

Heart valve disease – search strategy 1 – signs and symptoms

This literature search strategy was used for the following reviews:

- In adults with suspected heart valve disease what symptoms and signs indicate referral (for example from primary care) for echocardiography?
- In adults with suspected heart valve disease, what symptoms and signs indicate direct referral (for example from primary care) to a specialist?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.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 1: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 14 October 2020	Exclusions
Embase (OVID)	1974 – 14 October 2020	Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews 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 stenosis or atresia or insufficienc*).ti,ab.
7.	or/1-6
8.	letter/
9.	editorial/
10.	news/

11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/8-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice).ti.
25.	or/18-24
26.	7 not 25
27.	limit 26 to English language
28.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
29.	27 not 28
30.	exp Heart Murmurs/
31.	murm*r*.ti,ab.
32.	Heart Sounds/
33.	((heart or cardiac) adj sound*).ti,ab.
34.	(wooshing or blowing or flutter* or rasping).ti,ab.
35.	(heart beat* or heartbeat*).ti,ab.
36.	turbulent blood flow.ti,ab.
37.	Heart Auscultation/
38.	auscultation*.ti,ab.
39.	or/30-38
40.	29 and 39

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	or/1-6
8.	letter.pt. or letter/
9.	note.pt.
10.	editorial.pt.
11.	Case report/ or Case study/
12.	(letter or comment*).ti.
13.	or/8-12
14.	randomized controlled trial/ or random*.ti,ab.
15.	13 not 14
16.	animal/ not human/
17.	Nonhuman/
18.	exp Animal Experiment/
19.	exp Experimental animal/
20.	Animal model/
21.	exp Rodent/
22.	(rat or rats or mouse or mice).ti.
23.	or/15-22
24.	7 not 23
25.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
26.	24 not 25
27.	limit 26 to English language
28.	exp heart murmur/
29.	murm*r*.ti,ab.
30.	((heart or cardiac) adj sound*).ti,ab.
31.	(wooshing or blowing or flutter* or rasping).ti,ab.
32.	(heart beat* or heartbeat*).ti,ab.
33.	turbulent blood flow.ti,ab.
34.	heart sound/
35.	heart auscultation/
36.	auscultation*.ti,ab.
37.	or/28-36
38.	27 and 37

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Heart Valve Diseases] explode all trees
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#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.	(or #1-#6)
#8.	MeSH descriptor: [Heart Murmurs] explode all trees
#9.	murm*r*:ti,ab
#10.	MeSH descriptor: [Heart Sounds] this term only
#11.	((heart or cardiac) next sound*):ti,ab
#12.	(wooshing or blowing or flutter* or rasping):ti,ab
#13.	(heart next beat* or heartbeat*):ti,ab.
#14.	turbulent blood flow:ti,ab
#15.	MeSH descriptor: [Heart Auscultation] explode all trees
#16.	auscultation*:ti,ab
#17.	(or #8-#16)
#18.	#7 and #17

A.2 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 2: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 stenosis or atresia or insufficienc*)).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosthe* or bioprosathe* 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/
40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
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#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	(((heart or cardiac) 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*)))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosth* or bioprosth* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 2 - indications for specialist referral following echocardiography

This literature search strategy was used for the following reviews:

- In adults with heart valve disease who have had echocardiography, what are the indications for referral to a specialist?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.3 Clinical search literature search strategy

This search for a prognostic review used the following approach

- Population AND Prognostic/risk factor terms

Table 3: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 14 October 2020	Exclusions
Embase (OVID)	1974 – 14 October 2020	Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews 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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp Heart Murmurs/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter/
11.	editorial/
12.	news/
13.	exp historical article/
14.	Anecdotes as Topic/
15.	comment/
16.	case report/
17.	(letter or comment*).ti.
18.	or/10-17
19.	randomized controlled trial/ or random*.ti,ab.
20.	18 not 19
21.	animals/ not humans/
22.	exp Animals, Laboratory/
23.	exp Animal Experimentation/
24.	exp Models, Animal/
25.	exp Rodentia/
26.	(rat or rats or mouse or mice).ti.
27.	or/20-26
28.	9 not 27
29.	limit 28 to English language
30.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
31.	29 not 30
32.	Dyspnea/
33.	(breathless* or dyspnea or wheez*).ti,ab.
34.	shortness of breath.ti,ab.

35.	syncope/ or dizziness/
36.	(faint* or dizziness or syncop*).ti,ab.
37.	Cardiac arrhythmia/
38.	palpitat*.ti,ab.
39.	Cardiac arrhythm*.ti,ab.
40.	Edema/
41.	(oedema or edema).ti,ab.
42.	Chest pain/
43.	((chest or thorax) adj (pain* or tightness)).ti,ab.
44.	Exercise tolerance/
45.	((physical* or exercise or fitness) adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit* or tolera*)).ti,ab.
46.	or/32-45
47.	31 and 46
48.	Asymptomatic Diseases/
49.	asymptomatic.ti,ab.
50.	(symptom* adj3 (absent or non or none or no or missed or missing or unseen or "not apparent" or clinically silent or subclinical)).ti,ab.
51.	or/48-50
52.	31 and 50
53.	47 or 52

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart murmur/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	Case report/ or Case study/
14.	(letter or comment*).ti.

15.	or/10-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animal/ not human/
19.	Nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental animal/
22.	Animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice).ti.
25.	or/17-24
26.	9 not 25
27.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
28.	26 not 27
29.	limit 28 to English language
30.	*dyspnea/
31.	(breathless* or dyspn?ea or wheez*).ti,ab.
32.	shortness of breath.ti,ab.
33.	*dizziness/ or *faintness/
34.	(faint* or dizziness or syncop*).ti,ab.
35.	*heart arrhythmia/
36.	palpitat*.ti,ab.
37.	Cardiac arrhythm*.ti,ab.
38.	*edema/
39.	(oedema or edema).ti,ab.
40.	*thorax pain/
41.	((chest or thorax) adj (pain* or tightness)).ti,ab.
42.	*exercise tolerance/
43.	((physical* or exercise or fitness) adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit* or tolera*)).ti,ab.
44.	or/30-43
45.	29 and 44
46.	asymptomatic disease/
47.	asymptomatic.ti,ab.
48.	(symptom* adj3 (absent or non or none or no or missed or missing or unseen or "not apparent" or clinically silent or subclinical)).ti,ab.
49.	or/46-48
50.	29 and 49
51.	45 or 50

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 Murmurs] explode all trees
#8.	((heart or cardiac) NEXT murmur*):ti,ab
#9.	(or #1-#8)
#10.	MeSH descriptor: [Dyspnea] this term only
#11.	(breathless* or dyspnea or dyspnoea or wheez*):ti,ab
#12.	MeSH descriptor: [Dizziness] this term only
#13.	MeSH descriptor: [Syncope] this term only
#14.	(faint* or dizziness or syncop*):ti,ab
#15.	shortness of breath:ti,ab
#16.	MeSH descriptor: [Arrhythmias, Cardiac] this term only
#17.	palpitat*:ti,ab
#18.	cardiac NEXT arrhythm*:ti,ab
#19.	MeSH descriptor: [Edema] this term only
#20.	(oedema or edema):ti,ab
#21.	MeSH descriptor: [Chest Pain] this term only
#22.	((chest or thorax) NEXT (pain* or tightness)):ti,ab
#23.	MeSH descriptor: [Exercise Tolerance] this term only
#24.	((physical* or exercise or fitness) near/5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit* or tolera*)):ti,ab
#25.	(or #10-#24)
#26.	#9 and #25
#27.	MeSH descriptor: [Asymptomatic Diseases] this term only
#28.	asymptomatic:ti,ab
#29.	(symptom* near/3 (absent or non or none or no or missed or missing or unseen or subclinical)):ti,ab
#30.	"not apparent":ti,ab
#31.	"clinically silent":ti,ab
#32.	(or #27-#31)
#33.	#9 and #32

#34.	#26 or #33
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A.4 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 4: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 stenosis or atresia or insufficienc*)).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.

51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/
40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	((heart or cardiac) 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*))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosthe* or bioprosthe* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 3 - stress testing and echocardiography

This literature search strategy was used for the following reviews:

- In adults with heart valve disease, what is the prognostic value and cost effectiveness of stress testing and stress echocardiography to determine the need for intervention?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.5 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 5: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 14 October 2020	Exclusions
Embase (OVID)	1974 – 14 October 2020	Exclusions

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 stenosis or atresia or insufficienc*).ti,ab.
7.	exp Heart Murmurs/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter/
11.	editorial/
12.	news/
13.	exp historical article/
14.	Anecdotes as Topic/
15.	comment/
16.	case report/

17.	(letter or comment*).ti.
18.	or/10-17
19.	randomized controlled trial/ or random*.ti,ab.
20.	18 not 19
21.	animals/ not humans/
22.	exp Animals, Laboratory/
23.	exp Animal Experimentation/
24.	exp Models, Animal/
25.	exp Rodentia/
26.	(rat or rats or mouse or mice).ti.
27.	or/21-26
28.	9 not 27
29.	limit 28 to English language
30.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
31.	29 not 30
32.	Predictive Value of Tests/
33.	Echocardiography, Stress/
34.	Dobutamine/ or dobutamine.ti,ab.
35.	(stress adj2 (pharma* or drug* or chemical)).ti,ab.
36.	(stress adj (cardiac or heart or cardiograph* or echo* or ECG or ultrasonic or ultrasound)).ti,ab.
37.	exp Exercise Test/
38.	((physical* or exercise* or fitness) adj4 (endur* or exert* or capacit* or tolera* or test* or stress*)).ti,ab.
39.	or/32-38
40.	31 and 39

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart murmur/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8

10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	Case report/ or Case study/
14.	(letter or comment*).ti.
15.	or/10-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animal/ not human/
19.	Nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental animal/
22.	Animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice).ti.
25.	or/18-24
26.	9 not 25
27.	limit 26 to English language
28.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
29.	27 not 28
30.	predictive value/
31.	Echocardiography, Stress/
32.	Dobutamine/ or dobutamine.ti,ab.
33.	(stress adj2 (pharma* or drug* or chemical)).ti,ab.
34.	(stress adj (cardiac or heart or cardiograph* or echo* or ECG or ultrasonic or ultrasound)).ti,ab.
35.	exercise test/
36.	((physical* or exercise* or fitness) adj4 (endur* or exert* or capacit* or tolera* or test* or stress*)).ti,ab.
37.	or/30-36
38.	29 and 37

A.6 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 6: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 stenosis or atresia or insufficienc*).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/

40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	(((heart or cardiac) 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*)))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosth* or bioprosth* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 4 – Cardiac CT and cardiac MRI indications for intervention

This literature search strategy was used for the following reviews:

- In adults with heart valve disease, what is the prognostic value and cost effectiveness of cardiac MRI and cardiac CT to determine the need for intervention?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.7 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 7: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1995 - 14 October 2020	Exclusions
Embase (OVID)	1995 - 14 October 2020	Exclusions

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp Heart Murmurs/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter/
11.	editorial/
12.	news/
13.	exp historical article/
14.	Anecdotes as Topic/
15.	comment/
16.	case report/
17.	(letter or comment*).ti.
18.	or/10-17
19.	randomized controlled trial/ or random*.ti,ab.
20.	18 not 19
21.	animals/ not humans/
22.	exp Animals, Laboratory/
23.	exp Animal Experimentation/
24.	exp Models, Animal/

25.	exp Rodentia/
26.	(rat or rats or mouse or mice).ti.
27.	or/20-26
28.	9 not 27
29.	limit 28 to English language
30.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
31.	29 not 30
32.	Magnetic Resonance Imaging/
33.	magnetic resonance angiography/
34.	(mri* or nmr* or magnetic resonance).ti,ab.
35.	(cmr or ((cardiac or cardiovascular) adj mr)).ti,ab.
36.	tomography, x-ray computed/ or computed tomography angiography/
37.	((x-ray or radiograph* or compute*) adj3 tomograph*).ti,ab.
38.	Coronary Angiography/ and (compute* or ct or tomograph*).ti,ab.
39.	((compute* or ct or tomograph*) adj3 angiograph*).ti,ab.
40.	((heart or cardiac or myocardial or imag* or scan* or diagnos*) adj2 (ct or cat)).ti,ab.
41.	(cta or ccta or tro-cta or msct).ti,ab.
42.	or/32-41
43.	31 and 42

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart murmur/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	Case report/ or Case study/
14.	(letter or comment*).ti.
15.	or/10-14

16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animal/ not human/
19.	Nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental animal/
22.	Animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice).ti.
25.	or/17-24
26.	9 not 25
27.	limit 26 to English language
28.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
29.	27 not 28
30.	nuclear magnetic resonance imaging/ or magnetic resonance angiography/
31.	(mri* or nmr* or magnetic resonance).ti,ab.
32.	(cmr or ((cardiac or cardiovascular) adj mr)).ti,ab.
33.	computed tomographic angiography/
34.	x-ray computed tomography/
35.	tomography, x-ray computed/ or computed tomography angiography/
36.	((x-ray or radiograph* or compute*) adj3 tomograph*).ti,ab.
37.	coronary angiography/ and (compute* or ct or tomograph*).ti,ab.
38.	((compute* or ct or tomograph*) adj3 angiograph*).ti,ab.
39.	((heart or cardiac or myocardial or imag* or scan* or diagnos*) adj2 (ct or cat)).ti,ab.
40.	(cta or ccta or tro-cta or msct).ti,ab.
41.	or/30-40
42.	29 and 41

A.8 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 8: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 stenosis or atresia or insufficienc*)).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/

40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	(((heart or cardiac) 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*)))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficien*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosth* or bioprosth* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 5- pharmacological management with heart failure

This literature search strategy was used for the following reviews:

- In adults with heart failure and concomitant heart valve disease, what is the clinical and cost effectiveness of ACE inhibitors, ARBs, beta blockers, calcium channel blockers, digoxin, diuretics and nitrates to improve clinical outcome?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.9 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 9: 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 stenosis or atresia or insufficienc*).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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 psyclit 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/44-52
55.	35 and (43 or 54)
56.	exp Angiotensin-Converting Enzyme Inhibitors/
57.	((("angiotensin-converting enzyme" or ace) adj2 (inhibitor* or antagonist*)).ti,ab.
58.	(Captopril or cilazapril or enalapril or enalaprilat or fosinopril or lisinopril or perindopril or quinapril or ramipril or teprotide or imidapril ortrandolopril).ti,ab.
59.	exp Angiotensin Receptor Antagonists/
60.	(angiotensin adj3 receptor adj3 (antagonist* or blocker*)).ti,ab.
61.	(1-Sarcosine-8-Isoleucine or amlodipine or irbesartan or olmesartan or saralasin or telmisartan or valsartan or azilsartan or candesartan or eprosartan or losartan).ti,ab.
62.	exp Adrenergic beta-Antagonists/
63.	(Acebutolol or Atenolol or Bisoprolol or Carvedilol or Celiprolol or Esmolol or Labetalol or Metoprolol or Nadolol or Nebivolol or Oxprenolol or Propranolol or Pindolol or Sotalol or Timolol).ti,ab.
64.	(beta adj3 block*).ti,ab.
65.	((beta-adrenoceptor or b-adrenoceptor or beta-adrenergic) adj (block* or antagonist*)).ti,ab.
66.	(b adj3 block*).ti,ab.
67.	(beta adj2 antagonist*).ti,ab.
68.	exp Calcium Channel Blockers/
69.	(calcium adj3 (block* or antagonis* or inhibit*)).ti,ab.
70.	calcium channel receptor block*.ti,ab.
71.	(amlodipine or amrinone or bencyclane or bepridil or carvedilol or cinnarizine or conotoxin* or diltiazem or felodipine or fendiline or flunarizine or gallopamil or isradipine or lamotrigine or mibefradil or nicardipine or nifedipine or nimodipine or nisoldipine or nitrendipine or perhexiline or pregabalin or prenylamine or risedronic acid or tiapamil or verapamil or zonisamide or atenolol or clevidipine or lacidipine or lercanidipine or dihyropyridine*).ti,ab.
72.	exp Digoxin/
73.	digoxin.ti,ab.
74.	exp Diuretics/
75.	((oral* or subcut* or IV or intravenous* or iv or infusion* or drip or drips or augment* or sequential* or loop or "high ceiling") adj6 diuretic*).ti,ab.
76.	(augment* adj diuresis).ti,ab.
77.	(acetazolamide or amiloride or bendroflumethiazide or bumentanide or chlorothiazide or chlorthalidone or clopamide or cyclopheniazide or ethacrynic acid or ethoxzolamide or furosemide or hydrochlorothiazide or hydroflumethiazide or indapamide or mefruside or methazolamide or methyclothiazide or metolazone or muzolimine or polythiazide or potassium citrate or spironolactone or ticrynafen or torsemide or triamterene or

	trichlormethiazide or xipamide or isosorbide or mannitol or co-amilozone or co-triamterzide or co-flumactone or eplerenone or co-amilozone).ti,ab.
78.	exp Nitrates/
79.	Nitroglycerin/
80.	Nitroprusside/
81.	Isosorbide Dinitrate/
82.	(nitroglycerin or gtn or nitrate* or nitroprusside*).ti,ab.
83.	(glyceryl trinitrate or isosorbide dinitrate or isosorbide mononitrate).ti,ab.
84.	or/56-83
85.	55 and 84

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 stenosis or atresia or insufficienc*).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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 dipeptidyl carboxypeptidase inhibitor/
58.	(("angiotensin-converting enzyme" or ace) adj2 (inhibitor* or antagonist*)).ti,ab.
59.	(Captopril or cilazapril or enalapril or enalaprilat or fosinopril or lisinopril or perindopril or quinapril or ramipril or teprotide or imidapril or trandolopril).ti,ab.
60.	exp angiotensin receptor antagonist/
61.	(angiotensin adj3 receptor adj3 (antagonist* or blocker*)).ti,ab.

62.	(1-Sarcosine-8-Isoleucine or amlodipine or irbesartan or olmesartan or saralasin or telmisartan or valsartan or azilsartan or candesartan or eprosartan or losartan).ti,ab.
63.	exp beta adrenergic receptor blocking agent/
64.	(Acebutolol or Atenolol or Bisoprolol or Carvedilol or Celiprolol or Esmolol or Labetalol or Metoprolol or Nadolol or Nebivolol or Oxprenolol or Propranolol or Pindolol or Sotalol or Timolol).ti,ab.
65.	(beta adj3 block*).ti,ab.
66.	((beta-adrenoceptor or b-adrenoceptor or beta-adrenergic) adj (block* or antagonist*).ti,ab.
67.	(b adj3 block*).ti,ab.
68.	(beta adj2 antagonist*).ti,ab.
69.	exp Calcium Channel Blockers/
70.	(calcium adj3 (block* or antagonis* or inhibit*).ti,ab.
71.	calcium channel receptor block*.ti,ab.
72.	(amlodipine or amrinone or bencyclane or bepridil or carvedilol or cinnarizine or conotoxin* or diltiazem or felodipine or fendiline or flunarizine or gallopamil or isradipine or lamotrigine or mibefradil or nifedipine or nifedipine or nimodipine or nisoldipine or nitrendipine or perhexiline or pregabalin or prenylamine or risedronic acid or tiapamil or verapamil or zonisamide or atenolol or clevidipine or lacidipine or lercanidipine or dihydropyridine*).ti,ab.
73.	digoxin/
74.	digoxin.ti,ab.
75.	exp diuretic agent/
76.	((oral* or subcut* or IV or intravenous* or iv or infusion* or drip or drips or augment* or sequential* or loop or "high ceiling") adj6 diuretic*).ti,ab.
77.	(augment* adj diuresis).ti,ab.
78.	(acetazolamide or amiloride or bendroflumethiazide or bumentanide or chlorothiazide or chlorthalidone or clopamide or cyclopheniazide or ethacrynic acid or ethoxzolamide or furosemide or hydrochlorothiazide or hydroflumethiazide or indapamide or mefruside or methazolamide or methyclothiazide or metolazone or muzolimine or polythiazide or potassium citrate or spironolactone or ticrynafen or torsemide or triamterene or trichlormethiazide or xipamide or isosorbide or mannitol or co-amilozide or co-triamterzide or co-flumactone or eplerenone or co-amilofruse).ti,ab.
79.	nitrate/
80.	glyceryl trinitrate/
81.	nitroprusside sodium/
82.	isosorbide mononitrate/
83.	isosorbide dinitrate/
84.	(nitroglycerin or gtn or nitrate* or nitroprusside*).ti,ab.
85.	(glyceryl trinitrate or isosorbide dinitrate or isosorbide mononitrate).ti,ab.
86.	or/57-85
87.	56 and 86

Cochrane Library (Wiley) search terms

#1.	MeSH descriptor: [Heart Valve Diseases] explode all trees
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#2.	MeSH descriptor: [Heart Valves] explode all trees
#3.	((primary or secondary) NEXT valv* disease*):ti,ab
#4.	((valv* or flap* or leaflet*) near/2 (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 prosth* or bioprosth* 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: [Angiotensin-Converting Enzyme Inhibitors] explode all trees
#15.	(("angiotensin-converting enzyme" or ace) near/2 (inhibitor* or antagonist*)):ti,ab
#16.	(Captopril or cilazapril or enalapril or enalaprilat or fosinopril or lisinopril or perindopril or quinapril or ramipril or teprotide or imidapril or trandolopril):ti,ab
#17.	MeSH descriptor: [Angiotensin Receptor Antagonists] explode all trees
#18.	(angiotensin near/3 receptor near/3 (antagonist* or blocker*)):ti,ab
#19.	(amlodipine or irbesartan or olmesartan or saralasin or telmisartan or valsartan or azilsartan or candesartan or eprosartan or losartan):ti,ab
#20.	1-Sarcosine-8-Isoleucine:ti,ab
#21.	MeSH descriptor: [Adrenergic beta-Antagonists] explode all trees
#22.	(Acebutolol or Atenolol or Bisoprolol or Carvedilol or Celiprolol or Esmolol or Labetalol or Metoprolol or Nadolol or Nebivolol or Oxprenolol or Propranolol or Pindolol or Sotalol or Timolol):ti,ab
#23.	(beta near/3 block*):ti,ab
#24.	((beta-adrenoceptor or b-adrenoceptor or beta-adrenergic) NEXT (block* or antagonist*)):ti,ab
#25.	(b near/3 block*):ti,ab
#26.	(beta near/2 antagonist*):ti,ab
#27.	MeSH descriptor: [Calcium Channel Blockers] explode all trees
#28.	(calcium near/3 (block* or antagonis* or inhibit*)):ti,ab
#29.	'calcium channel receptor':ti,ab
#30.	(amlodipine or amrinone or bencyclane or bepridil or carvedilol or cinnarizine or conotoxin* or diltiazem or felodipine or fendiline or flunarizine or gallopamil or isradipine or lamotrigine or mibefradil or nicardipine or nifedipine or nimodipine or nisoldipine or nitrendipine or

	perhexiline or pregabalin or prenylamine or risedronic acid or tiapamil or verapamil or zonisamide or atenolol or clevidipine or lacidipine or lercanidipine or dihydropyridine*):ti,ab
#31.	MeSH descriptor: [Digoxin] explode all trees
#32.	digoxin:ti,ab
#33.	MeSH descriptor: [Diuretics] explode all trees
#34.	((oral* or subcut* or IV or intravenous* or iv or infusion* or drip or drips or augment* or sequential* or loop or "high ceiling") near/6 diuretic*):ti,ab
#35.	(acetazolamide or amiloride or bendroflumethiazide or bumetanide or chlorothiazide or chlorthalidone or clopamide or cyclopheniazide or ethacrynic acid or ethoxzolamide or furosemide or hydrochlorothiazide or hydroflumethiazide or indapamide or mefruside or methazolamide or methyclothiazide or metolazone or muzolimine or polythiazide or potassium citrate or spironolactone or ticrynafen or torsemide or triamterene or trichlormethiazide or xipamide or isosorbide or mannitol or co-amilozone or co-triamterzide or co-flumactone or eplerenone or co-amilofruse):ti,ab
#36.	MeSH descriptor: [Nitrates] explode all trees
#37.	MeSH descriptor: [Nitroglycerin] explode all trees
#38.	MeSH descriptor: [Nitroprusside] explode all trees
#39.	MeSH descriptor: [Isosorbide Dinitrate] explode all trees
#40.	(nitroglycerin or gtn or nitrate* or nitroprusside*):ti,ab
#41.	('glyceryl trinitrate' or 'isosorbide dinitrate' or 'isosorbide mononitrate'):ti,ab
#42.	(or #14-#41)
#43.	#13 and #42

A.10 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 10: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 stenosis or atresia or insufficienc*).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosthe* or bioprosathe* 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/
40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
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#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	(((heart or cardiac) 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*)))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosth* or bioprosth* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 6 - pharmacological management without heart failure

This literature search strategy was used for the following reviews:

- In adults with heart valve disease without concomitant heart failure, what is the clinical and cost effectiveness of alpha-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin-II receptor blockers (ARBs), beta blockers, calcium channel blockers, digoxin, diuretics, statins and nitrates to improve clinical outcome?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.11 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 11: 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 stenosis or atresia or insufficienc*)).ti,ab.
7.	Heart Valve Prosthesis/

Heart valve disease

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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 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/44-52
55.	35 and (43 or 54)
56.	exp Angiotensin-Converting Enzyme Inhibitors/
57.	(("angiotensin-converting enzyme" or ace) adj2 (inhibitor* or antagonist*)).ti,ab.
58.	(Captopril or cilazapril or enalapril or enalaprilat or fosinopril or lisinopril or perindopril or quinapril or ramipril or teprotide or imidapril or trandolopril).ti,ab.
59.	exp Angiotensin Receptor Antagonists/
60.	(angiotensin adj3 receptor adj3 (antagonist* or blocker*)).ti,ab.
61.	(1-Sarcosine-8-Isoleucine or amlodipine or irbesartan or olmesartan or saralasin or telmisartan or valsartan or azilsartan or candesartan or eprosartan or losartan).ti,ab.
62.	exp Adrenergic beta-Antagonists/
63.	(Acebutolol or Atenolol or Bisoprolol or Carvedilol or Celiprolol or Esmolol or Labetalol or Metoprolol or Nadolol or Nebivolol or Oxprenolol or Propranolol or Pindolol or Sotalol or Timolol).ti,ab.
64.	(beta adj3 block*).ti,ab.
65.	((beta-adrenoceptor or b-adrenoceptor or beta-adrenergic) adj (block* or antagonist*)).ti,ab.
66.	(b adj3 block*).ti,ab.
67.	(beta adj2 antagonist*).ti,ab.
68.	exp Calcium Channel Blockers/
69.	(calcium adj3 (block* or antagonis* or inhibit*)).ti,ab.
70.	calcium channel receptor block*.ti,ab.
71.	(amlodipine or amrinone or bencyclane or bepridil or carvedilol or cinnarizine or conotoxin* or diltiazem or felodipine or fendiline or flunarizine or gallopamil or isradipine or lamotrigine or mibefradil or nicardipine or nifedipine or nimodipine or nisoldipine or nitrendipine or perhexiline or pregabalin or prenylamine or risedronic acid or tiapamil or verapamil or zonisamide or atenolol or clevidipine or lacidipine or lercanidipine or dihydropyridine*).ti,ab.
72.	exp Digoxin/
73.	digoxin.ti,ab.
74.	exp Diuretics/

75.	((oral* or subcut* or IV or intravenous* or iv or infusion* or drip or drips or augment* or sequential* or loop or "high ceiling") adj6 diuretic*).ti,ab.
76.	(augment* adj diuresis).ti,ab.
77.	(acetazolamide or amiloride or bendroflumethiazide or bumentanide or chlorothiazide or chlorthalidone or clopamide or cyclopheniazide or ethacrynic acid or ethoxzolamide or furosemide or hydrochlorothiazide or hydroflumethiazide or indapamide or mefruside or methazolamide or methyclothiazide or metolazone or muzolimine or polythiazide or potassium citrate or spironolactone or ticrynafen or torsemide or triamterene or trichlormethiazide or xipamide or isosorbide or mannitol or co-amilozone or co-triamterzide or co-flumactone or eplerenone or co-amilofruse).ti,ab.
78.	exp Nitrates/
79.	Nitroglycerin/
80.	Nitroprusside/
81.	Isosorbide Dinitrate/
82.	(nitroglycerin or gtn or nitrate* or nitroprusside*).ti,ab.
83.	(glyceryl trinitrate or isosorbide dinitrate or isosorbide mononitrate).ti,ab.
84.	*hydroxymethylglutaryl-coa reductase inhibitors/ or atorvastatin calcium/ or pravastatin/ or rosuvastatin calcium/ or exp simvastatin/
85.	(atorvastatin* or pravastatin* or rosuvastatin* or simvastatin* or fluvastatin*).ti,ab.
86.	((Hydroxymethylglutaryl-CoA or HMG-CoA or Hydroxymethylglutaryl-Coenzyme A) adj3 (reductase* or inhibitor*).ti,ab.
87.	statin*.ti,ab.
88.	exp Adrenergic alpha-Antagonists/
89.	(alfuzosin or bunazosin or doxazosin or indoramin or metazosin or neldazosin or prazosin or silodosin or tamsulosin or terazosin or tiodazosin or trimazosin).ti,ab.
90.	(alpha adrenergic antagonist* or alpha adrenergic receptor antagonist* or adrenergic alpha antagonist*).ti,ab.
91.	((alpha or alpha-adrenergic) adj2 block*).ti,ab.
92.	or/56-91
93.	55 and 92

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 stenosis or atresia or insufficienc*).ti,ab.
7.	exp heart valve prosthesis/

8.	((mechanical or artificial or prosth* or bioprosth* 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 dipeptidyl carboxypeptidase inhibitor/
58.	(("angiotensin-converting enzyme" or ace) adj2 (inhibitor* or antagonist*)).ti,ab.
59.	(Captopril or cilazapril or enalapril or enalaprilat or fosinopril or lisinopril or perindopril or quinapril or ramipril or teprotide or imidapril ortrandolopril).ti,ab.
60.	exp angiotensin receptor antagonist/
61.	(angiotensin adj3 receptor adj3 (antagonist* or blocker*)).ti,ab.
62.	(1-Sarcosine-8-Isoleucine or amlodipine or irbesartan or olmesartan or saralasin or telmisartan or valsartan or azilsartan or candesartan or eprosartan or losartan).ti,ab.
63.	exp beta adrenergic receptor blocking agent/
64.	(Acebutolol or Atenolol or Bisoprolol or Carvedilol or Celiprolol or Esmolol or Labetalol or Metoprolol or Nadolol or Nebivolol or Oxprenolol or Propranolol or Pindolol or Sotalol or Timolol).ti,ab.
65.	(beta adj3 block*).ti,ab.
66.	((beta-adrenoceptor or b-adrenoceptor or beta-adrenergic) adj (block* or antagonist*)).ti,ab.
67.	(b adj3 block*).ti,ab.
68.	(beta adj2 antagonist*).ti,ab.
69.	exp Calcium Channel Blockers/
70.	(calcium adj3 (block* or antagonis* or inhibit*)).ti,ab.
71.	calcium channel receptor block*.ti,ab.
72.	(amlodipine or amrinone or bencyclane or bepridil or carvedilol or cinnarizine or conotoxin* or diltiazem or felodipine or fendiline or flunarizine or gallopamil or isradipine or lamotrigine or mibefradil or nicardipine or nifedipine or nimodipine or nisoldipine or nitrendipine or perhexiline or pregabalin or prenylamine or risedronic acid or tiapamil or verapamil or zonisamide or atenolol or clevidipine or lacidipine or lercanidipine or dihyropyridine*).ti,ab.
73.	digoxin/
74.	digoxin.ti,ab.
75.	exp diuretic agent/

76.	((oral* or subcut* or IV or intravenous* or iv or infusion* or drip or drips or augment* or sequential* or loop or "high ceiling") adj6 diuretic*).ti,ab.
77.	(augment* adj diuresis).ti,ab.
78.	(acetazolamide or amiloride or bendroflumethiazide or bumentanide or chlorothiazide or chlorthalidone or clopamide or cyclopheniazide or ethacrynic acid or ethoxzolamide or furosemide or hydrochlorothiazide or hydroflumethiazide or indapamide or mefruside or methazolamide or methyclothiazide or metolazone or muzolimine or polythiazide or potassium citrate or spironolactone or ticrynafen or torsemide or triamterene or trichlormethiazide or xipamide or isosorbide or mannitol or co-amilozide or co-triamterzide or co-flumactone or eplerenone or co-amilofruse).ti,ab.
79.	nitrate/
80.	glyceryl trinitrate/
81.	nitroprusside sodium/
82.	isosorbide mononitrate/
83.	isosorbide dinitrate/
84.	(nitroglycerin or gtn or nitrate* or nitroprusside*).ti,ab.
85.	(glyceryl trinitrate or isosorbide dinitrate or isosorbide mononitrate).ti,ab.
86.	*hydroxymethylglutaryl coenzyme a reductase inhibitor/ or exp atorvastatin/ or exp pravastatin/ or exp.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
87.	(atorvastatin* or pravastatin* or rosuvastatin* or simvastatin* or fluvastatin*).ti,ab.
88.	((Hydroxymethylglutaryl-CoA or HMG-CoA or Hydroxymethylglutaryl-Coenzyme A) adj3 (reductase* or inhibitor*).ti,ab.
89.	statin*.ti,ab.
90.	exp alpha adrenergic receptor blocking agent/
91.	(alfuzosin or bunazosin or doxazosin or indoramin or metazosin or neldazosin or prazosin or silodosin or tamsulosin or terazosin or tiodazosin or trimazosin).ti,ab.
92.	(alpha adrenergic antagonist* or alpha adrenergic receptor antagonist* or adrenergic alpha antagonist*).ti,ab.
93.	((alpha or alpha-adrenergic) adj2 block*).ti,ab.
94.	or/57-93
95.	56 and 94

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/2 (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 insufficiency*)):ti,ab
#7.	MeSH descriptor: [Heart Valve Prosthesis] explode all trees
#8.	((mechanical or artificial or prosthesis* or bioprosthesis* 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: [Angiotensin-Converting Enzyme Inhibitors] explode all trees
#15.	(("angiotensin-converting enzyme" or ace) near/2 (inhibitor* or antagonist*)):ti,ab
#16.	(Captopril or cilazapril or enalapril or enalaprilat or fosinopril or lisinopril or perindopril or quinapril or ramipril or teprotide or imidapril or trandolopril):ti,ab
#17.	MeSH descriptor: [Angiotensin Receptor Antagonists] explode all trees
#18.	(angiotensin near/3 receptor near/3 (antagonist* or blocker*)):ti,ab
#19.	(amlodipine or irbesartan or olmesartan or saralasin or telmisartan or valsartan or azilsartan or candesartan or eprosartan or losartan):ti,ab
#20.	1-Sarcosine-8-Isoleucine:ti,ab
#21.	MeSH descriptor: [Adrenergic beta-Antagonists] explode all trees
#22.	(Acebutolol or Atenolol or Bisoprolol or Carvedilol or Celiprolol or Esmolol or Labetalol or Metoprolol or Nadolol or Nebivolol or Oxprenolol or Propranolol or Pindolol or Sotalol or Timolol):ti,ab
#23.	(beta near/3 block*):ti,ab
#24.	((beta-adrenoceptor or b-adrenoceptor or beta-adrenergic) NEXT (block* or antagonist*)):ti,ab
#25.	(b near/3 block*):ti,ab
#26.	(beta near/2 antagonist*):ti,ab
#27.	MeSH descriptor: [Calcium Channel Blockers] explode all trees
#28.	(calcium near/3 (block* or antagonis* or inhibit*)):ti,ab
#29.	'calcium channel receptor':ti,ab
#30.	(amlodipine or amrinone or bencyclane or bepridil or carvedilol or cinnarizine or conotoxin* or diltiazem or felodipine or fendiline or flunarizine or gallopamil or isradipine or lamotrigine or mibefradil or nifedipine or nifedipine or nimodipine or nisoldipine or nitrendipine or perhexiline or pregabalin or prenylamine or risedronic acid or tiapamil or verapamil or zonisamide or atenolol or clevidipine or lacidipine or lercanidipine or dihydropyridine*):ti,ab
#31.	MeSH descriptor: [Digoxin] explode all trees
#32.	digoxin:ti,ab
#33.	MeSH descriptor: [Diuretics] explode all trees
#34.	((oral* or subcut* or IV or intravenous* or iv or infusion* or drip or drips or augment* or sequential* or loop or "high ceiling") near/6 diuretic*):ti,ab

#35.	(acetazolamide or amiloride or bendroflumethiazide or bumentanide or chlorothiazide or chlorthalidone or clopamide or cyclopheniazide or ethacrynic acid or ethoxzolamide or furosemide or hydrochlorothiazide or hydroflumethiazide or indapamide or mefruside or methazolamide or methyclothiazide or metolazone or muzolimine or polythiazide or potassium citrate or spironolactone or ticrynafen or torsemide or triamterene or trichlormethiazide or xipamide or isosorbide or mannitol or co-amilozide or co-triamterzide or co-flumactone or eplerenone or co-amilofruse):ti,ab
#36.	MeSH descriptor: [Nitrates] explode all trees
#37.	MeSH descriptor: [Nitroglycerin] explode all trees
#38.	MeSH descriptor: [Nitroprusside] explode all trees
#39.	MeSH descriptor: [Isosorbide Dinitrate] explode all trees
#40.	(nitroglycerin or gtn or nitrate* or nitroprusside*):ti,ab
#41.	('glyceryl trinitrate' or 'isosorbide dinitrate' or 'isosorbide mononitrate'):ti,ab
#42.	MeSH descriptor: [Hydroxymethylglutaryl-CoA Reductase Inhibitors] explode all trees
#43.	MeSH descriptor: [Atorvastatin] explode all trees
#44.	MeSH descriptor: [Pravastatin] explode all trees
#45.	MeSH descriptor: [Rosuvastatin Calcium] explode all trees
#46.	MeSH descriptor: [Simvastatin] explode all trees
#47.	(atorvastatin* or pravastatin* or rosuvastatin* or simvastatin* or fluvastatin*):ti,ab
#48.	((Hydroxymethylglutaryl-CoA or HMG-CoA or Hydroxymethylglutaryl-Coenzyme A) near/3 (reductase* or inhibitor*)):ti,ab
#49.	statin*:ti,ab
#50.	MeSH descriptor: [Adrenergic alpha-Antagonists] explode all trees
#51.	(alfuzosin or bunazosin or doxazosin or indoramin or metazosin or neldazosin or prazosin or silodosin or tamsulosin or terazosin or tiodazosin or trimazosin):ti,ab
#52.	(alpha next adrenergic):ti,ab
#53.	(adrenergic next alpha):ti,ab
#54.	((alpha or alpha-adrenergic) near/2 block*):ti,ab
#55.	(or #14-#54)
#56.	#13 and #55

A.12 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 12: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 stenosis or atresia or insufficienc*).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/

40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	(((heart or cardiac) 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*)))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosthe* or bioprosthe* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 7 - indications for specialist referral following echocardiography

This literature search strategy was used for the following review:

- What are the indications that interventions should be offered to adults with asymptomatic, severe heart valve disease?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.13 Clinical search literature search strategy

This prognostic search was constructed using one following approaches:

- Population AND Prognostic/risk factor terms

Table 13: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 - 14 October 2020	Exclusions
Embase (OVID)	1974 - 14 October 2020	Exclusions
The Cochrane Library (Wiley)	Cochrane Reviews 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 stenosis or atresia or insufficienc*).ti,ab.
7.	exp Heart Murmurs/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter/
11.	editorial/
12.	news/
13.	exp historical article/
14.	Anecdotes as Topic/
15.	comment/
16.	case report/
17.	(letter or comment*).ti.
18.	or/10-17
19.	randomized controlled trial/ or random*.ti,ab.

20.	18 not 19
21.	animals/ not humans/
22.	exp Animals, Laboratory/
23.	exp Animal Experimentation/
24.	exp Models, Animal/
25.	exp Rodentia/
26.	(rat or rats or mouse or mice).ti.
27.	or/20-26
28.	9 not 27
29.	limit 28 to English language
30.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
31.	29 not 30
32.	Asymptomatic Diseases/
33.	asymptomatic.ti,ab.
34.	(symptom* adj3 (absent or non or none or no or missed or missing or unseen or "not apparent" or clinically silent or subclinical)).ti,ab.
35.	or/32-34
36.	31 and 35

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart murmur/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	Case report/ or Case study/
14.	(letter or comment*).ti.
15.	or/10-14
16.	randomized controlled trial/ or random*.ti,ab.

17.	15 not 16
18.	animal/ not human/
19.	Nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental animal/
22.	Animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice).ti.
25.	or/17-24
26.	9 not 25
27.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
28.	26 not 27
29.	limit 28 to English language
30.	asymptomatic disease/
31.	asymptomatic.ti,ab.
32.	(symptom* adj3 (absent or non or none or no or missed or missing or unseen or "not apparent" or clinically silent or subclinical)).ti,ab.
33.	or/30-32
34.	29 and 33

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 Murmurs] explode all trees
#8.	((heart or cardiac) NEXT murmur*):ti,ab
#9.	(or #1-#8)
#10.	MeSH descriptor: [Asymptomatic Diseases] this term only
#11.	asymptomatic:ti,ab
#12.	(symptom* near/3 (absent or non or none or no or missed or missing or unseen or subclinical)):ti,ab
#13.	"not apparent":ti,ab
#14.	"clinically silent":ti,ab
#15.	(or #10-#14)

#16.	#9 and #15
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A.14 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 14: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 prosth* or bioprosth* 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.

51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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 stenosis or atresia or insufficienc*).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/
40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	((heart or cardiac) 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*))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosth* or bioprosth* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 8 - transcatheter intervention, surgery or conservative management

This literature search strategy was used for the following review:

- What is the clinical and cost-effectiveness of transcatheter intervention, surgery (with mechanical or biological valves) and conservative management compared with each other for adults with heart valve disease?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.15 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 15: 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 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 stenosis or atresia or insufficienc*).ti,ab.

Heart valve disease

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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 psychlit 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 heart surgery/
58.	exp valvular heart disease/su [Surgery]
59.	exp heart valve prosthesis/ or exp heart valve replacement/
60.	exp catheterization/
61.	exp minimally invasive surgery/
62.	((transcatheter or surg* or intervention*) adj3 (repair* or replac* or implant*)).ti,ab.
63.	(TAVR or TAVI or TMVR or TMVI).ti,ab.
64.	((cardiovascular or cardiac or heart or robotic) adj2 surg*).ti,ab.
65.	(commissurotomy or valvulotomy or valvotomy or valvuloplasty or valvoplasty or annuloplasty).ti,ab.
66.	(sternotomy or ministernotomy or mini-sternotomy or thoracotomy or port access or non-sternotomy).ti,ab.
67.	(mitra clip or MitraClip or edge to edge or chord* or balloon).ti,ab.
68.	or/57-67
69.	56 and 68

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 stenosis 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 psychlit 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 heart surgery/
58.	exp valvular heart disease/su [Surgery]
59.	exp heart valve prosthesis/ or exp heart valve replacement/
60.	exp catheterization/
61.	exp minimally invasive surgery/
62.	((transcatheter or surg* or intervention*) adj3 (repair* or replac* or implant*)).ti,ab.
63.	(TAVR or TAVI or TMVR or TMVI).ti,ab.
64.	((cardiovascular or cardiac or heart or robotic) adj2 surg*).ti,ab.
65.	(commissurotomy or valvulotomy or valvotomy or valvuloplasty or valvoplasty or annuloplasty).ti,ab.
66.	(sternotomy or ministernotomy or mini-sternotomy or thoracotomy or port access or non-sternotomy).ti,ab.
67.	(mitra clip or MitraClip or edge to edge or chord* or balloon).ti,ab.
68.	or/57-67
69.	56 and 68

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: [Cardiac Surgical Procedures] explode all trees
#15.	MeSH descriptor: [Heart Valve Diseases] explode all trees and with qualifier(s): [surgery - SU]
#16.	MeSH descriptor: [Heart Valve Prosthesis Implantation] explode all trees
#17.	MeSH descriptor: [Catheterization] explode all trees
#18.	MeSH descriptor: [Minimally Invasive Surgical Procedures] explode all trees
#19.	((transcatheter or surg* or intervention*) near/3 (repair* or replac* or implant*)):ti,ab
#20.	(TAVR or TAVI or TMVR or TMVI):ti,ab
#21.	((cardiovascular or cardiac or heart or robotic) near/2 surg*):ti,ab
#22.	(commissurotomy or valvulotomy or valvotomy or valvuloplasty or valvoplasty or annuloplasty):ti,ab
#23.	(sternotomy or ministernotomy or mini-sternotomy or thoracotomy or port access or non-sternotomy):ti,ab
#24.	(mitra NEXT clip or MitraClip or "edge to edge" or chord* or balloon):ti,ab
#25.	(or #14-#24)
#26.	#13 and #25

A.16 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 16: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018	None

Database	Dates searched	Search filter used
	NHSEED - Inception to 31 March 2015	

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 stenosis or atresia or insufficienc*).ti,ab.
7.	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 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp heart valve prosthesis/

8.	((mechanical or artificial or prosth* or bioprosth* 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/
40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.

46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	(((heart or cardiac) 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*)))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficien*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosthe* or bioprosthe* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 9 - repeat intervention for failure of biological or repaired valves

This literature search strategy was used for the following reviews:

- What is the clinical and cost effectiveness of transcatheter or surgical repeat valve intervention for people with biologic valves or repaired valves that require reintervention due to failure of the valve?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.17 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 17: 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 Observational studies
Embase (OVID)	1974 - 14 October 2020	Exclusions Randomised controlled trials Systematic review studies Observational 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 stenosis or atresia or insufficienc*)).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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 psyclit 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/44-52
55.	Epidemiologic studies/
56.	Observational study/
57.	exp Cohort studies/
58.	(cohort adj (study or studies or analys* or data)).ti,ab.
59.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
60.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
61.	Controlled Before-After Studies/
62.	Historically Controlled Study/
63.	Interrupted Time Series Analysis/
64.	(before adj2 after adj2 (study or studies or data)).ti,ab.
65.	exp case control study/
66.	case control*.ti,ab.
67.	Cross-sectional studies/
68.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
69.	or/55-68
70.	43 or 54 or 69
71.	35 and 70
72.	Reoperation/
73.	((reoperation* or revision) adj3 (valve or surgery or surgeries)).ti,ab.
74.	((redo or reoperative or repeat or reoperated) adj3 (surgery or surgical or procedure* or intervention* or valve replacement* or patient*)).ti,ab.
75.	((second or further or repeat*) adj2 ((transcatheter or surg* or intervention*) adj3 (repair* or replac* or implant*)).ti,ab.
76.	((second or further or repeat*) adj2 (TAVR or TAVI or TMVR or TMVI)).ti,ab.
77.	((second or further or repeat*) adj2 ((cardiovascular or cardiac or heart or robotic) adj2 surg*).ti,ab.
78.	((second or further or repeat*) adj2 (commissurotom* or valvulotom* or valvotom* or valvuloplast* or valvoplast* or annuloplast*).ti,ab.
79.	((second or further or repeat*) adj2 (sternotom* or ministernotom* or mini-sternotom* or thoracotom* or port access or non-sternotom*).ti,ab.
80.	((second or further or repeat*) adj2 (mitra clip or MitraClip or edge to edge or chord* or balloon)).ti,ab.
81.	or/72-80
82.	71 and 81

Embase (Ovid) search terms

1.	exp valvular heart disease/
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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 murmur/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	Case report/ or Case study/
14.	(letter or comment*).ti.
15.	or/10-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animal/ not human/
19.	Nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental animal/
22.	Animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice).ti.
25.	or/17-24
26.	9 not 25
27.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
28.	26 not 27
29.	limit 28 to English language
30.	random*.ti,ab.
31.	factorial*.ti,ab.
32.	(crossover* or cross over*).ti,ab.
33.	((doubl* or singl*) adj blind*).ti,ab.
34.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
35.	crossover procedure/
36.	single blind procedure/
37.	randomized controlled trial/

38.	double blind procedure/
39.	or/30-38
40.	systematic review/
41.	meta-analysis/
42.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
43.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
44.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
45.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
46.	(search* adj4 literature).ab.
47.	(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.
48.	cochrane.jw.
49.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
50.	or/40-49
51.	Clinical study/
52.	Observational study/
53.	family study/
54.	longitudinal study/
55.	retrospective study/
56.	prospective study/
57.	cohort analysis/
58.	follow-up/
59.	cohort*.ti,ab.
60.	58 and 59
61.	(cohort adj (study or studies or analys* or data)).ti,ab.
62.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
63.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
64.	(before adj2 after adj2 (study or studies or data)).ti,ab.
65.	exp case control study/
66.	case control*.ti,ab.
67.	cross-sectional study/
68.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
69.	or/51-57,60-68
70.	reoperation/
71.	((reoperation* or revision) adj3 (valve or surgery or surgeries)).ti,ab.
72.	((redo or reoperative or repeat or reoperated) adj3 (surgery or surgical or procedure* or intervention* or valve replacement* or patient*)).ti,ab.

73.	((second or further or repeat*) adj2 ((transcatheter or surg* or intervention*) adj3 (repair* or replac* or implant*))).ti,ab.
74.	((second or further or repeat*) adj2 (TAVR or TAVI or TMVR or TMVI)).ti,ab.
75.	((second or further or repeat*) adj2 ((cardiovascular or cardiac or heart or robotic) adj2 surg*)).ti,ab.
76.	((second or further or repeat*) adj2 (commissurotom* or valvulotom* or valvotom* or valvuloplast* or valvoplast* or annuloplast*)).ti,ab.
77.	((second or further or repeat*) adj2 (sternotom* or ministernotom* or mini-sternotom* or thoracotom* or port access or non-sternotom*)).ti,ab.
78.	((second or further or repeat*) adj2 (mitra clip or MitraClip or edge to edge or chord* or balloon)).ti,ab.
79.	or/70-78
80.	29 and 79 and (39 or 50 or 69)

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 Murmurs] explode all trees
#8.	((heart or cardiac) NEXT murmur*):ti,ab
#9.	(or #1-#8)
#10.	MeSH descriptor: [Reoperation] this term only
#11.	((reoperation* or revision) near/3 (valve or surgery or surgeries)):ti,ab
#12.	((redo or reoperative or repeat or reoperated) near/3 (surgery or surgical or procedure* or intervention* or valve replacement* or patient*)):ti,ab
#13.	((second or further or repeat*) near/2 ((transcatheter or surg* or intervention*) near/3 (repair* or replac* or implant*)):ti,ab
#14.	((second or further or repeat*) near/2 (TAVR or TAVI or TMVR or TMVI)):ti,ab
#15.	((second or further or repeat*) near/2 ((cardiovascular or cardiac or heart or robotic) near/2 surg*)):ti,ab
#16.	((second or further or repeat*) near/2 (commissurotom* or valvulotom* or valvotom* or valvuloplast* or valvoplast* or annuloplast*)):ti,ab
#17.	((second or further or repeat*) near/2 (sternotom* or ministernotom* or mini-sternotom* or thoracotom* or port access or non-sternotom*)):ti,ab
#18.	((second or further or repeat*) near/2 (mitra clip or MitraClip or "edge to edge" or chord* or balloon)):ti,ab

#19.	(or #10-#18)
#20.	#9 and #19

A.18 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 18: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 stenosis or atresia or insufficienc*)).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.

50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/
40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	(((heart or cardiac) 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*)))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosthe* or bioprosthe* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 10 - anticoagulant and/or antiplatelet therapy for biological prosthetic valves and after valve repair

This literature search strategy was used for the following review:

- What is the clinical and cost effectiveness of anticoagulant and/or antiplatelet therapy for adults with transcatheter or surgical biological prosthetic valves or after valve repair?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.19 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 19: 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 stenosis or atresia or insufficienc*)).ti,ab.
7.	Heart Valve Prosthesis/

8.	((mechanical or artificial or prosth* or bioprosth* 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

Heart valve disease

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 stenosis or atresia or insufficienc*).ti,ab.
7.	exp heart valve prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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

A.20 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 20: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions

Database	Dates searched	Search filter used
		Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 stenosis or atresia or insufficienc*)).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosthe* or bioproshe* 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51
53.	35 and 52

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 stenosis 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/
40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.

45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	((heart or cardiac) 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*))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosth* or bioprosth* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 11 - monitoring of people with heart valve disease and no current indication for intervention AND monitoring in people with repaired or replaced heart valves

This literature search strategy was used for the following reviews:

- Where there is no current indication for intervention, what is the most clinically and cost-effective type and frequency of test for monitoring in adults with heart valve disease?
- What is the most clinically and cost-effective frequency of echocardiography or clinical review for monitoring in adults with repaired or replaced heart valves?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.21 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 21: 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 Observational studies
Embase (OVID)	1974 - 14 October 2020	Exclusions Randomised controlled trials Systematic review studies Observational 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 stenosis or atresia or insufficienc*)).ti,ab.
7.	Heart Valve Prosthesis/
8.	((mechanical or artificial or prosth* or bioprosth* 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.	exp Natriuretic Peptide, Brain/
37.	Biomarker*.ti,ab.
38.	((brain or b-type) adj2 natriuretic peptide*).ti,ab.
39.	(bnp or nt-probnp or nt-pro bnp or nt-bnp).ti,ab.
40.	exp Echocardiography/
41.	(Echo* or transoesophageal or transesophageal or transthoracic or TOE or TEE or TTE).ti,ab.
42.	exp Electrocardiography/
43.	(electrocardio* or ECG or EKG).ti,ab.
44.	exp Tomography, X-Ray computed/
45.	(comput* adj2 tomograp*).ti,ab.
46.	(CT adj3 (cine or CAT or scan* or x ray* or xray* or imag*)).ti,ab.
47.	exp Magnetic Resonance Imaging/
48.	((magnetic or nuclear) adj2 resonance adj3 imag*).ti,ab.
49.	((cardiac or cardiovascular) adj mr).ti,ab.
50.	(mri* or nmr* or cmr*).ti,ab.
51.	patient reported outcome measures/
52.	("patient reported outcome measures" or PROM*).ti,ab.
53.	(euroqol* or eq5d* or eq 5*).ti,ab.

54.	("minnesota living with heart failure questionnaire" or MLHFQ or MLWHF).ti,ab.
55.	("Veterans Specific Activity Questionnaire" or VSAQ).ti,ab.
56.	(clinic* adj2 (assess* or general or special* or valve* or monitor* or examin*)).ti,ab.
57.	Exercise tolerance/ or Exercise Test/
58.	((physical* or exercise* or fitness) adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit* or tolera* or test*)).ti,ab.
59.	(stress test adj2 (cardiac or ECG)).ti,ab.
60.	bruce protocol.ti,ab.
61.	or/36-60
62.	Meta-Analysis/
63.	exp Meta-Analysis as Topic/
64.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
65.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
66.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
67.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
68.	(search* adj4 literature).ab.
69.	(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.
70.	cochrane.jw.
71.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
72.	or/62-71
73.	randomized controlled trial.pt.
74.	controlled clinical trial.pt.
75.	randomi#ed.ti,ab.
76.	placebo.ab.
77.	randomly.ti,ab.
78.	Clinical Trials as topic.sh.
79.	trial.ti.
80.	or/73-79
81.	Epidemiologic studies/
82.	Observational study/
83.	exp Cohort studies/
84.	(cohort adj (study or studies or analys* or data)).ti,ab.
85.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
86.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
87.	Controlled Before-After Studies/
88.	Historically Controlled Study/

89.	Interrupted Time Series Analysis/
90.	(before adj2 after adj2 (study or studies or data)).ti,ab.
91.	or/81-90
92.	35 and 61 and (72 or 80 or 91)

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 stenosis 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.	exp brain natriuretic peptide/
35.	Biomarker*.ti,ab.
36.	((brain or b-type) adj2 natriuretic peptide*).ti,ab.
37.	(bnp or nt-probnp or nt-pro bnp or nt-bnp).ti,ab.
38.	exp Echocardiography/
39.	(Echo* or transoesophageal or transesophageal or transthoracic or TOE or TEE or TTE).ti,ab.
40.	exp electrocardiography/
41.	(electrocardio* or ECG or EKG).ti,ab.
42.	exp x-ray computed tomography/
43.	(comput* adj2 tomograp*).ti,ab.
44.	(CT adj3 (cine or CAT or scan* or x ray* or xray* or imag*)).ti,ab.
45.	exp nuclear magnetic resonance imaging/
46.	((magnetic or nuclear) adj2 resonance adj3 imag*).ti,ab.
47.	((cardiac or cardiovascular) adj mr).ti,ab.
48.	(mri* or nmr* or cmr*).ti,ab.
49.	exp patient-reported outcome/
50.	("patient reported outcome measure*" or PROM*).ti,ab.
51.	(euroqol* or eq5d* or eq 5*).ti,ab.
52.	("minnesota living with heart failure questionnaire" or MLHFQ or MLWHF).ti,ab.
53.	("Veterans Specific Activity Questionnaire" or VSAQ).ti,ab.
54.	(clinic* adj2 (assess* or general or special* or valve* or monitor* or examin*)).ti,ab.
55.	Exercise tolerance/ or Exercise Test/
56.	((physical* or exercise* or fitness) adj5 (fit* or train* or therap* or activ* or strength or endur* or exert* or capacit* or tolera* or test*)).ti,ab.
57.	(stress test adj2 (cardiac or ECG)).ti,ab.
58.	bruce protocol.ti,ab.
59.	or/34-58
60.	systematic review/
61.	meta-analysis/
62.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
63.	((systematic or evidence) adj3 (review* or overview*)).ti,ab.
64.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
65.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
66.	(search* adj4 literature).ab.
67.	(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.

68.	cochrane.jw.
69.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
70.	or/60-69
71.	random*.ti,ab.
72.	factorial*.ti,ab.
73.	(crossover* or cross over*).ti,ab.
74.	((doubl* or singl*) adj blind*).ti,ab.
75.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
76.	crossover procedure/
77.	single blind procedure/
78.	randomized controlled trial/
79.	double blind procedure/
80.	or/71-79
81.	Clinical study/
82.	Observational study/
83.	family study/
84.	longitudinal study/
85.	retrospective study/
86.	prospective study/
87.	cohort analysis/
88.	follow-up/
89.	cohort*.ti,ab.
90.	88 and 89
91.	(cohort adj (study or studies or analys* or data)).ti,ab.
92.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
93.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
94.	(before adj2 after adj2 (study or studies or data)).ti,ab.
95.	or/81-87,90-94
96.	33 and 59 and (70 or 80 or 95)

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 insufficiency*)):ti,ab
#7.	MeSH descriptor: [Heart Valve Prosthesis] explode all trees
#8.	((mechanical or artificial or prosthesis* or bioprosthesis* 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: [Natriuretic Peptide, Brain] explode all trees
#15.	Biomarker*:ti,ab
#16.	((brain or b-type) near/2 natriuretic peptide*):ti,ab
#17.	(bnp or nt-probnp or nt-pro bnp or nt-bnp):ti,ab
#18.	MeSH descriptor: [Echocardiography] explode all trees
#19.	(electrocardio* or ECG or EKG):ti,ab
#20.	MeSH descriptor: [Tomography, X-Ray Computed] explode all trees
#21.	(comput* near/2 tomograph*):ti,ab
#22.	(CT near/3 (cine or CAT or scan* or x ray* or xray* or imag*)):ti,ab
#23.	MeSH descriptor: [Magnetic Resonance Imaging] explode all trees
#24.	((magnetic or nuclear) near/2 resonance near/3 imag*):ti,ab
#25.	((cardiac or cardiovascular) near/1 mr):ti,ab
#26.	(mri* or nmr* or cmr*):ti,ab
#27.	MeSH descriptor: [Patient Reported Outcome Measures] explode all trees
#28.	("patient reported outcome measures" or PROM).ti,ab
#29.	(euroqol* or eq5d* or eq 5*):ti,ab
#30.	("minnesota living with heart failure questionnaire" or MLHFQ or MLWHF):ti,ab
#31.	("Veterans Specific Activity Questionnaire" or VSAQ).ti,ab
#32.	(clinic* near/2 (assess* or general or special* or valve or monitor* or examin*)):ti,ab
#33.	MeSH descriptor: [Exercise Tolerance] explode all trees
#34.	MeSH descriptor: [Exercise Test] explode all trees
#35.	((physical* or exercise* or fitness) near/5 (fit* or train* or therap* or activ* or strength or endurance* or exert* or capacity* or tolerance* or test*)):ti,ab
#36.	("stress test" near/2 (cardiac or ECG)):ti,ab
#37.	bruce protocol:ti,ab
#38.	(OR #14-#37)
#39.	#13 and #38

A.22 Health Economics literature search strategy

Health economic evidence was identified by conducting a broad search relating to heart valve disease population in NHS Economic Evaluation Database (NHS EED) – (this ceased to be updated after March 2015) and the Health Technology Assessment database (HTA) – (this ceased to be updated after March 2018) with no date restrictions. NHS EED and HTA databases are hosted by the Centre for Research and Dissemination (CRD). Additional searches were run on Medline and Embase for health economics.

Table 22: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Embase	01 January 2014 – 15 October 2020	Exclusions Health economics studies
Centre for Research and Dissemination (CRD)	HTA - Inception – 31 March 2018 NHSEED - Inception to 31 March 2015	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 stenosis or atresia or insufficienc*)).ti,ab.
7.	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 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.	Economics/
37.	Value of life/
38.	exp "Costs and Cost Analysis"/
39.	exp Economics, Hospital/
40.	exp Economics, Medical/
41.	Economics, Nursing/
42.	Economics, Pharmaceutical/
43.	exp "Fees and Charges"/
44.	exp Budgets/
45.	budget*.ti,ab.
46.	cost*.ti.
47.	(economic* or pharmaco?economic*).ti.
48.	(price* or pricing*).ti,ab.
49.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
50.	(financ* or fee or fees).ti,ab.
51.	(value adj2 (money or monetary)).ti,ab.
52.	or/36-51

53.	35 and 52
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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 stenosis 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.	health economics/
35.	exp economic evaluation/
36.	exp health care cost/
37.	exp fee/
38.	budget/
39.	funding/
40.	budget*.ti,ab.
41.	cost*.ti.
42.	(economic* or pharmaco?economic*).ti.
43.	(price* or pricing*).ti,ab.
44.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
45.	(financ* or fee or fees).ti,ab.
46.	(value adj2 (money or monetary)).ti,ab.
47.	or/34-46
48.	33 and 47

NHS EED and HTA (CRD) search terms

#1.	MeSH DESCRIPTOR Heart Valve Diseases EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Heart Valves EXPLODE ALL TREES
#3.	(((primary or secondary) adj Valv* adj disease*))
#4.	(((valv* or flap* or leaflet*) adj (heart or cardiac) adj (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)))
#5.	((heart or cardiac) 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*))
#6.	(((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*)))
#7.	(((mitral or aortic or tricuspid or pulmon*) adj3 (prolapse or regurgitation or stenosis or atresia or insufficienc*)))
#8.	MeSH DESCRIPTOR Heart Valve Prosthesis EXPLODE ALL TREES
#9.	(((mechanical or artificial or prosthe* or bioprosthe* or biological or tissue) adj (valv* or flap* or leaflet*)))
#10.	(valve-in-valve)
#11.	((transcatheter adj2 (valve or valves)))
#12.	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11

Heart valve disease – search strategy 12 – patient information

This literature search strategy was used for the following review:

- What information and advice should adults with heart valve disease and their family and carers receive?

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

A.23 Clinical search literature search strategy

Searches for patient views were run in Medline (OVID), Embase (OVID), CINAHL, Current Nursing and Allied Health Literature (EBSCO) and PsycINFO (ProQuest). Search filters were applied to the search where appropriate.

Table 23: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	1946 - 14 October 2020	Exclusions
Embase (OVID)	1974 - 14 October 2020	Exclusions
CINAHL, Current Nursing and Allied Health Literature (EBSCO)	Inception – 14 October 2020	
PsycINFO (ProQuest)	Inception – 14 October 2020	

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 stenosis or atresia or insufficienc*)).ti,ab.
7.	exp Heart Murmurs/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter/
11.	editorial/
12.	news/
13.	exp historical article/
14.	Anecdotes as Topic/
15.	comment/

16.	case report/
17.	(letter or comment*).ti.
18.	or/10-17
19.	randomized controlled trial/ or random*.ti,ab.
20.	18 not 19
21.	animals/ not humans/
22.	exp Animals, Laboratory/
23.	exp Animal Experimentation/
24.	exp Models, Animal/
25.	exp Rodentia/
26.	(rat or rats or mouse or mice).ti.
27.	or/20-26
28.	9 not 27
29.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
30.	28 not 29
31.	limit 30 to English language
32.	"patient acceptance of health care"/ or exp patient satisfaction/ or consumer health information/ or needs assessment/
33.	Patient Education as Topic/ or exp patients/ or exp family/ or caregivers/ or patient preference/
34.	((client* or patient* or user* or carer* or consumer* or customer* or parent* or famil* or spouse*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or preference* or focus group*)).ti,ab.
35.	((educat* or learn* or support*) adj3 (service* or information* or material* or virtual* or app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or online or magazine* or mobile phone* or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster? or skype* or smartphone* or smart phone* or social media or social network* or sms or text messag* or twitter or tweet* or video* or web* or wiki* or youtube* or manual* or publication* or literature or computer* or interactive or telephone* or phone*)).ti,ab.
36.	((patient* or carer* or caregiver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or inpatient* or outpatient* or in patient* or out patient*) adj3 (service* or information* or material* or virtual* or app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or online or magazine* or mobile phone* or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster? or skype* or smartphone* or smart phone* or social media or social network* or sms or text messag* or

	twitter or tweet* or video* or web* or wiki* or youtube* or manual* or publication* or literature or computer* or interactive or telephone* or phone*).ti,ab.
37.	or/32-36
38.	31 and 37

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 stenosis or atresia or insufficienc*).ti,ab.
7.	exp heart murmur/
8.	((heart or cardiac) adj murmur*).ti,ab.
9.	or/1-8
10.	letter.pt. or letter/
11.	note.pt.
12.	editorial.pt.
13.	Case report/ or Case study/
14.	(letter or comment*).ti.
15.	or/10-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animal/ not human/
19.	Nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental animal/
22.	Animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice).ti.
25.	or/17-24
26.	9 not 25
27.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
28.	26 not 27
29.	limit 28 to English language
30.	patient attitude/ or patient preference/ or patient satisfaction/ or consumer attitude/ or needs assessment/

31.	*patient information/ or *consumer health information/ or *family/ or *caregivers/
32.	*patient education/
33.	((client* or patient* or user* or carer* or consumer* or customer* or parent* or famil* or spouse*) adj2 (attitud* or priorit* or perception* or preferen* or expectation* or choice* or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or preference* or focus group*)).ti,ab.
34.	((educat* or learn* or support*) adj3 (service* or information* or material* or virtual* or app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or online or magazine* or mobile phone* or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster? or skype* or smartphone* or smart phone* or social media or social network* or sms or text messag* or twitter or tweet* or video* or web* or wiki* or youtube* or manual* or publication* or literature or computer* or interactive or telephone* or phone*)).ti,ab.
35.	((patient* or carer* or caregiver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or inpatient* or outpatient* or in patient* or out patient*) adj3 (service* or information* or material* or virtual* or app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or online or magazine* or mobile phone* or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster? or skype* or smartphone* or smart phone* or social media or social network* or sms or text messag* or twitter or tweet* or video* or web* or wiki* or youtube* or manual* or publication* or literature or computer* or interactive or telephone* or phone*)).ti,ab.
36.	or/30-35
37.	29 and 36

CINAHL (EBSCO) search terms

S1.	(MH "Heart Valve Diseases+")
S2.	(MH "Heart Valves+")
S3.	TX (primary or secondary) AND TX valv* disease*
S4.	TX (valv* or flap* or leaflet*) AND TX (heart or cardiac) AND TX (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)
S5.	TX (mitral or aortic or tricuspid or pulmon*) AND TX (valv* or flap* or leaflet*) AND TX (disease* or disorder* or failure or failed or dysfunction* or insufficien* or repair* or replace* or damage* or leak*)
S6.	TX (mitral or aortic or tricuspid or pulmon) AND TX (prolapse or regurgitation or stenosis or stenoses or atresia or insufficienc*)
S7.	(MM "Heart Murmurs")
S8.	TX (heart or cardiac) AND TX murmur*
S9.	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8
S10.	TX (client* or patient* or user* or carer* or consumer* or customer* or parent* or famil* or spouse*) AND TX (attitud* or priorit* or perception* or preferen* or expectation* or choice*

	or perspective* or view* or satisfact* or inform* or experience or experiences or opinion* or preference* or focus group*)
S11.	TX (educat* or learn* or support*) AND TX (service* or information* or material* or virtual* or app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or online or magazine* or mobile phone* or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster* or skype* or smartphone* or smart phone* or social media or social network* or sms or text messag* or twitter or tweet* or video* or web* or wiki* or youtube* or manual* or publication* or literature or computer* or interactive or telephone* or phone*)
S12.	TX (patient* or carer* or caregiver* or famil* or parent* or father* or mother* or spouse* or wife or wives or husband* or next of kin or significant other* or partner* or guardian* or inpatient* or outpatient* or in patient* or out patient*) AND TX (service* or information* or material* or virtual* or app or apps or blog* or booklet* or brochure* or dvd* or elearn* or e-learn* or email* or e-mail* or e mail* or facebook or facetime or face time or forum* or handout* or hand-out* or hand out* or helpline* or hotline* or internet* or ipad* or iphone* or leaflet* or online or magazine* or mobile phone* or newsletter* or pamphlet* or palm pilot* or personal digital assistant* or pocket pc* or podcast* or poster* or skype* or smartphone* or smart phone* or social media or social network* or sms or text messag* or twitter or tweet* or video* or web* or wiki* or youtube* or manual* or publication* or literature or computer* or interactive or telephone* or phone*)
S13.	S10 OR S11 OR S12
S14.	S9 AND S13

PsycINFO (ProQuest) search terms

1.	((MAINSUBJECT.EXACT("Heart Valves") OR (heart valve disease*) OR ab(primary OR secondary NEAR/2 valv* diseases*) OR ti(primary OR secondary NEAR/2 valv* diseases*) OR ab(((mitral OR aortic OR tricuspid OR pulmon*) NEAR/1 (valv* OR flap* OR leaflet*) NEAR/1 (disease* OR disorder* OR failure OR failed OR dysfunction* OR insufficien* OR repair* OR replace* OR damage* OR leak*)) OR ti(((mitral OR aortic OR tricuspid OR pulmon*) NEAR/1 (valv* OR flap* OR leaflet*) NEAR/1 (disease* OR disorder* OR failure OR failed OR dysfunction* OR insufficien* OR repair* OR replace* OR damage* OR leak*)) OR ab(((valv* OR flap* OR leaflet*) NEAR/1 (heart OR cardiac) nearer (disease* OR disorder* OR failure OR failed OR dysfunction* OR insufficien* OR repair* OR replace* OR damage* OR leak*)) OR ti(((valv* OR flap* OR leaflet*) NEAR/1 (heart OR cardiac) nearer (disease* OR disorder* OR failure OR failed OR dysfunction* OR insufficien* OR repair* OR replace* OR damage* OR leak*)) OR ab(((mitral OR aortic OR tricuspid OR pulmon*) NEAR/3 (prolapse OR regurgitation OR stenosis OR stenoses OR atresia OR insufficienc*))) OR ti(((mitral OR aortic OR tricuspid OR pulmon*) NEAR/3 (prolapse OR regurgitation OR stenosis OR stenoses OR atresia OR insufficienc*)))) OR (MJMAINSUBJECT.EXACT("Heart Disorders") OR ti(((heart OR cardiac) NEAR/1 murmur*)) OR ab(((heart OR cardiac) NEAR/1 murmur*))) AND (ab(patient* OR carer* OR caregiver* OR famil* OR parent* OR father* OR mother* OR spouse* OR wife OR wives OR husband* OR next of kin OR significant other* OR partner* OR guardian* OR inpatient* OR outpatient* OR in patient* OR out patient*) OR ti(patient* OR carer* OR caregiver* OR famil* OR parent* OR father* OR mother* OR spouse* OR wife OR wives OR husband* OR next of kin OR significant other* OR partner* OR guardian* OR inpatient* OR outpatient* OR in patient* OR out patient*))
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Heart valve disease – health economic modelling search strategy

This literature search strategy was used for health economic modelling report

The literature searches for this review are detailed below and complied with the methodology outlined in Developing NICE guidelines: the manual.¹

For more information, please see the Methodology review published as part of the accompanying documents for this guideline.

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 24: Database date parameters and filters used

Database	Dates searched	Search filter used
Medline (OVID)	2010 – 15 October 2020	Exclusions Observational studies
Embase (OVID)	2010 – 15 October 2020	Exclusions Observational studies

Medline (Ovid) search terms

1.	exp Aortic valve stenosis/
2.	(aortic adj3 (stenos?s or atresia)).ti,ab.
3.	or/1-2
4.	letter/
5.	editorial/
6.	news/
7.	exp historical article/
8.	Anecdotes as Topic/
9.	comment/
10.	case report/
11.	(letter or comment*).ti.
12.	or/4-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animals/ not humans/
16.	exp Animals, Laboratory/
17.	exp Animal Experimentation/

18.	exp Models, Animal/
19.	exp Rodentia/
20.	(rat or rats or mouse or mice).ti.
21.	or/14-20
22.	3 not 21
23.	limit 22 to English language
24.	(exp child/ or exp pediatrics/ or exp infant/) not (exp adolescent/ or exp adult/ or exp middle age/ or exp aged/)
25.	23 not 24
26.	Epidemiologic studies/
27.	Observational study/
28.	exp Cohort studies/
29.	(cohort adj (study or studies or analys* or data)).ti,ab.
30.	((follow up or observational or uncontrolled or non random#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
31.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
32.	Controlled Before-After Studies/
33.	Historically Controlled Study/
34.	Interrupted Time Series Analysis/
35.	(before adj2 after adj2 (study or studies or data)).ti,ab.
36.	exp case control study/
37.	case control*.ti,ab.
38.	Cross-sectional studies/
39.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
40.	or/26-39
41.	25 and 40
42.	Transcatheter Aortic Valve Replacement/
43.	(TAVR or TAVI).ti,ab.
44.	((transcatheter or surg* or intervention*) adj3 (repair* or replac* or implant*)).ti,ab.
45.	(commissurotomy or valvulotomy or valvotomy or valvuloplasty or valvoplasty or annuloplasty).ti,ab.
46.	(sternotomy or ministernotomy or mini-sternotomy or thoracotomy or port access or non-sternotomy).ti,ab.
47.	Heart Valve Prosthesis Implantation/
48.	exp aortic valve stenosis/su
49.	Minimally Invasive Surgical Procedures/
50.	or/42-49
51.	41 and 50

Embase (Ovid) search terms

Heart valve disease

1.	exp aortic stenosis/
2.	(aortic adj3 (stenos?s or atresia)).ti,ab.
3.	1 or 2
4.	letter.pt. or letter/
5.	note.pt.
6.	editorial.pt.
7.	Case report/ or Case study/
8.	(letter or comment*).ti.
9.	or/4-8
10.	randomized controlled trial/ or random*.ti,ab.
11.	9 not 10
12.	animal/ not human/
13.	Nonhuman/
14.	exp Animal Experiment/
15.	exp Experimental animal/
16.	Animal model/
17.	exp Rodent/
18.	(rat or rats or mouse or mice).ti.
19.	or/11-18
20.	3 not 19
21.	limit 20 to English language
22.	(exp child/ or exp pediatrics/) not (exp adult/ or exp adolescent/)
23.	21 not 22
24.	Clinical study/
25.	Observational study/
26.	family study/
27.	longitudinal study/
28.	retrospective study/
29.	prospective study/
30.	cohort analysis/
31.	follow-up/
32.	cohort*.ti,ab.
33.	31 and 32
34.	(cohort adj (study or studies or analys* or data)).ti,ab.
35.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
36.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
37.	(before adj2 after adj2 (study or studies or data)).ti,ab.

38.	exp case control study/
39.	case control*.ti,ab.
40.	cross-sectional study/
41.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
42.	or/24-30,33-41
43.	23 and 42
44.	transcatheter aortic valve implantation/
45.	(TAVR or TAVI).ti,ab.
46.	((transcatheter or surg* or intervention*) adj3 (repair* or replac* or implant*)).ti,ab.
47.	(commissurotomy or valvulotomy or valvotomy or valvuloplasty or valvoplasty or annuloplasty).ti,ab.
48.	(sternotomy or ministernotomy or mini-sternotomy or thoracotomy or port access or non-sternotomy).ti,ab.
49.	minimally invasive surgery/
50.	aortic valve stenosis/su [Surgery]
51.	exp aortic valve prosthesis/
52.	aortic valve replacement/
53.	or/44-52
54.	43 and 53

1. National Institute for Health and Care Excellence. Developing NICE guidelines: the manual [updated 2020]. London. National Institute for Health and Care Excellence, 2014. Available from:
<http://www.nice.org.uk/article/PMG20/chapter/1%20Introduction%20and%20overview>