Risk of bias in included trials. Items for each trial are based on the Cochrane Risk of Bias Tool* and summary determination across all trials is based on the Cochrane Handbook†.

Study	Summary risk and number of subjects	Selection bias		Performance bias	Detection bias	Attrition bias	Reporting bias
		Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data‡	Selective reporting§
Svoboda, 2007	High risk 72	Low risk	Unclear risk	Unclear risk	Low risk	Low risk	High risk
Nobre, 2008 NCT00250666	High risk 79	Low risk	Low risk	High risk	High risk	Low risk	Low risk
Schroeder, 2009	High risk 27	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	High risk
Hochreiter, 2009 ISRCTN10288268	High risk 110	Unclear risk	High risk	High risk	High risk	Low risk	Low risk
Layios, 2012	High risk 509	Unclear risk	Unclear risk	Unclear risk	Unclear risk	Low risk	High risk

Annane, 2013 NCT01025180	High risk 62	Low risk	Low risk	High risk	High risk	Low risk	Low risk
Oliveira, 2013 NCT00934011	High risk 94	Low risk	High risk	High risk	Low risk	Low risk	Low risk
Deliberato, 2013 NCT01494675	High risk 81	Low risk	High risk	High risk	High risk	High risk	Low risk
Liu, 2013	High risk 82	Unclear risk	Unclear risk	Unclear risk	Unclear risk	High risk	High risk
Dharaniyadewi, 2013	High risk 197	Unclear risk	Unclear risk	Unclear risk	Unclear risk	High risk	High risk
ProGUARD, 2014 ACTRN12610000809033	High risk 394	Lower risk	Unclear risk	High risk	Low risk	Low risk	Low risk
De Jong, 2016 NCT01139489	High risk 1575	Low risk	High risk	High risk	Unclear risk	Low risk	Low risk
Bloos, 2016 NCT00832039	High risk 1089	Low risk	Low risk	High risk	Unclear risk	Low risk	Low risk

Summary across all trials	Subjects in low risk trials: 0% Subjects in trials of unclear risk: 0% Subjects in high risk trials: 100%						

Notes:

* Assessment of individual studies based on the Cochrane Handbook, Table 8.5.d. Available at http://handbook-5-1.cochrane.org/chapter_8/table_8_5_d_criteria_for_judging_risk_of_bias_in_the_risk_of.htm .

† Summary determination across studies based on Cochrane Handbook, Table 8.7. Available at http://handbook-5-1.cochrane.org/chapter_8/table_8_7_a_possible_approach_for_summary_assessments_of_the.htm .

‡ Lack of a Consort diagram, by itself, is considered unclear risk of incomplete outcome and attrition bias.

§ Lack of trial registration, by itself, is considered high risk of selective reporting.