

**96**

## Management of stable angina

A national clinical guideline

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February 2007

# KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

## LEVELS OF EVIDENCE

- 1<sup>++</sup> High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
- 1<sup>+</sup> Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
- 1<sup>-</sup> Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
- 2<sup>++</sup> High quality systematic reviews of case control or cohort studies  
High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
- 2<sup>+</sup> Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
- 2<sup>-</sup> Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
- 3 Non-analytic studies, eg case reports, case series
- 4 Expert opinion

## GRADES OF RECOMMENDATION

*Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.*

- A** At least one meta-analysis, systematic review of RCTs, or RCT rated as 1<sup>++</sup> and directly applicable to the target population; *or*  
A body of evidence consisting principally of studies rated as 1<sup>+</sup>, directly applicable to the target population, and demonstrating overall consistency of results
- B** A body of evidence including studies rated as 2<sup>++</sup>, directly applicable to the target population, and demonstrating overall consistency of results; *or*  
Extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>
- C** A body of evidence including studies rated as 2<sup>+</sup>, directly applicable to the target population and demonstrating overall consistency of results; *or*  
Extrapolated evidence from studies rated as 2<sup>++</sup>
- D** Evidence level 3 or 4; *or*  
Extrapolated evidence from studies rated as 2<sup>+</sup>

## GOOD PRACTICE POINTS

- Recommended best practice based on the clinical experience of the guideline development group

**Scottish Intercollegiate Guidelines Network**

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February 2007

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# 1 Introduction

## 1.1 WHY IS ANGINA IMPORTANT?

The recorded prevalence of angina varies greatly across UK studies.<sup>1</sup> The Scottish Health Survey (2003) reports the prevalence of angina, determined by the Rose Angina Questionnaire to be 5.1% and 6.7% in males aged 55-64 and 65-74 respectively.<sup>2</sup> For the same age groups in women the equivalent rates were 4% and 6.8%. This compares with general practitioner (GP) record data in the British Regional Heart Study from across the UK of 9.2% and 16.2% for men in the same age groups.<sup>3</sup> The average GP will see, on average, four new cases of angina each year.<sup>4</sup>

Practice team information submitted by Scottish general practices to Information Services Division (ISD) Scotland allows the calculation of an annual prevalence rate for Scotland (the proportion of the population who have consulted their general practice because of a definite diagnosis of angina based on ISD's standard morbidity grouping). In the year ending March 2005 the annual prevalence rate is given as 8.3 for men and 7.6 for women per 1,000 population. This equates to an estimated number of patients seen in Scotland in that year for angina of 42,600 with 68,200 patient contacts.<sup>5</sup>

A diagnosis of angina can have a significant impact on the patient's level of functioning. In one survey, angina patients scored their general health as twice as poor as those who had had a stroke.<sup>6</sup> In another survey, patients had a low level of factual knowledge about their illness and poor medication adherence.<sup>7</sup> A Tayside study showed that in patients with angina, symptoms are often poorly controlled, there is a high level of anxiety and depression, scope for lifestyle change and an ongoing need for frequent medical contact.<sup>8</sup>

## 1.2 THE NEED FOR A GUIDELINE

In recent years there has been a decline in the rate of major coronary events and death from coronary heart disease (CHD).<sup>9</sup> However, data from the British Regional Heart Study based on GP records which included Scotland has shown an annual increase of 2.6% in first diagnosed angina in the 20 years of follow up to the year 2000 in males aged 40-59 at entry.<sup>3</sup> This increase reflects the diagnosis as it occurred in clinical practice without objective criteria to confirm the presence of underlying CHD. The rise in the rate of new angina diagnoses eliminates any overall fall in the diagnosis of CHD.

General practitioners are being advised to ensure that patients presenting with symptoms consistent with angina are rapidly assessed. The development of rapid access chest pain clinics has been encouraged to allow this to happen.<sup>10</sup> Evidence based diagnostic practice and the prioritisation of investigation in patients with symptoms consistent with angina are required.

## 1.3 ANGINA AS A SYMPTOM

Angina is used to describe a clinical syndrome of chest pain or pressure precipitated by activities such as exercise or emotional stress which increase myocardial oxygen demand. Although classical stable angina can be predictable in onset, reproducible and relieved by rest or glyceryl trinitrate, other factors and circumstances can influence its development. Angina can be caused by various cardiovascular conditions but this guideline is restricted to the clinical situation where reduced myocardial perfusion is due to arterial narrowing resulting from underlying atherosclerotic coronary heart disease. A small minority of patients have objective evidence of myocardial ischaemia in the absence of any obvious structural abnormality of the coronary arteries.

Stable angina is usually assessed in the outpatient setting. It is important when taking a clinical history to identify and manage appropriately those patients whose symptoms may be due to the more severe changes of plaque erosion and rupture occurring as part of the spectrum of acute coronary syndrome (see *SIGN guideline 93 on acute coronary syndromes*).<sup>11</sup>

## 1.4 THE REMIT OF THE GUIDELINE

In addition to examining the most appropriate models of care and referral this guideline examines the investigations necessary to confirm the presence of CHD. The optimum medical treatment to relieve symptoms is considered as well as the optimum management of those patients with angina requiring non-cardiac surgery. In the 10 years up to 2004 the number of coronary artery bypass grafts carried out each year in Scotland has increased only slightly (2,452 to 2,637). In the same period percutaneous coronary interventions (PCI) have increased fourfold (1,028 to 4,133) with changing trends in stent implantation.<sup>12</sup> The relative benefits of different interventions and the provision of patient education are examined as well as whether psychological interventions can help improve symptoms and quality of life.

### 1.4.1 PATIENT VERSION

A patient version of this guideline is available from the SIGN website: [www.sign.ac.uk](http://www.sign.ac.uk)

### 1.4.2 ADDITIONAL ADVICE TO NHSSCOTLAND FROM NHS QUALITY IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

NHS QIS processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

SMC advice and NHS QIS validated NICE MTAs relevant to this guideline are summarised in the section on implementation.

## 1.5 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

## 1.6 REVIEW AND UPDATING

This guideline was issued in 2007 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: [www.sign.ac.uk](http://www.sign.ac.uk)

## 2 Diagnosis and assessment

### 2.1 ESTABLISHING A DIAGNOSIS

Angina is a symptom that suggests that an individual may have underlying CHD. Investigation to confirm the severity and extent of underlying CHD may also allow management strategies to be developed and optimise cardiovascular risk reduction.<sup>13</sup> A significant proportion of patients with chest pain may not have angina and assessment should also try to identify alternative diagnoses at an early stage.

Angina often varies in severity and patients who have unstable angina (acute coronary syndrome) are outside the remit of this guideline, as these patients usually require more urgent and immediate management (*see SIGN guideline 93 on acute coronary syndromes*).<sup>11</sup>

Patients with stable angina are usually managed in the primary care setting, but may present in a number of healthcare settings. An initial diagnosis of angina can be made within primary care but this should be supported by further assessment and risk stratification, which will normally require specialist input.

#### 2.1.1 CLINICAL ASSESSMENT

Patients with stable angina should have the diagnosis made, where possible, following a carefully obtained clinical assessment. Clinical history is the key component in the evaluation of the patient with angina; often the diagnosis can be made on the basis of clinical history alone. While a number of scoring systems are available to assess patients with chest pain and stable angina, an accurate clinical assessment is of key importance. There are several typical characteristics of stable angina which should increase the likelihood of underlying CHD. These include:<sup>14</sup>

- type of discomfort – often described as tight, dull or heavy
- location – often retrosternal or left side of chest and can radiate to left arm, neck, jaw and back
- relation to exertion – angina is often brought on with exertion or emotional stress and eased with rest
- duration – typically the symptoms last up to several minutes after exertion or emotional stress has stopped
- other factors – angina may be precipitated by cold weather or following a meal.

The predominant features described by some patients are discomfort and heaviness or breathlessness, rather than pain. Chest discomfort, irrespective of its site, is more likely to be angina when precipitated by exertion and relieved by rest. It is also characteristically relieved by glyceryl trinitrate. Not all patients will present with typical characteristics and the clinician should be aware of other symptoms such as breathlessness and burping which may be the initial presenting symptom.

Angina can be graded by severity on the Canadian Cardiovascular Society (CCS) class scale of I-IV<sup>15</sup> (*see Table 1*).

*Table 1: Canadian Cardiovascular Society Angina Classification*

Class	Description
Class I	Ordinary activity such as walking or climbing stairs does not precipitate angina
Class II	Angina precipitated by emotion, cold weather or meals and by walking up stairs
Class III	Marked limitations of ordinary physical activity
Class IV	Inability to carry out any physical activity without discomfort – anginal symptoms may be present at rest.

4

The likelihood of a diagnosis of angina increases with the number of cardiovascular risk factors in individual patients. These include:

- smoking
- hypertension
- diabetes
- family history of CHD (first degree relative – male < 55 years/female < 65 years)
- raised cholesterol and other lipids.

These risk factors are best initially addressed in the primary care setting where lifestyle advice can be provided and support offered, where necessary. If symptoms persist, more objective evaluation of symptoms may be necessary to establish the severity of any underlying CHD. In addition to assessment of conventional risk factors, (see *SIGN guideline 97 on risk estimation and the prevention of cardiovascular disease*)<sup>73</sup> patients should have the following evaluated:

- body mass index (BMI) or waist circumference
- murmur evaluation
- haemoglobin level
- fasting blood glucose
- thyroid function
- depression and social isolation
- physical activity.

A number of scoring systems have been proposed to assess the severity and prognostic impact of angina.<sup>16,17</sup> While these scoring systems may be accurate in the patient groups included in the cohorts studied, their use in routine clinical practice cannot be recommended, but they may have a role in influencing the clinical decision making process.

2++  
2+

When a general practitioner identifies a patient with stable angina, further assessment at a cardiology outpatient clinic is desirable.

- Patients with suspected angina should have a detailed initial clinical assessment which includes history, examination and an assessment of blood pressure, haemoglobin, thyroid function, cholesterol and glucose levels.
- Those patients who should be considered for early referral to secondary care include those with new onset angina and those with established coronary heart disease with an increase in symptoms.

### 2.1.2 NON-CARDIAC CHEST PAIN

Angina pain is not usually sharp or stabbing in nature. It is not usually influenced by respiration or eased with antacids and simple analgesia.

The initial clinical assessment is important as it may reduce anxiety and distress resulting in unnecessary hospital admissions and consultations.<sup>18</sup> Low risk patients, such as young women with atypical symptoms, should be assessed in primary care where possible. Much of this assessment includes explaining symptoms, discussing concerns and providing reassurance where necessary. A diagnosis of non-cardiac chest pain should be given early and confidently as correct management may reduce morbidity.<sup>19</sup>

2+  
4

A rehabilitation programme based on cognitive behaviour principles for patients with chest pain but normal coronary arteries, found that those who continued to attribute symptoms to cardiac causes had worse outcomes.<sup>20</sup>

- If the diagnosis is uncertain, clinicians should not give the impression that the patient has angina. This may lead the patient to have false beliefs, which may be difficult to change even after further investigations have ruled this out.



## 2.1.3 DIAGNOSTIC TOOLS

**Electrocardiography**

A baseline 12 lead electrocardiogram (ECG) should be performed in every patient with suspected angina.<sup>21</sup> A normal 12 lead ECG does not exclude a diagnosis of coronary heart disease.<sup>22</sup> An abnormal resting ECG increases the probability that a patient has CHD, but gives no indication as to the severity of any associated obstructive coronary heart disease.<sup>23</sup> A 12 lead ECG can also highlight the presence of atrial fibrillation or left ventricular hypertrophy. The interpretation of resting or exercise ECGs is operator-dependent.<sup>24</sup>

2++  
3**Exercise tolerance testing**

The majority of patients with suspected angina will be referred for exercise tolerance testing (ETT), which is also known as exercise ECG or stress ECG. Exercise is usually performed by treadmill testing or on a static bicycle and may be unsuitable for patients who have poor mobility, peripheral arterial disease or limiting respiratory or musculoskeletal conditions.

The sensitivity and specificity of ETT in establishing the diagnosis of CHD is dependent on the cohort of patients studied. Sensitivity is higher in patients with triple vessel disease and lower in patients with single vessel disease.<sup>25</sup> The true diagnostic value of exercise ECG lies in its relatively high sensitivity, but it is only moderately specific for the diagnosis of CHD in women.<sup>26</sup>

2++  
4

A normal exercise test may reassure many patients but it does not exclude a diagnosis of CHD. A highly abnormal ETT result is an indication for urgent further investigation.

**Myocardial perfusion scintigraphy**

Myocardial perfusion scintigraphy (MPS) with exercise or pharmacologic stress is an accurate and non-invasive investigation which reliably predicts the presence of CHD.<sup>27</sup> Myocardial perfusion scintigraphy may be the appropriate initial diagnostic test in patients with pre-existing ECG abnormalities (eg left bundle branch block) or in those unable to adequately exercise and as part of the diagnostic strategy for suspected CHD in people with lower likelihood of CHD.<sup>28</sup> It is also valuable in females who may have a low risk of underlying CHD but a high risk of a falsely positive ETT and in patients where identification of regional ischaemia would be of value (eg prior to PCI). Myocardial perfusion scintigraphy provides valuable independent and incremental prognostic information to that provided by ETT and this enables risk stratification of patients which informs treatment decisions.<sup>29</sup>

2++  
4

**C** Patients with suspected angina should usually be investigated by a baseline electrocardiogram and an exercise tolerance test.

**B** Patients unable to undergo exercise tolerance testing or who have pre-existing electrocardiogram abnormalities should be considered for myocardial perfusion scintigraphy.

**Coronary angiography**

Coronary angiography is the traditional benchmark investigation for establishing the nature, anatomy and severity of CHD. It is an invasive investigation and carries a mortality risk of around 0.1% for elective procedures.<sup>30</sup> It requires referral to a cardiologist and is best reserved for those patients who are at high risk or continue to have symptoms despite optimal medical treatment and may require revascularisation. It may also provide valuable information regarding valvular and left ventricular function.

4

Coronary angiography should be considered after non-invasive testing where patients are identified to be at high risk or where a diagnosis remains unclear.

**Other investigations**

Newer investigations including stress echocardiography, magnetic resonance perfusion imaging (MRI) and multislice computed tomography (CT) scanning are also effective in establishing a diagnosis of CHD when performed by trained and skilled teams.<sup>31-33</sup> These investigations are not part of routine clinical practice in NHSScotland, although their use may become more widespread as clinical and economic evaluations of their effectiveness become available.

1-4

**2.2 MODELS OF CARE**

A variety of models have been developed to facilitate prompt identification and optimum management of patients with angina from those with potentially less severe causes of chest pain. These models of care have been designed in varying ways emphasising the development of a service which reflects local health needs and demands. While many of these services have a triage role, their design facilitates the early detection of patients who may have severe CHD who would benefit from early intervention. Optimum management of angina requires reassurance of low risk patients while appropriately identifying high risk patients and making the most efficient use of available resources.

Rapid access chest pain clinics (RACPCs) have been advocated as a successful model of referral to secondary care for angina patients. These have been in existence for many years. The National Service Framework for Coronary Artery Disease suggested more of these clinics should be set up and rolled out across England and Wales to assess patients within two weeks of primary care referral.<sup>34</sup> No evidence was provided to explain the specific target of two weeks. These clinics are run in a variety of ways, depending on local resources, where patients can be seen by cardiologists, specialist registrars, nurse specialists or GPs with special interest in cardiology.

4

One detailed meta-analysis investigated a range of methods, including rapid access chest pain clinics, in the diagnosis and management of acute coronary syndromes (ACS), suspected myocardial infarction (MI) and exertional angina.<sup>21</sup> Weak evidence was found to suggest that RACPCs may be associated with reduced admission to hospital of patients with non-cardiac pain, better recognition of ACS, earlier specialist assessment of exertional angina and earlier diagnosis of non-cardiac chest pain. In a simulation exercise of models of care for investigation of suspected exertional angina, RACPCs were predicted to result in earlier diagnosis of both confirmed CHD and non-cardiac chest pain than models of care based around open access exercise tests or routine cardiology outpatients, but they were more expensive. The benefits of RACPCs disappeared if waiting times for further investigation (eg angiography) were long (six months).

2++

The evidence around the cost effectiveness of RACPC for patients with suspected angina is very limited. One study showed operating such a clinic can be cost saving, compared to standard care, potentially reducing costs by about £60 per patient, with the savings coming from fewer unnecessary hospitalisations.<sup>35</sup> However, the study is weak, results are very setting specific and may not generalise to other settings.

3

**B**

**Following initial assessment in primary care, patients with suspected angina should, wherever possible, have the diagnosis confirmed and the severity of the underlying coronary heart disease assessed in the chest pain evaluation service which offers the earliest appointment, regardless of model.**

## 3 Pharmacological management

This section deals with drugs that relieve and prevent angina symptoms.

### 3.1 DRUG MONOTHERAPY TO ALLEVIATE ANGINA SYMPTOMS

All the studies reported were carried out on a mixed population with males as a majority and included various age groups and patient entry criteria. Populations of patients with and without past medical histories of MI, heart failure and other cardiac and non-cardiac comorbidities were reported. The populations in the trials resemble the Scottish population who are treated for chest pain resulting from CHD. Drugs that are unlicensed for the treatment of CHD in the UK are not included in the guideline.

#### 3.1.1 BETA BLOCKERS

Beta blockers improve oxygen supply and demand balance by reducing heart rate and blood pressure, decreasing end systolic stress and contractility and prolonging diastole, allowing more coronary flow.

Meta-analyses have shown that beta blockers remain the first line drugs for the long term prevention of chest pain resulting from CHD.<sup>36-38</sup> This is because of their potential to reduce mortality in patients with acute MI or heart failure.<sup>39,40</sup> One observational study suggests a mortality benefit of beta blockers in patients with stable CHD and without a past medical history of MI or heart failure.<sup>41</sup>

1++  
3

Most randomised controlled trials (RCTs) have used older beta blockers such as propranolol, metoprolol and atenolol for the treatment of stable angina,<sup>36-38</sup> and newer beta blockers such as bisoprolol have also been shown to be effective.<sup>42</sup> The efficacy of beta blockers is due to a class effect mediated through blocking beta adrenoceptors rather than to individual characteristics of each drug. Comorbidity, eg heart failure, and other factors such as compliance and cost should be considered when selecting an individual beta blocker.

1++  
1+

The British National Formulary (BNF) indicates that the usual beta blocker regimens are: atenolol 100 mg daily in single or divided dosages, metoprolol 50-100 mg two to three times daily or bisoprolol 5-20 mg once daily. Doses should be tailored individually to ensure maximum beta blockade depending on the sensitivity of the patient to specific drugs. Resting heart rate less than 60 beats per minute is an indication of beta blockade.<sup>43</sup>

4

Beta blockers are contraindicated in patients with severe bradycardia, atrioventricular (AV) block, sick sinus syndrome, decompensated heart failure and asthma.<sup>43</sup> Diabetes mellitus is not a contraindication to beta blockers.

**A**

**Beta blockers should be used as first line therapy for the relief of symptoms of stable angina.**

#### 3.1.2 CALCIUM CHANNEL BLOCKERS

Calcium channel blockers (CCBs) inhibit calcium transport and induce smooth muscle relaxation.

Meta-analyses<sup>36-38</sup> and RCTs<sup>44,45</sup> have shown that CCBs are generally as effective as beta blockers in reducing angina symptoms.

1++  
1+

Few studies have directly compared individual CCBs using anginal symptoms as a clinical endpoint. In a small RCT diltiazem and amlodipine were similar in improving exercise tolerance in patients with CHD.<sup>45</sup> The choice of CCB may depend on comorbidity and drug interactions.

Rate-limiting CCBs (verapamil and diltiazem) are contraindicated in heart failure and in patients with bradycardia or AV block. Patients with heart failure and angina may be safely treated with the dihydropyridine derivatives amlodipine or felodipine<sup>46,47</sup> (see also SIGN guideline 95 on the management of chronic heart failure).<sup>48</sup>

1+

There is conflicting evidence regarding the safety of nifedipine in patients with angina. A meta-analysis has indicated that nifedipine monotherapy or short-acting nifedipine in combination with other anti-anginal drugs may increase the incidence of cardiovascular events, mainly angina episodes.<sup>49</sup>

1++

Prinzmetal (vasospastic) angina is a rare form of angina in which pain is experienced at rest rather than during activity. It is caused by narrowing or occlusion of proximal coronary arteries due to spasm and cannot be diagnosed by coronary angiography. Beta blockers should not be used in this form of angina because they may worsen the coronary spasm.<sup>50</sup> Patients with this condition may be treated effectively with a dihydropyridine derivative CCB such as amlodipine.<sup>51</sup>

1+  
2+

**B Patients with Prinzmetal (vasospastic) angina should be treated with a dihydropyridine derivative calcium channel blocker.**

3.1.3 POTASSIUM CHANNEL ACTIVATORS

There are few studies on the efficacy of nicorandil in the treatment and prevention of chest pain. One RCT showed that nicorandil was comparable to diltiazem in reducing angina.<sup>52</sup> Another trial demonstrated that nicorandil was as effective as amlodipine in patients with symptomatic stable angina.<sup>53</sup> In another RCT of over 5,000 patients, nicorandil was shown to significantly reduce the combined endpoint of CHD death, non-fatal myocardial infarction, or unplanned hospitalisation for cardiac chest pain (15.5% to 13.1% hazard ratio 0.83, 95% confidence interval, CI, 0.72 to 0.97; p=0.014).<sup>54</sup> A cost effectiveness analysis based on the results of this trial estimated that the additional costs of adding nicorandil to standard care for patients with angina were offset by the reduced hospitalisation costs.<sup>55</sup>

1++  
1+

3.1.4 NITRATES

These drugs act directly on the vascular smooth muscle to produce venous and arterial dilatation, reducing pre-load, after-load and oxygen demand.

Nitrates are effective drugs in the prevention and treatment of angina. In meta-analyses, there was no significant difference in the anti-anginal efficacy between long-acting nitrates and beta blockers or CCBs.<sup>36,37</sup> In a more recent RCT, the CCB amlodipine was shown to be more effective than nitrates in controlling exercise-induced angina in elderly patients with stable CHD.<sup>56</sup>

1++  
1+

Sublingual glyceryl trinitrate is effective for the immediate relief of angina and can also be used to prevent ischaemic episodes when used before planned exertion.<sup>57,58</sup>

1+

**A Sublingual glyceryl trinitrate tablets or spray should be used for the immediate relief of angina and before performing activities that are known to bring on angina.**

Nitrate tolerance can be avoided by prescribing modified release long acting preparations or by asymmetric dosing.<sup>59</sup> Such regimens can be confusing to patients and could lead to non-compliance and nitrate tolerance. Modified release oral nitrates that are given once daily provide therapeutic plasma nitrate levels over the initial few hours following ingestion. Compliance has been shown to improve when transferring from multiple dose regimens to once-daily regimens.<sup>60,61</sup> The low plasma nitrate level at 24 hours following ingestion appears to minimise tolerance.<sup>62,63</sup>

1+  
3+  
4

The main side effect of nitrates is headache, which usually wears off after continuous use, but in some patients this could become intolerable and necessitate change to another anti-anginal drug.

An economic model compared a single daily dose regimen using a modified release formulation with a twice-daily dose regimen, and assumed that better compliance with the single dose (88% vs 68%) would improve symptom control and result in fewer visits to GPs.<sup>62</sup> The two regimens had very similar annual costs (£248 vs £250). The sensitivity analysis showed that the result is highly sensitive to changes in the assumed compliance rates and drug costs. In Scotland, prescription of a generic drug for the two dose regimen would be cost saving compared to the single dose modified release option.

**A** Patients who are intolerant of beta blockers should be treated with either rate limiting calcium channel blockers, long-acting nitrates or nicorandil.

### 3.1.5 EFFECT OF OTHER DRUGS ON ANGINA

Ivabradine, a selective  $I_f$ -channel inhibitor, acts to lower heart rate. In a double blind randomised parallel-group trial ivabradine was shown to have equivalent anti-anginal efficacy to atenolol in patients with stable angina.<sup>64</sup> While symptomatic benefit has been clearly demonstrated long term protection against cardiovascular events has yet to be determined.

1+

## 3.2 COMBINATION THERAPY TO ALLEVIATE ANGINA SYMPTOMS

### 3.2.1 ADDING CALCIUM CHANNEL BLOCKERS TO BETA BLOCKERS

A meta-analysis of 22 RCTs demonstrated that the combination of a beta blocker with a CCB is more effective than monotherapy in improving exercise tolerance. Time to 1 mm ST-segment depression, total exercise duration and time to onset of anginal pain were significantly increased with the combined therapy compared to beta blocker alone (by 8, 5 and 12%, respectively). This benefit was only shown to be significant within six hours of drug intake.<sup>65</sup>

1++

Adding diltiazem to beta blockers produces a dose-dependent improvement in symptom control and exercise tolerance.<sup>66</sup> The British National Formulary suggests caution as this combination may cause severe bradycardia and heart block in some cases.<sup>43</sup>

1++  
4

Dihydropyridine derivatives are safe when combined with beta blockers. The combination of metoprolol with felodipine was shown to be slightly more effective than metoprolol alone in one RCT.<sup>67</sup> This trial showed a statistically significant improvement in time until end of exercise with felodipine-metoprolol combination (10/100 mg) compared with metoprolol 100 mg ( $p=0.04$ ) and felodipine 10 mg compared with metoprolol 100 mg ( $p=0.03$ ). For time until onset of pain or time until 1-mm ST-depression there were no significant differences among the treatment groups.

1++  
1+

Other RCTs have shown that adding CCBs to beta blockers, although safe, offered very little or no benefit in relief of anginal symptoms.<sup>68-70</sup>

**A** When adequate control of anginal symptoms is not achieved with beta-blockade a calcium channel blocker should be added.

Rate-limiting calcium channel blockers should be used with caution when combined with beta blockers.

### 3.2.2 ADDING NITRATES OR NICORANDIL TO OTHER ANTI-ANGINAL DRUGS

Adding isosorbide mononitrate to a beta blocker<sup>71</sup> or to a CCB<sup>72</sup> significantly improves performance on a range of clinical endpoints. Adding nicorandil to other anti-anginal drugs was effective in reducing combined cardiac events. One of these composite endpoints was hospital admission for refractory angina. There was no primary endpoint for reducing chest pain.<sup>54</sup>

1++  
1+

3.2.3 THE USE OF THREE DRUGS

The evidence for combining three drugs is very limited. In one study the combination of long acting nitrates, beta blockers and CCBs was ineffective in improving exercise testing when compared to a combination of two of the drugs.<sup>69</sup>

1+

The patients included in these trials were mostly stable patients who perhaps did not require another drug to control their angina. They were usually tested as to whether adding another drug would reduce their existing angina, measured by the number of angina episodes, exercise tolerance and amount of glyceryl trinitrate used. In ‘real life’ situations patients are given a second or a third anti-anginal drug usually when they become refractory to one or two drugs. More randomised trials are needed to test the efficacy of adding a third anti-anginal drug to patients whose angina is not optimally controlled on a combination of two drugs.

Patients whose symptoms are not controlled on maximum therapeutic doses of two drugs should be considered for referral to a cardiologist.

3.3 DRUG INTERVENTIONS TO PREVENT NEW VASCULAR EVENTS

Patients with angina due to CHD are at risk of cardiovascular events and are eligible for secondary preventative treatments to lower their risk of cardiovascular disease (CVD). These interventions are considered in more detail in SIGN guideline 97 on risk estimation and the prevention of cardiovascular disease.<sup>73</sup>

3.3.1 ANTIPLATELET THERAPY

Evidence from 287 studies involving a total of 135,000 patients with cardiovascular disease including stable angina has shown that antiplatelet therapy, mainly with aspirin, given in a dose ranging from 75 to 150 mg daily led to a significant reduction in serious vascular events, non-fatal myocardial infarction, non-fatal stroke and vascular mortality.<sup>74</sup>

1++

Enteric coated products do not prevent the major gastrointestinal complications of aspirin therapy and are significantly more expensive than the standard dispersible formulation.<sup>75-77</sup>

1++  
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3.3.2 LIPID LOWERING THERAPY WITH STATINS

A meta-analysis of data from 14 randomised trials of statins involving 90,056 patients including patients with stable angina has shown the overall benefit of statin therapy. There was a significant reduction in all-cause and coronary mortality, myocardial infarction, the need for coronary revascularisation and fatal or non-fatal stroke.<sup>78</sup>

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**A All patients with stable angina due to atherosclerotic disease should receive long term standard aspirin and statin therapy.**

3.3.3 ACE INHIBITORS

The question of whether patients with stable angina but without left ventricular systolic dysfunction benefit from angiotensin-converting enzyme (ACE) inhibition is controversial. Four large RCTs were identified which addressed this topic although the results are conflicting.<sup>79-82</sup> When re-analysed in two meta-analyses of these and other trials, ACE inhibitors significantly reduced all cause and cardiovascular mortality.<sup>83,84</sup>

The HOPE study involved 9,297 high-risk patients with vascular disease or diabetes plus one other cardiovascular risk factor without history of heart failure or left ventricular dysfunction. It showed that ramipril was associated with significant reductions in all-cause mortality, myocardial infarction and stroke in these patients.<sup>79</sup> The use of perindopril in the EUROPA study involving 13,655 patients with stable coronary disease and no clinical evidence of heart failure reduced the risk of cardiovascular death, myocardial infarction or cardiac arrest.<sup>80</sup> This significant reduction in cardiovascular events is mainly due to the reduction in the incidence of non-fatal myocardial infarction. Unlike the HOPE study, the effect on all-cause mortality did not reach a statistically significant level. Subgroup analysis of the trial showed that benefit from perindopril is mainly in patients with history of myocardial infarction.

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Two other trials of ACE inhibitors did not show any benefit in patients with stable coronary heart disease. The PEACE trial using trandolopril of 8,290 patients with no history of clinical heart failure or echocardiographic evidence of left ventricular systolic dysfunction did not reveal any benefit on cardiovascular events although the event rate was unexpectedly low.<sup>81</sup> The study population in this trial was of lower risk and received more intensive treatment of risk factors than did those in the HOPE and EUROPA trials.

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A smaller trial (QUIET) of 1,750 patients with coronary heart disease and normal left ventricular function found that the ACE inhibitor quinapril did not significantly affect clinical outcomes or the progression of coronary atherosclerosis.<sup>82</sup> All patients recruited to this trial had undergone successful coronary angioplasty involving the revascularisation of at least one coronary artery.

A meta-analysis of six randomised trials, including 33,500 patients with coronary artery disease and preserved left ventricular systolic function showed that ACE inhibitors significantly reduced cardiovascular (relative risk, RR 0.83, CI 0.72 to 0.96, absolute risk reduction, ARR 0.86%,  $p=0.01$ ) and all-cause mortality (RR 0.87, CI 0.81 to 0.94, ARR 1.06%,  $p=0.0003$ ).<sup>83</sup>

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When the findings of the HOPE, EUROPA, and PEACE trials were combined in a meta-analysis of 29,805 patients, ACE inhibitors significantly reduced all-cause mortality (7.8 vs 8.9%,  $p=0.0004$ ), cardiovascular mortality (4.3 vs 5.2%,  $p=0.0002$ ), non-fatal myocardial infarction (5.3 vs 6.4%,  $p=0.0001$ ) and all stroke (2.2 vs 2.8%,  $p=0.0004$ ).<sup>84</sup> Although PEACE and QUIET, which did not show a benefit of ACE inhibitors among their populations, both recruited patients at apparently lower CVD risk, the PEACE trial was underpowered rather than affected by low cardiovascular event rates in the study population.

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Patients with left ventricular systolic dysfunction (LVSD) or heart failure are at higher risk than those included in HOPE, EUROPA or PEACE and will gain relatively more benefit from ACE inhibitor therapy.<sup>84</sup> Systematic reviews in patients with chronic heart failure or LVSD indicate absolute risk reductions ranging from 3.8 - 6%.<sup>85,86</sup> All patients with stable vascular disease are likely to derive some benefit from these drugs, to a degree approximately proportional to the level of baseline risk.

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**A** All patients with stable angina should be considered for treatment with angiotensin-converting enzyme inhibitors.

## 4 Interventional cardiology and cardiac surgery

### 4.1 CORONARY ARTERY ANATOMY AND DEFINITIONS

The three principal coronary arteries are the left anterior descending (LAD), circumflex (Cx) and right coronary arteries (RCA). The right and left coronary arteries arise from their respective coronary ostia just above the aortic valve. The RCA supplies the right side of the heart and typically terminates as the posterior descending coronary artery supplying the diaphragmatic (inferior) surface of the left ventricle. The left coronary artery continues for a variable distance up to 3 cm as the left main stem (LMS) before dividing into LAD and Cx coronary arteries. The left coronary artery branches supply the anterior and lateral walls of the left ventricle and the majority of the septum. The clinically important distributions of coronary artery disease are:

- left main stem disease
- single, double or triple vessel coronary artery disease (SVD,DVD,TVD) depending on the number of principal arteries diseased.

Multivessel disease typically refers to disease in more than one coronary artery and is not the same as TVD.

Following coronary angiography, and assessment of left ventricular function, patients may be considered for coronary revascularisation by PCI (percutaneous intervention) or CABG (coronary artery bypass grafting).

The principal indications for revascularisation are symptomatic relief and prognostic gain (increased life expectancy). Published guidelines<sup>87</sup> recommend revascularisation for prognostic and symptomatic benefit in patients with the following anatomy:

- significant LMS disease (> 50% stenosis), or
- proximal three vessel disease, or
- two vessel disease involving the proximal LAD.

The benefit is greatest in patients with left ventricular dysfunction and/or evidence of reversible ischaemia at low or moderate workloads on exercise testing.<sup>87,187</sup>

Although not receiving prognostic advantage, the following groups of patients may receive symptomatic benefit from surgical revascularisation:

- those with single vessel disease not involving the LAD<sup>88-90</sup>
- those with two vessel disease not involving the LAD.<sup>89-91</sup>

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### 4.2 CHOICE OF REVASCULARISATION TECHNIQUE

Following the decision to intervene, the major consideration is whether this should be undertaken by PCI or surgery. Coronary artery bypass grafting has historically been the first line option but with the development of stenting with PCI, the role of surgery has been challenged.

The choice of revascularisation technique involves careful consideration of medical and surgical suitability, but informed patient choice must be of primary concern. In the context of stable angina where any intervention is essentially elective, an adequate amount of time can be allocated to allow appropriate clinical decision making and fully informed patient decision making. Ideally, revascularisation options should be jointly considered by a multidisciplinary "Heart Team" involving discussion between cardiac surgeons, cardiac anaesthetists, interventional cardiologists and the patient.

- Coronary artery bypass grafting and percutaneous coronary interventions are both appropriate options for the alleviation of anginal symptoms.



## 4.2.1 PERCUTANEOUS CORONARY INTERVENTION

Percutaneous coronary intervention defines angioplasty or percutaneous transluminal coronary angioplasty (PTCA) where the artery is dilated by inflating a fine balloon. In addition, PCI includes stenting which involves dilating the artery by angioplasty and then inserting a fine lattice scaffold to prevent the artery from recoiling (uncoated stent). More than 90% of PCI procedures now involve implantation of one or more coronary stents. Stent technology is developing rapidly and stents may be impregnated with drugs to prevent or retard endothelialisation and reduce restenosis (coated, or drug eluting stents).

Several RCTs have shown that both sirolimus and paclitaxel coated stents reduce the need for repeat revascularisation by around 50% when compared to uncoated stents.<sup>92-94</sup> One large RCT shows no difference in repeat revascularisation or major cardiac event rates between sirolimus and paclitaxel coated stents.<sup>95</sup> Coated stents delay re-endothelialisation and for this reason dual antiplatelet therapy (aspirin plus clopidogrel) is recommended for periods of at least three to six months post procedure as opposed to only four weeks for uncoated stents (see sections 5.2 and 5.3.4).

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There are anecdotal reports of late stent thrombosis even after this time period but no overall excess in the incidence of stent thrombosis has been shown in any RCT.

## 4.2.2 CORONARY ARTERY BYPASS GRAFTING

Coronary artery bypass grafting has been used for over three decades to bypass coronary stenoses. It is a major surgical procedure with a low mortality which involves the bypassing of a section of coronary artery narrowed by atheroma with a section of healthy saphenous vein or internal mammary artery. In the UK Cardiac Surgical Register (UKCSR) for 2003 the overall 30 day mortality was 2.0%.<sup>96</sup> This includes salvage procedures performed in patients who may have died even if surgery had not been undertaken.

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Coronary artery bypass grafting may be performed using cardiopulmonary bypass where a pump and oxygenator perform the role of the heart and lungs and permit the surgeon to operate on a still non-beating, protected heart. This "on-pump" surgery was considered to be responsible for some of the deleterious effects following CABG such as cognitive dysfunction or exaggerated systemic inflammatory response, and consequently off-pump coronary artery bypass surgery has emerged as a technique to perform CABG without cardiopulmonary bypass. Although considered minimally invasive, the procedure still involves a chest incision. Minimally invasive direct coronary bypass surgery attempts to reduce the major skin incision but its use is not widespread.

## 4.2.3 REVASCULARISATION TO RELIEVE ANGINA

Nine trials were identified which compare CABG with PCI without stenting<sup>97-105</sup> and a further six which compare CABG with PCI utilising a stent.<sup>106-111</sup>

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Patient groups known to benefit from CABG, eg those with LMS disease, were excluded from these trials and although 11 claimed to be trials of multivessel PCI, only around 35% of randomised patients in these multivessel trials had TVD. In all trials but one,<sup>107</sup> patients had good left ventricular function and patients with diabetes accounted for around 15% of the total.

Up to three years post intervention, studies demonstrate that PCI with uncoated stents has equivalent event rates for death, non-fatal MI and stroke to CABG. Although surgery is superior for freedom from angina and the need for repeat revascularisation, this has to be balanced against the invasive nature of CABG. In the trials comparing PCI with CABG, the average number of vessels revascularised is less in the PCI group. Incomplete revascularisation has deleterious effects on long term survival although this may be attenuated by improved secondary prevention.<sup>112</sup> Coronary artery bypass grafting is the preferred option if PCI cannot offer an equivalent degree of revascularisation.

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**Patients who have been assessed and are anticipated to receive symptomatic relief from revascularisation should be offered either coronary artery bypass grafting or percutaneous coronary interventions.**

4.2.4 REVASCULARISATION TO IMPROVE LONG TERM PROGNOSIS

Patients with significant left main stem stenosis were excluded from randomised controlled trials leaving no evidence to support the role of PCI to improve long term outcome in this group. In patients with multivessel disease, there is no robust evidence for a survival benefit with CABG. One meta-analysis showed a 1.9% absolute survival advantage in favour of CABG over PCI for all trials at five years ( $p < 0.02$ ), but no significant advantage at one, three, or eight years.<sup>113</sup> Given the absence of significant effect over a wider follow up period, it is possible that the apparent interim survival advantage may be due to a statistical anomaly. Patients randomised to PCI had more repeat revascularisations at all time points (risk difference; RD, 24% to 38%,  $p < 0.001$ ). With the use of stents, this RD was reduced to 15% at one and three years. As stenting was not available at the time some trials were carried out, a subgroup analysis was undertaken to analyse possible differences in results of CABG vs PCI with and without stenting. At three years, PCI with stent provided a statistically significant reduction in non-fatal MI compared to CABG (RD -2.9%, 95% CI -5.1 to -0.6%;  $p = 0.01$ ). Although subsequent revascularisation was still more frequent after PCI with stent than after CABG, the risk difference for revascularisation in trials with stents was about half that observed in trials without stents.

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For patients with diabetes, CABG provided a significant survival advantage over PCI at four years but not at 6.5 years. This subgroup analysis included patients from the trials using PCI alone making it less relevant to current practice. In the trials of uncoated stents PCI patients still had more repeat revascularisations at three years: risk difference 15% (95% CI 10 to 28%).

One meta-analysis comparing CABG with PCI in isolated LAD disease demonstrated CABG was associated with reduced multiple adverse cardiac events, reduced mortality and myocardial infarction at a median follow up of three years. In this study, which included both RCTs and observational data, six of the eight randomised trials used minimally invasive techniques and one study involved coated stents.<sup>114</sup>

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The BARI trial is the single largest randomised controlled trial of CABG vs PCI. The PCI arm did not use stents. Results compared various subsets of patients shown to derive prognostic benefit in previous RCTs of CABG vs medical therapy. These subsets were three vessel disease with or without left ventricular (LV) dysfunction (left ventricular ejection fraction, LVEF  $< 50\%$ ), and two vessel disease including the proximal LAD with or without LV dysfunction. After seven years of follow up there were no statistically significant mortality differences between CABG and PCI, even in patients with diabetes.<sup>115</sup>

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Well designed randomised controlled trials give statistically valid data in a highly selected group of patients but frequently less than 20% of eligible patients are randomised. Registry studies do not have the same statistical weight as RCTs as patients are not randomised, but they may provide an insight to current practice in a more clinically representative population.

Registry studies suggest that CABG results in better long term survival in patients with multivessel disease compared to PCI with stenting. They also confirm the need for repeat revascularisation in the PCI group.<sup>116,117</sup> One registry and one cohort study demonstrate increased long term mortality in patients with diabetes treated by PCI.<sup>118,119</sup>

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Further registry data show a reduction in long term mortality in those patients with severe proximal LAD disease who underwent CABG.<sup>116</sup> The stent usage in this registry was low. All studies confirm that CABG provides better relief of angina and less need for re-intervention.<sup>120,121</sup>

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- A** Patients with significant left main stem disease should undergo coronary artery bypass grafting.
- A** Patients with triple vessel disease should be considered for coronary artery bypass grafting to improve prognosis, but where unsuitable be offered percutaneous coronary intervention.
- A** Patients with single or double vessel disease, where optimal medical therapy fails to control angina symptoms, should be offered percutaneous coronary intervention or where unsuitable, considered for coronary artery bypass grafting.

## 4.2.5 CHOICE OF CONDUIT IN SURGICAL REVASCULARISATION

Long term patency rates in excess of 95% beyond ten years have been reported for anastomosis of the left internal mammary artery (IMA) to the LAD. This superior long term patency compared to saphenous vein grafts (SVG) leads to significant reduction in long term mortality, subsequent myocardial infarction, the need for further operation and freedom from late cardiac events.<sup>122,123</sup>

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Reports on the use of both IMAs have reinforced the benefits of arterial revascularisation. In patients where both IMAs were used, there was marginally improved long term survival at five, ten and 15 years (94%, 84% and 67% for bilateral IMA and 92%, 79% and 64% for single IMA). This prognostic benefit was accompanied by a reduced need for re-operation and PCI.<sup>124-126</sup>

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The radial artery is also a suitable conduit and may be used as a free graft applied to the aorta or as a composite "Y" graft from a left IMA. Five year angiographic patency in a small number (n = 50) of asymptomatic patients was 89% for radial artery with IMA patency exceeding 94% and SVG patency of 92%.<sup>127</sup>

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In one randomised trial of total arterial revascularisation (TAR) comparing IMA and SVG grafts at one year, angina recurrence, the need for reintervention with PCI and actuarial freedom from cardiac events were less in the TAR group. Angiography demonstrated SVG patency at around 90%.<sup>128</sup>

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The results of SVG patency may reflect the importance of secondary preventative therapy. Some studies have noted an increased rate of stenosis of radial artery grafts and have cautioned on their applicability in target vessels with only moderate stenosis. Total arterial revascularisation may confer long term benefit but application of the radial artery graft to sub-critical stenoses may not confer benefit.<sup>129-131</sup>

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**D Patients undergoing surgical revascularisation of the left anterior descending coronary artery should receive an internal mammary artery graft, where feasible.**

## 4.2.6 COST EFFECTIVENESS OF REVASCULARISATION TECHNIQUES

Several studies have compared the cost effectiveness of CABG and PCI.<sup>132-142</sup> The primary outcome in these studies was change in resource use (initial cost of procedure and future resources required, particularly those associated with revascularisation); the type and numbers of repeat revascularisation following the initial procedure was the key source of variability across studies.

Although the studies have different inclusion and exclusion criteria and have used different timeframes and costing techniques, the evidence suggests that CABG is the more expensive technology for the initial in-hospital stay and during the first few years of follow up. Thereafter the need for repeat revascularisation erodes the initial cost advantage of PCI so that by five years following any procedure the cost differences are unlikely to be significant.

Careful patient selection can improve cost effectiveness, with patients with two vessel disease having significantly lower cost long term (five to eight years) for PCI than CABG; whilst CABG is more cost effective in patients with severe multivessel disease.

Only one of these studies used drug eluting stents<sup>140</sup> and this limits the generalisability of the evidence to a setting which has a high utilisation of such stents.

The seven cost effectiveness studies comparing coated stents with uncoated stents<sup>140,143-148</sup> showed that using coated stents was only cost effective for a minority of patients who were at high risk of an adverse event such as those with multivessel disease or complex lesions.

### 4.3 POST INTERVENTION DRUG THERAPY

With the diagnosis of CVD, secondary prevention medication is mandatory and should include cholesterol lowering therapy usually with a statin, antiplatelet therapy and, if appropriate, antihypertensive and hypoglycaemic medications (see section 3.3 and SIGN guideline 97 on risk estimation and the prevention of cardiovascular disease).<sup>73</sup> Following CABG, aspirin (75-300 mg daily) is the routinely prescribed antiplatelet medication.<sup>149</sup> The administration of aspirin within 48 hours of CABG was associated with a 48% reduction in MI and a 50% reduction in stroke. The mortality in those receiving early aspirin was 1.3% compared to 4% amongst those who did not.<sup>150</sup> The Society of Thoracic Surgeons has recommended that aspirin should be stopped for three to five days before elective CABG and then restarted early after surgery.<sup>151</sup> In those intolerant of aspirin, clopidogrel (75 mg daily) should be considered.

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No evidence was identified for the use of dual antiplatelet therapy following PCI in patients with stable angina. Following PCI, there is evidence to support the use of daily aspirin (75 mg) combined with clopidogrel (75 mg) for one month in patients with acute coronary syndrome. One trial showed that long term administration of clopidogrel after PCI (mean length eight months) was associated with a lower rate of cardiovascular death, myocardial infarction, or any revascularisation ( $p=0.03$ ), and of cardiovascular death or myocardial infarction ( $p=0.047$ ) compared to placebo.<sup>152</sup> Dual therapy is associated with higher operative bleeding than single antiplatelet therapy.<sup>153</sup> The American College of Cardiology (ACC)/American Heart Association (AHA) guideline on percutaneous coronary intervention suggests that for coated stents the duration of therapy should be extended up to six months depending on the stent used.<sup>154</sup>

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No evidence was identified for the use of long term beta blockers for asymptomatic patients following CABG.

In all patients with evidence of left ventricular impairment, optimal medical therapy should include use of an ACE inhibitor (or angiotensin II receptor blocker if intolerant) and consider the use of beta blockers and further renin-angiotensin-aldosterone blockade (see SIGN guideline 95 on the management of chronic heart failure).<sup>48</sup>

### 4.4 POST INTERVENTION REHABILITATION

SIGN guideline 57, cardiac rehabilitation, recommends that patients who have undergone coronary revascularisation should receive comprehensive rehabilitation.<sup>155</sup>

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### 4.5 EFFECT OF ON-/OFF-PUMP CORONARY ARTERY BYPASS GRAFTING ON COGNITIVE IMPAIRMENT

The use of off-pump surgical techniques developed, in part, as a method of reducing potential cognitive impairment after surgery (see section 6.3). A meta-analysis comparing off-pump with conventional on-pump CABG did not demonstrate any significant differences in 30 day mortality, myocardial infarction, stroke or renal dysfunction but did show a reduced incidence of atrial fibrillation, transfusion, inotrope requirements with reduced length of ventilation time and intensive care unit (ITU) and hospital stay. The results for graft patency and neurocognitive function were inconclusive.<sup>156</sup> Two good quality RCTs were identified which indicate a benefit of off-pump surgery in reduction of cognitive impairment at three months for patients with one to three vessels bypassed, which is not sustained at 12 months (decline 21% in off-pump group and 29% in on-pump group at three months, 31% and 33% respectively at 12 months).<sup>157,158</sup> One cohort study also found a slight benefit for off-pump surgery at six months in younger patients.<sup>159</sup>

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A study looking at on- and off-pump surgical groups with cardiac and healthy controls found no evidence of cognitive decline at three or 12 months on objective testing, but significant baseline differences between surgical and non-surgical control groups in self reported cognitive problems. The study concludes that CABG patients, like similar patients with long-standing coronary artery disease, have some degree of cognitive dysfunction secondary to cerebrovascular disease before surgery.<sup>160</sup>

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In contrast, one RCT found no significant decline in cognitive function in either group immediately after surgery and at two and a half months.<sup>161</sup>

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Several variables appear to influence outcomes. Age did not predict decline in cognitive function although the patients tended to be relatively young (in their sixties).<sup>162</sup> Patients may have marked pre-surgical deficits which mask the potential effect on cognitive function of type of surgery.<sup>161</sup> Further evidence of the effect of CABG on cognitive function is reviewed in section 6.3.4.

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**A** Off-pump coronary artery bypass grafting should not be used as the basis of providing long term protection against cognitive decline.

## 4.6 MANAGING RESTENOSIS

Restenosis rates following uncoated stenting have been reduced, but not eliminated, by the use of coated stents.<sup>163</sup> No evidence was identified on which to base recommendations on the treatment of restenosis, although both CABG and PCI with coated stents may be considered.

## 4.7 MANAGING REFRACTORY ANGINA

Refractory angina can be defined as persisting unsatisfactory control of anginal symptoms despite maximal tolerated medical therapies and without further revascularisation options.

### 4.7.1 COGNITIVE BEHAVIOUR AND REHABILITATIVE APPROACHES TO MANAGEMENT

SIGN guideline 57 on cardiac rehabilitation recommends that patients with stable angina should be referred for rehabilitation if they have limiting symptoms and after revascularisation.<sup>155</sup> Patients presenting with refractory angina have often not received a comprehensive rehabilitation programme, which may improve management of symptoms. The initial treatment of these patients should follow an educational and rehabilitative approach, progressing to a cognitive behaviour approach where appropriate. The latter has demonstrated positive outcomes in both angina and chronic pain.<sup>164,165</sup> These approaches should be taken prior to considering the use of transcutaneous electrical nerve stimulation (TENS), temporary sympathectomy, use of opioids, destructive sympathectomy, and other interventions such as spinal cord stimulation, (see section 4.7.2) surgical transmyocardial revascularisation, (see section 4.7.3) and enhanced external counterpulsation (see section 4.7.4).

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**D** Patients with refractory angina may benefit from an educational and rehabilitation approach based on cognitive behaviour principles prior to considering other invasive treatments.

### 4.7.2 SPINAL CORD STIMULATION

This method consists of inserting a stimulating electrode into the thoracic epidural space under local anaesthetic with the final position of the electrode being determined by the patient's sensation of paraesthesia in the area where the angina pain is usually felt. One small randomised trial lasting six weeks showed a reduction in angina attacks ( $p=0.01$ ).<sup>166</sup> In this study although the control group had an inactive stimulator it is not possible to remove the bias of the lack of paraesthesia induced by the neurostimulator.

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## 4.7.3 SURGICAL TRANSMYOCARDIAL REVASCULARISATION

This procedure consists of using a laser to create between 20-40 one millimetre transmural channels in the exposed left ventricle. Suggested effects are the promotion of angiogenesis, restoring blood supply to the myocardium or destroying its innervation.

A meta-analysis of seven trials compared laser surgical transmyocardial revascularisation (TMR) plus continuing maximal medical therapy with continuing medical therapy alone in patients with ongoing symptoms but not amenable to revascularisation intervention. Overall, there was a non-significant reduction in survival after one year with TMR (odds ratio; OR, 1.17, 95% CI 0.74 to 1.83,  $p=0.75$ ), although angina class improvement was significantly better with TMR (OR 0.10, 95% CI 0.06 to 0.17,  $p<0.0001$ ).<sup>167</sup> In this type of trial with the lack of a sham procedure there is a built in bias towards a placebo effect and masking is impossible.

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One trial, based in the UK, showed a decrease of CCS score for angina of at least two classes in 25% of those receiving the procedure as opposed to 4% of patients receiving medical management alone at 12 months ( $p<0.001$ ). The operative risks need to be balanced against the potential benefits of moderate improvement in angina and only minimal improvement in exercise capacity ( $p=0.152$ ).<sup>168</sup>

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## 4.7.4 ENHANCED EXTERNAL COUNTERPULSATION

Enhanced external counterpulsation (EECP) involves the use of compressed air applied via cuffs to the patient's lower extremities in synchrony with the cardiac cycle. In early diastole, pressure is applied sequentially from the lower legs to the lower and upper thighs to propel blood back to the heart. This results in an increase of arterial blood pressure and retrograde aortic blood flow during diastole (diastolic augmentation). At end-diastole, air is released instantaneously from all the cuffs to remove the externally applied pressure, allowing the compressed vessels to reconform, thereby reducing vascular impedance.

One RCT showed that when comparing EECP and placebo, exercise duration increased in both groups, but the between-group difference was not significant ( $p>0.3$ ).<sup>169</sup> Time to  $\geq 1$ -mm ST-segment depression increased significantly from baseline in EECP compared with placebo ( $p=0.01$ ). More EECP patients reported a decrease and fewer experienced an increase in angina episodes as compared with placebo patients ( $p<0.05$ ). Glyceryl trinitrate usage decreased in EECP but did not change in the placebo group. The between-group difference was not significant ( $p>0.7$ ).

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## 5 Stable angina and non-cardiac surgery

Patients with coronary heart disease undergoing non-cardiac surgery are at increased risk of adverse cardiac events.<sup>170</sup> Perioperative conditions such as stress, tachycardia, hypovolaemia, hypotension, hypertension, anaemia, hypothermia, acute pain and hypercoagulable states can all affect the myocardium and coronary microcirculation and may precipitate myocardial infarction, myocardial ischaemia or significant arrhythmias. These cardiac events are associated with increased mortality and morbidity, length of stay and consequent higher costs. Prevention of perioperative cardiac complications is considered a priority and has been the subject of practice guidelines.<sup>171</sup> Patients who develop postoperative ischaemic events such as myocardial infarction or ischaemia are at increased risk of developing adverse cardiac outcomes within two years following surgery.<sup>172</sup>

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### 5.1 ASSESSMENT PRIOR TO SURGERY

An assessment of the risk of serious cardiac complications requires teamwork and good communication between surgeons, anaesthetists and physicians/cardiologists. This may be facilitated by preoperative clinics. Assessment for surgery should consider the inherent procedural risk, patient-specific factors and functional capacity. As myocardial ischaemia is an important predictor of major adverse cardiac events after non-cardiac surgery, a full clinical history and examination and resting electrocardiogram should be assessed.<sup>171</sup> Patients at increased risk may undergo additional risk stratification usually by exercise tolerance test.<sup>171</sup> Where this is impractical other non-invasive tests such as stress echocardiography or myocardial perfusion scintigraphy could be considered. Coronary angiography may be indicated where a high risk is identified and is the investigation of choice to define the coronary anatomy.

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Other patient-specific factors are listed in Table 2. The ACC/AHA guidelines on perioperative cardiovascular evaluation for non-cardiac surgery include a full discussion of preoperative assessment.<sup>171</sup>

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Table 2: Clinical predictors of major perioperative cardiovascular risk

#### Patient-specific risk factors

- Acute or recent myocardial infarction \*
- Unstable or severe angina
- Decompensated heart failure
- Significant arrhythmias
- Severe valvular heart disease

Adapted from American Heart Association/American College of Cardiology guidelines<sup>171</sup>

\* Acute myocardial infarction is defined as occurring within seven days of surgery and recent infarction occurring between seven days and one month of surgery.

If a recent stress test does not indicate residual myocardium is at risk, the likelihood of reinfarction is low and although no adequate clinical trials have been identified it seems reasonable to wait four to six weeks after MI to perform elective surgery. Historical recommendations to wait six months after MI before elective surgery are unsupported by evidence and the major determinant of risk is the amount of residual at-risk myocardium.<sup>171,173</sup>

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## 5.1.1 RISK SCORING SYSTEMS

The discovery of major risk factors before non-cardiac surgery will usually result in postponement of surgery and the investigation and treatment of that problem. Procedural risk should also be quantified (see *Table 3*), to help select patients who may benefit from further evaluation or investigation.

*Table 3: Surgical procedures stratified by cardiac risk level*

<b>HIGH RISK PROCEDURES reported cardiac risk &gt; 5%</b>
Emergency major operations, particularly in the elderly
Aortic and other major vascular surgery
Peripheral vascular surgery
Anticipated prolonged surgical procedures associated with large fluid shifts and/or blood loss
<b>INTERMEDIATE RISK PROCEDURES reported cardiac risk generally &lt; 5%</b>
Carotid endarterectomy
Head and neck surgery
Intraperitoneal and intrathoracic surgery
Orthopaedic surgery
Prostate surgery
<b>LOW RISK PROCEDURES reported cardiac risk generally &lt; 1%</b>
Endoscopic procedures
Superficial procedures
Cataract surgery
Breast surgery



The Revised Cardiac Risk Index (RCRI) is a simple risk stratification tool which combines patient risk and procedural risk and can aid clinical decision making (see *Table 4*).<sup>170</sup> In this report of the risk of major cardiac complications with major non-emergency, non-cardiac surgery, six factors with approximately equal prognostic importance were identified.

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*Table 4: Revised Cardiac Risk Index*

Clinical factors
High risk surgery
History of ischaemic heart disease
History of congestive heart failure
History of cerebrovascular disease
Preoperative insulin treatment
Preoperative creatinine > 180 micromol/l.

The rates of major cardiac complications postoperatively with 0, 1, 2, 3 or more risk factors were 0.5%, 1.3%, 4% and 9% respectively.

High risk surgery is defined as intraperitoneal, intrathoracic, or suprainguinal vascular procedures. A history of CHD is defined as any of the following: a history of MI, positive exercise tolerance test, current complaint of chest pain of ischaemic origin, use of nitrate therapy or pathological Q waves on ECG. Patients with prior revascularisation are only classified as having CHD if they have one of the above criteria.

Patients identified at high risk of cardiac complications using the RCRI may undergo further risk stratification with non-invasive testing or other risk reduction management strategies. These risk reduction strategies may involve preoperative revascularisation or medical therapy.<sup>174</sup> Those identified as low risk may proceed to surgery. The Revised Cardiac Risk Index has been modified for patients having vascular surgery.<sup>175</sup>

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The urgency of the surgical procedure and the presence of recent cardiac investigations will influence the decision on whether further cardiac investigations are appropriate. Clinical circumstances will determine whether a delay for investigation and preoperative optimisation can be justified.

Additional information can be derived from the functional capacity of patients and non-invasive tests such as exercise ECG tolerance testing, stress echocardiography and MPS. In general, indications for preoperative coronary angiography are similar to the non-operative setting. These are patients with known or suspected CHD and:

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- evidence of high risk of adverse outcome based on non-invasive test results, or
- unstable angina facing intermediate or major types of non-cardiac surgery, or
- equivocal non-invasive test results in a patient with high clinical risk undergoing high risk non-cardiac surgery.<sup>171</sup>

The risk of cardiac complications is significant (4% or greater) in patients undergoing high risk surgery and who have at least one CHD risk factor (see Table 4). These individuals should generally be considered for further investigation. Some combinations of risk factors may not predispose the individual to equal levels of risk for cardiac complications and clinical judgement should be used to stratify patients accordingly.

**B** As part of the routine assessment of fitness for non-cardiac surgery, a risk assessment tool should be used to quantify the risk of serious cardiac events in patients with coronary heart disease.

**B** Patients undergoing high risk surgery who have a history of coronary heart disease, stroke, diabetes, heart failure or renal dysfunction should have further investigation by either exercise tolerance testing or other non-invasive testing or coronary angiography, if appropriate.

Where a high risk is identified, a strategy for risk reduction should be agreed. This will require teamwork and good communication between surgeon, anaesthetist, physician/cardiologist and patient.

5.1.2 FUNCTIONAL CAPACITY

Functional capacity has been shown to predict perioperative and long term cardiac events and should be part of the preoperative assessment of patients with CHD undergoing major surgery.<sup>181,182</sup>

Functional capacity can be expressed in metabolic equivalents of task (METs). One MET is the oxygen consumption of a 40 year old 70 kg man at rest and is equal to 3.5 ml/min/kg. Patients who are unable to meet a four MET demand during most normal daily activities are at increased risk of perioperative and long term cardiac events.<sup>176</sup>

4

Different scoring systems are available to measure functional capacity objectively such as the NYHA Score,<sup>177</sup> Karnofsky Performance Scale<sup>178</sup> or the Duke Activity Score which is a self completed questionnaire using a set of common daily living items.<sup>179</sup> Simple exercise testing may further refine risk assessment. The failure to climb two flights of stairs, which is the equivalent of > four METs, is a good predictor of mortality associated with thoracic surgery and complications after major non-cardiac surgery.<sup>180</sup>

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Cardiopulmonary exercise testing has been used to identify high risk groups for major non-cardiac surgery. The measurement of anaerobic threshold (AT) may be a better predictor than the maximum oxygen consumption (VO<sub>2</sub> max) as it is more independent of patient motivation.<sup>181,182</sup> In elderly patients undergoing major abdominal surgery, a group of patients with an AT of < 11 ml/kg/min (three METs) had a higher mortality rate when compared to the group with an AT > 11 ml/kg/min. The anaerobic threshold is a better measure of the ability to meet the demands of prolonged stress associated with major surgery than VO<sub>2</sub> max. The anaerobic threshold may vary in any individual between 50% to 100% of the VO<sub>2</sub> max.

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Further studies are necessary to evaluate the cost effectiveness and clinical utility of cardiopulmonary exercise testing as a means of risk assessment before major surgery. Simple assessment of functional capacity by patient questionnaires and simple exercise testing such as stair climbing in thoracic surgery are valuable.<sup>179,180</sup> Many hospitals in Scotland do not have access to cardiopulmonary exercise testing.

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**D** An objective assessment of functional capacity should be made as part of the preoperative assessment of all patients with coronary heart disease before major surgery.

## 5.2 PREOPERATIVE REVASCULARISATION

Data from the Coronary Artery Surgery Study (CASS) registry confirmed that clinically stable patients ( $n = 1,297$ ) undergoing low risk surgery (urology, orthopaedic, breast, and skin surgery) had a low mortality ( $< 1\%$ ) regardless of prior coronary treatment.<sup>183</sup> Those ( $n = 1,961$ ) undergoing high risk surgery (abdominal, vascular, thoracic and head and neck surgery) had a combined MI/death rate among patients with non-revascularised CHD of  $> 4\%$ . Among these prior CABG was associated with fewer deaths (1.7% vs 3.3%) and myocardial infarctions (0.8% vs 2.7%) compared to medically managed coronary disease. These patients were enrolled between 1974 and 1979 and the results may not be applicable to contemporary practice.

3

The Coronary Artery Revascularisation Trial randomly assigned patients at risk for perioperative cardiac complications and clinically significant coronary heart disease to undergo either revascularisation or no revascularisation before elective major non-cardiac vascular surgery.<sup>184</sup> At 2.7 years after randomisation, mortality was 22% in the revascularisation group and 23% in the no revascularisation group. These results conflict with the CASS study and may reflect the bias of observational studies or that major vascular surgery is high risk and that advances in medicine resulted in many of the patients in the no revascularisation group receiving beta blockers, statins, aspirin and ACE inhibitors. After coronary catheterisation patients with significant left main stenosis (54 patients), poor left ventricular function (11 patients) and severe aortic stenosis (eight patients) were excluded from this study. Only 31% of the no revascularisation group had triple vessel disease.

1+

Preoperative CABG will be appropriate for only a minority of patients as the procedure carries a significant risk of mortality (around 3%) and morbidity, and these risks must be added to those of the coronary angiography and the non-cardiac surgery itself. Compared to case-matched controls, patients who underwent non-cardiac vascular surgery within a month of CABG suffered significantly greater mortality (20.6% vs 3.9%,  $p < 0.005$ ).<sup>185</sup> A significantly higher risk of cardiac complications (27%) was found in patients undergoing non-cardiac procedures in the first month after CABG.<sup>186</sup> This remained higher (17%) until the sixth month following CABG.

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Although definitive evidence for a safe period to delay non-cardiac surgery after CABG is lacking, it seems prudent to avoid elective non-cardiac surgery for at least one month and possibly up to six months. The timing of surgery will depend on the balance of risks and benefits which, in an individual patient, will depend on the severity of the coronary artery disease and the nature and urgency of the non-cardiac surgery.

Overall survival benefit is seen only in patients who would warrant CABG surgery independently of their major non-cardiac surgery. These indications are significant left main stenosis, triple vessel disease in conjunction with LV dysfunction, two vessel disease including proximal LAD, and unstable symptomatic CHD despite full medical therapy.<sup>187</sup> When time allows these patients may be offered preoperative CABG.

4

There is no evidence for the use of prophylactic percutaneous coronary intervention before non-cardiac surgery in patients with stable angina.

In the absence of any other data, indications for PCI are essentially identical to the non-operative setting, which are the relief of anginal symptoms resistant to medical therapy. Patients who have had PCI and stent insertion are at risk of stent thrombosis if their dual antiplatelet therapy is discontinued.<sup>188,189</sup> The risk of cardiac complications after non-cardiac surgery is greater if a recent ( $< 35$  days) coronary artery stent has been inserted compared to  $> 90$  days.<sup>190</sup>

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The combination of aspirin and clopidogrel increases the risk of bleeding during CABG, which may also be increased postoperatively.<sup>191,192</sup>

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There is limited evidence regarding the best time delay after PCI before proceeding to non-cardiac surgery. Following balloon angioplasty, at least one week should be left to allow healing of the traumatised vessel wall. After a bare metal stent insertion, four weeks of dual antiplatelet therapy are required. A delay of six weeks before non-cardiac surgery has been recommended by which time bare metal stents are generally re-endothelialised and clopidogrel can be discontinued.<sup>188,189</sup> Drug eluting stents delay re-endothelialisation and dual antiplatelet therapy (aspirin plus clopidogrel) must be continued for at least three months after sirolimus stents and six months after paclitaxel stents.<sup>193,194</sup> Thereafter, clopidogrel can be discontinued.

3

Elective non-cardiac surgery should be deferred until dual antiplatelet therapy is no longer required, to minimise the perioperative risks of bleeding and in-stent thrombosis.<sup>188</sup> If surgery cannot be delayed, dual antiplatelet therapy should be continued if possible.<sup>195</sup> Premature discontinuation of antiplatelet therapy is associated with a very high risk of stent thrombosis which is often fatal. The bleeding risk of the proposed emergency surgical procedure must be extremely high and the disease requiring surgery must be life threatening to justify stopping the antiplatelet agents.<sup>151</sup>

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**D** Coronary artery bypass grafting is not recommended before major or intermediate risk non-cardiac surgery unless cardiac symptoms are unstable and/or coronary artery bypass grafting would be justified on the basis of long term outcome.

**D** If emergency or urgent non-cardiac surgery is required after percutaneous coronary intervention, dual antiplatelet therapy should be continued whenever possible. If the bleeding risk is unacceptable and antiplatelet therapy is withdrawn, it should be reintroduced as soon as possible after surgery.

The indications used for revascularisation prior to non-cardiac surgery should be those used in the non-operative setting.

Where possible, non-cardiac surgery should be delayed for at least one month after coronary artery bypass grafting. When deciding when to operate, the balance of risks and benefits in an individual patient will depend on the severity of the coronary artery disease and the nature and urgency of the non-cardiac surgery.

### 5.3 DRUG THERAPY IN ANGINA PATIENTS UNDERGOING NON-CARDIAC SURGERY

In one study of histological analysis in patients who had suffered fatal postoperative MI, plaque rupture had occurred in almost half of the cases. This was commonly associated with multivessel coronary heart disease. The pathological findings are similar to myocardial infarction in the non-operative setting.<sup>196</sup> Most postoperative myocardial infarctions were associated with non-Q wave infarcts and were asymptomatic.<sup>197</sup> The risk of non-cardiac surgery in patients with stable angina can be minimised by optimising medical therapy in the perioperative period.

3

#### 5.3.1 BETA BLOCKERS

Beta blockers are an effective treatment for angina and are known to reduce mortality after MI and in stable heart failure.<sup>198</sup> It has been suggested that they may reduce the rate of perioperative MI and cardiac death. Beta blockers prolong coronary filling time and may prevent fatal ventricular arrhythmias and atheromatous plaque rupture in the presence of high sympathetic nervous system drive.

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A meta-analysis of 11 RCTs involving 694 surgical patients taking a beta blocker and undergoing non-cardiac surgery showed that beta blocker use was associated with a 75% relative reduction in risk of death from cardiac causes (OR 0.25, 95% CI 0.09 to 0.73; ARR 3.1%; number needed to treat, NNT 32).<sup>199</sup>

1++

Another meta-analysis of beta blocker use in patients undergoing non-cardiac surgery did not show any statistically significant beneficial effects on any individual cardiovascular endpoint. There was a 56% reduction in relative risk (5.02% absolute risk reduction, RR 0.44, 95% CI 0.20 to 0.97) for the composite outcome of cardiovascular mortality, non-fatal myocardial infarction, and non-fatal cardiac arrest. Beta blockers may reduce the risk of major perioperative cardiovascular events but increase the risk of bradycardia and hypotension needing treatment in patients having non-cardiac surgery. Caution is required in the interpretation of these results as only a moderate number of events occurred in the perioperative beta blocker trials and there was statistical heterogeneity.<sup>200</sup>

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The DECREASE trial studied 112 high risk patients with positive results of dobutamine stress echocardiography undergoing vascular surgery.<sup>201</sup> Those receiving bisoprolol at least one week preoperatively and continued for 30 days after surgery had a reduction of 90% in the primary endpoint of death from cardiac causes or non-fatal myocardial infarction which occurred in two patients in the bisoprolol group (3.4%) and 18 patients in the standard care group (34%,  $p < 0.001$ ). Another RCT found that atenolol administered intravenously 30 minutes before surgery and orally thereafter in high risk male patients reduced ischaemia but not cardiac death risk or MI during hospitalisation but did improve survival up to two years after discharge.<sup>202</sup>

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Another small RCT in patients undergoing vascular surgery showed that intravenous esmolol infusion from surgical recovery for 48 hours reduced the incidence of ischaemia. Ischaemia persisted in the postoperative period in eight of 11 patients taking placebo (73%), but only five of 15 patients taking esmolol (33%,  $p < 0.05$ ).<sup>203</sup>

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In summary, several RCTs and one meta-analysis have demonstrated that beta blockers reduce the incidence of intraoperative myocardial ischaemia and in high risk groups may reduce the risk of adverse cardiac events such as myocardial infarction and cardiac death after surgery. There is still a debate in the literature regarding which patients will benefit from beta blockade and on the optimal method of administration. The withdrawal of beta blocker therapy is associated with increased risk. A large international study which addresses the perioperative use of beta blockers is underway.

In a retrospective review of 782,969 patients beta blocker treatment was associated with significant reductions in mortality in the highest risk patients (RCRI score of three or greater) but was of no benefit among the lowest risk categories (those with a score of zero or one).<sup>204</sup>

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Generally, if time allows, it would seem safer to introduce the beta blocker in advance and allow time for dose titration and assessment of tolerance. Acute withdrawal of beta blockers in the postoperative period may increase the risk of postoperative cardiac complications.<sup>205</sup>

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SIGN guideline 77 on postoperative management in adults<sup>206</sup> and the American College of Cardiology/American Heart Association guideline on perioperative beta blocker therapy<sup>207</sup> recommend continuation of established beta blockade in patients undergoing surgery.

4

**A Preoperative beta blocker therapy should be considered in patients with coronary heart disease undergoing high or intermediate risk non-cardiac surgery who are at high risk of cardiac events.**

Where possible beta blockers should be started days or weeks in advance of surgery to allow for dose titration and to assess tolerance.

**B Pre-existing beta blocker therapy should be continued in the perioperative period.**

### 5.3.2 ALPHA 2 AGONISTS

Alpha 2 agonists inhibit the sympathetic outflow, reduce peripheral noradrenaline release and dilate post stenotic coronary arteries and may be beneficial in the perioperative setting. One meta-analysis identified 23 studies comprising 3,395 patients. Alpha 2 agonists significantly reduced mortality (RR 0.47; 95% CI 0.25 to 0.90; ARR 1.9%;  $p = 0.02$ ) and myocardial infarction (RR = 0.66; 95% CI 0.46 to 0.94; ARR 3.3%;  $p = 0.02$ ) after vascular surgery.<sup>208</sup> The largest benefits were seen in vascular and cardiac surgery. Non-significant increases in bradycardia and hypotension were also seen. Minimal data was identified on the use of alpha 2 agonists in non-vascular surgery. There has been no direct comparison of alpha 2 agonists with beta blockers. Further large RCTs are needed in non-cardiac surgical patients.

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In a study of 2,854 patients with or at risk of coronary heart disease mivazerol administered during anaesthesia and surgery on a double blind placebo controlled basis led to a significant reduction in all cause and cardiac mortality (RR = 0.67, CI 0.45 to -0.98; ARR 4.3%) in patients undergoing major reconstructive vascular surgery.<sup>209</sup>

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Mivazerol and dexmedetomidine are not licensed in the UK. Clonidine is available and although the potential benefits do seem to be a class effect, the data on clonidine are limited to smaller studies.

One RCT of 190 patients with or at risk of CHD investigated the effect of clonidine in patients undergoing non-cardiac surgery. The study group was given 0.2 mg oral clonidine followed by a patch for four days. Prophylactic administration of clonidine reduced the postoperative mortality for up to two years (RR 0.43, CI 0.21 to 0.89; ARR 14%; p=0.035).<sup>210</sup> Clonidine is not licensed for this indication.

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5.3.3 CALCIUM CHANNEL BLOCKERS

There is some evidence that CCBs may reduce the cardiac risk of non-cardiac surgery. The evidence base is weak, consisting of small, often unblinded studies. One meta analysis included 11 studies of 1,007 patients in which diltiazem, verapamil or nifedipine were assessed in major non-cardiac surgery.<sup>211</sup> Calcium channel blockers reduced by half perioperative ischaemia (RR 0.49, CI 0.30 to 0.80; p=0.004) and supraventricular tachyarrhythmia (RR 0.52, CI 0.37 to 0.72; p<0.0001). There was no effect on heart failure. Trends toward a reduction in MI (RR 0.25, CI 0.05 to 1.18) or mortality (RR 0.4, CI 0.14 to 1.16) were seen. Post hoc analyses showed a significant reduction in death/MI (RR 0.35, CI 0.15 to 0.86; p=0.02). The majority of these effects were attributable to diltiazem. Further large well designed studies are required to confirm any benefit. There are no comparative studies with other drugs.

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A meta-analysis of RCTs for the prevention of cardiovascular complications of non-cardiac surgery found no benefit for the use of perioperative CCB on cardiac death.<sup>199</sup>

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Further evidence is required before CCB can be recommended as a form of medical therapy to reduce the cardiac risk of non-cardiac surgery.

5.3.4 ANTIPLATELET THERAPY

Aspirin has both antiplatelet and anti-inflammatory effects and is known to reduce mortality in unstable angina and after MI and stroke. Most patients with stable angina will be prescribed low-dose aspirin therapy for secondary cardiovascular prevention.

In five RCTs, preoperative administration of aspirin resulted in increased blood loss, blood transfusion and reoperation after cardiac surgery.<sup>212-216</sup>

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1++

The benefits of aspirin administration before or after non-cardiac surgery are less well defined. SIGN guideline 62 on prophylaxis of venous thromboembolism recommends pre- and postoperative aspirin as prophylaxis of asymptomatic and symptomatic venous thromboembolism (VTE) in surgical patients.<sup>217</sup>

4

Aspirin may be stopped five days before major non-cardiac surgery because of the bleeding risks but these must be balanced against the risk of postoperative thrombotic complications such as VTE, MI and stroke. A meta-analysis showed that whilst the rate of bleeding complications was increased by low-dose aspirin by a factor of 1.5, it did not lead to a higher severity of bleeding complications (with the exception of intracranial surgery and possibly transurethral prostatectomy) nor of perioperative mortality because of bleeding complications.<sup>218</sup>

2+

There is evidence that low-dose aspirin reduces the risks of stroke associated with carotid endarterectomy and should be continued preoperatively.<sup>219</sup> The American Association of Colleges of Pharmacy recommends aspirin in patients receiving prosthetic femoropopliteal bypass grafts with therapy starting preoperatively.<sup>220</sup>

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**C** Low-dose aspirin therapy should only be withheld before non-cardiac surgery in patients with coronary heart disease where the aspirin related bleeding complications are expected to be significant (VTE, MI, stroke, peripheral vascular occlusion, or cardiovascular death).

**D** If low-dose aspirin therapy is withdrawn before non-cardiac surgery in patients with coronary heart disease, it should be recommenced as soon as possible after surgery.

## 5.3.5 NITRATES AND POTASSIUM CHANNEL ACTIVATORS

Glyceryl trinitrate infusions do not reduce perioperative ischaemia<sup>221</sup> and a systematic review concluded that there was insufficient evidence to support the use of nitrates in the perioperative period.<sup>199</sup> No evidence was identified on nicorandil use in this setting.

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## 5.3.6 STATINS

In the operative setting statins may influence plaque instability and rupture and subsequent thrombosis and coronary artery occlusion. One RCT of 100 patients undergoing vascular surgery showed that 20 mg of simvastatin administered daily for 45 days reduced the incidence of cardiac events (RR 0.31; ARR 18%).<sup>222</sup> Observational studies have shown associations between statin use and reduced cardiac events after non-cardiac surgery.<sup>223,224</sup>

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Early concerns about the use and safety of statins during hospitalisation for major surgery have not been confirmed.<sup>225</sup> In a study of 981 patients undergoing non-cardiac surgery, perioperative statin use was not associated with an increased risk of myopathy (ie creatine phosphokinase elevation with or without muscle complaints after major vascular surgery).<sup>226</sup>

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**B** Patients with coronary heart disease undergoing major non-cardiac vascular surgery should be established on a statin before surgery.

Patients presenting for non-cardiac surgery on statin therapy should have the statin continued through the perioperative period.

## 5.4 ADJUNCTIVE ANAESTHETIC TECHNIQUES

## 5.4.1 FACTORS ASSOCIATED WITH ISCHAEMIA

Myocardial ischaemia is associated with hypoxia, hypothermia, anaemia, hypovolaemia, unstable haemodynamics and inadequate pain control. These factors may adversely affect the oxygen supply/demand relationship in the myocardium and must be considered in any preventative strategy (see *SIGN guideline 77 on postoperative management in adults*).<sup>206</sup>

## 5.4.2 EPIDURAL ANALGESIA

One systematic review of randomised trials of epidural anaesthesia indicated that the incidence of myocardial infarction was reduced by about one third with neuraxial blockade (OR 0.70, 95% CI 0.54 to 0.90; ARR 0.9%; p = 0.006).<sup>227</sup> A smaller trial showed that myocardial ischaemia was reduced with epidural infusions after hip fracture surgery.<sup>228</sup>

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The MASTER study did not show any improvement in outcomes after abdominal surgery with epidural analgesia.<sup>229</sup>

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## 5.4.3 INTRA-AORTIC BALLOON PUMP IN NON-CARDIAC SURGERY

The use of an intra-aortic balloon pump (IABP) has an established place in the management of acute coronary syndromes complicated by cardiogenic shock, myocardial infarction complicated by ventricular septal defects or papillary muscle rupture and refractory myocardial ischaemia prior to revascularisation (see *SIGN guideline 93 on acute coronary syndromes*).<sup>11</sup>

No RCTs were identified on the use of IABP in non-cardiac surgery. Case reports have suggested that some patients with severe CHD requiring urgent non-cardiac surgery may benefit from the support of an IABP.<sup>155</sup> Experience in the insertion of and the management of the IABP is an essential prerequisite to safe use.

2+

## 6 Psychological and cognitive issues

Psychological factors exert an influence on patients with angina in several ways:

- limitations and concerns related to living with angina can influence mood, degree of disability, quality of life and mortality<sup>230-232</sup>
- beliefs and misconceptions about heart disease have been shown to influence outcome (see *SIGN guideline 57 on cardiac rehabilitation, section 2.1.4*), and eliciting and reframing unhelpful beliefs decreases disability<sup>155,233</sup>
- depression and anxiety influence health service use (see *SIGN guideline 57 on cardiac rehabilitation, sections 2.1.1 and 2.1.2*)<sup>155</sup>
- the presence of depression influences mortality and morbidity<sup>234-238</sup>
- patients commonly report cognitive difficulties following CABG<sup>160,261</sup>

This section addresses the evidence about these issues.

### 6.1 HOW DOES ANGINA AFFECT QUALITY OF LIFE?

The impact of angina on psychological health and function can be measured by assessing mood and quality of life (QoL) using validated measures such as Hospital Anxiety and Depression Scale (HAD). The evidence reviewed indicates a considerable impact of angina on QoL status. Depression was associated with poorer function.<sup>230,239-242</sup>

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Two large Scandinavian surveys of quality of life using the questionnaires SF-36 and Swed-Qual found that patients with mild and moderate angina have significantly lower quality of life ratings compared with the general population and those with diabetes, epilepsy, and asthma.<sup>230,232</sup> The same study group also demonstrated reduced and impaired sexual functioning in angina patients compared with normal population.<sup>243</sup>

3

Two studies comparing patients with angina who were awaiting revascularisation with the normal population found limitations in quality of life compared with the general Swedish population on all domains of Swed-Qual, and SF-36. Persistence of angina after intervention (four year follow up) was associated with reduced QoL.<sup>244,245</sup> A large scale well conducted study of 1,025 patients with CHD and angina, looked at the association between depression, physical limitations and QoL over a three month period. Twenty eight per cent of patients were depressed, which was significantly associated with poorer scores on the Seattle Angina questionnaire ( $p < 0.001$ ). At three month follow up, depression was associated with deterioration of functional status.<sup>230</sup>

2+  
3

A small, well conducted study based in Scotland followed up patients from a chest pain service for six months. Standardised measures demonstrated presence of significant symptoms of angina (58%) and breathlessness (72%), with more than half affected by tiredness, mobility problems and a restricted social and domestic life. More than 75% of patients had anxiety and depression above the normal range, with risk factors poorly controlled.<sup>8</sup>

3

**D Patients with angina should be assessed for the impact of angina on mood, quality of life and function, to monitor progress and inform treatment decisions.**

Mood, quality of life and function in angina patients can be assessed using validated measures such as:

- SF-36
- Hospital Anxiety and Depression Scale (generic)
- The Dartmouth Primary Care Co-operative Information Project Functional Health Assessment Chart
- Seattle Angina Questionnaire – UK version
- Cardiovascular Limitations and Symptoms profile (CHD specific).



Quality outcomes framework (QOF) targets for 2006 include two screening questions for depression in patients with CHD for whom case finding has been undertaken in the previous 15 months:

- “During the last month, have you often been bothered by feeling down, depressed or hopeless?”
- “During the last month, have you often been bothered by having little interest or pleasure in doing things?”

## 6.2 IMPROVING SYMPTOM CONTROL WITH BEHAVIOURAL INTERVENTIONS

A systematic review of four RCTs reported that the evidence of efficacy of psychoeducational intervention for the management of chronic stable angina was inconclusive. Individually, the trials indicated some positive effects on angina symptoms, angina symptom-related distress and physical functioning, however they used different outcome measures, timing of outcomes and heterogeneous analyses of measures.<sup>246</sup>

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An RCT evaluating the use of the Angina Plan delivered by a nurse in primary care (patient held workbook and relaxation programme) to patients who had begun treatment for angina within the preceding 12 months, showed significant reduction in mean number of self reported angina attacks and physical limitation with reduction in anxiety and depression ( $p < 0.05$ ).<sup>247</sup>

1++

One RCT of autogenic relaxation training (guided relaxation focused on somatic sensations) after angioplasty found that it reduced anxiety at two and five months, although high drop-outs reduce the strength of this study.<sup>248</sup>

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**B Patients with stable angina whose symptoms remain uncontrolled or who are experiencing reduced physical functioning despite optimal medical therapy should be considered for the Angina Plan.**

- Any psychoeducational treatments which are shown to reduce distress should be considered alongside interventional treatments.

## 6.3 THE EFFECT OF TREATMENT FOR ANGINA ON COGNITION

Patients' reports of cognitive problems following CABG are common.<sup>160</sup> The guideline has not looked at the evidence for the mechanisms by which impairment may occur, apart from off- and on-pump procedures (see section 4.5) and hypothermia (see section 6.3.3). Nor has it looked at evidence for whether major surgery other than CABG affects cognitive impairment, nor the prevalence of cognitive impairment in a CHD population as a whole.

### 6.3.1 DEFINITION OF COGNITIVE DECLINE

An international consensus agreement defines cognitive decline as a 20% decrease in 20% of tests.<sup>249</sup> This definition allows comparison between studies but may produce a high proportion of false positives due to natural fluctuations in performance during repeated testing.<sup>250</sup> A further consideration is whether objective evidence of cognitive decline correlates with patient perception of decline.

Outcomes from different studies are not always comparable as not all studies employ neuropsychological measures consistent with the consensus agreement, there are differing time periods for follow up and difficulties controlling for other factors that might influence outcomes, eg age, pre-morbid levels of impairment and other variables.

### 6.3.2 PERCUTANEOUS CORONARY INTERVENTION

There is little evidence on the effect of PCI on cognitive function. One underpowered study compared PCI with CABG and found no difference in cognitive function at six or 12 months in either treatment.<sup>251</sup>

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A further study with poor methodology assessed patient and spouse perception of memory problems one to two years post CABG and angioplasty. This found no difference between CABG and PTCA patients.<sup>252</sup> 3

6.3.3 CORONARY ARTERY BYPASS GRAFTING

**Medical factors**

Hypothermia during CABG does not affect cognitive function postoperatively or at three month follow up. Use of hypothermia showed a non-significant trend to reduction of non-fatal strokes (OR 0.68, 95% CI 0.43-1.05).<sup>253</sup> 1++

One observational study found no relationship between the increase in lesions found on MRI scan post CABG and increase in cognitive decline.<sup>254</sup> 2+

**Patterns of cognitive decline**

The degree of decline varies depending on the length of time since surgery. Cognitive decline is relatively common in the early period following surgery and, in some patients, the initial decline may improve over the first three months. A systematic review of 12 cohort studies and 11 intervention studies found that 22% of patients had evidence of cognitive decline at two months post CABG. The relatively early follow up period used may overestimate the longer term severity of the problem.<sup>255</sup> 2++

Papers published subsequent to this review describe conflicting results for decline in later time periods post surgery. Two robust longitudinal studies of cognitive decline post CABG found decline at six months in 24% and in 39% of those with pre-surgical impairment.<sup>256,257</sup> This pattern was also found by two less robust studies.<sup>258,259</sup> 3

Longer term follow up of patients indicates an increase in the prevalence of decline from 24% at six months to 42% at five years,<sup>256</sup> with similar results from another study.<sup>260</sup> The Octopus study group found an increase in decline in both on- and off-pump surgical groups from six to 12 months (21-33% in off-pump group, 29% to 33% in on-pump group).<sup>157</sup> These findings indicate that other factors may influence continuing decline related to presence of cardiovascular disease and the ageing process. 2++

**B Patients undergoing coronary artery bypass grafting should be advised that cognitive decline is relatively common in the first two months after surgery.**

A robust cohort study compared on-pump and off-pump surgical patients, CHD patients without surgery and 'heart healthy' controls to try to control for the presence of cardiovascular and cerebrovascular disease.<sup>160</sup> Both objective and subjective complaints of cognitive decline over 12 months were assessed. All three cardiac groups had lower cognitive scores at baseline (before surgery), indicating some degree of impairment related to CHD status. All four groups showed improvement in function over 12 month follow up with no evidence that surgical patients did less well than cardiac controls. Subjective reports of deterioration in memory, personality and reading were significantly more frequent in both surgical groups compared with controls. Surgery appears to exert a significant influence on patient perception of decline. Although this self report is related to presence of depression, mood did not explain the higher incidence in the surgical groups. These results conflict with other studies and indicate that use of appropriate controls may produce a different pattern of evidence of decline. 2++

A further study found that 37% of patients showed a decline in cognitive function on formal testing at six weeks post CABG but this did not correlate with patient perception of cognitive difficulties.<sup>261</sup> 3

The following factors predict poor cognitive outcome:

- age<sup>256,257,259</sup>
- evidence of decline preoperatively and at discharge<sup>256,257,259</sup>
- fewer years of education<sup>256,258,259</sup>
- anxiety and depression<sup>257,261</sup>
- female gender<sup>259</sup>
- hypertension<sup>259</sup>
- non-coronary atherosclerosis<sup>258,259</sup>
- chronic disabling neurological illness<sup>258</sup>
- limited social support.<sup>258</sup>

3

A cohort study looked at cognitive impairment and driving performance post CABG and angioplasty (four to six weeks). Performance was worst in post CABG group (48% vs 10% of patients showing cognitive impairment) but lack of long term follow up means results should be viewed with caution.<sup>262</sup>

2+

A single study with a small sample indicated potential benefit of pre CABG treatment with hyperbaric oxygen in reducing neuropsychological dysfunction. Lack of availability of facilities will limit availability of this treatment.<sup>263</sup>

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**D Patients who are older and have other evidence of atherosclerosis and/or existing cognitive impairment may be more at risk of increasing decline and these factors should be considered when evaluating options for revascularisation to achieve symptom relief.**

#### 6.3.4 EFFECT OF MEDICATION ON PSYCHOLOGICAL FACTORS

Patients often report perceived changes in psychological functioning while taking cardiac medications. There is very limited evidence available to address this question. An RCT comparing lovastatin with placebo in healthy volunteers found no effect on measures of mental health and inconclusive minor reductions in cognitive function (NB lovastatin is not licensed in the UK).<sup>264</sup> An RCT comparing losartan with atenolol in elderly patients with hypertension indicated some minor benefit of losartan in improving immediate and delayed memory ( $p < 0.05$ ). However, small numbers and the non-standard outcome measures used mean these results are inconclusive.<sup>265</sup>

1+

There is no robust evidence in patients with angina demonstrating any effect of medication on psychological functioning.

### 6.4 THE EFFECT OF PSYCHOLOGICAL FACTORS ON CLINICAL OUTCOMES INCLUDING MORTALITY

Depression in post MI patients predicts mortality and morbidity<sup>155</sup> and psychological distress is associated with higher healthcare costs.<sup>266</sup> Evidence reviewed elsewhere (see *SIGN guideline 97 on risk estimation and the prevention of cardiovascular disease*),<sup>73</sup> indicates that depression is also a primary risk factor for the development of CHD of similar magnitude to standard risk factors. The pattern in patients after CABG is similar, indicating that depression should be treated with the same importance as other risk factors. A review of depression in CHD indicates the need to address this problem systematically, and describes potential screening measures.<sup>267</sup>

#### 6.4.1 ANXIETY AND DEPRESSION

Depression is a significant factor influencing mortality and morbidity post CABG. The prevalence of depression before surgery ranged from 10% to 43%,<sup>234-238,268,269</sup> and persisted at one year in up to 21% of patients.<sup>234</sup> Anxiety and depression were assessed using validated measures, with classification of anxiety and depression being determined by scoring above a certain cut-off point (clinical caseness) on the standardised measure of psychiatric adjustment used.

3

<p>Three studies<sup>234-236</sup> examined the relationship between depression and mortality including one large robust study with long follow up (n= 817, mean follow up 5.2 years).<sup>234</sup> Moderate to severe depression pre CABG or persistent depression up to six months was associated with two- to threefold increase in risk of death.</p>	3
<p>Another study showed highest fear and anxiety prevalence just after being put on the CABG waiting list (50%) with levels clearly dropping at admission (30%) and continuing to drop slightly at three months after surgery (20%). Differing anxiety measures gave different rates. Those under 55 years remained more fearful.<sup>270</sup> Women were more anxious and depressed preoperatively than men<sup>234,270-272</sup> and one study indicated that women living alone were more distressed than those living with partners.<sup>270</sup></p>	3
<p>One study shows high rates of anxiety and depression pre CABG (anxiety 55%, depression 32%) which reduced to 32% and 26% three months after CABG. High levels preoperatively predicted high levels three months after surgery.<sup>268</sup></p>	3
<p>Three studies found early depression either pre-CABG or immediately post-CABG to predict cardiac hospitalisation and poorer function/activity at six months.<sup>234,236,238</sup> One study showed that somatic complaints were associated with a similar prediction.<sup>273</sup> This effect was independent of other risk factors. Early depression also predicted likelihood of persisting depression and was associated with less education, life stressors, low social support and dyspnoea.<sup>269</sup> One study found that two screening questions for depression identified those more likely to be readmitted in the following six months, indicating that a simple screening method can identify those at risk (see section 6.1).<sup>274</sup></p>	3
<p>Two studies looked at the impact of gender in CABG and found that women tend to have poorer psychological health than men preoperatively. They do less well than men postoperatively at three and 12 months on function, overall health rating and depression.<sup>271,272</sup></p>	3
<p>A study of the influence of depression on outcomes after angiography found it predicted CABG and PCI rates over the next five years.<sup>275</sup></p>	
<p>One case series found a high positive view of self, future and personal control over daily life reduced likelihood of subsequent cardiac event over four years, in patients undergoing angioplasty.<sup>276</sup></p>	3
<p>The evidence indicates that depression and anxiety have similar detrimental effects on outcomes in patients with CABG and angina as in post-MI patients. The SIGN guideline on cardiac rehabilitation reported that comprehensive cardiac rehabilitation programmes improved mortality, psychological and physical outcomes, and such rehabilitation programmes should be considered for patients with stable angina after interventions.<sup>155</sup></p>	4
<p><b>D Patients undergoing coronary artery bypass grafting should receive screening for anxiety and depression pre-surgery and during the following year as part of postsurgical assessment, rehabilitation and coronary heart disease secondary prevention clinics. Where required patients should receive appropriate treatment (psychological therapy, rehabilitation, medication).</b></p>	
<p><b>D Rehabilitation programmes should be implemented after revascularisation for patients with stable angina.</b></p>	
<p><input checked="" type="checkbox"/> Particular attention should be paid to women, those living alone and those under 55 years.</p>	
<p>The NICE guidelines on management of depression<sup>277</sup> and anxiety disorders<sup>278</sup> in primary and secondary care provide recommendations for appropriate treatments.</p>	4

## 6.5 THE EFFECT OF HEALTH BELIEFS ON SYMPTOMS AND FUNCTIONAL STATUS

Individuals' beliefs about their condition are derived from many sources in addition to medical ones (eg, family, cultural group, media).<sup>233,282,283</sup> Information from clinicians may be adapted to fit existing beliefs or ignored, thereby influencing behaviour.<sup>279</sup> Commonly found beliefs such as 'angina is like a mini-heart attack' or 'every time I get angina I am damaging my heart', influence mood and degree of disability.

Observational studies from the same research group have examined the causal attributions and beliefs about appropriate coping strategies in patients with stable angina. The two qualitative studies found that causal attributions appear similar to those with MI.<sup>280,281</sup> Most patients thought stress was the cause of their angina, women were more likely to attribute angina to stress or uncontrollable causes than their own previous behaviour and a large number do not cite risk factors they are known to have. Beliefs were also likely to lead to avoidance of activity and were maintained by partners. 3

A similar study compared views of angina patients and peers, finding that peers have greater misconceptions than patients, which may reinforce the network of misconceptions held by angina sufferers.<sup>282</sup> 3

The York Angina Beliefs questionnaire is a 14 item measure of beliefs about angina. It was demonstrated to be a reliable and valid tool to measure misconceptions and beliefs in angina patients, which may lead to avoidance of activity, disability and anxiety.<sup>283</sup> 3

A study of 140 patients examined causal attributions of patients awaiting PCI. Stress, family history and cholesterol are cited as causes of CHD prior to PCI by more females than males. Females were more likely to blame uncontrollable factors (biological) than men who cited behavioural factors. There was a discrepancy between patients' and healthcare professionals' views of causes.<sup>284</sup> 3

The Angina Plan is an intervention which identifies beliefs about angina, with educational and management advice tailored to alter erroneous beliefs and their impact (see *section 6.2*). An RCT showed that the Angina Plan successfully changed beliefs and improved functional outcomes in patients three months following MI. The intervention group were more optimistic that illness could be controlled or cured.<sup>233</sup> 1+

**D** Patients' beliefs about angina should be assessed when discussing management of risk factors and how to cope with symptoms.

**B** Interventions based on psychological principles designed to alter beliefs about heart disease and angina, such as the Angina Plan, should be considered.

## 7 Patient issues and follow up

During their journey of care a patient is likely to come in contact with a range of healthcare professionals whose individual roles should be made clear.

A sympathetic approach is needed at all times, with the opportunity for reflection and further questioning as required. There may be a need for verbal information to be reinforced by written or visual information and there should always be an opportunity to involve family members and carers.

### 7.1 DELIVERING INFORMATION TO PATIENTS WITH ANGINA – AT DIAGNOSIS AND PRIOR TO INTERVENTIONS

Patient information can be provided by means of prepared resources such as books, pamphlets and other printed material. Use can also be made of audio or video tapes as well as computer software and the internet. Very limited evidence was identified for the effectiveness of any individual format over another.

#### 7.1.1 INFORMATION AND EDUCATION ABOUT SURGERY AND OTHER INTERVENTIONS

Preparing patients for surgery by provision of information and addressing concerns, reduces distress, length of stay and the need for analgesia.<sup>285</sup>

The educational interventions described in the evidence were not standard or delivered at the same point in time in relation to interventions. Outcomes also varied between studies.

One RCT providing educational intervention for angina patients awaiting angiography showed no effect on measures of anxiety or well-being after the procedure.<sup>293</sup> One observational study showed the waiting period prior to elective catheterisation is associated with a negative impact on patients' anxiety, and reduction in functioning and quality of life.<sup>286</sup>

1+  
3

Two RCTs provided differing educational-type interventions prior to CABG, (pain management booklet, and an educational session early in the long wait for CABG). There was no effect on pain scores, pain-related interference with activities or on postoperative analgesia in the first study, nor on anxiety, depression, pain score, general well-being and length of stay. Patients in both studies received other educational input as part of standard care. All patients received inadequate analgesia, women had higher pain scores and longer length of stay.<sup>287,288</sup>

1++

One RCT of a protocol delivered telephone educational intervention post CABG did not show any effect on anxiety of patient or partner at eight weeks.<sup>289</sup>

1+

Motivational interviewing is a structured approach to helping people change behaviour, using patient-centred but directed strategies (see *SIGN guideline 97 on risk estimation and the prevention of cardiovascular disease*<sup>73</sup> and *SIGN guideline 57, cardiac rehabilitation*<sup>155</sup>). One RCT delivering education using a motivational interviewing approach by a specialist cardiac nurse, shared with community nurses and the support of medical practitioners, was shown to provide effective reduction in risk factors, anxiety and depression and improved perception of general health status during the period of wait prior to CABG. The health of patients not assigned to the treatment intervention deteriorated as assessed by outcome measures.<sup>290</sup>

1+

One RCT provided audio-taped information on strategies to deal with expected physical sensations and their management following CABG. This tape was listened to in the ward on the fourth or fifth postoperative day and was taken home by the patient. This showed benefit in physical functioning in women and psychological distress, vigour and fatigue in men compared to usual care.<sup>291</sup>

1+

- ☑ Educational programmes delivered pre- and post-coronary artery bypass grafting should consider the use of strategies based on psychological principles to improve management of risk factors, psychological distress and physical functioning.
- ☑ Patients newly diagnosed with angina and those who are immediately pre- and postinterventions and revascularisation, should be given appropriate information to help them understand their condition and how to manage it, and any procedure being undertaken.
- ☑ Health beliefs and misconceptions should be addressed when delivering information.

## 7.2 CARDIAC WAITING TIMES

In 2007 the specified standard waiting time for surgery is 18 weeks from the time of angiography.<sup>292</sup> Adverse effects in terms of morbidity and mortality occurring in patients waiting for investigative or revascularisation procedures may be preventable if waiting times are eliminated.

One RCT of 228 patients which measured a variety of health related quality of life parameters revealed that a waiting period prior to elective cardiac catheterisation has a negative impact on patients' anxiety, with reduction in functioning and quality of life.<sup>293</sup> 1+

For patients waiting for cardiac interventions, enrolment in a nurse-led education programme may help improve short term quality of life.

In an American cohort patients waiting for coronary angiography were followed up for an average of eight months following the procedure and significant adverse events classified. Compared with the event free group, patients with adverse events more frequently had a history of known CHD (55% vs 35%;  $p=0.03$ ), CCS angina class III or IVa (42% vs 22%;  $p=0.01$ ), and positive stress test results (69% vs 46%;  $p=0.001$ ).<sup>294</sup> 2+

Long waiting times for coronary artery bypass grafting have been shown to have an adverse effect on physical and social functioning before and after surgery with an increase in postoperative adverse effects. In a cohort study of 360 Dutch patients, the median waiting time for patients placed on the elective surgical waiting list (186 patients) was 100 days. The primary outcome measures of death, myocardial infarction or unstable angina requiring hospital admission occurred in around 5% of this group of patients. The majority of events occurred within 30 days of being listed for surgery.<sup>295</sup> 2+

**C** Early access to angiography and coronary artery bypass surgery may reduce the risk of adverse cardiac events and impaired quality of life.

## 7.3 FOLLOW UP IN PATIENTS WITH ANGINA

Patients presenting with angina to their general practitioners have often been managed without appropriate assessment and referral for possible intervention.<sup>296</sup>

A meta-analysis of cardiac secondary prevention programmes with or without an exercise programme indicated that such programmes can have a positive effect on the process of care, quality of life as well as reducing the reinfarction and mortality rates.<sup>297</sup> 1+

Multidisciplinary disease management programmes for patients with CHD have been shown in a systematic review to have a beneficial impact on the uptake of secondary prevention drugs and addressing risk factor profiles.<sup>298</sup> Three trials address follow up in patients with angina. 1++

In the SHIP trial, a cardiac liaison nurse coordinated care with general practitioners in patients discharged from hospital with newly diagnosed angina.<sup>299</sup> Although this approach encouraged follow up it did not improve objective measures of risk except in relation to blood pressure in the patients with angina  $p<0.05$ .

Health promotion provided by health visitors in Belfast to patients with angina showed improved physical activity and diet with less angina and social isolation after two years. At five year follow up after recruitment, three years after the end of the intervention, most of the benefits had worn off. Benefits in respect of exercise and taking prophylactic drugs, although less, were still evident ( $p < 0.001$  to  $p < 0.05$  for both categories).<sup>300</sup> This would suggest that to be effective health promotion advice needs to be provided on a long term basis.

1+

In the third trial, patients with a diagnosis of coronary heart disease were recruited to the Grampian nurse-led secondary prevention clinics versus routine care with the aim of promoting lifestyle change and secondary prevention. After attending the clinics for one year there was an improvement in quality of life and secondary prevention components except smoking. These improvements were sustained after four years except for exercise. Those attending the clinics also had fewer total deaths and coronary events.<sup>301</sup> After adjusting for age, sex and baseline secondary prevention, the proportional hazard ratios were 0.75 for all deaths (95% CI 0.58 to 0.98;  $p = 0.036$ ) and 0.76 for coronary events (95% CI 0.58 to 1.00;  $p = 0.049$ ).

1++

Two further studies consisting of nurse or GP follow up with audit feedback<sup>302</sup> and postal prompts<sup>303</sup> did not lead to significant benefits in secondary prevention. Provision of the Angina Plan to patients with angina did lead to an improvement in reported diet and daily walking ( $p < 0.001$ ).<sup>4</sup>

3

**A** Patients presenting with angina and with a diagnosis of coronary heart disease should receive long term structured follow up in primary care.



## 8 Sources of further information and support for patients and carers

### **British Cardiac Patients Association**

BCPA Head Office  
2 Station Road  
Swavesey, Cambridge, CB4 5QJ  
Tel: 0800 479 2800 • Fax: 01954 202 022  
Email: enquiries@bcpa.co.uk • www.bcpa.co.uk

The British Cardiac Patients Association is a charitable organisation run by volunteers providing support, advice and information to cardiac patients and their carers.

### **British Heart Foundation (Scotland)**

4 Shore Place  
Edinburgh  
EH6 6WW  
Tel: 0131 555 5891 • Heart Information line: 08450 70 80 70 (available Mon-Fri 9am-5pm)  
Email: scotland@bhf.org.uk • www.bhf.org.uk

British Heart Foundation provides a telephone information service for those seeking information on heart health issues. Also provides a range of written materials offering advice and information to CHD patients and carers. Topics include physical activity, smoking and diabetes.

### **Chest Heart and Stroke Scotland**

65 North Castle Street  
Edinburgh  
EH2 3LT  
Tel: 0131 225 6963 • Helpline: 0845 0776000  
Email: admin@chss.org.uk • www.chss.org.uk

Chest Heart and Stroke Scotland provides a 24 hour advice line offering confidential, independent advice on all aspects of chest, heart and stroke illness. A series of information booklets, factsheets and videos is available free of charge to patients and carers. There are over 30 cardiac support groups in Scotland which are affiliated to CHSS, patients can contact CHSS for details of their nearest local support group.

### **Depression Alliance Scotland**

3 Grosvenor Gardens  
Edinburgh  
EH12 5JU  
Tel: 0131 467 3050  
Email: info@dascot.org • www.depressionalliance.org

Depression Alliance Scotland provides information and support for people in Scotland who have depression.

### **Heart Surgery in Great Britain**

<http://heartsurgery.healthcarecommission.org.uk/>

This website has been developed by the Healthcare Commission and the Society for Cardiothoracic Surgery in Great Britain and Ireland to help heart surgery patients make informed choices about their treatment. It provides patients and carers with information on the different operations available and the benefits of having heart surgery.

**NHS Health Scotland**

Woodburn House  
Canaan Lane  
Edinburgh, EH10 4SG  
Tel: 0131 536 5500 • Textphone: 0131 536 5503  
Fax: 0131 536 5501 • Email: [publications@health.scot.org.uk](mailto:publications@health.scot.org.uk) (information on obtaining Health Scotland publications); [library.enquiries@health.scot.nhs.uk](mailto:library.enquiries@health.scot.nhs.uk) (help with general health information enquiries) • [www.hebs.com](http://www.hebs.com)

NHS Health Scotland is a special health board within NHS Scotland. The organisation provides information on projects, publications, support groups and information leaflets relating to CHD.

**Heart Manual Department**

Administration Building,  
Astley Ainslie Hospital,  
Grange Loan, Edinburgh EH9 2HL  
Tel: 0131 537 9127 / 9137  
Email: [heart.manual@lpct.scot.nhs.uk](mailto:heart.manual@lpct.scot.nhs.uk) • [www.theheartmanual.com](http://www.theheartmanual.com)

The Heart Manual is the UK's leading home based rehabilitation programme for patients recovering from acute myocardial infarction. The programme is delivered by health professionals who have completed a two day facilitator training course. It provides a standardised approach for more than 250 major NHS users across the UK and Ireland, and is in use in a number of overseas countries. It contributes to the recovery of more than 12,000 heart attack patients per year and has been shown to be clinically effective in studies.

**NHS 24**

[www.nhs24.com](http://www.nhs24.com)  
Tel: 0845 4 24 24 24

NHS 24 is a nurse-led service for members of the public. It is a helpline offering health information, advice and help over the phone.

**Scotland's Health on the Web**

[www.show.scot.nhs.uk](http://www.show.scot.nhs.uk)

This website provides public access to publications relating to CHD such as the strategy for CHD and stroke in Scotland.

## 9 Implementation and audit

### 9.1 LOCAL IMPLEMENTATION

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. It is acknowledged that every Board cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

### 9.2 KEY POINTS FOR AUDIT

The National Clinical Datasets Development Programme and ISD Scotland are working to develop national standard datasets for implementation in IT systems supporting patient care. The following clinical datasets have been developed and are available at [www.datadictionary.scot.nhs.uk](http://www.datadictionary.scot.nhs.uk)

- CHD core
- Acute coronary syndromes
- Cardiac rehabilitation
- Heart failure
- Electrophysiology

The CHD and Stroke Programme is setting up working groups to develop methods and coding definitions to support monitoring of the implementation of the SIGN guidelines from new datasets and existing data collections. Where there are gaps in the data ISD Scotland will work to support the necessary information collection.

### 9.3 RECOMMENDATIONS FOR RESEARCH

#### *Diagnosis and assessment*

- What is the effectiveness of a RACPC compared to a traditional clinic in controlling angina symptoms and reducing mortality and morbidity when patients access these services within the recommended National Service Framework threshold of two weeks from primary care referral?
- What is the role of multislice CT scanning in the diagnosis of coronary artery disease?
- More evidence is needed to identify the most effective model for the early assessment of patients with suspected stable angina.

#### *Pharmacological management*

- Further information is required on the role of ACE inhibitors in patients with stable angina without further cardiovascular risk factors (eg diabetes, hypertension, MI).
- What is the effectiveness of adding a third anti-anginal drug to patients whose symptoms are not controlled with a combination of two drugs?

#### *Interventional cardiology and cardiac surgery*

- For how long should beta blockers be continued after successful revascularisation?
- What is appropriate management of restenosis following coronary artery revascularisation?

***Psychological and cognitive issues***

- What are the mechanisms by which depression influences mortality following CABG?
- More robust studies are required on the relationship between patient reporting of cognitive impairment and measurable impairment.
- Further clarification is needed on the role of non-surgical factors in determining which patients will demonstrate continued cognitive impairment following CABG.
- An intervention study is needed on the effect of screening for high levels of depression and anxiety pre-CABG and delivery of early postoperative rehabilitation and psychological intervention, on patient outcomes and use of health service resources.
- An economic analysis of health service use is required in patients with angina with high levels of misconceptions and emotional distress.

***Patient issues and follow up***

- What is the optimum review interval in primary care for patients with established cardiovascular disease?

**9.4 ADDITIONAL ADVICE TO NHSSCOTLAND FROM NHS QIS AND THE SCOTTISH MEDICINES CONSORTIUM****9.4.1 NHS QIS APPROVED NICE MTAS**

The following reports have been approved by NHS Quality Improvement Scotland.

NICE Technology Appraisal Guidance No 51 – The use of computerised cognitive behaviour therapy for anxiety and depression.<sup>304</sup>

NICE Technology Appraisal Guidance No 52 – The use of drugs for early thrombolysis in the treatment of acute myocardial infarction.<sup>305</sup>

NICE Technology Appraisal Guidance No 71 – Ischaemic heart disease - coronary artery stents (review).<sup>306</sup>

NICE Technology Appraisal Guidance No 80 – Acute coronary syndromes – clopidogrel.<sup>307</sup>

NICE Technology Appraisal Guidance 90 – Clopidogrel and modified-release dipyridamole in the prevention of occlusive vascular events.<sup>308</sup>

NICE Technology Appraisal Guidance No 94 – Statins for the prevention of cardiovascular events.<sup>309</sup>

**9.4.2 SMC ADVICE**

The Scottish Medicines Consortium has issued advice on the use of ivabradine (October 2006).<sup>310</sup> Advice on a number of individual products within the following drug classes; statins, angiotensin receptor blockers, beta blockers and direct thrombin inhibitors is also available.

Further details are available from [www.scottishmedicines.org.uk](http://www.scottishmedicines.org.uk)

# 10 Development of the guideline

## 10.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. Further details about SIGN and the guideline development methodology are contained in “SIGN 50: A Guideline Developer’s Handbook”, available at [www.sign.ac.uk](http://www.sign.ac.uk)

## 10.2 THE GUIDELINE DEVELOPMENT GROUP

Dr Alan Begg (Chair)	<i>General Practitioner, Montrose</i>
Ms Shona Black	<i>Cardiovascular Facilitator, Dundee Community Health Partnership</i>
Mr Tom Brighton	<i>Lay Representative, Montrose</i>
Dr Rob Cargill	<i>Consultant Cardiologist, Victoria Hospital, Kirkcaldy</i>
Ms Joyce Craig	<i>Senior Health Economist, NHS Quality Improvement Scotland</i>
Dr Mohamed Elfellah	<i>Cardiovascular Lead Pharmacist, Aberdeen Royal Infirmary</i>
Dr Neil Gillespie	<i>Senior Lecturer, Section of Ageing and Health, University of Dundee</i>
Mr Bob Jeffrey	<i>Consultant Cardiothoracic Surgeon, Aberdeen Royal Infirmary</i>
Dr Alistair Macfie	<i>Consultant Anaesthetist, Western Infirmary, Glasgow</i>
Mrs Catriona McGregor	<i>Head of Clinical Physiology, Ayr Hospital</i>
Mr Alexander Masson	<i>Lay Representative, Montrose</i>
Dr John Milne	<i>General Practitioner, Leslie Medical Practice, Glenrothes</i>
Dr Moray Nairn	<i>Programme Manager, SIGN Executive</i>
Dr Keith Oldroyd	<i>Interventional Cardiologist, Western Infirmary, Glasgow</i>
Mr Dennis Sandeman	<i>Chest Pain Nurse Specialist, Victoria Hospital, Kirkcaldy</i>
Mr Duncan Service	<i>Information Officer, SIGN Executive</i>
Ms Nicola Stuckey	<i>Consultant Clinical Psychologist, Astley Ainslie Hospital, Edinburgh</i>

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive. Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive.

### 10.3 THE STEERING GROUP

A steering group comprising the chairs of the five SIGN CHD guidelines and other invited experts was established to oversee the progress of guideline development. This group met regularly throughout the development of the guidelines.

Dr Kevin Jennings	<i>Co-chair and Consultant Cardiologist, Aberdeen Royal Infirmary</i>
Professor Lewis Ritchie	<i>Co-chair and Mackenzie Professor of General Practice, University of Aberdeen</i>
Dr Alan Begg	<i>Chair of SIGN stable angina guideline</i>
Dr Nick Boon	<i>Consultant Cardiologist, Royal Infirmary of Edinburgh</i>
Ms Marjory Burns	<i>Director for Scotland, British Heart Foundation</i>
Mr David Clark	<i>Chief Executive, Chest, Heart and Stroke Scotland</i>
Professor Stuart Cobbe	<i>Chair of SIGN arrhythmias guideline</i>
Ms Joyce Craig	<i>Senior Health Economist, NHS Quality Improvement Scotland</i>
Dr Iain Findlay	<i>Chair of SIGN acute coronary syndromes guideline</i>
Professor Keith Fox	<i>Professor of Cardiology, University of Edinburgh</i>
Dr James Grant	<i>Chair of SIGN prevention guideline</i>
Mr James Grant	<i>Lay representative, Balerno</i>
Dr Grace Lindsay	<i>Reader in Clinical Nursing Research, Glasgow Caledonian University</i>
Dr Moray Nairn	<i>Programme Manager, SIGN</i>
Professor Allan Struthers	<i>Chair of SIGN heart failure guideline</i>
Dr Lorna Thompson	<i>Programme Manager, SIGN</i>

### 10.4 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Information Officer. Searches were focused on existing guidelines, systematic reviews, randomised controlled trials, and (where appropriate) observational and/or diagnostic studies. Databases searched include Medline, Embase, Cinahl, PsychINFO, and the Cochrane Library. The year range covered was 1999-2005. Internet searches were carried out on various websites including those for the Australian Centre for Clinical Effectiveness, National Institute for Health and Clinical Excellence, the National Library for Health, Swedish Council on Technology Assessment in Healthcare, US Agency for Healthcare Research and Quality, and the US National Guidelines Clearinghouse. The Medline version of the main search strategies can be found on the SIGN website, in the section covering supplementary guideline material. The main searches were supplemented by material identified by individual members of the development group. Each of the selected papers was evaluated by two members of the group using standard SIGN methodological checklists before conclusions were considered as evidence.

### 10.5 CONSULTATION AND PEER REVIEW

#### 10.5.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for the five parallel SIGN guidelines on aspects of cardiovascular disease was held on 16 September 2005 and was attended by over 600 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

## 10.5.2 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. SIGN is very grateful to all of these experts for their contribution to the guideline.

Professor Adrian Bagust	<i>Professor of Cardiology, University of Liverpool</i>
Mr Alex Cale	<i>Cardiac Surgeon, Castle Hill Hospital, North Humbershire</i>
Professor Stuart Cobbe	<i>Consultant Cardiologist, Glasgow Royal Infirmary</i>
Ms Irene Crawford	<i>Senior Chief Cardiac Physiologist, Golden Jubilee Hospital, Glasgow</i>
Dr Malcolm Daniel	<i>Consultant Anaesthetist, Glasgow Royal Infirmary</i>
Mrs Frances Divers	<i>Cardiac Nurse Specialist, St John's Hospital, Livingston</i>
Dr Frank Dunn	<i>Consultant Cardiologist, Stobhill Hospital, Glasgow</i>
Ms Karen Fletcher	<i>CHD and Stroke Prevention Coordinator, Angus CHP, Forfar</i>
Professor Kim Fox	<i>Professor of Cardiology, Royal Brompton Hospital, London</i>
Dr John Gillies	<i>General Practitioner, The Health Centre, Selkirk</i>
Dr Grant Haldane	<i>Consultant Anaesthetist, Hairmyres Hospital, East Kilbride</i>
Mr Martin Hayes	<i>Senior Chief Cardiac Physiologist, Western General Hospital, Edinburgh</i>
Dr Graham Hilditch	<i>Consultant Anaesthetist, Gartnavel General Hospital, Glasgow</i>
Dr Graham Hillis	<i>Senior Lecturer and Honorary Consultant Cardiologist, Aberdeen Royal Hospitals NHS Trust</i>
Dr Harpreet Kohli	<i>Head of Health Services Research and Development, NHS Quality Improvement Scotland, Glasgow</i>
Dr Sandy Kopyto	<i>Principal Clinical Pharmacist, Victoria Hospital, Kirkcaldy</i>
Professor Chim Lang	<i>Professor of Cardiology, Ninewells Hospital and Medical School, Dundee</i>
Ms Lynne MacBeth	<i>Senior Chief Cardiac Physiologist, Aberdeen Royal Infirmary</i>
Dr Malcolm Metcalfe	<i>Consultant Cardiologist, Aberdeen Royal Infirmary</i>
Dr Stewart Milne	<i>Consultant Anaesthetist, Glasgow Royal Infirmary</i>
Professor David Newby	<i>British Heart Foundation Reader and Consultant Cardiologist, University of Edinburgh</i>
Dr Alistair Nimmo	<i>Consultant Anaesthetist, Royal Infirmary of Edinburgh</i>
Mr David Paul	<i>Lay Reviewer, Glasgow</i>
Professor Stuart Pringle	<i>Consultant Cardiologist, Ninewells Hospital and Medical School, Dundee</i>
Ms Fiona Reid	<i>Pharmacist, NHS Lothian</i>
Dr Karen Smith	<i>Clinical Research Fellow (Cardiac Nursing), Ninewells Hospital and Medical School, Dundee</i>
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### 10.5.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising members of SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows:

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# Abbreviations

<b>ACC</b>	American College of Cardiology
<b>ACE</b>	angiotensin converting enzyme
<b>ACS</b>	acute coronary syndrome
<b>ADP</b>	adenosine diphosphate
<b>AHA</b>	American Heart Association
<b>ARB</b>	angiotensin receptor blocker
<b>ARR</b>	absolute risk reduction
<b>AT</b>	anaerobic threshold
<b>AV</b>	atrioventricular
<b>BARI</b>	Bypass Angioplasty Revascularization Investigation trial
<b>BMI</b>	body mass index
<b>BNF</b>	British National Formulary
<b>CABG</b>	coronary artery bypass grafting
<b>CASS</b>	Coronary Artery Surgery Study
<b>CCB</b>	calcium channel blocker
<b>CCS</b>	Canadian Cardiovascular Society
<b>CHD</b>	coronary heart disease
<b>CI</b>	confidence interval
<b>CT</b>	computed tomography
<b>CVD</b>	cardiovascular disease
<b>Cx</b>	circumflex
<b>DECREASE</b>	Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography trial
<b>DVD</b>	double vessel coronary artery disease
<b>ECG</b>	electrocardiogram
<b>EECP</b>	enhanced external counterpulsation
<b>ETT</b>	exercise tolerance test
<b>EUROPA</b>	EUROpean trial On reduction of cardiac events with Perindopril in stable coronary Artery disease trial
<b>GP</b>	general practitioner
<b>HAD</b>	Hospital Anxiety and Depression Scale
<b>HOPE</b>	Heart Outcomes Prevention Evaluation trial
<b>IABP</b>	intra aortic balloon pump
<b>IMA</b>	internal mammary artery
<b>ISD</b>	Information and Statistics Division
<b>ITU</b>	intensive care unit
<b>LAD</b>	left anterior descending

<b>LMS</b>	left main stem
<b>LV</b>	left ventricular
<b>LVEF</b>	left ventricular ejection fraction
<b>LVSD</b>	left ventricular systolic dysfunction
<b>MASTER</b>	Multicentre Australian Study of Epidural Anaesthesia trial
<b>MET</b>	metabolic equivalent of task
<b>MI</b>	myocardial infarction
<b>MPS</b>	myocardial perfusion scintigraphy
<b>MRI</b>	magnetic resonance imaging
<b>MTA</b>	multiple technology assessment
<b>NICE</b>	National Institute for Health and Clinical Excellence
<b>NNT</b>	number needed to treat
<b>NYHA</b>	New York Heart Association
<b>OR</b>	odds ratio
<b>PEACE</b>	Prevention of Events with Angiotensin Converting Enzyme inhibition trial
<b>PCI</b>	percutaneous coronary intervention
<b>PTCA</b>	percutaneous transluminal coronary angioplasty
<b>QOF</b>	quality outcomes framework
<b>QoL</b>	quality of life
<b>QUIET</b>	QUinapril Ischemic Event Trial
<b>RACPC</b>	rapid access chest pain clinic
<b>RCA</b>	right coronary arteries
<b>RCRI</b>	revised cardiac risk index
<b>RCT</b>	randomised controlled trial
<b>RD</b>	risk difference
<b>RR</b>	relative risk
<b>SHIP</b>	Southampton Heart Integrated care Project trial
<b>SIGN</b>	Scottish Intercollegiate Guidelines Network
<b>SMC</b>	Scottish Medicines Consortium
<b>SVD</b>	single vessel coronary artery disease
<b>SVG</b>	saphenous vein grafts
<b>SVT</b>	supraventricular tachycardia
<b>TAR</b>	total arterial revascularisation
<b>TENS</b>	transcutaneous electrical nerve stimulator
<b>TMR</b>	transmyocardial revascularisation
<b>TVD</b>	triple vessel coronary artery disease
<b>UKCSR</b>	UK Cardiac Surgical Register
<b>VO<sub>2</sub> max</b>	maximum oxygen consumption
<b>VTE</b>	venous thromboembolism

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Risk assessment

The Revised Cardiac Risk Index is a simple risk stratification tool which combines patient risk and procedural risk and can aid clinical decision making. Six factors for major cardiac complications with approximately equal prognostic importance are defined.

- High risk surgery
- History of ischaemic heart disease
- History of congestive heart failure
- History of cerebrovascular disease
- Preoperative insulin treatment
- Preoperative creatinine > 180 micromol/l

**B** As part of the routine assessment of fitness for non-cardiac surgery, a risk assessment tool should be used to quantify the risk of serious cardiac events in patients with coronary heart disease.

- Patients undergoing high risk surgery who have a history of coronary heart disease, stroke, diabetes, heart failure or renal dysfunction should have further investigation by either exercise tolerance testing or other non-invasive testing or coronary angiography, if appropriate.

**D** An objective assessment of the functional capacity should be made as part of the preoperative assessment of all patients with coronary heart disease before major surgery.

Preoperative revascularisation

**D** Coronary artery bypass grafting is not recommended before major or intermediate risk non-cardiac surgery unless cardiac symptoms are unstable and/or coronary artery bypass grafting would be justified on the basis of long term outcome.

**D** If emergency or urgent non-cardiac surgery is required after percutaneous coronary intervention, dual antiplatelet therapy should be continued whenever possible. If the bleeding risk is unacceptable and antiplatelet therapy is withdrawn, it should be reintroduced as soon as possible after surgery.

The indications used for revascularisation prior to non-cardiac surgery should be those used in the non-operative setting.

Where possible, non-cardiac surgery should be delayed for at least one month after coronary artery bypass grafting. When deciding when to operate, the balance of risks and benefits in an individual patient will depend on the severity of the coronary artery disease and the nature and urgency of the non-cardiac surgery.

Drug therapy

**A** Preoperative beta blocker therapy should be considered in patients with coronary heart disease undergoing high or intermediate risk non-cardiac surgery who are at high risk of cardiac events.

**B** Pre-existing beta blocker therapy should be continued in the perioperative period.

Where possible beta blockers should be started days or weeks in advance of surgery to allow for dose titration and to assess tolerance.

**C** Low-dose aspirin therapy should only be withheld before non-cardiac surgery in patients with coronary heart disease where the aspirin related bleeding complications are expected to be significant (VTE, MI, stroke, peripheral vascular occlusion, or cardiovascular death).

**D** If low-dose aspirin therapy is withdrawn before non-cardiac surgery in patients with coronary heart disease, it should be recommenced as soon as possible after surgery.

Patients presenting for non-cardiac surgery on statin therapy should have the statin continued through the perioperative period.

Delivering information

Patients newly diagnosed with angina and those who are immediately pre- and postinterventions and revascularisation, should be given appropriate information to help them understand their condition and how to manage it, and any procedure being undertaken.

- Health beliefs and misconceptions should be addressed when delivering information.

Follow up

**A** Patients presenting with angina and with a diagnosis of coronary heart disease should receive long term structured follow up in primary care.

**D** Patients with angina should be assessed for the impact of angina on mood, quality of life and function, to monitor progress and inform treatment decisions.

**B** Patients with stable angina whose symptoms remain uncontrolled or who are experiencing reduced physical functioning despite optimal medical therapy should be considered for the Angina Plan.

**D** Patients who are older and have other evidence of atherosclerosis and/or existing cognitive impairment may be more at risk of increasing decline and these factors should be considered when evaluating options for revascularisation to achieve symptom relief.

Depression is a significant factor influencing mortality and morbidity post CABG.

**D** Patients undergoing coronary artery bypass grafting should receive screening for anxiety and depression pre-surgery and during the following year as part of post-surgical assessment, rehabilitation and coronary heart disease secondary prevention clinics. Where required patients should receive appropriate treatment (psychological therapy, rehabilitation, medication).

**D** Rehabilitation programmes should be implemented after revascularisation for patients with stable angina.

**D** Patients' beliefs about angina should be assessed when discussing management of risk factors and how to cope with symptoms.

**B** Interventions based on psychological principles designed to alter beliefs about heart disease and angina, such as the Angina Plan, should be considered.

## DIAGNOSIS AND ASSESSMENT

## Clinical assessment

Some patients describe discomfort and heaviness or breathlessness, rather than pain. Chest discomfort, irrespective of its site, is more likely to be angina when precipitated by exertion and relieved by rest. It is also characteristically relieved by glyceryl trinitrate.

Characteristic features of stable angina include:

- tight, dull or heavy feeling of discomfort
- discomfort is often retrosternal or left side of chest and can radiate to left arm, neck, jaw and back
- angina is often brought on with exertion or emotional stress and eased with rest
- typically the symptoms last up to several minutes after exertion or emotional stress has stopped
- other factors – angina may be precipitated by cold weather or following a meal.

Patients with suspected angina should have a detailed initial clinical assessment which includes history, examination and an assessment of blood pressure, haemoglobin, thyroid function, cholesterol and glucose levels.

Those patients who should be considered for early referral to secondary care include those with new onset angina and those with established coronary heart disease with an increase in symptoms.

## Diagnosis

Patients with suspected angina should usually be investigated by a baseline electrocardiogram and an exercise tolerance test.

Patients unable to undergo exercise tolerance testing or who have pre-existing electrocardiogram abnormalities should be considered for myocardial perfusion scintigraphy.

Coronary angiography should be considered after non-invasive testing where patients are identified to be at high risk or where a diagnosis remains unclear.

Following initial assessment in primary care, patients with suspected angina should, wherever possible, have the diagnosis confirmed and the severity of the underlying coronary heart disease assessed in the chest pain evaluation service which offers the earliest appointment, regardless of model.

## PHARMACOLOGICAL MANAGEMENT

## First line therapy

Beta blockers should be used as first line therapy for the relief of symptoms of stable angina.

Patients who are intolerant of beta blockers should be treated with either rate limiting calcium channel blockers, long-acting nitrates or nicorandil.

## Nitrates

Sublingual glyceryl trinitrate tablets or spray should be used for the immediate relief of angina and before performing activities that are known to bring on angina.

## Combination therapy

When adequate control of anginal symptoms is not achieved with beta-blockade a calcium channel blocker should be added.

Rate-limiting calcium channel blockers should be used with caution when combined with beta blockers.

Patients whose symptoms are not controlled on maximum therapeutic doses of two drugs should be considered for referral to a cardiologist

## Drug interventions to prevent new vascular events

All patients with stable angina due to atherosclerotic disease should receive long term standard aspirin and statin therapy.

All patients with stable angina should be considered for treatment with angiotensin-converting enzyme inhibitors.

## REVASCULARISATION

## All patients

Coronary artery bypass grafting and percutaneous coronary interventions are both appropriate options for the alleviation of anginal symptoms.

## Patients with triple vessel disease

Patients with triple vessel disease should be considered for coronary artery bypass grafting to improve prognosis, but where unsuitable be offered percutaneous coronary intervention.

## Patients with left main stem disease

## Patients with single/double vessel disease

Patients with single or double vessel disease, where optimal medical therapy fails to control angina symptoms, should be offered percutaneous coronary intervention or where unsuitable, considered for coronary artery bypass grafting.

Patients with significant left main stem disease should undergo coronary artery bypass grafting.