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2 **NATIONAL INSTITUTE FOR HEALTH AND CARE**
3 **EXCELLENCE**

4 # Guideline

5 # Heart valve disease presenting in adults:
6 # investigation and management

7 ## Draft for consultation, March 2021

This guideline covers investigating and managing heart valve disease presenting in adults. It aims to improve diagnosis and raise awareness of the indications for intervention. Timely and appropriate intervention benefits quality of life and survival for people with heart valve disease.

This guideline will update and replace the recommendations on valve surgery and percutaneous intervention in the NICE guideline on acute heart failure (published October 2014).

Who is it for?

- Healthcare professionals
- Commissioners and providers
- People with heart valve disease, their families and carers

What does it include?

This draft guideline contains:

- the draft recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the recommendations and how they might affect practice
- the guideline context.

Information about how the guideline was developed is on the guideline's webpage. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

The recommendations in this guideline were partially developed before the COVID-19 pandemic. Please tell us if there are any particular issues relating to COVID-19 that we should take into account when finalising the guideline for publication.

1

2

3

Contents

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Referral for echocardiography and specialist assessment

Referral for echocardiography

1.1.1 Consider an echocardiogram for adults with a murmur and no other signs or symptoms if valve disease is suspected (based on the nature of the murmur, family history, age or medical history).

1.1.2 Offer an echocardiogram to adults with a murmur if valve disease is suspected (based on the nature of the murmur, family history, age or medical history) and they have:

- signs (such as peripheral oedema) or symptoms (such as angina or breathlessness) or an abnormal ECG, or
- an ejection systolic murmur with a reduced second heart sound but no other signs or symptoms.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on referral for echocardiography.

Full details of the evidence and the committee's discussion are in evidence review A: Symptoms or signs indicating referral for echocardiography or specialist assessment.

Referral for urgent specialist assessment or urgent echocardiography

1.1.3 If valve disease is suspected (based on the nature of the murmur, family history, age or medical history):

- Offer urgent (ideally within 4 weeks) specialist assessment or an urgent echocardiogram to adults with a systolic murmur and exertional syncope.
- Consider urgent specialist assessment for adults with a murmur and severe symptoms (angina or breathlessness on minimal exertion or at rest).

1.1.4 For guidance on referral and assessment for adults with murmur and non-exertional syncope, follow the recommendations in the NICE guideline on transient loss of consciousness ('blackouts') in over 16s.

1.1.5 For guidance on referral and assessment for adults with breathlessness but no murmur, follow the recommendations in the NICE guideline on chronic heart failure in adults.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on referral for urgent specialist assessment or urgent echocardiography.

Full details of the evidence and the committee's discussion are in evidence review A: Symptoms or signs indicating referral for echocardiography or specialist assessment.

Referral to a specialist following echocardiography

1.1.6 Advise adults with mild valve disease that this seldom causes symptoms, but they should seek advice from a healthcare professional if they develop symptoms.

1.1.7 Offer specialist assessment to:

- adults with moderate or severe valve disease of any type

- adults with bicuspid aortic valve disease of any severity (including mild valve disease)
- adults with mitral valve prolapse with documented ventricular arrhythmia.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on referral to a specialist following echocardiography.

Full details of the evidence and the committee's discussion are in evidence review B: Referral to a specialist following echocardiography.

Referral and specialist assessment for pregnant women and women considering pregnancy

These recommendations are for cardiologists.

1.1.8 Be aware that most women with valve disease can have a pregnancy without complications.

1.1.9 Consider seeking specialist advice on the choice of replacement valve for women of childbearing potential.

1.1.10 Refer pregnant women or women who are considering a pregnancy to a cardiologist with expertise in the care of pregnant women, if they have any of the following:

- moderate or severe valve disease
- bicuspid aortic valve disease of any severity (including mild disease) and associated aortopathy
- a mechanical prosthetic valve.

Refer irrespective of whether they have symptoms.

1.1.11 For guidance on intrapartum care, follow the recommendations on heart disease in the NICE guideline on intrapartum care for women with existing medical conditions or obstetric complications and their babies.

For a short explanation of why the committee made these recommendations and how they might affect practice, see the rationale and impact section on referral and specialist assessment for pregnant women and women considering a pregnancy.

Full details of the evidence and the committee's discussion are in evidence review A: Symptoms or signs indicating referral for echocardiography or specialist assessment.

1.2 Pharmacological management

To improve prognosis

1.2.1 For guidance on statins, follow the recommendations in the NICE guideline on cardiovascular disease: risk assessment and reduction, including lipid modification.

For a short explanation of why the committee made this recommendation and how it might affect practice, see the rationale and impact section on pharmacological management to improve prognosis.

Full details of the evidence and the committee's discussion are in evidence review C: Pharmacological management of heart valve disease.

To manage heart failure in valve disease

1.2.2 Consider a beta-blocker for adults with moderate to severe mitral stenosis and heart failure.

For a short explanation of why the committee made this recommendation and how it might affect practice, see rationale and impact section on pharmacological management of heart failure in heart valve disease.

Full details of the evidence and the committee's discussion are in evidence review C: Pharmacological management of heart valve disease.

1.3 Indications for interventions

1.3.1 Offer an intervention to adults with symptomatic severe heart valve disease.

> For a short explanation of why the committee made the recommendation, see the rationale and impact section on indications for interventions.
>
> Full details of the evidence and the committee's discussion are in evidence review H: Interventions

Aortic stenosis

1.3.2 Consider referring adults with asymptomatic severe aortic stenosis for surgery, if suitable, if they have any of the following:

- Vmax (peak aortic jet velocity) more than 5 m/s on echocardiography
- aortic valve area less than 0.6 cm^2 on echocardiography
- LVEF (left ventricular ejection fraction) less than 60% on echocardiography
- BNP/NT-proBNP level more than twice the upper limit of normal
- symptoms unmasked on exercise testing.

1.3.3 Consider referring adults with symptomatic low-flow low-gradient aortic stenosis with LVEF less than 50% for intervention if they have all of the following:

- mean gradient across the aortic valve less than 40 mmHg on echocardiography
- a valve area less than 1.0 cm^2, which does not increase on dobutamine stress echocardiography.

1.3.4 If the severity of symptomatic aortic stenosis is uncertain, consider measuring aortic valve calcium score on cardiac CT to assess the need for intervention.

1.3.5 Take into account the degree and distribution of calcium in the aortic valve when deciding if transcatheter aortic valve intervention (TAVI) is appropriate for adults with severe aortic stenosis.

1.3.6 Offer enhanced follow up (for example, more frequent reviews) and further assessment (for example, stress echocardiography) to monitor the need for intervention if midwall fibrosis is detected on cardiac MRI in adults with severe aortic stenosis.

For a short explanation of why the committee made the recommendations, see the rationale and impact section on indications for interventions for adults with aortic stenosis.

Full details of the evidence and the committee's discussion are in evidence review D: Echocardiography to determine the need for intervention, evidence review E: Stress testing and stress echocardiography to determine the need for intervention, and evidence review F: Cardiac MRI and cardiac CT to determine the need for intervention.

Aortic regurgitation

1.3.7 Consider referring adults with asymptomatic severe aortic regurgitation for surgery, if suitable, if they have any of the following:

- LVEF less than 55% on echocardiography
- ESDI (end-systolic diameter index) more than 2.4 cm/m^2 on echocardiography.

For a short explanation of why the committee made the recommendations, see the rationale and impact section on indications for interventions for adults with aortic regurgitation.

Full details of the evidence and the committee's discussion are in evidence review D: Echocardiography to determine the need for intervention.

Mitral regurgitation

1.3.8 Consider referring adults with asymptomatic severe mitral regurgitation for surgery, if suitable, if they have any of the following:

- LVEF less than 60% on echocardiography
- ESDI more than 2.2 cm/m^2 on echocardiography
- an increase of systolic pulmonary artery pressure to more than 60 mgHg on exercise testing.

Take into account the suitability of the valve for repair and the presence of atrial fibrillation, or systolic pulmonary artery pressure more than 50 mmHg on echocardiography at rest, when making decisions about referral for surgery.

For a short explanation of why the committee made the recommendations, see the rationale and impact section on indications for intervention for adults with mitral regurgitation.

Full details of the evidence and the committee's discussion are in evidence review D: Echocardiography to determine the need for intervention and evidence review E: Stress testing and stress echocardiography to determine the need for intervention.

1.4 Monitoring where there is no current need for intervention

1.4.1 Offer clinical review every 6 to 12 months, with an echocardiogram, to adults with asymptomatic severe valve disease if an intervention is suitable but not currently needed. Base the frequency of the review, within the 6- to 12-month timeframe, on echocardiography findings and discussion with the patient.

For a short explanation of why the committee made the recommendation and how it might affect practice, see the rationale and impact section on monitoring where there is no current need for intervention.

Full details of the evidence and the committee's discussion are in evidence review G: Monitoring where there is no current need for intervention.

1.5 Interventions

See the recommendations on indications for interventions.

Decisions about interventions

1.5.1 Discuss the possible benefits and risks of interventions with adults who have an indication for valve intervention. Include in the discussion:

- the benefits to quality of life (both in the short and long term)
- valve durability
- the risks associated with the procedure
- the type of access for surgery (median sternotomy or minimally invasive surgery)
- the possible need for other cardiac procedures in the future.

Follow the recommendations on shared decision making in the NICE guideline on patient experience in adult NHS services and base decisions on type of intervention on patient characteristics and preferences.

1.5.2 When surgery is agreed, base the decision on the type of surgery (median sternotomy or minimally invasive surgery) on patient characteristics and patient preferences. If minimally invasive surgery is the agreed option and is not available locally, refer the person to another centre.

For a short explanation of why the committee made the recommendations and how they might affect practice, see the rationale and impact section for decisions about interventions.

Full details of the evidence and the committee's discussion are in evidence review H: Interventions.

Aortic valve disease

1.5.3 Offer surgery, if suitable (by median sternotomy or minimally invasive surgery), as first-line intervention for adults with severe aortic stenosis, aortic regurgitation or mixed aortic valve disease.

1.5.4 Offer TAVI, if suitable, to adults with non-bicuspid severe aortic stenosis, if surgery is unsuitable.

1.5.5 See NHS England's clinical commissioning policy on transcatheter aortic valve implantation for aortic stenosis and the recommendations on using TAVI in the NICE interventional procedures guidance on transcatheter aortic valve implantation for aortic stenosis, including entering the details of all people undergoing TAVI into the UK Central Cardiac Audit database.

For a short explanation of why the committee made the recommendations and how they might affect practice, see the rationale and impact section on interventions for aortic valve disease.

Full details of the evidence and the committee's discussion are in evidence review H: Interventions.

Mitral stenosis

1.5.6 Consider transcatheter valvotomy for adults with rheumatic severe mitral stenosis, if the valve is suitable for this procedure.

1.5.7 Offer surgical mitral valve replacement to adults with rheumatic severe mitral stenosis if transcatheter valvotomy is unsuitable.

For a short explanation of why the committee made the recommendations and how they might affect practice, see the rationale and impact section on interventions for mitral stenosis.

Full details of the evidence and the committee's discussion are in evidence review H: Interventions.

Mitral regurgitation

Primary mitral regurgitation

1.5.8 Offer surgical mitral valve repair (by median sternotomy or minimally invasive surgery) to adults with severe primary mitral regurgitation and an indication for repair, if surgery is suitable.

1.5.9 Offer surgical mitral valve replacement (by median sternotomy or minimally invasive surgery) to adults with severe primary mitral regurgitation and an indication for surgery, if the valve is not suitable for repair and surgery is suitable.

1.5.10 Consider transcatheter edge-to-edge repair, if suitable, for adults with severe primary mitral regurgitation and symptoms, if surgery is unsuitable.

See NHS England's clinical commissioning policy on percutaneous mitral valve leaflet repair for primary degenerative mitral regurgitation in adults and the NICE interventional procedures guidance on percutaneous mitral valve leaflet repair for mitral regurgitation.

Secondary mitral regurgitation

1.5.11 Consider surgical mitral valve repair (by median sternotomy or minimally invasive surgery) for adults with severe secondary mitral regurgitation and an indication for surgery, if surgery is suitable.

1.5.12 Consider surgical mitral valve replacement (by median sternotomy or minimally invasive surgery) for adults with severe secondary mitral

regurgitation and an indication for surgery, if the valve is not suitable for repair and surgery is suitable.

1.5.13 Offer medical management in preference to transcatheter mitral edge-to-edge repair to adults with heart failure and severe secondary mitral regurgitation, if surgery is unsuitable.

> For a short explanation of why the committee made the recommendations and how they might affect practice, see the rationale and impact section on interventions for mitral regurgitation.
>
> Full details of the evidence and the committee's discussion are in evidence review H: Interventions.

1.6 Repeat intervention

1.6.1 Consider transcatheter or redo surgical intervention for adults with severe aortic degeneration of a biological prosthetic valve and symptoms. Take into account the following factors to inform a shared decision about choice of intervention:

- the short and long-term benefits
- type of valve dysfunction and prosthesis
- the risks associated with the procedure
- the possible need for other cardiac procedures in the future.

> For a short explanation of why the committee made the recommendation and how it might affect practice, see rationale and impact section on repeat intervention.
>
> Full details of the evidence and the committee's discussion are in evidence review I: Repeat intervention.

1.7 Anticoagulation and antiplatelet therapy

1.7.1 Do not offer anticoagulation after surgical biological valve replacement unless there are other indications for anticoagulation.

1.7.2 Consider aspirin, or clopidogrel if aspirin is not tolerated, after TAVI.

1.7.3 If people have other indications for anticoagulation or antiplatelet therapy, follow the recommendations in the NICE guidelines on atrial fibrillation and acute coronary syndromes

> For a short explanation of why the committee made the recommendations and how they might affect practice, see the rationale and impact section on anticoagulation and antiplatelet therapy.
>
> Full details of the evidence and the committee's discussion are in evidence review J: Antithrombotic therapy.

1.8 Monitoring after an intervention

1.8.1 Base decisions on the frequency and type of monitoring for adults who have had an intervention (valve repair or replacement) for valve disease on:

- durability of the prosthetic valve or durability of the repair
- the presence of another condition, including other heart disease
- residual valve abnormality or consequences of the procedure, for example, paravalvular leak
- concerns about abnormal function of the prosthetic valve
- the patient's wishes.

Advise people and their family members or carers (as appropriate) to seek advice if the heart condition deteriorates.

For a short explanation of why the committee made the recommendations and how they might affect practice, see the rationale and impact section on monitoring after an intervention.

Full details of the evidence and the committee's discussion are in evidence review K: Monitoring after an intervention.

1.9 Information and advice

1.9.1 Follow the recommendations in the NICE guideline on patient experience in adult NHS services on:

- involvement of family members and carers
- communication
- information
- tailoring healthcare services
- shared decision making

1.9.2 Consider providing a point of contact for accessing specialist advice between appointments.

1.9.3 Consider providing psychological support for people receiving a diagnosis of valve disease, whether or not they have symptoms.

1.9.4 Provide information and advice, as appropriate, to adults with valve disease about:

- the expected progression and prognosis of their condition, including the likely length of an asymptomatic stage
- any need for intervention, including the type of intervention
- pregnancy, if appropriate
- the possible effects of other conditions on long-term outcomes
- rehabilitation and long-term outcomes
- palliative care, if appropriate, including how to access this.

1.9.5 Provide information and support to young adults regarding transition from paediatric to adult services, in line with the NICE guideline on transition from children's to adults' services for young people using health or social care services.

For a short explanation of why the committee made the recommendations and advice and how they might affect practice, see the rationale and impact section on information and advice.

Full details of the evidence and the committee's discussion are in evidence review L: Information and advice.

Terms used in this guideline

This section defines terms that have been used in a particular way for this guideline.

Degenerated

Degenerated covers progressive degeneration and does not include failure of the valve due to endocarditis or thrombosis.

Severe valve disease

Severity of valve disease is defined in line with the British Society of Echocardiography guidelines on the British Heart Foundation's website.

Suitability for TAVI

Suitability for TAVI depends on:

- an appropriate access for inserting the TAVI catheter
- the morphology of the valve, aortic root and ascending aorta
- the degree and distribution of calcium in the aortic valve.

Suitability for transcatheter edge-to-edge repair

Suitability for transcatheter edge-to-edge repair depends on:

- the morphology of the valve
- the feasibility of using transoesophageal echocardiography to guide the procedure

- fitness for general anaesthesia.

Recommendations for research

The guideline committee has made the following recommendations for research.

Key recommendations for research

1 Monitoring where there is no current need for intervention

What is the most clinically and cost-effective monitoring (type and frequency of test) for adults with asymptomatic mild or moderate heart valve disease (aortic stenosis, aortic regurgitation, mitral stenosis, mitral regurgitation and tricuspid regurgitation) and no current need for intervention?

> For a short explanation of why the committee made the research recommendation see the rationale and impact section on monitoring where there is no current need for intervention.
>
> Full details of the evidence and the committee's discussion are in evidence review G: Monitoring where there is no current need for intervention.

2 Interventions for tricuspid regurgitation

What is the most clinically and cost-effective management strategy for adults with tricuspid regurgitation?

> For a short explanation of why the committee made the research recommendation see the rationale section on interventions for tricuspid regurgitation.
>
> Full details of the evidence and the committee's discussion are in evidence review H: Interventions.

3 Interventions for a failed valve

What is the clinical and cost effectiveness of transcatheter intervention compared with surgical redo intervention for adults with failing biological prosthetic tricuspid valves or failing repaired native tricuspid valves when either procedure is suitable?

For a short explanation of why the committee made the research recommendation see the rationale and impact section on repeat intervention.

Full details of the evidence and the committee's discussion are in evidence review I: Repeat interventions.

4 Monitoring after an intervention

What is the most clinically and cost-effective timing, nature and frequency of follow up for different types of valve interventions, including repair and replacement with tissue or mechanical valves?

For a short explanation of why the committee made the research recommendation see rationale and impact section on monitoring after an intervention.

Full details of the evidence and the committee's discussion are in evidence review K: Monitoring after an intervention.

5 Information and advice

What are the information and advice needs of all adult age groups with heart valve disease of all severities and stages?

For a short explanation of why the committee made the research recommendation see the rationale and impact section on information and advice

Full details of the evidence and the committee's discussion are in evidence review L: Information and advice.

Other recommendations for research

Indications for interventions – stress testing/echocardiography

What is the prognostic value of severe mitral regurgitation unmasked on exercise echocardiography in adults with symptomatic non-severe mitral regurgitation at rest?

What is the prognostic value of parameters observed on exercise stress testing and exercise stress echocardiography in asymptomatic severe aortic regurgitation?

Indications for interventions – CT/MRI

In adults with aortic or primary mitral regurgitation in whom the need for intervention is unclear after echocardiography, what is the prognostic value and cost effectiveness of cardiac MRI to assess the severity of valvular regurgitation?

In adults with aortic or mitral regurgitation in whom the need for intervention is unclear after echocardiography, what is the prognostic value and cost effectiveness of left ventricular ejection fraction measured on cardiac MRI to assess the need for intervention?

In adults with asymptomatic severe aortic stenosis what is the prognostic value and cost effectiveness of left ventricular ejection fraction measured on cardiac MRI to assess the need for intervention?

In adults with asymptomatic severe tricuspid regurgitation what is the prognostic value and cost effectiveness of cardiac MRI for assessment of the right ventricle to assess the need for intervention?

Indications for interventions – global longitudinal strain

In adults with severe heart valve disease what is the prognostic value and cost effectiveness of global longitudinal strain to assess the need for intervention?

In adults with asymptomatic, severe aortic regurgitation or mitral regurgitation what is the prognostic value and cost effectiveness of BNP to assess the need for intervention?

Pharmacological management for adults with heart valve disease

What is the clinical and cost effectiveness of ACE inhibitors, beta-blockers and diuretics for adults with severe aortic stenosis?

What is the clinical and cost effectiveness of ACE inhibitors, angiotensin II receptor antagonists, beta-blockers and calcium channel blockers, including compared with placebo, for adults with aortic regurgitation?

What is the clinical and cost effectiveness of ACE inhibitors, beta-blockers and diuretics for adults with primary severe mitral regurgitation?

What is the clinical and cost effectiveness of beta-blockers for adults over 75 years with non-rheumatic/calcific mitral stenosis, in both sinus rhythm and atrial fibrillation?

What is the clinical and cost effectiveness of pharmacological management of heart failure for adults with heart failure and severe aortic stenosis, severe aortic regurgitation or severe mitral regurgitation?

Monitoring where there is no current need for intervention

What is the most clinically and cost-effective monitoring strategy (type and frequency of test) for adults with asymptomatic severe heart valve disease (aortic regurgitation, mitral stenosis, mitral regurgitation or tricuspid regurgitation) and no current indication for intervention?

What is the most clinically and cost-effective monitoring strategy (type and frequency of test) for adults with symptomatic moderate heart valve disease (aortic stenosis, aortic regurgitation, mitral stenosis, mitral regurgitation and tricuspid regurgitation) and no current indication for intervention?

Interventions

What is the most clinically and cost-effective management strategy for adults with calcific mitral stenosis and an indication for intervention?

Anticoagulation and antiplatelet therapy

What is the clinical and cost effectiveness of single or dual antiplatelet therapies or anticoagulants compared with placebo following transcatheter or surgical valve replacement (implantation) with biological prosthesis and following valve repair?

In adults with biological valve replacement, what effect does anticoagulation or antiplatelet therapy have on long-term valve function and outcomes?

Repeat interventions

What is the clinical and cost effectiveness of transcatheter intervention compared with surgical redo intervention for adults with failing biological prosthetic aortic valves when either procedure is suitable?

What is the clinical and cost effectiveness of transcatheter intervention compared with surgical redo intervention for adults with failing biological prosthetic mitral valves when either procedure is suitable?

Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice.

Referral for echocardiography

Recommendations 1.1.1 to 1.1.2

Why the committee made the recommendations

Murmur alone

Limited evidence showed that murmur is an indicator of valve disease. But the evidence also showed that a substantial proportion of people with a murmur do not have valve disease confirmed by a reference test. The committee agreed that 'innocent' murmurs can occur, particularly during the teenage/young adult years and pregnancy. These are difficult to differentiate from pathological murmurs by clinical examination alone. The evidence was not strong enough to recommend that

everyone with a murmur should be referred for echocardiography. The committee agreed that this would be a change in practice, would increase pressure on echocardiography services and would offer uncertain benefit. However, when the nature of the murmur, family history, age or medical history suggest possible valve disease, echocardiography should be considered to establish a diagnosis.

Systolic murmur with a reduced second heart sound

Evidence suggested that the presence of a systolic heart murmur plus a reduced second heart sound had good specificity for aortic stenosis confirmed by echocardiography. The recommendation specifies ejection systolic murmur as this combined with a reduced second heart sound is a classic indicator of aortic stenosis and is most often present in severe aortic stenosis. Although this was based on only a few studies, the committee agreed that people with these features should be referred for echocardiography. Due to the limited evidence identified, this recommendation was limited to those in whom heart valve disease was considered to be a possible explanation of these signs based on the nature of the murmur, family history, age or medical history.

Murmur with other symptoms or signs

Studies showed that echocardiography detected valve disease in a higher proportion of people with murmur plus other signs and symptoms (abnormal ECG, angina, breathlessness, peripheral oedema) than in people with murmur alone. That is, murmur plus other signs or symptoms had a higher specificity for echocardiography confirmed valve disease. Again, this was based on a few studies only so the committee agreed that the nature of the murmur, family history, age or medical history should also suggest valve disease as a possibility.

How the recommendations might affect practice

The recommendations reflect current practice.

Return to recommendations

Referral for urgent specialist assessment or urgent echocardiography

Recommendations 1.1.3 to 1.1.5

Why the committee made the recommendations

Evidence showed that more cases of severe valve disease were picked up when a murmur plus other signs or symptoms were present. The committee agreed that mild and moderate valve disease does not usually present with these symptoms and using these criteria for referral would not result in unnecessary referral for urgent specialist assessment or echocardiography in most cases.

People with exertional syncope and a systolic murmur need an urgent diagnosis because if exertional syncope is caused by aortic stenosis there is a high risk of a poor outcome. The diagnosis needs to be made quickly to allow appropriate management, which would likely include intervention if severe aortic stenosis is confirmed. Depending on local availability, an echocardiogram may be faster than direct specialist referral, so the committee agreed to recommend either for this group. The committee agreed that the assessment or echocardiogram should be done within 4 weeks.

For people with severe symptoms (New York Heart Association classification III to IV or perceived by the person as severe) and a murmur, but without exertional syncope, the committee agreed that urgent specialist assessment, which would include echocardiography, should be considered.

How the recommendations might affect practice

The recommendations reflect current practice.

Return to recommendations

Referral to a specialist following echocardiography

Recommendations 1.1.6 to 1.1.7

Why the committee made the recommendations

Across the included studies, moderate and/or severe valve disease was consistently associated with more adverse outcomes than 'mild' or 'mild and moderate' valve disease. Despite limited evidence for each specific type of valve disease, the committee agreed that specialist referral should be offered to those with moderate or severe disease and this is consistent with current practice.

The evidence could not be used to recommend that people with mild valve disease should never be referred to a specialist, because outcomes were not compared with those without valve disease. However, the committee stressed that mild valve disease is very common in people over 70, seldom causes symptoms and does not progress in most cases. The committee recommended that people with bicuspid aortic valve disease of any severity (including mild disease) should be offered specialist referral as it differs in terms of its progression to other types of valve disease, can be associated with aortopathy and in practice is usually referred. A similar recommendation was made for those with mitral valve prolapse and documented ventricular arrhythmia because this confers an increased risk of sudden death.

How the recommendations might affect practice

The committee agreed that it is current practice for everyone with moderate or severe valve disease to be referred to a specialist, regardless of the type of disease and whether it is primary or secondary. The recommendation on moderate and severe valve disease would therefore not lead to a change in practice.

For mild valve disease, there is currently variation in specialist referral, with some unnecessary referrals being made. Although the recommendation does not preclude referral for this group, it may reassure individuals with mild valve disease and it may reduce the number of unnecessary referrals and be cost saving. The recommendations covering bicuspid aortic valve disease and mitral valve prolapse with documented ventricular arrhythmia were considered to reflect current practice.

Return to recommendations

Referral and specialist assessment for pregnant women and women considering pregnancy

Recommendations 1.1.8 to 1.1.11

Why the committee made the recommendations

The committee recognised that the proportion of pregnant women with valve disease is small compared with the number of women with valve disease who may be considering pregnancy. These women need to carefully consider the impact of treatment on any future pregnancy and should be given advice before making a treatment decision. This should include consideration of the type of valve they receive if surgery is performed and it may be appropriate for their clinician to seek specialist advice from a cardiologist with expertise in the care of pregnant women, to inform this decision. The committee noted that healthcare professionals without specialist expertise may inappropriately advise women against becoming pregnant. They agreed that a woman with valve disease who may wish to become pregnant or who is pregnant should be referred to a cardiologist with specialist expertise. The committee highlighted that only women with moderate or severe disease on echocardiography, bicuspid aortic valve disease with associated aortopathy or mechanical prosthetic valves need referral. Women with mild disease, for example, aortic regurgitation or mitral valve prolapse without regurgitation, do not need a referral. The committee acknowledged that an ejection systolic flow murmur is present in most pregnant women and is not a cause for concern. They also noted that there is no official subspecialty or national accreditation for cardiologists with a specialist interest in pregnancy.

How the recommendations might affect practice

The committee agreed that the recommendations reflect current practice and would not require additional resource.

Return to recommendations

Pharmacological management to improve prognosis

Recommendation 1.2.1

Why the committee made the recommendations

There was no evidence that pharmacological management can slow the progression of heart valve disease, there was only evidence that statins improve prognosis in aortic stenosis. The evidence showed that statins reduced cardiac mortality compared with placebo for adults with aortic stenosis. The committee agreed that this benefit is due to an improvement in overall cardiovascular health rather than a direct effect on the aortic stenosis and agreed to refer to the recommendations on statins in the NICE guideline on cardiovascular disease: risk assessment and reduction, including lipid modification.

There was not enough evidence for the committee to make recommendations on pharmacological management of other conditions (for example, systemic hypertension) when heart valve disease coexists.

The committee decided to make research recommendations to inform the pharmacological management with a series of commonly used drugs (ACE inhibitors, angiotensin II receptor antagonists, beta-blockers, calcium channel blockers, diuretics) in adults with aortic stenosis, aortic regurgitation or mitral regurgitation. These are important areas of uncertainty in current UK clinical practice.

How the recommendations might affect practice

The recommendation reflects current practice so the committee agreed there is unlikely to be a significant resource impact.

Return to recommendations

Pharmacological management of heart failure in heart valve disease

Recommendations 1.2.2

Why the committee made the recommendation

Some evidence showed that beta-blockers reduced hospital stay for heart failure and increased exercise tolerance for adults with mitral stenosis compared with usual care. As with all other indications for beta-blockers, some adults with mitral stenosis stopped beta-blockers because of adverse events (weakness, dizziness and

shortness of breath), but the committee agreed that in their experience these drugs offer overall benefit for people in the UK with moderate to severe mitral stenosis and heart failure.

The studies included younger people than in UK clinical practice, with mitral stenosis often being due to rheumatic fever. Patients also had atrial fibrillation. The committee agreed to make a research recommendation to inform future use of beta-blockers for older adults with non-rheumatic calcific mitral stenosis, more common currently in the UK than rheumatic mitral stenosis, in sinus rhythm or atrial fibrillation.

There was not enough evidence for the committee to make recommendations on the use of other drugs for the management of heart failure in heart valve disease or for beta-blockers in other types of valve disease. They agreed to make a research recommendation on the pharmacological management of heart failure in adults with severe aortic stenosis, aortic regurgitation and mitral regurgitation.

How the recommendation might affect practice

The recommendation reflects current practice so the committee agreed there is unlikely to be a significant resource impact.

Return to recommendations

Indications for interventions

Recommendation 1.3.1

Why the committee made the recommendation

Severe symptomatic heart valve disease has a poor prognosis and there is no treatment for the symptoms other than an intervention on the valve. Because of this, the committee recommended that an intervention should be offered to this group. The evidence to support this recommendation is discussed under the different types of valve disease in the section on intervention.

How the recommendation might affect practice

The recommendation reflects current practice.

Return to the recommendations

Indications for interventions for adults with aortic stenosis

Recommendations 1.3.2 to 1.3.6

Why the committee made the recommendations

Echocardiography

A peak aortic jet velocity more than 5 m/s was a risk factor for increased mortality (all-cause and cardiac or cardiovascular) and sudden death in people with asymptomatic severe aortic stenosis who had not had a valve intervention. An aortic valve area less than 0.6 cm^2 was also associated with increased all-cause mortality, both before and after valve intervention in adults with asymptomatic severe aortic stenosis.

A left ventricular ejection fraction (LVEF) less than 60% was the best marker of early myocardial decompensation, being linked to increased mortality (all-cause and cardiovascular), sudden death and hospital admission for heart failure in adults with asymptomatic severe aortic stenosis.

Raised BNP, particularly when 2 to 3 times the normal level, was a risk factor for all-cause mortality, before and after valve intervention, for people with asymptomatic severe aortic stenosis and a preserved ejection fraction. The committee agreed that this would also apply to NT pro-BNP which is more widely used currently in the UK than BNP.

Some of these indicators were broadly in line with current practice and the experience of the committee. In addition, the evidence for increased mortality was strong, including for BNP. Therefore the committee agreed that these indicators of poorer prognosis should prompt a discussion about the possible need for referral for intervention in people with asymptomatic severe aortic stenosis. Recommendations were limited to considering referral because the evidence was low to very low quality.

There was some evidence of increased mortality in people with asymptomatic severe aortic stenosis and a global longitudinal strain less than 14.7% or 15%, even when ejection fraction was preserved. However, there is some concern about

reproducibility of measurements. The committee agreed that further research in this area would help to inform future guidance and they made a research recommendation.

Stress testing and stress echocardiography

The committee agreed that there was enough evidence that symptoms unmasked during exercise testing predict a poor outcome in those with asymptomatic severe aortic stenosis, despite limitations in the quality of the evidence. They noted that some people may not report symptoms because they have adapted, for example, by reducing their activity. Exercise testing may reveal symptoms masked by reduced activity and is an indication for intervention.

There was evidence from 2 studies, but with limitations, that no increase in valve area on dobutamine stress testing was associated with worse outcome in symptomatic low-flow low-gradient aortic stenosis. Point estimates and confidence intervals from both studies were consistent with this being a risk factor for poor outcome. For those with low-flow low-gradient aortic stenosis and a valve area suggesting potential severe aortic stenosis at rest (less than 1.0 cm^2), no increase in valve area on dobutamine stress testing confirms severe aortic stenosis and is an indication for intervention.

Cardiac MRI and cardiac CT

The evidence showed that a higher aortic valve calcium score measured by cardiac CT indicates a worse prognosis for people with aortic stenosis. This could be because it is an index of the severity of aortic stenosis or because it is a marker of more widespread vascular disease. This was supported by the knowledge and experience of the committee, who noted that a more calcified aortic valve is associated with more severe aortic stenosis. However, the mechanism of aortic stenosis in bicuspid aortic valves or in rheumatic disease is different, and cardiac CT would not be as relevant to monitor valve calcium. The committee agreed that aortic valve calcium scoring is useful to assess the need for intervention in adults with symptomatic aortic stenosis of uncertain severity. Based on their expert opinion and the evidence of a worse prognosis after transcatheter aortic valve implantation (TAVI) among those with a very high calcium score, the committee recommended

that the amount and distribution of calcium in the aortic valve should be taken into account when deciding on the intervention. A very high calcium score or calcium in the left ventricular outflow tract may increase the risk associated with TAVI.

Most of the evidence suggested that myocardial fibrosis was associated with increased risk of a poor outcome in severe aortic stenosis. This was in line with the committee's experience that myocardial fibrosis in general, not only in aortic stenosis, is associated with a worse prognosis. Furthermore, myocardial fibrosis in people with severe aortic stenosis indicates early decompensation and the possible need for early intervention to stop progression, because midwall fibrosis cannot be reversed or improved by intervention. The committee agreed that follow up should be enhanced and further assessment should be offered in those with midwall fibrosis to check for symptoms and enable earlier aortic valve intervention to improve prognosis.

How the recommendations might affect practice

These recommendations largely reflect current best practice, although there is local variation and not all healthcare professionals will know that all of these thresholds should lead to referral for intervention.

However, the threshold of LVEF less than 60% does represent a significant change from current practice, because some centres use less than 50%. However, when LVEF starts to decline, it does so quite quickly, moving from 60% to 50% in under a year. Therefore for most adults this will mean earlier rather than additional intervention, with subsequent improvement in survival and quality of life.

Cardiac MRI is not currently used by all centres to assess aortic stenosis. The recommendation to consider enhanced follow up and further assessment if midwall fibrosis is detected by cardiac MRI should not mean a change in practice because it will be implemented only when cardiac MRI data are available.

Return to recommendations

Indications for intervention for adults with aortic regurgitation

Recommendation 1.3.7

Why the committee made the recommendation

Echocardiography

The committee agreed that it is established practice to consider intervention for people with severe aortic regurgitation and reduced cardiac function. Severity is defined in line with British Society of Echocardiography guidelines. People with aortic regurgitation are often younger than people with other types of valve disease and gain from timely intervention.

Evidence showed that when LVEF was less than 55% the risk of cardiovascular mortality or heart failure after intervention was higher. End-systolic diameter index (ESDI) is also a measure of systolic dysfunction. Evidence showed an increased risk of left ventricular systolic dysfunction or death when ESDI was more than 2.4 cm/m^2. The committee agreed that either of these 2 indicators of early myocardial decompensation should prompt discussion of possible intervention for asymptomatic severe aortic regurgitation. Recommendations were limited due to the evidence included being low to very low quality.

There was not enough evidence to include BNP level as an indicator for referral for intervention for people with asymptomatic severe aortic regurgitation. The committee agreed to make a research recommendation to inform future practice.

Stress testing and stress echocardiography

No evidence was identified for stress testing and stress echocardiography in adults with asymptomatic severe aortic regurgitation. The committee agreed that further research could answer questions about when to intervene in this population. Therefore, they made a research recommendation to identify prognostic factors in this population on stress testing.

How the recommendations might affect practice

The recommendations are in line with current practice.

Return to recommendations

Indications for intervention for adults with mitral regurgitation

Recommendation 1.3.8

Why the committee made the recommendation

Echocardiography

Evidence showed that LVEF less than 60% was a risk factor for increased cardiac mortality after intervention for asymptomatic severe mitral regurgitation. An ESDI greater than 2.2 cm/m^2 was associated with onset of symptoms, left ventricular dysfunction, or death without intervention. The committee agreed that either of these indicators of early myocardial decompensation should prompt consideration of an intervention for people with asymptomatic severe mitral regurgitation. Recommendations were limited to considering an intervention because the evidence was low to very low quality. The evidence on valve morphology, atrial fibrillation and pulmonary hypertension was not robust enough to include these as independent indicators for referral for intervention. However, the evidence suggested that these were associated with increased mortality so the committee agreed their presence should be considered when discussing the possibility of intervention.

There was not enough evidence to include BNP level as an indicator for referral for intervention for people with asymptomatic severe mitral regurgitation. The committee agreed to make a research recommendation to inform future practice.

Stress testing and stress echocardiography

Evidence from 2 studies showed that an increase of systolic pulmonary artery pressure (SPAP) to more than 60 mmHg on exercise was associated with worse outcomes in people with mitral regurgitation (asymptomatic or asymptomatic/mildly symptomatic, moderate or severe). This agreed with the committee's experience. Although there is limited evidence that in severe mitral regurgitation, intervening before symptoms develop results in better outcomes, the committee agreed that this may be better. Evidence from 1 study showed that SPAP above 60 mmHg on exercise was associated with symptoms developing during follow up.

There was not enough evidence for the committee to make a recommendation about symptomatic non-severe mitral regurgitation. The single small study identified suggested that an increase in effective regurgitant orifice area by 13 mm^2 or more on exercise may indicate a worse outcome for this group. But the committee were not confident in this result and so made a research recommendation to inform future practice.

How the recommendations might affect practice

These recommendations largely reflect current best practice, although there is local variation and not all healthcare professionals will know that all of these thresholds should lead to referral for intervention.

Return to recommendations

Monitoring where there is no current need for intervention

Recommendation 1.4.1

Why the committee made the recommendations

A single study from the USA suggested that regular monitoring for people with severe asymptomatic aortic stenosis reduced all-cause mortality and hospital admission for heart failure. However, the study had limitations, including lack of applicability to UK clinical practice.

The committee discussed that although frequency of monitoring currently varies in the UK, it is usually every 6 to 12 months. Some adults find 6-monthly monitoring reassuring. For others this leads to anxiety and they would prefer less frequent monitoring (for example, every 12 months). The committee agreed that the exact frequency of monitoring within the 6- to 12-month timeframe should be determined by discussions with the patient. Monitoring less often than every 12 months would be likely to lead to negative outcomes for the patient because valve changes in this group occur over months rather than years. The recommendation covers all types of asymptomatic severe valve disease.

No evidence was found for mild or moderate valve disease so the committee made research recommendations.

How the recommendations might affect practice

The recommendation is in line with current practice.

Return to recommendations

Decisions about interventions

Recommendations 1.5.1 to 1.5.2

Why the committee made the recommendations

The committee highlighted the importance of shared decision making when discussing interventions. This is to ensure that treatment options are fully explored, along with their risks and benefits. Specifically, the committee highlighted valve durability, the risks associated with the procedure and the possible need for other cardiac procedures in the future.

The committee agreed that in their clinical experience there was no difference between minimally invasive and standard surgery replacement in terms of outcomes when performed by those with expertise in minimally invasive surgery. The decision should be based on patient characteristics and preferences. A lack of expertise in minimally invasive surgery locally should not be used as a reason for not performing a minimally invasive procedure. Adults should be referred to a centre where this expertise is available if the procedure is agreed as most suitable. The evidence to support this recommendation is reported under the different types of valve disease.

How the recommendations might affect practice

The recommendations are expected to have a very small impact on current practice. Minimally invasive surgery will not be suitable for most patients. Those for whom it is suitable may decide not to opt for a minimally invasive surgery after considering the increased likelihood of failure of repair, needing redo surgery or other complications.

Return to recommendations

Interventions for aortic valve disease

Recommendations 1.5.3 to 1.5.5

Why the committee made the recommendations

Aortic stenosis when surgery is suitable

Evidence from 7 randomised controlled trials showed no large or clear differences for most outcomes between TAVI and surgery for adults with non-bicuspid aortic stenosis, including mortality outcomes and quality of life. However, a benefit of TAVI was identified for major bleeding and atrial fibrillation at 30 days, and length of hospital stay after the intervention. Absolute effects for other outcomes also suggested a benefit, but there was more uncertainty based on the confidence intervals. A harm of TAVI was identified for pacemaker implantation at 30 days. Although absolute effects also suggested a possible harm of TAVI in terms of mortality, need for reintervention, rehospitalisation and major vascular complications, the direction and size of the effect was much more uncertain for these outcomes and no clear difference between the 2 groups could be identified.

Only 1 study reported data beyond 5 years, but only for all-cause mortality. The health economic model developed as part of the guideline looked for cost effectiveness over a lifetime, so it included evidence regarding impact of complications in the long term, beyond 5 years, given the longer life expectancy for people with lower surgical risk and younger age. The results of the health economic model showed that TAVI was not cost effective when surgery was also an option. This applied to people at low, intermediate and high risk for surgery and for different age groups. The committee agreed that if surgery is an option, it should be offered to those with severe aortic stenosis requiring intervention. Although all of the evidence identified was for non-bicuspid aortic stenosis, it was agreed that the recommendation should also apply to bicuspid aortic stenosis, because suitability of surgery does not depend on the type of aortic stenosis. TAVI is also considered to be more difficult in bicuspid aortic stenosis.

Aortic stenosis when surgery is unsuitable

Evidence showed benefits for TAVI for people with inoperable non-bicuspid severe aortic stenosis compared with pharmacological management at 1 to 5 years. These included benefits in all-cause mortality, cardiac mortality, need for another intervention during follow up and hospital admission. However, at 30 days TAVI was

associated with increased mortality, stroke or TIA, major bleeding and major vascular complications. The committee noted that TAVI is the only intervention available for some people with symptomatic severe aortic stenosis. They agreed that pharmacological management is not sufficient to help symptoms in severe aortic stenosis and for some aortic stenosis can be fatal without an intervention. TAVI can improve outcomes in many cases. Two UK-based studies indicated that TAVI offers a good balance of benefits and costs in adults who cannot have surgery. The committee agreed to recommend TAVI, if suitable, for those with non-bicuspid severe aortic stenosis if surgery is unsuitable. TAVI is the only option for this group and was deemed cost effective in this population.

All of the evidence identified was for non-bicuspid aortic stenosis. TAVI is considered to be more difficult for bicuspid aortic stenosis and the committee could not extrapolate the evidence to cover this population.

Invasiveness of surgery

Evidence was identified from 14 RCTs comparing minimally invasive surgery for aortic valve replacement with standard surgery by median sternotomy across different aortic valve disease populations. Some harms of minimally invasive surgery were observed and 1 health economic study suggested that minimally invasive surgery was less cost effective than median sternotomy. However, the RCTs were small and a small number of events were observed for many outcomes. The health economic study was limited for the same reasons, because it was based on 1 of the RCTs and was limited to a 12-month time-horizon. Although the committee agreed it is likely there would not be a large difference in outcomes after 12 months, this may be too short to draw conclusions about cost effectiveness over a lifetime. The committee highlighted that in their experience there was no difference between minimally invasive surgery and median sternotomy when performed by those with expertise. The committee were also aware of certain advantages of minimally invasive surgery, for example, smaller incisions. The committee agreed not to limit the use of minimally invasive surgery and to recommend a choice with the decision based on patient characteristics and preferences. A lack of expertise in minimally invasive surgery locally should not be used as a reason for not performing a

minimally invasive procedure and adults should be referred to a centre where there is expertise if this procedure is agreed as most suitable.

Despite no direct evidence for bicuspid aortic stenosis, aortic regurgitation (bicuspid or non-bicuspid) and mixed aortic valve disease (aortic stenosis and regurgitation in the same person), the committee agreed that the type of aortic valve disease would not affect decisions about the invasiveness of surgery and the evidence could be extrapolated to any aortic valve disease.

How the recommendations might affect practice

TAVI for non-bicuspid aortic stenosis when surgery is unsuitable

The committee agreed that the use of TAVI is increasing, particularly when surgery is unsuitable and there are no other options for interventional procedures. It would be rare not to perform TAVI in these circumstances, but palliative care with pharmacological management is sometimes agreed. Therefore, the committee considered that the recommendation would represent a minimal change in practice and would not increase the number of TAVI procedures.

Surgery for aortic stenosis when this is suitable

The committee agreed that TAVI is usually reserved for when surgery is unsuitable . The recommendation to offer surgery when suitable therefore reflects current practice.

Minimally invasive surgery or median sternotomy for aortic valve disease

The committee agreed that between 10 and 20% of surgical isolated aortic valve replacements are performed by minimally invasive surgery. If the recommendation leads to an increase in the number of aortic valve replacements being performed by minimally invasive surgery, this could represent a change in practice. There may be no increase in the short term, because more training in these procedures will be needed. But in the longer term there may be a change in practice.

Return to recommendations

Interventions for mitral stenosis

Recommendations 1.5.6 and 1.5.7

Why the committee made the recommendations

Evidence from 7 RCTs comparing transcatheter valvotomy with surgical valvotomy (either by minimally invasive or standard surgery) in people with rheumatic severe mitral stenosis demonstrated very few differences in outcomes. The committee agreed that surgical valvotomy is no longer commonly used in practice because similar results can be achieved with the transcatheter procedure, with less trauma and scarring and at a lower cost to the NHS. The evidence was limited by small studies, often with only a small number of events, and most outcomes being graded as very low quality. The committee agreed that transcatheter valvotomy could be considered for adults with rheumatic severe mitral stenosis who need an intervention and for whom this procedure would be suitable.

No evidence was identified for mitral valve replacement in those with rheumatic mitral stenosis when transcatheter valvotomy is not suitable. The committee agreed this it was important to make a recommendation for these people. Although no evidence was included, the condition would likely deteriorate without an intervention.

It was not appropriate to extrapolate evidence from rheumatic mitral stenosis to calcific mitral stenosis because they are 2 very different pathologies. Because there was no evidence included for calcific mitral stenosis, the committee made a research recommendation to inform future practice.

How the recommendations might affect practice

The recommendations are in line with current practice.

Return to the recommendations

Interventions for mitral regurgitation

Recommendations 1.5.8 to 1.5.13

Why the committee made the recommendations

Repair or replacement when surgery is suitable

Evidence from 3 RCTs demonstrated few differences between surgical repair and surgical replacement in those with severe mitral regurgitation. (One study included both primary and secondary mitral regurgitation; the other 2 studies covered secondary mitral regurgitation only). The largest effect was for the need for reintervention for secondary mitral regurgitation, with fewer repeat interventions needed in the replacement group. Overall, the included evidence was limited; all studies were very small, with very few events reported for most outcomes and substantial uncertainty in the effects reported. Most outcomes were graded as very low quality. The lack of stronger evidence is likely to be because surgical repair has been preferred to replacement in mitral valve surgery for the past few decades based on observational evidence, and randomising to repair or replacement in those suitable for repair was thought to be unethical. Based on these limitations, the committee made recommendations reflecting current practice for those with severe mitral regurgitation requiring an intervention, with surgical repair recommended in those for whom it is suitable and replacement when repair is not suitable.

The committee noted that there are differences in the aetiology and treatment of primary and secondary mitral regurgitation. Although valve intervention is the next step for primary mitral regurgitation and an indication for intervention, for secondary mitral regurgitation the underlying heart failure is usually treated first. Therefore, the committee recommended that an intervention should be offered for severe primary mitral regurgitation and considered for secondary mitral regurgitation following optimisation of medical management.

Invasiveness of surgery

Evidence from 5 RCTs comparing minimally invasive surgery with median sternotomy for mitral regurgitation or mixed/unclear mitral valve disease demonstrated few differences. The studies were limited by small participant numbers and a small number of events for many reported outcomes. There was substantial uncertainty for most reported outcomes, a lack of long-term data for many outcomes, and most outcomes were graded as low or very low quality. Overall, where any

larger differences were observed (for example, length of stay), these were for a benefit of minimally invasive procedures. A single health economic study suggested the cost of minimally invasive surgery was less per person than median sternotomy. However, the committee did not consider the included evidence to be strong enough to support recommending one type of surgery over the other. They agreed that median sternotomy and minimally invasive surgery should be options for those with mitral regurgitation requiring mitral valve surgery, with the decision being based on patient characteristics and patient preferences. A lack of expertise in minimally invasive surgery locally should not be used as a reason for not performing a minimally invasive procedure and patients should be referred to a centre where there is expertise if this procedure is agreed as most suitable

Transcatheter mitral valve repair in primary mitral regurgitation when surgery is unsuitable

No clinical evidence was identified comparing transcatheter mitral valve repair with medical management for primary mitral regurgitation when surgery is not suitable. The committee noted that the lack of evidence may be because it is well established that medical management does not improve outcomes and transcatheter mitral valve repair is useful when surgery cannot be performed. One health economic study, based on a non-randomised registry, reported that transcatheter repair was cost effective compared with medical management in those with severe mitral regurgitation when surgery was not suitable. This study had limitations because it included people with secondary mitral regurgitation and used data from a prospective, single-arm registry with a control group obtained retrospectively. A second Japanese study on a mixed population with secondary and primary mitral regurgitation found transcatheter repair with the MitraClip device to be cost effective. This study had some limitations too as the relative treatment effects were informed from a propensity score matching study rather than an RCT.

A health economic model developed as part of this guideline did not find MitraClip to be cost effective for adults with secondary mitral regurgitation. However, the committee agreed that it was plausible that MitraClip would offer more benefits for people with primary mitral regurgitation because they are likely to have less residual disease affecting quality of life after the intervention. The committee agreed to

recommend that transcatheter mitral valve repair should be considered for primary severe mitral regurgitation with symptoms when surgery is unsuitable.

Transcatheter mitral valve repair in secondary mitral regurgitation when surgery is unsuitable

Evidence was included from 3 RCTs comparing transcatheter mitral valve repair with medical management for secondary mitral regurgitation. Two of these were clearly in a population not suitable for surgery and covered the use of the MitraClip device; the third study covered a Carillon device rather than MitraClip and the population was unclear. Outcomes from all 3 studies were pooled where possible in the clinical review, but the health economic modelling was limited to the population not suitable for surgery.

The clinical review highlighted uncertainty in the results for 3 outcomes (all-cause mortality, cardiac mortality and onset/exacerbation of heart failure at 1 to 2 years). Some studies demonstrated a benefit of transcatheter repair, some a harm and some no difference. One UK health economic study based on the results of the COAPT trial, which enrolled people with very severe secondary mitral regurgitation deemed inoperable, found that transcatheter edge-to-edge repair with MitraClip device had an incremental cost per QALY of about £30,000.

A health economic model was developed as part of the guideline to investigate the cost effectiveness of using the MitraClip device when surgery is not suitable. The model demonstrated that transcatheter mitral valve repair had a low chance of being cost effective at £20,000 per QALY gained, with an incremental cost-effectiveness ratio of £30,000 per QALY gained. These results are in line with the UK study identified in the literature review. The health economic model was largely based on results from the COAPT trial, which covered transcatheter mitral valve repair in severe secondary mitral regurgitation. This trial demonstrated substantial benefits over medical management alone when surgery was unsuitable. However, it was not considered to be cost effective at the current list price. For this reason, edge-to-edge mitral valve repair was not recommended over medical management.

How the recommendations might affect practice

Repair or replacement when surgery is suitable

The recommendations are in line with current practice.

Invasiveness of surgery

The recommendations are in line with current practice.

Transcatheter mitral valve repair in primary mitral regurgitation when surgery is unsuitable

Transcatheter mitral valve repair is rarely performed for primary mitral regurgitation when an intervention is required and surgery is unsuitable, so the recommendation may lead to a change in practice. This procedure has only recently been commissioned by the NHS and its use is likely to increase now based on this commissioning. The recommendation is unlikely to increase use much beyond this.

Transcatheter mitral valve repair in secondary mitral regurgitation when surgery is unsuitable

Transcatheter mitral valve repair is not currently used for secondary mitral regurgitation because it has not been commissioned by the NHS for this. The recommendation is unlikely to lead to a change in practice.

Return to recommendations

Interventions for tricuspid regurgitation

Research recommendation

Why the committee made the research recommendation

A single RCT was identified comparing transcatheter repair plus optimal medical management with optimal medical management alone in people with severe, symptomatic tricuspid regurgitation and a high surgical risk score. Although some possible benefits and harms of the transcatheter procedure were identified, the study was extremely small (with only 14 participants randomised to each arm) and there was uncertainty in the results for all outcomes. This was not enough evidence for the committee to make a recommendation and they were unable to base a

recommendation on their experience because of a lack of consensus in this area. They made a recommendation for research to inform future guidance.

Repeat intervention

Recommendation 1.6.1

Why the committee made the recommendations

No evidence was identified comparing surgery with medical management for people with failing biological prosthetic aortic valves. However, the committee agreed that surgery should be considered in this group because their condition may deteriorate if left without intervention on medical management.

Similarly, no evidence was identified comparing transcatheter repeat intervention with medical management when surgery is unsuitable for people with failing biological prosthetic aortic valves. However, the committee agreed that repeat transcatheter intervention should be considered in this group because their condition may deteriorate if left without intervention on medical management.

For people who can have surgery, there were no RCTs comparing transcatheter intervention and surgery for repeat intervention and the only included studies were non-randomised. The committee were not able to base recommendations on this because of the limitations with non-randomised evidence. They therefore recommended that a shared decision should be based on short and longer-term benefits, the type of valve dysfunction and prosthesis, the risks associated with the procedure and the possible need for other cardiac procedures. The term 'degenerated' refers to progressive degeneration and does not include failure of the valve due to endocarditis or thrombosis. The recommendation was limited to those with symptoms because this was considered to be an indication for repeat intervention

The committee also made research recommendations for repeat intervention for failing biological prosthetic aortic, mitral and tricuspid valves because the only available evidence was non-randomised.

How the recommendations might affect practice

When both transcatheter and surgical procedures are options for repeat intervention, the choice of procedure is usually based on individual patient characteristics although surgery may be performed more often. When surgery is not an option, transcatheter intervention is used as the only alternative to medical management. The recommendations will therefore not represent a change in practice.

Return to recommendations

Anticoagulation and antiplatelet therapy

Recommendations 1.7.1 to 1.7.3

Why the committee made the recommendations

Anticoagulant and antiplatelet treatment after surgical biological valve replacement

Evidence from a population without atrial fibrillation demonstrated an increased risk of major bleeding with vitamin K antagonist compared with single antiplatelet therapy (aspirin). No clear reduction in mortality or thromboembolic events was observed with vitamin K antagonist. Therefore, the committee agreed that anticoagulation should not be offered after surgical biological valve replacement unless there are other indications for anticoagulation. This covers both vitamin K antagonists and direct-acting oral anticoagulants (DOACs) because there was no evidence to show that DOACs are safe. One small study in people with atrial fibrillation suggested there may be no clear differences in outcomes between DOACs and vitamin K antagonists, and it is not common practice to use DOACs for this group. The committee agreed that if there is already an indication for anticoagulation or antiplatelet therapy, for example, because of atrial fibrillation, the existing NICE guidelines for these indications should be followed.

Despite 1 study demonstrating a potential reduction in arterial thromboembolic events and vascular mortality with combined anticoagulant and antiplatelet therapy compared with anticoagulant therapy alone after surgical biological valve replacement, there was uncertainty around this result. This uncertainty, combined

with further study limitations, including issues with the target INR used and the selective population, meant that the study could not be used to inform general recommendations for surgical biological valve replacement.

There was a lack of evidence comparing anticoagulant or antiplatelet therapy with no treatment after surgical biological valve replacement, so the committee made a research recommendation. They made another research recommendation to investigate the long-term effect of anticoagulant or antithrombotic therapy on valve function and outcomes after biological valve replacement because no long-term data were available.

Single antiplatelet therapy after transcatheter aortic valve implantation

Evidence from 4 studies demonstrated a clinically important benefit of single antiplatelet therapy (aspirin) compared with dual antiplatelet therapy in reducing major and minor bleeding in the short to medium term. Based on this, the committee agreed that single rather than dual antiplatelet therapy should be considered after transcatheter aortic valve implantation. As aspirin is used in practice, and this was used in all of the studies, aspirin was recommended, with clopidogrel specified as the alternative if aspirin was not tolerated.

The committee were also aware of observational evidence that antiplatelets reduced the risk of valve thrombosis and improved valve durability over the long term. There was also evidence from 1 study demonstrating harms of DOACs compared with single antiplatelet therapy for most reported outcomes, including mortality, bleeding and withdrawal because of adverse events. This further supported the recommendation for single antiplatelet therapy. Because of the lack of evidence comparing anticoagulant and antiplatelet therapy with no treatment after TAVI, the committee made a research recommendation.

Valve repair

No evidence was identified comparing different anticoagulant and antiplatelet treatments in adults who have had valve repair. The committee made a recommendation for research comparing anticoagulant and antiplatelet treatments with placebo after valve repair.

How the recommendations might affect practice

Anticoagulant and antiplatelet treatment after surgical biological valve replacement

Practice is currently variable, with some centres offering vitamin K antagonists after surgical biological valve replacement. Therefore the recommendation will lead to a change in practice in some centres.

Single antiplatelet therapy after transcatheter aortic valve implantation

It is unusual for people not to receive at least single antiplatelet therapy after TAVI and many people receive dual antiplatelet therapy. The recommendation was not thought to represent a change in practice in terms of the number of people who receive some form of antiplatelet therapy following a transcatheter procedure.

Return to recommendations

Monitoring after an intervention

Recommendation 1.8.1

Why the committee made the recommendations

No evidence was found for the frequency of monitoring after an intervention for valve disease. Current practice is variable and depends on patient factors, such as comorbidities, other cardiac disease or previous heart surgery, as well as the type of procedure performed (repair or replacement). Follow up also depends on the type of valve used for a replacement. The committee agreed that mechanical valves have good durability with a low risk of failure. In contrast, biological valves have lower durability with deterioration possible within 10 years. The committee noted that, although practice varies, mechanical valves may be monitored over the first 12 months and then only checked if problems develop. Monitoring is usually more frequent for biological valves – with some centres offering annual follow up starting from the year of the operation and others starting annual follow up after 5 years. Any concerns about abnormal valve function may also affect the frequency of monitoring, with more frequent follow up if there are concerns.

The committee agreed that frequency of follow up should be discussed with the patient. Some people find more frequent monitoring reassuring whereas for others this leads to increased anxiety. People should be encouraged to seek advice if they feel that their condition has deteriorated. There is a higher risk of endocarditis in replacement valves and people should be encouraged to report symptoms.

How the recommendations might affect practice

The recommendation reflects current practice, which is variable and depends on various factors, such as valve durability and patient comorbidities and preferences.

Return to recommendations

Information and advice

Recommendations 1.9.1 to 1.9.5

Why the committee made the recommendations

Clear and consistent evidence outlined the negative impact of symptoms of valve disease and loss of control that led to feelings of despair and insecurity. In this context, a single point of contact for some people may increase the hope and security afforded between appointments.

The committee also agreed that it was useful to list areas of information and advice that are important to people with valve disease to ensure that their expectations accurately match the likely course of their condition. Having this information will be beneficial for planning, reducing anxiety and supporting shared decision making. This may include relevant information for patients and carers (when appropriate) about the possibility of delirium after valve surgery, in line with the NICE guideline on delirium.

The committee noted from the evidence and their experience the psychological impact of valve disease, whether or not the person currently has symptoms. They agreed that psychological support should be considered.

The committee stressed the importance of individualised care and shared decision making and referenced the relevant NICE guidelines. Specific advice and support at

the point of transition from paediatric to adult services was also agreed to be important to ensure young adults are given appropriate information on the likely progression of their valve disease and referrals to adult valve clinics.

The committee noted the limitations of the available evidence, which was mostly from those being considered for TAVI. These people typically have more complex comorbidities, and their older age means that their hopes and fears are different from those of younger adults. Therefore, the committee made a research recommendation on the information and advice needs of all adult age groups with valve disease of all severities and stages. Studies should include patient-reported outcomes and experiences of decision aids.

How the recommendations might affect practice

Currently not all adults with valve disease have a point of contact between appointments or psychological support, and so these recommendations will need a change by some providers.

Return to recommendations

Context

The heart has 4 valves (aortic, mitral, tricuspid and pulmonary) that control blood flow.

In heart valve disease, valve function can be impaired by:

- stenosis, a narrowing or stiffening of the valve, which restricts its opening and obstructs the forward flow of blood
- regurgitation, failure of the valve to close completely, which allows blood to flow backward.

There can be stenosis and regurgitation of the same valve (mixed valve disease) or disease may affect more than one valve (multiple valve disease).
Mitral and tricuspid heart valve disease can be primary or secondary. Primary disease affects the valve structure, whereas secondary disease results from enlargement or dysfunction of the heart chambers (atria or ventricles) with otherwise normal mitral or tricuspid valve structure.

Heart valve disease can be congenital or acquired. Acquired valve degeneration is currently the main cause of heart valve disease, leading to the most common types of heart valve disease, as for example calcific aortic stenosis and myxomatous or calcific degeneration of the mitral valve.

Secondary heart valve disease can be classified as:

- ventricular-secondary mitral or tricuspid regurgitation
- atrial-secondary mitral or tricuspid regurgitation.

Among people aged 65 years or over the prevalence of asymptomatic heart valve disease may be more than 50%, whereas the prevalence of clinically significant heart valve disease is around 11%. It is predicted that for people over 65, the prevalence of heart valve disease will increase, from 1.5 million people currently to more than 3 million in 2046.

People with heart valve disease may have no symptoms or may have symptoms that can depend on the affected valve. Associated heart rhythm problems, such as atrial

fibrillation or heart block, may cause palpitations and breathlessness, or dizziness and light-headedness, respectively. Untreated severe disease can lead to valvular heart failure, with symptoms including breathlessness, reduced exercise capacity, tiredness and swollen ankles. Heart valves stiffen as part of the ageing process, making dysfunction more likely in older people. We hope that this guideline will raise awareness of heart valve disease and improve diagnosis and management.

Finding more information and committee details

To find out what NICE has said on topics related to this guideline, see our web page on cardiovascular conditions.

For details of the guideline committee see the committee member list.