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S1. Summary of search strategy

MEDLINE	887
EMBASE	1475
Cochrane	329
Web of Science	388
Subtotal	3079
-dupes	-740
Total	2339

Oct 13, 2021

MEDLINE
Database: OVID Medline Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:
---
1 Hepatorenal Syndrome/ (1430)
2 ("hepatorenal disease" or "hepatorenal failure" or "hepatorenal insufficiency" or "hepatorenal syndrome" or HRS).mp. (37057)
3 1 or 2 (37057)
4 (((kidney* or renal) adj3 (failure* or injur*)) or AKI).mp. (233713)
5 exp Liver Cirrhosis/ (94358)
6 Hypertension, Portal/ (17085)
7 ((liver adj3 (fibroses or fibrosis)) or cirrhoses or cirrhosis).mp. (145100)
8 5 or 6 or 7 (154722)
9 4 and 8 (3432)
10 3 or 9 (39874)
11 Terlipressin/ (747)
12 (glipressin or glipressina or glycylpressin or glypressin or remestyp or terlipressin or triglycyllypressin or triglycyllysylvasopressin or triglycylvasopressin or "val 283" or val283 or vasopressin).mp. (40103)
13 Midodrine/ (468)
14 ("a 4020 linz" or "a4020 linz" or alphamine or amatine or gutron or metligine or midodrin or midodrine or "midodrine hydrochloride" or midon or midron or misodrine or mitodrine or orvaten or proamatine or "st 1085" or st1085 or "st-1085").mp. (733)
15 Octreotide/ (7840)
16 ("compound 201 995" or "compound 201995" or longastatin or longastatina or octreotide or oncolar or samilstin or "san 201 995" or "san 201995" or sandostatin or sandostatina or

sandostatine or "sandoz 201 995" or "sandoz 201995" or sandstatin or "sdz 201995" or sdz201995 or "sm 201 995" or "sm 201995" or "sms 201 995" or "sms 201995" or "sms 995" or "sms 995 aaa" or "sms 995aaa" or "sms201 995" or sms201995 or sms995 or "sms995 aaa" or sms995aaa or "somatuline la").mp. (11175)
17 exp Norepinephrine/ (86390)
18 (adrenor or alginodia or arterenal or arterenol or "baycain green" or levarterenol or levonor or levonorepinephrine or levophed or neomelubrin or noradrec or noradrenalin or noradrenaline or noradrine or norepinephrin or norepinephrine or norexadrin or revarterenol or sympathin or "sympathin e").mp. (126327)
19 Dopamine/ (71357)
20 ("asl 279" or asl279 or cardiopal or cardiosteril or catabon or dihydroxyphenylethylamine or docard or dopamex or dopamin or dopamina or dopamine or dopaminergic or dopaminex or dopaminum or dopastat or dopinga or dopmin or drynalken or dynatra or dynos or giludop or hydroxytyramine or inopan or inopin or inotropin or inovan or intropin or "intropin iv" or levodopamine or revivan or tensamin or uramin).mp. (186148)
21 exp Albumins/ (183539)
22 albumin.mp. (191347)
23 Furosemide/ (12039)
24 (furosemide or aldic or aluzine or anfuramaide or aquarid or arasemide or cetasix or desal or diamazon or dirine or diumide or diural or diuresal or diurin or diurix or diurolasa or diusemide or diuspec or dryptal or durafurid or edenol or errolon or eutensin or eutensine or flurosemide or franyl or fretic or frumid or frusedan or frusehexal or frusema or frusemide or frusid or fruzex or fumarenid or fumide or furanthril or furantril or furanturil or furosemide or furesin or furesis or furetic or furix or furmid or furo puren or furobasan or furomen or furomex or furomide or furomin or furopuren or furorese or furosemide or furoscan or furose or furosemide or furosemide or furosemix or furosemide or furosix or furovite or furosemide or fusid or fusimex or hissuflux or hydro rapid or impugan or jufurix or kofuzon or kutrix or lasiletten or lasilix or lasix or laxis or laxur or lb 502 or lb502 or luramide or marsemide or mirfat or odemase or odemex or oedemase or oedemex or pharmix or promedes or radisemide or rasitol or retep or salinex or seguril or selectofur or sigasalur or uremide or uresix or vesix or zafurida).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (17717)
25 or/11-24 (623034)
26 10 and 25 (2422)
27 randomized controlled trial.pt. (546156)
28 controlled clinical trial.pt. (94452)
29 randomi?ed.ab. (641966)
30 placebo.ab. (222197)
31 drug therapy.fs. (2385050)
32 randomly.ab. (367613)
33 trial.ab. (571598)
34 groups.ab. (2257900)

35 or/27-34 (5160085)
36 exp animals/ not humans.sh. (4897169)
37 35 not 36 (4490617)
38 26 and 37 (887)

Oct 14, 2021

EMBASE
Database: Embase <1974 to 2021 October 13>
Search Strategy:
---
1 hepatorenal syndrome/ (5826)
2 ("hepatorenal disease" or "hepatorenal failure" or "hepatorenal insufficiency" or "hepatorenal syndrome" or HRS).mp. (73815)
3 1 or 2 (73815)
4 (((kidney* or renal) adj3 (failure* or injur*)) or AKI).mp. (438626)
5 exp liver cirrhosis/ (169148)
6 exp portal hypertension/ (33845)
7 ((liver adj3 (fibroses or fibrosis)) or cirrhoses or cirrhosis).mp. (238172)
8 5 or 6 or 7 (253559)
9 4 and 8 (11289)
10 3 or 9 (83518)
Annotation: hepatorenal syndrome
11 terlipressin/ (3256)
12 (glipressin or glipressina or glycylpressin or glypressin or remestyp or terlipressin or triglycyllypressin or triglycyllysylvasopressin or triglycylvasopressin or "val 283" or val283 or vasopressin).mp. (64015)
13 midodrine/ (3052)
14 ("a 4020 linz" or "a4020 linz" or alphamine or amatine or gutron or metligine or midodrin or midodrine or "midodrine hydrochloride" or midon or midron or misodrine or mitodrine or orvaten or proamatine or "st 1085" or st1085 or "st-1085").mp. (3124)
15 octreotide/ (23280)
16 ("compound 201 995" or "compound 201995" or longastatin or longastatina or octreotide or oncolar or samilstin or "san 201 995" or "san 201995" or sandostatin or sandostatina or sandostatine or "sandoz 201 995" or "sandoz 201995" or sandstatin or "sdz 201995" or sdz201995 or "sm 201 995" or "sm 201995" or "sms 201 995" or "sms 201995" or "sms 995" or "sms 995 aaa" or "sms 995aaa" or "sms201 995" or sms201995 or sms995 or "sms995 aaa" or sms995aaa or "somatuline la").mp. (25746)
17 noradrenalin/ (124746)
18 (adrenor or alginodia or arterenal or arterenol or "baycain green" or levarterenol or levonor or levonorepinephrine or levophed or neomelubrin or noradrec or noradrenalin or noradrenaline

or noradrine or norepinephrin or norepinephrine or norexadrin or revarterenol or sympathin or "sympathin e").mp. (168757)
19 dopamine/ (118674)
20 ("asl 279" or asl279 or cardiopal or cardiosteril or catabon or dihydroxyphenylethylamine or docard or dopamex or dopamin or dopamina or dopamine or dopaminergic or dopaminex or dopaminum or dopastat or dopinga or dopmin or drynalken or dynatra or dynos or giludop or hydroxytyramine or inopan or inopin or inotropin or inovan or intropin or "intropin iv" or levodopamine or revivan or tensamin or uramin).mp. (267079)
21 albumin/ (139271)
22 albumin.mp. (284527)
23 furosemide/ (60215)
24 (furosemide or aldic or aluzine or anfuramaide or aquarid or arasemide or cetasix or desal or diamazon or dirine or diumide or diural or diuresal or diurin or diurix or diurolasa or diusemide or diuspec or dryptal or durafurid or edenol or errolon or eutensin or eutensine or flurosemide or franyl or fretic or frumid or frusedan or frusehexal or frusema or frusemide or frusid or fruzex or fumarenid or fumide or furanthril or furantril or furanturil or furosemide or furesin or furesis or furetic or furix or furmid or furo puren or furobasan or furomen or furomex or furomide or furomin or furopuren or furorese or furosemide or furoscan or furose or furosemide or furosemide or furosemix or furosemide or furosix or furovite or furosemide or fusid or fusimex or hissuflux or hydro rapid or impugan or jufurix or kofuzon or kutrix or lasiletten or lasilix or lasix or laxis or laxur or lb 502 or lb502 or luramide or marsemide or mirfat or odemase or odemex or oedemase or oedemex or pharmix or promedes or radisemide or rasitol or retep or salinex or seguril or selectofur or sigasalur or uremide or uresix or vesix or zafurida).mp. (62757)
25 or/11-24 (805451)
26 10 and 25 (6569)
27 randomized controlled trial/ (679862)
28 Controlled clinical study/ (464158)
29 random$.ti,ab. (1714729)
30 randomization/ (92009)
31 intermethod comparison/ (275971)
32 placebo.ti,ab. (330767)
33 (compare or compared or comparison).ti. (548338)
34 ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab. (2381681)
35 (open adj label).ti,ab. (91644)
36 ((double or single or doubly or singly) adj (blind or blinded or blindly)).ti,ab. (249306)
37 double blind procedure/ (188665)
38 parallel group$1.ti,ab. (28229)
39 (crossover or cross over).ti,ab. (113029)
40 ((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant$1)).ti,ab. (364685)
41 (assigned or allocated).ti,ab. (429819)
42 (controlled adj7 (study or design or trial)).ti,ab. (390059)

43 (volunteer or volunteers).ti,ab. (261385)
44 human experiment/ (556892)
45 trial.ti. (340928)
46 or/27-45 (5543599)
47 (random$ adj sampl$ adj7 ("cross section$" or questionnaire$1 or survey$ or database$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.) (8733)
48 Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or randomi?ed controlled.ti,ab. or control group$1.ti,ab.) (284883)
49 (((case adj control$) and random$) not randomi?ed controlled).ti,ab. (19019)
50 (Systematic review not (trial or study)).ti. (188582)
51 (nonrandom$ not random$).ti,ab. (17302)
52 "Random field$".ti,ab. (2595)
53 (random cluster adj3 sampl$).ti,ab. (1388)
54 (review.ab. and review.pt.) not trial.ti. (930981)
55 "we searched".ab. and (review.ti. or review.pt.) (38621)
56 "update review".ab. (118)
57 (databases adj4 searched).ab. (45809)
58 (rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/ (1124945)
59 Animal experiment/ not (human experiment/ or human/) (2360480)
60 or/47-59 (3803886)
61 46 not 60 (4918786)
62 26 and 61 (1475)

Cochrane Library

Search Name:
Date Run: 14/10/2021 11:35:03
Comment:

ID	Search	Hits
#1	MeSH descriptor: [Hepatorenal Syndrome] explode all trees	76
#2	hepatorenal near/2 (disease or failure or insufficiency or syndrome)	514
#3	#1 or #2	514
#4	(kidney* or renal) near/3 (failure* or injur*)	23187
#5	AKI	1877
#6	#4 or #5	23429
#7	MeSH descriptor: [Liver Cirrhosis] explode all trees	3037
#8	MeSH descriptor: [Hypertension, Portal] explode all trees	1208
#9	((liver NEAR/3 (fibroses or fibrosis)) or cirrhoses or cirrhosis)	11233
#10	#7 or #8 or #9	11695

#11 #6 and #10 574
#12 #3 or #11 993
#13 MeSH descriptor: [Terlipressin] explode all trees 192
#14 (glipressin or glipressina or glycylpressin or glypressin or remestyp or terlipressin or triglycyllypressin or triglycyllysylvasopressin or triglycylvasopressin or "val 283" or val283 or vasopressin) 2965
#15 MeSH descriptor: [Midodrine] explode all trees 139
#16 ("a 4020 linz" or "a4020 linz" or alphamine or amatine or gutron or metligine or midodrin or midodrine or "midodrine hydrochloride" or midon or midron or misodrine or mitodrine or orvaten or proamatine or "st 1085" or st1085 or "st-1085") 313
#17 MeSH descriptor: [Octreotide] explode all trees 700
#18 ("compound 201 995" or "compound 201995" or longastatin or longastatina or octreotide or oncolar or samilstin or "san 201 995" or "san 201995" or sandostatin or sandostatina or sandostatine or "sandoz 201 995" or "sandoz 201995" or sandstatin or "sdz 201995" or sdz201995 or "sm 201 995" or "sm 201995" or "sms 201 995" or "sms 201995" or "sms 995" or "sms 995 aaa" or "sms 995aaa" or "sms201 995" or sms201995 or sms995 or "sms995 aaa" or sms995aaa or "somatuline la") 1660
#19 MeSH descriptor: [Norepinephrine] explode all trees 2851
#20 (adrenor or alginodia or arterenal or arterenol or "baycain green" or levarterenol or levonor or levonorepinephrine or levophed or neomelubrin or noradrec or noradrenalin or noradrenaline or noradrine or norepinephrin or norepinephrine or norexadrin or revarterenol or sympathin or "sympathin e") 8927
#21 MeSH descriptor: [Dopamine] explode all trees 1316
#22 ("asl 279" or asl279 or cardiopal or cardiosteril or catabon or dihydroxyphenylethylamine or docard or dopamex or dopamin or dopamina or dopamine or dopaminergic or dopaminex or dopaminum or dopastat or dopinga or dopmin or drynalken or dynatra or dynos or giludop or hydroxytyramine or inopan or inopin or inotropin or inovan or intropin or "intropin iv" or levodopamine or revivan or tensamin or uramin) 10042
#23 MeSH descriptor: [Albumins] explode all trees 8141
#24 albumin 16091
#25 MeSH descriptor: [Furosemide] explode all trees 1198
#26 (furosemide or aldic or aluzine or anfuramaide or aquarid or arasemide or cetasix or desal or diamazon or dirine or diumide or diural or diuresal or diurin or diurix or diurolasa or diusemide or diuspec or dryptal or durafurid or edenol or errolon or eutensin or eutensine or flurosemide or franyl or fretic or frumid or frusedan or frusehexal or frusema or frusemide or frusid or fruzex or fumarenid or fumide or furanthril or furantril or furanturil or furosemide or furesin or furesis or furetic or furix or furmid or furo puren or furobasan or furomen or furomex or furomide or furomin or furopuren or furorese or furosemide or furoscan or furose or furosemide or furosemide or furosemix or furosemide or furosix or furovite or furosemide or fusid or fusimex or hissuflux or hydro rapid or impugan or jufurix or kofuzon or kutrix or lasiletten or lasilix or lasix or laxis or laxur or lb 502 or lb502 or luramide or marsemide or mirfat or odemase or odemex or oedemase or oedemex or pharmix or promedes or radisemide or rasitol or retep or salinex or seguril or selectofur or sigasalur or uremide or uresix or vesix or zafurida) 3074

#27 #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 44935
#28 #12 and #27 in Trials 329

Web of Science (Clarivate)

9
(#8) AND #7
Edit
Add to Search
388

8
TS=(randomised OR randomized OR randomisation OR randomisation OR placebo* OR (random* AND (allocat* OR assign*)) OR (blind* AND (single OR double OR treble OR triple)))
Edit
Add to Search
1,310,907

7
(#5) AND #6
Edit
Add to Search
1,592

6
TS=((glipressin or glipressina or glycylpressin or glypressin or remestyp or terlipressin or triglycyllypressin or triglycyllysylvasopressin or triglycylvasopressin or "val 283" or val283 or vasopressin or "a 4020 linz" or "a4020 linz" or alphamine or amatine or gutron or metligine or midodrin or midodrine or "midodrine hydrochloride" or midon or midron or misodrine or mitodrine or orvaten or proamatine or "st 1085" or st1085 or "st-1085" or "compound 201 995" or "compound 201995" or longastatin or longastatina or octreotide or oncolar or samilstin or "san 201 995" or "san 201995" or sandostatin or sandostatina or sandostatine or "sandoz 201 995" or "sandoz 201995" or sandstatin or "sdz 201995" or sdz201995 or "sm 201 995" or "sm 201995" or "sms 201 995" or "sms 201995" or "sms 995" or "sms 995 aaa" or "sms 995aaa" or "sms201 995" or sms201995 or sms995 or "sms995 aaa" or sms995aaa or "somatuline la" or adrenor or alginodia or arterenal or arterenol or "baycain green" or levarterenol or levonor or levonorepinephrine or levophed or neomelubrin or noradrec or noradrenalin or noradrenaline or noradrine or norepinephrin or norepinephrine or norexadrin or revarterenol or sympathin or "sympathin e" or "asl 279" or asl279 or cardiopal or cardiosteril or catabon or dihydroxyphenylethylamine or docard or dopamex or dopamin or dopamina or dopamine or dopaminergic or dopaminex or dopaminum or dopastat or dopinga or dopmin or drynalken or dynatra or dynos or giludop or hydroxytyramine or inopan or inopin or inotropin or inovan or intropin or "intropin iv" or levodopamine or revivan or tensamin or uramin or albumin or furosemide or aldic or aluzine or anfuramaide or aquarid or arasemide or cetasix or desal or

diamazon or dirine or diumide or diural or diuresal or diurin or diurix or diurolasa or diusemide or diuspec or dryptal or durafurid or edenol or errolon or eutensin or eutensine or flurosemide or franyl or fretic or frumid or frusedan or frusehexal or frusema or frusemide or frusid or fruzex or fumarenid or fumide or furanthril or furantril or furanturil or furosemide or furesin or furesis or furetic or furix or furmid or furo puren or furobasan or furomen or furomex or furomide or furomin or furopuren or furorese or furosemide or furoscan or furose or furosemide or furosemide or furosemix or furosemide or furosix or furovite or furosemide or fusid or fusimex or hissuflux or hydro rapid or impugan or jufurix or kofuzon or kutrix or lasiletten or lasilix or lasix or laxis or laxur or lb 502 or lb502 or luramide or marsemide or mirfat or odemase or odemex or oedemase or oedemex or pharmix or promedes or radisemide or rasitol or retep or salinex or seguril or selectofur or sigasalur or uremide or uresix or vesix or zafurida))
Edit
Add to Search

523,672

5
(#1) OR #4
Edit
Add to Search

5,484

4
(#3) AND #2
Edit
Add to Search

2,874

3
TS=(((liver NEAR/3 (fibroses or fibrosis)) or cirrhoses or cirrhosis))
Edit
Add to Search

131,258

2
TS=((kidney* or renal) near/3 (failure* or injur*))
Edit
Add to Search

168,556

1
TS=(hepatorenal near/2 (disease or failure or insufficiency or syndrome))
Edit
Add to Search

S2. Risk of bias tool

Bias from the randomization process	
Issues to consider: Random sequence generation Allocation concealment	
Definitely low risk of bias	Trials that assign participants to alternative interventions using a randomly generated sequence and maintain allocation concealment. Examples of methods for developing a randomly generated allocation sequence include a random number generator, random number table, coin tossing, shuffling cards or envelopes, and throwing dice. If a trial is described as 'randomized' without any additional details related to how the allocation sequence was developed, we will assume that the allocation sequence was appropriately developed. Examples of methods for maintaining allocation concealment include using central allocation via a computer or phone system, pharmacy-controlled allocation, opaque sealed envelopes, and sequentially numbered drug containers. *Note that an explicit description of random sequence generation is not necessary for a rating of low risk of bias.*
Probably low risk of bias	Trials in which healthcare providers were blind to the intervention but which provide no information on allocation concealment and in which there are no major baseline imbalances. *Note that an explicit description of random sequence generation is not necessary for a rating of probably low risk of bias.*
Probably high risk of bias	Trials in which healthcare providers were not blind to the intervention and which provide no information on allocation concealment. Trials in which there are substantial baseline differences between trial arms that suggest a problem with the randomization process but there are no other limitations related to randomization.
Definitely high risk of bias	Trials in which allocation is by judgment of the clinician, by preference of the participant, by availability of the intervention, based on the results of a laboratory test, or other non-random rules (e.g., birthdate, etc.).

	Trials in which investigators enrolling participants could possibly foresee the arm to which each subsequent patient would be randomized, such as allocation using an open allocation schedule (e.g. a list of random numbers), assignment envelopes used without appropriate safeguards (e.g. use of unsealed, non-opaque or not sequentially numbered envelopes), alternation between arms, case record number, or any other explicitly unconcealed procedure, rate as high risk.
Bias due to deviations from the intended intervention	
Issues to consider: Blinding of healthcare providers/clinicians and participants Imbalances in cointerventions or behaviors	
Definitely low risk of bias	Therapy trials in which healthcare providers are blind to the intervention administered and in which there are no significant differences in administered co-interventions. Therapy trials that are described as double or triple blind.
Probably low risk of bias	
Probably high risk of bias	Therapy trials in which healthcare providers are not blind to the intervention administered. Therapy trials in which healthcare providers are blind to the intervention administered but there are significant differences in administered co-interventions that suggests that blinding may have been compromised. Therapy trials in which healthcare providers are described as being blind to the intervention but allocation concealment was inadequate.
Definitely high risk of bias	Therapy trials in which healthcare providers are not blind to the intervention and in which there are significant differences in administered co-interventions.
Bias due to missing data	
Issues to consider: Missing outcome measures Loss to follow-up	
Definitely low risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) < 10%. For in-patient trials, we will assume low risk of bias due to missing data unless otherwise specified.

Probably low risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) is between 10% to 15% and missing outcome data is unlikely to be related to the true outcome and there is no imbalance in numbers of or reasons for missing data across intervention groups.
Probably high risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) is between 10% to 15% and missing outcome data is likely to be related to the true outcome or there are imbalances in numbers of or reasons for missing data across intervention groups.
Definitely high risk of bias	Trials in which missing outcome data (including outcome data that has been imputed) > 15%.
Bias due to measurement of the outcome	
Issues to consider: Blinding of outcome adjudicators Objectivity of outcome *Note that the judgments may differ across outcomes.*	
Definitely low risk of bias	Trials in which patients are blind to the intervention and in which outcomes are patient-reported. Trials in which outcomes are measured by a third-party (investigator or clinician) and in which the third-party is blind to the intervention. Trials in which the outcomes are objective. Trials that are described as double or triple blind.
Probably low risk of bias	
Probably high risk of bias	
Definitely high risk of bias	Trials in which patients are not blind and in which outcomes are patient-reported (e.g., time to symptom resolution). Trials in which outcome adjudicators are not blind and the outcomes are not objective (e.g., adverse effects leading to discontinuation, transfusion-related acute lung injury, transfusion-associated circulatory overload, allergic reactions, infection with suspected/symptomatic COVID-19, venous thromboembolism, time to symptom resolution including fever, time to clinical improvement if the criteria for clinical improvement are not objective).
Bias in selection of the reported results	
Issues to consider: Selective reporting of timepoints	

Selective reporting of outcome measures *Note that we are only interested in selective reporting for the outcomes for which we are extracting data.* *Note that the judgments may differ across outcomes.*	
Definitely low risk of bias	Results for outcomes that were analyzed and reported according to a pre-specified statistical analysis plan or protocol (including the timepoint for the measurement of the outcome).
Probably low risk of bias	Results for outcomes that were analyzed and reported but that were not prespecified in a statistical analysis plan or protocol but the timepoint at which results are reported is consistent with the timepoint for other outcomes in the trial report or there is little reason to believe the outcome was selectively reported. Please note that outcomes that were not prespecified in a protocol or statistical analysis plan and that are reported in the trial preprint or publication should be rated at probably low risk of bias unless there are other important reasons to suspect that results for those outcomes were selectively reported (e.g., results are presented at timepoints that don't match the timepoints reported for other outcomes).
Probably high risk of bias	Results for outcomes that were analyzed and reported but that were not prespecified in a statistical analysis plan or protocol but the timepoint at which results are reported is not consistent with the timepoint for other outcomes in the trial report or there are other reasons to believe that the outcome is selectively reported.
Definitely high risk of bias	Results for outcomes that were analyzed and reported for which there are inconsistencies with the statistical analysis plan or protocol. These inconsistencies may include outcome measures of interest or the timepoints for the measurement of outcomes.

S3. Methods terminology for GRADE and network meta-analysis

Terms:

Network meta-analysis - a type of meta-analysis that compares more than two treatments against one another in the same analytic framework using both direct and indirect evidence to inform network estimates.

Frequentist network meta-analysis - a method of analysis that relies on traditional hypothesis-testing. This is compared to Bayesian analysis which uses probabilities generated from 'priors' and treatment effects.

Node splitting – a method for dividing network estimates into indirect and direct components to facilitate inspecting for coherence.

Heterogeneity estimators - methods for calculating heterogeneity (differences between studies) in meta-analysis. Restricted Maximum Likelihood (REML) estimator is one such example. Simulation studies show that this method produces better error rates.

ICEMAN tool - is a validated instrument designed to evaluate the credibility of a subgroup.

Imprecision - using minimally important differences, we rated down the certainty of evidence once, twice or three times, depending on how uncertain the result is.

Using a minimally contextualized framework, we rated down once for imprecision if the confidence intervals included the MID. If the confidence interval included the MID in both directions we rated down twice. We did not rate down three times for any estimate.

Indirectness - This is assessed whether the population and intervention of interest are congruent with the research question. If it is not, researchers may rate down the certainty of evidence.

We assessed this by evaluating each trial and making judgements on the included trials, interventions (dose, route, duration) and how each outcome was measured (i.e., definition of reversal for example).

Publication bias - In estimates with 10 more studies, publication bias can be assessed. If there is publication bias, investigators may rate down. We assessed publication bias by inspecting funnel plots and Egger's statistical test.

There were two instances where we rated down for publication bias in our analysis.

Inconsistency - The individual study estimates may be inconsistent with each other. If this is detected, we may further rate down the certainty of evidence.

We assessed for inconsistency by reviewing forest plots for each estimate. Both the width and overlap of confidence intervals were measured. I^2 statistics were also assessed. If inconsistency was detected, we rated down if removal of that study changed the results.

Incoherence - coherence refers to consistency between direct and indirect estimates

We planned to down for incoherence when the indirect and direct estimates were different enough such that there was no overlap in confidence intervals. We did not detect incoherence in our networks and therefore never rated down for this.

Intransitivity - Intransitivity is the dissimilarity of important factors that may affect the outcome being investigated (i.e., effect modifiers) across comparisons.

We looked at multiple possible effect modifiers across the network to determine whether there was intransitivity.

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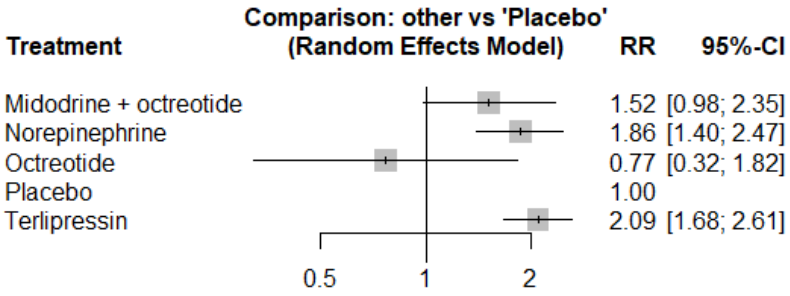
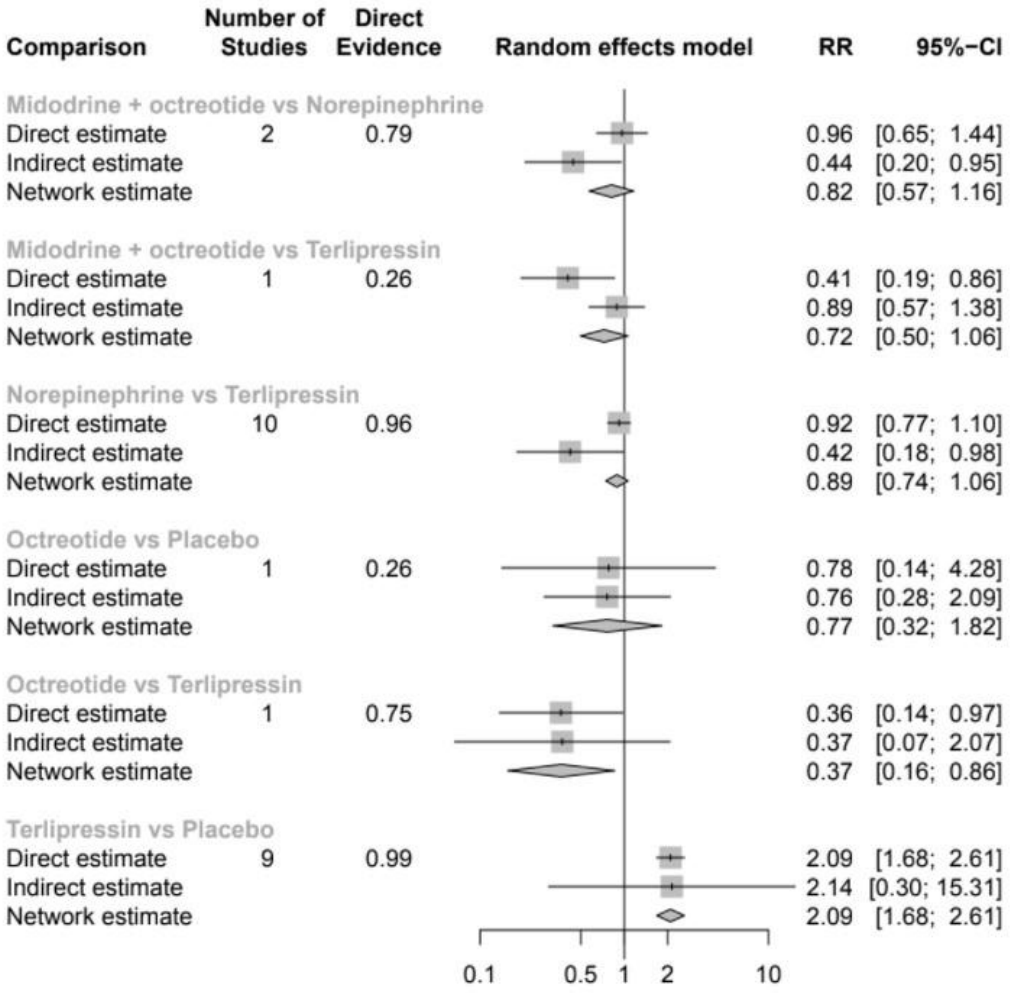
S4. Forest plots, node splitting, and funnel plot

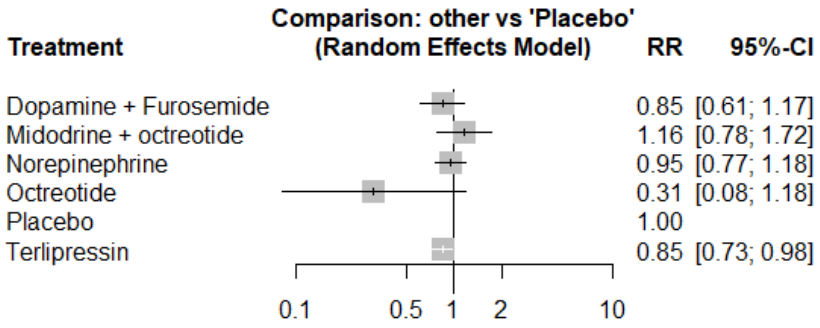
HRS reversal network plot



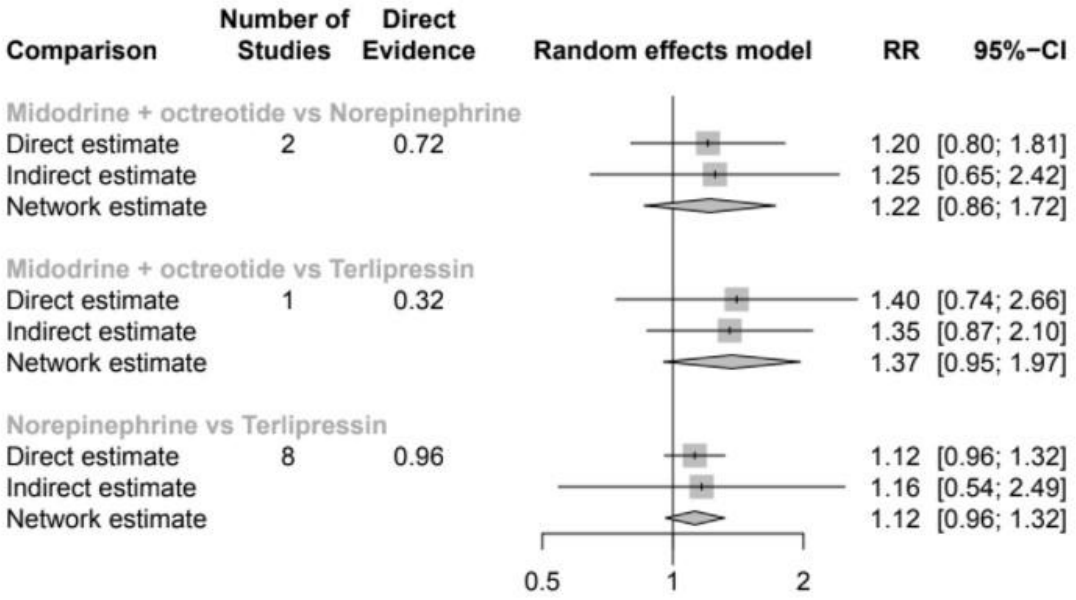
HRS reversal node splitting plot



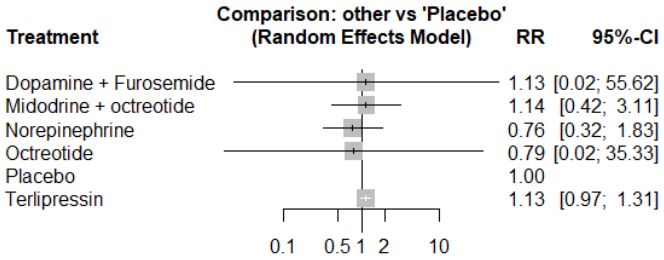
HRS mortality network plot



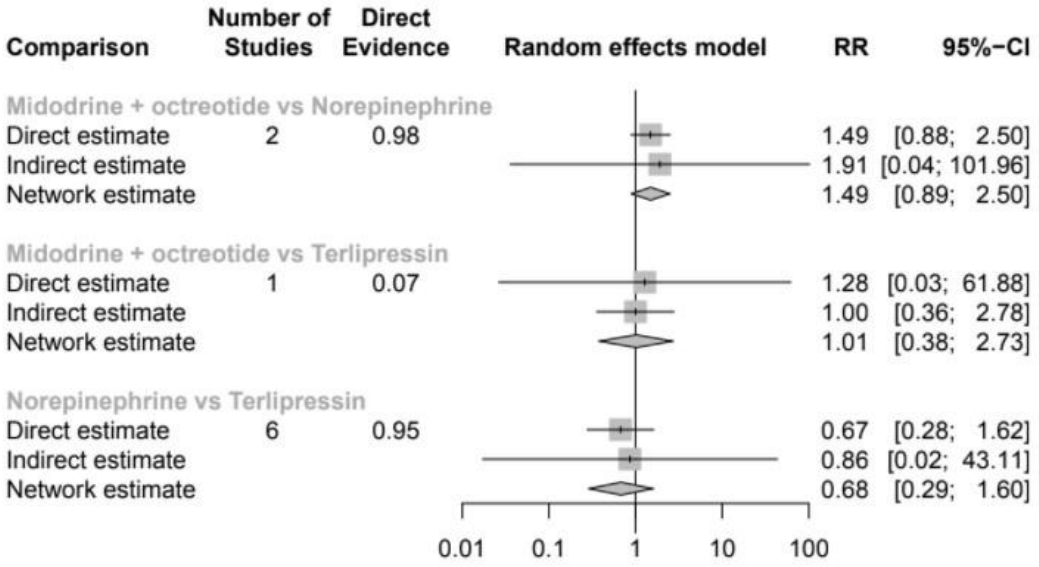
HRS mortality node splitting plot



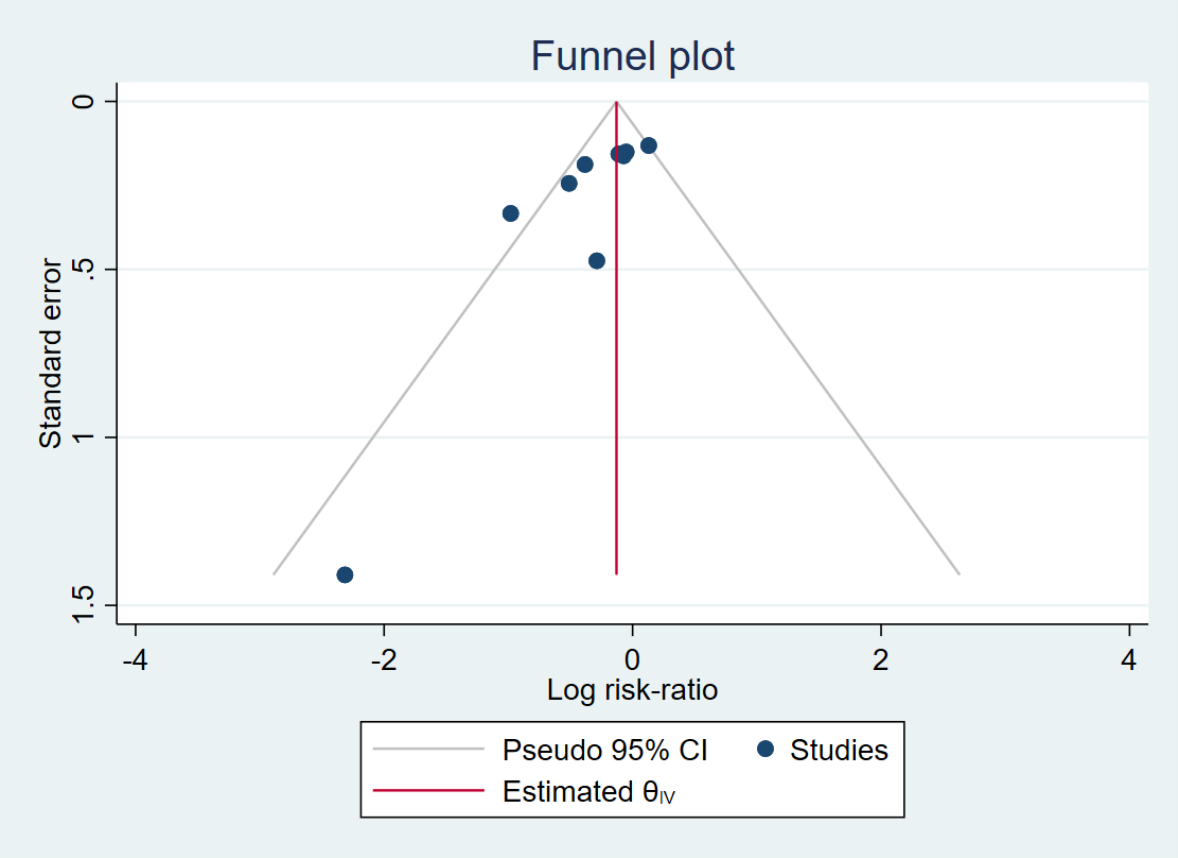
HRS SAE network plot



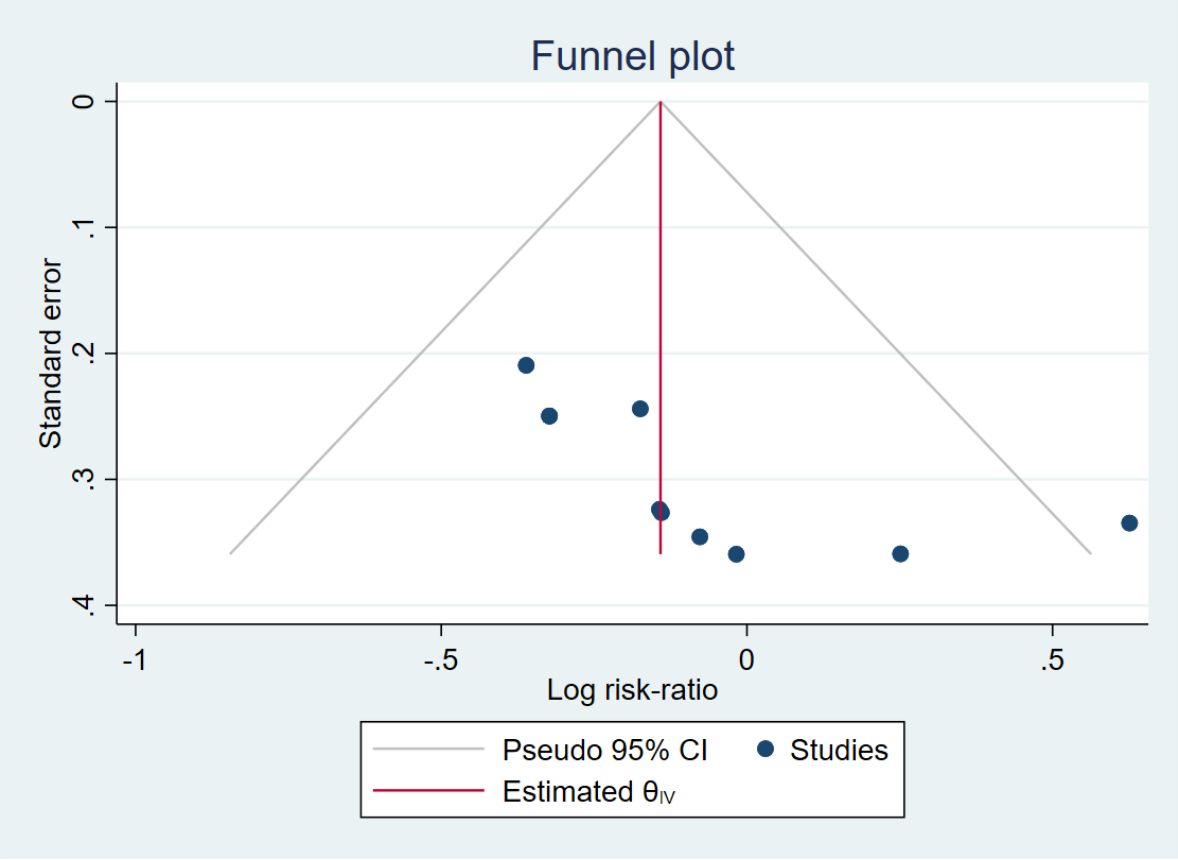
HRS SAE node splitting plot



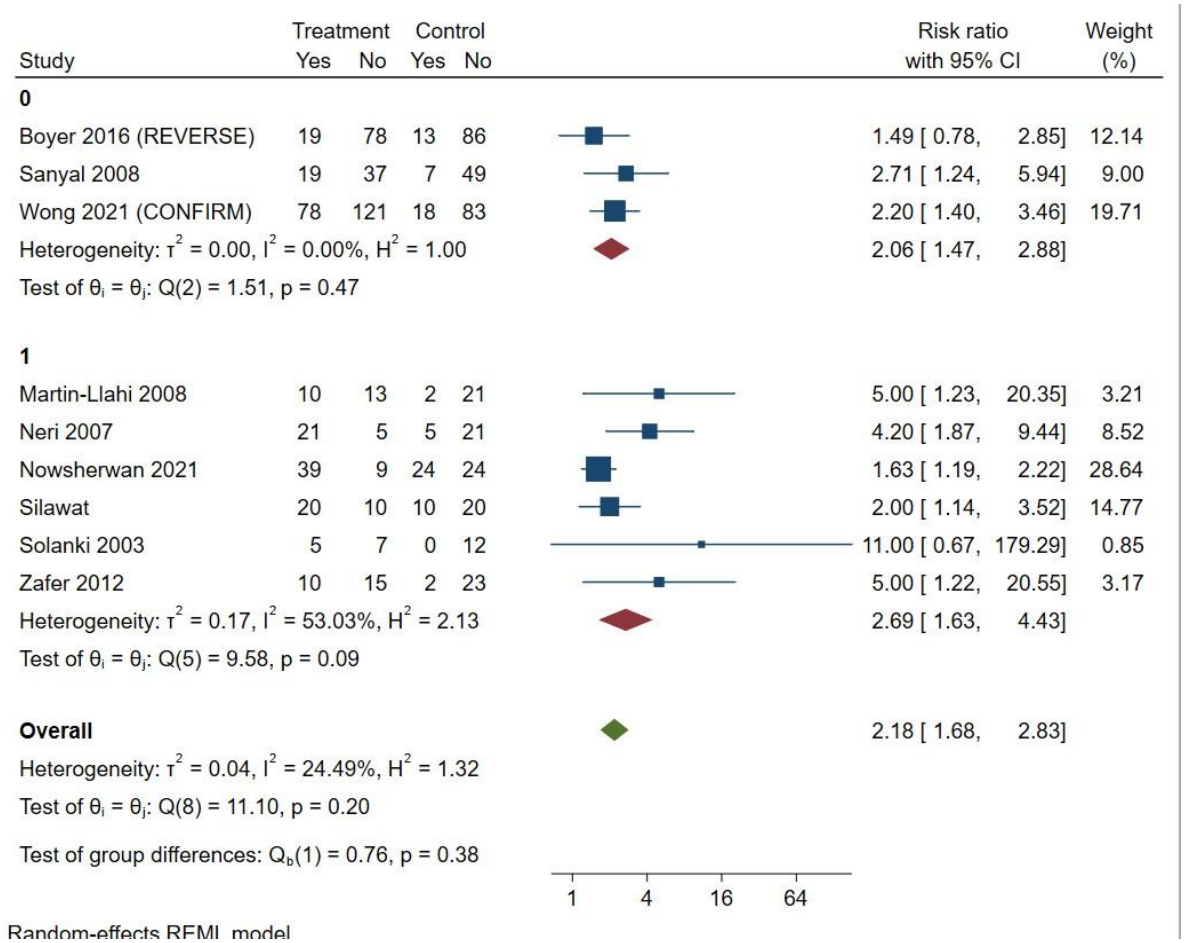
Funnel plot for terlipressin vs placebo (mortality)



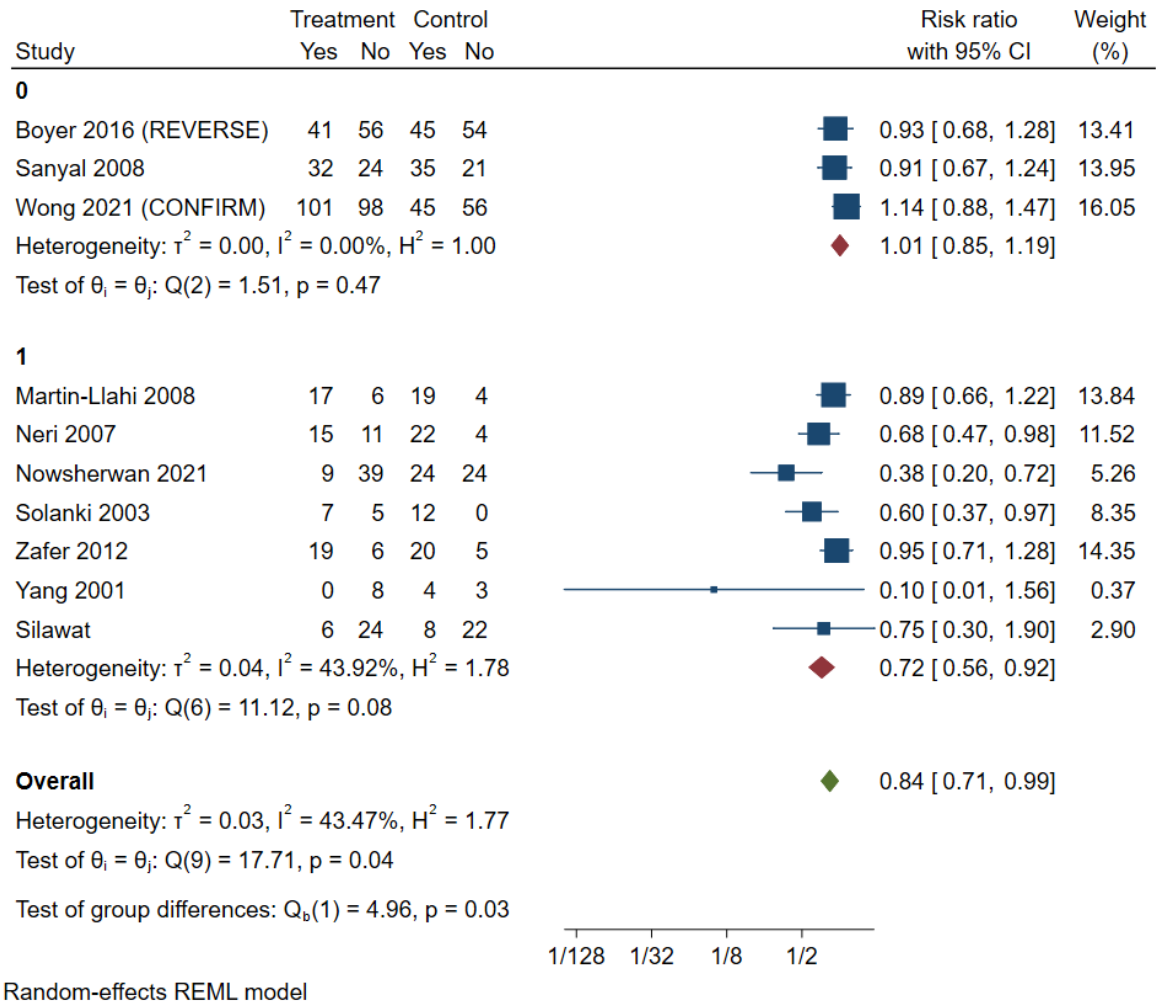
Funnel plot for terlipressin vs norepinephrine (HRS reversal)



Forest plot for the subgroup analysis of reversal of HRS for low risk of bias (0) versus high risk of bias (1) trials.



Subgroup analysis of mortality for low risk of bias (0) versus high risk of bias (1) trials.



S5. Trial characteristics.

Study	Intervention	Country of recruitment	Trial registration number	N	Age	Male (%) total	Type 1 HRS (%)	Type 2 HRS (%)	Child-Pugh	MELD
Nowsherwan 2021	TERLI vs Placebo	India	NR	96	41.5	45.8	100	0	NR	NR
Solanki 2003	TERLI vs Placebo	India	NR	24	51.5	70.8	100	0	NR	NR
Neri 2007	TERLI vs Placebo	Italy	NR	52	59.5	40.3	100	0	11.3	NR
Zafer 2012	TERLI vs Placebo	Pakistan	NR	50	NR	NR	NR	NR	NR	NR
Martin-Llahi 2008	TERLI vs Placebo	Spain	NCT00287664	46	57	63	76.1	23.9	10.5	29
Boyer 2016 (REVERSE)	TERLI vs Placebo	USA, Canada	NCT01143246	196	55.3	60.7	100	0	10.3	33
Wong 2021 (CONFIRM)	TERLI vs Placebo	USA, Canada	NCT02770716	300	53.8	59.3	100	0	10.6	33

Sanyal 2008	TERLI vs Placebo	USA, Germany, Russia	NCT00089570	112	51.7	71.4	100	0	11.4	33.4
Yang 2001	TERLI vs Placebo	China	NR	15	NR	66	NR	NR	NR	NR
Silawat 2011	TERLI vs Placebo	Egypt	NR	60	NR	NR	NR	NR	NR	NR
Cavallin 2015	TERLI vs O+M	Italy	NCT00742339	48	62.2	65.1	91.5	8.5	NR	30.3
Srivastava 2015	TERLI vs D+F	India	CTRI/2011/07/001860	80	43	86.2	50	50	12.2	NR
Pomier-Layrargues 2003	O vs Placebo	Canada	NR	16	52.1	74.6	30.9	69.1	12.2	NR
Copaci 2016	TERLI vs O	Romania	NR	40	NR	NR	100	0	NR	NR
Ghosh 2013	NE vs TERLI	India	NCT01637454	46	47	78.3	0	100	10.2	21.1
Goyal 2016	NE vs TERLI	India	NR	41	55.7	90.2	100	0	10.8	29.6
Indrabi 2013	NE vs TERLI	India	NR	60	NR	NR	NR	NR	NR	NR

Saif 2018	NE vs TERLI	India	CTRI/2011/09/002032	60	52.6	NR	100	0	11.9	29.7
Sharma 2008	NE vs TERLI	India	NR	40	48	85	100	0	10.8	30.6
Singh 2012	NE vs TERLI	India	NR	46	49.8	82.6	100	0	10.5	25.5
Arora 2018	NE vs TERLI	India	NCT02573727	120	39.5	94	NR	NR	11	33.5
Alessandria 2007	NE vs TERLI	Italy	NR	22	55.4	72.5	40.8	59.2	10.5	26
Badawy 2013	NE vs TERLI	Egypt	NR	51	NR	NR	NR	NR	NR	NR
Goyal 2008	NE vs TERLI	India	NR	32	55	76	100	NR	NR	NR
Mahmoud 2021	NE vs O+M	Egypt	NCT03455322	60	60.9	50	100	0	11.7	NR
Tavakkoli 2012	NE vs O+M	Iran	IRCT201107217085N1	23	52.5	65.1	64.7	35.3	11.8	33.7

Legend:

N = total number of patients randomized

TERLI=terlipressin

O = octreotide

M = midodrine

NE= norepinephrine

NR = not reported

S6. Study characteristics for intervention, background therapy and definition for response to therapy.

StudyID	**Solanki 2003**
Intervention	Terlipressin vs. Placebo
Intervention details	Terlipressin given at 1mg IV at 12-h intervals and placebo patients received distilled water 1mL IV at 12-h intervals for the study period.
Background therapy	The patients from both groups received i.v. albumin infusion, 20 g/day and fresh frozen plasma (FFP) 150 mL every 8h, until central venous pressure reached the upper normal range (10–12cm of H2O). None of the investigated patients showed improvement of renal function after volume expansion. Nearly all the patients received daily i.v. albumin until the end of the study period or until they died. The patients also received dopamine in the renal vasodilatory doses (≤4μg/min) only for the initial 24–48h.
Response definition	Not defined.
StudyID	**Arora 2020**
Intervention	Norepinephrine vs. Terlipressin
Intervention details	Terlipressin was started at 2 mg/hour. Dosage of terlipressin was doubled every 48 hours in case of nonresponse (<25% of pretreatment value) to the maximum dosage of 12 mg/24 h. Noradrenaline was given as a continuous intravenous infusion starting at 0.5 mg/h with doubling of dose after every 4 hours designed to achieve an increase in mean arterial pressure (MAP) of at least 10 mm Hg or an increase in 4-hour urine output >200 mL. When one of these goals was not achieved, noradrenaline dose was increased every 4 hours in steps of 0.5 mg/h, up to a maximum dose of 3 mg/h.
Background therapy	Plasma expansion was done with albumin for the initial 2 days (1 g/kg/day dose titrated as per signs of volume overload. Daily albumin (20-40 g/day) was given in both groups until the end of reversal of HRS-AKI or evidence of volume overload (CVP >18 cm of H20 or IVC >22 mm) or requirement of RRT.
Response definition	Defined by a decrease in SCr level to ≤1.5 mg/dL.
StudyID	**Neri 2007**

Intervention	Terlipressin vs. placebo
Intervention details	Intravenous boluses of terlipressin at the dose of 1 mg/8 h/5 days followed by 0.5 mg/8 h for two weeks plus albumin or intravenous boluses of albumin alone. Albumin was given at a weight-based dosage (1 g/kg body weight during the first day and 20–40 g/day thereafter)
Background therapy	Both groups received albumin.
Response definition	Complete response: decrease of serum creatinine to a value of 132 µmol/l (1.5 mg/dl) or lower, during treatment.
StudyID	**Sanyal 2008**
Intervention	Terlipressin vs. Placebo
Intervention details	Terlipressin at a dose of 1 mg administered by slow intravenous (IV) push every 6 hours or matching placebo. If after 3 days of therapy, SCr level had not decreased by at least 30% from the baseline value, the dose of the study drug (terlipressin or placebo) was increased to 2 mg every 6 hours.
Background therapy	Concomitant use of the following medications was prohibited during the period of study drug administration: vasoactive drugs (such as dopamine or noradrenaline), prostaglandin analogues and nonsteroidal anti-inflammatory drugs. Patients received concomitant IV albumin (100 g on day 1 and 25 g daily until end of treatment) as per standard medical practice.
Response definition	Defined by a decrease in SCr level to ≤1.5 mg/dL.
StudyID	**Boyer 2016 (REVERSE)**
Intervention	Terlipressin vs. Placebo
Intervention details	Terlipressin 1 mg or placebo was administered via a slow intravenous bolus injection over 2 minutes every 6 hours (total amount of terlipressin, 4 mg/day).
Background therapy	Both groups received albumin.
Response definition	Defined as 2 SCr values of 1.5 mg/dL or less, collected at least 40 hours apart

	(48 hours minus an 8-hour window) while on treatment, defined as within 24 hours of the last dose of study treatment, and without intervening RRT or liver transplant
StudyID	**Martin-Llahi 2008**
Intervention	Terlipressin vs. Placebo
Intervention details	Terlipressin and albumin, terlipressin (Glypressin, Ferring AB, Sweden) was administered initially at a dose of 1 mg/4 hour as IV bolus for 3 days. If after the first 3 days serum creatinine had decreased at least 25% of the pretreatment values, the dose was not modified. In patients in whom serum creatinine had not decreased at least 25% of the pretreatment values within the first 3 days, the dose was increased to a maximum of 2 mg/4 hour. Terlipressin was given until serum creatinine had decreased below 133 µmol/L or for a maximum of 15 days.
Background therapy	Both groups received albumin.
Response definition	Defined as a reduction in serum creatinine below 133 µmol/L during treatment or partial response when there was a reduction in serum creatinine of greater than 50% of the pretreatment value but with an end-of-treatment value equal to or greater than 133 µmol/L.
StudyID	**Zafer 2012 (Abstract only)**
Intervention	Terlipressin
Intervention details	Terlipressin (1mg/4 hourly, IV), and albumin (1 g/kg followed by 20-40 g/day)
Background therapy	Both groups received albumin
Response definition	Not defined.
StudyID	**Indrabi 2013 (Abstract only)**
Intervention	Terlipressin vs. Norepinephrine
Intervention details	Not reported
Background therapy	Both groups received albumin.
Response definition	Not defined.

StudyID	**Sharma 2008**
Intervention	Norepinephrine vs. Terlipressin
Intervention details	Group A patients received continuous infusion of noradrenaline at an initial dose of 0.5 mg/h, designed to achieve an increase in mean arterial pressure (MAP) of at least 10 mmHg or an increase in 4-h urine output to more than 200 mL. When one of these goals was not achieved, the noradrenaline dose was increased every 4 h in steps of 0.5 mg/h, up to the maximum dose of 3 mg/h. Patients in group B received terlipressin as an IV bolus of 0.5 mg every 6 h. If a significant reduction in serum creatinine level (≥1 mg/dL) was not observed during each 3-day period, the dose of terlipressin was increased in a stepwise fashion every 3 days to a maximum of 2 mg every 6 h.
Background therapy	Both groups received albumin.
Response definition	Decrease in serum creatinine to a value of 1.5 mg/dL or lower during the treatment.
StudyID	**Singh 2012**
Intervention	Norepinephrine vs. Terlipressin
Intervention details	Patients in group A received terlipressin as an intravenous bolus of 0.5 mg every 6 h. If a significant reduction in serum creatinine level (⩾1 mg/dl) was not observed during a 3-day period, the dose of terlipressin was increased in a stepwise fashion every 3 days to a maximum of 2 mg every 6 h. Patients in group B received a continuous infusion of noradrenaline at an initial dose of 0.5 mg/h, designed to achieve an increase in MAP of at least 10 mmHg or an increase in 4-h urine output of more than 200 ml. When one of these goals was not achieved, the noradrenaline dose was increased every 4 h in steps of 0.5 mg/h, up to the maximum dose of 3 mg/h.
Background therapy	Both groups received albumin.
Response definition	Defined as serum creatinine less than 1.5 mg
StudyID	**Alessandria 2007**
Intervention	Norepinephrine vs. Terlipressin

Intervention details	Noradrenalin was given by continuous infusion at an initial dose of 0.1 µg/kg/min and then increased every 4 h according to a protocol based on arterial blood pressure response to the treatment. In the case of a lack of increase in baseline mean arterial pressure (MAP) of at least 10 mmHg, noradrenalin was increased every 4 h in steps of 0.05 µg/kg/min up to the maximum dose of 0.7 µg/kg/min. Terlipressin was given as an intravenous bolus of 1 mg every 4 h and increased to 2 mg every 4 h after 3 days of treatment if a significant reduction in serum creatinine (reduction of at least 25% of the basal value) was not observed during the first 3-day period
Background therapy	Both groups received albumin
Response definition	Decrease of 30% or greater of serum creatinine level compared with the baseline value to a final value of 1.5 mg/dL (133 µmol/L) or lower during treatment.
StudyID	**Srivastava 2015**
Intervention	Terlipressin vs. Dopamine and furosemide
Intervention details	A dose of 0.5 mg intravenous terlipressin was administered every 6 hr along with albumin 20% (100 ml) per day for 5 days in the terlipressin arm. Patients under the triple therapy arm received, in addition to albumin 20% (100 ml), concurrent intravenous dopamine infusion in the dose of 2 µg/kg/min, and furosemide in the dose of 0.01 mg/kg/hr for 5 days.
Background therapy	Both groups received albumin
Response definition	N/A
StudyID	**Tavakkoli 2012**
Intervention	Norepinephrine vs. Octreotide + Midodrine
Intervention details	Continuous infusion of NA at an initial dose of 0.1 µg/kg/min, aimed to attain an increase in MAP of at least 10 mm Hg. In case of lack of increase in baseline MAP of at least 10 mmHg, noradrenalin was increased every 4 hours in steps of 0.05 µg/kg/min up to the maximum dose of 0.7 µg/kg/min. Octreotide was administered subcutaneously at an initial dose of 100 µg 3 times daily and then, if necessary, increased to 200 µg 3 times daily.

	Midodrine was administered orally at an initial dose of 5 mg 3 times daily, and in case of lack of increase in baseline MAP of at least 15 mmHg, midodrine was increased every 24 hours in steps of 5 mg 3 times daily up to the maximum dose of 15 mg 3 times daily, if needed
Background therapy	Both groups received albumin
Response definition	Decreases of 30% or greater of serum creatinine level compared with the baseline value to a final value of 1.5 mg/dL (133 µmol/L) or lower during treatment were observed.
StudyID	**Cavallin 2015**
Intervention	Terlipressin vs. Octreotide + Midodrine
Intervention details	The TERLI group received terlipressin by intravenous infusion, initially 3 mg/24 hours, progressively increased to 12 mg/24 hours if there was no response. The MID/OCT group received midodrine orally at an initial dose of 7.5 mg thrice daily, with the dose increased to a maximum of 12.5 mg thrice daily, together with octreotide subcutaneously: initial dose 100 µg thrice daily and up to 200 µg thrice daily
Background therapy	Both groups received albumin
Response definition	Defined as a decrease in serum creatinine to ≤133 µmol/L (≤1.5
StudyID	**Wong 2021 (CONFIRM)**
Intervention	Terlipressin vs. Placebo
Intervention details	1 mg of terlipressin or placebo was administered intravenously over 2 minutes every 5.5 to 6.5 hours.
Background therapy	A total of 121 patients (61%) in the terlipressin group and 61 patients (60%) in the placebo group had previously received midodrine and octreotide. All patients received albumin.
Response definition	HRS reversal was defined as any serum creatinine level of 1.5 mg per deciliter or less while receiving terlipressin or placebo.
StudyID	**Ghost 2013**
Intervention	Norepinephrine vs. Terlipressin

Intervention details	Patients in group A received terlipressin as an intravenous bolus of 0.5 mg every 6 h. If a significant reduction in serum creatinine level (≥1 mg/dL) was not observed during the 3-day period, the dose of terlipressin was increased in a stepwise fashion every 3 days to a maximum of 2 mg every 6 h. Patients in group B received a continuous infusion of noradrenaline at an initial dose of 0.5 mg/h, designed to achieve an increase in mean arterial pressure (MAP) of at least 10 mmHg or an increase in 4-h urine output to more than 200 ml.
Background therapy	Both groups received albumin.
Response definition	Serum creatinine less than 1.5 mg
StudyID	**Pomier-Layrargues 2003**
Intervention	Octreotide vs. Placebo
Intervention details	Octreotide infusion (50 ug/h)
Background therapy	Both groups received albumin.
Response definition	Improvement was defined as a 20% decrease in serum creatinine value as compared with the pretreatment value.
StudyID	**Saif 2018**
Intervention	Norepinephrine vs. Terlipressin
Intervention details	Noradrenaline at an initial dose of 0.5 mg/h, designed to achieve an increase in mean arterial pressure (MAP) of at least 10 mmHg, or an increase in 4-h urine output to more than 200 mL. When one of these goals was not achieved, the noradrenaline dose was increased every 4 h in steps of 0.5 mg/h, up to the maximum dose of 3 mg/h Terlipressin as an IV bolus of 0.5 mg every 6 h; if a significant reduction in serum creatinine level (≥ 1 mg/dL) was not observed during each 3-day period, the dose of terlipressin was increased in a stepwise fashion every 3 days to a maximum of 2 mg every 6 h to maximum of 8 mg per day.
Background therapy	Both groups received albumin
Response definition	Decrease in serum creatinine to a value of ≤ 1.5 mg/dL.

StudyID	**Mahmoud 2021**
Intervention	Norepinephrine vs Midodrine+Octreotide
Intervention details	Patients received either a continuous infusion of norepinephrine at an initial dose of 0.5 mg/h (maximum 3 mg/h) or 5 mg of oral midodrine three times/day (maximum 12.5 mg three times/day) plus octreotide (100 µg/6 h) as subcutaneous injection (maximum 200 µg/6 h).
Background therapy	Albumin
Response definition	Defined as the return of sCr to a value within 0.3 mg/dl of the baseline at the end of treatment
StudyID	**Nowsherwan 2021**
Intervention	Terlipressin vs Placebo
Intervention details	Patients were treated with terlipressin initially 2-4mg per day along with intravenous albumin 20-40mg/day in group I as compared to this group II received 20-40mg albumin alone per a day for duration of 14-days
Background therapy	Albumin
Response definition	NR
StudyID	**Yang 2001**
Intervention	Terlipressin vs Placebo
Intervention details	NR
Background therapy	Albumin
Response definition	NR
StudyID	**Badawy 2013**
Intervention	Norepinephrine vs Terlipressin
Intervention details	NR
Background therapy	Albumin
Response definition	NR

StudyID	**Silawat 2011**
Intervention	Terlipressin vs Placebo
Intervention details	NR
Background therapy	Albumin
Response definition	NR
StudyID	**Copaci 2016**
Intervention	Terlipressin vs Octreotide
Intervention details	NR
Background therapy	Albumin
Response definition	NR
StudyID	**Goyal 2008**
Intervention	Norepinephrine vs Terlipressin
Intervention details	Intravenous noradrenaline infusion (0.5-3 mg/h) and group B received intravenous terlipressin (0.5-2 mg/6h) for 2 weeks. Intravenous albumin (20 g/day) was given to both groups.
Background therapy	Albumin
Response definition	NR
StudyID	**Goyal 2016**
Intervention	Norepinephrine vs Terlipressin
Intervention details	Intravenous noradrenaline infusion (0.5-3 mg/h) and group B received intravenous terlipressin (0.5-2 mg/6h) for 2 weeks. Intravenous albumin (20 g/day) was given to both groups.
Background therapy	Albumin
Response definition	NR

S7. Risk of bias assessments and judgements

StudyID	Outcomes	Bias from the randomization process	Bias due to deviations from the intended intervention	Bias due to missing data	Bias due to measurement of the outcome	Bias in selection of the reported results
Zafer 2012	Mortality	Definitely high risk	Definitely high risk	Definitely low risk	Probably low Risk	Probably low Risk
Indrabi 2013	Mortality	Definitely high risk	Definitely high risk	Definitely low risk	Probably low Risk	Probably low Risk
Zafer 2012	Reversal	Definitely high risk	Definitely high risk	Definitely low risk	Probably low Risk	Probably low Risk
Indrabi 2013	Reversal	Definitely high risk	Definitely high risk	Definitely low risk	Probably low Risk	Probably low Risk
Sanyal 2008	Mortality	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Boyer 2016 (REVERSE)	Mortality	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Wong 2021 (CONFIRM)	Mortality	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Pomier-Layrargues 2003	Mortality	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Sanyal 2008	Reversal	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Boyer 2016 (REVERSE)	Reversal	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Wong 2021 (CONFIRM)	Reversal	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Pomier-Layrargues 2003	Reversal	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Sanyal 2008	SAE	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk

Boyer 2016 (REVERSE)	Serious adverse events	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Wong 2021 (CONFIRM)	Serious adverse events	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Pomier-Layrargues 2003	Serious adverse events	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk	Definitely low risk
Alessandria 2007	Mortality	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Tavakkoli 2012	Mortality	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Cavallin 2015	Mortality	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Saif 2018	Mortality	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Alessandria 2007	Reversal	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Tavakkoli 2012	Reversal	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Cavallin 2015	Reversal	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Saif 2018	Reversal	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Alessandria 2007	Serious adverse events	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Tavakkoli 2012	Serious adverse events	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Cavallin 2015	Serious adverse events	Probably high risk	Definitely high risk	Definitely low risk	Definitely low risk	Definitely low risk
Martin-Llahi 2008	Mortality	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Srivastava 2015	Mortality	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Ghosh 2013	Mortality	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Goyal 2016	Mortality	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk

Mahmoud 2021	Mortality	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Nowsherwan 2021	Mortality	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Yang 2001	Mortality	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Silawat	Mortality	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Martin-Llahi 2008	Reversal	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Ghosh 2013	Reversal	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Goyal 2016	Reversal	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Mahmoud 2021	Reversal	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Nowsherwan 2021	Reversal	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Goyal 2016	SAE	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Mahmoud 2021	SAE	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Goyal 2008	SAE	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Martin-Llahi 2008	Serious adverse events	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Srivastava 2015	Serious adverse events	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Ghosh 2013	Serious adverse events	Probably high risk	Probably high risk	Definitely low risk	Definitely low risk	Definitely low risk
Silawat	Reversal	Probably high risk	Probably low Risk	Definitely low risk	Definitely low risk	Definitely low risk
Badawy	Reversal	Probably high risk	Probably low Risk	Definitely low risk	Definitely low risk	Definitely low risk
Goyal 2008	Reversal	Probably high risk	Probably low Risk	Definitely low risk	Definitely low risk	Definitely low risk
Capaci 2016	Reversal	Probably high risk	Probably low Risk	Definitely low risk	Definitely low risk	Definitely low risk
Arora 2020	Mortality	Probably high risk	Definitely low risk	Definitely low risk	Probably high risk	Definitely low risk

Neri 2007	Mortality	Probably high risk	Probably high risk	Definitely low risk	Probably high risk	Definitely low risk
Neri 2007	Reversal	Probably high risk	Probably high risk	Definitely low risk	Probably high risk	Definitely low risk
Arora 2020	Reversal	Probably high risk	Probably high risk	Definitely low risk	Probably high risk	Definitely low risk
Neri 2007	Serious adverse events	Probably high risk	Probably high risk	Definitely low risk	Probably high risk	Definitely low risk
Arora 2020	Serious adverse events	Probably high risk	Probably high risk	Definitely low risk	Probably high risk	Definitely low risk
Singh 2012	Mortality	Probably high risk	Definitely high risk	Definitely low risk	Probably low Risk	Definitely low risk
Singh 2012	Reversal	Probably high risk	Definitely high risk	Definitely low risk	Probably low Risk	Definitely low risk
Singh 2012	Serious adverse events	Probably high risk	Definitely high risk	Definitely low risk	Probably low Risk	Definitely low risk
Solanki 2003	Mortality	Probably high risk	Probably high risk	Definitely low risk	Probably high risk	Probably low Risk
Solanki 2003	Reversal	Probably high risk	Probably high risk	Definitely low risk	Probably high risk	Probably low Risk
Sharma 2008	Mortality	Probably high risk	Definitely high risk	Definitely low risk	Probably low Risk	Probably low Risk
Sharma 2008	Reversal	Probably high risk	Definitely high risk	Definitely low risk	Probably low Risk	Probably low Risk
Sharma 2008	Serious adverse events	Probably high risk	Definitely high risk	Definitely low risk	Probably low Risk	Probably low Risk

S8. Network estimates for head-to-head comparisons.

Reversal

Reversal network	**Comparison**	**Network estimate**						
		Relative estimate			**Absolute risk difference (per 1,000)**			
Treatment 1	Treatment 2	Point estimate	95% Confidence intervals		Pointe estimate	95% Confidence intervals		GRADE rating
Midodrine + octreotide	Norepinephrine	0.8157	0.5712	1.1648	-44.906538	-104.481408	40.155168	Very low
Midodrine + octreotide	Octreotide	1.9829	0.7791	5.0466	100.2558	-22.5318	412.7532	Very low
Midodrine + octreotide	Placebo	1.5175	0.978	2.3546	67.7925	-2.882	177.4526	
Norepinephrine	Octreotide	2.4309	1.0168	5.8118	145.9518	1.7136	490.8036	Very low
Norepinephrine	Placebo	1.8604	1.4019	2.4687	112.7124	52.6489	192.3997	Low
Octreotide	Placebo	0.7653	0.3214	1.8226	-30.7457	-88.8966	107.7606	very low

Terlipressin	Midodrine + octreotide	1.37	0.94	2.01	72.52	-11.76	197.96	Low
Terlipressin	Norepinephrine	1.125	0.94	1.34	30.4575	-14.6196	82.8444	Low
Terlipressin	Octreotide	2.73	1.16	6.42	176.46	16.32	552.84	Moderate
Terlipressin	Placebo	2.09	1.67	2.61	142.79	87.77	210.91	High

Mortality

Mortality network	**Comparison**	**Network estimate**						
		Relative risk			**Absolute risk reduction (per 1,000)**			
Treatment 1	Treatment 2	Point estimate	95% CI		Point estimate	95% CI		GRADE rating
Dopamine + Furosemide	Midodrine + octreotide	0.731	0.4607	1.1599	-193.3303	-387.59491	114.92013	Very low
Dopamine + Furosemide	Norepinephrine	0.8893	0.6419	1.232	-65.72259	-212.60397	137.7384	Very low
Dopamine + Furosemide	Octreotide	2.7225	0.6901	10.7407	306.605	-55.1622	1733.8446	Very low
Dopamine + Furosemide	Placebo	0.847	0.6134	1.1696	-95.625	-241.625	106	Very low
Midodrine + octreotide	Norepinephrine	1.2165	0.859	1.723	128.53605	-83.7117	429.2451	Low
Midodrine + octreotide	Octreotide	3.7243	0.9272	14.9595	484.9254	-12.9584	2484.791	Very low

Midodrine + octreotide	Placebo	1.1587	0.7827	1.7153	99.1875	-135.8125	447.0625	Very low
Norepinephrine	Octreotide	3.0613	0.7924	11.8266	366.9114	-36.9528	1927.1348	Very low
Norepinephrine	Placebo	0.9524	0.7668	1.183	-29.75	-145.75	114.375	Very low
Octreotide	Placebo	0.3111	0.082	1.181	-430.5625	-573.75	113.125	Very low
Terlipressin	Dopamine + Furosemide	1	0.751	1.33	0	-132.2688	175.296	Very low
Terlipressin	Midodrine + octreotide	0.73	0.51	1.05	-194.049	-352.163	35.935	Low
Terlipressin	Norepinephrine	0.889	0.76	1.04	-65.9007	-142.488	23.748	Low
Terlipressin	Octreotide	2.722	0.711	10.42	306.516	-51.442	1676.76	Very low
Terlipressin	Placebo	0.85	0.73	0.98	-93.75	-168.75	-12.5	Low

Serious adverse events

SAE network	**Comparison**	**Network estimate**						
		Relative risk			**Absolute risk reduction (per 1,000)**			
Treatment 1	Treatment 2	Point estimate	95% CI		Point estimate	95% CI		**GRADE rating**
Dopamine + Furosemide	Midodrine + octreotide	0.9877	0.0177	54.998	-2.3862	-190.5662	10475.612	**very low**
Dopamine + Furosemide	Norepinephrine	1.4744	0.0273	79.6636	61.1976	-125.4783	10147.6044	**very low**
Midodrine + octreotide	Norepinephrine	1.4928	0.8898	2.5044	63.5712	-14.2158	194.0676	**low**
Dopamine + Furosemide	Octreotide	1.4284	0.0062	330.778	56.9772	-132.1754	43860.474	**very low**
Midodrine + octreotide	Octreotide	1.4462	0.0284	73.6942	59.3446	-129.2228	9668.3286	**very low**
Norepinephrine	Octreotide	0.9688	0.0196	47.868	-4.1496	-130.3932	6233.444	**very low**
Dopamine + Furosemide	Placebo	1.1277	0.0229	55.622	21.709	-166.107	9285.74	**very low**

Midodrine + octreotide	Placebo	1.1417	0.4193	3.1088	24.089	-98.719	358.496	**very low**
Norepinephrine	Placebo	0.7648	0.3195	1.8309	-39.984	-115.685	141.253	**very low**
Octreotide	Placebo	0.7895	0.0176	35.3335	-35.785	-167.008	5836.695	**very low**
Terlipressin	Placebo	1.12	0.97	1.3	20.4	-5.1	51	**moderate**
Dopamine + Furosemide	Terlipressin	1	0.0203	49.1883	0	-186.143	9155.777	**very low**
Midodrine + octreotide	Terlipressin	1.0125	0.3759	2.7271	2.375	-118.579	328.149	**very low**
Norepinephrine	Terlipressin	0.6782	0.2869	1.6035	-61.142	-135.489	114.665	**very low**
Octreotide	Terlipressin	0.7001	0.0156	31.4222	-56.981	-187.036	5780.218	**very low**