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Consensus Definitions for Sepsis and Septic Shock (Sepsis-III)

Advantages and Disadvantages

Dr. Luis García-Castrillo

Sepsis II /Sepsis III

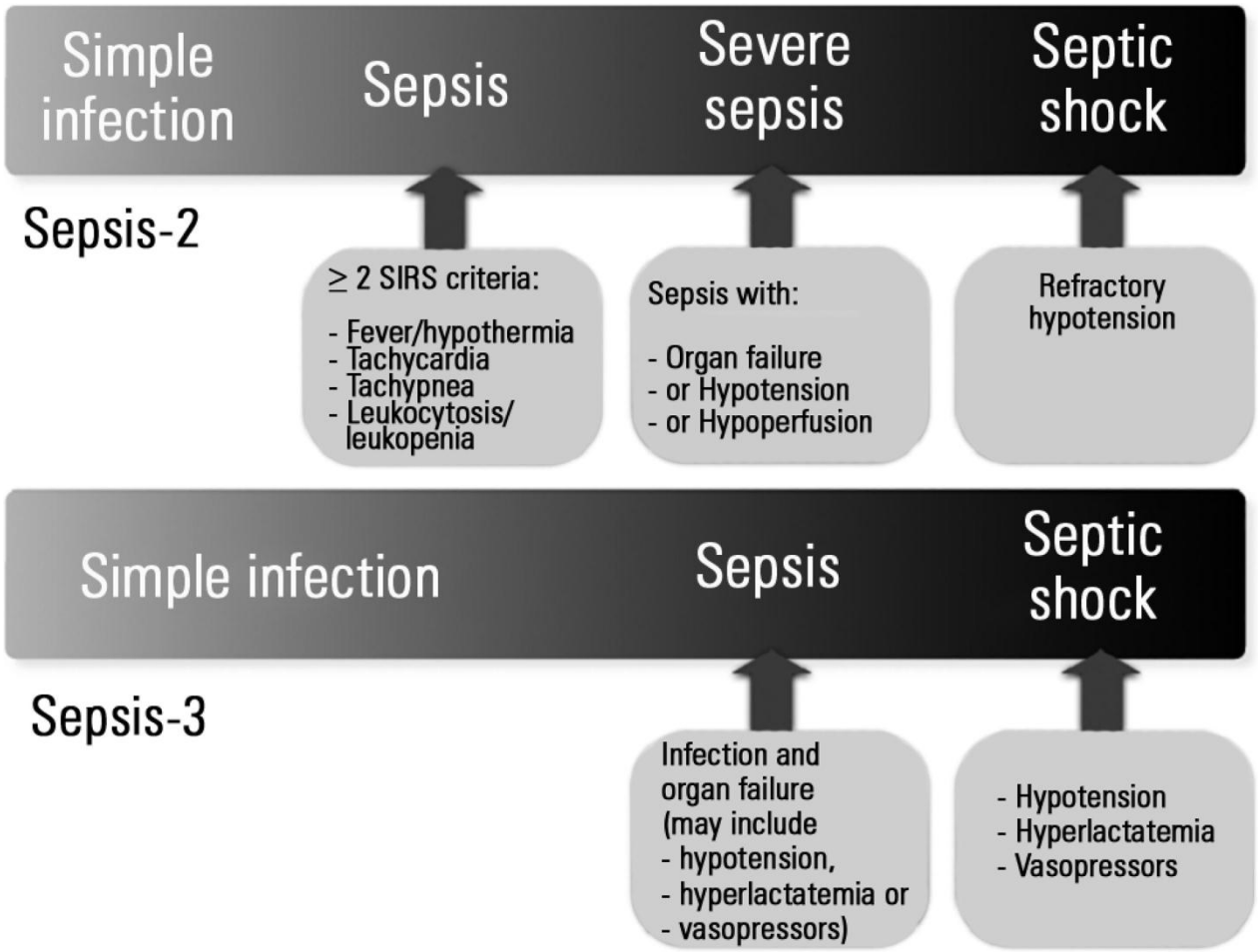
- Content:
  - ✓ Reasons for new definition.
  - ✓ Advantages of Sepsis III.
  - ✓ Disadvantages of Sepsis III.
  - ✓ To take home.

Sepsis II /Sepsis III

- Sepsis I (1991) SIRS (Systemic Inflammatory Response Syndrome)
- Sepsis II (2001)
- Sepsis III (2016)

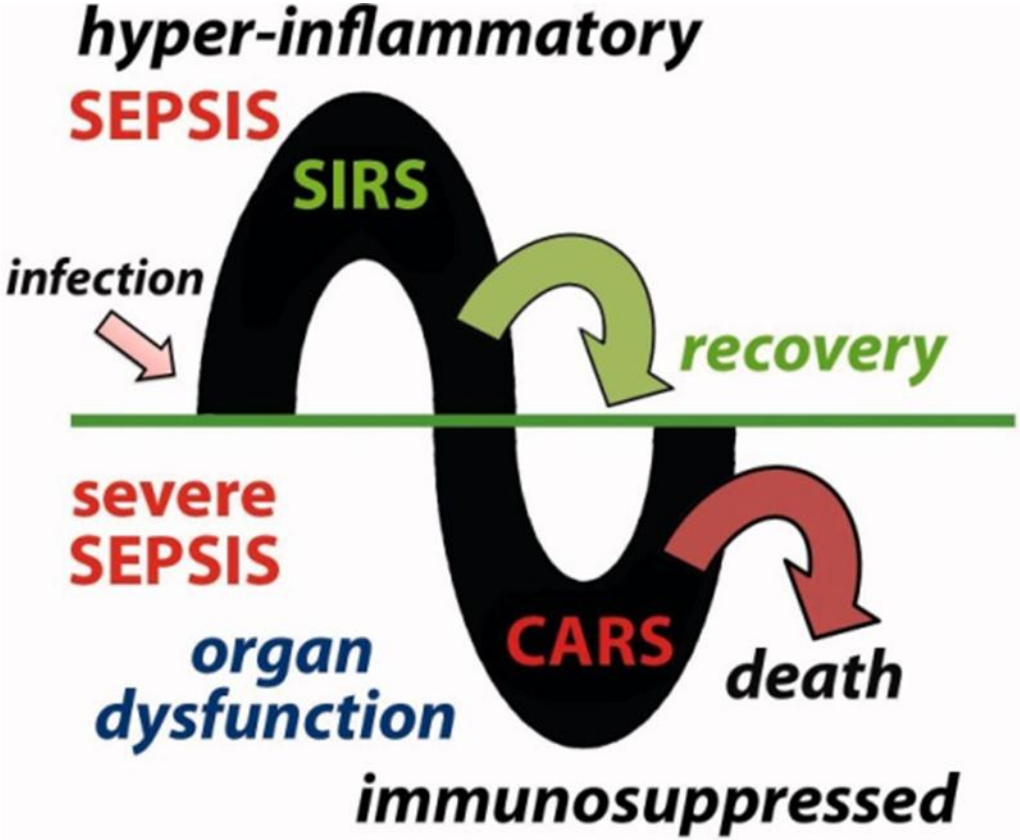
- *European Society of Intensive Care, Society of Critical Care Medicine.*

Sepsis II /Sepsis III



Sepsis II /Sepsis III

- Revision justification:
  - Better *pathophysiology compression.*
    - *Disbalance between proinflamatory and antinflamatory*



https://openi.nlm.nih.gov/detailedresult.php?img=PMC3613962_LAB-50-23-g001&query=&req=4&npos=-1

Sepsis II /Sepsis III

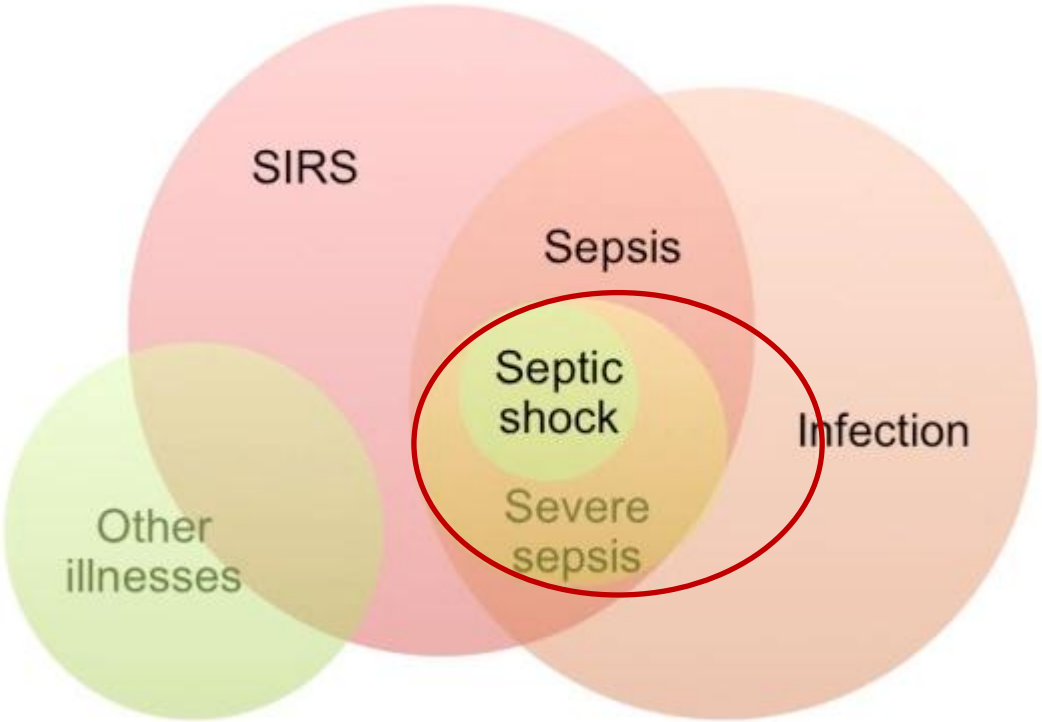
- Revision justification:
  - *Lack of specificity of SIRS*
    - *1/8 patients of severe sepsis do not have SIRS criteria*
    - *SIRS criteria are too sensitive and lack clinical specificity.*
    - *SIRS for infection has sensitivity 87%*
    - *12% of iCU patients with infection, organ failure, and significant mortality did not meet SIRS criteria*

Vincent JL. Dear SIRS, I'm sorry to say that I don't like you. Crit Care Med. 1997; 25:372–374

N Engl J Med 2015;372:1629-38. DOI: 10.1056/NEJMoa1415236

Sepsis II /Sepsis III

SIRS/INFECCTION/SEPSIS

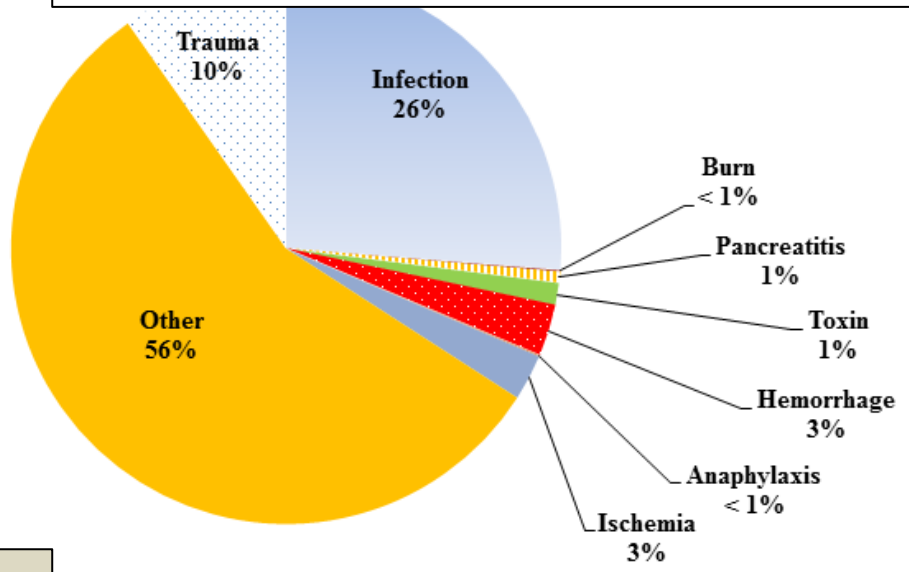


Sepsis II /Sepsis III

SIRS in EDs

ED national representative survey		≥ Two SIRS %
2007-10 EDs	Horeczko,	9-26% (17%)

Distribution of patients at ED with Two SIRS



Two SIRS

- Higher admission rate
- Higher level of complexity (ICU)
- Longer LOS
- Higher 28 days mortality

https://doi.org/10.5811/westjem.2013.9.1806

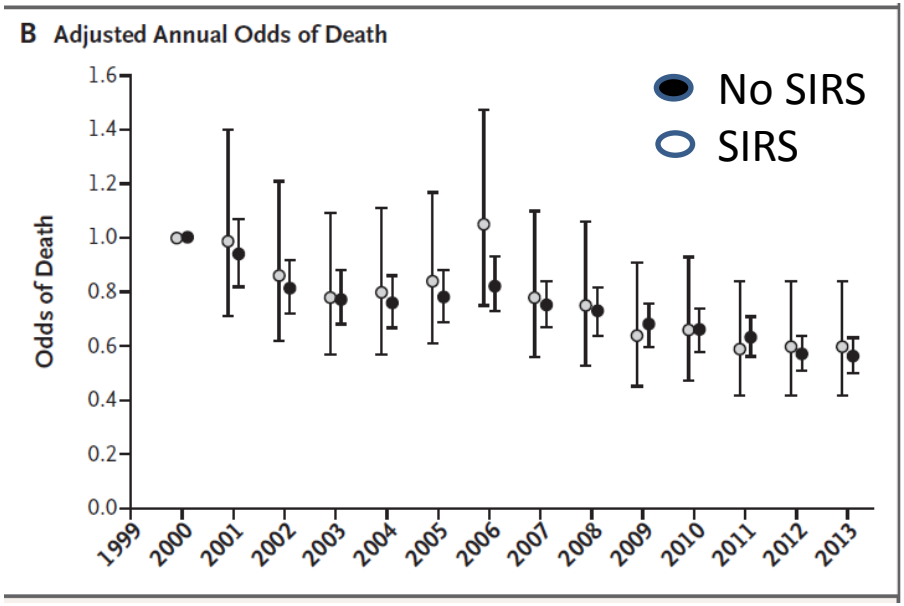
Sepsis II /Sepsis III

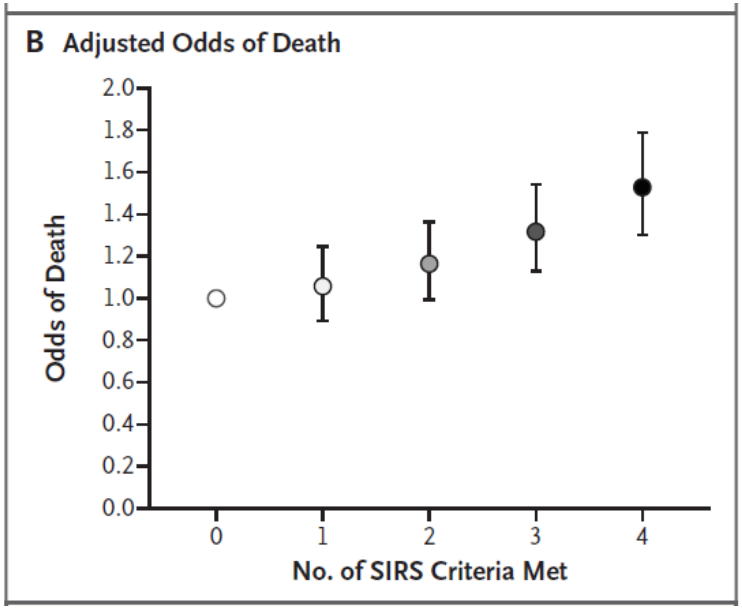
SIRS in Sepsis

- 172 ICU 1999-2013 (109.663) Severe Sepsis at admission

  Sepsis and SIRS 96,385 patients (87.9%)
  Sepsis and negative SIRS 13,278 (12.1%)

Sensitivity 87%





N Engl J Med 2015;372:1629-38.

Sepsis II /Sepsis III

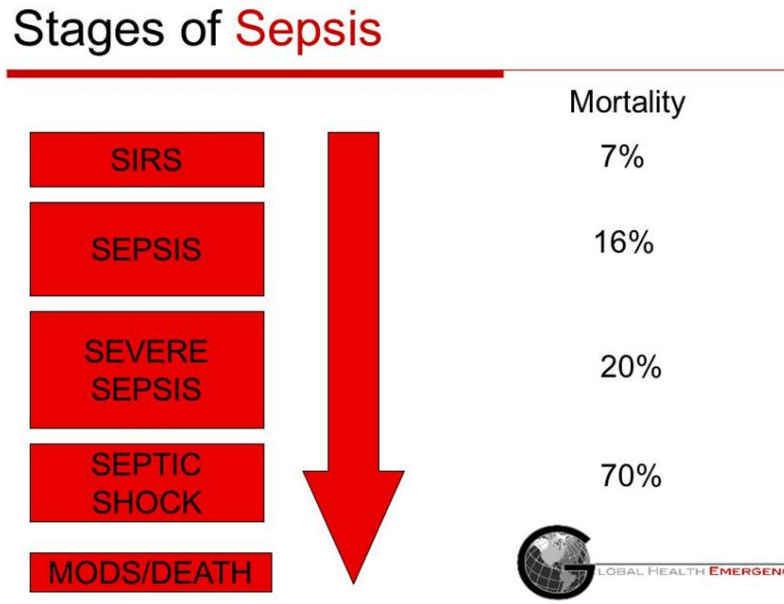
- Can reduction in mortality be due to inclusion of patients with only two SIRS.

Presence of SIRS in ICUs and out ICUs

Setting		> Two SIRs %
ICUs, Wards	Rangel-Frausto	68%
EU. 198 ICUs	Sprung	98%
Australian ICUs	Dulhunty	88.4%
Wards at any time	Churpek	50%

Sepsis II /Sepsis III
SIRS evolution to Sepsis

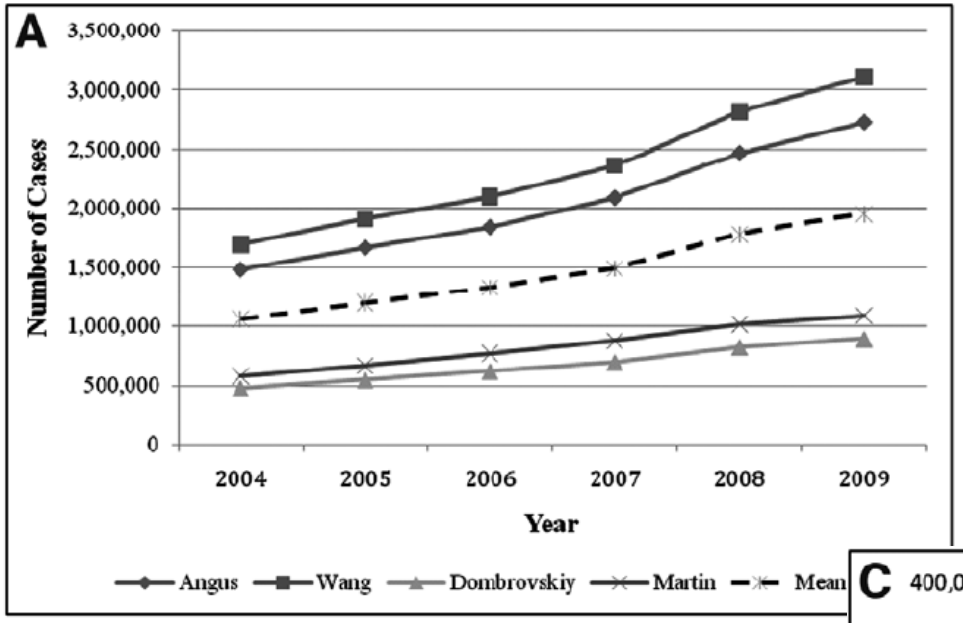
- Sepsis is a continuum that starts with the infection and can end in death.
- The median interval from SIRS to sepsis is inversely correlated with the number of SIRS criteria.



Rangel-Frausto MS, Pittet D, Costigan M, et al. The natural history of the systemic inflammatory response syndrome (SIRS). A prospective study. JAMA. 1995; 273:117–123

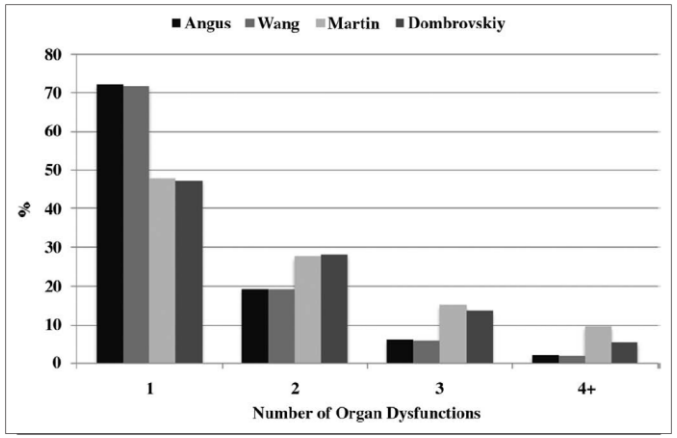
Sepsis II /Sepsis III

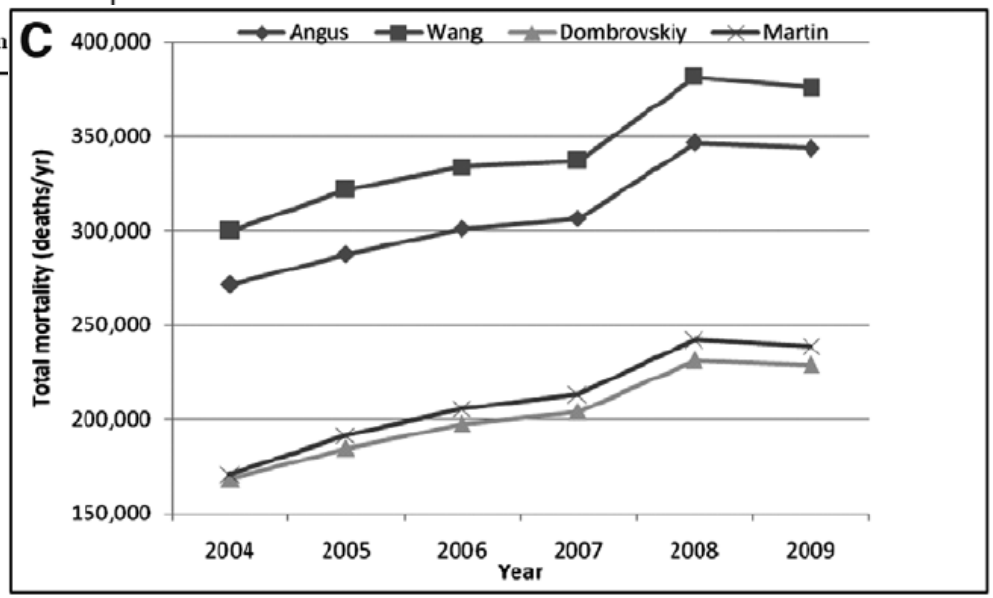
Different survival results



Gaieski

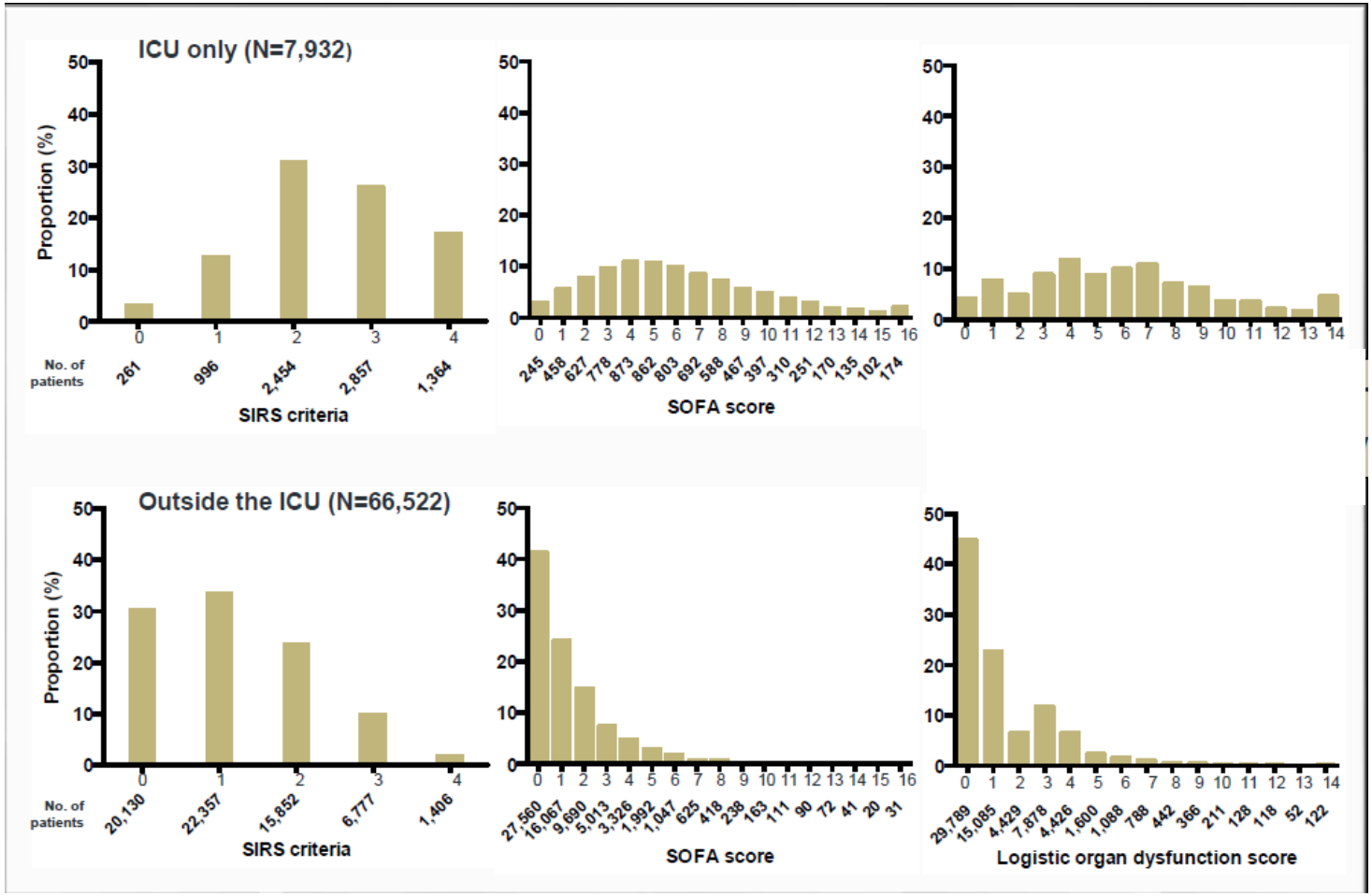
Crit Care Med 2013; 41:1167–1174





Sepsis II /Sepsis III

SIRS and SOFA different settings



Sepsis II /Sepsis III

- Revision justification:
  - *Lack of specificity of SIRS*
    - *1/8 patients of severe sepsis do not have SIRS criteria*
  - *Different outcomes on clinical trails*
  - *Better physiopathology understanding*
  - *“Definition in progress”*

Sepsis III Definitions

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

- Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.

Sepsis III Definitions

- ✓ SIRS are not included in the screening process.
- ✓ Severe sepsis is not use any more.
- ✓ For sepsis we need some level of cell damage.
- ✓ Organ dysfunction is not any more assessed trough markers on each of the six evaluated.
- ✓ Suspected infection is still in the definition.

Sepsis II /Sepsis III

- Diagnostic criteria
  - Sepsis
    - SOFA ≥2
    - qSOFA ≥2
  - Septic Shock
    - Need of vasopressor to maintain MAP ≥ 65 mmHg.
    - Lactate ≥ 2 mmol/L.

- This tools are design to identify severity not to identify septic patients.

Dear SIRS,

This just isn't working.

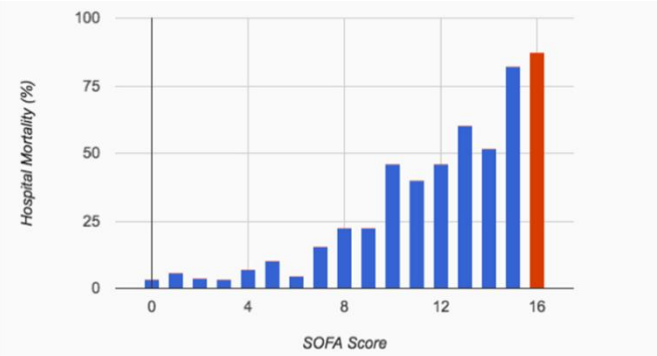
Goodbye,

Sepsis

Sepsis III Definitions

Table 1. The Sequential Organ Failure Assessment (SOFA) Score*

Variables	SOFA Score 0	1	2	3	4
Respiratory Pao_2/Fio_2, mm Hg	>400	≤400	≤300	≤200†	≤100†
Coagulation Platelets $\times 10^3/\mu L$‡	>150	≤150	≤100	≤50	≤20
Liver Bilirubin, mg/dL‡	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular Hypotension	No hypotension	Mean arterial pressure <70 mm Hg	Dop ≤5 or dob (any dose)§	Dop >5, epi ≤0.1, or norepi ≤0.1§	Dop >15, epi >0.1, or norepi >0.1§
Central nervous system Glasgow Coma Score Scale	15	13-14	10-12	6-9	<6
Renal Creatinine, mg/dL or urine output, mL/d‖	<1.2	1.2-1.9	2.0-3.4	3.5-4.9 or <500	>5.0 or <200



Above: Hospital mortality rate associated with maximum SOFA score. The mortality rate was nearly 90% in patients with a SOFA score of more than 15.

Sepsis III Validations

qSOFA ≥2

Generation 74453
Validation 74454

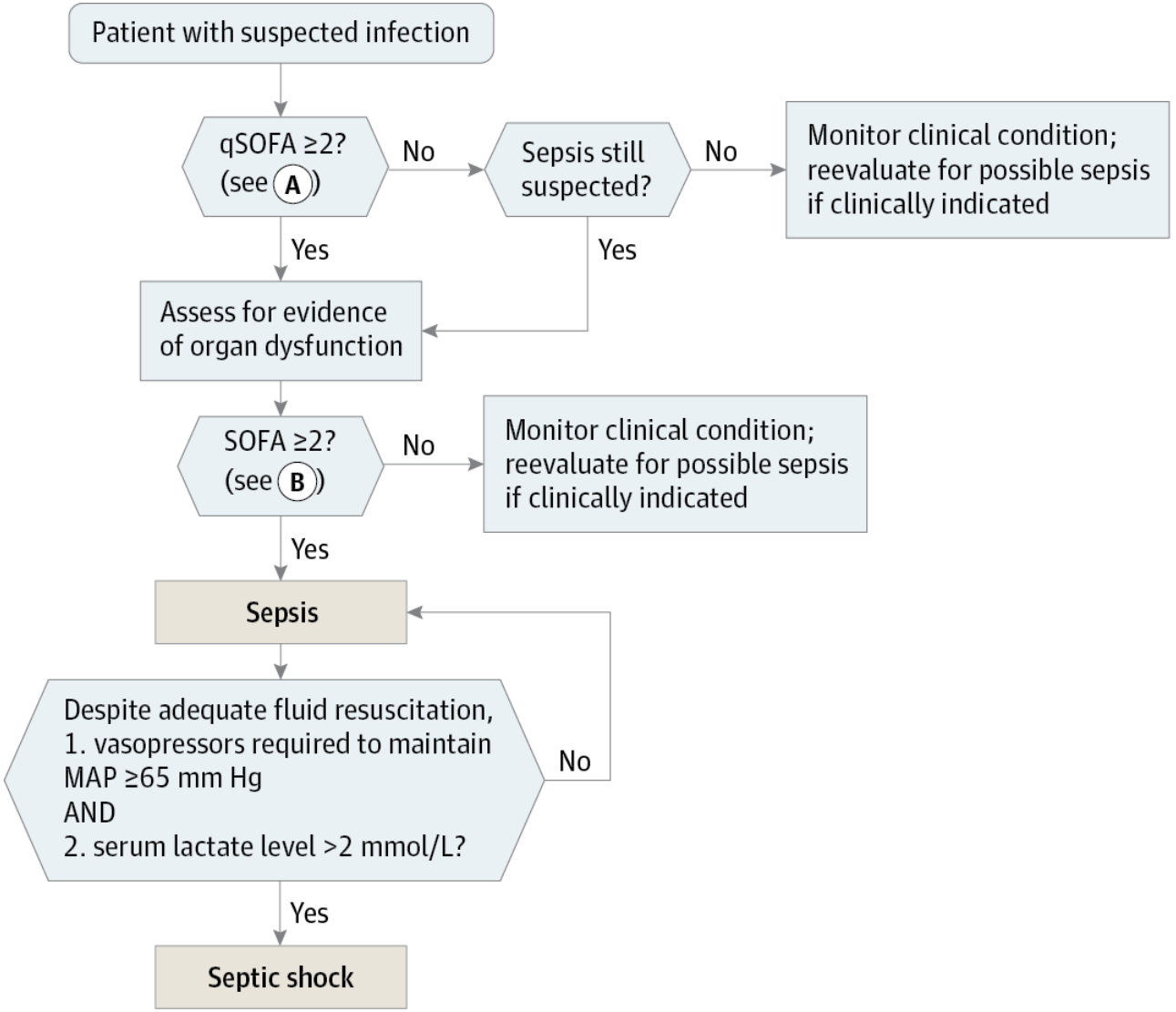
Inhospital mortality 4-18%

qSOFA	
RR > 22bpm	0 = Mortality < 1%
sBP < 100mmHg	1 = Mortality 2-3%
Altered GCS	⩾2 = Mortality ⩾10%
Screening for outcome rather than diagnosis	

	AUROC SOFA	AUROC SIRS	AUROC qSOFA
ICU	0.74 (0.73-0.75)	0.64 (0.62-0.66)	0.66 (0.64-0.68)
ED	0.79 (0.78-0.80)	0.76 (0,75-0.77)	0..81 (0.80-0.82)

JAMA 2016;315(8):762-774

Sepsis III Operationalization



Sepsis II /Sepsis III

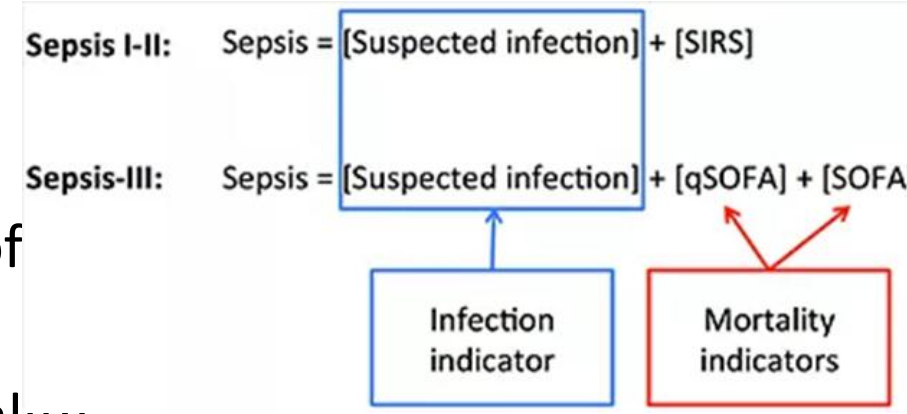
- Advantages of the new definition.
  - Well researched publication. Beyond the expert opinion.
  - Large data based in and out UCI.
  - Clear definition of organ dysfunction.
  - SOFA is powerful tool to predict mortality 2 points of change, 25- fold increase in mortality.
  - qSOFA better than SOFA in the out-of-ICU (AUROC=0.81 vs AUROC=0.74).

Sepsis II /Sepsis III

- Disadvantages
  - Designed to gain validity and lose of scope in early identification.
  - Severity prediction trough in hospital mortality.
  - Subjectivity “Suspected Infection” depending on the prevailing levels of paranoia.
  - qSOFA is a mortality predictors
  - Rentability of SIRS and qSOFA are similar…. or not?

Sepsis II /Sepsis III
Disadvantages

- Is this the type of information we will like to see:
  - No subjective definition
  - Tool for early identification of septic patients ??
  - ICU admission criteria/mortality



Ability to predict mortality among patients with possible infection outside the ICU

Test	Area under ROC curve	Sensitivity for mortality	Specificity for mortality
SIRS ≥ 2	0.76	64%	65%
SOFA ≥ 2	0.79	68%	67%
qSOFA ≥ 2	0.81	55%	84%

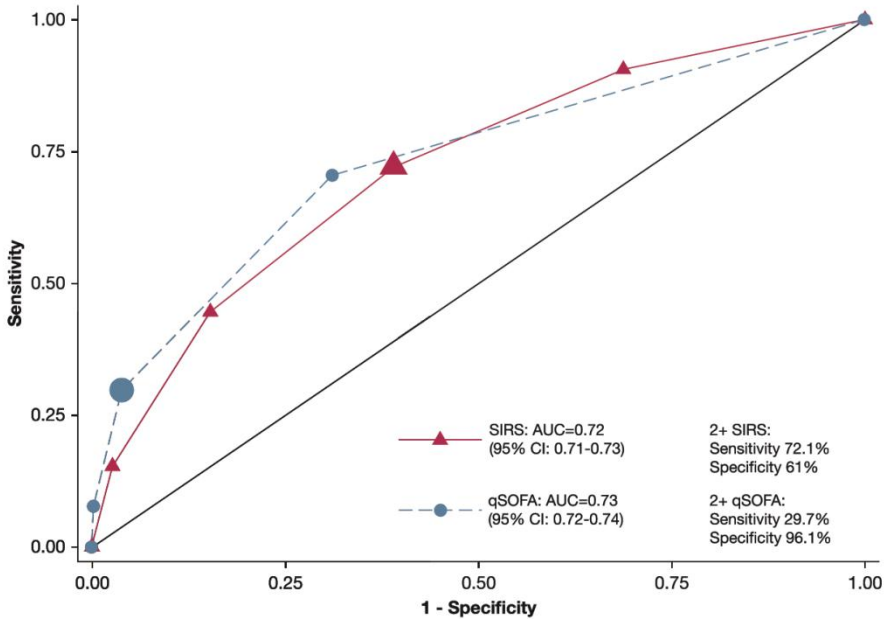
Sepsis II /Sepsis III
Disadvantages

Author	Outcome	Setting	Patients (mortality)	AUROC qSOFA	AUROC SIRS	NEWS
Yonathan	IHM	ED(pr)	879 (8%)	0.80 (0.74 - 0.85)	0.65 (0.59 - 0.70)	
Finkelsztein	IHM	ED+from ICU	152 (19%)	0.74 (0.66–0.81]	0.59 (0.51–0.67)	
Rath	IHM/ ICU>3d	ICU	184.875 (18.7%)	0.60 (0.60-.61]	0.59 (0.58-0.59)	
Churpek	IHM/ICU Ad	ED(re)	30.677 (5%)	0.69 (0.67–0.70)	0.65 (0.63–0.66)	0.73
WIlliams	IHH/ Organ Dam	ED(pr)	8.871 (3.7%)	0.73 (0.72-0.74)	0.72 (0.71-0.73)	

Sepsis II /Sepsis III
Disadvantages(Williams)

- Consecutive ED presumed infection 8871 SIRS(47%)
- Mortality 30d- 3.7%.
- For organ dysfunction SOFA ≥ 2 24%

	Sensitivity	Specificity
qSOFA	29.9	96.1
SIRS	72	61

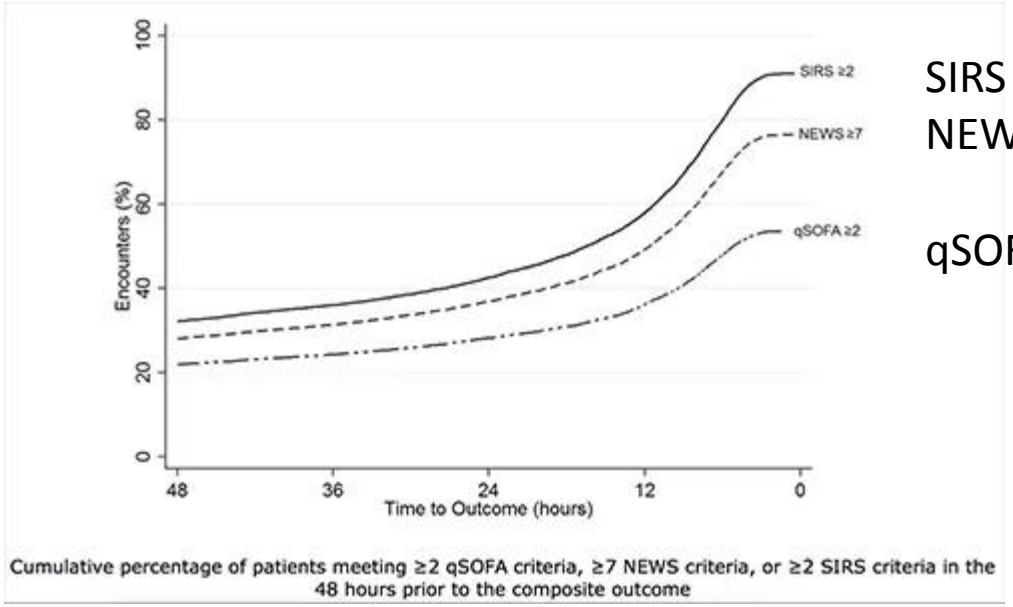


- Organ dysfunction > 10% mortality
- 24-26,7% of organ dysfunction has no SIRS

Williams CHEST 2017;151(3):586-596

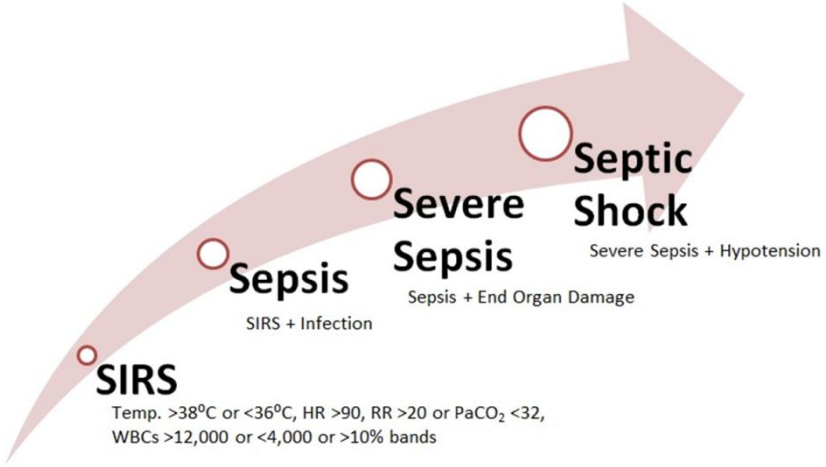
Sepsis III
Disadvantages

- "Sepsis" without organ dysfunction that have progressed to sepsis with organ dysfunction or septic shock, the Sepsis-3 consensus disputes the existence of this continuum.



Cumulative percentage of patients meeting ≥2 qSOFA criteria, ≥7 NEWS criteria, or ≥2 SIRS criteria in the 48 hours prior to the composite outcome

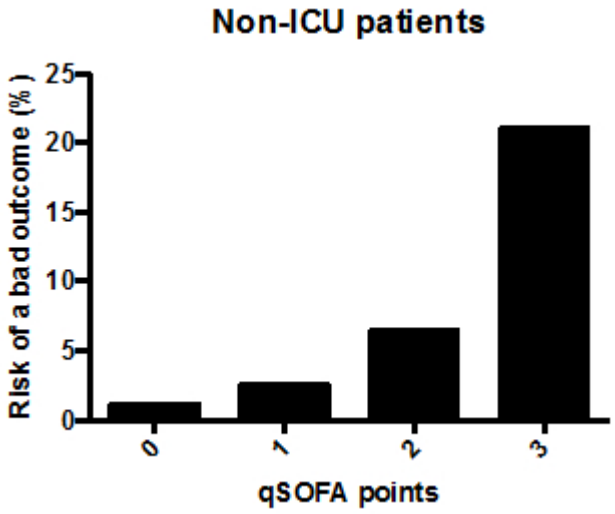
SIRS
NEWS
qSOFA



Churpek

Sepsis II /Sepsis III
Disadvantages

- Non supported by previous scores



qSOFA	CURB65
Criteria • Abnormal mental status • RR ≥22 • SBP ≤ 100	**Criteria** • Confusion • RR ≥ 30 • SBP <90 *or* diastolic Bp ≤ 60 mm • BUN > 19 mg/dL • Age ≥ 65 YO
Interpretation • >1: sepsis (mortality ~10%)	**Interpretation** • 0: 0.6% mortality • 1: 2.7% mortality • 2: 6.8% mortality • 3: 14% mortality • 4-5: 28% mortality

Sepsis III

- Endorse by 31 SS
  - Society of Critical Care Medicine,
  - American Thoracic Society,
  - American Association of Critical Care Nurses.
  - European Society Intensive Care
  - EUSEM
  - ERC
- Surviving Sepsis Campaign
- Sepsis III is not endorsed by:
  - American College of Chest Physicians,
  - Infectious Disease Society of America,
  - any of the Emergency Medicine societies
    - ACEP
    - SAEM
    - AAEM
  - NICE, Royal Colleague of Emergency Physicians, UK Sepsis Trust

Sepsis Management Clinical needs

- To provide a rapid screening test and to render a definitive diagnosis.
- The primary clinical utility of sepsis definitions is to determine who is sick and who needs to be admitted to the ICU.
- An ideal screening test has a high sensitivity sacrifying specificity. Fast and easy to perform.
- Are the new definitions going to improve patient care.

Sepsis III Take Home

- Some methodological problems in the evaluation of qSOFA: Outcome, Population.
- qSOFA performance compare to SIRS.
- Is important to see concordance with other well stablish scores.
- We need new publications that address these controversies.

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Thank you for your attention.¡