

**Patients With Severe Sepsis Should  
Receive a 30 mL/kg IV Fluid Bolus**

# Scope

- The premise of the discussion is 30ml/kg of IVF for initial resuscitation for patients with (severe) sepsis and septic shock
- ICU fluid balance is a different question/discussion

# Outline

- 30 ml/kg – where does this come from?
- What are the data overall?
- What are the data in specific populations of heart failure and renal failure

Sepsis and septic shock are medical emergencies and we recommend that treatment and resuscitation begin immediately. (Best practice statement)

Rhodes et al Crit Care Med. 2017 Mar;45(3):486-552.

# Recommendation for initial fluid management

- We recommend that in the resuscitation from sepsis-induced hypoperfusion, at least 30ml/kg of intravenous crystalloid fluid be given within the first 3 hours.

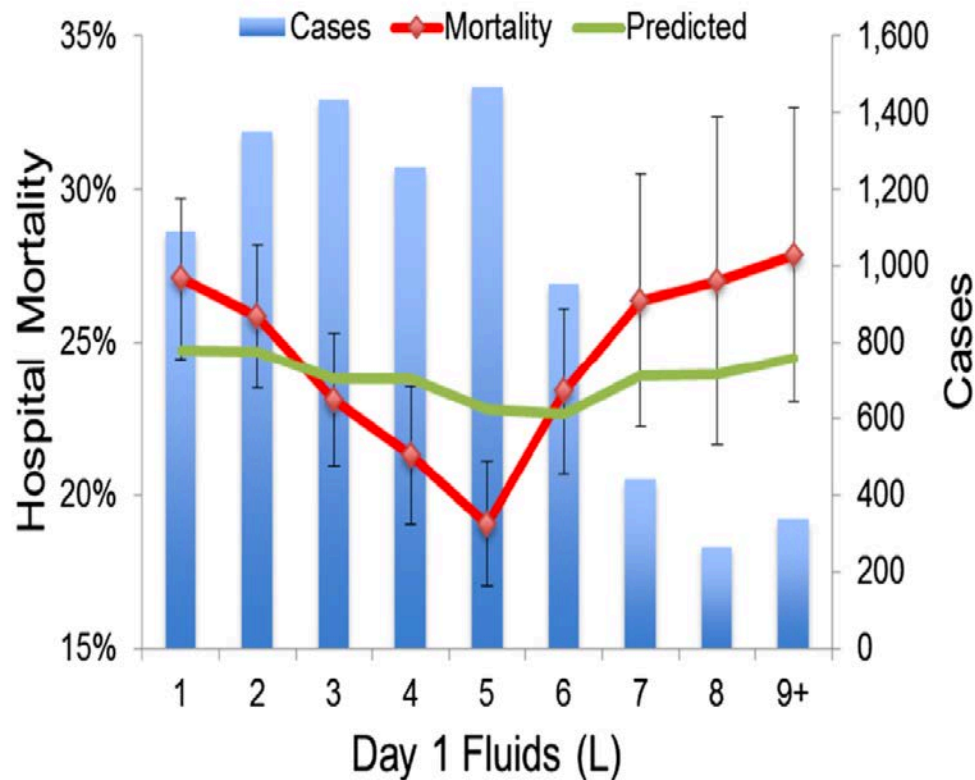
(Strong recommendation; low quality of evidence)

# So why 30 ml/Kg?

# Fluid administration in severe sepsis and septic shock, patterns and outcomes: an analysis of a large national database

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## Shock Day 1 but no Mechanical Ventilation



*Intensive Care Med* (2017) 43:625–632  
DOI 10.1007/s00134-016-4675-y

# 30 ml/Kg seems to be standard practice...

Trial	Time to randomization (hours)	Fluids received prior to randomization (mL)	Fluids Received prior to randomization (mL/kg)	Between 0 and 6 h after randomization (mL)
Rivers	0.8	NA	NA	3499 ± 2438
ProCESS	3.0	2083 ± 1405	28 ± 21	2279 ± 1881
ARISE	2.7	2591 ± 1331	34.7 ± 20.1	1713 ± 1401
PROMISE*	2.5	1790 (1000, 2500)	NA	2022 ± 1271

\* Plus 500 (255, 500) ml pre-hospital



# The IMPRESS-SSC Study

An International Multi-Centre Prevalence Study of Sepsis



## 3 Hour Bundle Compliance

%

Measurement of Lactate

56

Obtain Blood Cultures Prior to Antibiotics

49

Administer Broad Spectrum Antibiotics

64

Administer 30 mL/kg crystalloid for hypotension or lactate  $\geq 4$  mmol/L

57

# Relationship Between Bundle Compliance and Outcome

GEE population-averaged logistic regression model  
adjusted hospital mortality odds ratios

Variable	Hospital mortality odds ratio <sup>1</sup>	95% CI	p-value
Full 3 hour bundle	0.70	0.51 – 0.96	0.026
Full 6 hour bundle	0.75	0.58 – 0.96	0.020

<sup>1</sup>Adjusted for ICU admission, sepsis status (severe vs. shock), location (ED, ward, ICU, OR, unknown), and APACHE II



**IMPRESS**  
INTERNATIONAL MULTICENTRE PREVALENCE STUDY ON SEPSIS

# Surviving Sepsis Campaign: Association Between Performance Metrics and Outcomes in a 7.5-Year Study

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Initial Care Bundle (First 6 hr of presentation)	Participation in SSC, yr	Hospital Mortality OR <sup>a</sup>	95% CI	p
Measured lactate	< 2	0.80	0.73–0.89	< 0.001
	2 to < 3	0.67	0.59–0.76	< 0.001
	≥ 3	0.69	0.63–0.75	< 0.001
Blood cultures before antibiotics	Not applicable <sup>b</sup>	0.82	0.77–0.87	< 0.001
Broad-spectrum antibiotics	Not applicable <sup>b</sup>	0.85	0.81–0.90	< 0.001
Fluids and vasopressors	< 2	0.86	0.73–1.01	0.074
	2 to < 3	0.63	0.48–0.81	< 0.001
	≥ 3	0.74	0.62–0.88	0.001

# What about patients with heart failure or renal failure?

## ORIGINAL ARTICLE

### Multicenter Implementation of a Treatment Bundle for Patients with Sepsis and Intermediate Lactate Values

Vincent X. Liu<sup>1,2</sup>, John W. Morehouse<sup>2</sup>, Gregory P. Marelich<sup>2</sup>, Jay Soule<sup>2</sup>, Thomas Russell<sup>2</sup>, Melinda Skeath<sup>3</sup>, Carmen Adams<sup>3</sup>, Gabriel J. Escobar<sup>1,2</sup>, and Alan Whippy<sup>2</sup>

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Liu et al Am J Respir Crit Care Med Vol 193(11):1264–1270

**Table 4.** Hospital Mortality in Heart Failure and Chronic Kidney Disease Subgroups

	n	Mortality (%)			P Value
		Prior (2011)	Prebundle (2012)	Postbundle (2013)	
All patients	18,122				
Hospital		8.8	9.3	7.9	0.02
30 d		13.7	14.1	12.6	0.03
History of heart failure	4,144				
Hospital		13.0	14.8	11.6	0.03
30 d		18.8	20.7	17.8	0.13
History of kidney disease	6,265				
Hospital		9.7	11.5	7.5	<0.01
30 d		15.9	17.7	13.3	<0.01
Heart failure or kidney disease	8,322				
Hospital		10.7	12.5	8.7	<0.01
30 d		16.8	18.3	14.5	<0.01
No heart failure or kidney disease	9,800				
Hospital		7.4	6.5	7.2	0.40
30 d		11.3	10.5	10.8	0.60

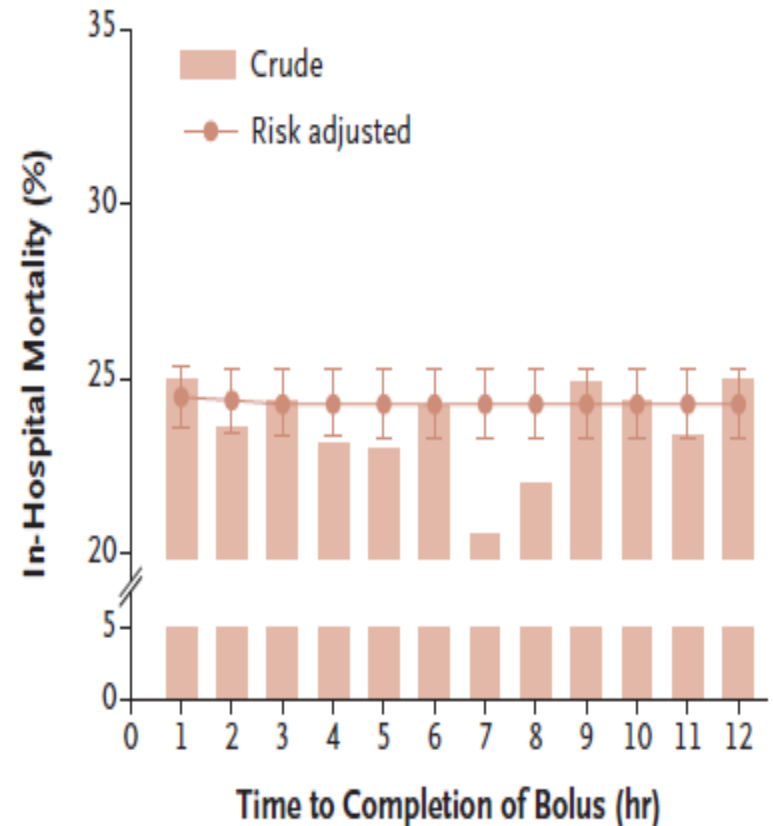
Hemodynamically stable patients with intermediate lactate levels (2-4 mmol/L) in the ED

# Time to Treatment and Mortality during Mandated Emergency Care for Sepsis

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Gary S. Phillips, M.A.S., Stanley Lemeshow, Ph.D., Tiffany Osborn, M.D., M.P.H.,  
Kathleen M. Terry, Ph.D., and Mitchell M. Levy, M.D.

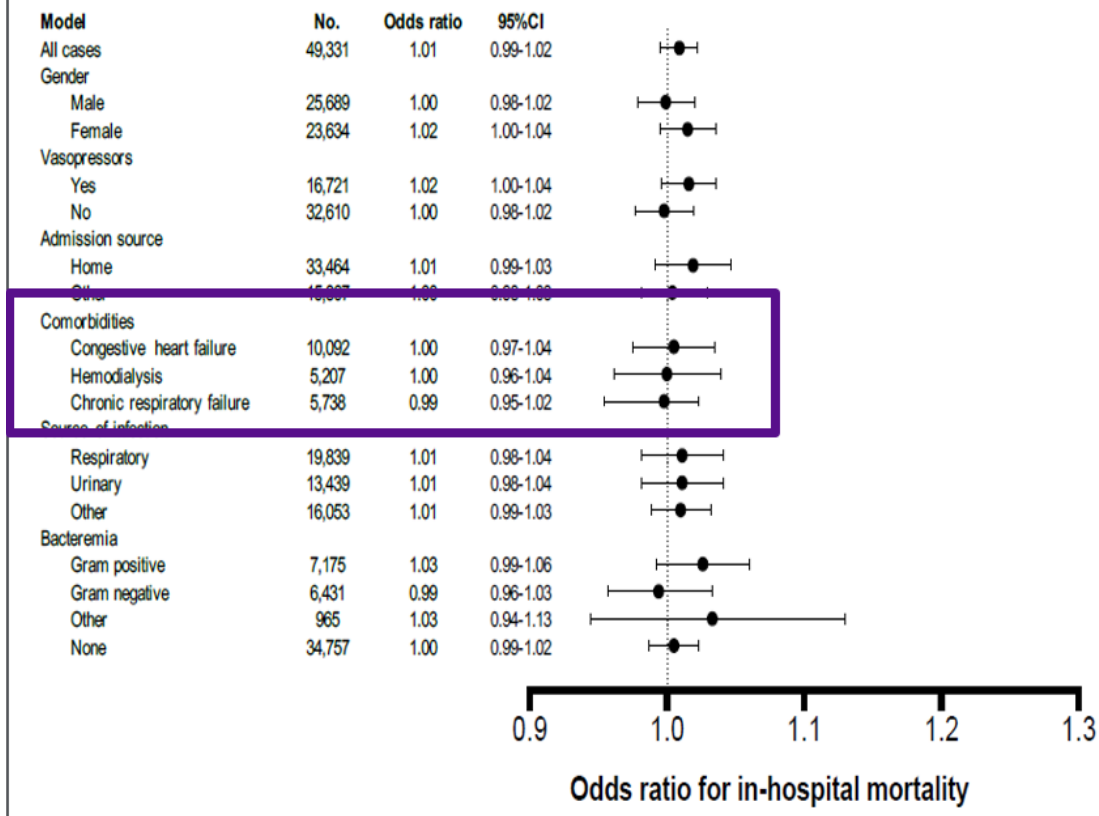
- 49,331 patients with sepsis presenting to EDs in New York State
- Examined time to antibiotics and fluids and 3 hour sepsis bundle adherence

C Initial Bolus of Intravenous Fluids



# NYS Sepsis Initiative

**Figure S4.** Risk-adjusted odd ratios of in-hospital mortality with 95% confidence interval for each hour in time to completion of the initial IV fluid bolus from primary model and multiple *a priori* subgroups





# NYS Sepsis Initiative

**Appendix Table 6: Probabilities and odds ratios of In-Hospital Mortality based on separate logistic regression models containing the compliance risk factor along with each of the variables in the risk adjusted model for hospital mortality developed through collaboration with the State of New York.**

Compliance risk factor	N	Probability of in-hospital mortality %	95% CI	OR for In-hospital mortality	95% CI	p-value
3-hour bundle						
No	29,134	29.3	28.8 – 29.8	0.73	0.70 – 0.76	< 0.001
Yes	44,996	24.2	23.9 – 24.6			
6-hour bundle						
No	46,390	27.4	27.1 – 27.8	0.74	0.71 – 0.77	< 0.001
Yes	27,361	22.8	22.3 – 23.3			
Lactate reported in 3 hours						
No	7,721	30.2	29.3 – 31.1	0.76	0.72 – 0.81	< 0.001
Yes	66,409	25.8	25.5 – 26.1			
Blood cultures obtained prior to antibiotics						
No	18,179	30.2	29.6 – 30.8	0.72	0.69 – 0.75	< 0.001
Yes	55,951	24.9	24.6 – 25.3			
Antibiotics started in 3 hours						
No	11,448	29.7	28.9 – 30.4	0.78	0.74 – 0.82	< 0.001
Yes	62,682	25.7	25.4 – 26.0			
Adequate fluids in hypotensive or elevated lactate						
No	24,052	32.1	31.6 – 32.7	0.79	0.76 – 0.83	< 0.001
Yes	27,855	28.1	27.6 – 28.6			
Vasopressors if refractory hypotension						
No	12,449	38.2	37.4 – 39.0	1.03	0.97 – 1.09	0.32
Yes	12,145	38.8	38.0 – 39.6			



# Patterns and Outcomes Associated With Timeliness of Initial Crystalloid Resuscitation in a Prospective Sepsis and Septic Shock Cohort\*

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- 11,182 patients in 9 hospitals
- Time to initiation of fluid resuscitation associated with reduced risk of death

**TABLE 3. Distribution of Patient Outcomes Across Fluid Initiation Time Groups**

Variables	All Patients	≤ 30 min	31–120 min	> 120 min or No Fluids in First 6 hr
<i>n</i>	11,182	5,336	2,388	3,458
Outcomes <sup>a,b,c</sup>				
All in-hospital mortality, <i>n</i> (%) 95% CI	2,241 (20.0)	949 (17.8) (16.8–18.8)	446 (18.7) (17.2–20.3)	846 (24.5) (23.1–25.9)
60-d in-hospital mortality	2,219 (19.8)	941 (17.6) (16.6–18.7)	444 (18.6) (17.1–20.2)	834 (24.1) (22.7–25.6)
28-d in-hospital mortality	2,029 (18.1)	889 (16.7) (15.7–17.7)	414 (17.3) (15.9–18.9)	726 (21.0) (19.7–22.4)
ICU LOS (d) (ICU admitted only, <i>n</i> = 5,185), <sup>b</sup> (95% CI)	12.8	10.4 (9.4–11.3)	10.9 (9.6–12.3)	16.7 (15.0–18.4)
Hospital LOS (d), <sup>b</sup> (95% CI)	14.9	12.8 (12.3–13.3)	13.1 (12.4–13.8)	19.6 (18.4–20.7)
Mean percentage lactate clearance, <sup>c</sup> (%) (95% CI), <i>n</i>	5,963 (19.7)	(23.8) (22.3–25.2), 3,055	(23.0) (20.5–25.5), 1,284	(9.5) (6.7–12.4), 1,624

**TABLE 4. Interaction Coefficients for the Association of Timeliness and Volume of Initial Crystalloid Resuscitation With Outcomes by Presentation Phenotype**

Phenotype	Time to Fluid Initiation		Initial Fluid Volume	
	Interaction Term (95% CI)	<i>p</i> (Interaction)	Interaction Term (95% CI)	<i>p</i> (Interaction)
Hospital mortality				
Heart failure	0.96 (0.91–1.01)	0.13	1.01 (0.93–1.09)	0.80
Renal failure	0.98 (0.92–1.05)	0.58	0.99 (0.91–1.08)	0.81
Mechanical ventilation				
Heart failure	0.99 (0.94–1.05)	0.78	1.01 (0.93–1.09)	0.88
Renal failure	0.99 (0.93–1.05)	0.77	0.99 (0.91–1.08)	0.80

# Summary

- Start resuscitation early
- 30ml/Kg crystalloid is a pragmatic choice to begin resuscitation
- At this time there are strong observational data of benefit and no convincing evidence of harm, especially in well-resourced environments, even for patients with heart failure and renal failure
- Fluid resuscitation after an initial 30ml/kg is an area of active controversy and research