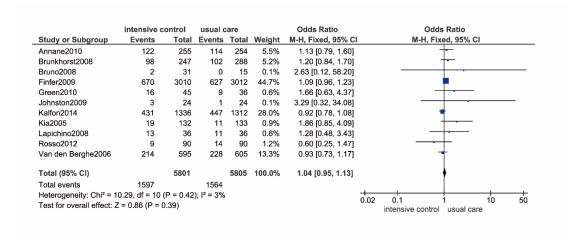
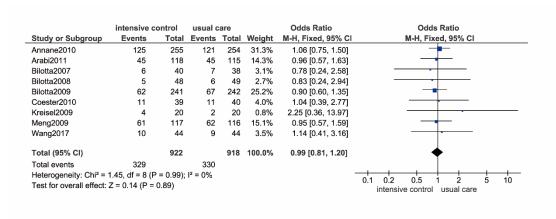
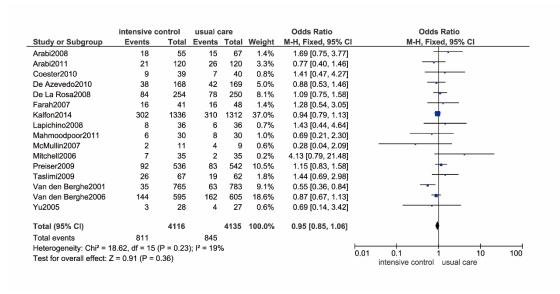
Supplementary Figure S1.



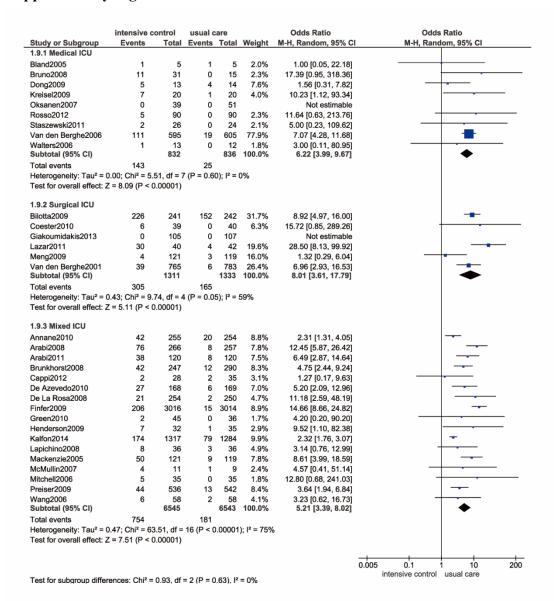
Supplementary Figure S2.



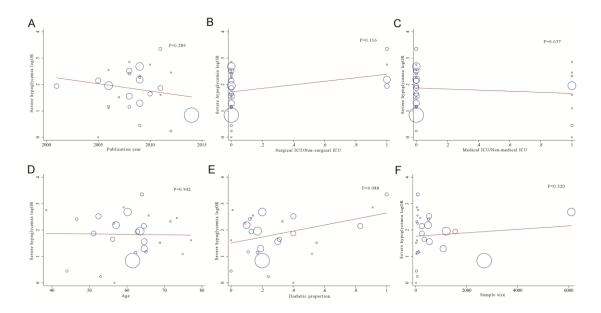
Supplementary Figure S3.



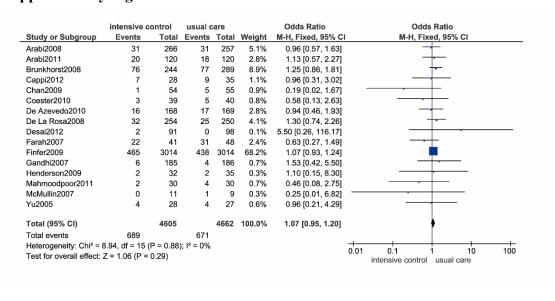
Supplementary Figure S4.



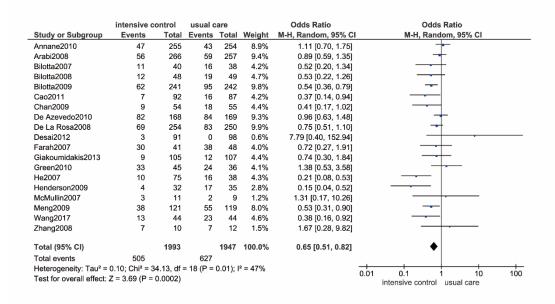
Supplementary Figure S5.



Supplementary Figure S6.



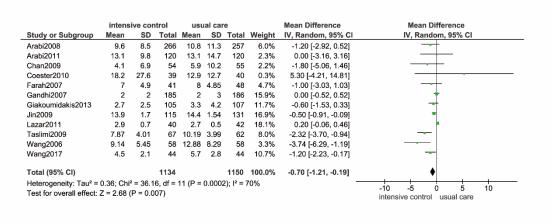
Supplementary Figure S7.



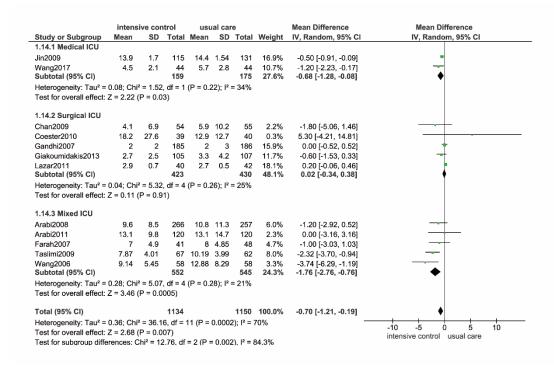
Supplementary Figure S8.

	intensive co	ontrol	usual care			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	CI M-H, Fixed, 95% CI
Arabi2008	98	266	105	257	34.2%	0.84 [0.59, 1.20]]
Arabi2011	59	120	50	120	12.9%	1.35 [0.81, 2.25]	†
Bilotta2008	2	48	3	49	1.4%	0.67 [0.11, 4.18]	
Bilotta2009	7	241	8	242	3.9%	0.88 [0.31, 2.45]	1
Cao2011	2	92	3	87	1.5%	0.62 [0.10, 3.82]	· · · · ·
Chan2009	2	54	2	55	1.0%	1.02 [0.14, 7.51]]
Coester2010	33	39	32	40	2.5%	1.38 [0.43, 4.41]	<u> </u>
Farah2007	11	41	17	48	5.8%	0.67 [0.27, 1.66]	<u> </u>
Mahmoodpoor2011	7	30	9	30	3.5%	0.71 [0.22, 2.25]	1
Meng2009	5	121	7	119	3.4%	0.69 [0.21, 2.24]	1
Van den Berghe2001	32	765	61	783	29.3%	0.52 [0.33, 0.80]	_ - _
Wang2017	1	44	1	44	0.5%	1.00 [0.06, 16.51]	
Total (95% CI)		1861		1874	100.0%	0.80 [0.65, 0.99]	ı •
Total events	259		298				
Heterogeneity: Chi ² = 9	9.27, df = 11 (P	= 0.60);	$I^2 = 0\%$				+ + + + + +
Test for overall effect:	Z = 2.04 (P = 0	.04)					0.05 0.2 1 5 20 intensive control usual care

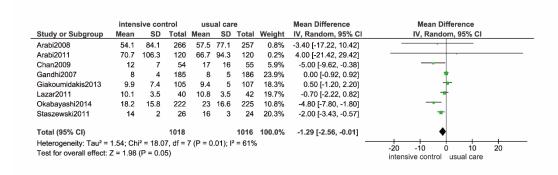
Supplementary Figure S9.



Supplementary Figure S10.



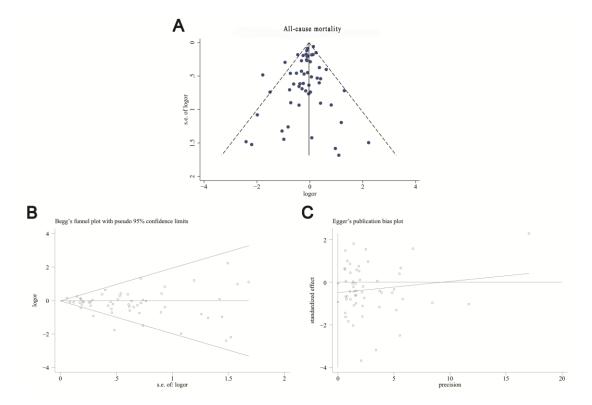
Supplementary Figure S11.



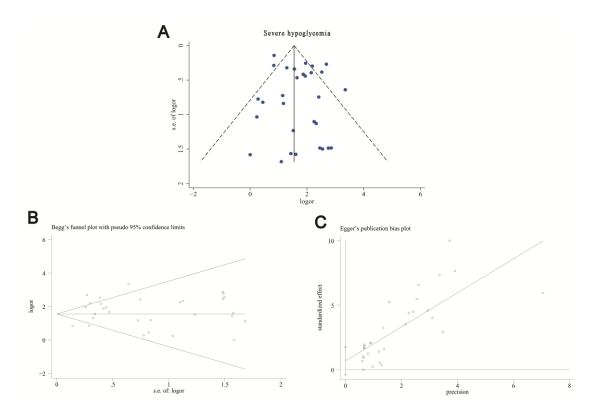
Supplementary Figure S12.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Annane2010	•	•	•	•	•	•	•
Arabi2008 Arabi2011	•	•	•	•	•	•	•
Bilotta2007	•	•	•	•	•	?	•
Bilotta2008	•	•	•	•	•	?	•
Bilotta2009	?	?	•	•	•	?	•
Bland2005	•	•		•	•	?	•
Brunkhorst2008	•	•	•	•	•	•	•
Bruno2008	•	?	•	•	•	?	•
Cao2011	•	?	•	•	•	?	•
Cappi2012	•	•	•	•	•	•	•
Chan2009 Coester2010	•	?	•	•	•	?	•
Davies1991	?	?	•	?	•	?	•
De Azevedo2010	•	•	•	•	•	?	•
De La Rosa2008	•	?	•	•	•	•	•
Desai2012	?	?	•	•	•	?	•
Dong2009	?	?	•	•	•	?	•
Farah2007	?	?	•	•	•	?	•
Fernandez2005	?	?	•	•	•	?	?
Finfer2009	•	•	•	•	•	•	•
Gandhi2007 Giakoumidakis2013	?	?	_	2	•	?	•
Gray2007	•	•	_	•	•	•	•
Green2010	?	•	•	?	•	?	•
Grey2004	?	•	•	•	•	?	•
He2007	•	•	•	?	•	?	•
Henderson2009	•	•		•	•	•	•
Jin2009	?	?	•	?	•	?	?
Johnston2009	•	•	•	•	•	•	•
Kalfon2014 Kia2005	•	?	•	•	•	?	•
Kreisel2009	-	?	_	•	•	•	?
Lapichino2008	•	?	•	•	•	?	•
Lazar2011	•	?	•	•	•	•	•
Mackenzie2005	•	•	•	•	•	?	•
Mahmoodpoor2011	?	•		?	•	?	
McMullin2007	•	•		•	•	?	•
Meng2009	•	?	•	•	•	?	•
Miranda2013	•	?	•	•	•	•	•
Mitchell2006	-		_	•	•		-
Okabayashi2014 Oksanen2007	•	?	•	•	•	?	●●
Preiser2009	•	•	•	•	•	•	•
Rosso2012	•	•	•	•	•	•	•
Savioli2009	•	?	•	•	•	•	•
Staszewski2011	•	?	•	•	•	?	•
Stecher2006	?	?	•	?	•	?	?
Taslimi2009	•	•	•	•	•	?	•
Van den Berghe2001	•	•	•	•	•	?	•
Van den Berghe2006 Walters2006	•	?		•	•	?	•
Walters2006 Wang2006	•	•	-	2		?	•
Wang2017	•	•	•	•	•	•	•
Yang2009	•	•	•	?	•	?	•
Yu2005	?	?	•	•	•	•	•

Supplementary Figure S13.



Supplementary Figure S14.





PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Checklist

www.prisma-statement.org

You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Section/Topic	Item No.	Checklist item	Reported on Page No.
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	

Section/Topic	Item No.	Checklist item	Reported on Page No.
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION	1		
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			

Section/Topic	Item No.	Checklist item	Reported on Page No.
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Once you have completed this checklist, please save a copy and upload it as part of your submission. Please DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.