

## Supplementary Online Content

Alobaidi R, Morgan C, Basu RK, et al. Association between fluid balance and outcomes in critically ill children: a systematic review and meta-analysis. *JAMA Pediatr*. Published online January 22, 2018. doi: 10.1001/jamapediatrics.2017.4540

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Search Strategy**

<b>Database: Epub Ahead of Print, In-Process &amp; Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present</b>	
1. Acute Kidney Injury/	42. (respiratory care adj (department* or unit* or ward or wards)).tw,kf.
2. Acute Lung Injury/	43. respiratory failure.tw,kf.
3. exp Cardiac Surgical Procedures/	44. RRT.tw,kf.
4. exp Critical Care/	45. (sepsis or septic*).tw,kf. 46. transplant*.tw,kf.
5. Critical Illness/	47. or/1-46
6. Heart Defects, Congenital/su	48. Body Fluids/
7. exp Intensive Care Units/	49. Diuretics/
8. Kidney/in	50. Fluid Therapy/
9. Multiple Organ Failure/	51. exp Solutions/ad, ae
10. Multiple Trauma/	52. Water-Electrolyte Imbalance/
11. exp Organ Transplantation/	53. Water Intoxication/
12. Postoperative Complications/	54. diuretic*.tw,kf.
13. exp Renal Replacement Therapy/	55. (fluid* adj1 (accumulat* or administ* or balance or excess* or imbalance or manag* or over load* or overload* or retain* or retention or remov*)).tw,kf.
14. Respiration, Artificial/	56. or/48-55
15. Respiratory Insufficiency/	57. exp Adolescent/
16. exp Sepsis/	58. exp Child/
17. Transplant Recipients/	59. exp Infant/
18. Transplantation/	60. exp Infant, Newborn Diseases/
19. Transplants/	61. exp Infant, Premature, Diseases/
20. (acute kidney adj (failure or injur* or insufficien*)).tw,kf.	62. exp Minors/
21. acute lung injur*.tw,kf.	63. Neonatology/
22. (acute renal adj (failure or injur* or insufficien*)).tw,kf.	64. exp Pediatrics/
23. (AKI or ALI).tw,kf.	65. Perinatal Care/
24. ((artificial* or mechanic*) adj (respirat* or ventilat*)).tw,kf.	66. Perinatology/
25. ((cardiac or heart) adj surg*).tw,kf.	67. Postnatal Care/
26. (coronary care adj (department* or unit* or ward or wards)).tw,kf.	68. Premature Birth/
27. critical care.tw,kf,jw.	69. exp Puberty/
28. (critical* adj2 (department* or unit* or ward or wards)).tw,kf.	70. (baby* or babies or infant* or infancy or newborn* or newborn*).tw,kf.
29. critical* ill*.tw,kf.	71. (boy* or girl* or teen*).tw,kf.
30. CRRT.tw,kf.	72. (child* or kid or kids or pre school* or preschool* or school age* or schoolchild* or toddler*).tw,kf.
31. CVVH.tw,kf.	73. (ELBW* or VLBW*).tw,kf.
32. (haemo filtrat* or haemofiltrat* or hemo filtrat* or hemofiltrat*).tw,kf.	74. low birth weight.tw,kf.
33. intensive care*.tw,kf,jw.	75. minors*.tw,kf.
34. (intensive adj2 (department* or unit* or ward or wards)).tw,kf.	76. (neonat* or perinat* or postnat*).tw,kf.
35. intensivist*.tw,kf.	77. (paediatric* or peadiatric* or pediatric*).tw,kf,jw.
36. (ICU* or NICU* or PICU* or SICU*).tw,kf.	78. (prepubescen* or pubescen* or pubert*).tw,kf.
37. (multi* organ adj (dysfunction* or dis function* or dysfunction* or dys function* or failure*)).tw,kf.	79. small for gestational age.tw,kf.
38. (multi* system adj (dysfunction* or dis function* or dysfunction* or dys function* or failure*)).tw,kf.	80. or/57-79
39. (polytrauma* or trauma*).tw,kf.	81. and/47,56,80
40. (post op* or postop*).tw,kf.	82. animals/ not (animals/ and humans/)
41. (renal replacement adj2 (therap* or treatm* or support*)).tw,kf.	83. 81 not 82
	84. (case reports or comment or editorial or letter).pt. 85. 83 not 84
	86. remove duplicates from 85

**eTable 2.** List of Conference Proceedings Searched

- The Society of Critical Care Medicine (SCCM)
- Canadian Critical Care Society
- The European Society of Intensive Care Medicine (ESICM)
- The International Symposium on Intensive Care and Emergency Medicine (ISICEM)
- The World Federation of Pediatric Intensive and Critical Care Societies
- American Society of Nephrology (ASN)
- International Society of Nephrology (ISN)
- International Symposium on AKI in Children
- International Conference on Pediatric Continuous Renal Replacement Therapy (pCRRT)

**eTable 3.** Newcastle-Ottawa Quality Assessment Scale

**1. Cohort studies**

Newcastle-Ottawa Scale (Cohort Studies)										
		Selection				Comparability	Outcome			Total
Author and Year	Study Design	Representativeness of cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome of interest	Comparability of cohorts	Assessment of outcome	Adequate duration of follow-up	Adequate follow-up of cohort	Total Score
Abulebda, 2014 <sup>1</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8
Arikan, 2012 <sup>2</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Askenazi, 2013 <sup>3</sup>	PC	0	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	7
Baird, 2010 <sup>4</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	7
Boschee, 2014 <sup>5</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	7
Chen, 2016 <sup>6</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Choi, 2017 <sup>7</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8
De Galasso, 2016 <sup>8</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Diaz, 2017 <sup>9</sup>	PC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Elbahlawan, 2010 <sup>10</sup>	RC	0	A (1*)	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	6
Flores, 2008 <sup>11</sup>	PC	0	A (1*)	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	6
Flori, 2011 <sup>12</sup>	PC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8
Foland, 2004 <sup>13</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8
Gillespie, 2004 <sup>14</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8
Goldstein, 2005 <sup>15</sup>	PC	0	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	7
Goldstein, 2001 <sup>16</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8
Gulla, 2015 <sup>17</sup>	RC	0	A (1*)	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	6
Hassinger, 2014 <sup>18</sup>	PC	1*	A (1*)	A (1*)	A (1*)	A (1) B (0)	A (1*)	A (1*)	A (1*)	8

Hayes, 2009 <sup>19</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Hazle, 2013 <sup>20</sup>	PC	0	A (1*)	A (1*)	A (1*)	A (1) B (1)	A (1*)	A (1*)	A (1*)	8
Ingelse, 2017 <sup>21</sup>	RC	0	A (1*)	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	6
Jhang, 2014 <sup>22</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8
Kaempfer, 2017 <sup>23</sup>	RC	0	A (1*)	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	6
Ketharanathan, 2014 <sup>24</sup>	PC	1*	A (1*)	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	7
Lex, 2016 <sup>25</sup>	PC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Li, 2016 <sup>26</sup>	PC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Lombel, 2012 <sup>27</sup>	RC	0	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	7
Michael, 2004 <sup>28</sup>	PC	0	A (1*)	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	6
Modem, 2014 <sup>29</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8
Naveda, 2016 <sup>30</sup>	PC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Park, 2016 <sup>31</sup>	RC	0	A (1*)	A (1*)	A (1*)	A (1) B (0)	A (1*)	A (1*)	A (1*)	7
Randolph, 2005 <sup>32</sup>	PC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Sampaio, 2015 <sup>33</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Seguin, 2014 <sup>34</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1) B (1*)	A (1*)	A (1*)	A (1*)	9
Selewski, 2011 <sup>35</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Selewski, 2012 <sup>36</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Sinitsky, 2015 <sup>37</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1)	A (1*)	A (1*)	A (1*)	8
Sutherland, 2010 <sup>38</sup>	PC	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8
Valentine, 2012 <sup>39</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Vidal, 2016 <sup>40</sup>	RC	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9

RC = retrospective cohort; PC= prospective cohort  
For comparability: A is age, B is illness severity

## 2. Case Control studies

Newcastle-Ottawa Scale (Case control studies)									
	Selection				Comparability	Outcome			Total
Author and Year	Case definition adequate?	Representativeness of cases	Select ion of Controls	Definit ion of Controls	Comparability of cases and controls	Assess ment of exposure	Same method of ascertain ment	Non-Respo nse rate	Total Score
Bhask ar, 2015 <sup>41</sup>	1*	A (1*)	A (1*)	A (1*)	A (1*) B (1*)	A (1*)	A (1*)	A (1*)	9
Hoove r, 2008 <sup>42</sup>	1*	0	A (1*)	A (1*)	A (0) B (0)	A (1*)	A (1*)	A (1*)	6
Sutaw an, 2016 <sup>43</sup>	1*	A (1*)	A (1*)	A (1*)	A (0) B (1*)	A (1*)	A (1*)	A (1*)	8

For comparability: A is age, B is illness severity

**eTable 4.** Fluid Balance Assessment Methods

Main Fluid Balance Measure	Assessment Period		Paper(s)		
	Start	End			
Percent Fluid Overload (FO%) (intake-output based)	PICU admission	24 hours	Chen, 2016 <sup>6</sup> Li, 2016 <sup>26</sup> Hassinger, 2014 <sup>18</sup>		
		48 hours	Sinitsky, 2015 <sup>37</sup> Vidal, 2016 <sup>40</sup>		
		72 hours	Hazle, 2013 <sup>20</sup>		
		7 days	Abulebda, 2014 <sup>1</sup> Bhaskar, 2015 <sup>41</sup> Sampaio, 2015 <sup>33</sup>		
		14 days	Arikan, 2012 <sup>2</sup>		
		PICU discharge	Diaz, 2017 <sup>9</sup> Ketharanathan, 2014 <sup>24</sup> Michael, 2004 <sup>28</sup> Naveda, 2016 <sup>30</sup> Sutawan, 2016 <sup>43</sup>		
	CRRT initiation		Askenazi, 2013 <sup>3</sup> Boschee, 2014 <sup>5</sup> de Galasso, 2016 <sup>8</sup> Flores, 2008 <sup>11</sup> Gillespie, 2004 <sup>14</sup> Goldstein, 2001 <sup>16</sup> Goldstein, 2005 <sup>15</sup> Gulla, 2015 <sup>17</sup> Hayes, 2009 <sup>19</sup> Jhang, 2014 <sup>22</sup> Kaempfen, 2017 <sup>23</sup> Lombel, 2012 <sup>27</sup> Modem, 2014 <sup>29</sup> Selewski, 2011 <sup>35</sup> Sutherland, 2010 <sup>38</sup>		
			24 hours before CRRT initiation	Elbahlawan, 2010 <sup>10</sup> Choi, 2017 <sup>7</sup>	
			7 days before CRRT initiation	Baird, 2010 <sup>4</sup> Foland, 2004 <sup>13</sup>	
			Intra-operative	48 hours	Lex, 2016 <sup>25</sup>
				72 hours	Park, 2016 <sup>31</sup>
	PICU discharge	Seguin, 2014 <sup>34</sup>			
	Percent Fluid Overload FO% (weight based)	PICU admission	7 days	Hazle, 2013 <sup>20</sup>	
CRRT initiation			Lombel, 2012 <sup>27</sup> Selewski, 2011 <sup>35</sup> Selewski, 2012 <sup>36</sup>		
Net Fluid Balance (ml/kg)	PICU admission	7 days	Valentine, 2012 <sup>39</sup>		
		PICU discharge	Ingelse, 2017 <sup>21</sup>		
	Intubation	Extubation	Randolph, 2005 <sup>32</sup>		
	Onset of ALI	72 hours post ALI	Flori, 2011 <sup>12</sup>		
ECMO start	ECMO end	Hoover, 2008 <sup>42</sup>			
Net Fluid Balance (L/m <sup>2</sup> )	PICU admission	7 days	Willson, 2013 <sup>44</sup>		

**eTable 5. Weights Used in FO Definitions**

<b>Weight used</b>	<b>Paper (s)</b>
PICU admission weight	Chen, 2016 <sup>6</sup> Choi, 2017 <sup>7</sup> Diaz, 2017 <sup>9</sup> Li, 2016 <sup>26</sup> Abulebda, 2014 <sup>1</sup> Bhaskar, 2015 <sup>41</sup> Arikan, 2012 <sup>2</sup> Askenazi, 2013 <sup>3</sup> Boschee, 2014 <sup>5</sup> de Galasso, 2016 <sup>8</sup> Flores, 2008 <sup>11</sup> Gillespie, 2004 <sup>14</sup> Goldstein, 2001 <sup>16</sup> Goldstein, 2005 <sup>15</sup> Gulla, 2015 <sup>17</sup> Jhang, 2014 <sup>22</sup> Ketharanathan, 2014 <sup>24</sup> Lombel, 2012 <sup>27</sup> Modem, 2014 <sup>29</sup> Selewski, 2011 <sup>35</sup> Sutherland, 2010 <sup>38</sup> Sutawan, 2016 <sup>43</sup>
Hospital admission weight	Hayes, 2009 <sup>19</sup> Lombel, 2012 <sup>27</sup> Michael, 2004 <sup>28</sup> Selewski, 2011 <sup>35</sup> Selewski, 2012 <sup>36</sup> Baird, 2010 <sup>4</sup> Sinitsky, 2015 <sup>37</sup>
Hospital admission weight or the most recent available PICU weight	Lex, 2016 <sup>25</sup>
The lowest patient weight from either hospital admission or the most recent within 1 month of admission	Foland, 2004 <sup>13</sup>
PICU dry or ideal bodyweight *	Lombel, 2012 <sup>27</sup> Randolph, 2005 <sup>32</sup>
Outpatient weight	Hazle, 2013 <sup>20</sup> Lombel, 2012 <sup>27</sup>
Not specified	Elbahlawan, 2010 <sup>10</sup> Flori, 2011 <sup>12</sup> Hassinger, 2014 <sup>18</sup> Hoover, 2008 <sup>42</sup> Ingelse, 2017 <sup>21</sup> Kaempfen, 2017 <sup>23</sup> Naveda, 2016 <sup>30</sup> Park, 2016 <sup>31</sup> Sampaio, 2015 <sup>33</sup> Seguin, 2014 <sup>34</sup> Valentine, 2012 <sup>39</sup> Vidal, 2016 <sup>40</sup> Willson, 2013 <sup>44</sup>

\* Randolph et al used "ideal body weight": Estimated as the 50th percentile for recumbent length and sex from the National Center for Health Statistics growth charts.

\* Lombel et al used "PICU dry weight": assigned at the time of PICU admission by the PICU staff based on clinical judgment of pre-morbid weight



**eTable 6. Studies Reporting Respiratory Dysfunction and Outcomes**

<b>Study</b>	<b>Population</b>	<b>Main Respiratory Outcomes</b>
Arikan, 2012 <sup>2</sup>	Multisystem (ventilated only)	<ul style="list-style-type: none"> <li>• Peak %FO correlated significantly with peak OI (<math>r = 0.26</math>, <math>p &lt; 0.02</math>)</li> <li>• Higher peak %FO was an independent predictor of higher peak OI (<math>p = 0.009</math>) on multivariate regression analysis</li> <li>• Daily %FO &gt;15% was independently associated with that day's OI (regression coefficient= 0.12, <math>p = 0.004</math>)</li> <li>• %FO and OI regression coefficient progressively increased with increased %FO cut-off</li> <li>• %FO&gt;15% was independently associated with longer duration of MV (OR 0.46, <math>p = 0.01</math>)</li> </ul>
Bhaskar, 2015 <sup>41</sup>	Sepsis/shock	<ul style="list-style-type: none"> <li>• MV was longer in patients with FO (median 2 vs 6 days, <math>p = 0.004</math>). However, the difference was not significant in matched analysis (5 vs 6 days, <math>p = 0.36</math>)</li> </ul>
Elbahlawan, 2010 <sup>10</sup>	Stem cell transplant on CRRT	<ul style="list-style-type: none"> <li>• Improvement of PaO<sub>2</sub>/FiO<sub>2</sub> correlated significantly with reduction of fluid balance after initiation of CRRT (median PaO<sub>2</sub>/FiO<sub>2</sub> increase of 30.51 after 24 hours, and 43 after 48 hours, <math>p &lt; 0.05</math>)</li> </ul>
Flori, 2011 <sup>12</sup>	ALI	<ul style="list-style-type: none"> <li>• Positive fluid balance (in 10 mL/kg/day increments) was independently associated with fewer ventilator-free days (regression coefficient = - 0.21, <math>p = 0.02</math>)</li> </ul>
Hassinger, 2014 <sup>18</sup>	Post cardiac surgery	<ul style="list-style-type: none"> <li>• Early FO was associated with prolonged MV (43% vs 8.8%). However, the association was not significant after adjusting for severity of illness (OR 3.15, <math>p = 0.18</math>)</li> </ul>
Hayes, 2009 <sup>19</sup>	CRRT	<ul style="list-style-type: none"> <li>• Higher %FO was associated with longer MV (median 7 vs 16 days, <math>p = 0.02</math>). The association was not significant on multivariable regression.</li> </ul>
Ketharanathan, 2014 <sup>24</sup>	Multisystem	<ul style="list-style-type: none"> <li>• %FO correlated significantly with OI (<math>r = 0.33</math>, <math>p = 0.01</math>) and length of MV (<math>r = 0.34</math>, <math>p &lt; 0.001</math>)</li> </ul>
Lex, 2016 <sup>25</sup>	Post cardiac surgery	<ul style="list-style-type: none"> <li>• Higher %FO was independently associated with prolonged MV (OR 1.01, <math>p = 0.03</math>)</li> </ul>
Li, 2016 <sup>26</sup>	Multisystem	<ul style="list-style-type: none"> <li>• There was a trend towards prolonged MV in the early FO group but it was not significant statistically (26.6% vs 17%, <math>p = 0.07</math>)</li> </ul>
Sampaio, 2015 <sup>33</sup>	Post cardiac surgery	<ul style="list-style-type: none"> <li>• %FO was independently associated with Length of MV in multiple linear regression (<math>p &lt; 0.01</math>)</li> <li>• Peak %FO correlated significantly with maximum OI (Spearman's test = 0.37, <math>p = 0.01</math>)</li> <li>• Peak %FO was associated with chest wall edema (<math>p = 0.003</math>) and pleural effusion (<math>p = 0.01</math>)</li> <li>• Peak %FO was not associated with extubation failure (<math>p = 0.98</math>)</li> </ul>
Seguin, 2014 <sup>34</sup>	Post cardiac Surgery	<ul style="list-style-type: none"> <li>• Peak %FO correlated significantly with maximum OI (<math>r = 0.32</math>, <math>p = 0.001</math>)</li> <li>• Higher FO % was independently associated with worse OI (HR 0.16, <math>p = 0.03</math>)</li> <li>• %FO at day 2 was independently associated with length of mechanical ventilation (HR 0.97, <math>p = 0.03</math>)</li> </ul>

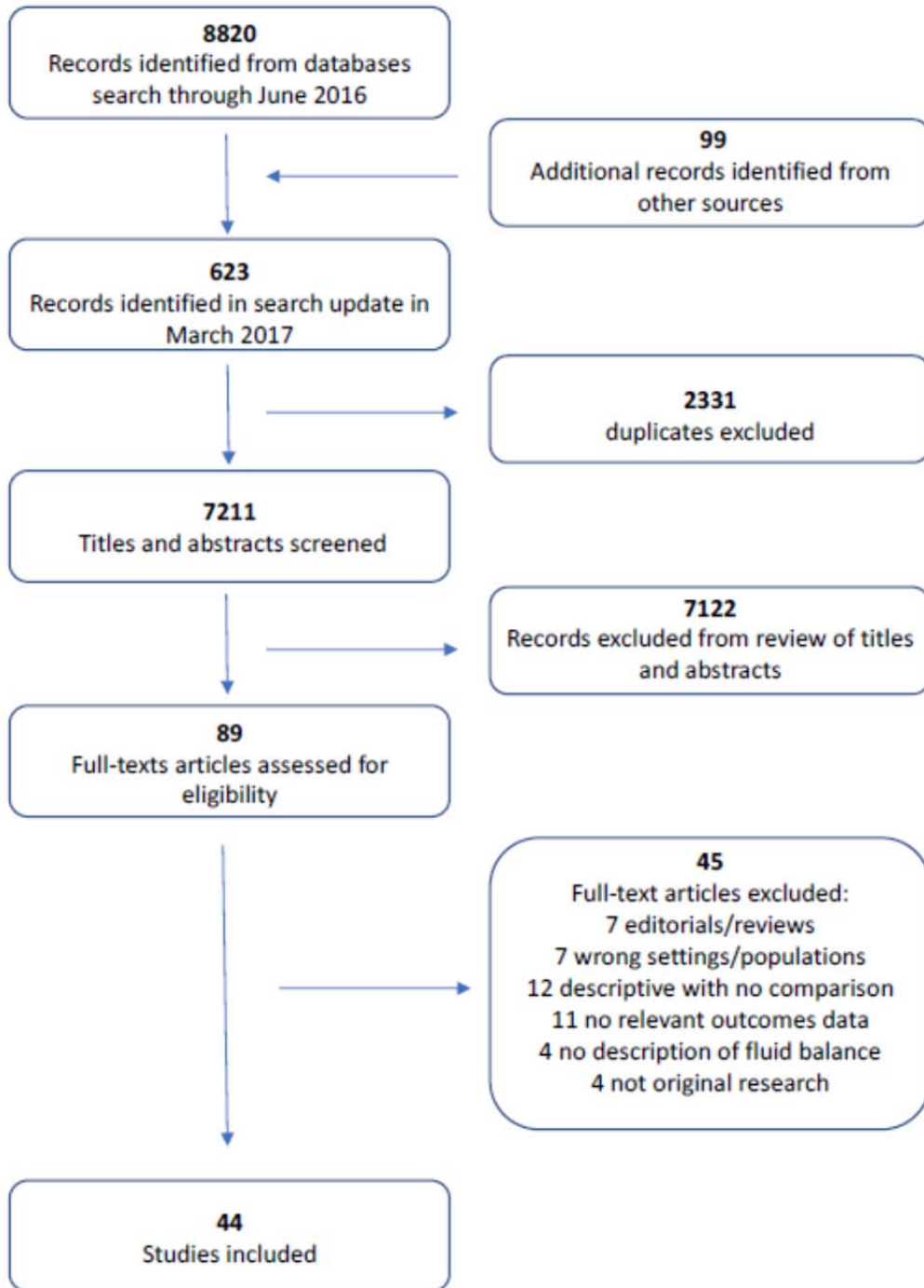
Study	Population	Main Respiratory Outcomes
Sinitsky, 2015 <sup>37</sup>	Multisystem	<ul style="list-style-type: none"> <li>• %FO correlated significantly with oxygenation index (Spearman's test = 0.32, p &lt; 0.001) and with length of MV (Spearman's test = 0.27; p &lt; 0.001)</li> <li>• %FO was independently associated with OI at 48 hours (regression coefficient 0.26, p &lt; 0.001)</li> <li>• %FO was independently associated with MV days (regression coefficient 0.14, p = 0.002)</li> </ul>
Valentine, 2012 <sup>39</sup>	ALI	<ul style="list-style-type: none"> <li>• Higher fluid balance (mL/kg/day) at day 3 was independently associated with fewer ventilator-free days (regression coefficient = -0.02, p = 0.01)</li> </ul>
Willson, 2013 <sup>44</sup>	ALI	<ul style="list-style-type: none"> <li>• Higher fluid balance (L/m<sup>2</sup>) was associated with fewer ventilation-free days (p &lt; 0.001)</li> <li>• Fluid balance (L/m<sup>2</sup>) was independently associated with OI (regression coefficient 0.52, p = 0.01)</li> </ul>
Randolph, 2005 <sup>32</sup>	Multisystem (ventilated only)	<ul style="list-style-type: none"> <li>• Higher fluid balance (ml/kg/day) was associated with nonsignificant trend towards longer duration of ventilation weaning (HR 0.94, P = 0.051)</li> <li>• Positive fluid balance did not predict extubation failure</li> </ul>
Chen, 2016 <sup>6</sup>	Sepsis	<ul style="list-style-type: none"> <li>• Early FO was an independent predictor for the need of MV (OR 1.2, p = 0.04)</li> <li>• However, FO was not associated with the duration of MV (p = 0.3)</li> </ul>
Diaz, 2017 <sup>9</sup>	Multisystem	<ul style="list-style-type: none"> <li>• Peak %FO correlated with length of MV (r = 0.67, p &lt; 0.01)</li> </ul>
Ingelse, 2017 <sup>21</sup>	Multisystem (ventilated only)	<ul style="list-style-type: none"> <li>• Fluid balance (mL/kg/day) on day 3 was independently associated with duration of MV (p = 0.048), but not with OI</li> </ul>
Vidal, 2016 <sup>40</sup>	Multisystem (ventilated only)	<ul style="list-style-type: none"> <li>• FO was associated with prolonged MV (OR 4.02, p = 0.04). However, the association was not significant after adjusting for severity of illness (OR 3.7, p = 0.06)</li> </ul>

OI = Oxygenation index  
 MV = Mechanical ventilation  
 ALI = Acute lung injury  
 OR = Odds ratio  
 HR = Hazard ratio

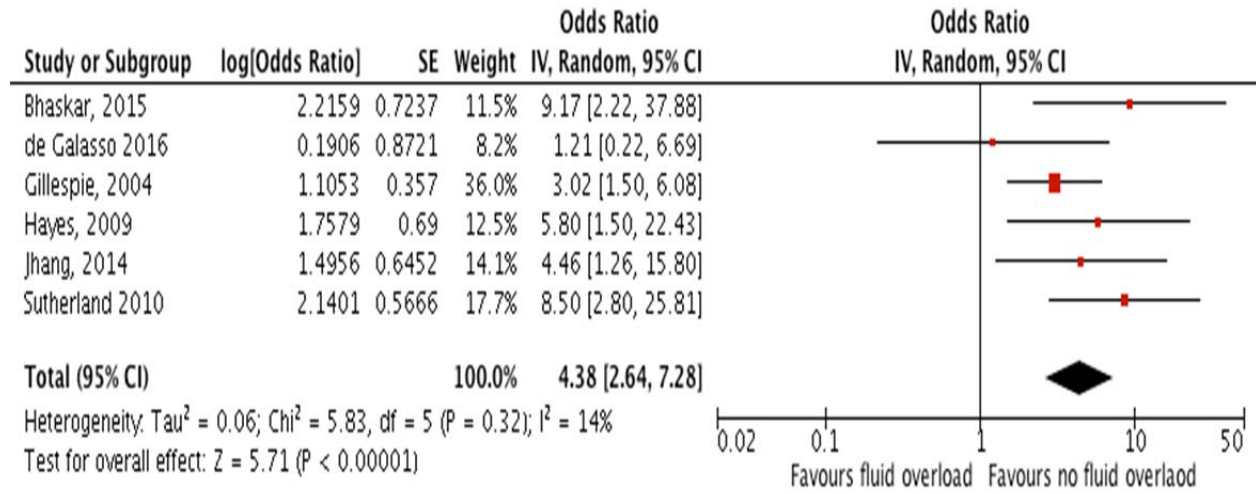
**eTable 7.** Other Outcomes From Individual Studies

<b>Study</b>	<b>Outcome</b>	<b>Result</b>
Abulebda, 2014 <sup>1</sup>	Composite of “complicated course”: death within the 28-day study period or persistence of >2 organ failures at day-7 post admission.	<ul style="list-style-type: none"> <li>Those with complicated course had higher %FO (8.5% Vs 3.8%, P &lt;0.001)</li> </ul>
Bhaskar, 2015 <sup>41</sup>	ECMO use	<ul style="list-style-type: none"> <li>FO group had more ECMO use compared to no FO (OR 6.2, P=0.01)</li> </ul>
Hassinger, 2014 <sup>18</sup>	Hemodynamic variables	<p>In FO group:</p> <ul style="list-style-type: none"> <li>Later first inotrope-free day (day 5 Vs day 3, P &lt;0.001)</li> <li>Higher peak inotropic score (P &lt;0.01)</li> <li>More likely to have escalation in inotropic support (20% vs 4.4%) (p = 0.01)</li> </ul>
Hazle, 2013 <sup>20</sup>	Composite of poor outcome: need for CRRT, upper quartile time to first extubation or intensive care length of stay, or death within 30 days of surgery	<ul style="list-style-type: none"> <li>Maximum %FO was higher in patients who developed “poor outcome” (24% vs 14%, p=0.02)</li> </ul>
Lex, 2016 <sup>25</sup>	Post cardiac bypass low cardiac output syndrome	<ul style="list-style-type: none"> <li>Cumulative %FO on day of surgery was independently associated with low cardiac output syndrome (OR 1.21, P= 0.002)</li> </ul>

**eFigure 1.** Flow Diagram of the Study Selection Process



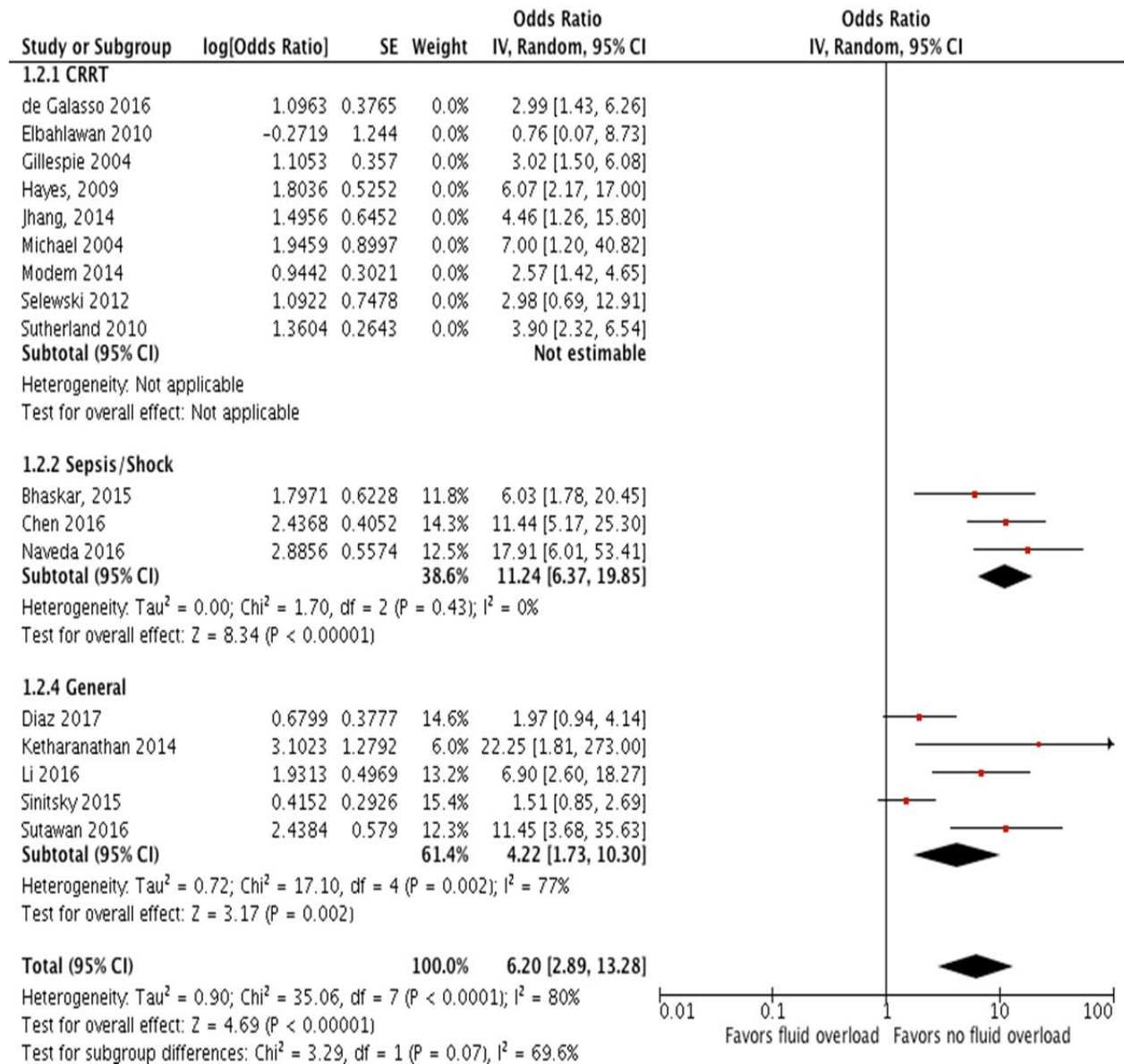
**eFigure 2.** Association Between FO (Categorical Exposure) and Mortality in Studies Adjusting for Severity of Illness



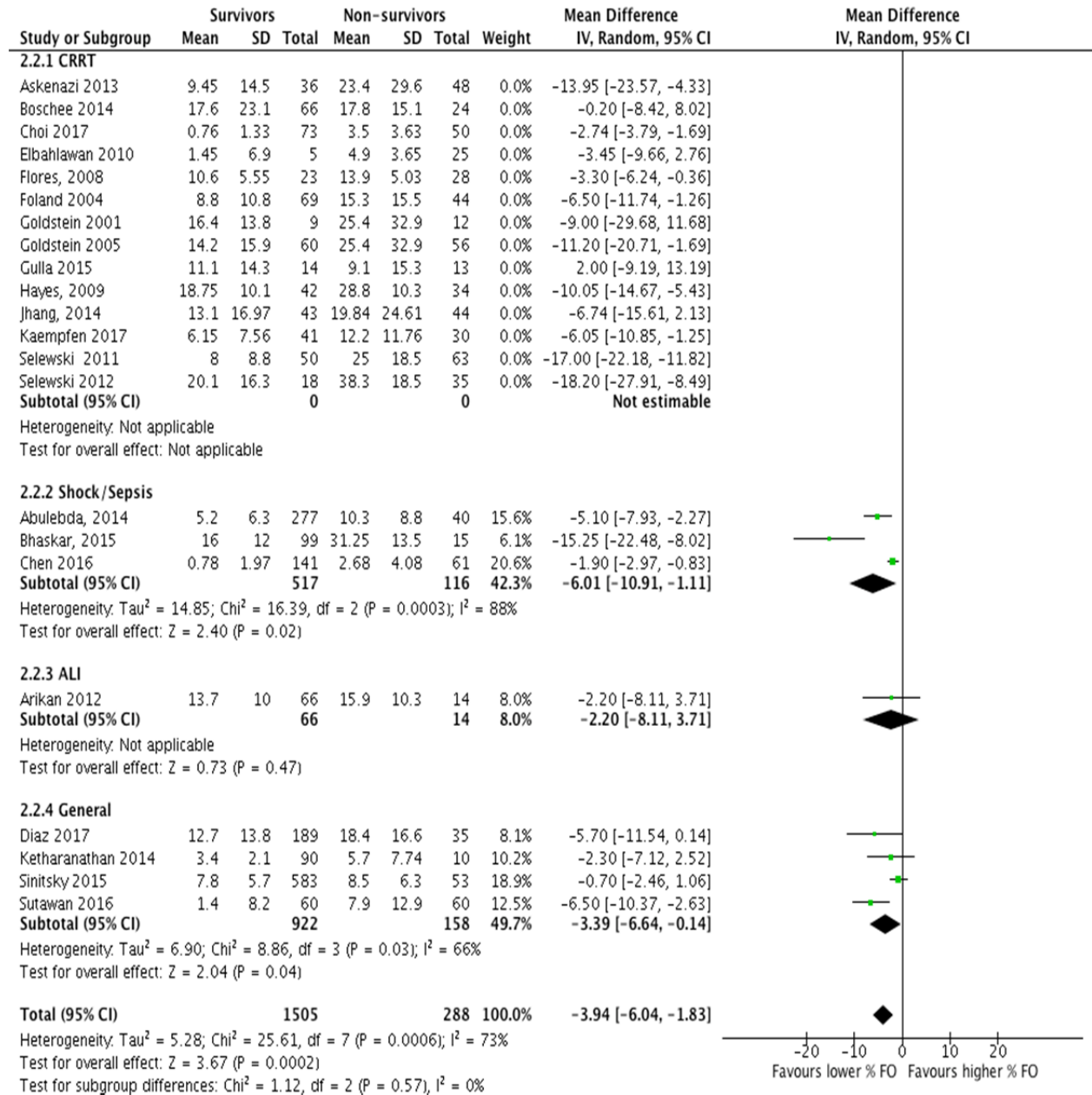
Studies adjusted for:

- Bhaskar, 2015: PIM 2, age, indication for ICU admission, duration of hospitalization prior to ICU transfer, presence of infectious diagnoses, presence of oncologic disease(s), presence of respiratory failure, need for vasopressor support and presence of renal dysfunction.
- De Galasso, 2016: PIM2, diagnosis, MODS at CRRT initiation, hypotension at CRRT initiation
- Gillespie, 2004: PRISM2, dose of CVVH replacement of fluid, number of inotropes
- Hayes, 2009: PRISM 2, age, race, sex
- Jhang, 2014: SOFA score
- Sutherland, 2010: PRISM, MODS, CRRT modality, number of inotropes

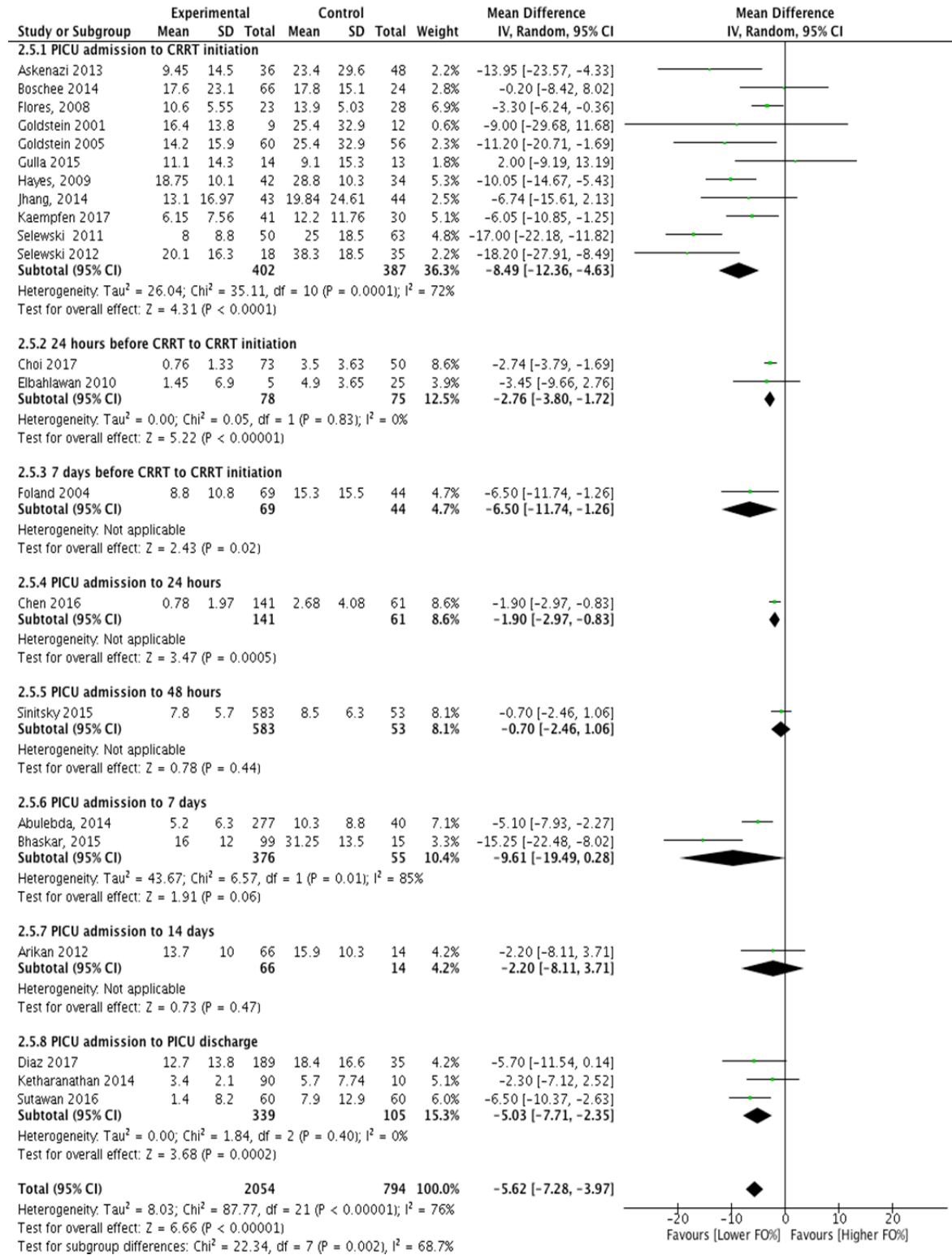
**eFigure 3.** Association Between Fluid Overload (Categorical Exposure) and Mortality Omitting Studies of Children Receiving CRRT



## Association between fluid overload (continuous exposure) and mortality omitting studies of children receiving CRRT

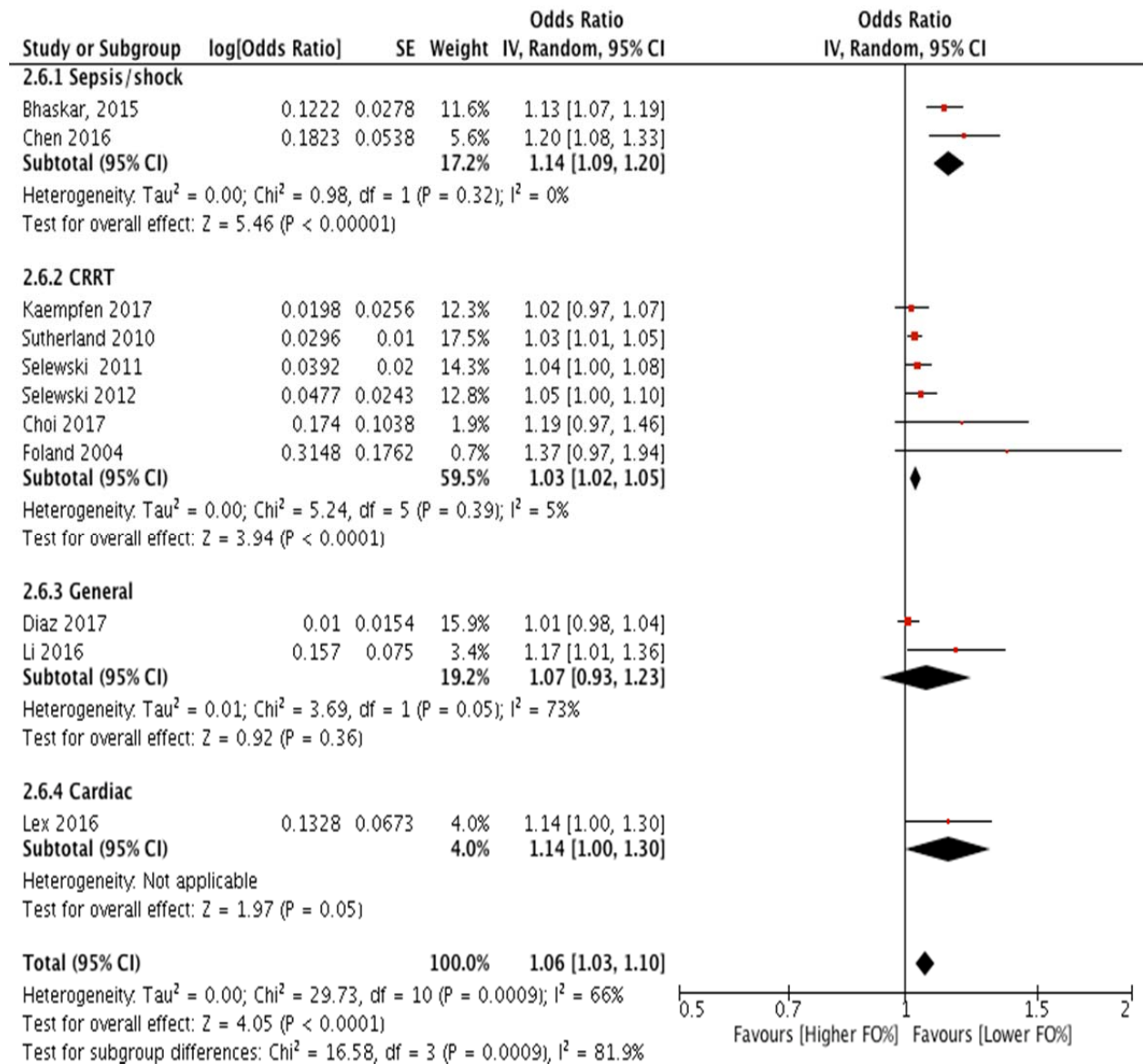


**eFigure 4** Percent Fluid Overload (%FO) (Continuous Variable) Association With Mortality, Stratified by Assessment Period





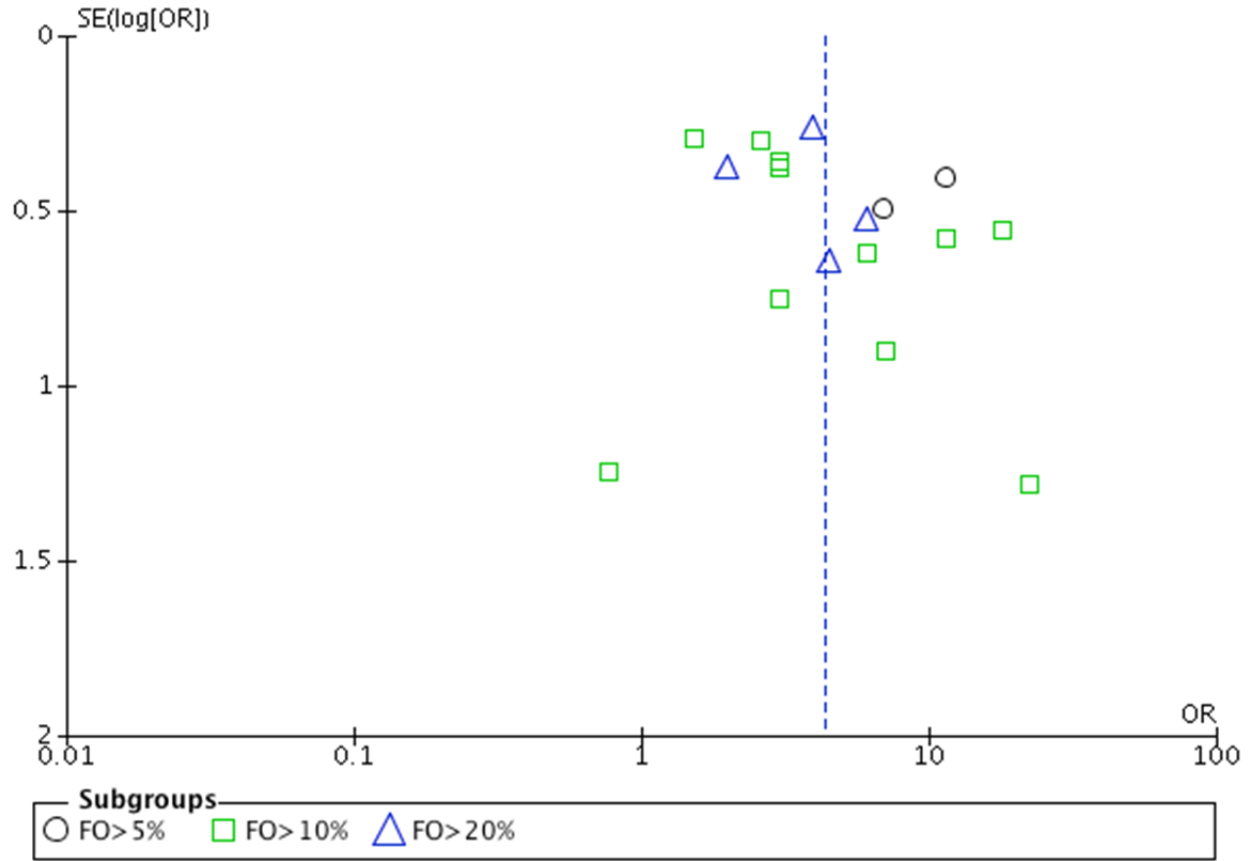
**eFigure 5.** Percent Fluid Overload (%FO) (Continuous Variable) Association With Mortality in Studies Adjusting for Severity of Illness (Stratified by Case-Mix)



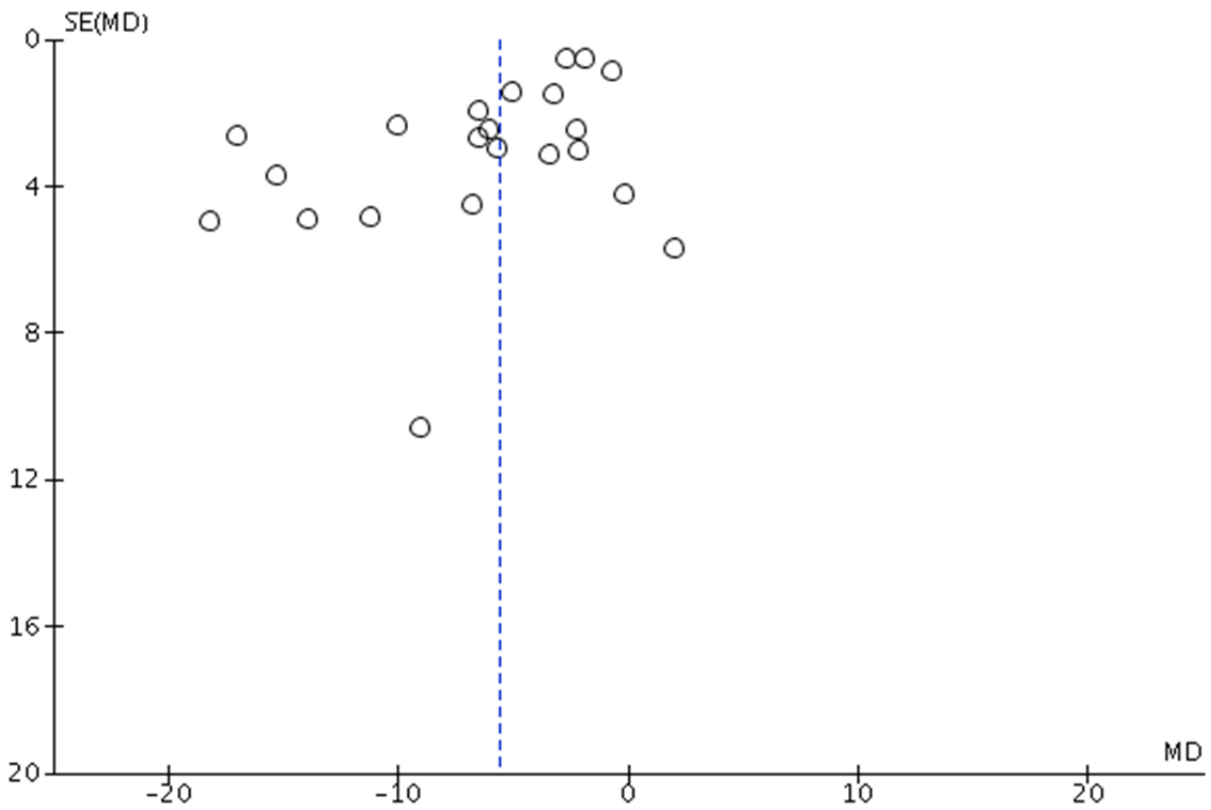
Studies adjusted for:

- Bhaskar, 2015: PIM 2, age, indication for ICU admission, duration of hospitalization prior to ICU transfer, presence of infectious diagnoses, presence of oncologic disease(s), presence of respiratory failure, need for vasopressor support and presence of renal dysfunction.
- Chen, 2016: PIM2, age
- Kaempfen, 2017: Weight, length of stay prior to CRRT, inotrope need, mean blood pressure prior to CRRT
- Sutherland, 2010: PRISM, MODS, CRRT modality, number of inotropes
- Selewski, 2011: Age, hospital days pre CRRT, extracorporeal life support status, pRIFLE status, and number of vasoactive agents
- Selewski, 2012: Age, PRISM
- Choi, 2017: PRISM III, inotrope score, length of PICU stay, length of stay prior to CRRT, duration of CRRT, lactic acid, Creatinine, Urea
- Foland, 2004: PRISM III
- Diaz, 2017: PRISM II, age, AKI status, vasoactive support, >3 organ failure
- Li, 2016: PRISM III, age, need for mechanical ventilation, AKI
- Lex, 2016: age, emergency operation, cardiac bypass time, CRRT, low cardiac output syndrome

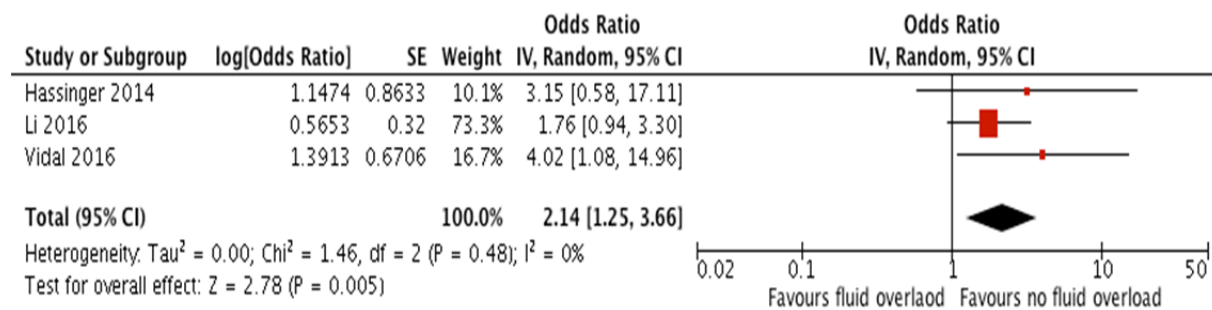
**eFigure 6.** Funnel Plot of FO Odds of Mortality (Categorical Exposure) Analysis



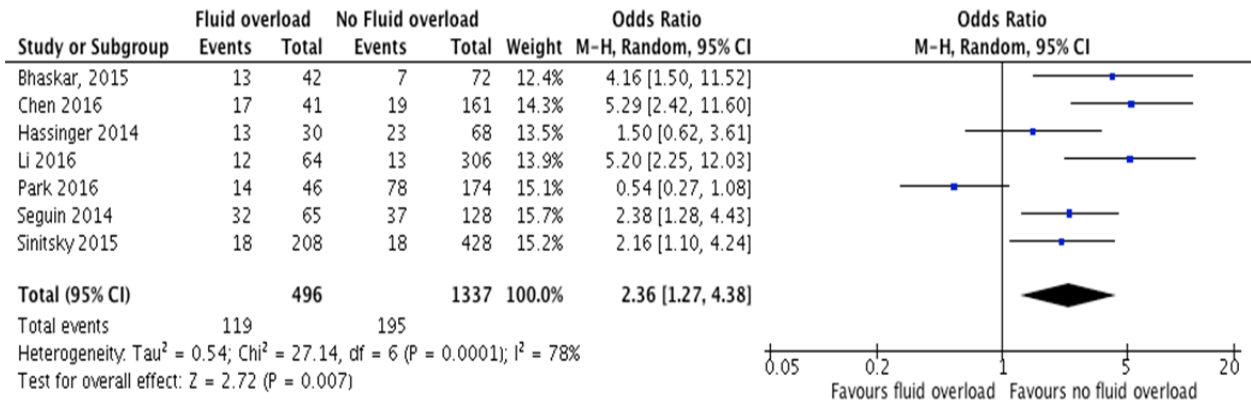
**eFigure 7.** Funnel Plot of Fluid Overload Percent (%FO) (Continuous Variable) Association With Mortality Analysis



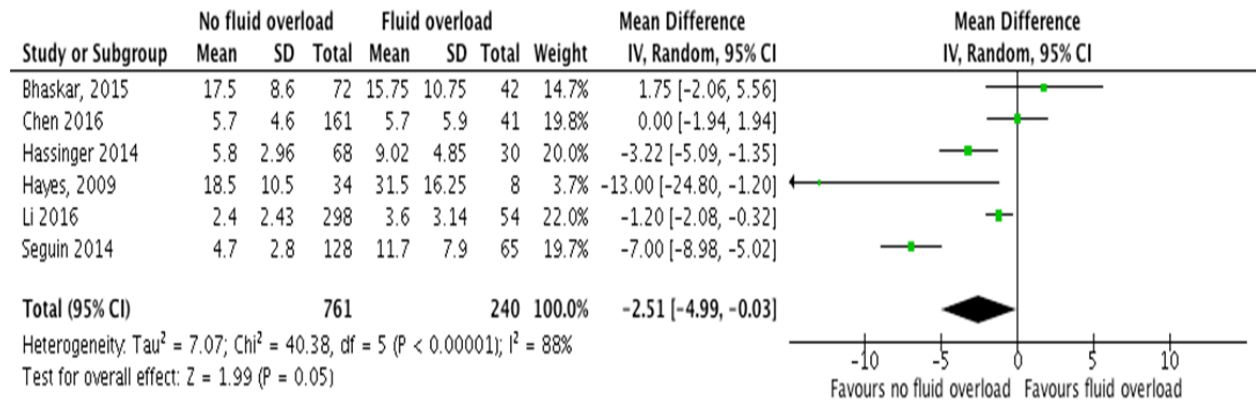
**eFigure 8.** Random-Effects Meta-analysis of FO and Prolonged Mechanical Ventilation



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



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



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