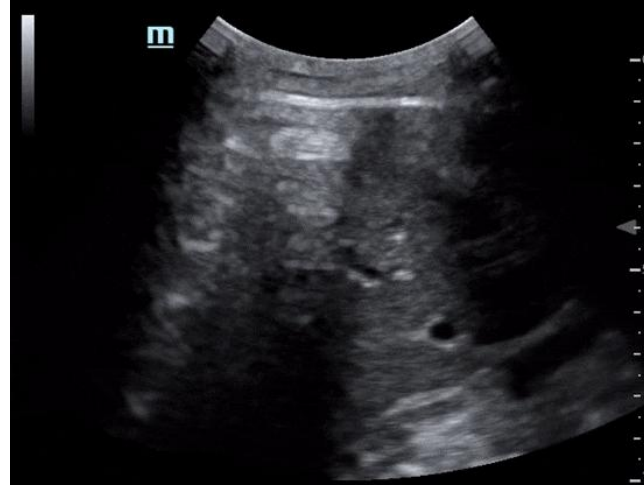
Monitor



Treat

# Source identification





## EVALUATE

Quickly differentiate between cardiogenic, hypovolemic, obstructive and distributive shock

## DIAGNOSE

Make fast decisions with immediate access to vital information

## POINT OF CARE ULTRASOUND

## MONITOR

Get up-to-the-minute insight into the effectiveness of fluid treatment

## TREAT

Change therapeutic plans based on the real-time status of a variety of indicators



**Avoid premature closure**



# References

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- **[Oxford Textbook of Medicine \(6 ed.\) 2020,](#)**  
DOI: 10.1093/med/9780198746690.001.0001
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- <https://sepsistrust.org/wp-content/uploads/2018/06/ED-toolkit-2016-Final-1.pdf>