Association Between Fluid Balance and Outcomes in Critically Ill Children

A Systematic Review and Meta-analysis

Dr Nguyen Hoang Phuong Anh

Introduction

- Fluid therapy: cornerstone of resuscitation in Critically ill children
- Adequate volume using early aggresive fluid administration can be lifesaving.
- Critically ill children often receive “obligatory” fluid intake (nutrition, medication, and mainstenance fluid)

→ positive fluid balance.

- Many evidence suggests that fluid accumulation after initial resucitation may exert hazard for major morbidity and mortality.
- Defined as a fluid accumulation > 10% of baseline weight.
- It is an independent factor of worse outcome in ICU patients

→ importance of monitoring fluid status daily for avoidable fluid accumalation.

ORIGINAL INVESTIGATION

Association Between Fluid Balance and Outcomes in Critically Ill Children

A Systematic Review and Meta-analysis

Rashid Alobaidi, MD [1]; Catherine Morgan, MD, MSc [2]; Rajit K. Basu, MD [3]; Erin Stenson, MD [4]; Robin Featherstone, MLIS [5]; Sumit R. Majumdar, MD, MPH [6]; Sean M. Bagshaw, MD, MSc [7]

JAMA Pediatr. Published online January 22, 2018. doi:10.1001/jamapediatrics.2017.4540.

[+]Author Affiliations

ABSTRACT

Importance

After initial resuscitation, critically ill children may accumulate fluid and develop fluid overload. Accruing evidence suggests that fluid overload contributes to greater complexity of care and worse outcomes.

Objective

Question

- Is there an association between fluid balance and outcomes in critically ill children admitted to pediatric intensive care?

Main Outcomes and Measures

- Primary outcome: Mortality
- Secondary outcomes included treatment intensity, organ failure, and resource use.

- This systematic review and meta-analysis of 44 studies including 7507 children
- showed strong and consistent evidence of an association between fluid overload and poor outcomes in critically ill children.
- Including
  - worsening respiratory function
  - development of acute kidney injury,
  - longer pediatric intensive care stay
  - death.

Fluid Balance Assessment

- Peak percentage fluid overload (37)
- Peak percentage weight change (4)
- Net fluid balance in relation to weight (5)
- Net fluid balance in relation to body surface area (1)

- Despite many studies show the harmful effect of fluid overload on outcomes
- No consensus on how best to define it.
- Definition of fluid over load include 3 components
  - Methods of fluid balance assessment
  - Methods used to quantify fluid overload
  - Fluid Overload Definitions

Methods of fluid balance assessment

- Recorded daily intake-output
- Serial weight mesuarements

Methods used to quantify fluid overload

- Method: proposed by Goldstein and colleages most frequencently used.
- Method: % WEIGHT CHANGE

→Both methods clinically usefull.

% fluid overload= [(total fluid intake in Liters – total fluid Output in Liters)]/Admission Weight In Kilogram] x 100%

% weight change= [(current weight – admission Weight)/ admission Weight] X 100

Fluid Overload Definitions

- # threshold of 10% that used in studies and show association with worse outcomes.

Table 2. Fluid Overload Definitions

%FO Cutoff	Weight Used	Assessment Period		Source
		Start	End	
%FO>5%	Not specified	PICU admission	POD 1	Hassinger et al,[34] 2014
	PICU admission weight	PICU admission	24 h After admission	Chen et al,[24] 2016
	PICU admission weight	PICU admission	24 h After admission	Li et al,[6] 2016
	Hospital admission weight or the most recent PICU weight	Intraoperative	POD 2	Lex et al,[41] 2016
%FO>7%	Not specified	Intraoperative	POD 3	Park et al,[45] 2016
%FO>10%	PICU admission weight	PICU admission	CRRT initiation	Askenazi et al,[21] 2013; Boschee et al,[23] 2014; de Galasso et al,[27] 2016; Gillespie et al,[31] 2004; Selewski et al,[49] 2012; Sutherland et al,[51] 2010
	PICU admission weight	Not specified	CRRT initiation	Modem et al,[43] 2014
	Not specified	24 h Before CRRT	CRRT initiation	Elbahlawan et al,[28] 2010
	Hospital admission weight	Hospital admission	Not specified	Michael et al,[42] 2004
	Hospital admission weight	PICU admission	PICU day 2	Sinitsky et al,[50] 2015
	PICU admission weight	PICU admission	PICU day 3	Bhaskar et al,[5] 2015
	PICU admission weight	Not specified	Not specified	Sutawan et al,[52] 2016
	Preoperative weight	PICU admission	PICU day 7	Hazle et al,[10] 2013
	PICU admission weight	PICU admission	PICU discharge	Ketharanathan et al,[40] 2014
	Not specified	PICU admission	PICU discharge	Naveda et al,[44] 2016
%FO>13%	Not specified	PICU admission	PICU day 2	Vidal et al,[54] 2016
%FO>15%	PICU admission weight	PICU admission	14d	Arikan et al,[20] 2012
%FO>20%	PICU admission weight	PICU admission	PICU discharge	Diaz et al,[26] 2017
	PICU admission weight	PICU admission	CRRT initiation	Askenazi et al,[21] 2013; Goldstein et al,[32] 2005; Jhang et al,[38] 2014; Selewski et al,[49] 2012; Sutherland et al,[51] 2010
	PICU admission weight	Not specified	CRRT initiation	Modem et al,[43] 2014
	Hospital admission weight	PICU admission	CRRT initiation	Hayes et al,[35] 2009
	Hospital admission weight	PICU admission	PICU day 2	Sinitsky et al,[50] 2015
	Preoperative weight	PICU admission	PICU day 7	Hazle et al,[10] 2013

Result

- The proportion of children with fluid overload varied by case mix and fluid overload definition (median, 33%; range, 10%-83%).
- Maximum percentage fluid overload was achieved on day 5.7 (±4.2) after PICU admission in cohort pts mechanical ventilation.
- In pts with cardiac surgery, percentage fluid overload within the first 24-48h after surgery.

Mortality

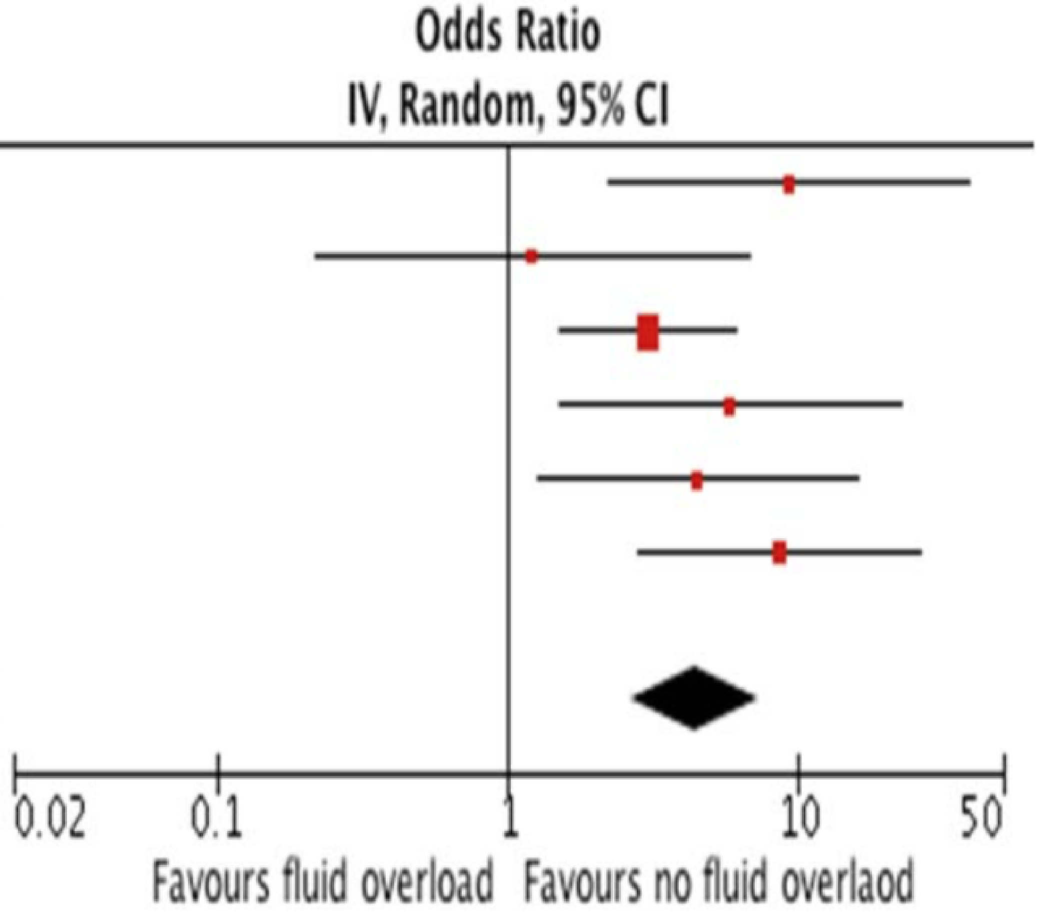
- Fluid overload associated with increased in-hospital mortality (17 studies [n = 2853]; odds ratio [OR], 4.34 [95% CI, 3.01-6.26]; I^2 = 61%).
- Survivors had lower percentage fluid overload than nonsurvivors (22 studies [n = 2848]; mean difference, −5.62 [95% CI, −7.28 to −3.97]; I^2 = 76%).
- After adjustment for illness severity, every 1% increase in percentage fluid overload → 6% increase mortality (11 studies [n = 3200]; adjusted OR, 1.06 [95% CI, 1.03-1.10]; I^2 = 66%).

eFigure 2. Association Between FO (Categorical Exposure) and Mortality in Studies Adjusting for Severity of Illness

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Bhaskar, 2015	2.2159	0.7237	11.5%	9.17 [2.22, 37.88]
de Galasso 2016	0.1906	0.8721	8.2%	1.21 [0.22, 6.69]
Gillespie, 2004	1.1053	0.357	36.0%	3.02 [1.50, 6.08]
Hayes, 2009	1.7579	0.69	12.5%	5.80 [1.50, 22.43]
Jhang, 2014	1.4956	0.6452	14.1%	4.46 [1.26, 15.80]
Sutherland 2010	2.1401	0.5666	17.7%	8.50 [2.80, 25.81]
Total (95% CI)			**100.0%**	**4.38 [2.64, 7.28]**

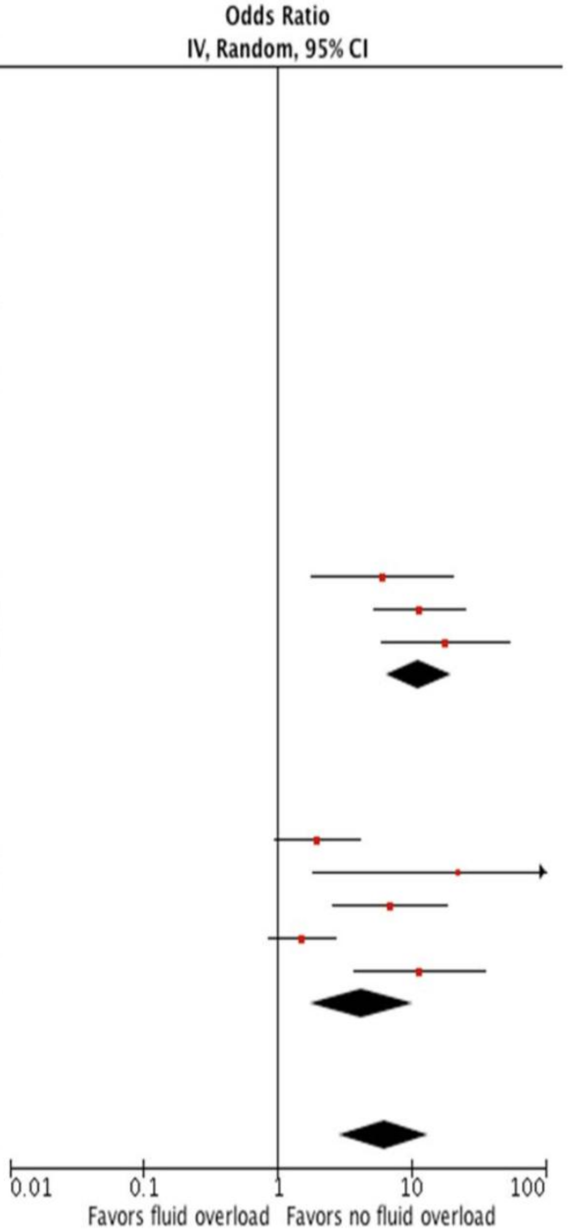
Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 5.83$, df = 5 ($P = 0.32$); $I^2 = 14\%$

Test for overall effect: $Z = 5.71$ ($P < 0.00001$)



eFigure 3. Association Between Fluid Overload (Categorical Exposure) and Mortality Omitting Studies of Children Receiving CRRT

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.2.1 CRRT				
de Galasso 2016	1.0963	0.3765	0.0%	2.99 [1.43, 6.26]
Elbahlawan 2010	-0.2719	1.244	0.0%	0.76 [0.07, 8.73]
Gillespie 2004	1.1053	0.357	0.0%	3.02 [1.50, 6.08]
Hayes, 2009	1.8036	0.5252	0.0%	6.07 [2.17, 17.00]
Jhang, 2014	1.4956	0.6452	0.0%	4.46 [1.26, 15.80]
Michael 2004	1.9459	0.8997	0.0%	7.00 [1.20, 40.82]
Modem 2014	0.9442	0.3021	0.0%	2.57 [1.42, 4.65]
Selewski 2012	1.0922	0.7478	0.0%	2.98 [0.69, 12.91]
Sutherland 2010	1.3604	0.2643	0.0%	3.90 [2.32, 6.54]
Subtotal (95% CI)				**Not estimable**
Heterogeneity: Not applicable				
Test for overall effect: Not applicable				
1.2.2 Sepsis/Shock				
Bhaskar, 2015	1.7971	0.6228	11.8%	6.03 [1.78, 20.45]
Chen 2016	2.4368	0.4052	14.3%	11.44 [5.17, 25.30]
Naveda 2016	2.8856	0.5574	12.5%	17.91 [6.01, 53.41]
Subtotal (95% CI)			**38.6%**	**11.24 [6.37, 19.85]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.70$, df = 2 (P = 0.43); $I^2 = 0\%$				
Test for overall effect: Z = 8.34 (P < 0.00001)				
1.2.4 General				
Diaz 2017	0.6799	0.3777	14.6%	1.97 [0.94, 4.14]
Ketharanathan 2014	3.1023	1.2792	6.0%	22.25 [1.81, 273.00]
Li 2016	1.9313	0.4969	13.2%	6.90 [2.60, 18.27]
Sinitsky 2015	0.4152	0.2926	15.4%	1.51 [0.85, 2.69]
Sutawan 2016	2.4384	0.579	12.3%	11.45 [3.68, 35.63]
Subtotal (95% CI)			**61.4%**	**4.22 [1.73, 10.30]**
Heterogeneity: $Tau^2 = 0.72$; $Chi^2 = 17.10$, df = 4 (P = 0.002); $I^2 = 77\%$				
Test for overall effect: Z = 3.17 (P = 0.002)				
Total (95% CI)			**100.0%**	**6.20 [2.89, 13.28]**
Heterogeneity: $Tau^2 = 0.90$; $Chi^2 = 35.06$, df = 7 (P < 0.0001); $I^2 = 80\%$				
Test for overall effect: Z = 4.69 (P < 0.00001)				
Test for subgroup differences: $Chi^2 = 3.29$, df = 1 (P = 0.07), $I^2 = 69.6\%$				



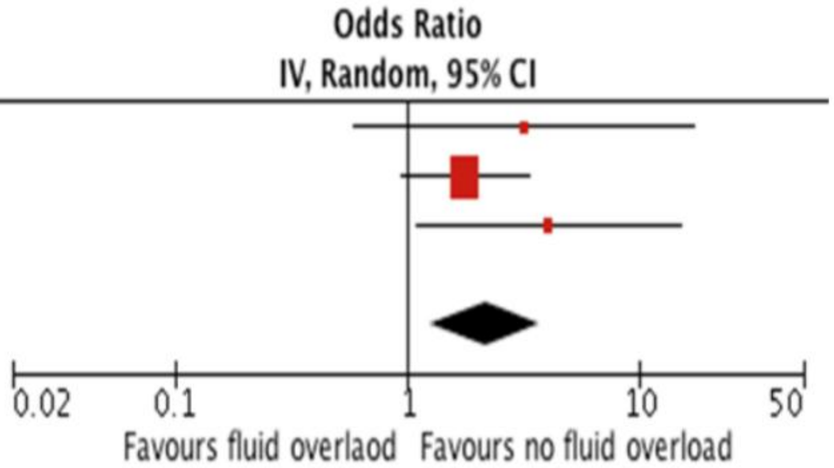
Prolonged mechanical ventilation

eFigure 8. Random-Effects Meta-analysis of FO and Prolonged Mechanical Ventilation

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Hassinger 2014	1.1474	0.8633	10.1%	3.15 [0.58, 17.11]
Li 2016	0.5653	0.32	73.3%	1.76 [0.94, 3.30]
Vidal 2016	1.3913	0.6706	16.7%	4.02 [1.08, 14.96]
Total (95% CI)			**100.0%**	**2.14 [1.25, 3.66]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.46$, $df = 2$ ($P = 0.48$); $I^2 = 0\%$

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



Fluid overload was associated with increased risk for prolonged mechanical ventilation (>48 hours) (3 studies [n = 631]; OR, 2.14 [95% CI, 1.25-3.66]; $I^2 = 0\%$)

Acute kidney injury

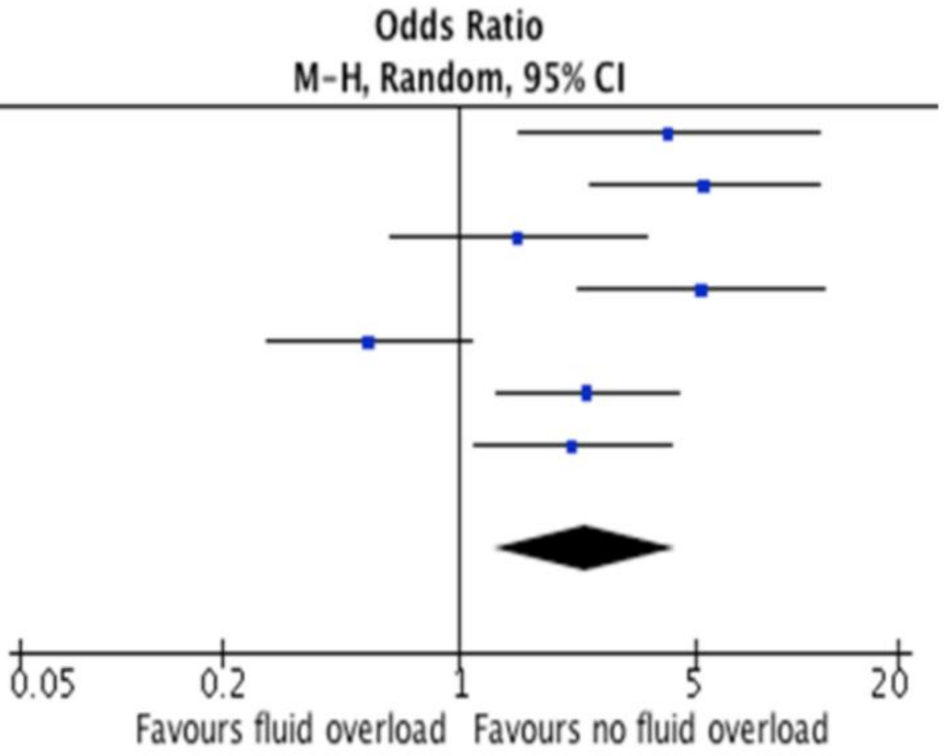
Acute kidney injury (7 studies [n = 1833]; OR, 2.36 [95% CI, 1.27-4.38]; I^2 = 78%).

eFigure 9. Random-Effects Meta-analysis of FO and Acute Kidney Injury

Study or Subgroup	Fluid overload Events	Fluid overload Total	No Fluid overload Events	No Fluid overload Total	Weight	Odds Ratio M-H, Random, 95% CI
Bhaskar, 2015	13	42	7	72	12.4%	4.16 [1.50, 11.52]
Chen 2016	17	41	19	161	14.3%	5.29 [2.42, 11.60]
Hassinger 2014	13	30	23	68	13.5%	1.50 [0.62, 3.61]
Li 2016	12	64	13	306	13.9%	5.20 [2.25, 12.03]
Park 2016	14	46	78	174	15.1%	0.54 [0.27, 1.08]
Seguin 2014	32	65	37	128	15.7%	2.38 [1.28, 4.43]
Sinitsky 2015	18	208	18	428	15.2%	2.16 [1.10, 4.24]
Total (95% CI)		**496**		**1337**	**100.0%**	**2.36 [1.27, 4.38]**
Total events	119		195			

Heterogeneity: $Tau^2 = 0.54$; $Chi^2 = 27.14$, df = 6 (P = 0.0001); $I^2 = 78\%$

Test for overall effect: Z = 2.72 (P = 0.007)



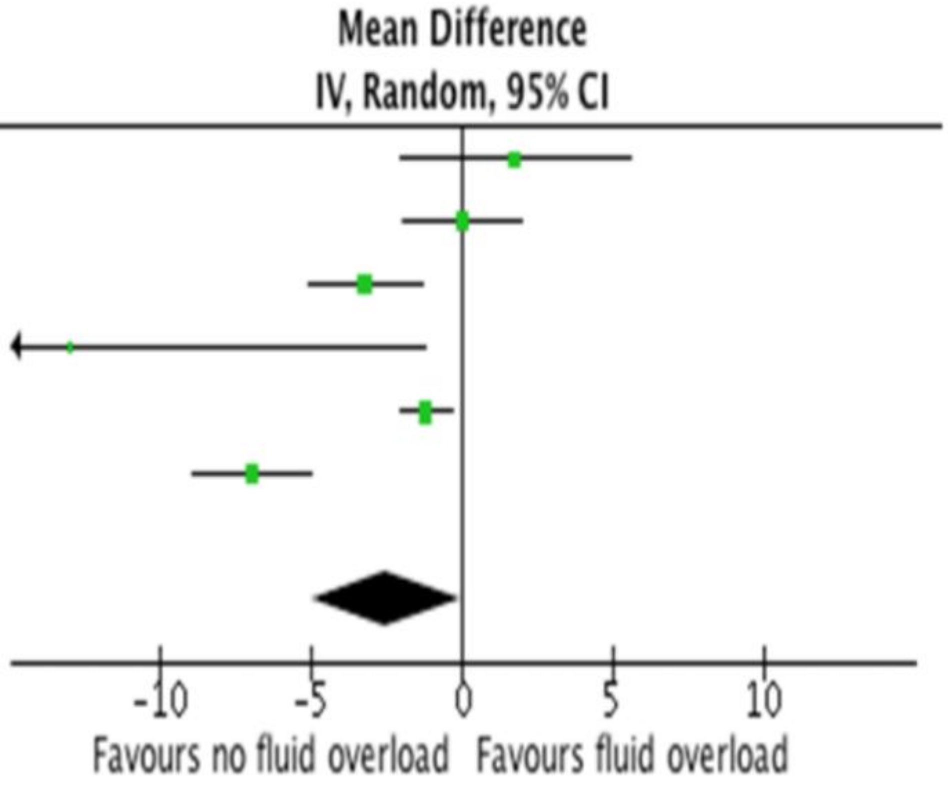
PICU Lenght of Stay

eFigure 10. Random-Effects Meta-analysis of FO and PICU Length of Stay

	No fluid overload			Fluid overload				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Bhaskar, 2015	17.5	8.6	72	15.75	10.75	42	14.7%	1.75 [-2.06, 5.56]
Chen 2016	5.7	4.6	161	5.7	5.9	41	19.8%	0.00 [-1.94, 1.94]
Hassinger 2014	5.8	2.96	68	9.02	4.85	30	20.0%	-3.22 [-5.09, -1.35]
Hayes, 2009	18.5	10.5	34	31.5	16.25	8	3.7%	-13.00 [-24.80, -1.20]
Li 2016	2.4	2.43	298	3.6	3.14	54	22.0%	-1.20 [-2.08, -0.32]
Seguin 2014	4.7	2.8	128	11.7	7.9	65	19.7%	-7.00 [-8.98, -5.02]
Total (95% CI)			**761**			**240**	**100.0%**	**-2.51 [-4.99, -0.03]**

Heterogeneity: $Tau^2 = 7.07$; $Chi^2 = 40.38$, df = 5 ($P < 0.00001$); $I^2 = 88\%$

Test for overall effect: $Z = 1.99$ ($P = 0.05$)



Conclusions and Relevance

- Fluid overload is common and is associated with substantial morbidity and mortality in critically ill children.
- A threshhold may exist beyond which fluid accumulation becomes unhelpful or frankly harmful.
- Clinicians should monitor fluid balance and consider the hazard associated with avoidable fluid acucumulation and overload.