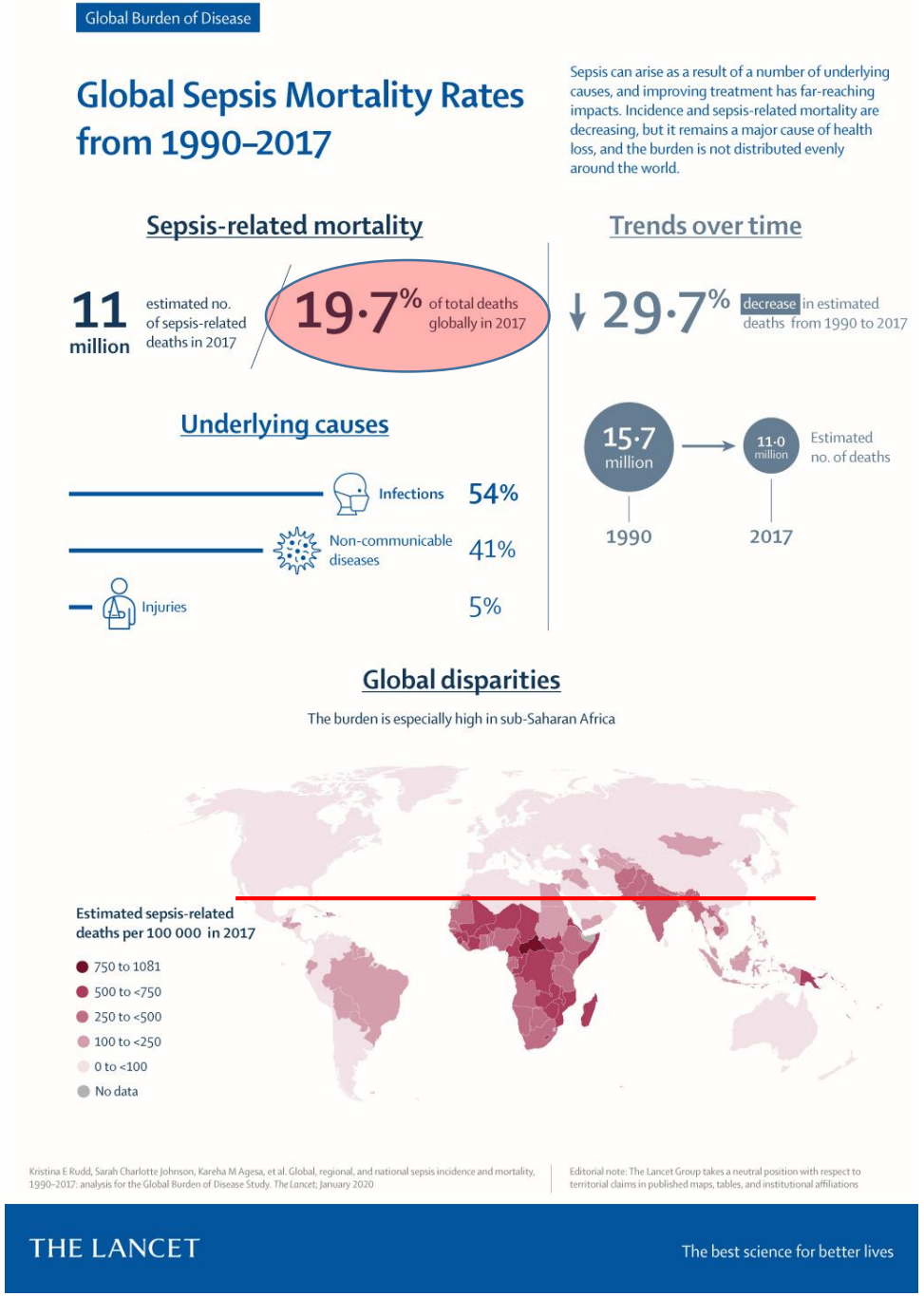
Sepsis : que faire avant d'appeler le réanimateur ?

Prise en charge hémodynamique

Mohamed Boussarsar, MD Professor
Sousse, Tunisia

Sepsis worldwide burden



Sepsis / Septic Shock definition

Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

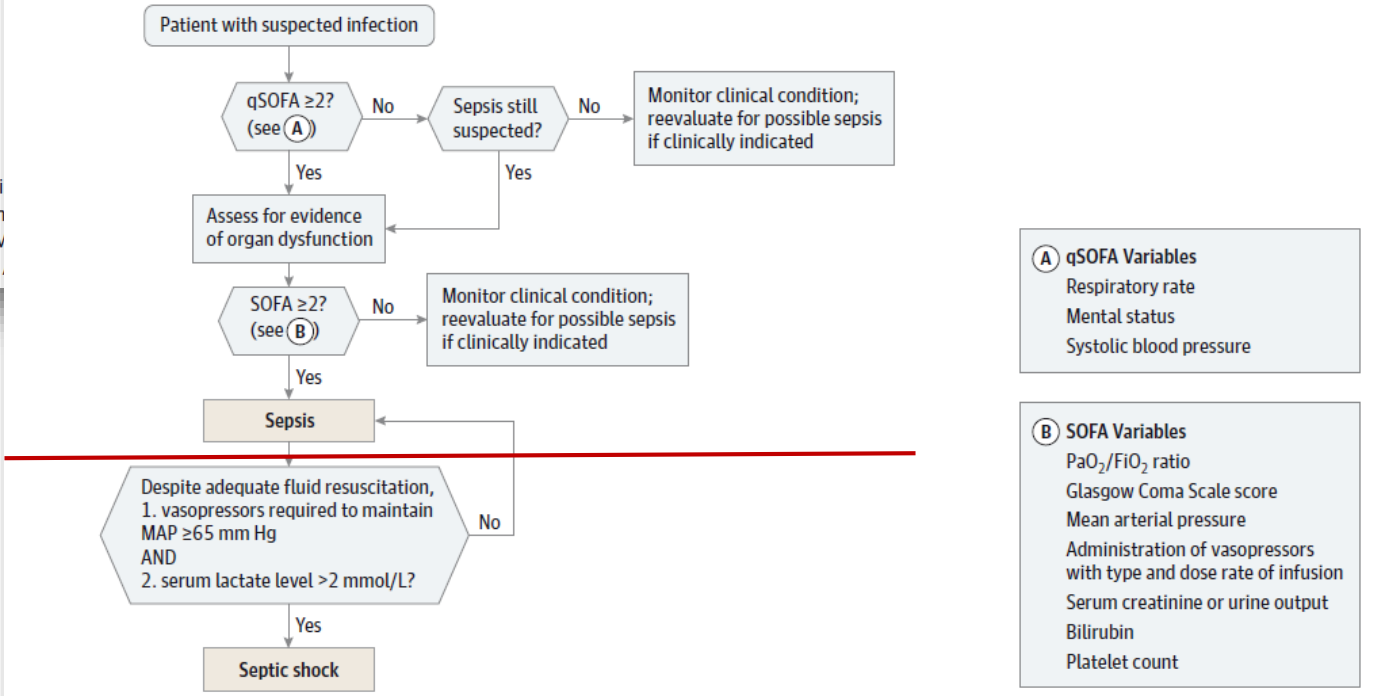
The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari
Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, Ph
Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, M
Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C.

Box 3. New Terms and Definitions

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection.
- Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
- Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40%.

Figure. Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock



The baseline Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score should be assumed to be zero unless the patient is known to have preexisting (acute or chronic) organ dysfunction before the onset of infection. qSOFA indicates quick SOFA; MAP, mean arterial pressure.

Sepsis / Septic Shock at the era of precision medicine

nature medicine

PERSPECTIVE

https://doi.org/10.1038/s41591-022-01843-x

Check for updates

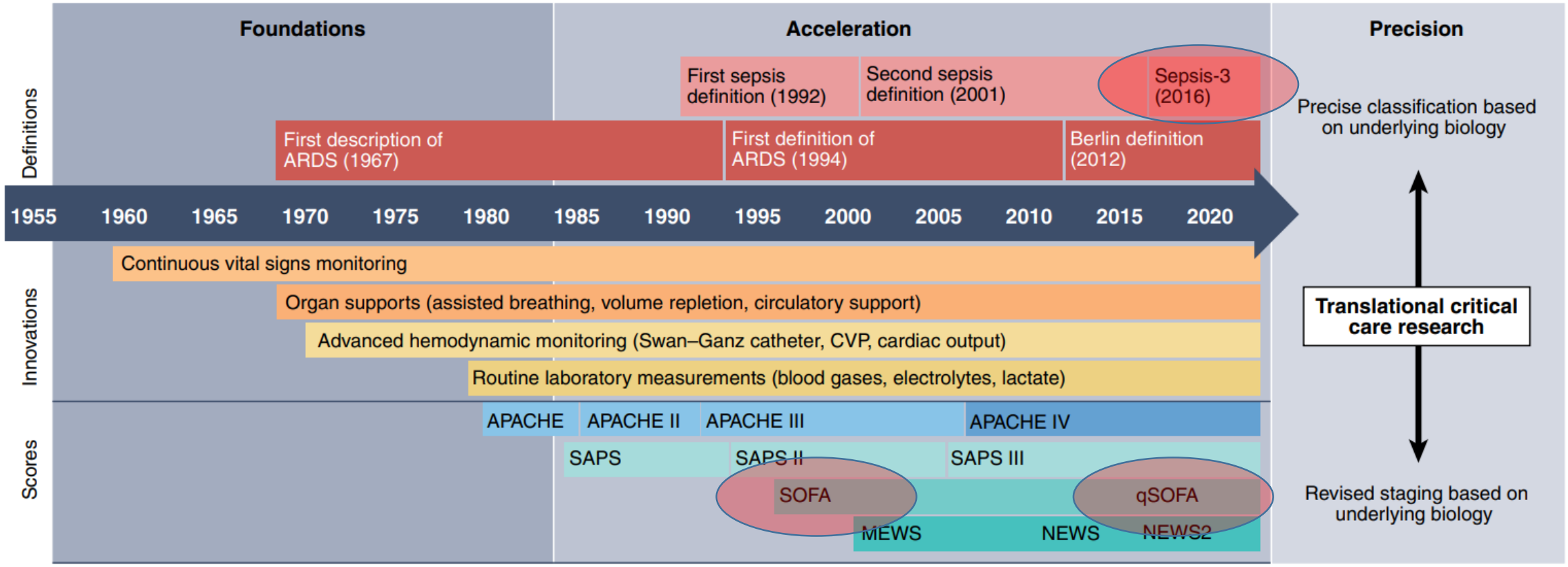
Redefining critical illness

David M. Maslove[1,2,45] ✉, Benjamin Tang[3,45], Manu Shankar-Hari[4,5], Patrick R. Lawler[6,7], Derek C. Angus[8,9], J. Kenneth Baillie[5,10,11], Rebecca M. Baron[12,13], Michael Bauer[14,15], Timothy G. Buchman[16,17], Carolyn S. Calfee[18], Claudia C. dos Santos[7,19], Evangelos J. Giamarellos-Bourboulis[20], Anthony C. Gordon[21], John A. Kellum[8], Julian C. Knight[22], Aleksandra Leligdowicz[23,24], Daniel F. McAuley[25,26], Anthony S. McLean[3], David K. Menon[27], Nuala J. Meyer[28], Lyle L. Moldawer[29], Kiran Reddy[25,26], John P. Reilly[28], James A. Russell[30], Jonathan E. Sevransky[16,31], Christopher W. Seymour[8], Nathan I. Shapiro[13,32], Mervyn Singer[33], Charlotte Summers[34], Timothy E. Sweeney[35], B. Taylor Thompson[13,36], Tom van der Poll[37], Balasubramanian Venkatesh[38,39], Keith R. Walley[30], Timothy S. Walsh[40], Lorraine B. Ware[41], Hector R. Wong[42,46], Zsolt E. Zador[43] and John C. Marshall[7,43,44]

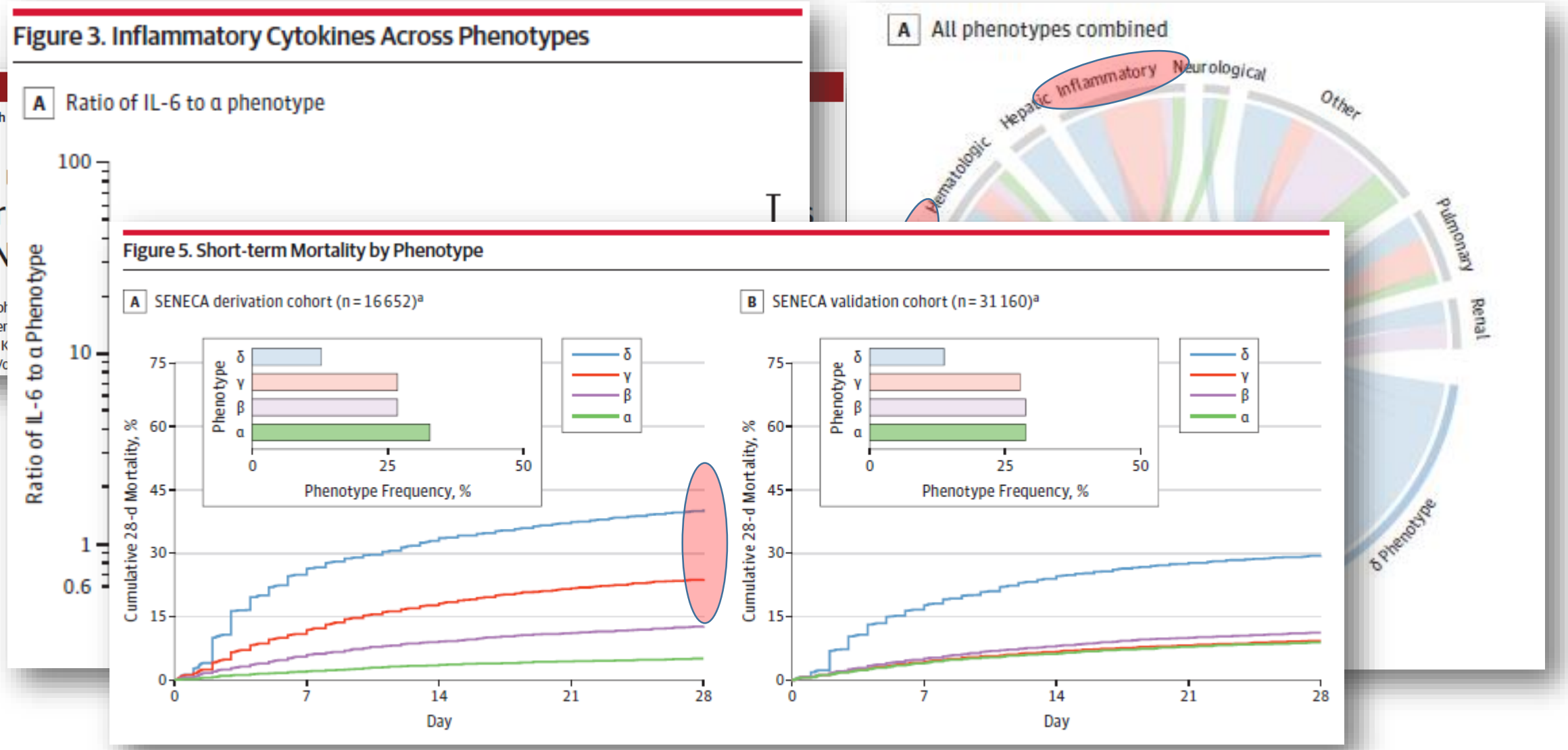
Research and practice in critical care medicine have long been defined by syndromes, which, despite being clinically recognizable entities, are, in fact, loose amalgams of heterogeneous states that may respond differently to therapy. Mounting translational evidence—supported by research on respiratory failure due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection—suggests that the current syndrome-based framework of critical illness should be reconsidered. Here we discuss recent findings from basic science and clinical research in critical care and explore how these might inform a new conceptual model of critical illness. De-emphasizing syndromes, we focus on the underlying biological changes that underpin critical illness states and that may be amenable to treatment. We hypothesize that such an approach will accelerate critical care research, leading to a richer understanding of the pathobiology of critical illness and of the key determinants of patient outcomes. This, in turn, will support the design of more effective clinical trials and inform a more precise and more effective practice at the bedside.

Sepsis / Septic Shock at the era of precision medicine

PERSPECTIVE NATURE MEDICINE



Sepsis / Septic Shock at the era of precision medicine



Sepsis / Septic Shock at the era of precision medicine

REVIEW

Heterogeneity in
evidence with cli

Aleksandra Leligdowicz[1,2*] and Michae

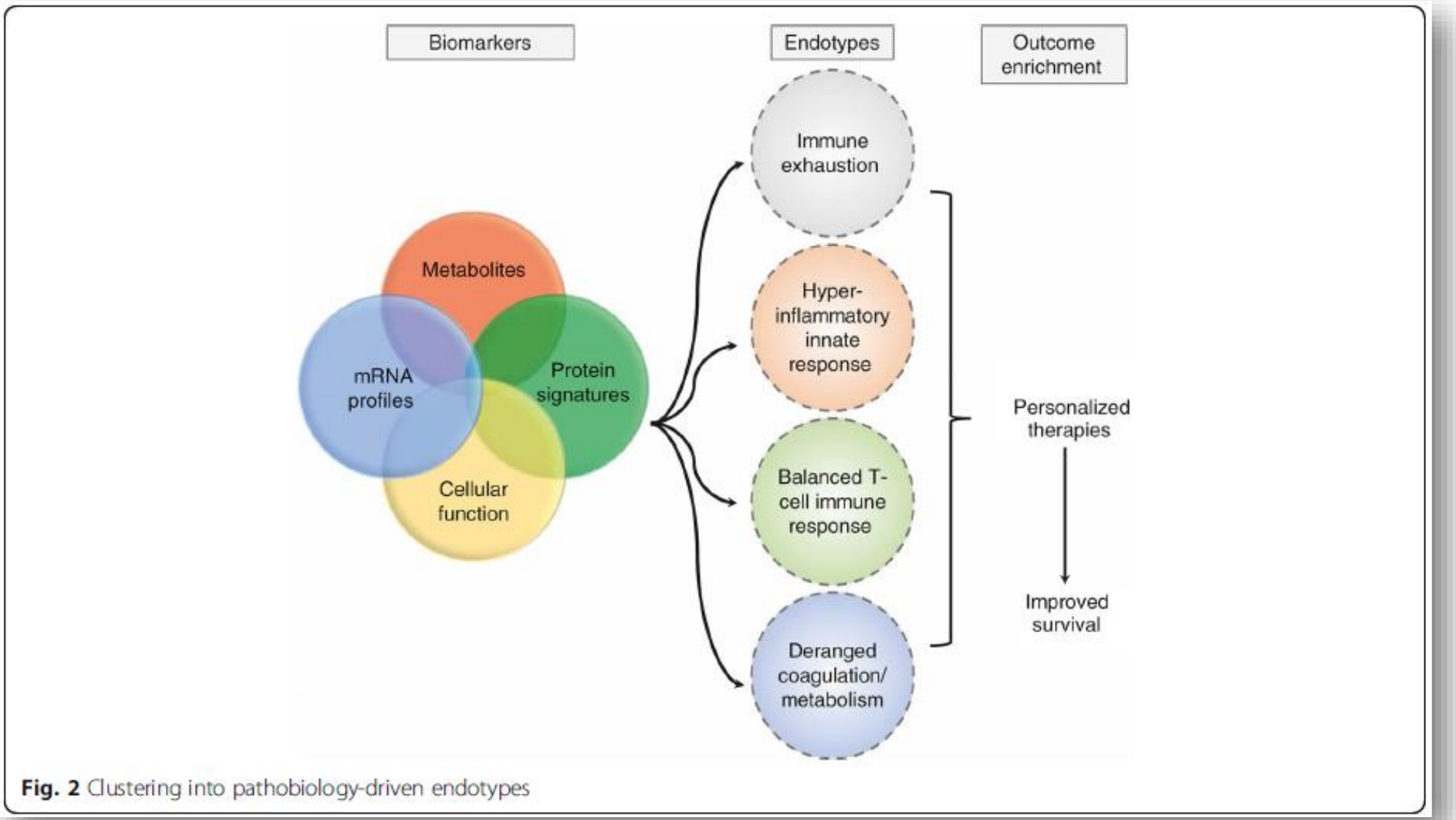


Fig. 2 Clustering into pathobiology-driven endotypes

Sepsis / Septic Shock at the era of precision medicine

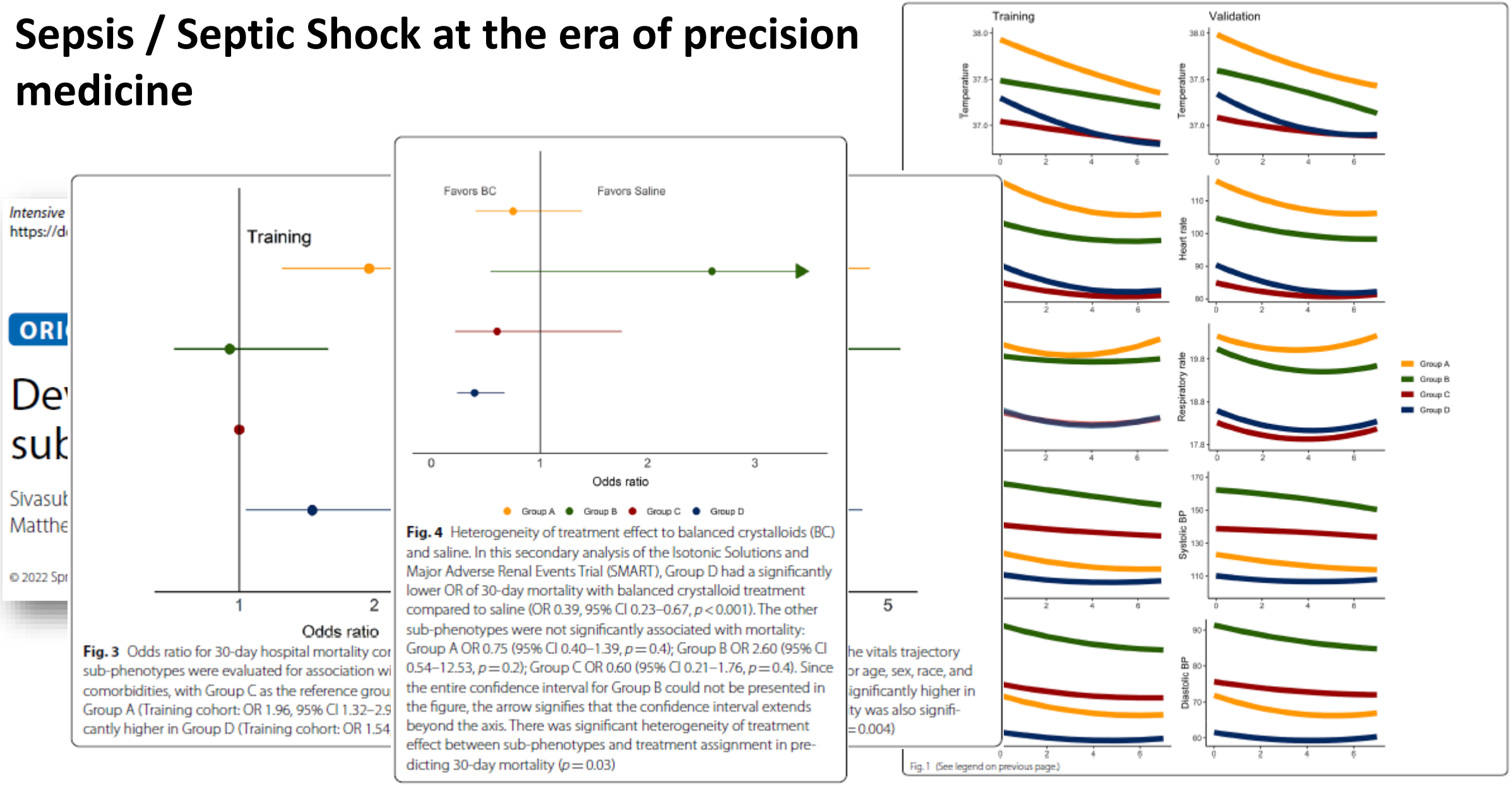


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Fig. 3 Odds ratio for 30-day hospital mortality cor
sub-phenotypes were evaluated for association wi
comorbidities, with Group C as the reference grou
Group A (Training cohort: OR 1.96, 95% CI 1.32–2.9
cantly higher in Group D (Training cohort: OR 1.54

Fig. 4 Heterogeneity of treatment effect to balanced crystalloids (BC) and saline. In this secondary analysis of the Isotonic Solutions and Major Adverse Renal Events Trial (SMART), Group D had a significantly lower OR of 30-day mortality with balanced crystalloid treatment compared to saline (OR 0.39, 95% CI 0.23–0.67, $p < 0.001$). The other sub-phenotypes were not significantly associated with mortality: Group A OR 0.75 (95% CI 0.40–1.39, $p = 0.4$); Group B OR 2.60 (95% CI 0.54–12.53, $p = 0.2$); Group C OR 0.60 (95% CI 0.21–1.76, $p = 0.4$). Since the entire confidence interval for Group B could not be presented in the figure, the arrow signifies that the confidence interval extends beyond the axis. There was significant heterogeneity of treatment effect between sub-phenotypes and treatment assignment in predicting 30-day mortality ($p = 0.03$)

he vitals trajectory
or age, sex, race, and
ignificantly higher in
ty was also signifi-
= 0.004)

Fig. 1 (See legend on previous page.)

Sepsis / Septic Shock redefinition

Published in final edited form as:
Crit Care Med. 2021 May 01; 49(5): 748–759. doi:10.1097/CCM.0000000000004842.

Sepsis Subclasses: A Framework for Development and Interpretation*

, MPH[1], J. Kenneth Baillie, MD, PhD[2],
Joseph Carcillo, MD[4], Chung-Chou H.
ns, MD, MSc[1], Anthony C. Gordon, MD[8],
istopher J. Lindsell, PhD[10], Vincent Liu,
Randolph, MD, MSc[13], Brendon P. Scicluna,
an I. Shapiro, MD[18], Timothy E. Sweeney,
ng, MD, PhD[20], B. Taylor Thompson, MD[21],
MD, PhD[14], Lonneke A. van Vught, MD,
, MS[1], Huiying Zhao, MD[24], Christopher W.

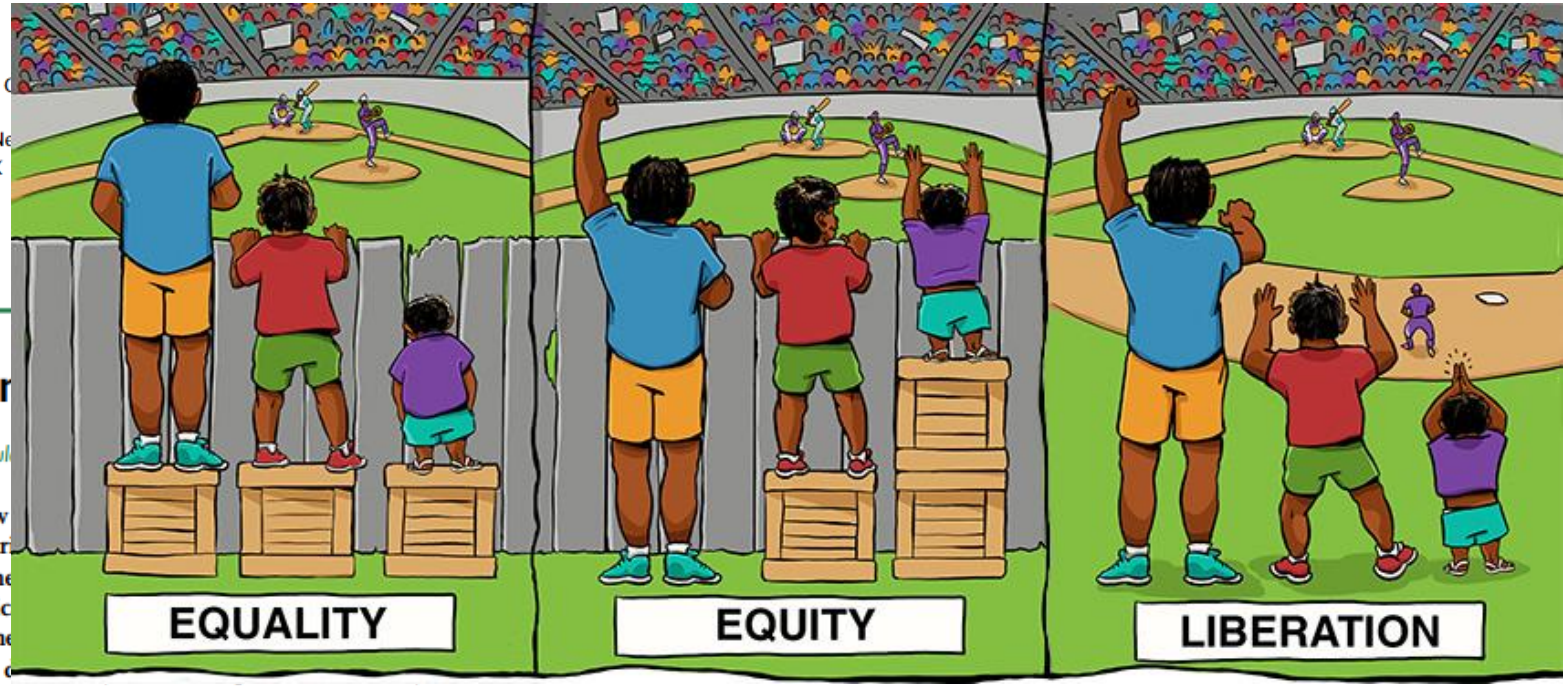
Before the broad use of sepsis subclasses at the bedside, it is helpful to consider the many issues related to purpose, statistical methods, data sources, timing, and assessment of truth. Is it enough to identify groups of patients in a single dataset, hitherto not recognized to cluster together, for prognosis or a precision treatment? Or is the goal a truly individualized strategy? Rather than "subclasses," per se, perhaps we should be searching for "clinically relevant, nonsynonymous, biologically plausible, treatment-responsive, and reproducible" subgroups. Once tested in randomized trials with accompanying treatments, these subclasses would have the potential to inform not only the pathophysiology of sepsis, but future efforts to improve patient outcomes.

Sepsis / Septic Shock definition, E Q U I T Y

Equitable endotyping is essential to achieve a global standard of precise, effective, and locally-relevant sepsis care

Matthew J. Cummings[a,b] *and Shevin T. Jacob*[c,d,*]

[a]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine, Vagelos C
Columbia University, New York, NY, USA
[b]Center for Infection and Immunity, Mailman School of Public Health, Columbia University, Ne
[c]Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool L3 5QA, UK
[d]Walimu, Kampala, Uganda



Subphenotypes in critical care: translation

Kiran Reddy, Pratik Sinha, Cecilia M O'Kane, Anthony C Gordon, Carolyn S Calfee, Daniel F McAul

Despite progress in the supportive care available for critically ill patients, few for effective disease-modifying therapeutic options. The fact that many tr identified a treatment benefit is probably due, in part, to the underlying he Numerous approaches have been proposed to divide populations of critic subgroups (subphenotypes), some of which might be more useful than othe clinical features and biomarkers have been proposed for acute respiratory d injury, and pancreatitis. Identifying the systems that are most useful and biologically meaningful could lead to a better understanding of the pathophysiology of critical care syndromes and the discovery of new treatment targets, and allow recruitment in future therapeutic trials to focus on predicted responders. This Review discusses proposed subphenotypes of critical illness syndromes and highlights the issues that will need to be addressed to translate subphenotypes into clinical practice.

Division of Pulmonary, Critical Care, Allergy and Sleep Medicine, and Department of Anesthesia, University of California, San Francisco, CA, USA (P Sinha PhD, Prof C S Calfee MD); **Wellcome-**

Cas Clinique, Maladies Infectieuses

- Mr AB, 53 ans, HTA, Amlodipine, Valsartan
- 5 mai 2022, fièvre, douleur abdominale
- 7 mai 2022, ictère
- 11h00 am, aux urgences
- FC, 105b/mn ; PA, 92/36/55mmHg ; T°, 39°C ; ictère ; triade de Charcot ; marbrures ; TRC, 5s

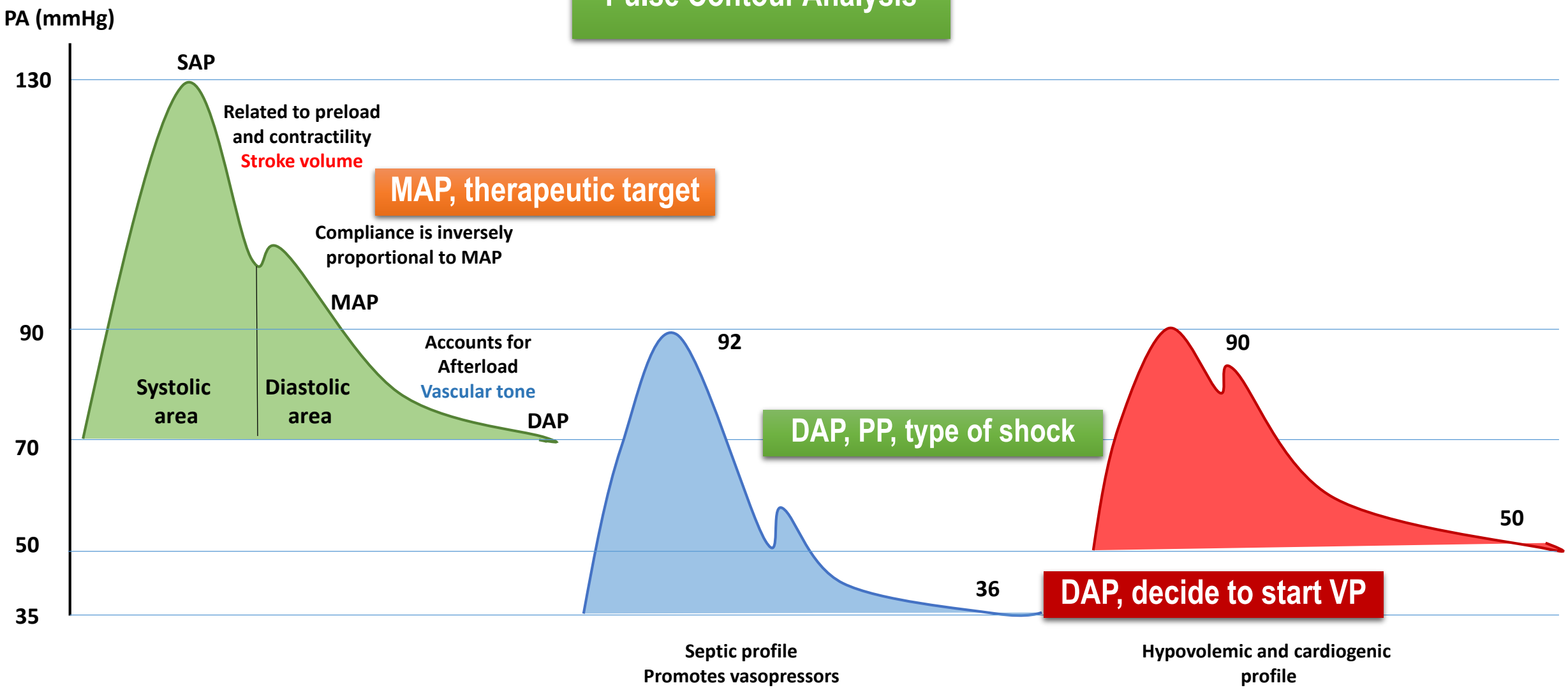
- Qu'est ce que vous ferez à ce stade?
- Expansion volémique
- Norépinephrine
- Les deux

Monitorage HD basique?

Pression artérielle

Beaucoup d'informations

Pulse Contour Analysis



How about BP components in sepsis and septic shock?

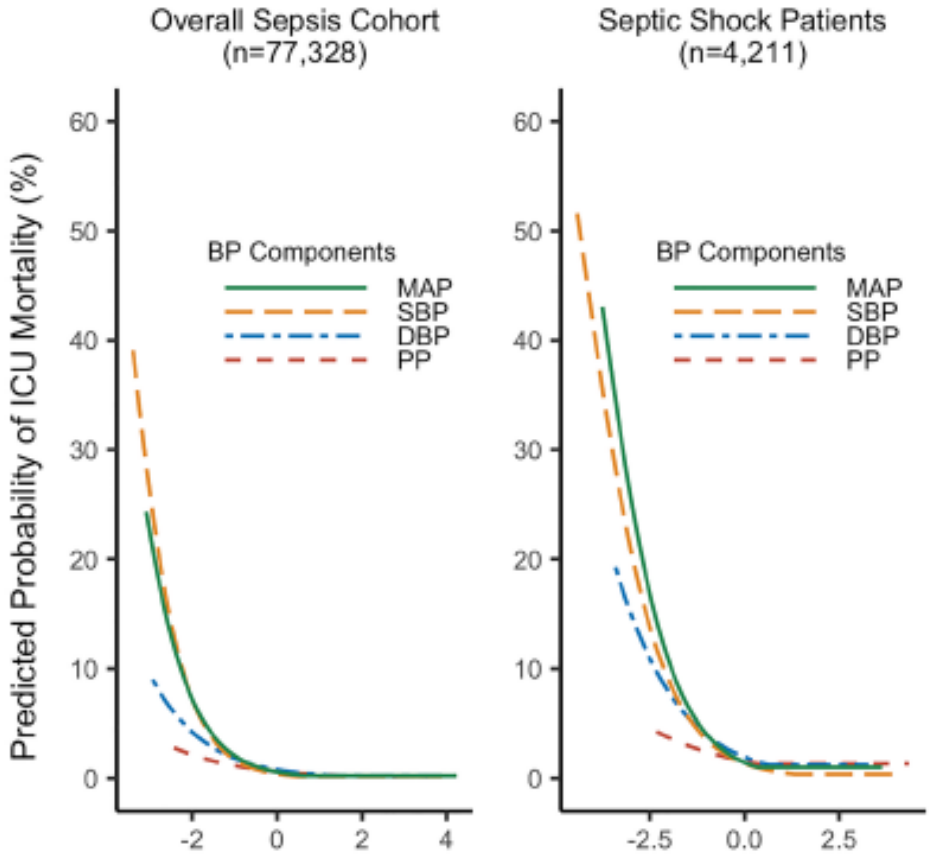
Khanna *et al. Annals of Intensive Care* (2023) 13:9
https://doi.org/10.1186/s13613-023-01101-4

Annals of Intensive Care

RESEARCH Open A

Association of systolic, diastolic, mean, and pulse pressure with morbidity and morta in septic ICU patients: a nationwide observational study

Ashish K. Khanna[1,2*†], Takahiro Kinoshita[3†], Annamalai Natarajan[3], Emma Schwager[3], Dustin D. Linn[3], Junzi Dong[3], Erina Ghosh[3], Francesco Vicario[3] and Kamal Maheshwari[4]



Component	-2SD	0(mean)	+2SD	+4SD
MAP	42	62	82	102
SBP	66	94	122	150
DBP	30	48	66	84
PP	11	35	59	83

Component	-2.5SD	0(mean)	+2.5SD
MAP	36	56	76
SBP	59	84	109
DBP	24	44	64
PP	3	28	53

Fig. 3 Predicted probabilities of ICU mortality under the hinge model with a single change-point

Lowest BP components maintained for 2h?

Khanna *et al. Annals of Intensive Care* (2023) 13:9
https://doi.org/10.1186/s13613-023-01101-4

Annals of Intensive Care

RESEARCH

Association of systolic, diastolic, mean and pulse pressure with morbidity and in septic ICU patients: a nationwide observational study

Ashish K. Khanna[1,2*†], Takahiro Kinoshita[3†], Annamalai Natarajan[3], Emma Schwager[3], Junzi Dong[3], Erina Ghosh[3], Francesco Vicario[3] and Kamal Maheshwari[4]

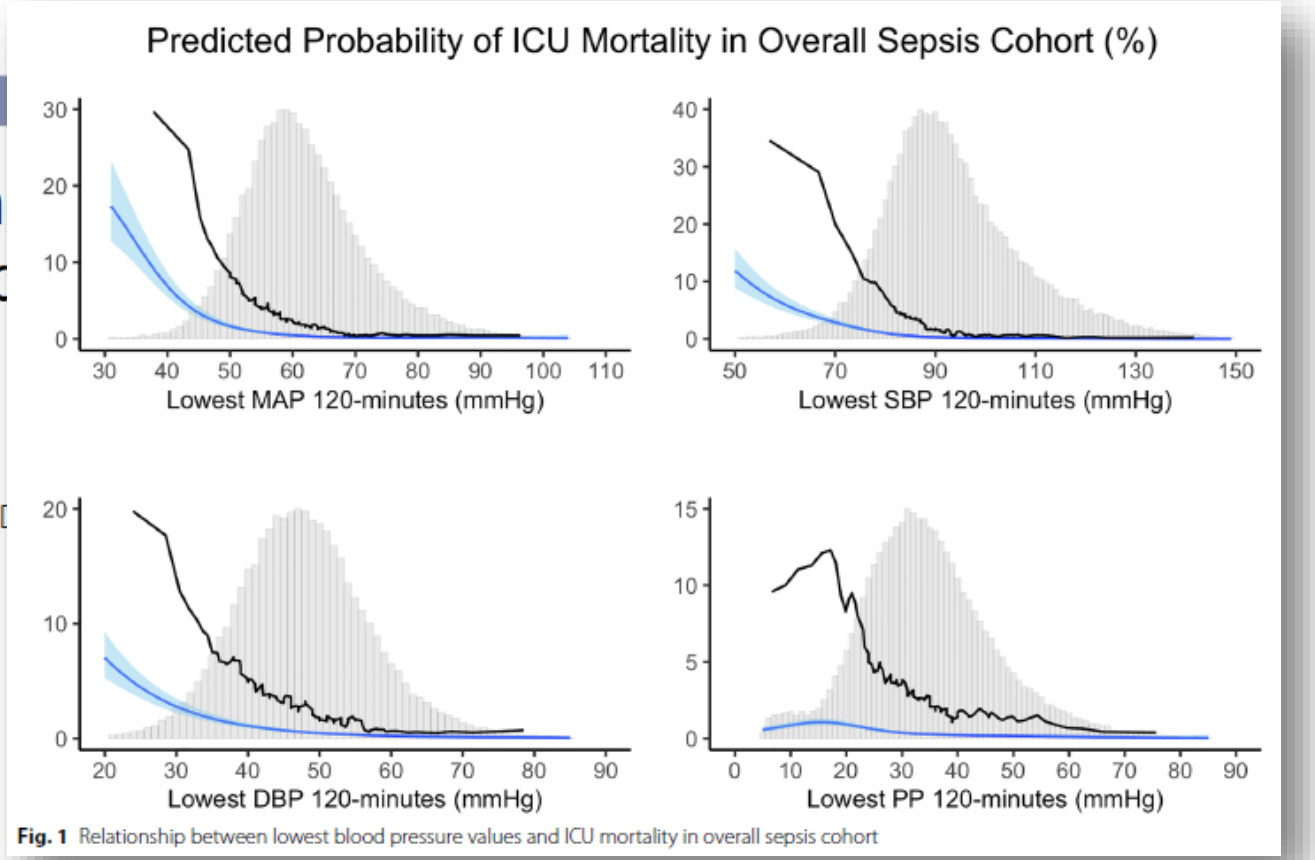


Fig. 1 Relationship between lowest blood pressure values and ICU mortality in overall sepsis cohort

Vasopressors

Intensive Care Med (2021) 47:1181–1247
https://doi.org/10.1007/s00134-021-06506-y

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

...[4], Craig M. Coopersmith[5],
...[9], Hallie C. Prescott[10],
...[14], Derek C. Angus[15], Yaseen Arabi[16],
...[19], Lisa Burry[20], Maurizio Cecconi[21,22],
...[11], Kent Doi[26], Bin Du[27],
Morten Hylander Møller[32],
...[36,37], Younsuck Koh[38], Anand Kumar[39],
Sangeeta Mehta[44], Yatin Mehta[45],
...zabeth Papathanassoglou[49],
...weickert[56], Maureen Seckel[57],
...erman[61] and Mitchell Levy[62]

Vasoactive Agent Management

Use norepinephrine as first-line vasopressor

For patients with septic shock on vasopressor

Target a MAP of 65mm 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

Strong recommendations Weak recommendations

*When using vasopressors peripherally, they should be administered only for a short period of time and in a vein proximal to the antecubital fossa.

Fig. 2 Summary of vasoactive agents recommendations

Cas Clinique, 60 mn plutard, Toujours pas de lit de en réanimation

- Saline: 1500 ml
- Norepi: 0.2 µg/Kg/mn
- FC, 102 b/mn
- PA, 83/50/59 mmHg

- Urée, 17 mmol/L
- Creat, 150 µmol/L
- Bili, 65 µmol/L
- Lactates, 2.7 mmol/L

- Qu'est ce que vous ferez à ce stade?

- Augmenter Norepi
- Rajouter 500 ml de fluide
- Tester la réponse au remplissage

Fluid management

4 Ds, Dose, Duration, De-escalation, De-resuscitation

Malbrain *et al. Ann. Intensive Care (2018) 8:66*
https://doi.org/10.1186/s13613-018-0402-x

Annals o

REVIEW

Principles of fluid management and stewardship in septic shock: it is ti to con four ph of fluic

Manu L. N. G. M De Tavernier[3], F
Olivier Joanne and Xavier Mc

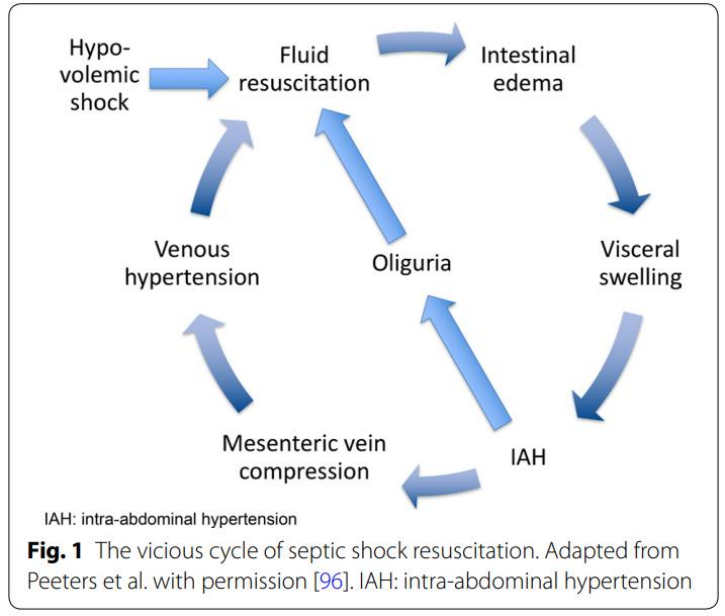
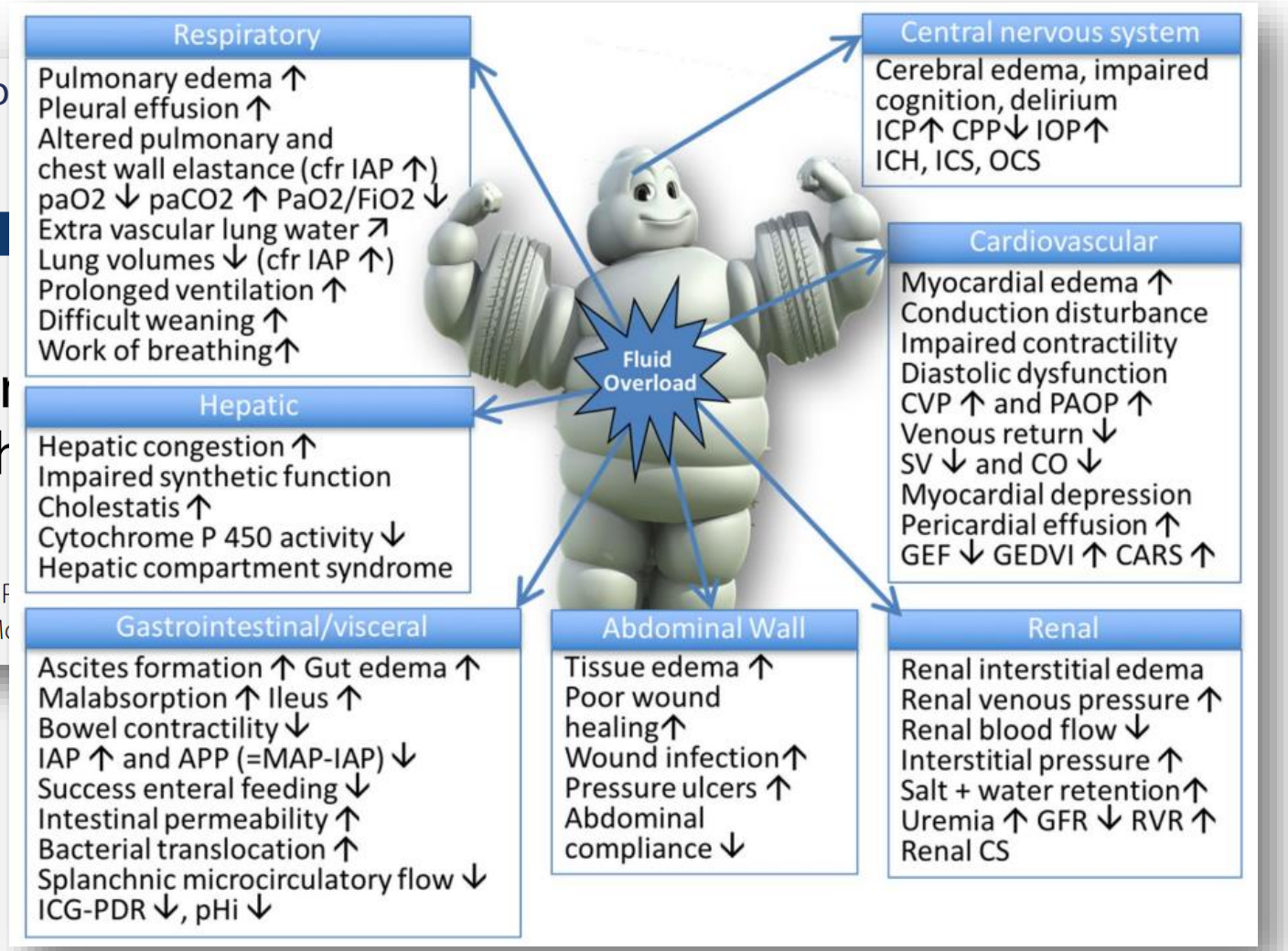


Fig. 1 The vicious cycle of septic shock resuscitation. Adapted from Peeters et al. with permission [96]. IAH: intra-abdominal hypertension



Fluid management

Intensive Care Med (2021) 47:1181–1247
https://doi.org/10.1007/s00134-021-06506-y

GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Laura Evans[1*], Andrew Rhodes[2], Waleed Alhazzani[3], Massimo Antonelli[4], Craig M. Coopersmith[5], Craig French[6], Flávia R. Machado[7], Lauralyn Mcintyre[8], Marlies Ostermann[9], Hallie C. Prescott[10], Christa Schorr[11], Steven Simpson[12], W. Joost Wiersinga[13], Fayez Alshamsi[14], Derek C. Angus[15], Yaseen Arabi[16], Luciano Azevedo[17], Richard Beale[9], Gregory Beilman[18], Emilie Belley-Cote[19], Lisa Burry[20], Maurizio Cecconi[21,22]

Recommendations

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

5. For patients with sepsis induced hypoperfusion or septic shock we **suggest** that at least 30 mL/kg of intravenous (IV) crystalloid fluid should be given within the first 3 h of resuscitation
Weak recommendation, low-quality evidence

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 recommendation, very low-quality evidence

Remarks

Dynamic parameters include response to a passive leg raise or a fluid bolus, using stroke volume (SV), stroke volume variation (SVV), pulse pressure variation (PPV), or echocardiography, where available

Recommendations

32. For adults with sepsis or septic shock, we **recommend** using crystalloids as first-line fluid for resuscitation
Strong recommendation, moderate quality of evidence

33. For adults with sepsis or septic shock, we **suggest** using balanced crystalloids instead of normal saline for resuscitation
Weak recommendation, low quality of evidence

34. For adults with sepsis or septic shock, we **suggest** using albumin in patients who received large volumes of crystalloids over using crystalloids alone
Weak recommendation, moderate quality of evidence

35. For adults with sepsis or septic shock, we **recommend against** using starches for resuscitation
Strong recommendation, high quality of evidence

36. For adults with sepsis and septic shock, we **suggest against** using gelatin for resuscitation
Weak recommendation, moderate quality

Check for updates

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Sepsis

A Secondary Analysis of the SMART Clinical Trial

Ryan M. Brown[1], Li Wang[2], Taylor D. Coston[3], Nathan I. Krishnan[3], Jonathan D. Casey[1], Jonathan P. Wanderer[4,5], Jesse M. Ehrenfeld[4,5,6,7], Daniel W. Byrne[2], Joanna L. Stollings[8], Edward D. Siew[9], Gordon R. Bernard[1], Wesley H. Self[10], Todd W. Rice[1], and Matthew W. Semler[1]; for the SMART Investigators* and the Pragmatic Critical Care Research Group

[1]Division of Allergy, Pulmonary, and Critical Care Medicine, [2]Department of Biostatistics, [3]Department of Medicine, [4]Department of Anest
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Neph

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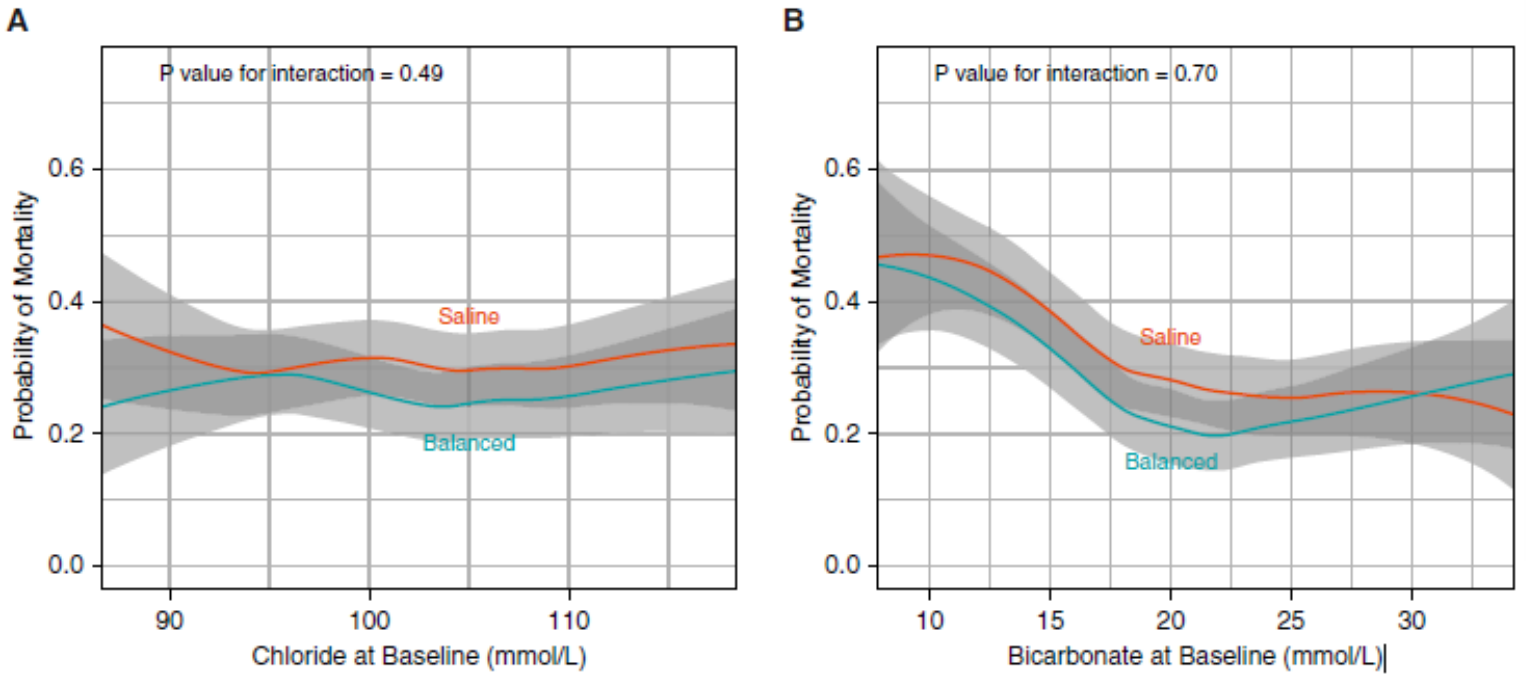

Figure 2. Relationship between baseline chloride and bicarbonate concentration, study groups, and 30-day in-hospital mortality. The mean and 95% confidence interval (denoted by gray shading) for the probability of 30-day in-hospital mortality is displayed for patients in the balanced crystalloids group (blue) and in the saline group (red) relative to (*A*) baseline plasma chloride concentration and (*B*) baseline bicarbonate concentration, with locally weighted scatterplot smoothing. Although 30-day in-hospital mortality overall was lower in the balanced crystalloids group than the saline group, neither baseline chloride nor baseline bicarbonate concentration modified the effect of study group on in-hospital mortality.

In conclusion, in this secondary analysis of 1,641 critically ill adults with sepsis from a large pragmatic trial, the use of balanced crystalloids was associated with a lower incidence of 30-day in-hospital mortality than saline. These results should be viewed as hypothesis-generating. Future research should examine the effect of crystalloid composition on mortality in sepsis and explore mechanisms linking crystalloid composition to clinical outcomes. ■

Journal of
Clinical Medicine

MDPI

Review

Balanced Crystalloids versus Normal Saline in Adults with Sepsis: A Comprehensive Systematic Review and Meta-Analysis

Azizullah Beran [1,*], Nehaya Altorok [1], Omar Srour [1], Saif-Eddin Malhas [1], Waleed Khokher [1], Mohammed Mhanna [1], Hazem Ayesh [1], Nameer Aladamat [2], Ziad Abuhelwa [1], Khaled Srour [3], Asif Mahmood [1], Nezam Altorok [1,4], Mohammad Taleb [5] and Ragheb Assaly [1,5]

1 Department of Internal Medicine, University of Toledo, Toledo, OH 43606, USA; nehayamunir@gmail.com (N.A.); omar.srour@utoledo.edu (O.S.); saif-eddin.malhas@utoledo.edu (S.-E.M.); waleed.khokher@utoledo.edu (W.K.); mohammed.mhanna@utoledo.edu (M.M.); hazem.ayesh@utoledo.edu (H.A.); ziad.abuhelw
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mohammad.taleb@utoledo.edu
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5. Conclusions

Our meta-analysis demonstrates that overall balanced crystalloids were associated with reduced mortality and acute kidney injury in patients with sepsis compared to normal saline. However, subgroup analysis of RCTs showed no significant differences in overall mortality and AKI between the groups. There was no significant difference in the need for renal replacement therapy and ICU length of stay between the groups. Pending further data, our meta-analysis support using balanced crystalloid over normal saline for fluid resuscitation in adults with sepsis. Future large-scale RCTs with better stratification for the source and severity of sepsis are necessary to validate our findings.

Fluid management

Sepsis in European intensive care units: Results of the SOAP study*

Jean-Louis Vincent, MD, PhD, FCCM; Yasser Sakr, MB, BCh, MSc; Charles L. Sprung, MD; V. Marco Ranieri, MD; Konrad Reinhart, MD, PhD; Herwig Gerlach, MD, PhD; Rui Moreno, MD, PhD; Jean Carlet, MD, PhD; Jean-Roger Le Gall, MD; Didier Payen, MD; on behalf of the Sepsis Occurrence in Acutely Ill Patients Investigators

Table 7. Multivariate, forward stepwise logistic regression analysis in sepsis patients (n = 1177), with intensive care unit mortality as the dependent factor

	OR (95% CI)	*p* Value
SAPS II score[a] (per point increase)	1.0 (1.0–1.1)	<.001
Cumulative fluid balance[b] (per liter increase)	1.1 (1.0–1.1)	.001
Age (per year increase)	1.0 (1.0–1.0)	.001
Initial SOFA score (per point increase)	1.1 (1.0–1.1)	.002
Blood stream infection	1.7 (1.2–2.4)	.004
Cirrhosis	2.4 (1.3–4.5)	.008
Pseudomonas infection	1.6 (1.1–2.4)	.017
Medical admission	1.4 (1.0–1.8)	.049
Female gender	1.4 (1.0–1.8)	.044

OR, odds ratio; CI, confidence interval; SAPA, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment.

[a]At admission; [b]within the first 72 hrs of onset of sepsis.

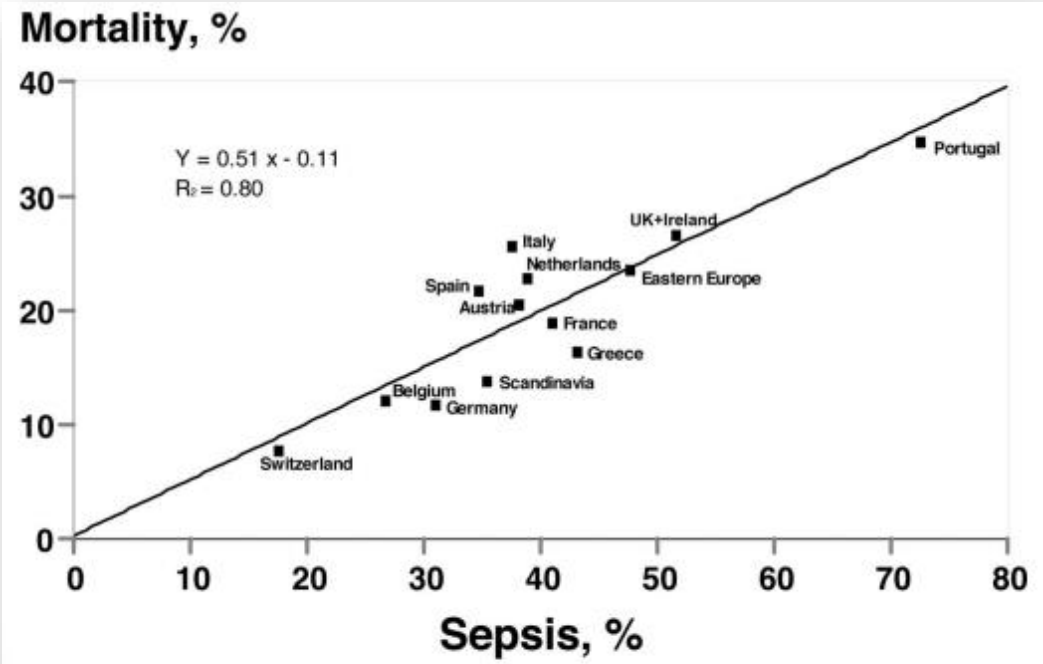


Figure 2. Relationship between intensive care unit mortality rates for all patients and frequency of sepsis in the various European countries.

Fluid management

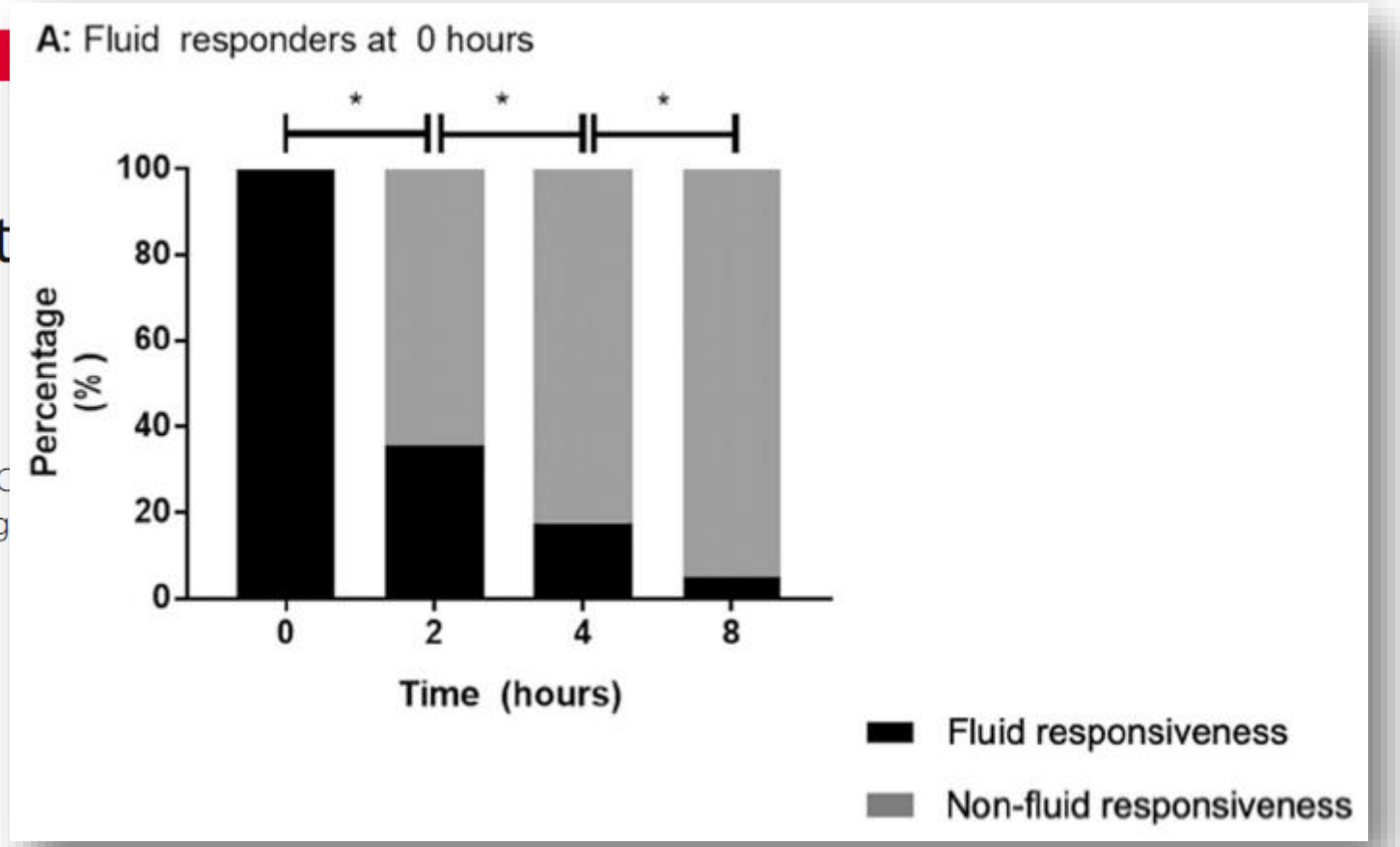
Kattan *et al. Critical Care* (2020) 24:23
https://doi.org/10.1186/s13054-020-2732-y

Critical Care

RESEARCH

Systematic assessment of fluid responsiveness during early sept resuscitation: secondary analysis ANDROMEDA-SHOCK trial

Eduardo Kattan[1], Gustavo A. Ospina-Tascón[2], Jean-Louis Teboul[3], Ricardo C
Jan Bakker[6,1,7,8], Glenn Hernández[1*] and The ANDROMEDA-SHOCK Investig



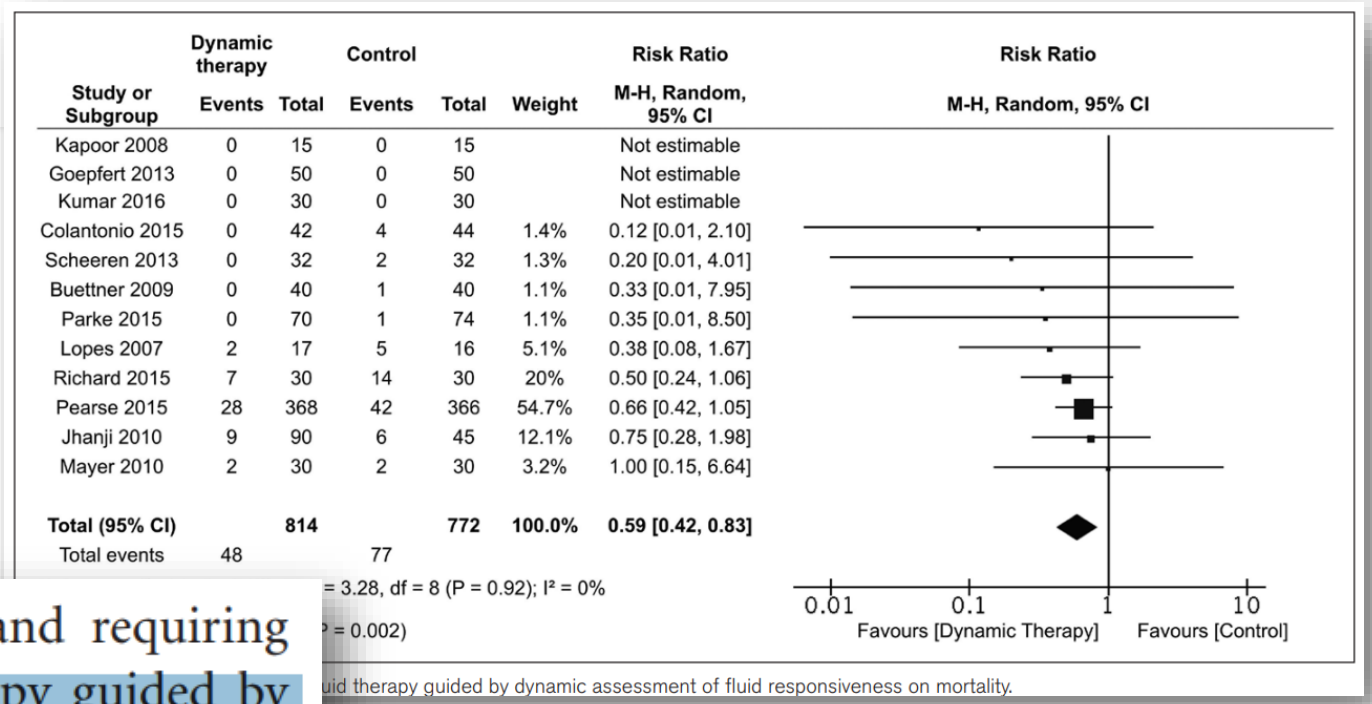
Fluid management

Review Article

OPEN

Incorporating Dynamic Assessment of Fluid Responsiveness Into Goal-Directed Therapy: A Systematic Review and Meta-Analysis

In adult patients admitted to intensive care and requiring acute volume resuscitation, goal-directed therapy guided by assessment of fluid responsiveness appears to be associated with reduced mortality, ICU length of stay, and duration of mechanical ventilation. High risk of bias due to lack of blinding limits the internal validity of published trials. High-quality clinical trials in both medical and surgical ICU populations are warranted to inform routine care.



Study or Subgroup	Dynamic therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Kapoor 2008	0	15	0	15		Not estimable
Goepfert 2013	0	50	0	50		Not estimable
Kumar 2016	0	30	0	30		Not estimable
Colantonio 2015	0	42	4	44	1.4%	0.12 [0.01, 2.10]
Scheeren 2013	0	32	2	32	1.3%	0.20 [0.01, 4.01]
Buettner 2009	0	40	1	40	1.1%	0.33 [0.01, 7.95]
Parke 2015	0	70	1	74	1.1%	0.35 [0.01, 8.50]
Lopes 2007	2	17	5	16	5.1%	0.38 [0.08, 1.67]
Richard 2015	7	30	14	30	20%	0.50 [0.24, 1.06]
Pearse 2015	28	368	42	366	54.7%	0.66 [0.42, 1.05]
Jhanji 2010	9	90	6	45	12.1%	0.75 [0.28, 1.98]
Mayer 2010	2	30	2	30	3.2%	1.00 [0.15, 6.64]
Total (95% CI)		**814**		**772**	**100.0%**	**0.59 [0.42, 0.83]**
Total events	48		77			

= 3.28, df = 8 (P = 0.92); I² = 0%

= 0.002)

Risk Ratio M-H, Random, 95% CI

0.01 0.1 1 10

Favours [Dynamic Therapy] Favours [Control]

uid therapy guided by dynamic assessment of fluid responsiveness on mortality.

Fluid management

De Backer *et al. Criti*
https://doi.org/10.1

REVIEW

A plea
of the
shock

Daniel De Back
Gustavo A. Osp

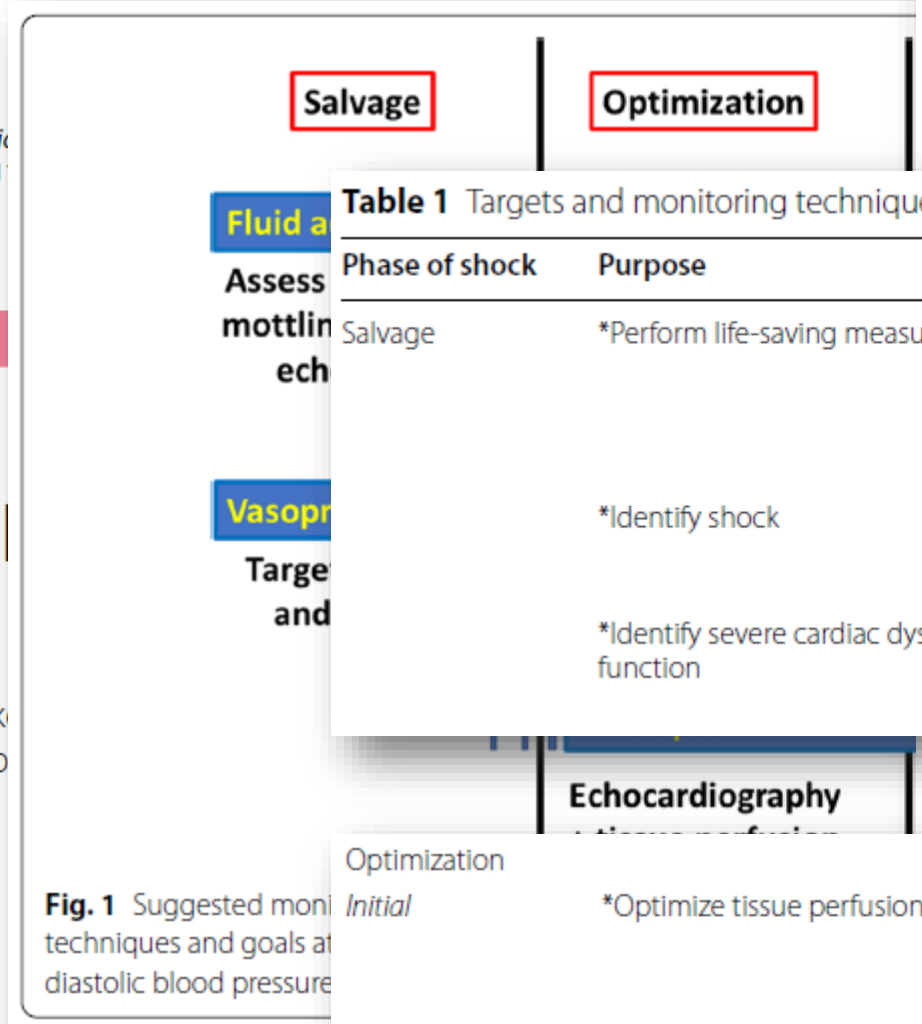


Fig. 1 Suggested moni
techniques and goals at
diastolic blood pressure

Table 1 Targets and monitoring techniques at the different phases of shock

Phase of shock	Purpose	Targets	Interventions	Monitoring tools
Salvage	*Perform life-saving measures	*Maintain minimal MAP and CO	*Fluids *Vasopressors according to MAP and DAP	*Arterial pressure (often non-invasive, turn to invasive if not responding) *CRT *Lactate
	*Identify shock			*Clinical examination *Arterial pressure *Lactate
	*Identify severe cardiac dys-function			*Echocardiography *CRT *Jugular vein distension
Optimization				
Initial	*Optimize tissue perfusion	*Normalize indices of tissue perfusion *Optimize MAP *Optimize CO	*Fluids according to fluid responsiveness and tolerance *Vasopressors *Inotropes according to CO and echocardiography	*CRT *Lactate *CVP – ScvO2-PvaCO2 *Urine output *Minimally invasive CO *Echocardiography if not yet performed *Evaluation of fluid responsiveness

Cas Clinique, 60 mn plutard, Toujours pas de lit de en réanimation

- Saline: 1500 ml
- Norepi: 0.2 µg/Kg/mn
- FC, 102b/mn
- PA, 83/50/59 mmHg

- Urée, 17 mmol/L
- Creat, 150 µmol/L
- Bili, 65 µmol/L
- Lactates, 2.7 mmol/L

- A ce stade quell est votre avis?

- PA est largement suffisante pour apprécier Qc
- Mesurer le Qc permet un meilleur monitorage
- Ce monitorage n'est pas nécessaire

Intensive Care Med (2012) 38:422–428
DOI 10.1007/s00134-011-2457-0

ORIGINAL

PA = VES x RVS

Charalampos Pierrakos
Dimitrios Velissaris
Sabino Scolletta
Sarah H
Daniel I
Jean-Lo

Can changes in arterial pressure be used to detect changes in cardiac index during fluid

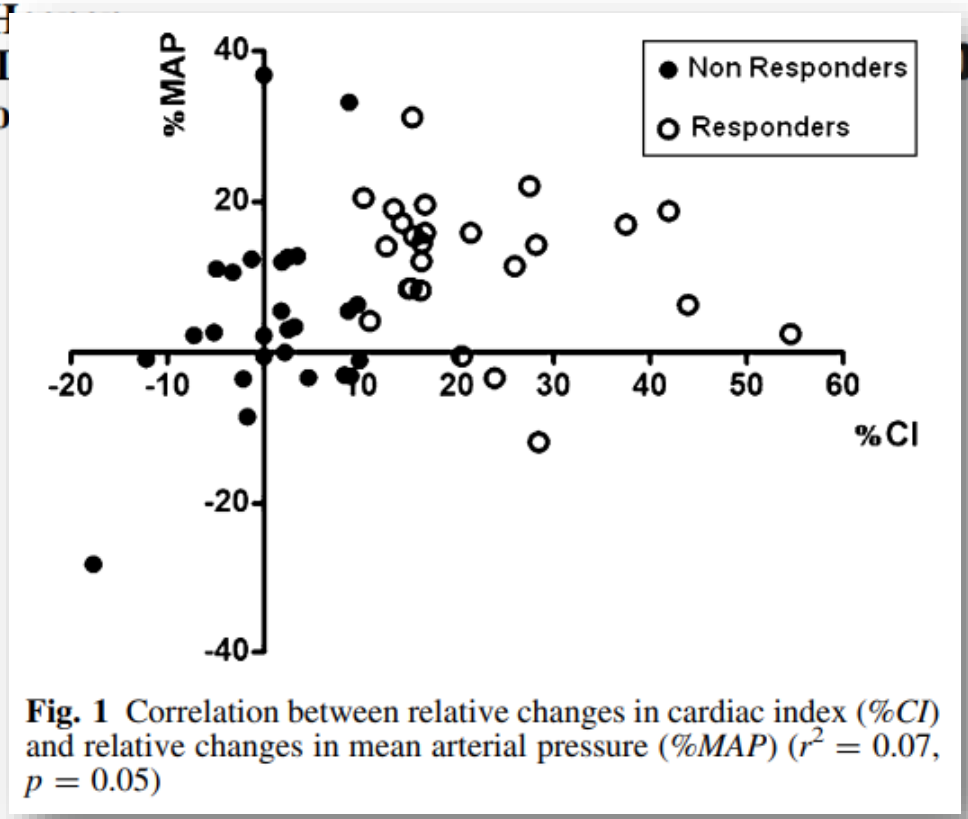


Fig. 1 Correlation between relative changes in cardiac index (*%CI*) and relative changes in mean arterial pressure (*%MAP*) ($r^2 = 0.07$, $p = 0.05$)

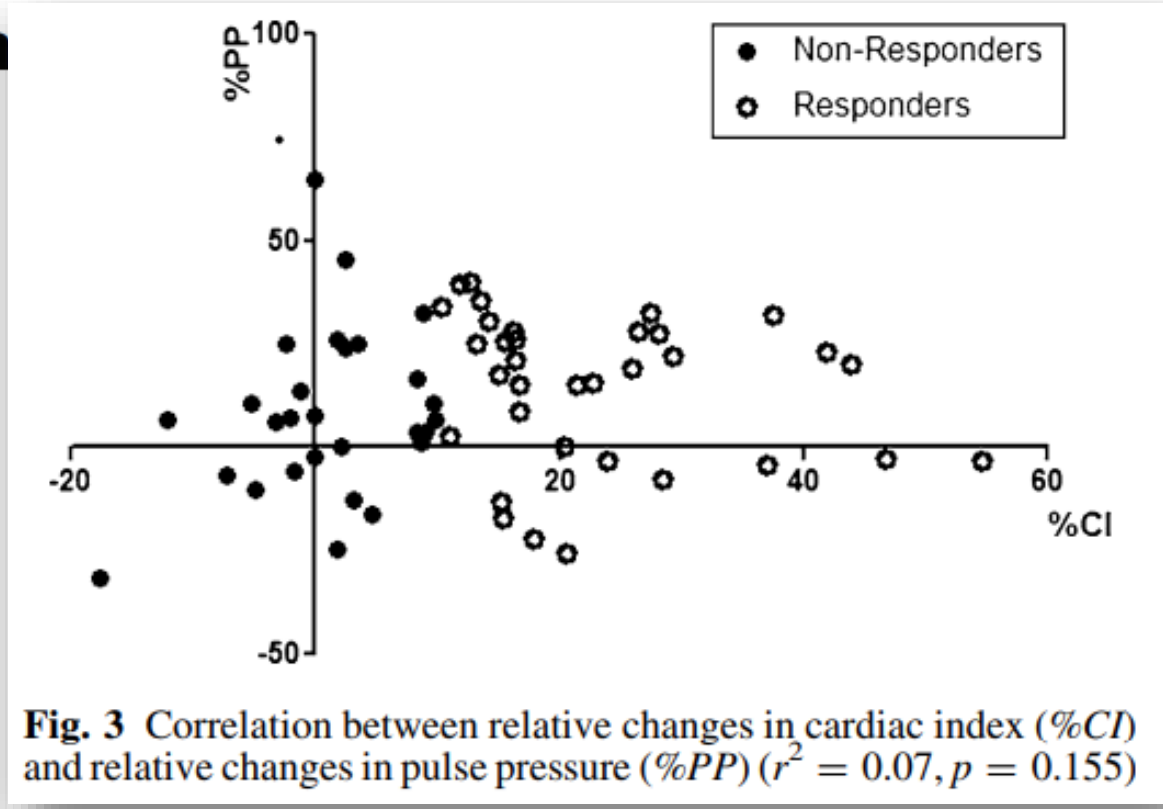


Fig. 3 Correlation between relative changes in cardiac index (*%CI*) and relative changes in pulse pressure (*%PP*) ($r^2 = 0.07, p = 0.155$)

Intensive Care Med (2014) 40:1795–1815
DOI 10.1007/s00134-014-3525-z

Maurizio Cecconi
Daniel De Backer
Massimo Antonelli
Richard Beale
Jan Bakker
Christoph Hofer
Roman Jaeschke
Alexandre Mebazaa
Michael R. Pinsky
Jean Louis Teboul
Jean Louis Vincent
Andrew Rhodes

Consensus on circulatory shock and hemodynamic monitoring. Task force

Table 6 Summary of the consensus statements—part 4

No.	Statement/recommendation	GRADE level of recommendation; quality of evidence	Type of statement
37.	We do not recommend routine measurement of cardiac output for patients with shock responding to the initial therapy	Level 1; QoE low (C)	Recommendation
38.	We recommend measurements of cardiac output and stroke volume to evaluate the response to fluids or inotropes in patients that are not responding to initial therapy	Level 1; QoE low (C)	Recommendation
	and right ventricular dysfunction		
43.	We suggest the use of transpulmonary thermodilution or pulmonary artery catheterization in patients with severe shock especially in the case of associated acute respiratory distress syndrome	Level 2; QoE low (C)	Recommendation
44.	We recommend that less invasive devices are used, instead of more invasive devices, only when they have been validated in the context of patients with shock	Ungraded	Best practice

Statements in this table are related to cardiac function and cardiac output assessment and monitoring. These are also presented in the main text together with the rationale. The order of presentation in the table has been changed from that in the main text to allow for better reading in the table

We recommend measurements of cardiac output and stroke volume to evaluate the response to fluids or inotropes in patients that are not responding to initial therapy. Level 1; QoE low (C)

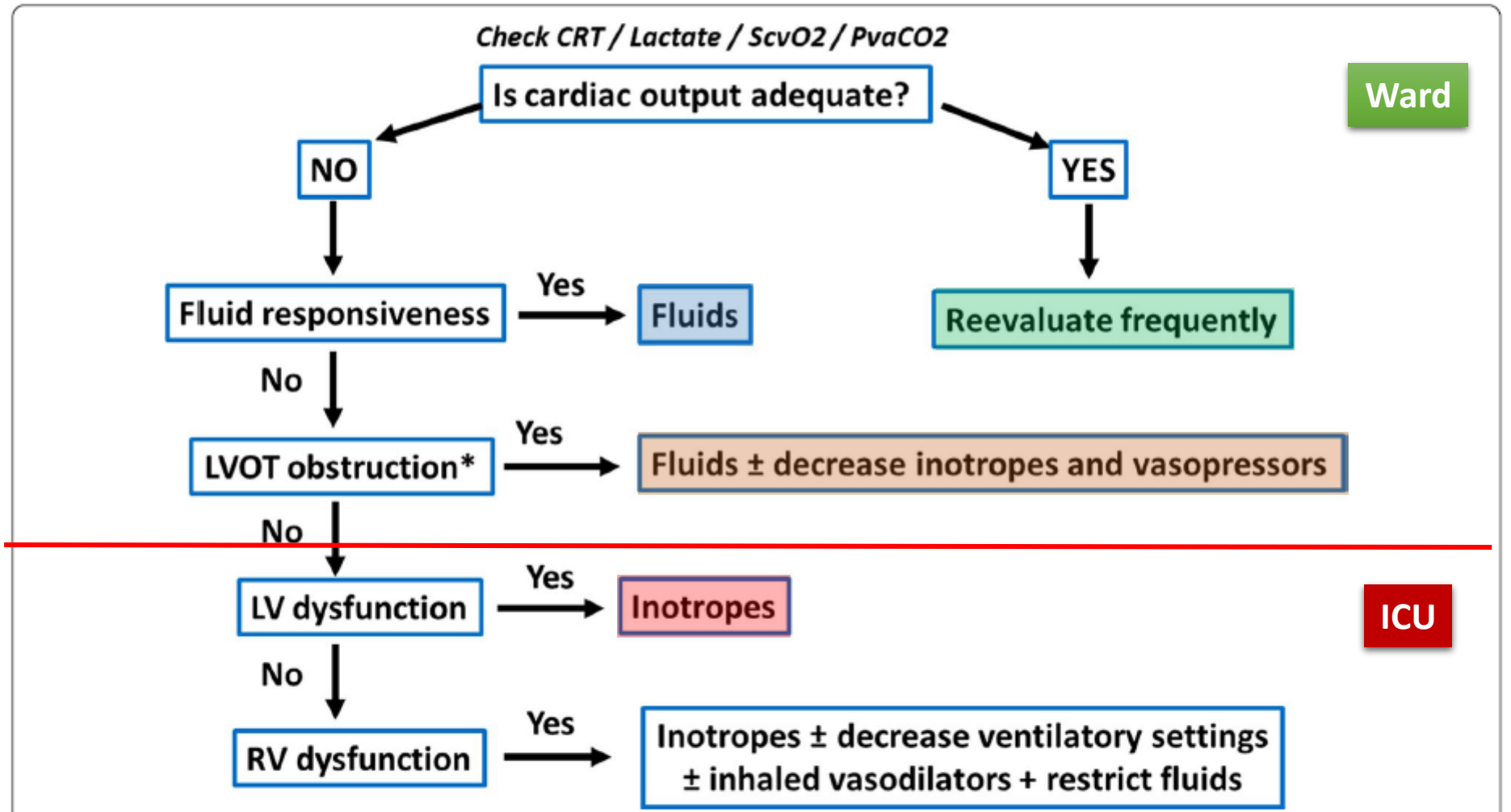


Fig. 2 Therapeutic approach based on assessment of cardiovascular function. LVOT left ventricular outflow tract, LV left ventricle, RV right ventricle, NO nitric oxide. LVOT obstruction can only be observed with echocardiography. The other measurements can be obtained by echocardiography as well as other monitoring techniques

Cas Clinique, 60 mn plutard, Toujours pas de lit de en réanimation

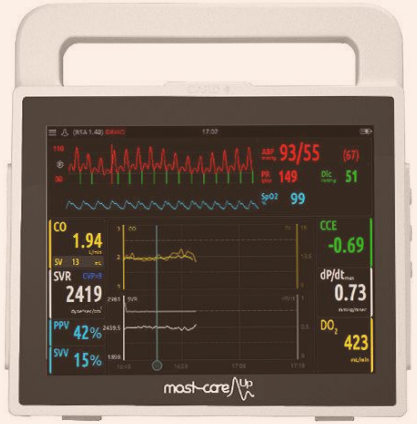
- Saline: 1500 ml
- Norepi: 0.2 µg/Kg/mn
- FC, 102b/mn
- PA, 83/50/59 mmHg

- Urée, 17 mmol/L
- Creat, 150 µmol/L
- Bili, 65 µmol/L
- Lactates, 2.7 mmol/L

- Quel outil de monitorage?

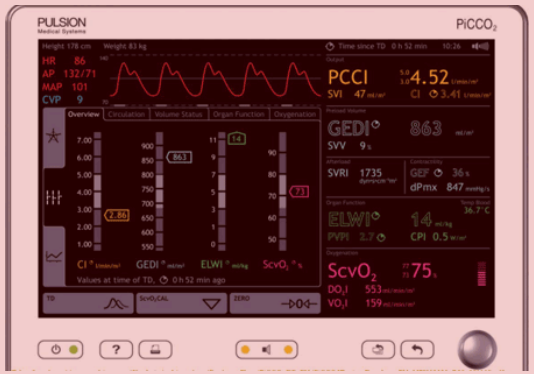
- Uncalibrated PCA
- Bioreactance
- Pulmonary artery catheter
- Transpulmonary thermodilution

PA invasive

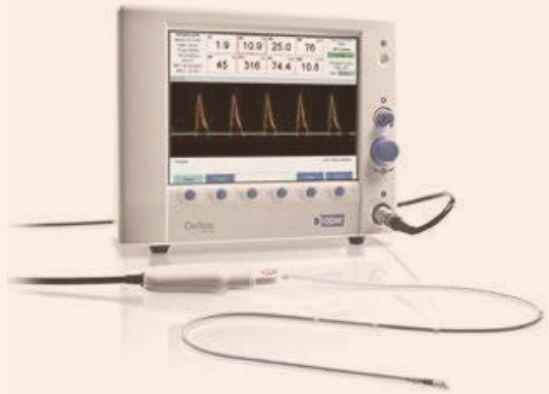


UC Pulse Contour Analysis

Volume Clamp Devices



Thermodilution TP



Oesophageal Doppler

Bioreactance

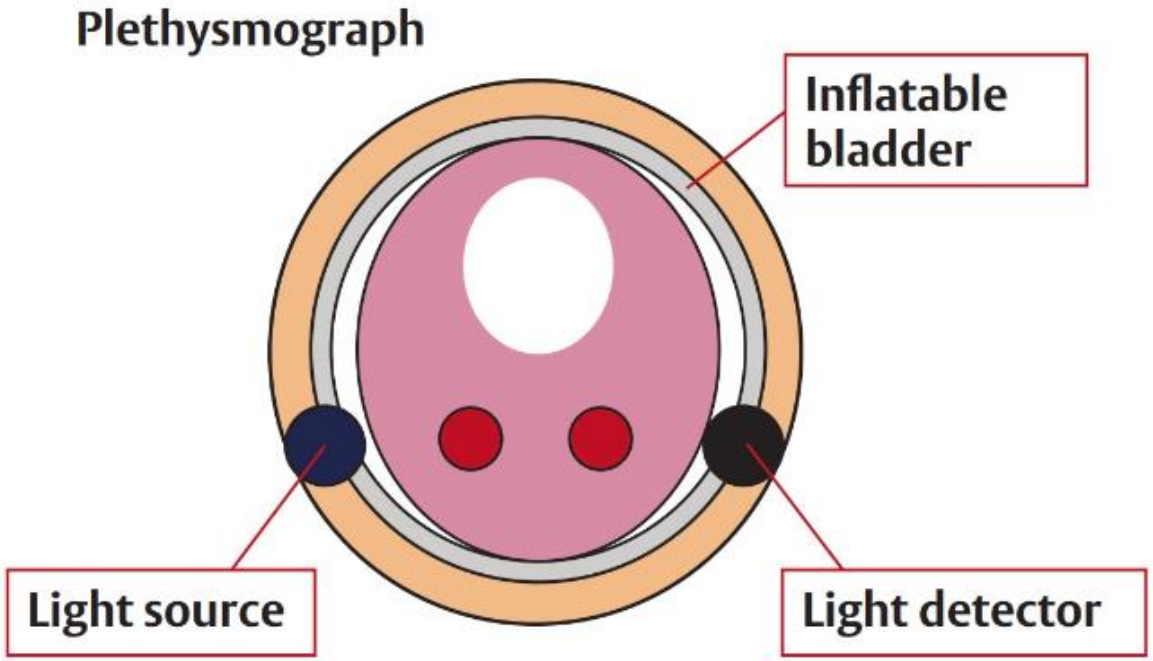
Invasive Devices

Minimally-Invasive Devices

Non-Invasive devices

Volume Clamp Devices

Photo-Plethysmography measures the diameter of the finger arteries



Volume Clamp Devices

The cuff inflates/relaxes to keep the diameter constant

Non-Invasive devices

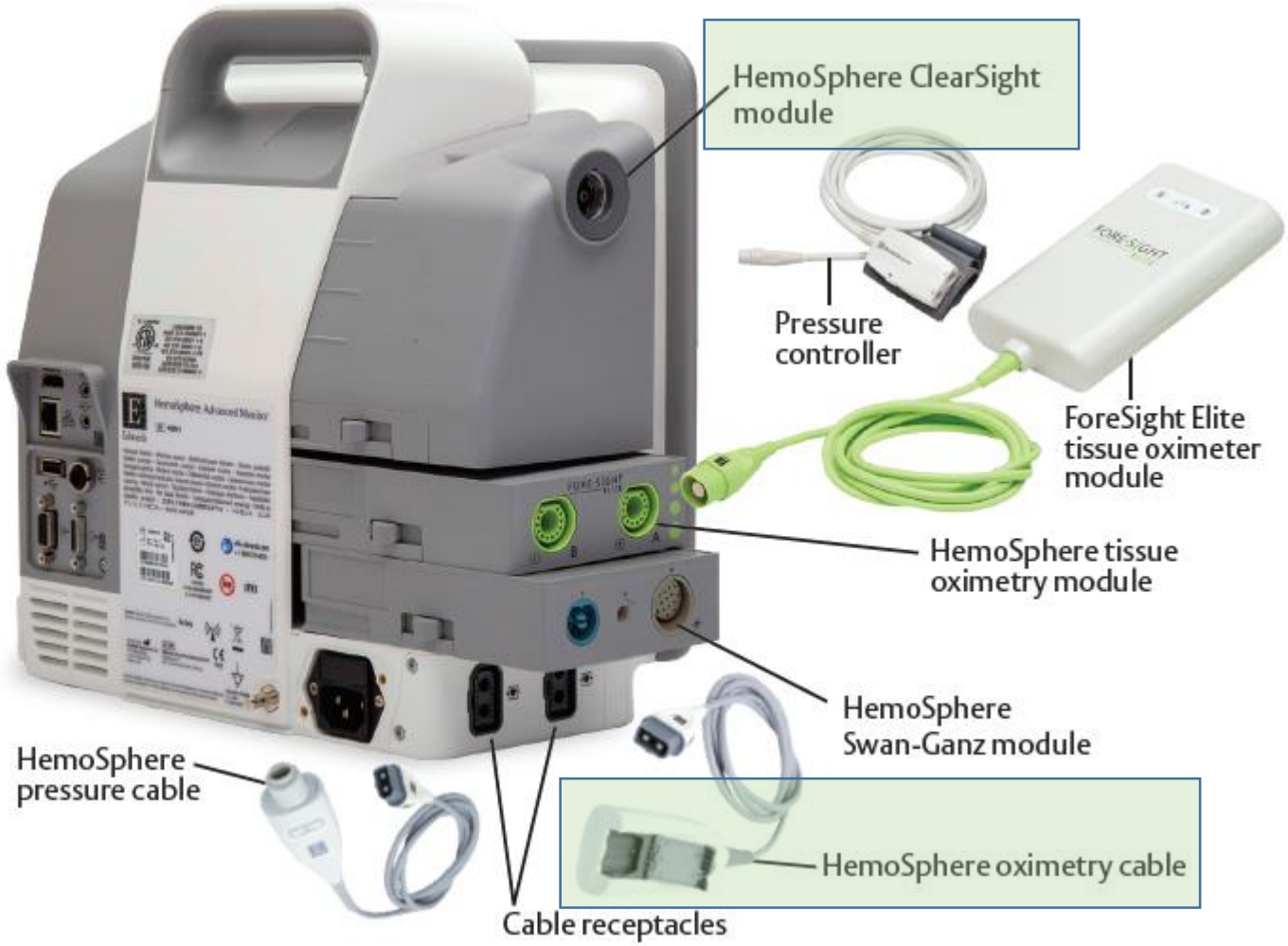
Volume Clamp Devices

	Noninvasive		Minimally-invasive		Invasive	
	ClearSight finger cuff	ForeSight Elite sensor	Acumen IQ sensor	FloTrac sensor	Swan-Ganz catheter	PediaSat oximetry catheter
StO_2		●				
HPI			●			
Ea_{dyn}			●			
dP/dt			●			
CO/CI	●		●			
SV/SVI	●		●			
SVV/PPV	●		●			
SVR/SVRI	●		●			
PVR/PVRI						
SvO_2						
$ScvO_2$						
RVEF/EDV						
MAP	●		●			
PAP						
CVP						

HPI secondary screen*

Physiology screen

Fluid responsiveness result screen



PE ward patients, 15-40%
PE ICU patients, 44-57%

Bioreactance

[Critical Care Original Research] CHEST

Fluid Response Evaluation in Sepsis Hypotension and Shock

A Randomized Clinical Trial

Ivor S. Douglas, MD; Philip M. Alapat, MD; Keith A. Corl, MD; Matthew C. Exline, MD, MPH; Lui G. Forni, PhD; Andre L. Holder, MD; David A. Kaufman, MD; Akram Khan, MD; Mitchell M. Levy, MD; Gregory S. Martin, MD; Jennifer A. Sahatjian, PsyD; Eric Seeley, MD; Wesley H. Self, MD; Jeremy A. Weingarten, MD; Mark Williams, MD; and Douglas M. Hansell, MD

Bioreactance

Non-Invasive devices

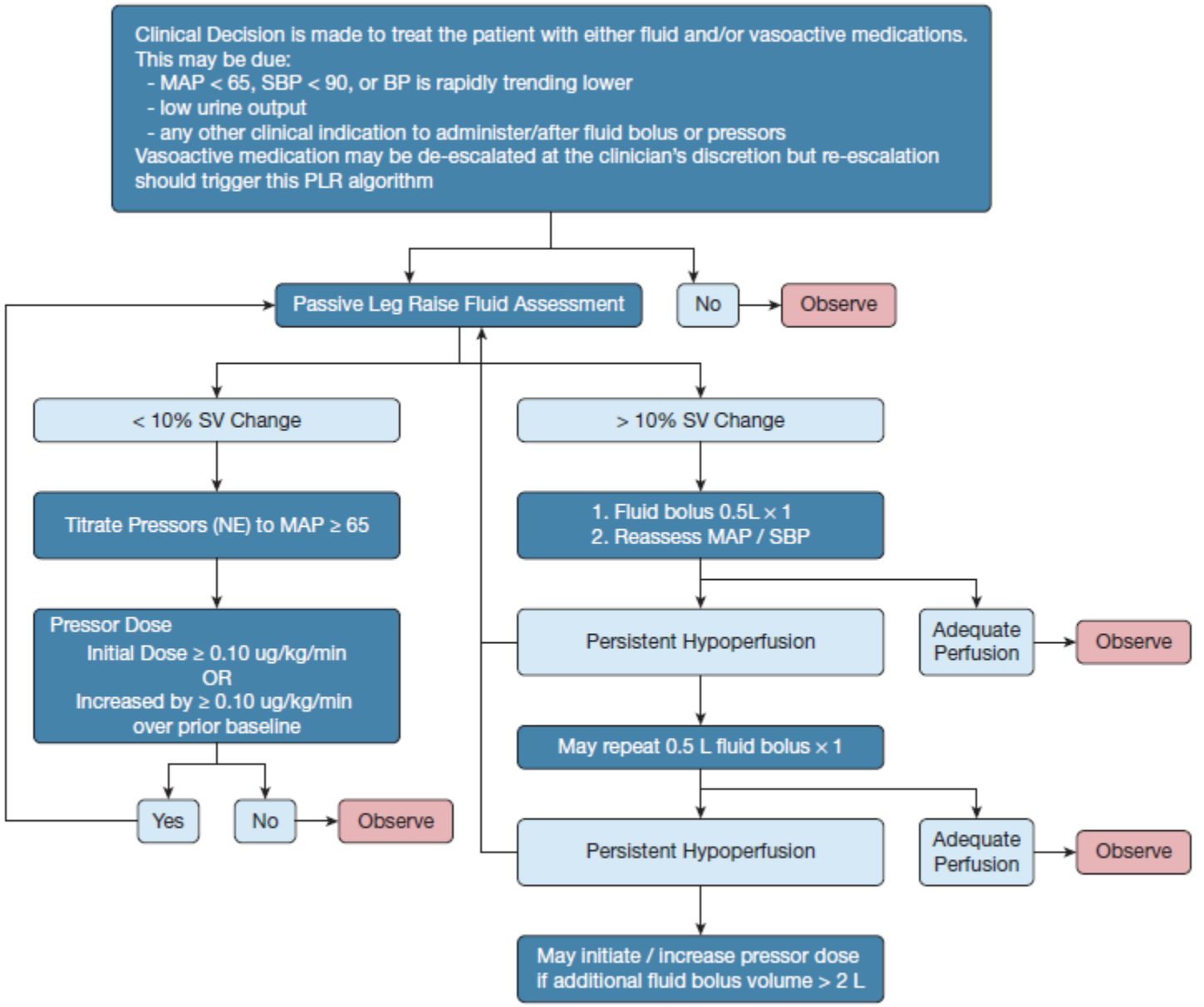


Figure 1 – *Flow chart model of the algorithm used to guide treatment in the Fluid Responsiveness Evaluation in Sepsis-associated Hypotension study. MAP = mean arterial pressure; NE = norepinephrine; PLR = passive leg raise; SBP = systolic BP; SV = stroke volume.*

Sepsis / Septic shock, frugal management, Mottling

Trans R Soc Trop Med Hyg 2017; **111**: 483–489
doi:10.1093/trstmh/try007 Advance Access publication 9 February 2018

REVIEW

Haemodynamic assessment and support in sepsis and septic shock in resource-limited settings

David Misango[a], Rajyabardhan Pattnaik[b], Tim Baker[c,d], Martin W. Dünser[e], Arjen M. Dondorp[f,g,h] and Marcus J. Schultz[f,h,*], for the Global Intensive Care Working Group[†], of the European Society of Intensive Care Medicine (ES[illegible]) and the Mahidol Oxford Tropical Medicine Research Unit (MORU) in Bangkok, Thailand

[a]*Department of Anc… Medicine, Ispat Gen… Karolinska Universit… Care, University Co… Medicine, Mahidol… Nuffield Departme…* … *Department of Intensive Care …e Care and Surgical Services, …utet; [e]Department of Critical …(MORU), Faculty of Tropical …edicine and Global Health, …Academic Medical Center,*

[†]Task… …e supplement

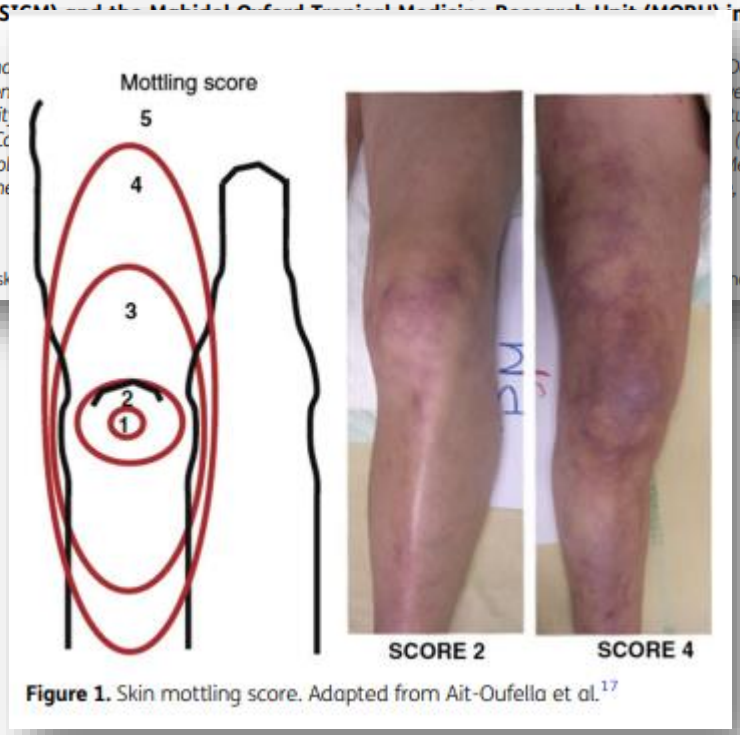


Figure 1. Skin mottling score. Adapted from Ait-Oufella et al.[17]

Recommendations for simple bedside tools

(1) Which simple bedside tools for assessing tissue perfusion could be useful in sepsis and septic shock in resource-limited settings?

Recommendation: We suggest using capillary refill time, skin mottling scores and, if affordable, skin temperature gradients to assess the adequacy of tissue perfusion in paediatric and adult sepsis and septic shock, either alone or in combination (UG). It remains uncertain whether these tools are effective in malaria.

Sepsis / Septic shock, frugal management, CRT

Dumas *et al. Critical Care* (2019) 23:211
https://doi.org/10.1186/s13054-019-2496-4

Critical Care

RESEARCH

Mottling score is a strong predicto day mortality in septic patients wh vasopressor doses and other tissue perfusion parameters

Guillaume Dumas[1,2,3*], Jean-Rémi Lavillegrand[1,2], Jérémie Joffre[1], Naïke Bigé[1], Ec
Jean-Luc Baudel[1], Sylvie Chevret[3], Bertrand Guidet[1,2,5], Eric Maury[1,2,5], Fabio Am

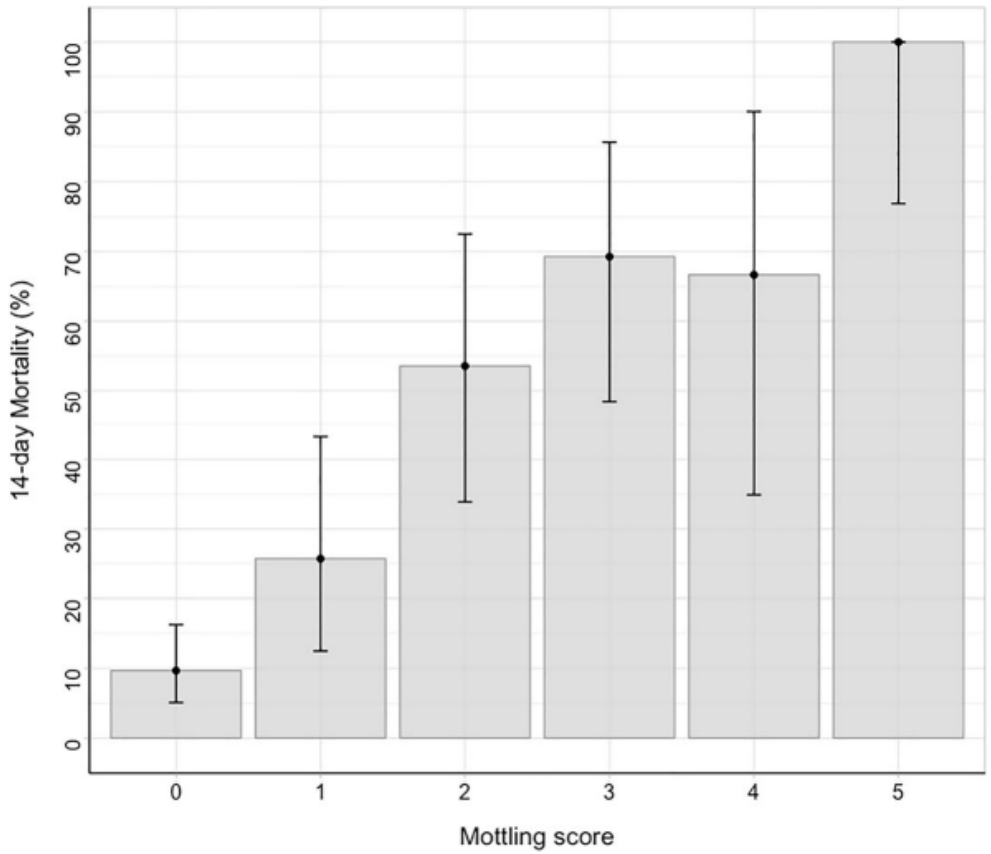


Fig. 1 14-day mortality according to mottling score value at H-6. Error-bars represent 95% confidence interval

Sepsis / Septic shock, frugal management, CRT

Research

JAMA | Original Investigation | CARING

Effect of a Resuscitat
Perfusion Status vs S
Among Patients With
The ANDROMEDA-SH

Glenn Hernández, MD, PhD; Gustavo A. Ospina-Tasc
Arnaldo Dubin, MD, PhD; Javier Hurtado, MD; Gilbe
Leyla Alegría, RN, MSc; Jean-Louis Teboul, MD, PhD
Manuel Jibaja, MD; Ronald Pairumani, MD; Paula Fe
Vladimir Granda-Luna, MD, PhD; Alexandre Biasi Ca
ANDROMEDA-SHOCK Investigators and the Latin A

JAMA Network™

QUESTION Does a resuscitation strategy targeting normalization of capillary refill time, compared with targeting serum lactate levels, reduce mortality in patients with septic shock?

CONCLUSION This randomized clinical trial of adults with septic shock found that use of a peripheral perfusion–targeted resuscitation strategy, compared with targeting serum lactate, did not significantly reduce mortality.

POPULATION

198 Men 226 Women

Adults in the ICU with septic shock

Mean age: 63 years

LOCATIONS

28 ICUs in 5 countries in South America

INTERVENTION

424 Patients randomized

212

Peripheral perfusion group

Resuscitation protocol of normalizing capillary refill time (measured in seconds)

212

Lactate group

Resuscitation protocol of normalizing or decreasing lactate levels (>20% per 2 hours)

PRIMARY OUTCOME

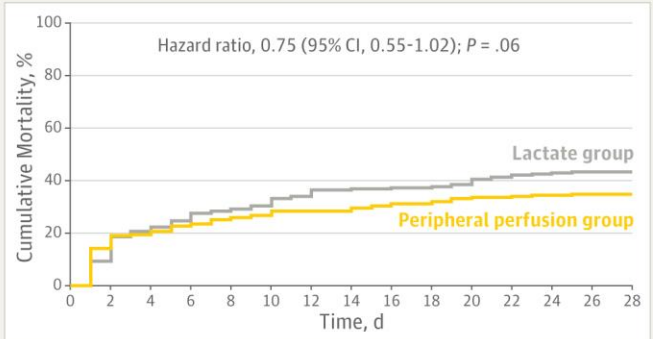
All-cause mortality at 28 days

FINDINGS

All-cause mortality at 28 days

Peripheral perfusion group 34.9% (74 patients died)

Lactate group 43.4% (92 patients died)



No significant risk difference between groups:
-8.5% (95% CI, -18.2% to 1.2%),

Hernández G, Ospina-Tascón GA, Petri Damiani L, et al. Effect of a resuscitation strategy targeting peripheral perfusion status vs serum lactate levels on 28-day mortality among patients with septic shock: the ANDROMEDA-SHOCK randomized clinical trial [published February 17, 2019]. *JAMA*. doi:10.1001/jama.2019.0071

Sepsis / Septic shock, frugal management, CRT re-analysis

ORIGINAL ARTICLE

Effects of a Resuscitation Strategy Targeting Peripheral Perfusion Status versus Serum Lactate Levels among Patients with Septic Shock

A Bayesian Reanalysis of the ANDROMEDA-SHOCK Trial

Fernando G. Zampieri[1,2], Lucas P. Damiani[1], Jan Bakker[3,4,5,6], Gustavo A. Ospina-Tascón[7], Ricardo Castro[3], Alexandre B. Cavalcanti[1], and Glenn Hernandez[3]; for the ANDROMEDA-SHOCK Investigators and the Latin America Intensive Care Network (LIVEN)

Conclusions: Peripheral perfusion–targeted resuscitation may result in lower mortality and faster resolution of organ dysfunction when compared with a lactate-targeted resuscitation strategy.

Sepsis / Septic shock, frugal management, CRT / PLR

Jacquet-Lagrèze *et al. Critical Care* (2019) 23:281
https://doi.org/10.1186/s13054-019-2560-0

RESEARCH

Capillary refill time varia passive leg raising pred time response to volum

Matthias Jacquet-Lagrèze[1,2*], Nourredine Bouhamri[1], Marc Lilot[4,5,6,7], William Fornier[1,2] and Jean-Luc Fellahi

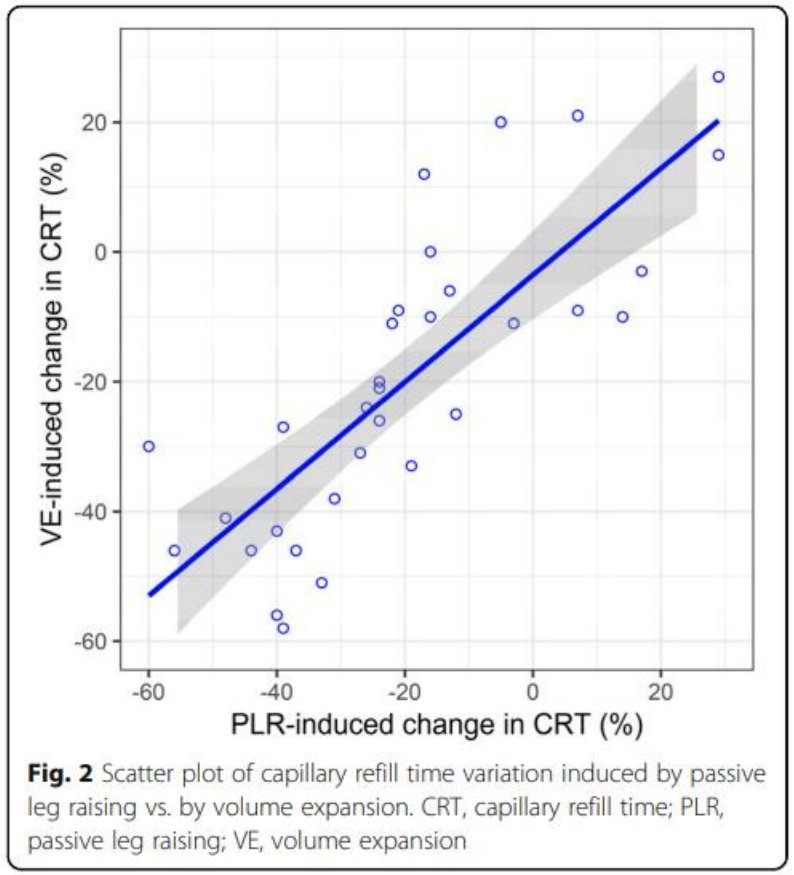


Fig. 2 Scatter plot of capillary refill time variation induced by passive leg raising vs. by volume expansion. CRT, capillary refill time; PLR, passive leg raising; VE, volume expansion

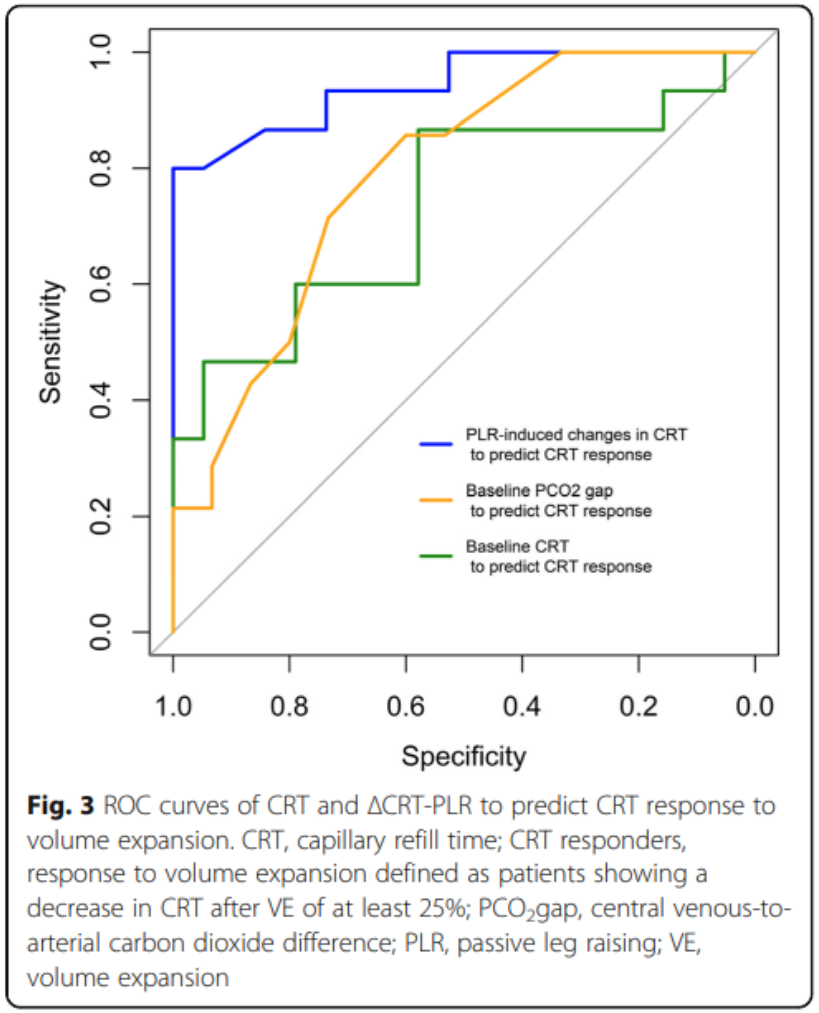


Fig. 3 ROC curves of CRT and ΔCRT-PLR to predict CRT response to volume expansion. CRT, capillary refill time; CRT responders, response to volume expansion defined as patients showing a decrease in CRT after VE of at least 25%; PCO_2gap, central venous-to-arterial carbon dioxide difference; PLR, passive leg raising; VE, volume expansion

Delayed presentation of septic shock!

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CLINICAL SCIENCE ASPECTS

TIME FROM HOSPITAL ADMISSION TO ONSET OF SEPTIC SHOCK IS ASSOCIATED WITH HIGHER IN-HOSPITAL MORTALITY

Sato, Ryota[*]; Dugar, Siddharth[*,†]; Han, Xiaozhen[‡]; Siuba, Matthew T.[*,†]; Mucha, Simon[*,†]; Dettmer, Matthew[*,†,§]; Wang, Xiaofeng[‡]; Yataco, Angel Coz[*,†]; Choudhary, Chirag[*,†]; Khanna, Ashish K.[‖,¶]; Duggal, Abhijit[*,†]

between 54.6 and 148.4 h of the time from the hospital admission to shock onset. **Conclusion:** In-hospital mortality continued to rise as admission-shock-onset-time increased in patients with septic shock. No clear dichotomization between early and late septic shock could be ascertained, and this categorization may limit our understanding of the temporal relationship of shock onset to mortality.

Predicting progression to septic shock

INFECTIOUS DISEASE/ORIGINAL RESEARCH

Predicting Progression to Septic Shock in the Emergency Department Using an Externally Generalizable Machine-Learning Algorithm

Gabriel Wardi, MD, MPH*; Morgan Carlile, MD; Andre Holder, MD, MSc; Supreeth Shashikumar, PhD; Stephen R. Hayden, MD; Shamim Nemati, PhD

*Corresponding Author. E-mail: gwardi@health.ucsd.edu, Twitter: @WardiGabriel.

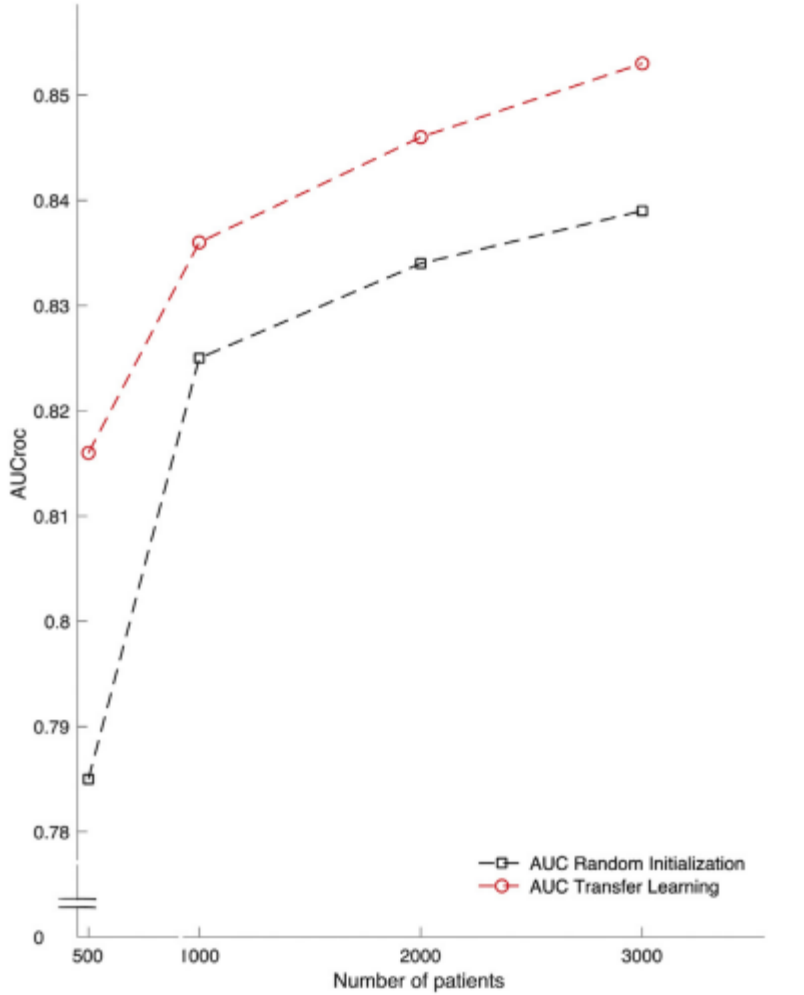
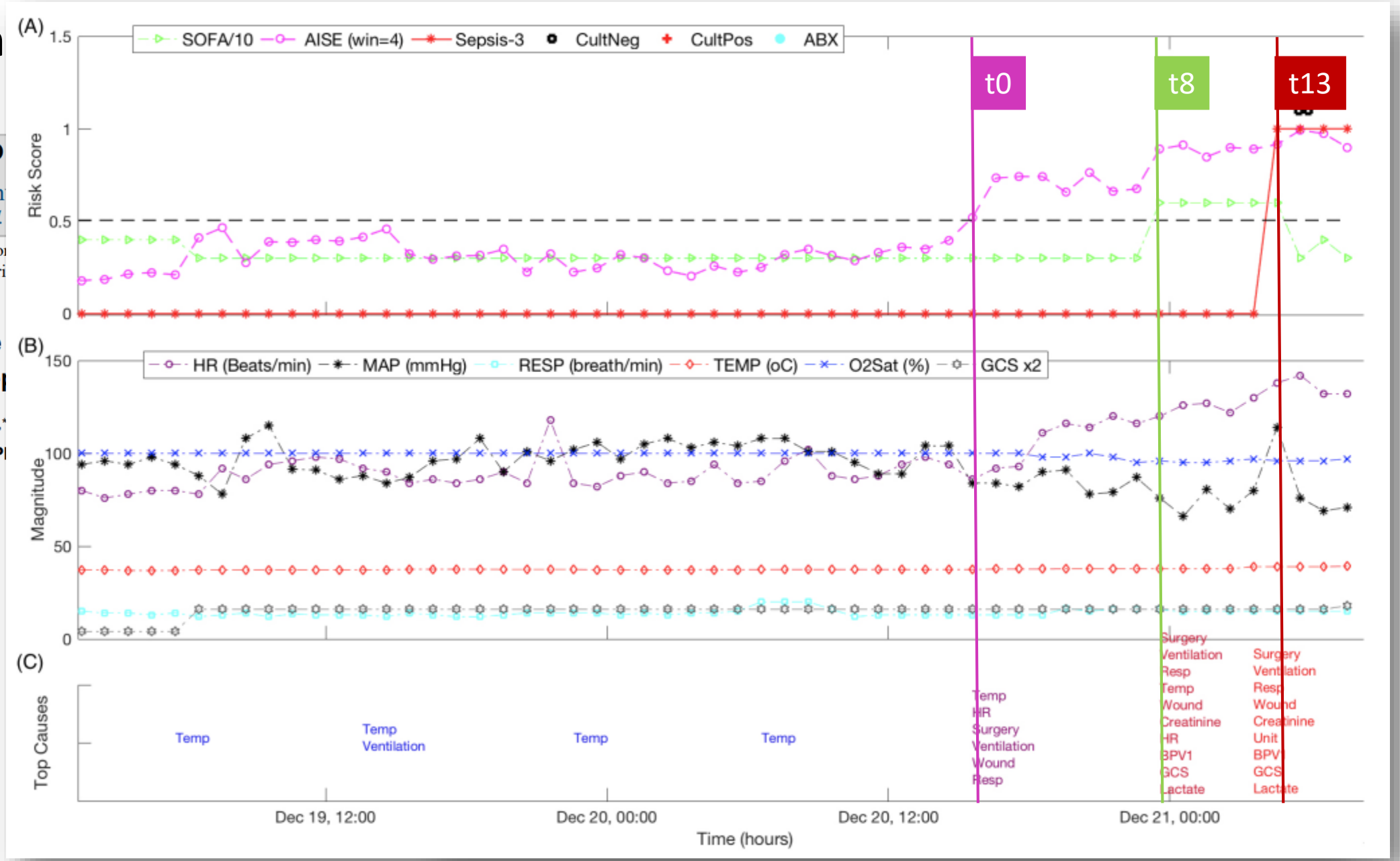


Figure 5. AUC ROC of the ability of the Artificial Intelligence Sepsis Expert algorithm to detect septic shock 12 hours ahead of time in the validation cohort with and without transfer learning (red and black dashed lines, respectively) based on increasing amounts of patient encounters in model development.

All septic sh

An Interpretable
Prediction of Sep

Shamim Nemati, PhD[1,]
MD[3], Gari D. Clifford, Pl



How about the “pre-shock” state?

SCIENTI

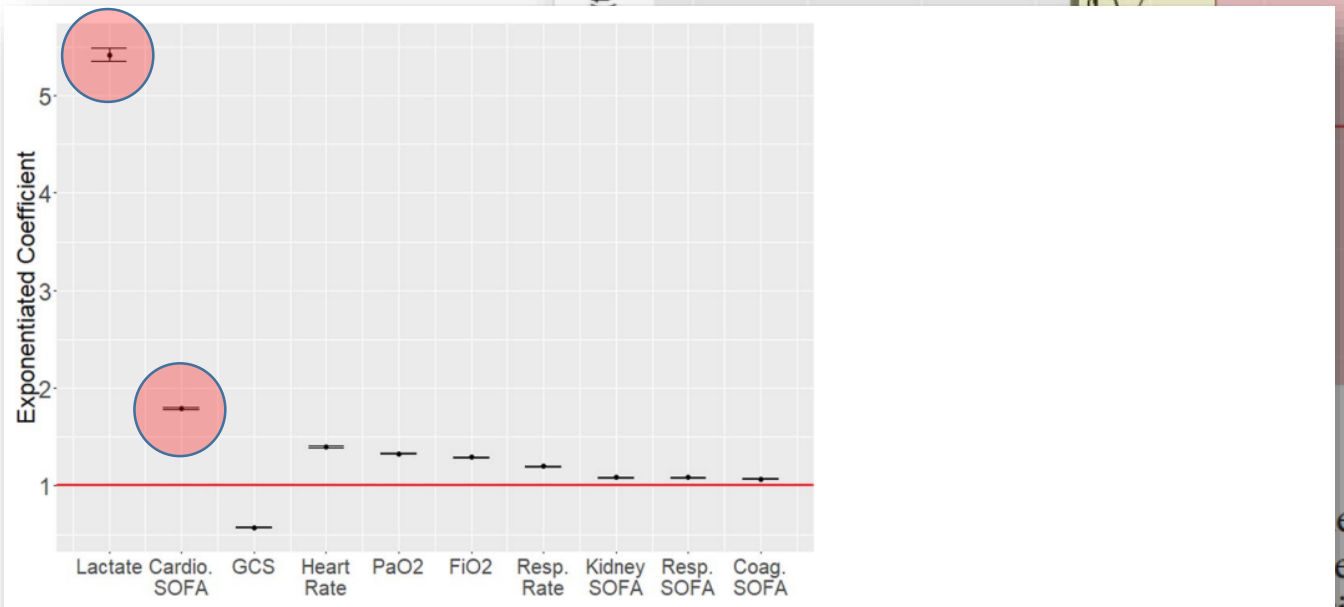
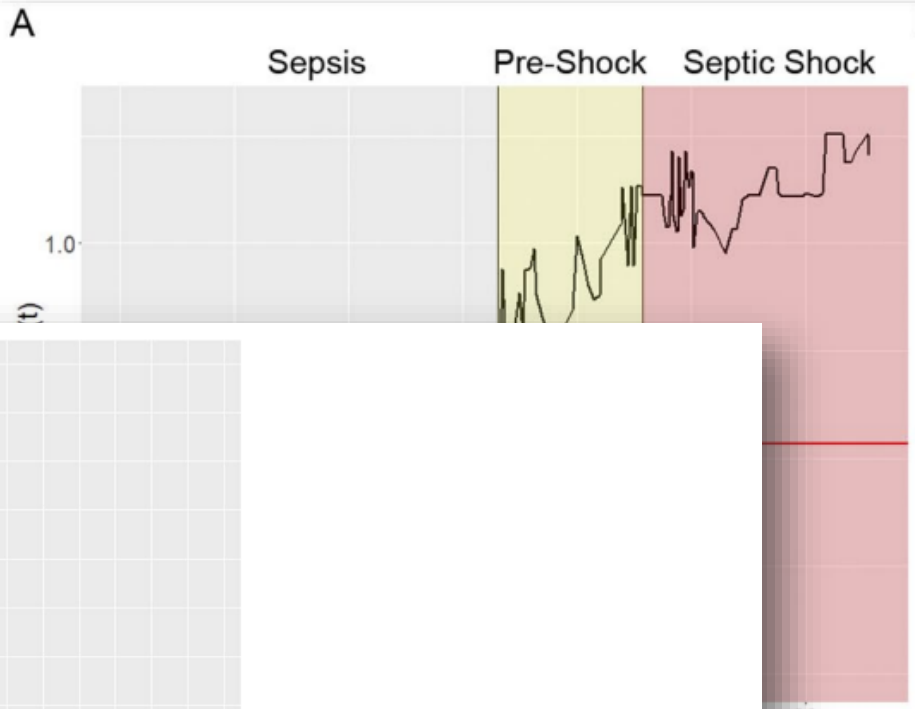
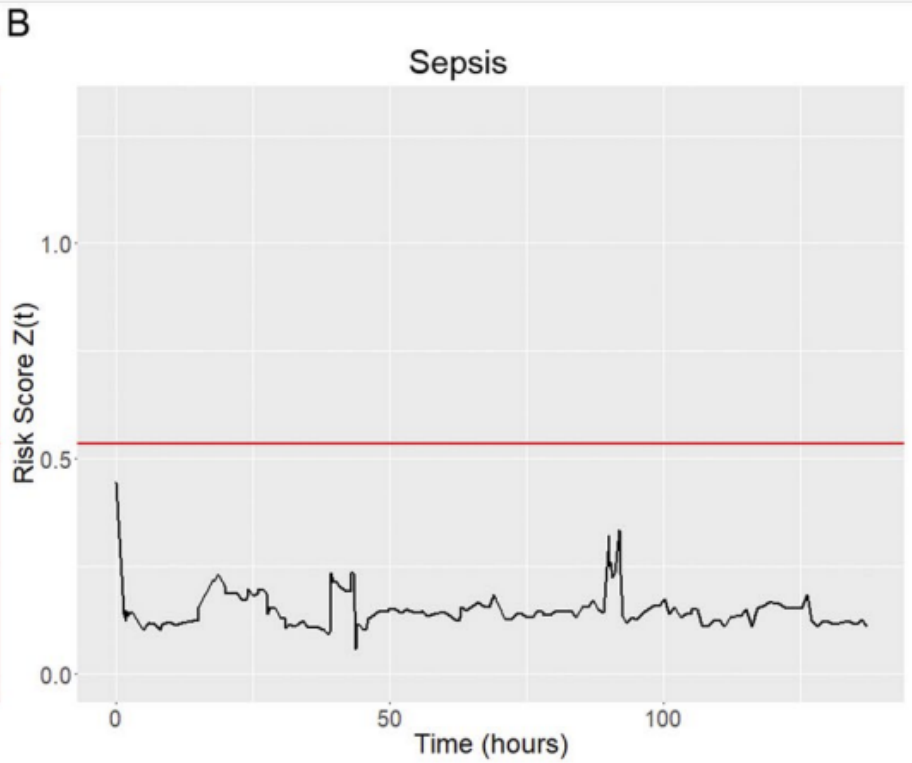


Figure 3. Exponentiated model coefficients and 95% confidence bounds for the ten selected features from one sample train/test iteration. These coefficients were learned using features normalized to a mean of 0 and unit standard deviation. Abbreviations: Cardio SOFA – Cardiovascular SOFA score; PaO2 – Partial pressure of oxygen; FiO2 – Fraction of inspired oxygen; Resp. Rate – Respiratory Rate; Resp. SOFA – Respiratory SOFA score; Coag. SOFA – Coagulatory SOFA score.





es for a septic shock patient ((**A**) MIMIC-III subject 250) and
e detection threshold θ applied to $z(t)$ is indicated by the red
ions into the pre-shock state when the risk exceeds the threshold
diagnosed at onset time t_o. Time is given in hours relative to the
is ~6 hours.

The future? Predicting instability (hypotension) in sepsis?

Machine-learning Algorithm to Pre
Hypotension Based on High-fidelity
Pressure Waveform Analysis

Feras Hatib,
Karen Sibert,

Conclusions: The results demonstrate that a mac
arterial waveforms, to predict hypotension in surg

Journal of Clinical Monitoring and Computing (2020) 34:1135–1138
https://doi.org/10.1007/s10877-020-00465-3

EDITORIAL

Hypotension Prediction Index: from proof-of-concept to proof-of-feasibility

Ilonka N. de Keijzer[1] · Jaap Jan Vos[1] · Thomas W. L. Scheeren[1]

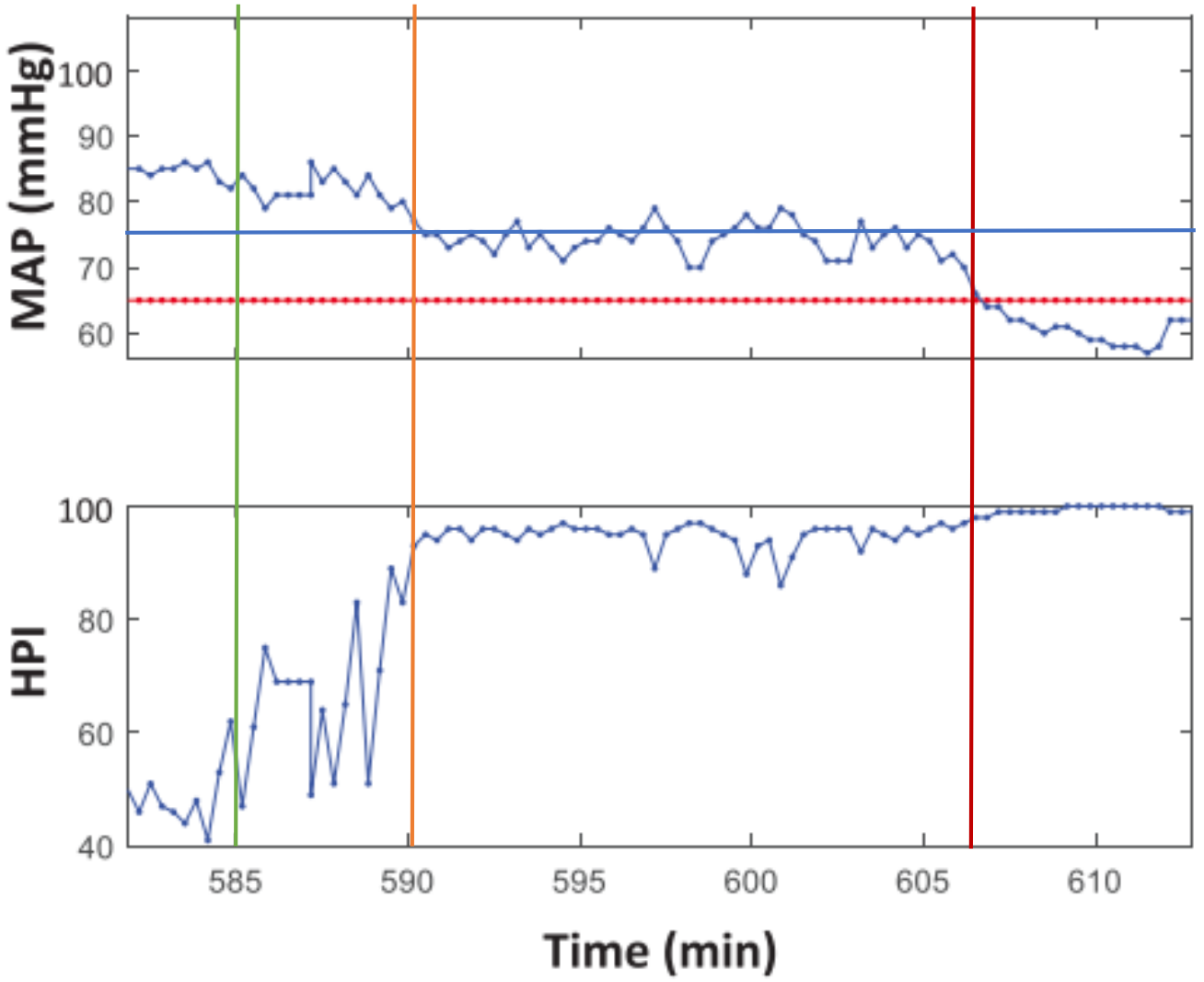
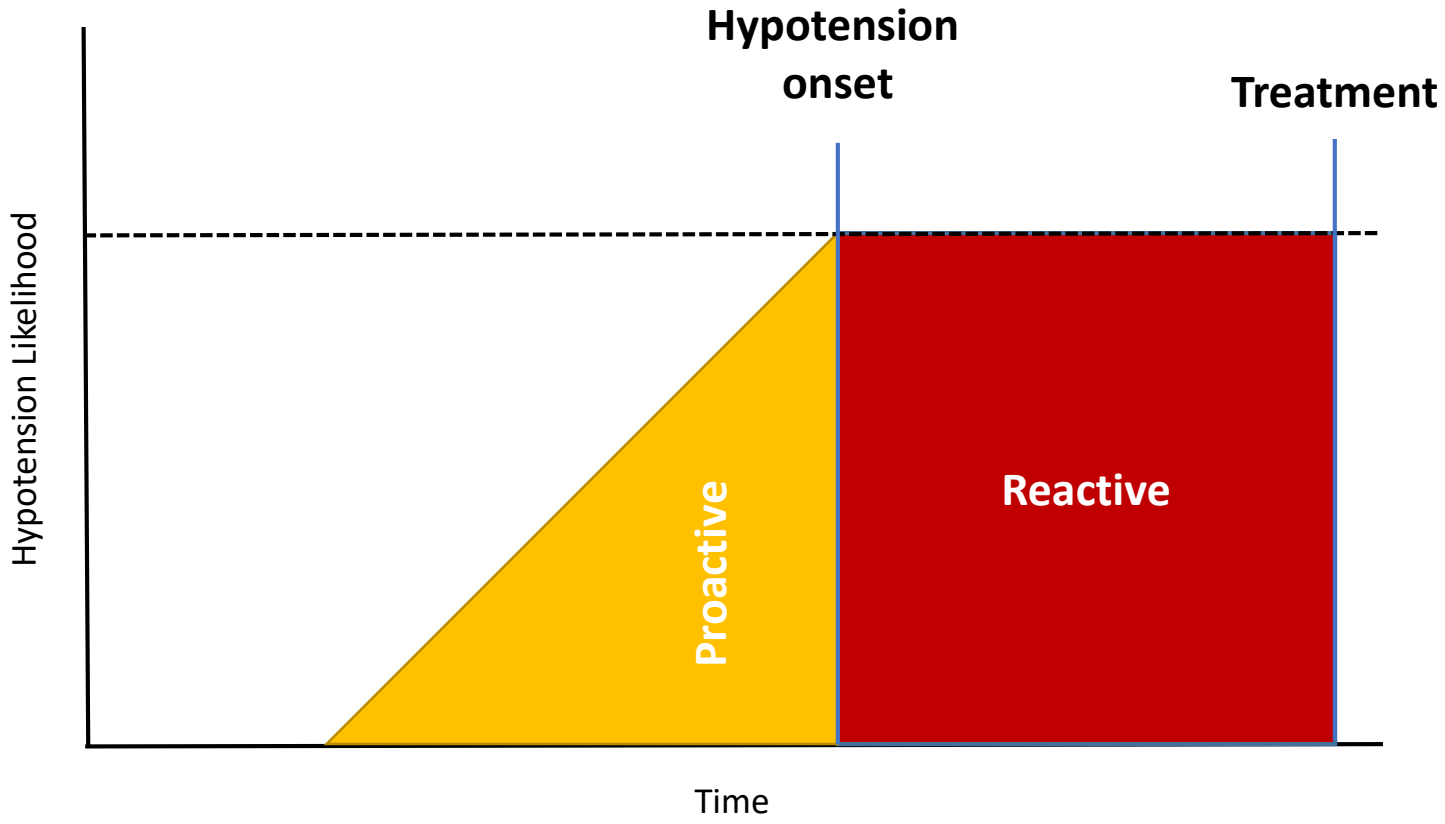


Fig. 5. One illustrative patient record showing the association between the algorithm output (Hypotension Prediction Index [HPI]) and the evolution of mean arterial pressure (MAP) over time.

Can we move from a reactive to a proactive approach?



The future? Using more features from vital signs

Prediction of Septic Shock Onset in ICU by Instantaneous Monitoring of Vital Signs*

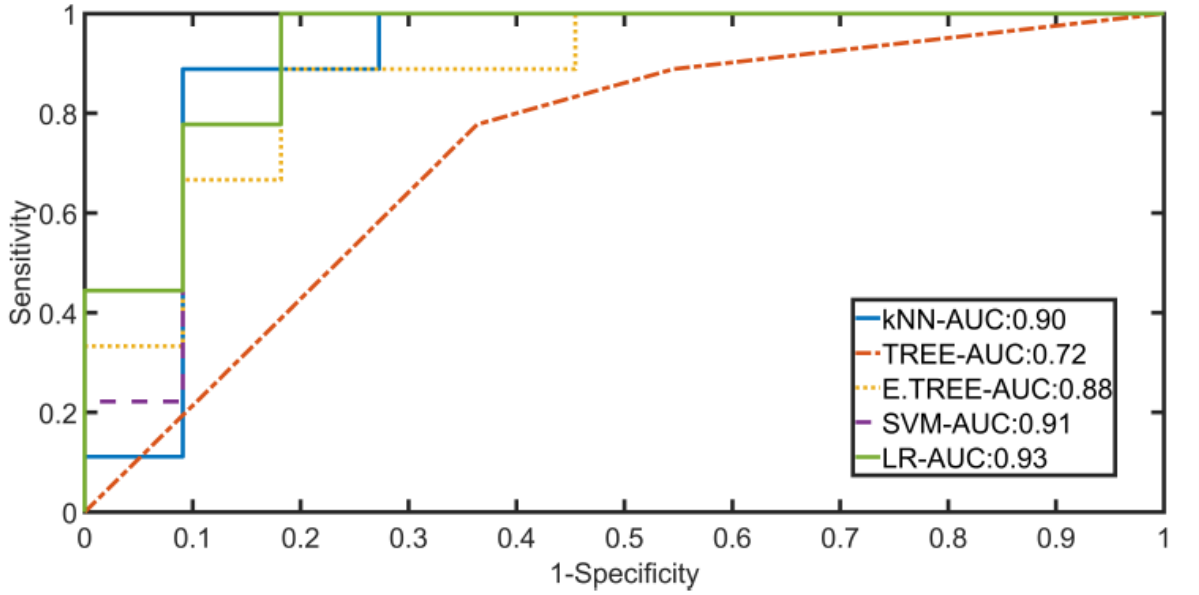


Fig. 1. ROCs obtained on the test set with kNN, Tree, Ensemble Tree, SVM and Logistic Regression algorithms.

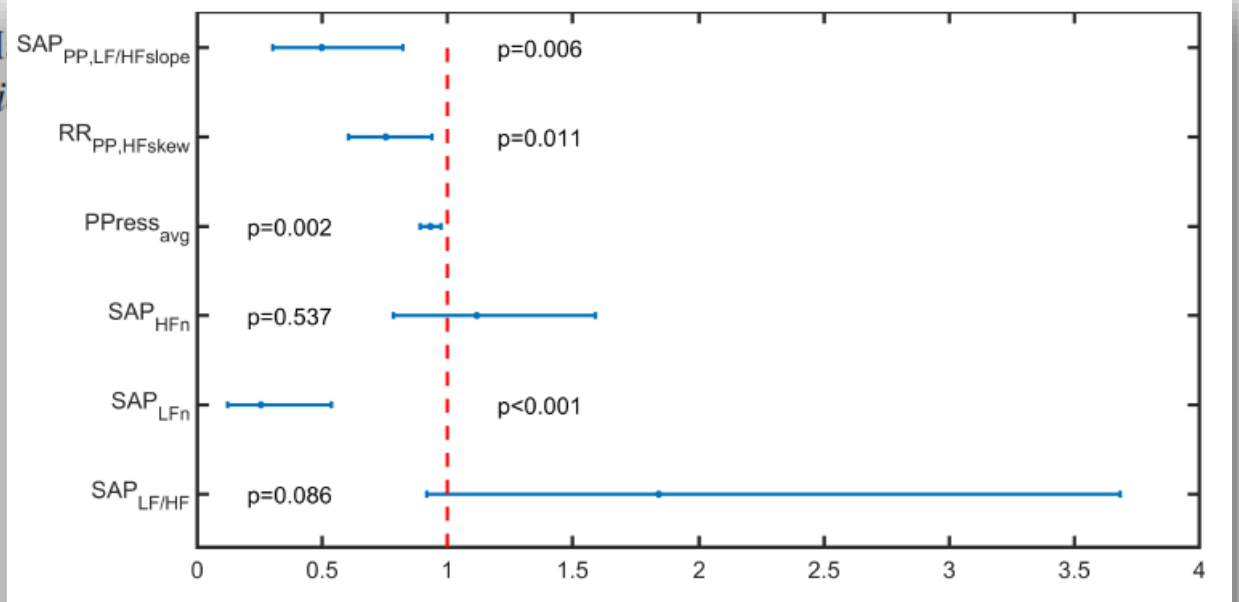


Fig. 2. Odds ratios and 95% confidence intervals of features included in the Logistic Regression classifier.

The future? Early diagnosis outside the ICU using “dense” monitoring data.

CLINICAL FOCUS REVIEW

Jerrold H. Levy, M.D., F.A.H.A., F.C.C.M., Editor

Rethinking Patient Surveillance on Hospital Wards

Frederic Michard, M.D., Ph.D., Cor J. Kalkman, M.D., Ph.D.

	Heart rate	Heart rate variability	Blood pressure	Respiratory rate	Oxygen saturation	Tempera-ture	Numerical pattern
No event/alarm							333333
Cardiac arrhythmia	↑	↑↑	↓				452333
Shock	↑↑		↓↓	↑		↑*	531433/531434*
Respiratory depression				↓↓	↓		333123
Respiratory failure	↑			↑↑	↓↓	↑**	433513/433514**
Sepsis	↑		↓	↑		↑↑	432435
Bleeding	↑		↓				432333

Fig. 3. Concept of automatic pattern recognition of clinical deterioration. Clinicians integrate information to suspect specific diagnoses. Similarly, simple algorithms could be used to automatically identify specific vital sign patterns and suggest possible diagnoses. Examples of numerical patterns are presented in the *right column*, assuming that for each variable, 1 means “major decrease,” 2 means “decrease,” 3 means “stable,” 4 means “increase,” and 5 means “major increase.” The numerical pattern “333333” would mean all variables remain stable, whereas the pattern “433514” could suggest pneumonia-related acute respiratory failure. *If septic shock. **If pneumonia.

The future? Predicting interventions

Rahman *et al. Critical Care* (2021) 25:388
https://doi.org/10.1186/s13054-021-03808-x

Critical

RESEARCH Open A

Early prediction of hemodynamic interventions in the intensive care unit using machine learning

Asif Rahman[1*], Yale Chang[1], Junzi Dong[1], Bryan Conroy[1], Annamalai Natarajan[1], Takahiro Kinoshita[1], Francesco Vicario[1], Joseph Frassica[1,2] and Minnan Xu-Wilson[1]

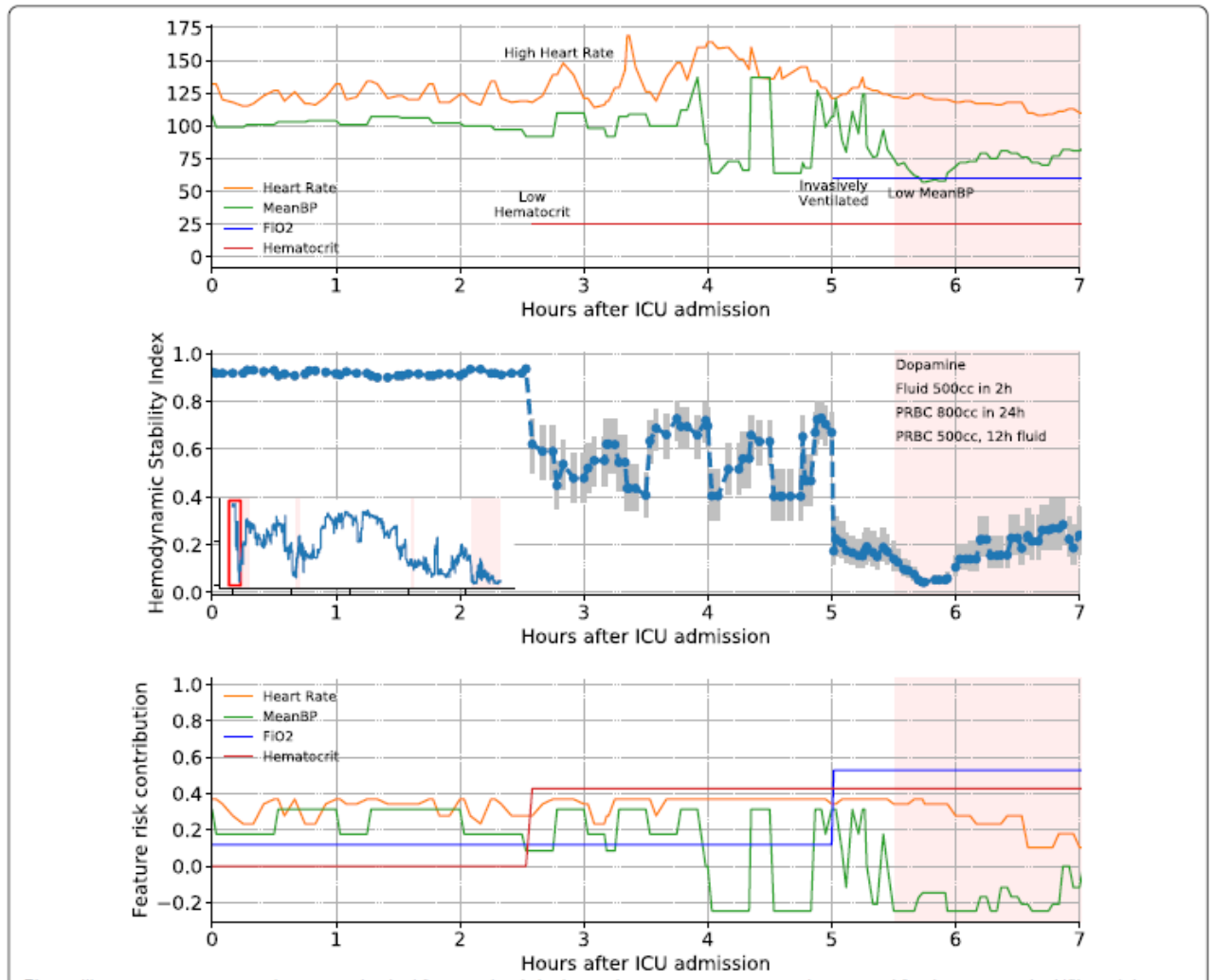


Fig. 2 Illustrative patient case showing individual features (top) the hemodynamic interventions administered for this patient, the HSI model predictions with confidence intervals (middle), and univariate risk scores contributed by select features from the HSI model (bottom). There is an emergent hemodynamic situation within the first day of ICU admission leading to a blood transfusion along with fluid and dopamine administration. HSI acts as an early indicator by responding to a sudden decrease in blood pressure and initiation of invasive mechanical ventilation

The future? Wireless wearables – bridge outside the ICU and capture dense data?

- FDA cleared blood pressure and cardiac output
- Pulse decomposition analysis
- Completely wireless technology
- Wearable technology
- Continuous ECG, HR, SpO2, BP, RR, Position, Skin temperature
- Q15 seconds data point
- Standard of care in >75% inpatients
- Alarms and nursing interventions

Khanna AK group

The future? Wireless US

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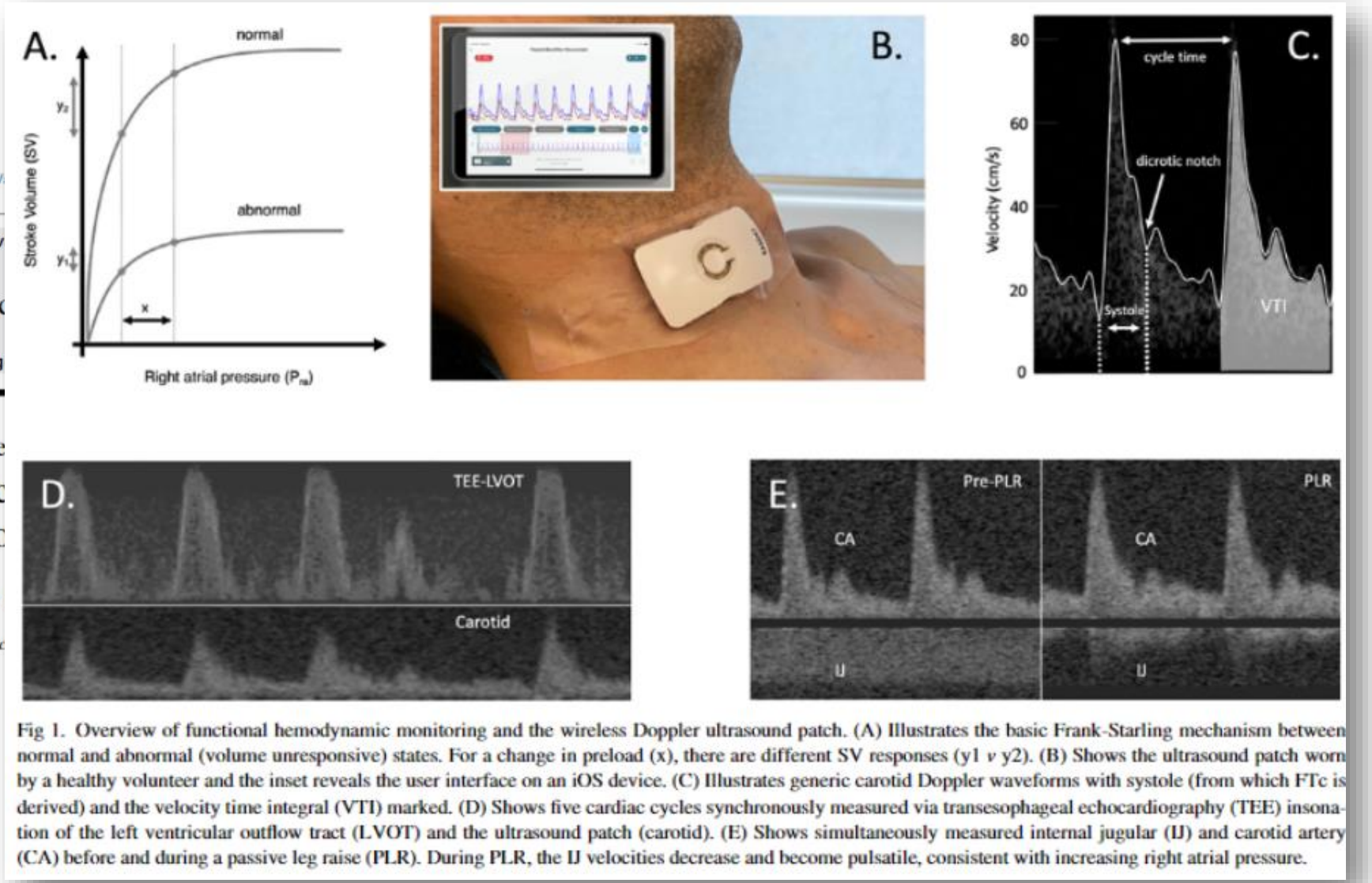

Fig 1. Overview of functional hemodynamic monitoring and the wireless Doppler ultrasound patch. (A) Illustrates the basic Frank-Starling mechanism between normal and abnormal (volume unresponsive) states. For a change in preload (x), there are different SV responses (y1 *v* y2). (B) Shows the ultrasound patch worn by a healthy volunteer and the inset reveals the user interface on an iOS device. (C) Illustrates generic carotid Doppler waveforms with systole (from which FTc is derived) and the velocity time integral (VTI) marked. (D) Shows five cardiac cycles synchronously measured via transesophageal echocardiography (TEE) insonation of the left ventricular outflow tract (LVOT) and the ultrasound patch (carotid). (E) Shows simultaneously measured internal jugular (IJ) and carotid artery (CA) before and during a passive leg raise (PLR). During PLR, the IJ velocities decrease and become pulsatile, consistent with increasing right atrial pressure.

Hemodynamic monitoring in the future

Frugality	Low-middle income countries / promoting equity
Proactive	Preventive vs curative
Noninvasive	Miniaturised wearable wireless
Accurate / discriminative	MCID
Simple	Usable in the ward and even at home
Smart	Detecting treatable traits / phenotypes / Clinical trajectories / equity

We are “at a state where the line between the normal and the pathological became a numerical abstraction.”

Prescribing by numbers. **Jeremy A Greene.** Drugs and the Definition of Disease

We should never treat (or not) a sepsis or septic shock based only on a “number” (biomarker or MAP)!