Fluid resuscitation and de-resuscitation?

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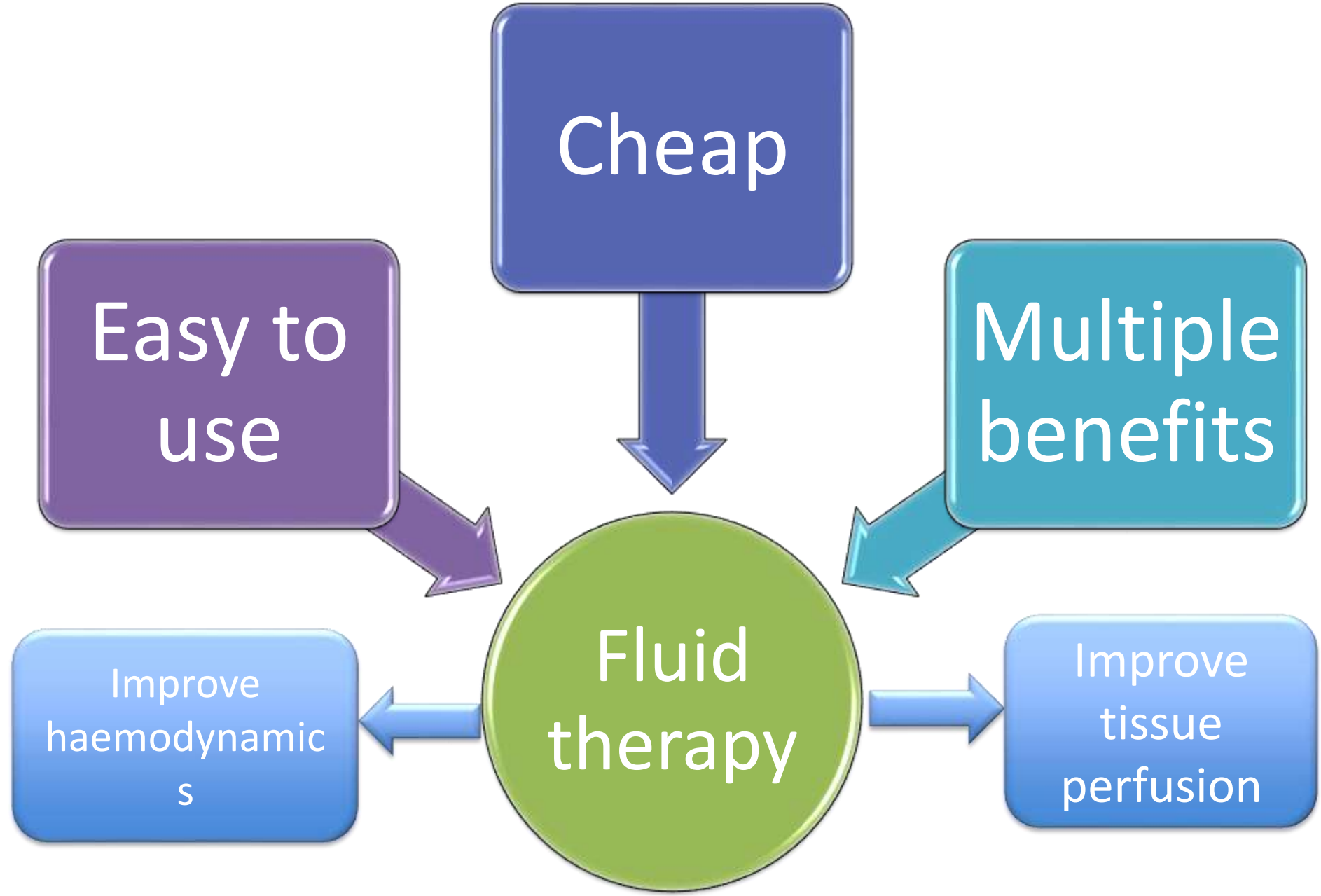
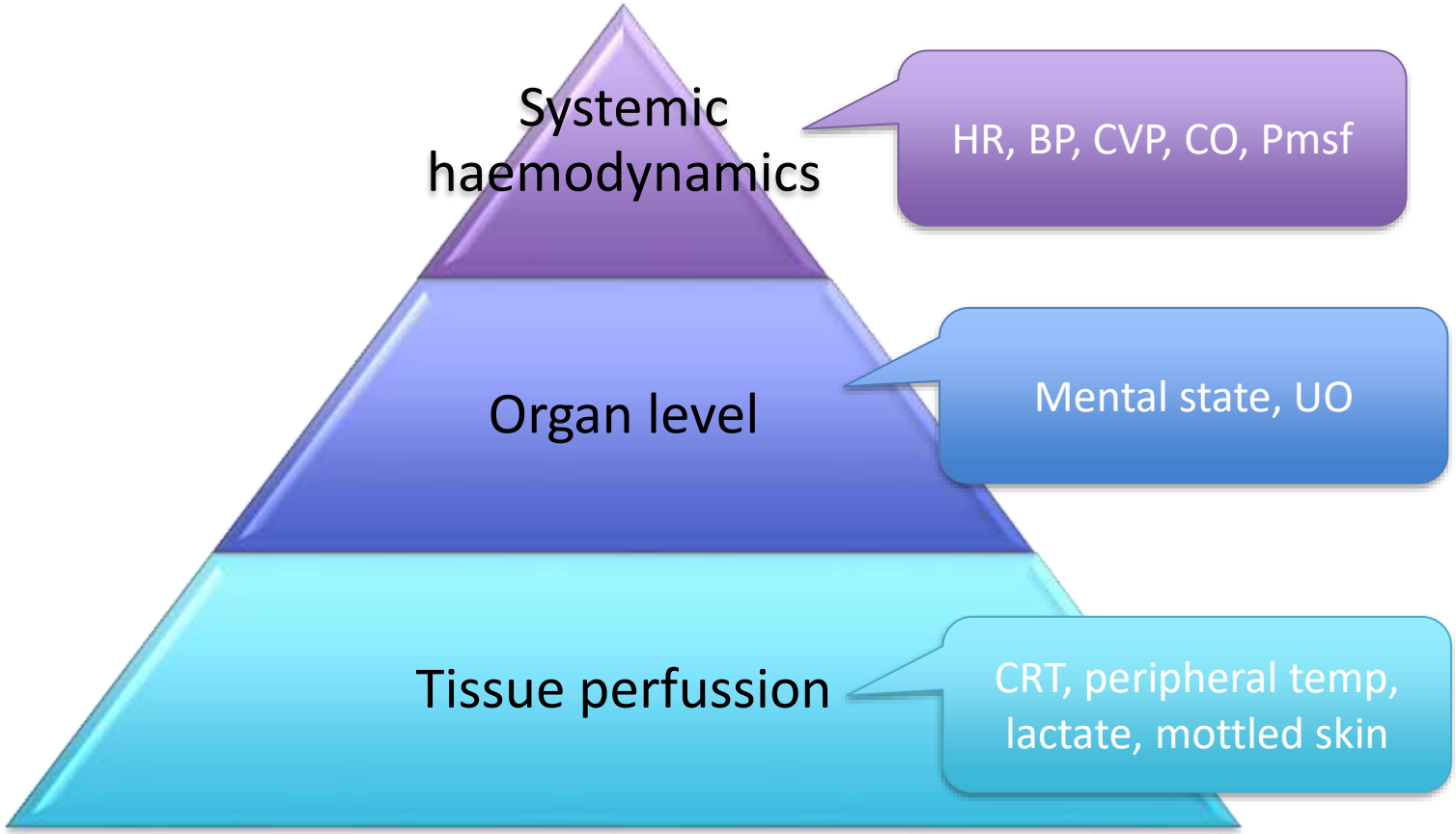
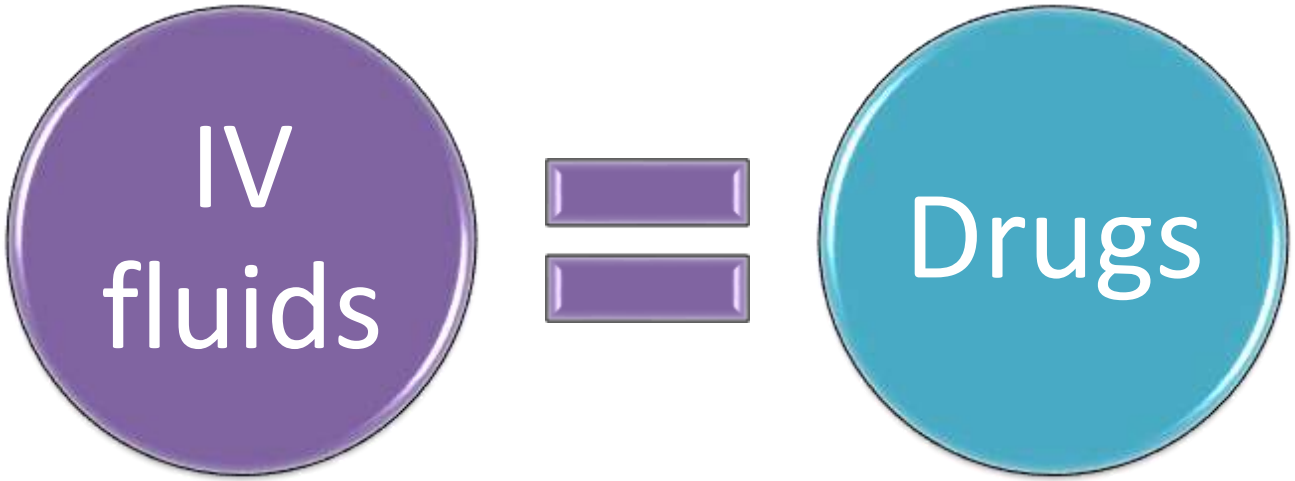
NEICS Meeting 2017

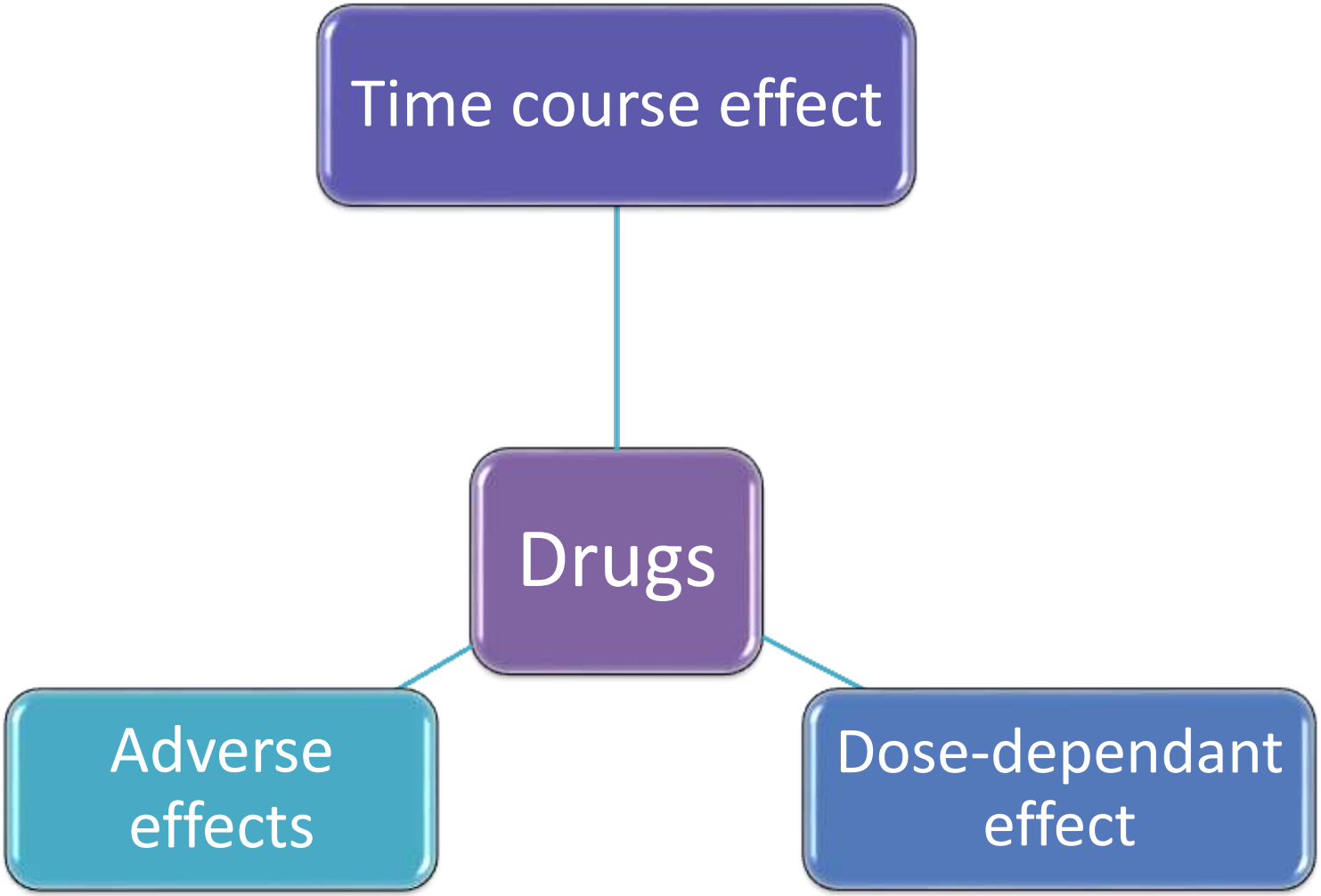

Cheap
Easy to use
Multiple benefits
Fluid therapy
Improve haemodynamics
Improve tissue perfusion


Systemic haemodynamics
HR, BP, CVP, CO, Pmsf
Organ level
Mental state, UO
Tissue perfussion
CRT, peripheral temp, lactate, mottled skin



***Drug**: A medicine or other substance which has a physiological effect when ingested or otherwise introduced into the body*

Oxford Dictionary


Time course effect
Drugs
Adverse effects
Dose-dependant effect

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*

Measured intravascular pressure (mm Hg)				MAP <60 mm Hg or a need for any vasopressor (except dopamine ≤5 μg/kg/min); consider correctable causes of shock first	MAP ≥60 mm Hg without vasopressors (except dopamine ≤5 μg/kg/min)			
CVP		PAOP[G]			Average urinary output <0.5 ml/kg/hr		Average urinary output ≥0.5 ml/kg/hr	
Conservative strategy	Liberal strategy	Conservative strategy	Liberal strategy		**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation	**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation
Range 1				1 Vasopressor[F] Fluid bolus[F]	3 KVO IV Dobutamine[A] Furosemide[B,1,2,4]	7 KVO IV Furosemide[B,1,2,4]	11 KVO IV Dobutamine[A] Furosemide[B,1,3,4]	15 KVO IV Furosemide[B,1,3,4]
>13	>18	>18	>24					
Range 2					4 KVO IV Dobutamine[A]	8 KVO IV Furosemide[B,1,2,4]	12 KVO IV Dobutamine[A]	16 KVO IV Furosemide[B,1,3,4]
9–13	15–18	13–18	19–24					
Range 3				2 Fluid bolus[F] Vasopressor[F]	5 Fluid bolus[C]	9 Fluid bolus[C]	13 Fluid bolus[C]	17 Liberal KVO IV
4–8	10–14	8–12	14–18					18 Conservative Furosemide[B,1,3,4]
Range 4					6 Fluid bolus[C]	10 Fluid bolus[C]	14 Fluid bolus[C]	19 Liberal fluid bolus
<4	<10	<8	<14					20 Conservative KVO IV

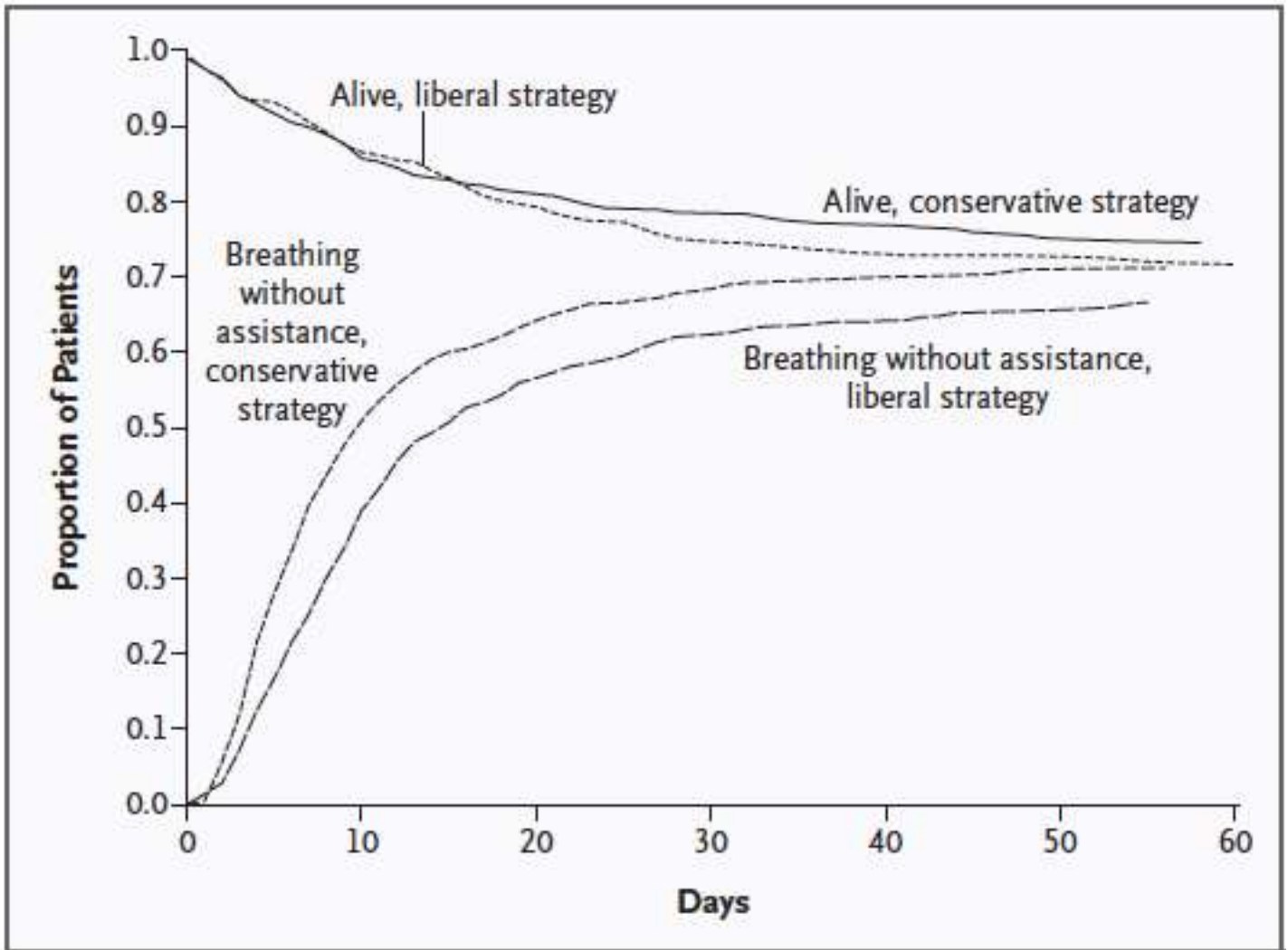


Figure 3. Probability of Survival to Hospital Discharge and of Breathing without Assistance during the First 60 Days after Randomization.

Restricting volumes of resuscitation fluid in adults with septic shock after initial management: the CLASSIC randomised, parallel-group, multicentre feasibility trial

Peter B. Hjortrup[1], Nicolai Haase[1], Helle Bundgaard[2], Simon L. Thomsen[3], Robert Winding[4], Ville Pettilä[5], Anne Aaen[6], David Lodahl[7], Rasmus E. Berthelsen[8], Henrik Christensen[9], Martin B. Madsen[1], Per Winkel[10], Jørn Wetterslev[10], Anders Perner[1,11*], The CLASSIC Trial Group, The Scandinavian Critical Care Trials Group

Restriction Group

- Lactate > 4
- MAP < 50 mmHg
- Mottling score > 2
- Oliguria (first 2h) UO < 0.1 mL/Kg IBW

Standard Care

- Improvement of haemodynamic variables

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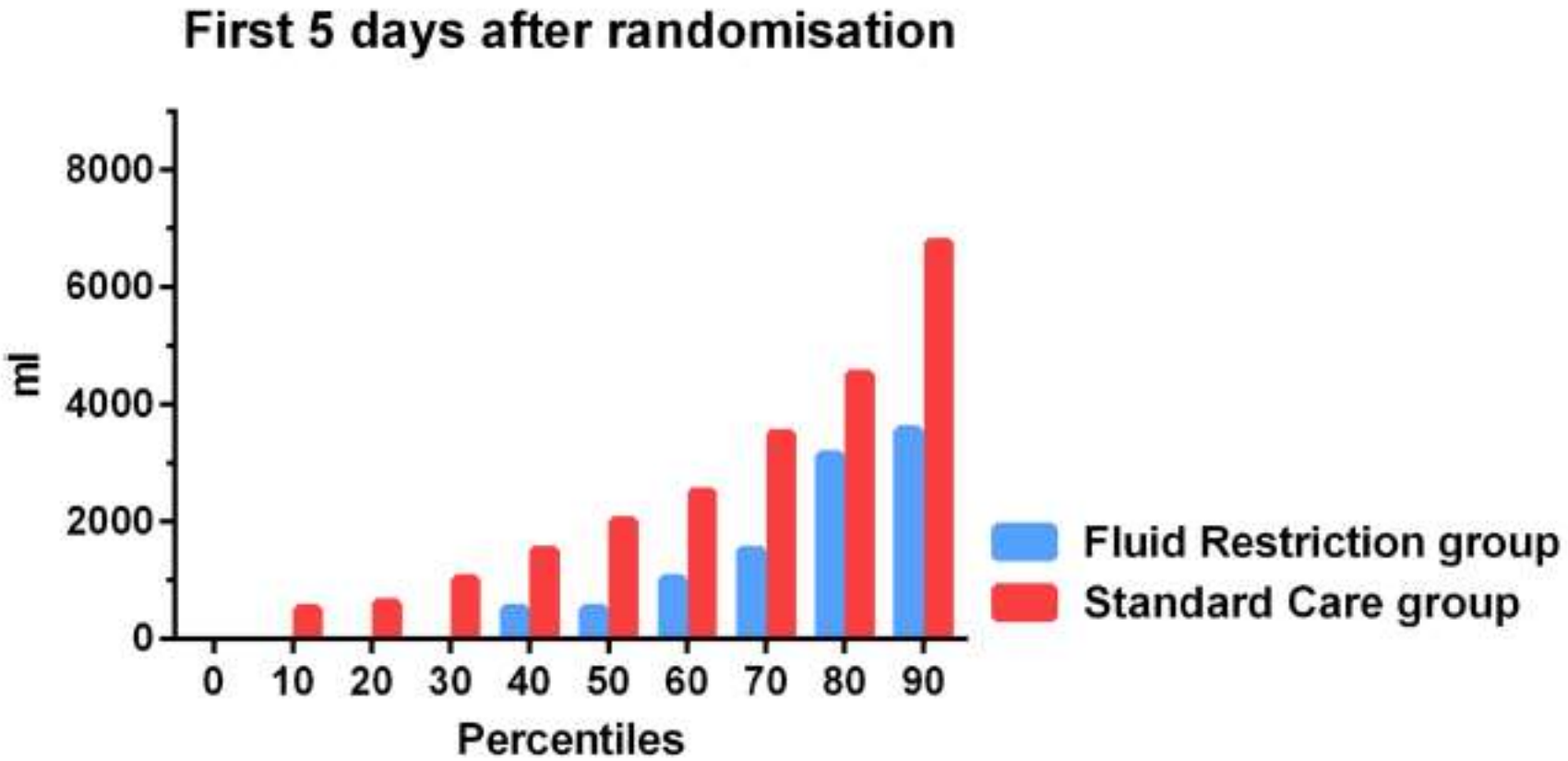

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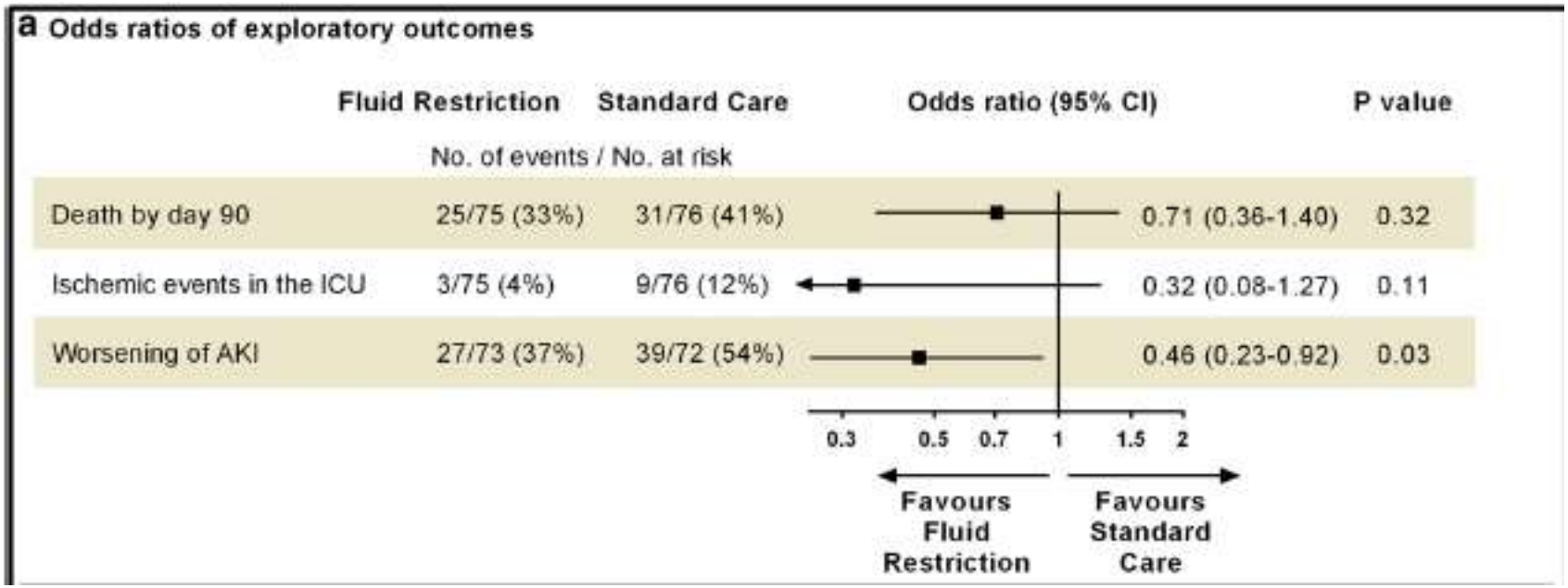
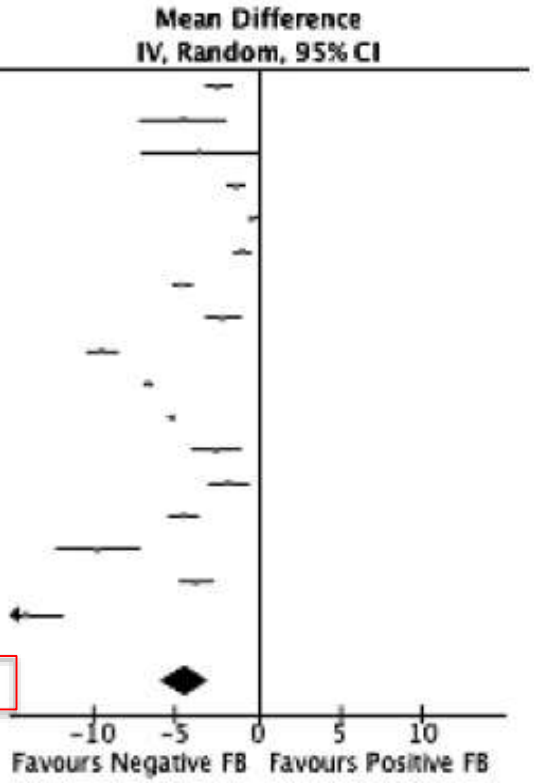


Fluid overload, de-resuscitation, and outcomes in critically ill or injured patients: a systematic review with suggestions for clinical practice

Manu L.N.G. Malbrain[1], Paul E. Marik[2], Ine Witters[1], Colin Cordemans[1], Andrew W. Kirkpatrick[3], Derek J. Roberts[3,4], Niels Van Regenmortel[1]

Study or Subgroup	Survivors Mean	SD	Total	Nonsurvivors Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Alsous 2000	0.05	0.4	16	2.4	1.7	20	6.1%	-2.35 [-3.12, -1.58]
Cordemans 2012 (CLI)	4.971	7.737	58	9.503	6.91	65	5.1%	-4.53 [-7.14, -1.93]
Cordemans 2012 (PAL)	3.419	7.842	70	6.982	9.875	44	4.5%	-3.56 [-7.01, -0.12]
Dabrowski 2014	-0.963	1.089	24	0.333	0.401	6	6.2%	-1.30 [-1.84, -0.75]
Goldstein 2005	0.457	0.403	60	0.805	0.858	56	6.3%	-0.35 [-0.59, -0.10]
Kuzkov 2006	0.893	0.668	16	1.782	0.75	15	6.2%	-0.89 [-1.39, -0.39]
Malbrain 2005	1.643	1.5	192	6.214	2.143	73	6.2%	-4.57 [-5.11, -4.04]
Malbrain 2014	3.862	6.904	314	5.994	7.546	413	6.1%	-2.13 [-3.19, -1.08]
Micek 2013	2.709	2.585	162	12.124	5.463	163	6.1%	-9.42 [-10.34, -8.49]
Murphy 2009	9.25	0.625	125	15.875	1.125	87	6.3%	-6.63 [-6.89, -6.36]
Rosenberg 2009	5.154	0.769	159	10.308	1.923	635	6.3%	-5.15 [-5.35, -4.96]
Sakr 2005	1.4	6.5	239	3.9	7.8	153	5.9%	-2.50 [-3.99, -1.01]
Schuller 1991	0.25	1.6	43	2	2.8	26	6.0%	-1.75 [-2.93, -0.57]
Shum 2011	0.88	2.32	505	5.41	5.05	134	6.1%	-4.53 [-5.41, -3.65]
Simmons 1987	7.5	4.09	11	17.22	2.045	26	5.2%	-9.72 [-12.26, -7.18]
The RENAL Study 2012	-1.94	11	808	1.755	9.061	644	6.1%	-3.69 [-4.73, -2.66]
Vidal 2008	2.1	3.9	34	16.1	6.4	49	5.4%	-14.00 [-16.22, -11.78]
Total (95% CI)			2836			2609	100.0%	**-4.43 [-5.83, -3.04]**

Heterogeneity: Tau² = 8.09; Chi² = 1894.59, df = 16 (P < 0.00001); I² = 99%
Test for overall effect: Z = 6.23 (P < 0.00001)



Conservative fluid management or deresuscitation for patients with sepsis or acute respiratory distress syndrome following the resuscitation phase of critical illness: a systematic review and meta-analysis

Jonathan A. Silversides[1,2*], Emmet Major[2], Andrew J. Ferguson[3], Emma E. Mann[2], Daniel F. McAuley[1,4], John C. Marshall[5,6], Bronagh Blackwood[1] and Eddy Fan[5]

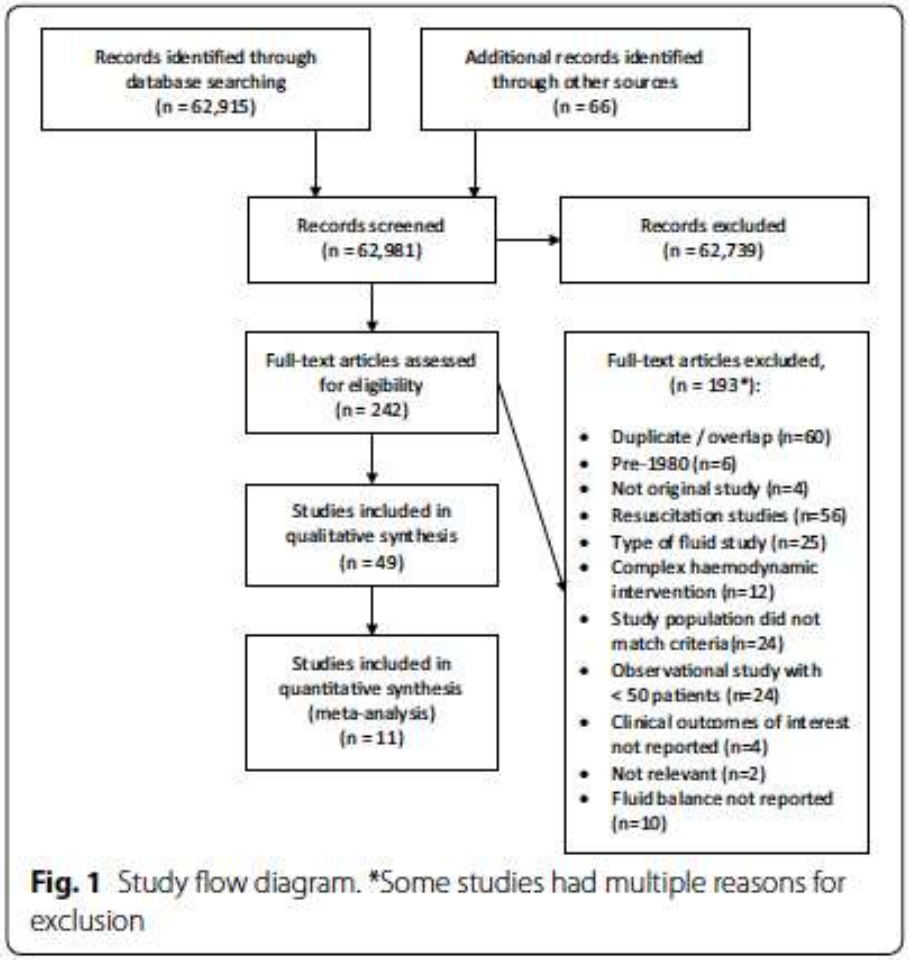


Fig. 1 Study flow diagram. *Some studies had multiple reasons for exclusion

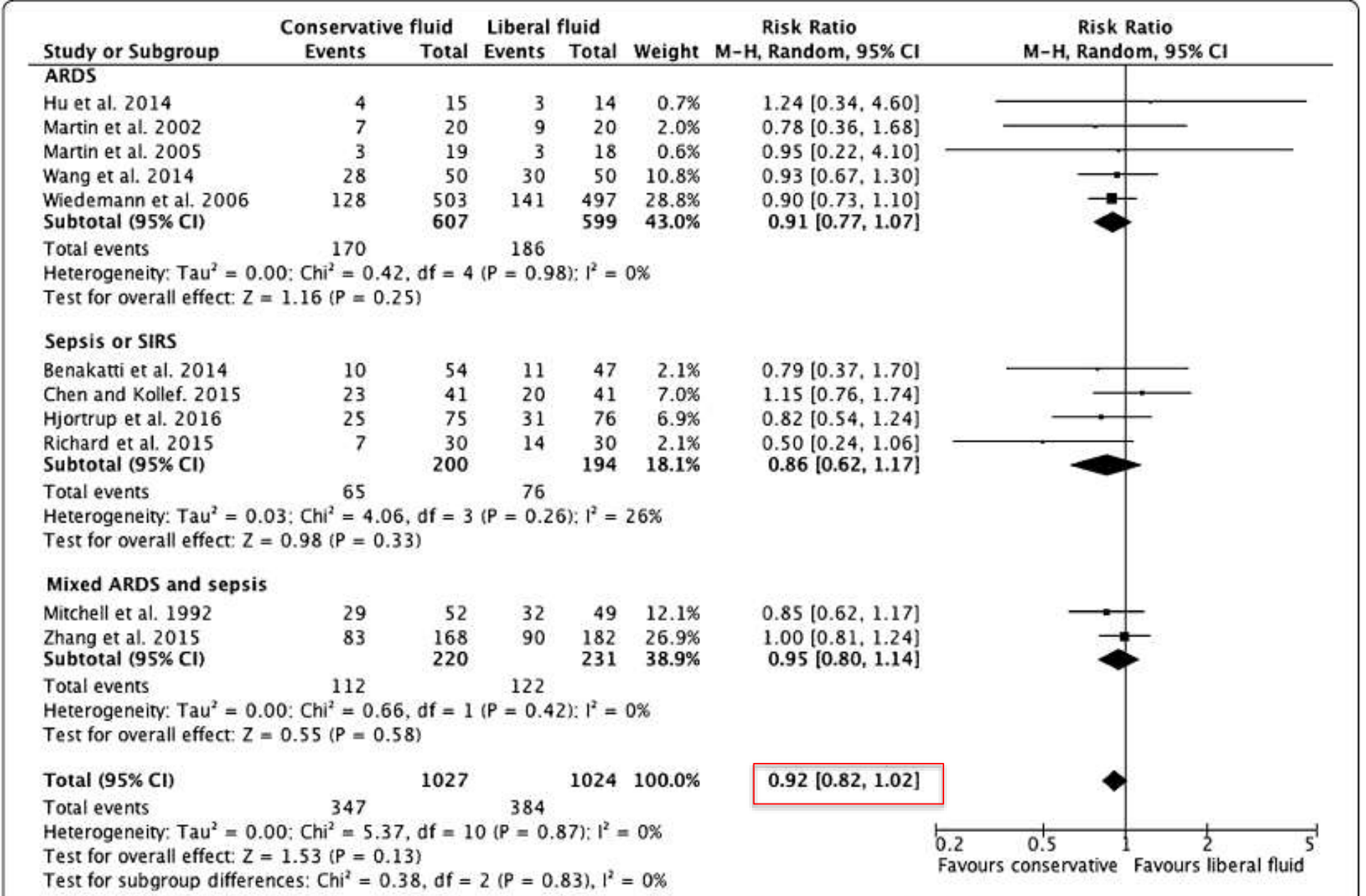


Fig. 3 Forest plot for mortality at most protracted time point available, conservative or deresuscitative fluid strategy versus standard care or liberal fluid strategy

Study or Subgroup	Conservative fluid Mean [Days]	SD [Days]	Total	Liberal fluid Mean [Days]	SD [Days]	Total	Weight	Mean Difference IV, Random, 95% CI [Days]
Chen and Kollef. 2015	5.5	9.4	41	7.4	12.9	41	6.5%	
Zhang et al. 2015	9	17.9	168	10.3	18.7	182	10.3%	
Hjortrup et al. 2016	21.4	9.7	75	19.8	11.1	76	13.3%	
Martin et al. 2005	10.3	8	20	8	8	20	6.4%	
Wiedemann et al. 2006	14.6	11.2	503	12.1	11.1	497	51.6%	
Richard et al. 2015	12.7	18.7	30	9.7	16.3	30	2.1%	
Benakatti et al. 2014	15.8	10.8	54	12.1	9.4	47	9.8%	
Total (95% CI)			**891**			**893**	**100.0%**	

Heterogeneity: $Tau^2 = 0.33$; $Chi^2 = 6.63$, df = 6 (P = 0.36); $I^2 = 9\%$

Test for overall effect: Z = 2.78 (P = 0.005)

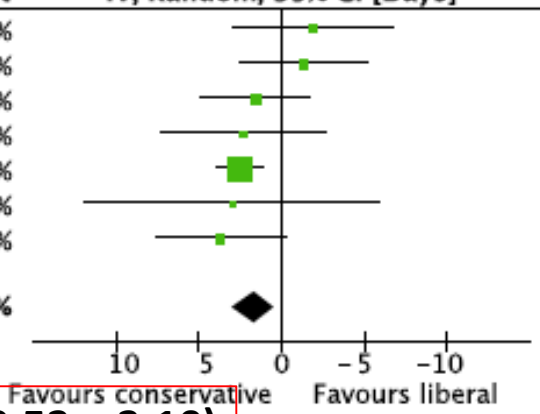


Fig. 4 Forest plot for outcome of ventilator-free days

MD 1.82 (95% CI 0.53 – 3.10)

Study or Subgroup	Conservative fluid Mean [Days]	SD [Days]	Total	Liberal fluid Mean [Days]	SD [Days]	Total	Weight	Mean Difference IV, Random, 95% CI [Days]
Benakatti et al. 2014	7.1	5.5	54	10.3	6.5	47	15.5%	-3.20 [-5.57, -0.83]
Hjortrup et al. 2016	6.7	6.1	75	6	5.3	76	17.5%	0.70 [-1.12, 2.52]
Hu et al. 2014	12.5	3.5	15	15.5	2.5	14	16.1%	-3.00 [-5.20, -0.80]
Mitchell et al. 1992	13.5	10.7	52	18	10.7	49	9.8%	-4.50 [-8.68, -0.32]
Richard et al. 2015	18.7	17.1	30	17	14.8	30	3.9%	1.70 [-6.39, 9.79]
Wang et al. 2014	12.1	3.2	50	15.8	4.6	50	18.5%	-3.70 [-5.25, -2.15]
Zhang et al. 2015	9	6	168	8.8	8.2	182	18.7%	0.20 [-1.30, 1.70]
Total (95% CI)			**444**			**448**	**100.0%**	**-1.88 [-3.64, -0.12]**

Heterogeneity: $Tau^2 = 3.74$; $Chi^2 = 24.47$, df = 6 (P = 0.0004); $I^2 = 75\%$

Test for overall effect: Z = 2.09 (P = 0.04)

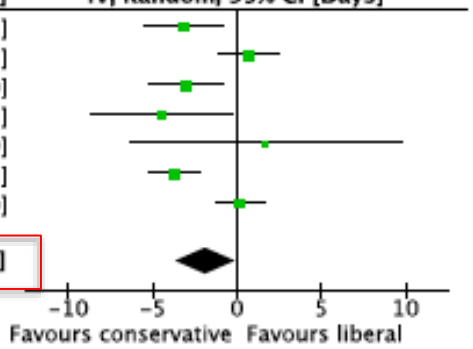
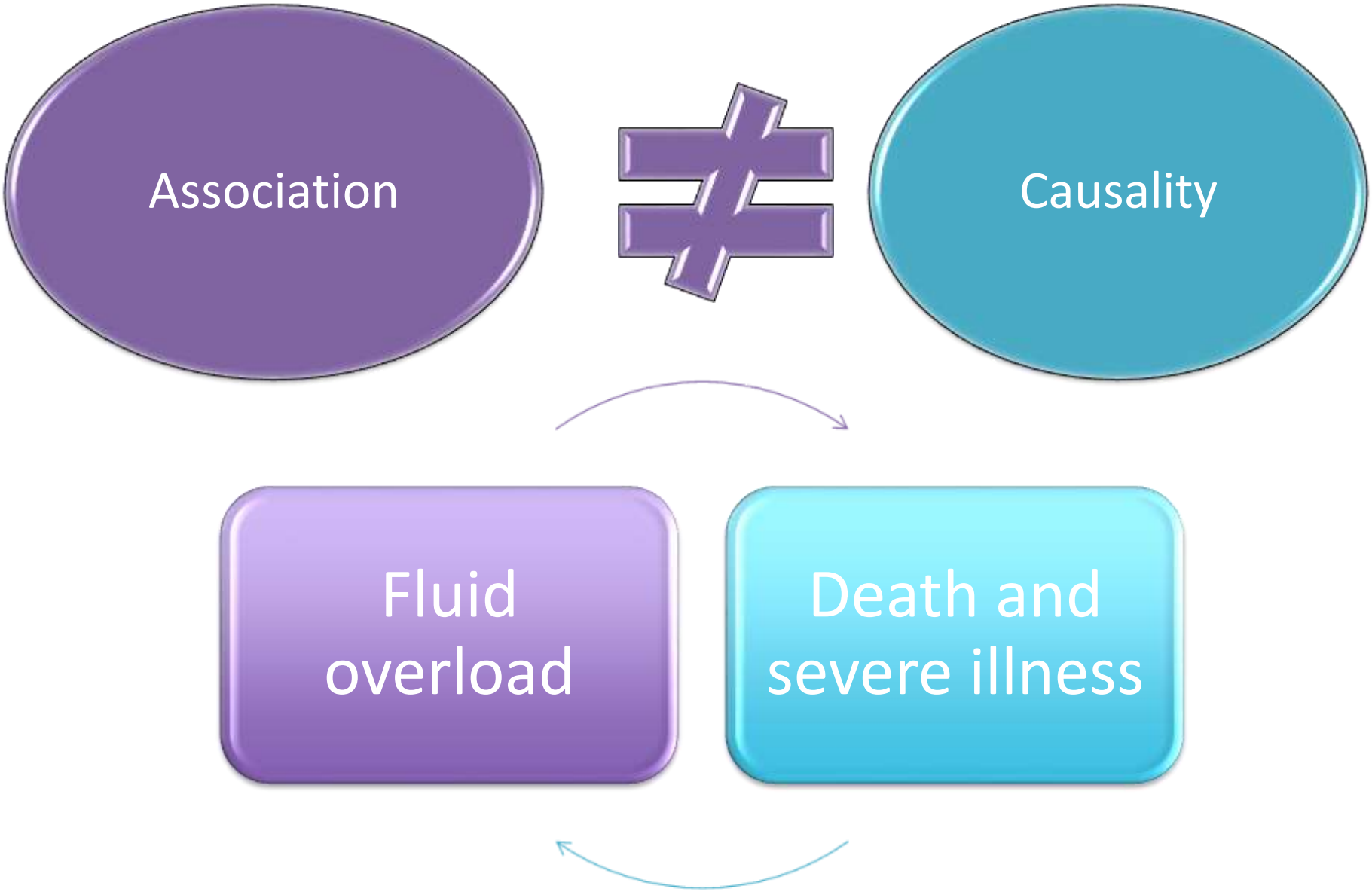


Fig. 5 Forest plot for ICU length of stay, conservative or deresuscitative fluid strategy versus standard care or liberal fluid strategy


Association
≠
Causality
Fluid overload
Death and severe illness

RESUSCITATION

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

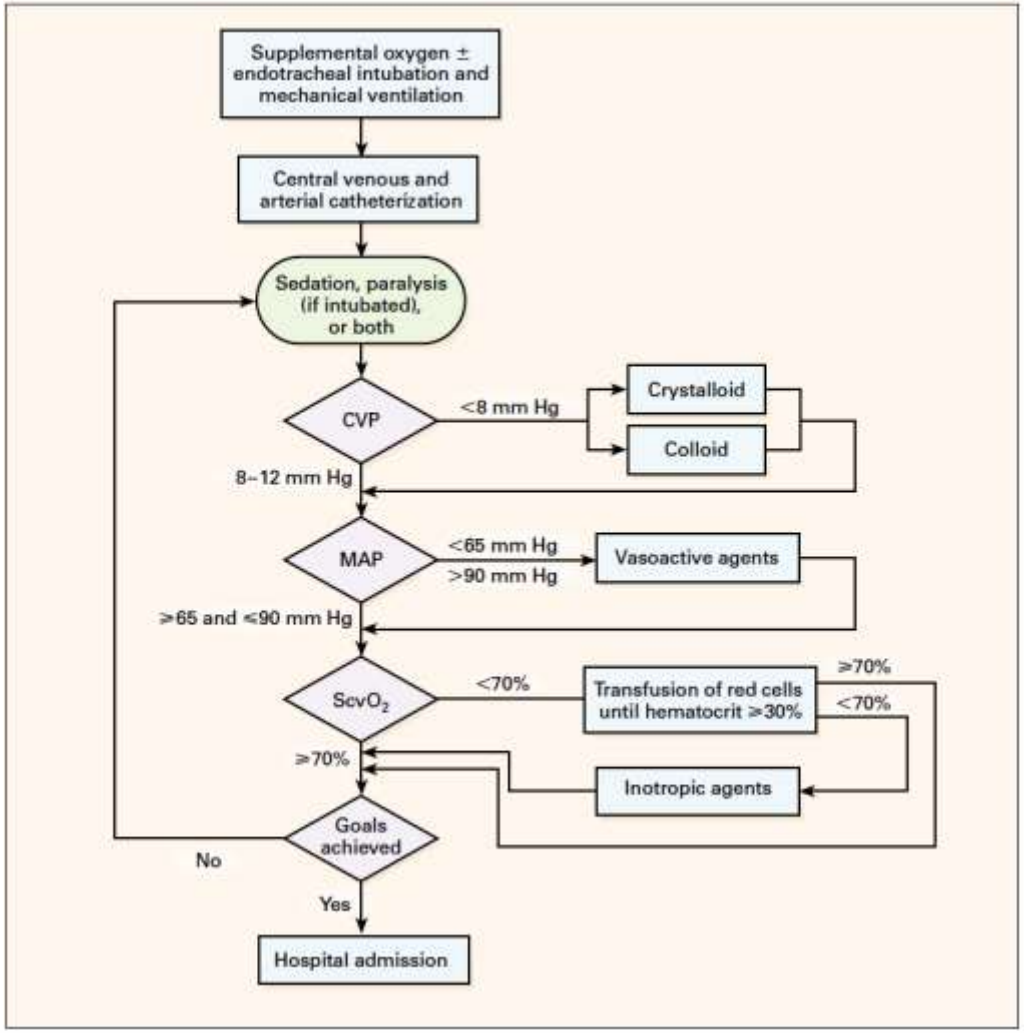


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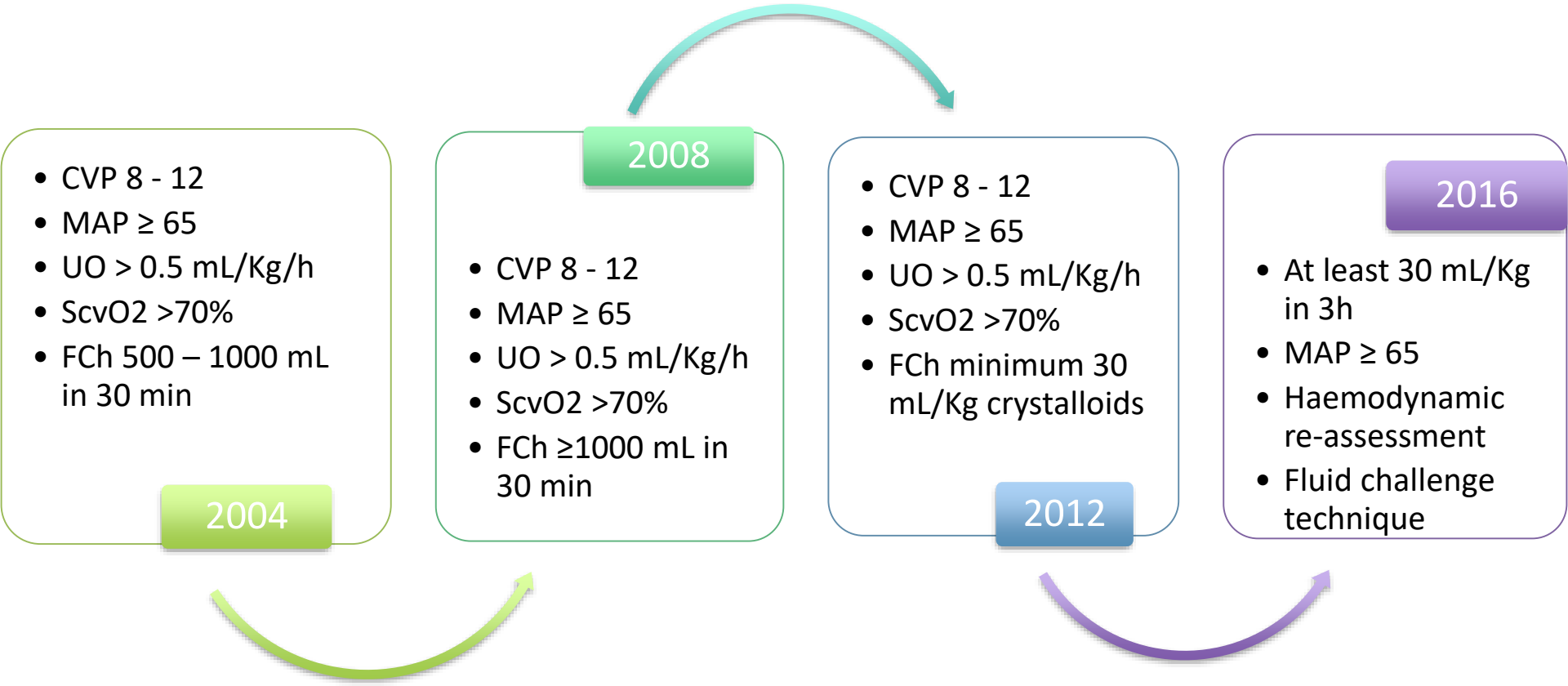
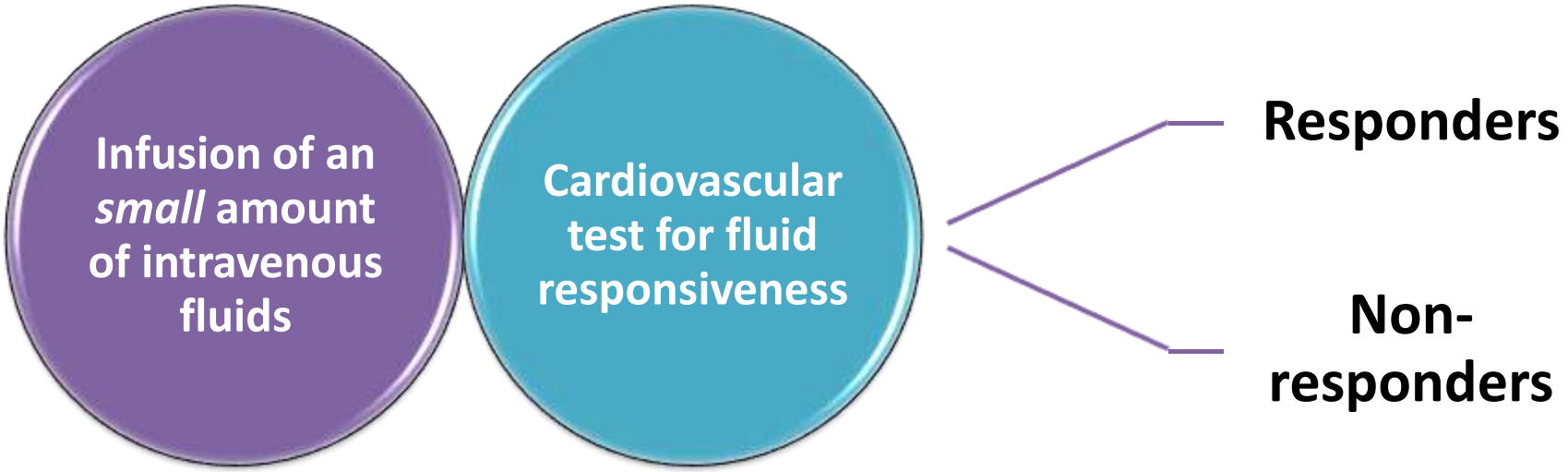
TABLE 4. TREATMENTS ADMINISTERED.*

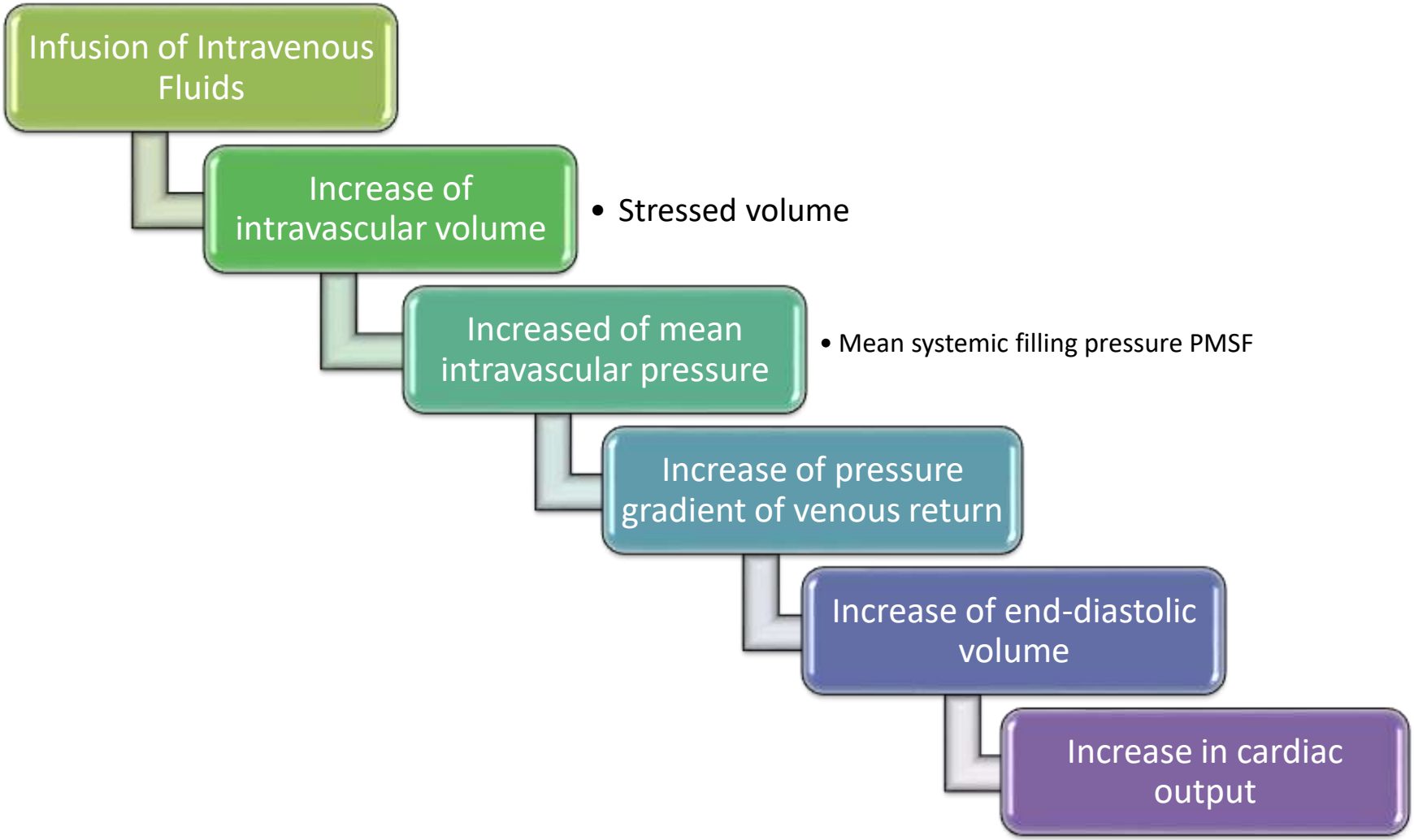
TREATMENT	HOURS AFTER THE START OF THERAPY		
	0–6	7–72	0–72
Total fluids (ml)			
Standard therapy	3499±2438	10,602±6,216	13,358±7,729
EGDT	4981±2984	8,625±5,162	13,443±6,390
P value	<0.001	0.01	0.73
Mechanical ventilation (%)			
Standard therapy	53.8	16.8	70.6
EGDT	53.0	2.6	55.6
P value	0.90	<0.001	0.02

Surviving sepsis campaign recommendation

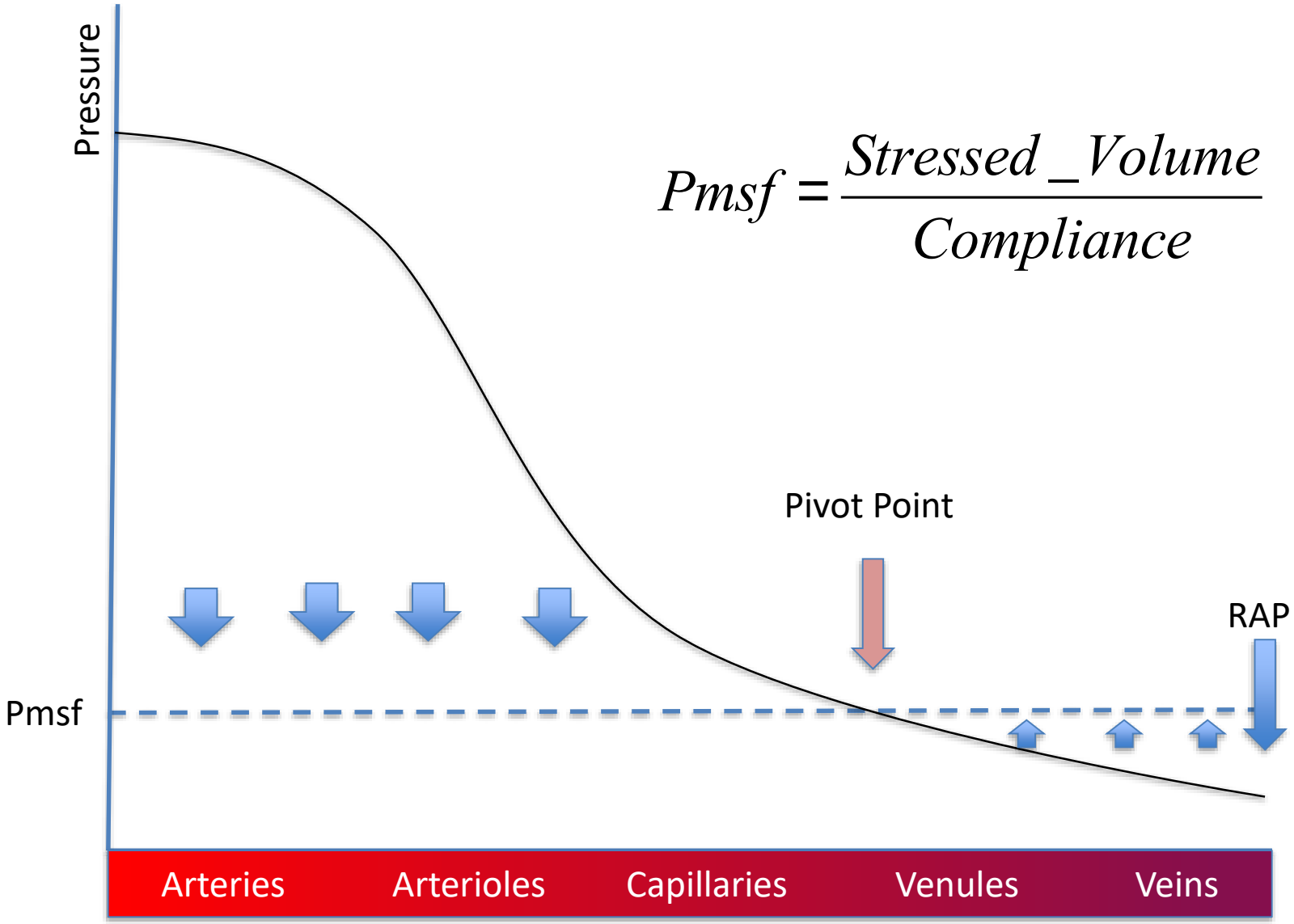


What is a fluid challenge?




Infusion of Intravenous Fluids
Increase of intravascular volume
• Stressed volume
Increased of mean intravascular pressure
• Mean systemic filling pressure PMSF
Increase of pressure gradient of venous return
Increase of end-diastolic volume
Increase in cardiac output

Mean systemic filling pressure

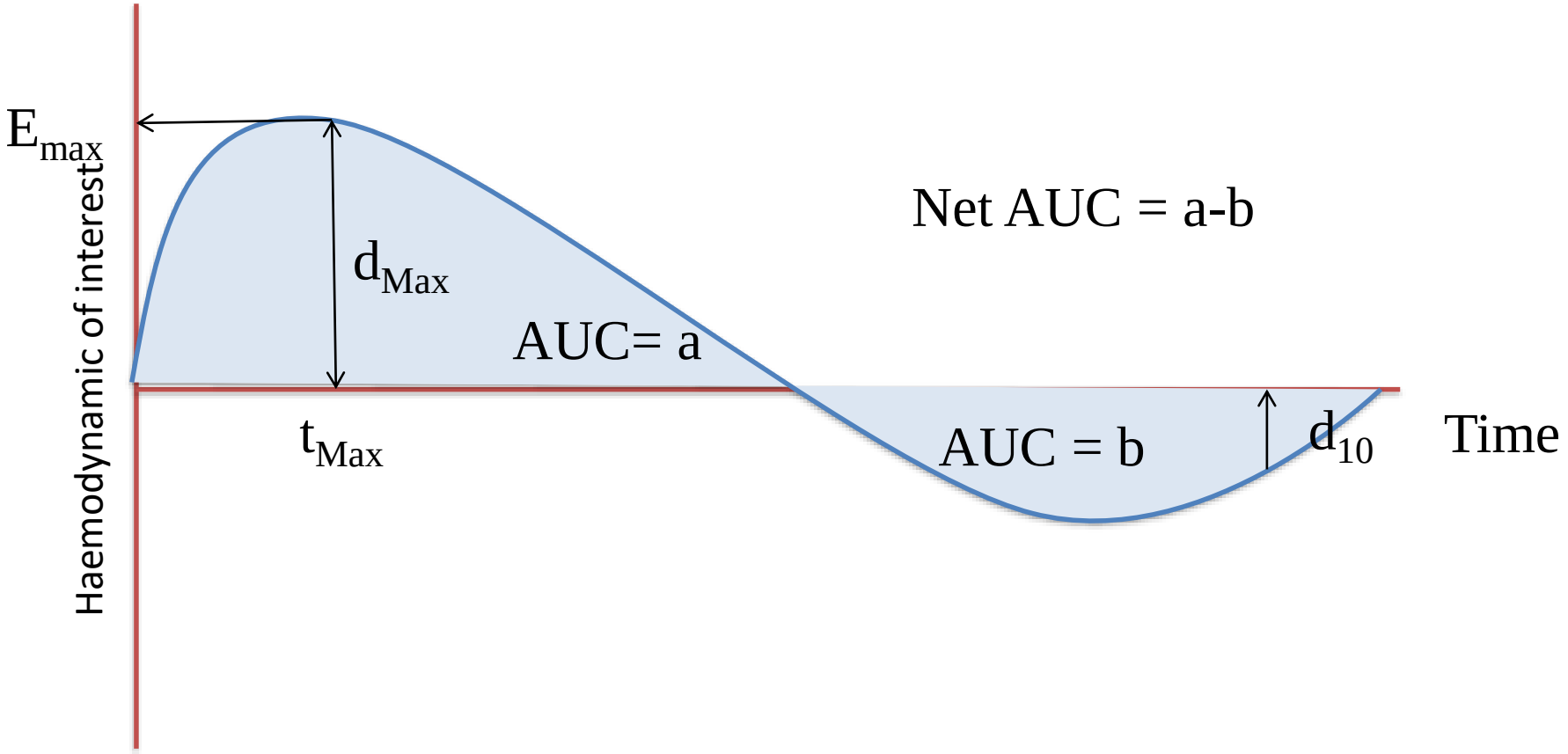


What is the **time course effect** of a fluid challenge?

Pharmacodynamics of a fluid challenge

- **50 Fluid challenges (250 mL Crystalloids) in 26 patients infused over 5 min**
  - No septics
  - No bleeding
- **Haemodynamics:**
  - arterial pressure
  - heart rate,
  - cardiac output (LiDCOplus),
  - CVP
  - Pmsa: Pmsf analogue (calculated by a computer)

Pharmacodynamic outcomes



Statistical analysis

- **Multi-level analysis**
- **Bayesian framework**
  - Probability >0.95 or < 0.05 = strong evidence
  - Probability > 0.79 or < 0.21 = fairly good evidence

RESULTS

Pharmacodynamic Analysis of a Fluid Challenge

Hollmann D. Aya, MD[1]; Irina Chis Ster, PhD[2]; Nick Fletcher, MD[1]; R. Michael Grounds, MD[1]; Andrew Rhodes, MD[1]; Maurizio Cecconi, MD[1]

TABLE 2. The Predicted Means in Each Group After a Fluid Challenge With Crystalloids, the Estimated Difference Between Groups Adjusted for the Baseline and the Bayesian Probability That the Difference Between Responders and Nonresponders Is Greater Than Zero

	Responders, Mean (95% CrI)	Nonresponders, Mean (95% CrI)	Δ(R – NR), Mean (95% CrI)	Probability (Δ(R – NR) > 0)
Mean arterial pressure				
AUC (mm Hg·min)	54.39 (18.14 to 88.82)	63.06 (29.04 to 97.06)	−8.67 (−57.70 to 38.72)	0.36
d_{max} (mm Hg)	9.35 (4.30 to 14.36)	12.15 (7.13 to 17.23)	−2.80 (−10.02 to 4.22)	0.21
T_{max} (min)	1.58 (−0.15 to 3.31)	4.50 (2.67 to 6.33)	−2.92 (−5.44 to −0.41)	0.01
E_{max} (mm Hg)	82.76 (77.71 to 87.77)	85.51 (80.49 to 90.59)	−2.75 (−9.97 to 4.28)	0.22
d_{10} (mm Hg)	3.84 (0.95 to 6.66)	4.22 (1.22 to 7.26)	−0.39 (−4.52 to 3.70)	0.43
Cardiac output				
AUC (L)	4.64 (2.63 to 6.64)	2.72 (1.12 to 4.39)	1.93 (−0.70 to 4.50)	0.93
d_{max} (mm Hg)	0.87 (0.51 to 1.22)	0.58 (0.27 to 0.90)	0.29 (−0.20 to 0.75)	0.89
T_{max} (min)	1.16 (−0.56 to 2.84)	3.77 (2.28 to 5.28)	−2.61 (−4.86 to −0.39)	0.01
E_{max} (mm Hg)	5.65 (5.29 to 6.00)	5.37 (5.06 to 5.69)	0.28 (−0.20 to 0.74)	0.88
d_{10} (mm Hg)	0.23 (−0.09 to 0.55)	0.15 (−0.12 to 0.43)	0.08 (−0.35 to 0.50)	0.65

TABLE 2. The Predicted Means in Each Group After a Fluid Challenge With Crystalloids, the Estimated Difference Between Groups Adjusted for the Baseline and the Bayesian Probability That the Difference Between Responders and Nonresponders Is Greater Than Zero

	Responders, Mean (95% CrI)	Nonresponders, Mean (95% CrI)	Δ(R − NR), Mean (95% CrI)	Probability (Δ(R − NR) > 0)
Pmsf analogue				
AUC (mm Hg·min)	21.78 (16.69 to 26.61)	23.31 (18.20 to 28.49)	−1.52 (−8.77 to 5.50)	0.34
d_{max} (mm Hg)	3.72 (2.74 to 4.66)	3.76 (2.80 to 4.70)	−0.03 (−1.38 to 1.30)	0.48
T_{max} (min)	1.50 (0.15 to 2.85)	2.73 (1.28 to 4.20)	−1.23 (−3.21 to 0.72)	0.11
E_{max} (mm Hg)	19.41 (18.43 to 20.35)	19.45 (18.49 to 20.39)	−0.04 (−1.38 to 1.30)	0.48
d_{10} (mm Hg)	1.69 (0.97 to 2.41)	1.68 (0.90 to 2.47)	0.01 (−1.05 to 1.07)	0.51
Central venous pressure				
AUC (mm Hg·min)	15.54 (9.55 to 21.36)	20.45 (14.69 to 26.49)	−4.91 (−13.45 to 3.30)	0.12
d_{max} (mm Hg)	3.02 (1.91 to 4.12)	3.49 (2.43 to 4.55)	−0.47 (−2.00 to 1.03)	0.27
T_{max} (min)	1.08 (−0.17 to 2.37)	1.71 (0.47 to 2.99)	−0.63 (−2.42 to 1.13)	0.23
E_{max} (mm Hg)	12.27 (11.16 to 13.38)	12.74 (11.69 to 13.80)	−0.47 (−2.00 to 1.03)	0.27
d_{10} (mm Hg)	1.16 (0.38 to 1.93)	1.58 (0.81 to 2.35)	−0.41 (−1.52 to 0.66)	0.22
Heart rate				
AUC (beats)	7.34 (−5.56 to 19.14)	11.04 (−4.52 to 26.48)	−3.71 (−23.39 to 15.69)	0.35
d_{max} (beats/min)	−1.53 (−3.43 to 0.22)	−0.57 (−2.78 to 1.65)	−0.96 (−3.80 to 1.82)	0.24
T_{max} (min)	2.52 (0.81 to 4.23)	1.72 (−0.21 to 3.71)	0.80 (−1.82 to 3.38)	0.73
E_{max} (beats/min)	83.26 (81.36 to 85.01)	84.21 (82.00 to 86.42)	−0.95 (−3.79 to 1.83)	0.25
d_{10} (beats/min)	0.62 (−1.02 to 2.28)	0.65 (−1.29 to 2.65)	−0.03 (−2.61 to 2.55)	0.49

This is a very small dose of fluids….

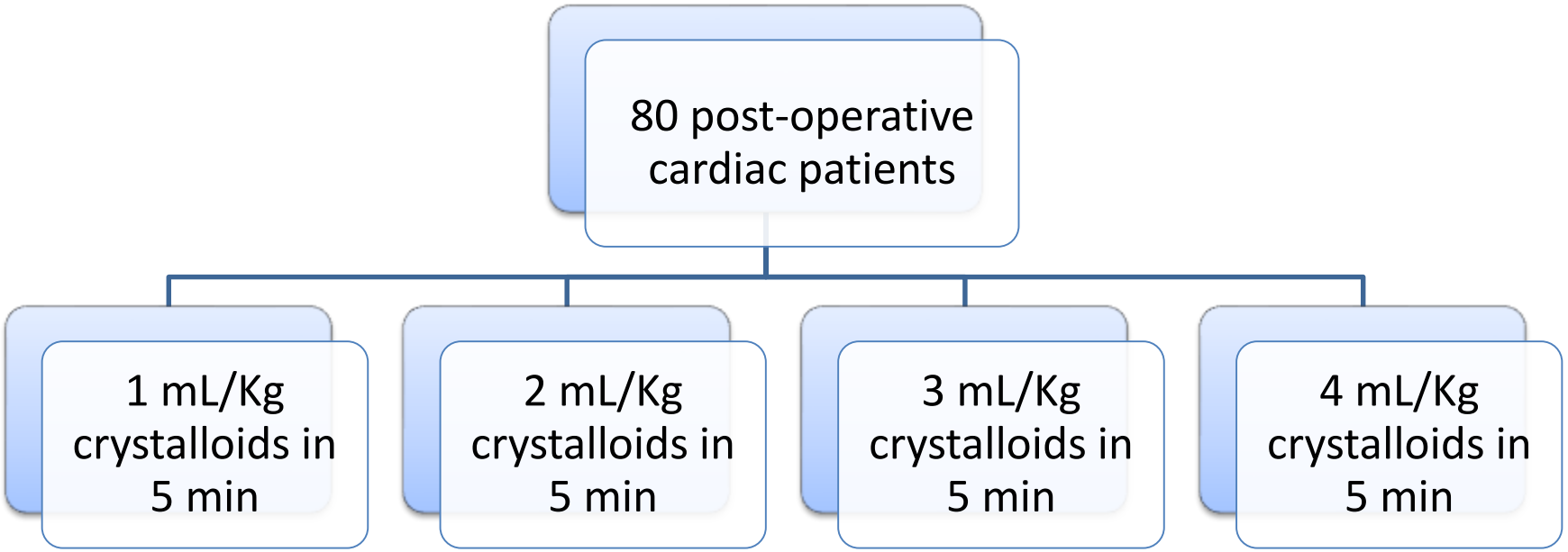
What is the minimal volume for a fluid challenge?

- **What is the minimal volume required to increase the Pmsf?**
- **May Different doses of fluids affect the changes in Cardiac Output?**
- **May different doses of fluids affect the proportion of responders and non-responders?**

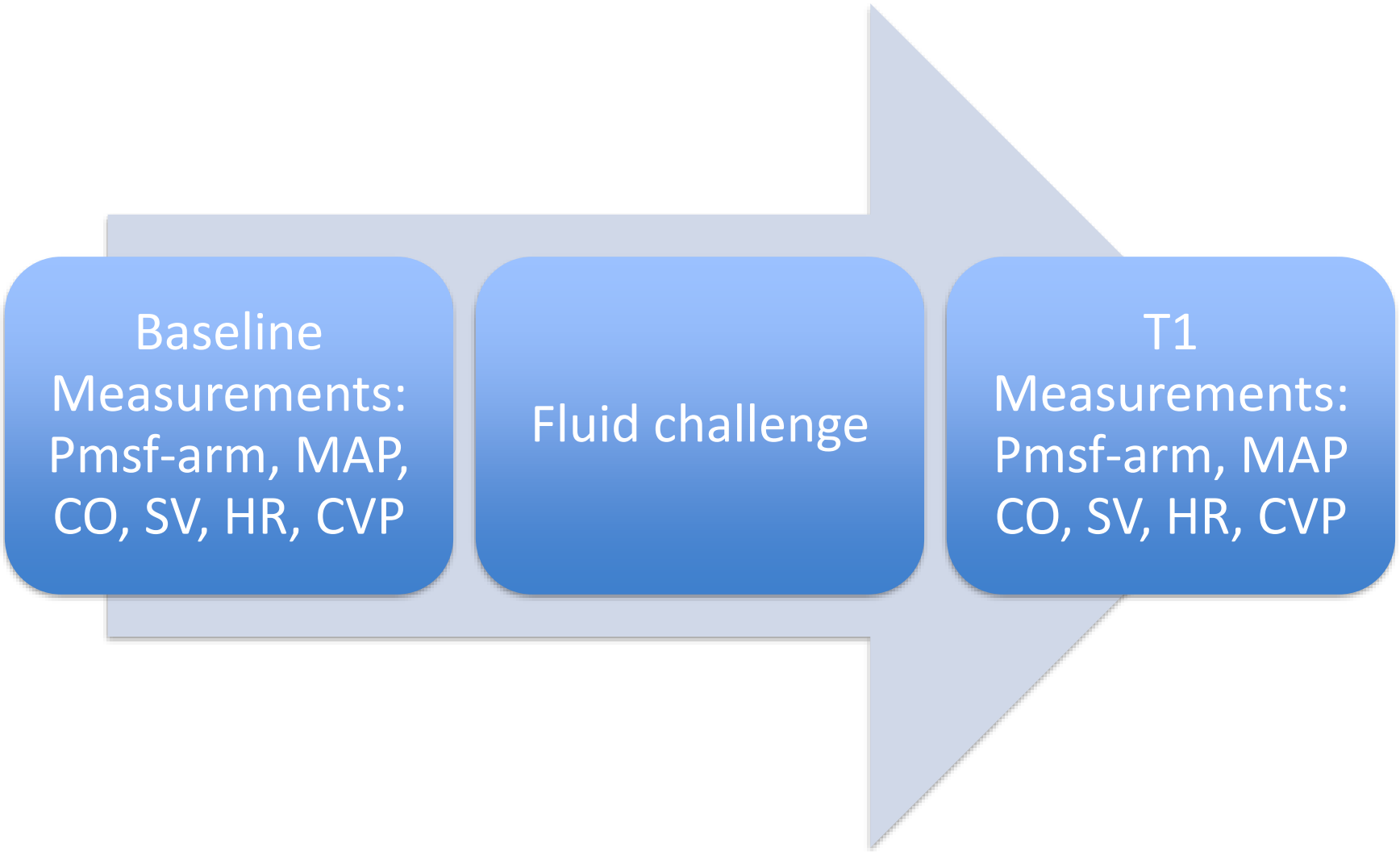
Hemodynamic Effect of Different Doses of Fluids for a Fluid Challenge: A Quasi-Randomized Controlled Study

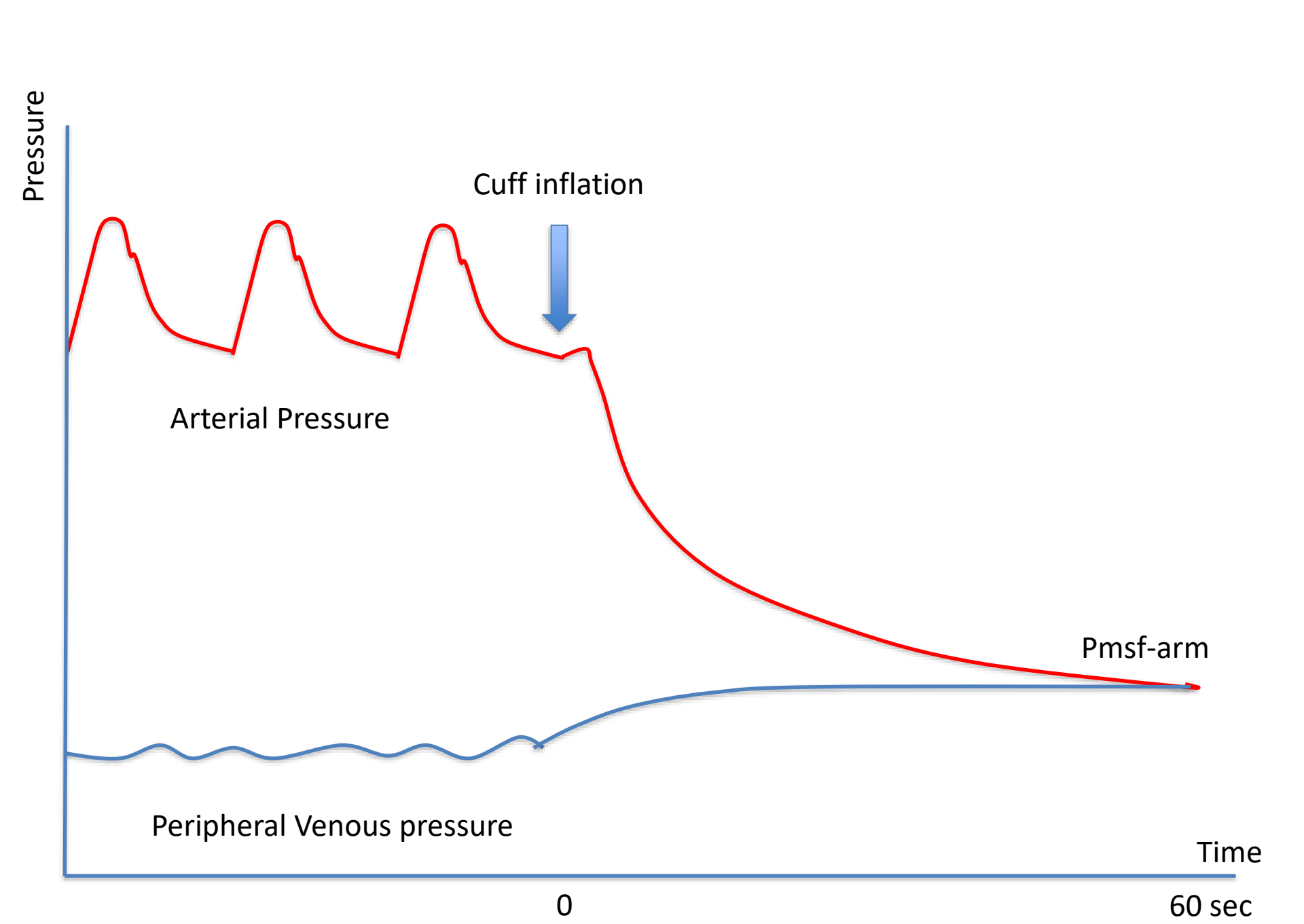
Hollmann D. Aya, MD[1]; Andrew Rhodes, MD(Res)[1]; Irina Chis Ster, PhD[2]; Nick Fletcher, MD(Res)[1]; R. Michael Grounds, MD(Res)[1]; Maurizio Cecconi, MD(Res)[1]

Methods


80 post-operative cardiac patients
1 mL/Kg crystalloids in 5 min
2 mL/Kg crystalloids in 5 min
3 mL/Kg crystalloids in 5 min
4 mL/Kg crystalloids in 5 min

Study protocol




Pressure
Cuff inflation
Arterial Pressure
Pmsf-arm
Peripheral Venous pressure
Time
0
60 sec

Transient stop-flow arm arterial–venous equilibrium pressure measurement: determination of precision of the technique

Hollmann D. Aya[1] · Andrew Rhodes[1] · Nick Fletcher[1] · R. Michael Grounds[1] · Maurizio Cecconi[1]

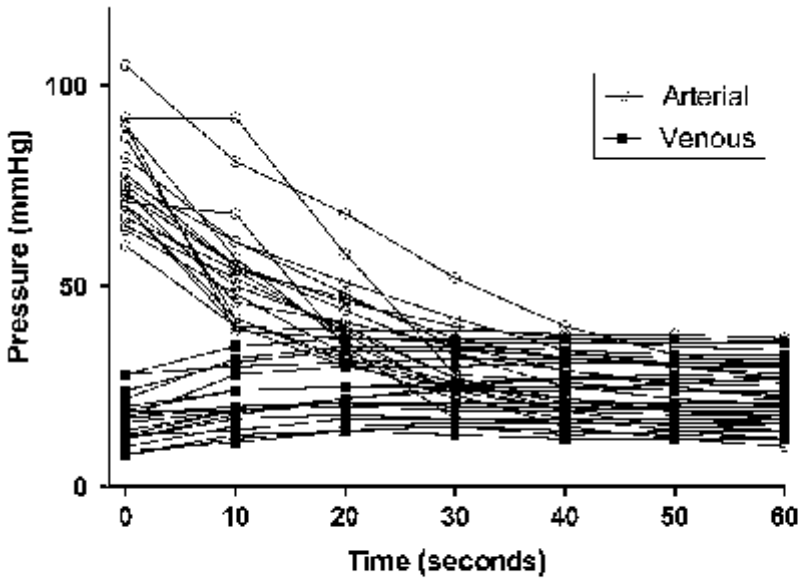


Fig. 1 Mean radial arterial pressure (Pa) and forearm venous pressure (Pv) during one cuff inflation

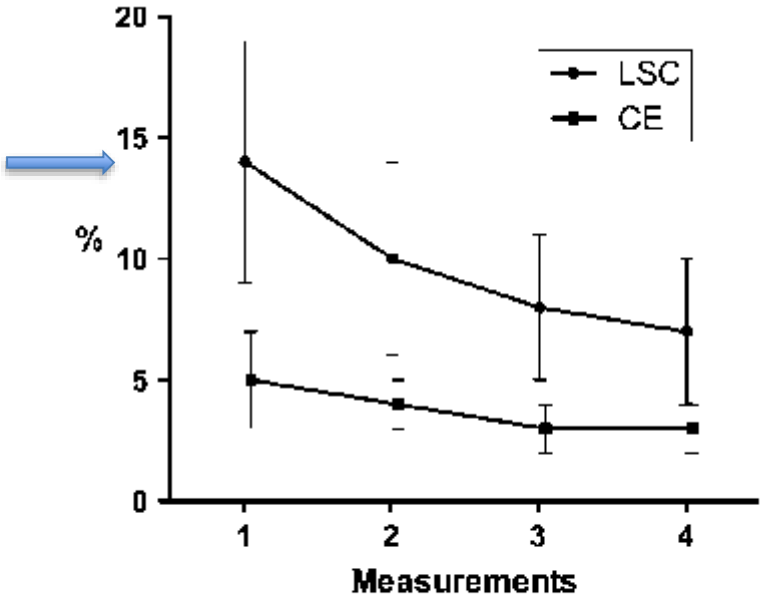
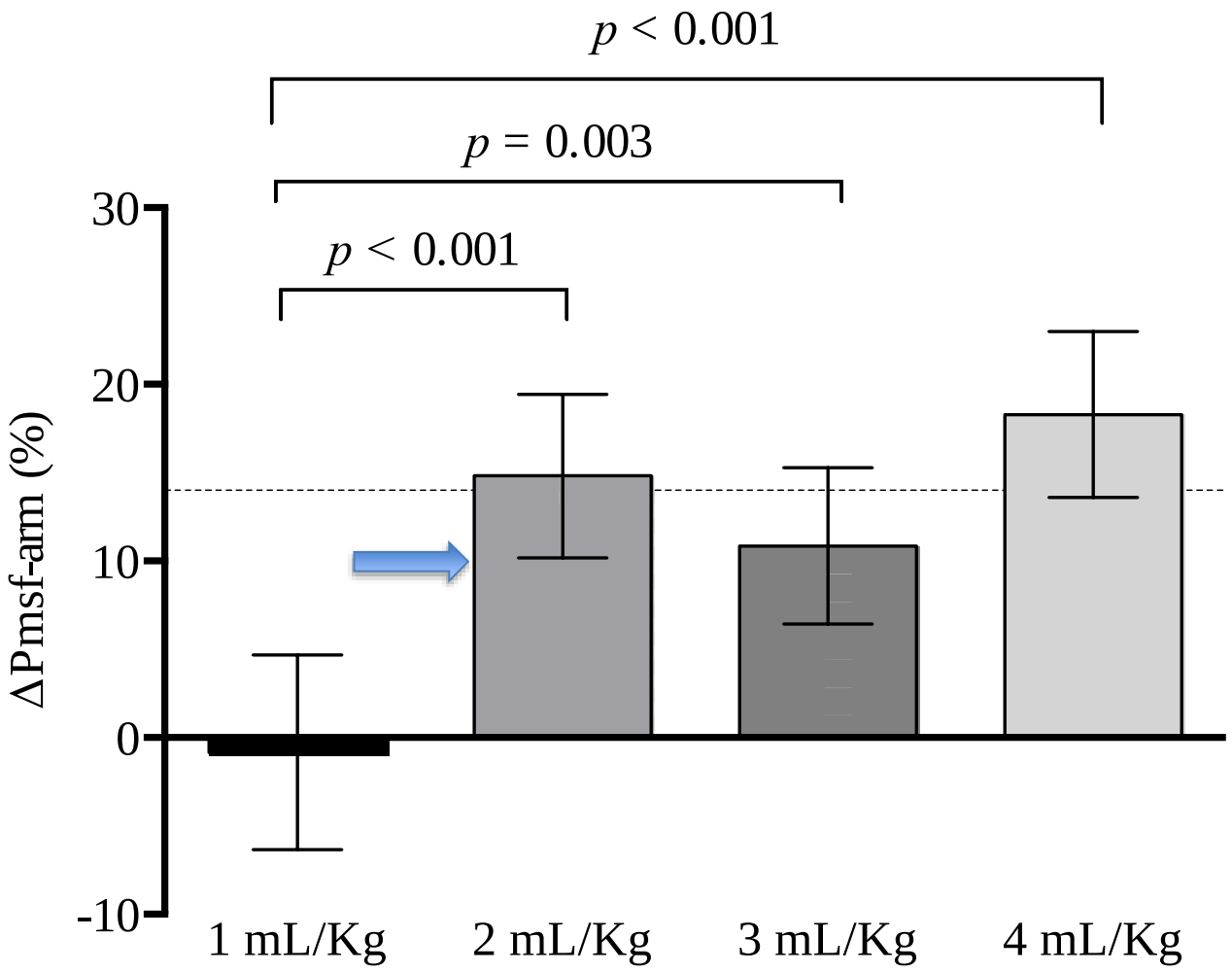
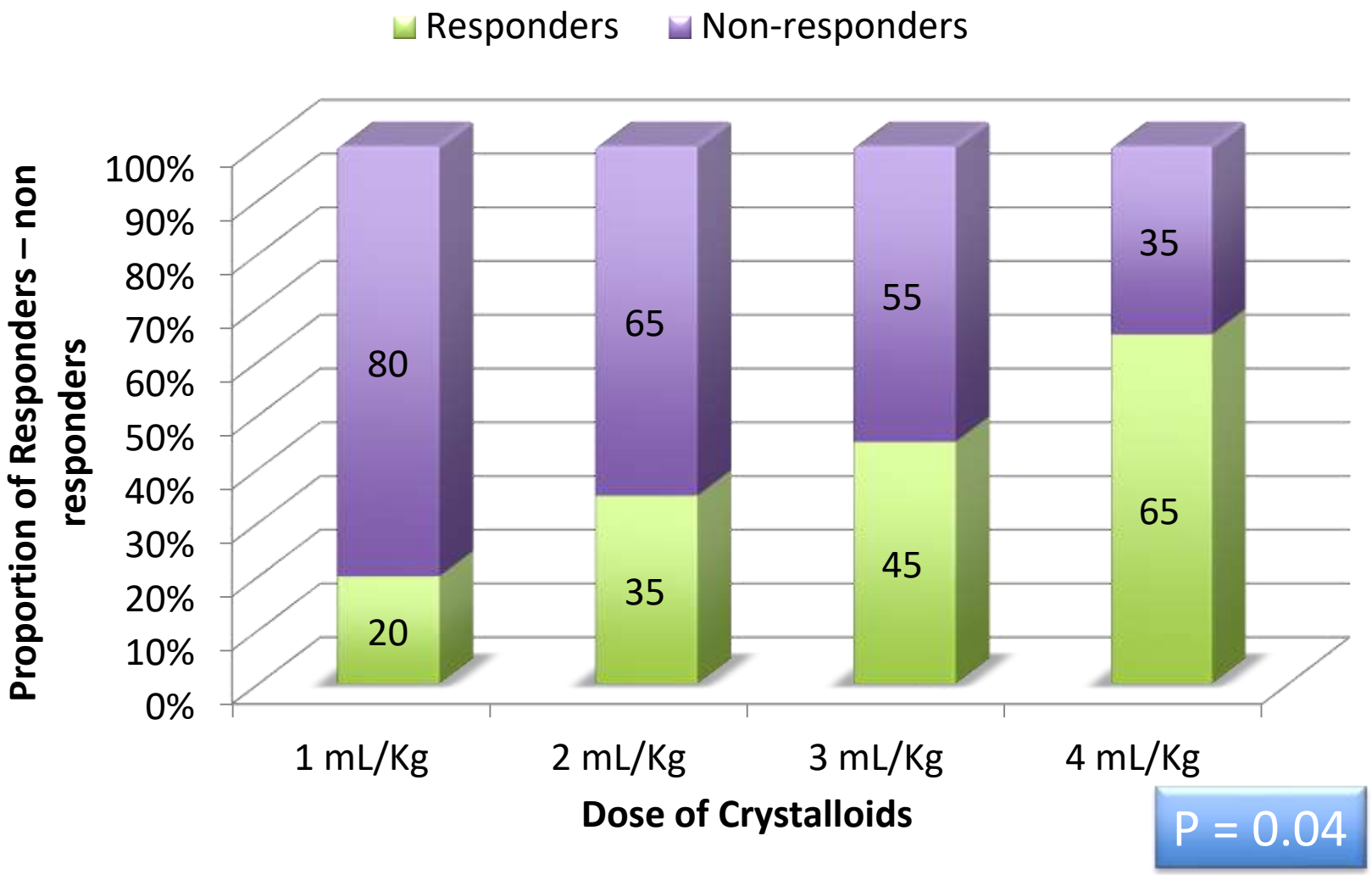


Fig. 3 Relationship between the least significant change (LSC) and coefficient error (CE) for the Pmsf-arm measurement technique and the number of replicates used to calculate the average

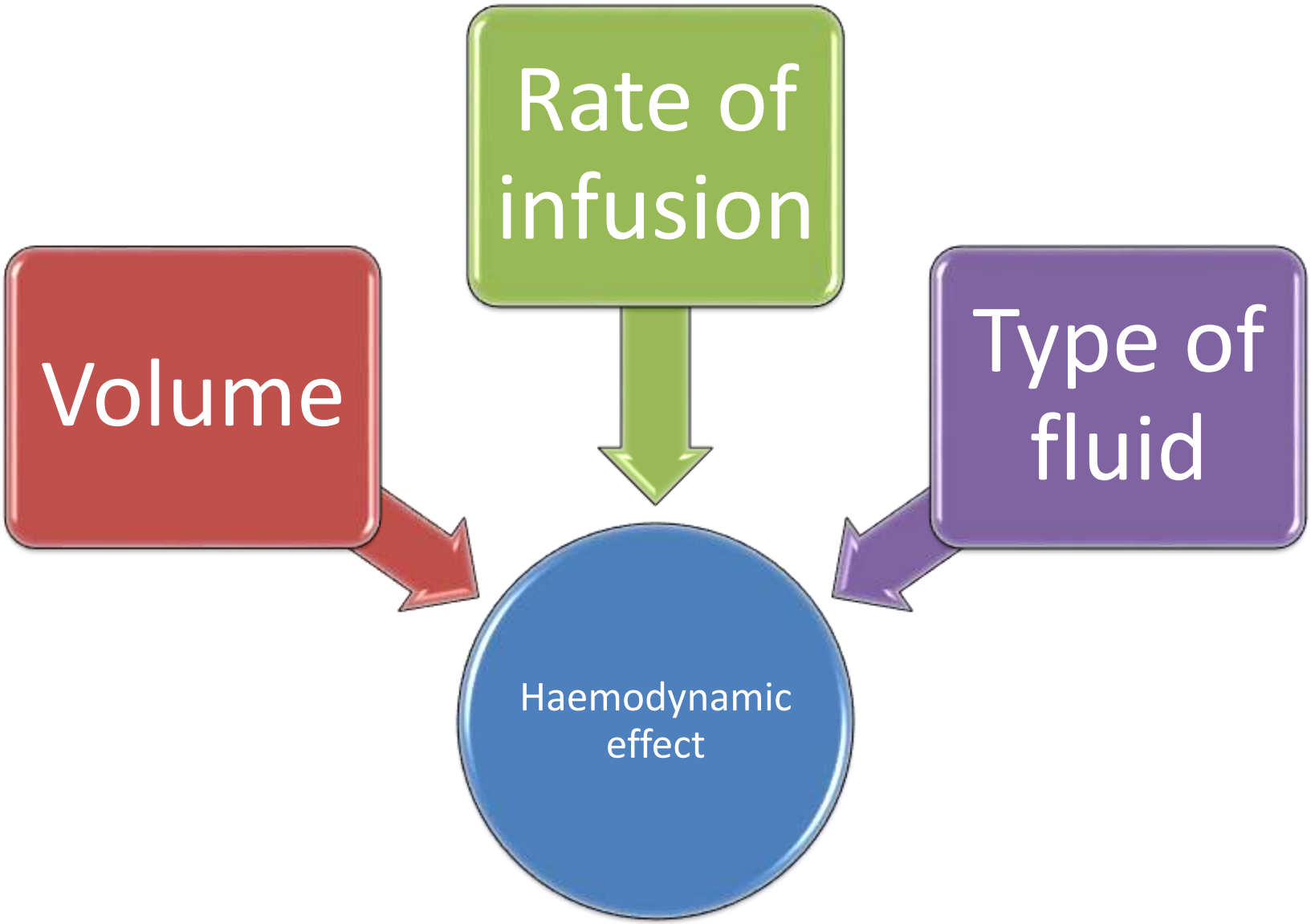
Change in Pmsf-arm by dose of crystalloids



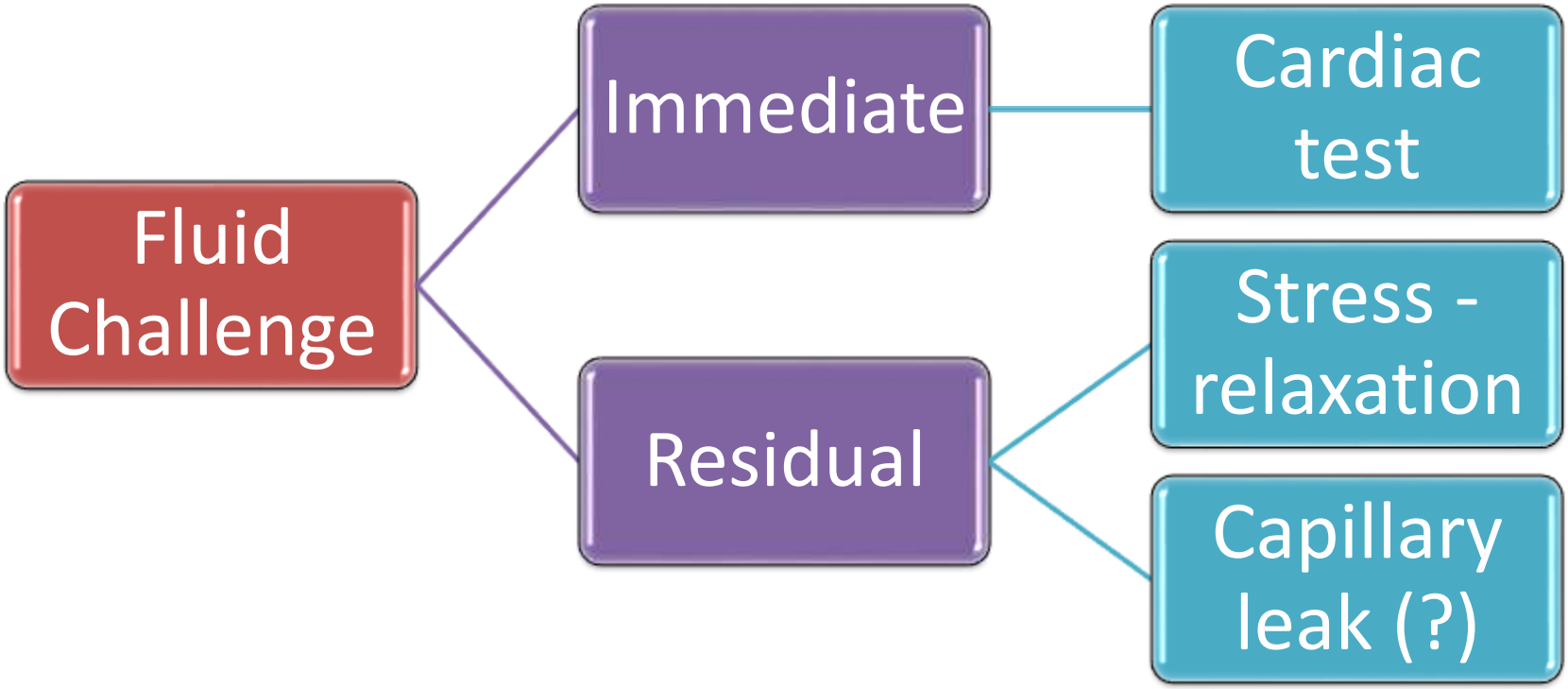
Percentage of responders and non-responders by dose of crystalloids in a fluid challenge



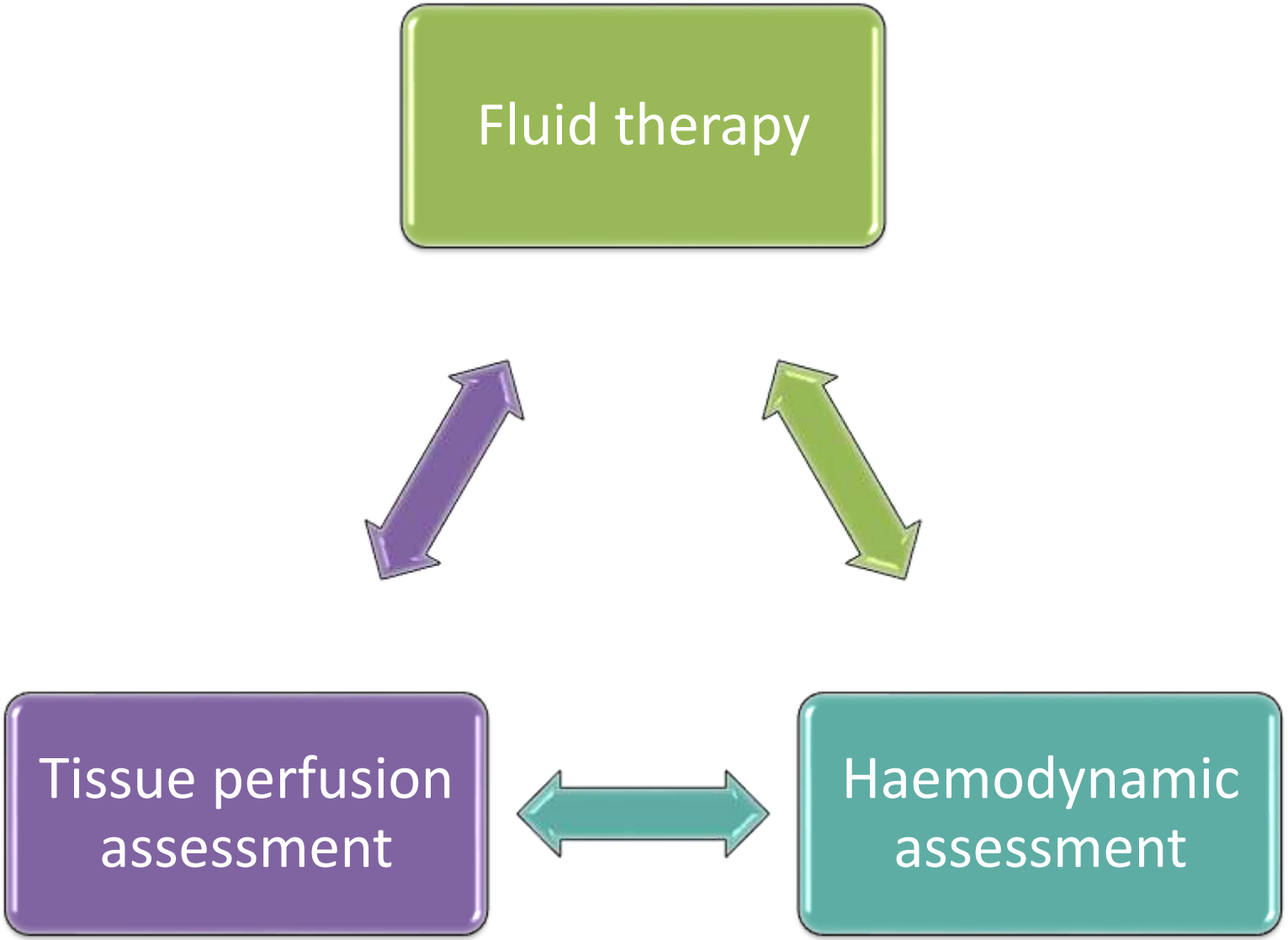
1. We need a standard technique



2 Points for interpretation



Conclusion


Fluid therapy
Tissue perfusion assessment
Haemodynamic assessment

Take home message 1

Do we need a de-resuscitation stage?

WHAT ABOUT A MORE CAUTIOUS RESUSCITATION?


thank you
danke
謝謝
ngiyabonga
teşekkür ederim
gracias
merci
obrigado
dziękuję
bedankt
go raibh maith agat
sukriya
kop khun krap
lerima kasih
arigatō
dakujem
grazie
takk
tapadh leat
mochchakkeram
mauruuru
hvala
sagolun
dank je
спасибо
рахмат
Баярлалаа
faafetai lava
kiitos
dankie
vinaka
blagodaram
barka
welalin
tack
mersi
spas
paldies
mahalo
matondo
misaotra
хвала
asante
manana
tenki
murakoze
mamnun
djiere dieuf
tau
enkosi
bayarlalaa
gracie
koszonom
akun
dankon
obrigado
sobodi
dekuji
mesi
didi madloba
najis tuke
kam sah hamnida
rahmat
rahmet
tanemirt
diolch
dhanyavadagalu
shukriya
merce
мерси
trugarez
xiexie
감사합니다
ευχαριστώ
chnorakaloutioun
gracies
sulpay
taiku
ありがとう
তোমাকে ধন্যবাদ