SUPPLEMENTAL MATERIAL

Intended for publication as a data supplement

Supplementary Table 1. Search strategies for (A) MEDLINE, (B) EMBASE, (C) CENTRAL, and (D) CINAHL without language restriction from database inception to August 2019.

(A) MEDLINE (1946-2019)

#	Searches	Results	Search type
1	exp Syncope, Vasovagal/	1,869	Advanced
2	(vasovagal adj2 (syncop* or faint* or collapse* or shock* or reaction)).ti,ab.	1,552	Advanced
3	((neurocardiogenic or neuro-cardiogenic or neurogenic or neurally-mediated or neural* or cerebral or reflex) adj2 (syncop* or faint*)).ti,ab.	1,157	Advanced
4	or/1-3	3,070	Advanced
5	exp Adrenergic Uptake Inhibitors/	68,893	Advanced
6	((adrenergic or norepinephrine) adj2 (uptake or reuptake or transport*) adj2 inhibit*).ti,ab.	2,286	Advanced
7	exp Reboxetine/	592	Advanced
8	exp Atomoxetine Hydrochloride/	1,130	Advanced
9	sibutramine.ti,ab.	1,060	Advanced
10	(reboxetine or atomoxetine or sibutramine).ti,ab.	3,066	Advanced
11	or/5-10	71,854	Advanced
12	4 and 11	10	Advanced
13	remove duplicates from 12	10	Advanced
14	((randomized controlled trial or controlled clinical trial).pt. or randomized.ab. or randomised.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (exp animals/ not humans.sh.)	3,546,227	
15	Case Reports/ or Letter/ or Historical Article/ or Review/	5,301,793	
16	14 not 15	2,691,504	Advanced
17	13 and 16	5	Advanced

(B) EMBASE (1974-2019)

#	Searches	Results	Search type
1	exp faintness/	21,687	Advanced
2	(vasovagal adj2 (syncop* or faint* or collapse* or shock* or reaction)).ti,ab.	2,766	Advanced
3	((neurocardiogenic or neuro-cardiogenic or neurogenic or neurally-mediated or neural* or cerebral or reflex) adj2 (syncop* or faint*)).ti,ab.	1,838	Advanced
4	or/1-3	24,356	Advanced
5	exp noradrenalin uptake inhibitor/	205,581	Advanced
6	((adrenergic or norepinephrine or noradrenalin*) adj2 (uptake or reuptake or transport*) adj2 inhibit*).ti,ab.	3,718	Advanced
7	exp reboxetine/	3,314	Advanced
8	exp atomoxetine/	5,157	Advanced
9	sibutramine.mp.	1,636	Advanced
10	(reboxetine or atomoxetine or sibutramine).ti,ab.	5,013	Advanced
11	or/5-10	206,193	Advanced
12	4 and 11	520	Advanced
13	remove duplicates from 12	512	
14	crossover-procedure/ or double-blind procedure/ or randomized controlled trial/ or single-blind procedure/ or (random* or factorial* or crossover* or cross over* or placebo* or (doubl* adj blind*) or (singl* adj blind*) or assign* or allocat* or volunteer*).tw.	2,205,370	Advanced
15	case report/ or letter/ or review/	5,543,541	
16	14 not 15	2,024,683	
17	13 and 16	66	Advanced

(C) CENTRAL (1995-2019)

#	Searches	Results	Search type
1	MeSH descriptor: [Syncope, Vasovagal] explode all trees	158	Advanced
2	(vasovagal near/2 (syncop* or faint* or collapse* or shock* or reaction)):ti,ab,kw	344	Advanced
3	((neurocardiogenic or neuro-cardiogenic or neurogenic or neurally-mediated or neural* or cerebral or reflex) near/2 (syncop* or faint*)):ti,ab,kw	127	Advanced
4	#1 or #2 or #3	408	Advanced
5	MeSH descriptor: [Adrenergic Uptake Inhibitors] explode all trees	460	Advanced
6	((adrenergic or norepinephrine) adj2 (uptake or reuptake or transport*) adj2 inhibit*):ti,ab,kw	1,013	Advanced
7	MeSH descriptor: [Reboxetine] explode all trees	143	Advanced
8	MeSH descriptor: [Atomoxetine Hydrochloride] explode all trees	317	Advanced
9	(sibutramine):ti,ab,kw	357	Advanced
10	(reboxetine or atomoxetine or sibutramine):ti,ab,kw	1,305	Advanced
11	#5 or #6 or #7 or #8 or #9 or #10	1,993	Advanced
12	#4 or #11	7	Advanced

(D) CINAHL (1937-2019)

#	Searches	Results	Search type
S1	(MH "Syncope, Vasovagal")	742	Advanced
S2	(vasovagal W2 (syncop* or faint* or collapse* or shock* or reaction))	580	Advanced
S3	((neurocardiogenic or neuro-cardiogenic or neurogenic or neurally-mediated or neural* or cerebral or reflex) W2 (syncop* or faint*))	770	Advanced
S4	S1 or S2 or S3	1,487	Advanced
S5	(MH "Adrenergic Uptake Inhibitors+")	8,092	Advanced
S6	(adrenergic or norepinephrine) W2 (uptake or reuptake or transport*) W2 inhibit*	1,042	Advanced
S7	reboxetine	91	Advanced
S8	(MH "Atomoxetine")	264	Advanced
S9	(MH "Sibutramine")	239	Advanced
S10	reboxetine or atomoxetine or sibutramine	1,192	Advanced
S11	S5 or S6 or S7 or S8 or S9 or S10	9,259	Advanced
S12	((MH "Random Assignment") or (MH "Random Sample+") or (MH "Crossover Design") or (MH "Clinical Trials+") or (MH "Comparative Studies") or (MH "Control (Research)+") or (MH "Control Group") or (MH "Factorial Design") or (MH "Quasi-Experimental Studies+") or (MH "Placebos") or (MH "Meta Analysis") or (MH "Sample Size") or (MH "Research, Nursing") or (MH "Research Question") or (MH "Research Methodology+") or (MH "Evaluation Research+") or (MH "Concurrent Prospective Studies") or (MH "Prospective Studies") or (MH "Nursing Practice, Research-Based") or (MH "Solomon Four-Group Design") or (MH "One-Shot Case Study") or (MH "Pretest-Posttest Design+") or (MH "Static Group Comparison") or (MH "Study Design") or (MH "Clinical Research+")) or (clinical nursing research or random* or cross?over or placebo* or control* or factorial or sham* or meta?analy* or systematic review* or blind* or mask* or trial*)	2,587,090	Advanced
S13	S4 and S11 and S12	6	Advanced

Supplementary Table 2. Individual characteristics and risk of bias assessments of included studies.

Birkenfeld, 2002		
Study Design	Double-blind crossover randomized controlled trial	
Participants	11 healthy volunteers randomized: 7 males, 4 females; mean age of 27 ± 2 *Inclusion criteria:* healthy volunteers without diagnosis of vasovagal syncope *Exclusion criteria:* diagnosis of vasovagal syncope	
Interventions	Sibutramine: 10 mg PO x2 plus 20 mg PO, 12 hours apart (26 h, 14 h, and 2 h before testing) *versus* Placebo: matched	
Outcome	HUT-induced presyncope (with decrease in blood pressure and heart rate of at least 30 mmHg and 20 bpm, respectively) or intolerable pre-syncopal symptoms to warrant premature abortion of HUT testing (dizziness, nausea, visual disturbances) *	
Risk of Bias		
Bias Domain	*Judgement*	*Support for Judgement*
Random Sequence Generation (Selection Bias)	Unclear	Randomization method not specified.
Allocation Concealment (Selection Bias)	Unclear	Randomization method not specified.
Blinding of Participants and Personnel (Performance Bias)	Low	Participants and investigators were blinded to treatment allocation until the end of the study.
Blinding of Outcome Assessment (Detection Bias)	Low	Outcomes were clearly defined; blinding was maintained during outcome assessments.
Incomplete Outcome Data (Attrition Bias)	Low	No loss to follow-up.
Selective Reporting (Reporting Bias)	Low	All pre-specified outcomes were reported.
Other Bias	Low	Not applicable.
* Blood pressure and heart rate decreases, as well as the scope of pre-syncopal symptoms warranting premature HUT abortion, were specifically defined in *Schroeder 2006*, which combines data from three separate study cohorts, including *Birkenfeld 2002*		

Schroeder, 2002		
Study Design	Double-blind crossover randomized controlled trial	
Participants	18 patients randomized: 8 males, 10 females; mean age of 30 ± 2 *Inclusion criteria:* healthy volunteers without diagnosis of vasovagal syncope *Exclusion criteria:* diagnosis of vasovagal syncope	
Interventions	Reboxetine: 8 mg PO x2, 11 hours apart (12 h and 1 h before testing) *versus* Placebo: matched	
Outcome	HUT-induced presyncope (with decrease in blood pressure and heart rate of at least 30 mmHg and 20 bpm, respectively) *	
Risk of Bias		
Bias Domain	*Judgement*	*Support for Judgement*
Random Sequence Generation (Selection Bias)	Unclear	Randomization method not specified.
Allocation Concealment (Selection Bias)	Unclear	Randomization method not specified.
Blinding of Participants and Personnel (Performance Bias)	Low	Participants and investigators were aware of treatment allocation.
Blinding of Outcome Assessment (Detection Bias)	Low	Outcome was clearly defined; blinding was maintained during outcome assessments.
Incomplete Outcome Data (Attrition Bias)	Low	No loss to follow-up.
Selective Reporting (Reporting Bias)	Low	All pre-specified outcomes were reported.
Other Bias	Low	Not applicable.
* Blood pressure and heart rate decreases, as well as the scope of pre-syncopal symptoms warranting premature HUT abortion, were specifically defined in *Schroeder 2006*, which combines data from three separate study cohorts, including *Schroeder 2002*		

Schroeder, 2006		
Study Design	Double-blind crossover randomized controlled trial	
Participants	16 patients randomized: 16 males, 0 females; mean age of 26 ± 1 *Inclusion criteria: healthy volunteers without diagnosis of vasovagal syncope* *Exclusion criteria:* diagnosis of vasovagal syncope	
Interventions	Reboxetine: 8 mg PO x1 (1.5 h before testing) *versus* Placebo: matched	
Outcome	HUT-induced presyncope (with decrease in blood pressure and heart rate of at least 30 mmHg and 20 bpm, respectively) or HUT-induced vasodepressor-type presyncope (with decrease in blood pressure of at least 20 mmHg)	
Risk of Bias		
Bias Domain	*Judgement*	*Support for Judgement*
Random Sequence Generation (Selection Bias)	Unclear	Randomization method not specified.
Allocation Concealment (Selection Bias)	Unclear	Randomization method not specified.
Blinding of Participants and Personnel (Performance Bias)	Low	Participants and investigators were blinded to treatment allocation until the end of the study.
Blinding of Outcome Assessment (Detection Bias)	Low	Outcomes were clearly defined; blinding was maintained during outcome assessments.
Incomplete Outcome Data (Attrition Bias)	Low	No loss to follow-up.
Selective Reporting (Reporting Bias)	Low	All pre-specified outcomes were reported.
Other Bias	Low	Not applicable.

Sheldon, 2019		
Study Design	Double-blind randomized controlled trial	
Participants	56 patients randomized: 15 males, 41 females; mean age of 35 ± 14 *Inclusion criteria:* ≥1 syncopal recurrence in the year preceding enrolment; ≥-2 points on the Syncope Symptom Score *Exclusion criteria:* syncope due to other causes	
Interventions	Atomoxetine: 40 mg PO x2, 12 hours apart (1 h before testing) *versus* Placebo: matched	
Outcome	Syncope induced by head-up-tilt testing	
Risk of Bias		
Bias Domain	*Judgement*	*Support for Judgement*
Random Sequence Generation (Selection Bias)	Low	Eligible patients were randomly assigned using a computer-generated random number sequence.
Allocation Concealment (Selection Bias)	Low	Eligible patients were randomly assigned using a computer-generated random number sequence.
Blinding of Participants and Personnel (Performance Bias)	Low	Participants and investigators were blinded to treatment allocation until the end of the study.
Blinding of Outcome Assessment (Detection Bias)	Low	Outcome was clearly defined; blinding was maintained during outcome assessments.
Incomplete Outcome Data (Attrition Bias)	Low	No loss to follow-up.
Selective Reporting (Reporting Bias)	Low	All pre-specified outcomes were reported.
Other Bias	Low	Not applicable.