

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies for interventions as these concepts may not be well described in title, abstract or indexes and therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 12: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 - 14 October 2020	Exclusions Randomised controlled trials Systematic review studies
Embase (OVID)	1974 - 14 October 2020	Exclusions Randomised controlled trials Systematic review studies
The Cochrane Library (Wiley)	Cochrane Reviews to 2020 Issue 10 of 12 CENTRAL to 2020 Issue 10 of 12	None

Medline (Ovid) search terms

1.	exp Heart Valve Diseases/
2.	exp heart valves/
3.	((primary or secondary) adj valv* disease*).ti,ab.
4.	((valv* or flap* or leaflet*) adj1 (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*).ti,ab.
5.	((mitral or aortic or tricuspid or pulmon*) adj (valv* or flap* or leaflet*) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*).ti,ab.
6.	((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenos?s or atresia or insufficienc*).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosthe* or bioprothe* or biological or tissue) adj (valv* or flap* or leaflet*).ti,ab.
9.	valve-in-valve.ti,ab.
10.	(transcatheter adj2 (valve or valves)).ti,ab.
11.	exp Heart Murmurs/
12.	((heart or cardiac) adj murmur*).ti,ab.
13.	or/1-12
14.	letter/
15.	editorial/
16.	news/
17.	exp historical article/
18.	Anecdotes as Topic/
19.	comment/
20.	case report/
21.	(letter or comment*).ti.
22.	or/14-21

23.	randomized controlled trial/ or random*.ti,ab.
24.	22 not 23
25.	animals/ not humans/
26.	exp Animals, Laboratory/
27.	exp Animal Experimentation/
28.	exp Models, Animal/
29.	exp Rodentia/
30.	(rat or rats or mouse or mice).ti.
31.	or/24-30
32.	13 not 31
33.	limit 32 to English language
34.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
35.	33 not 34
36.	randomized controlled trial.pt.
37.	controlled clinical trial.pt.
38.	randomi#ed.ti,ab.
39.	placebo.ab.
40.	randomly.ti,ab.
41.	Clinical Trials as topic.sh.
42.	trial.ti.
43.	or/36-42
44.	Meta-Analysis/
45.	exp Meta-Analysis as Topic/
46.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
47.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
48.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
49.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
50.	(search* adj4 literature).ab.
51.	(medline or pubmed or cochrane or embase or psychlit or psychlit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
52.	cochrane.jw.
53.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
54.	or/44-53
55.	35 and (43 or 54)
56.	exp Anticoagulants/
57.	anticoag*.ti,ab.
58.	anti coag*.ti,ab.
59.	"antivitamin k".ti,ab.
60.	acenocoumarol.ti,ab.
61.	aspirin*.ti,ab.
62.	clopidogrel.ti,ab.
63.	Phenindione.ti,ab.

64.	Phytomenadione.ti,ab.
65.	warfarin.ti,ab.
66.	Heparin.ti,ab.
67.	((novel or direct) adj oral anticoag*).ti,ab.
68.	exp Platelet Aggregation Inhibitors/
69.	antiplatelet*.ti,ab.
70.	anti platelet*.ti,ab.
71.	antiaggregant*.ti,ab.
72.	anti aggregant*.ti,ab.
73.	platelet antagonist*.ti,ab.
74.	(platelet adj2 inhibitor*).ti,ab.
75.	Cangrelor.ti,ab.
76.	dipyridamole.ti,ab.
77.	Prasugrel.ti,ab.
78.	Ticagrelor.ti,ab.
79.	or/56-78
80.	55 and 79

Embase (Ovid) search terms

1.	exp valvular heart disease/
2.	exp heart valve/
3.	((primary or secondary) adj valv* disease*).ti,ab.
4.	((valv* or flap* or leaflet*) adj1 (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)).ti,ab.
5.	((mitral or aortic or tricuspid or pulmon*) adj (valv* or flap* or leaflet*) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)).ti,ab.
6.	((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenos?s or atresia or insufficienc*)).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosthe* or bioprosthe* or biological or tissue) adj (valv* or flap* or leaflet*)).ti,ab.
9.	valve-in-valve.ti,ab.
10.	(transcatheter adj2 (valve or valves)).ti,ab.
11.	exp heart murmur/
12.	((heart or cardiac) adj murmur*).ti,ab.
13.	or/1-12
14.	letter.pt. or letter/
15.	note.pt.
16.	editorial.pt.
17.	Case report/ or Case study/
18.	(letter or comment*).ti.
19.	or/14-18
20.	randomized controlled trial/ or random*.ti,ab.
21.	19 not 20
22.	animal/ not human/

23.	Nonhuman/
24.	exp Animal Experiment/
25.	exp Experimental animal/
26.	Animal model/
27.	exp Rodent/
28.	(rat or rats or mouse or mice).ti.
29.	or/21-28
30.	13 not 29
31.	limit 30 to English language
32.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
33.	31 not 32
34.	random*.ti,ab.
35.	factorial*.ti,ab.
36.	(crossover* or cross over*).ti,ab.
37.	((doubl* or singl*) adj blind*).ti,ab.
38.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
39.	crossover procedure/
40.	single blind procedure/
41.	randomized controlled trial/
42.	double blind procedure/
43.	or/34-42
44.	systematic review/
45.	meta-analysis/
46.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
47.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
48.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
49.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
50.	(search* adj4 literature).ab.
51.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
52.	((pool* or combined) adj2 (data or trials or studies or results)).ab.
53.	cochrane.jw.
54.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
55.	or/44-53
56.	33 and (43 or 55)
57.	exp anticoagulant agent/
58.	anticoag*.ti,ab.
59.	anti coag*.ti,ab.
60.	antivitamin K/
61.	"antivitamin k".ti,ab.
62.	acenocoumarol/
63.	acenocoumarol.ti,ab.
64.	aspirin*.ti,ab.

65.	clopidogrel/
66.	clopidogrel.ti,ab.
67.	phenindione/
68.	Phenindione.ti,ab.
69.	phytomenadione/
70.	phytomenadione.ti,ab.
71.	warfarin/
72.	warfarin.ti,ab.
73.	heparin/
74.	heparin.ti,ab.
75.	((novel or direct) adj oral anticoag*).ti,ab.
76.	exp antithrombocytic agent/
77.	antithrombocytic.ti,ab.
78.	antiplatelet*.ti,ab.
79.	anti platelet*.ti,ab.
80.	antiaggregant*.ti,ab.
81.	anti aggregant*.ti,ab.
82.	platelet antagonist*.ti,ab.
83.	(platelet adj2 inhibitor*).ti,ab.
84.	cangrelor/
85.	Cangrelor.ti,ab.
86.	dipyridamole/
87.	dipyridamole.ti,ab.
88.	prasugrel/
89.	Prasugrel.ti,ab.
90.	ticagrelor/
91.	Ticagrelor.ti,ab.
92.	or/57-91
93.	56 and 92

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Heart Valve Diseases] explode all trees
#2.	MeSH descriptor: [Heart Valves] explode all trees
#3.	((primary or secondary) NEXT valv* disease*).ti,ab
#4.	((valv* or flap* or leaflet*) near/1 (heart or cardiac) NEXT (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)):ti,ab
#5.	((mitral or aortic or tricuspid or pulmon*) NEXT (valv* or flap* or leaflet*) NEXT (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)):ti,ab
#6.	((mitral or aortic or tricuspid or pulmon*) NEAR/3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)):ti,ab
#7.	MeSH descriptor: [Heart Valve Prosthesis] explode all trees
#8.	((mechanical or artificial or prosthe* or bioprosthe* or biological or tissue) NEXT (valv* or flap* or leaflet*)):ti,ab
#9.	valve-in-valve:ti,ab

#10.	(transcatheter NEAR/2 (valve or valves)):ti,ab
#11.	MeSH descriptor: [Heart Murmurs] explode all trees
#12.	((heart or cardiac) NEXT murmur*):ti,ab
#13.	(or #1-#12)
#14.	MeSH descriptor: [Anticoagulants] explode all trees
#15.	anticoag*:ti,ab
#16.	anti coag*:ti,ab
#17.	antivitamin k:ti,ab
#18.	acenocoumarol:ti,ab
#19.	aspirin*:ti,ab
#20.	clopidogrel:ti,ab
#21.	Phenindione:ti,ab
#22.	Phytomenadione:ti,ab
#23.	warfarin:ti,ab
#24.	Heparin:ti,ab
#25.	((novel or direct) NEXT oral anticoag*):ti,ab
#26.	MeSH descriptor: [Platelet Aggregation Inhibitors] explode all trees
#27.	antiplatelet*:ti,ab
#28.	anti platelet*:ti,ab
#29.	antiaggregant*:ti,ab
#30.	anti aggregant*:ti,ab
#31.	platelet antagonist*:ti,ab
#32.	(platelet NEAR/2 inhibitor*):ti,ab
#33.	Cangrelor:ti,ab
#34.	dipyridamole:ti,ab
#35.	Prasugrel:ti,ab
#36.	Ticagrelor:ti,ab
#37.	(or #14-#36)
#38.	#13 and #37