

APPENDICES

Appendix 1: Search strategy for MEDLINE In-Process & Other Non-Indexed Citations (1946 to Present)

#	Searches
1	adrenergic beta-antagonists.mp. or exp Adrenergic beta-Antagonists/
2	alprenolol.mp. or exp Alprenolol/
3	bunolol.mp.
4	bupranolol.mp. or exp Bupranolol/
5	carteolol.mp. or exp Carteolol/
6	dihydroalprenolol.mp. or exp Dihydroalprenolol/
7	iodocyanopindolol.mp. or exp Iodocyanopindolol/
8	labetalol.mp. or exp Labetalol/
9	levobunolol.mp. or exp Levobunolol/
10	metipranolol.mp. or exp Metipranolol/
11	nadolol.mp. or exp Nadolol/
12	oxprenolol.mp. or exp Oxprenolol/
13	penbutolol.mp. or exp Penbutolol/
14	pindolol.mp. or exp Pindolol/
15	propranolol.mp. or exp Propranolol/
16	sotalol.mp. or exp Sotalol/
17	exp Timolol/ or timolol.mp.
18	adrenergic beta-1 receptor antagonists.mp. or exp Adrenergic beta-1 Receptor Antagonists/

19	acebutolol.mp. or exp Acebutolol/
20	atenolol.mp. or exp Atenolol/
21	betaxolol.mp. or exp Betaxolol/
22	bisoprolol.mp. or exp Bisoprolol/
23	exp Celiprolol/ or celiprolol.mp.
24	metoprolol.mp. or exp Metoprolol/
25	practolol.mp. or exp Practolol/
26	beta-blockers.mp.
27	esmolol.mp.
28	Bucindolol.mp.
29	Carvedilol.mp.
30	Nebivolol.mp. or exp Nebivolol/
31	sepsis.mp. or exp Sepsis/
32	septic shock.mp. or exp Shock, Septic/
33	septicemia.mp.
34	severe sepsis.mp.
35	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
36	31 or 32 or 33 or 34
37	35 and 36

Appendix 2: A priori hypotheses for subgroup effects

Subgroup	a priori hypotheses of subgroup effect by outcome					
	Mortality	Lengths of ICU and hospital stay	Heart Rate	Mean arterial pressure	Cardiac index	Vasopressor dose
Patients						
Sepsis vs severe sepsis vs septic shock	Greater reduction with beta-blockade in more severe illness	Greater reduction with beta-blockade in more severe illness	Greater reduction with beta-blockade in more severe illness	Greater reduction with beta-blockade in more severe illness	Greater reduction with beta-blockade in more severe illness	Greater increase with beta-blockade in more severe illness
Intervention						
esmolol vs other beta blockers	Greater reduction with beta-blockade in esmolol	Greater reduction with beta-blockade in esmolol	Greater reduction with beta-blockade in esmolol	Greater reduction with beta-blockade in esmolol	Smaller reduction with beta-blockade in esmolol	Smaller increase with beta-blockade in esmolol
Methodology						
high or unclear vs low risk of bias studies	Greater treatment effect with beta-blockade in high risk of bias studies					

Appendix 3. PRISMA-P 2015 checklist

Section and topic	Item No	Location in systematic review protocol
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Title
Update	1b	Title
Registration	2	Review registration
Authors:		
Contact	3a	Authors
Contributions	3b	Contributions
Amendments	4	N/A
Support:		
Sources	5a	Funding
Sponsor	5b	N/A
Role of sponsor	5c	N/A
INTRODUCTION		
Rationale	6	Introduction
Objectives	7	Introduction
METHODS		
Eligibility criteria	8	Methods: Criteria for selecting studies for this review
Information sources	9	Methods: Search methods for identification of studies, Additional search methods (grey literature)
Search strategy	10	Appendix 1
Study records:		
Data management	11a	Methods: Trial records, Data collection
Selection process	11b	Methods: Trial records
Data collection process	11c	Methods: Data collection
Data items	12	Methods: Types of outcomes, Data collection, Summarizing data and treatment effect

Outcomes and prioritization	13 Methods: Types of outcomes
Risk of bias in individual studies	14 Methods: Assessment of risk of bias
Data synthesis	15a Methods: Summarizing data and treatment effect 15b Methods: Summarizing data and treatment effect, Assessment of heterogeneity 15c Methods: Subgroup analysis and investigation of heterogeneity 15d Methods: Summarizing data and treatment effect
Meta-bias(es)	16 Methods: Assessment of reporting bias
Confidence in cumulative evidence	17 Methods: Assessment of confidence in estimates of effect