By kind permission, these guidelines are adapted from the Cheshire and Merseyside Cardiac Network Guidelines and represent the consensus views of the North Wales Cardiac Network (NWCN).

They were developed following consideration of the available evidence and aim to ensure equity and best practice.

Health professionals are asked to take them into account when exercising their clinical judgement and are encouraged to discuss with colleagues those cases where the assessment of likely benefit from a particular intervention is equivocal. The guidelines do not override the responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient in consultation with the patient and/or guardian or carer.
CONTENTS

OVERVIEW OF GUIDELINES ................................................................. 1
INTRODUCTION ................................................................................... 4

1. What is Angina?
2. Why Is Angina Important?
3. The Need for Guidelines
4. Principles Underpinning Guidelines

STAGE 1 CASE MANAGEMENT AND REFERRAL PATHWAYS .............. 8
1. Patients with Known Stable Angina
2. Patients with Worsening Known Angina
3. New Patients with Recent Onset Chest Pain - Suspected Angina
4. Communications

STAGE 2 DIAGNOSIS ........................................................................... 13
1. Use of Algorithm 2
2. Clinical Assessment
3. Pre-test Probability of CAD
4. Non-invasive Diagnostic Testing to Produce Post-test Probability of CAD

STAGE 3 RISK STRATIFICATION ...................................................... 23

STAGE 4 CORONARY ANGIOGRAPHY ............................................. 26

STAGE 5 LIFESTYLE AND RISK FACTOR MODIFICATION .......... 29
1. Cardiac Rehabilitation
2. Refractory Angina

STAGE 6 DRUG TREATMENT .............................................................. 40
1. Drug Treatment of Acute Episode
2. Prophylactic Drug Treatment of Symptoms
3. Drug Treatment to Improve Prognosis in Stable Angina

STAGE 7 REvascularisation ............................................................... 49
1. Selection of Patients for Revascularisation Therapy
2. Selection of Method of Revascularisation
3. Contraindications to Myocardial Revascularisation
4. Specific Patient and Lesion Subsets

STAGE 8 ASSESSMENT AND MANAGEMENT OF CVD RISK PRIOR TO NON-CARDIAC SURGERY ........................................... 55
1. Use of Algorithm 3
2. Mechanisms of Perioperative Acute Coronary Syndrome (ACS)
3. Accuracy of Non-invasive Testing in Pre-operative Assessment
4. Classical Approach
5. Preferred (Modern) Approach

APPENDIX TO STAGE 8 ASSESSMENT AND MANAGEMENT OF CVD RISK OF POTENTIAL CANDIDATES FOR RENAL TRANSPLANTATION ........................................................................ 62
1. Objectives
2. Special Considerations (Why Renal Transplant and Pancreatic-renal Transplant Differ)
3. CMCN Pathway
4. Re-assessment of Patients Accepted on to Transplant Waiting List
OVERVIEW OF GUIDELINES

Wherever possible the guidelines are in the format of clinical algorithms supported by tables with a minimum of text. The component parts of the Stable Angina Pathway are discussed in eight management stages as follows and the overall pathway is outlined in Algorithm 1.

Table 1

<table>
<thead>
<tr>
<th>Stage</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Case management and referral pathways</td>
</tr>
<tr>
<td></td>
<td>Models of care within primary care and between primary and secondary care.</td>
</tr>
<tr>
<td>2</td>
<td>Diagnostic pathway</td>
</tr>
<tr>
<td></td>
<td>Initial clinical assessment giving a pre-test probability of angina; then appropriate non-invasive investigations; followed by a re-assessment of the likelihood of angina modified by the investigation results giving a post-test probability.</td>
</tr>
<tr>
<td>3</td>
<td>Risk Stratification</td>
</tr>
<tr>
<td></td>
<td>Based on clinical and non-invasive investigational data.</td>
</tr>
<tr>
<td>4</td>
<td>Coronary angiography</td>
</tr>
<tr>
<td></td>
<td>Indications for, and interpretation of, results of invasive investigation by coronary angiography (and left ventricular angiography) to confirm diagnosis, refine prognosis and identify need for interventional therapy.</td>
</tr>
<tr>
<td>5</td>
<td>Lifestyle and risk factor modification</td>
</tr>
<tr>
<td></td>
<td>As a complement to medical and/or interventional treatment including the roles of cardiac rehabilitation and refractory angina management.</td>
</tr>
<tr>
<td>6</td>
<td>Drug treatment</td>
</tr>
<tr>
<td></td>
<td>Acute and prophylactic drug treatment, either as a primary treatment modality or as an adjunct to cardiac revascularisation.</td>
</tr>
<tr>
<td>7</td>
<td>Revascularisation</td>
</tr>
<tr>
<td></td>
<td>Interventional treatment including the indications and standards for either percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery (CABG).</td>
</tr>
<tr>
<td>8</td>
<td>Assessment and management of patients for non-cardiac surgery</td>
</tr>
<tr>
<td></td>
<td>Focussing on patients undergoing elective surgery. In addition, the specific problems relating to renal transplantation are addressed in an appendix.</td>
</tr>
</tbody>
</table>
**ALGORITHM 1**
**STABLE ANGINA PATHWAY**

- **New/suspected angina**
  - Diagnosis
    - Pre-test probability
    - Testing
    - Post-test probability
  - Worsening angina
  - Symptom severity assessment
  - Risk stratification
  - Known angina
  - Coronary angio indicated for diagnosis/prognosis
  - Coronary angio not indicated
  - Lifestyle/risk factor modification
  - Cardiac rehab
  - Refractory angina
  - Drug treatment
  - Non-cardiac pre-op assessment/management
  - Revasc. PCI CABG
1. What Is Angina?

Angina pectoris (angina) is a clinical syndrome characterised by discomfort in the chest, jaw, shoulder, back or arms, brought on by exercise or emotion and relieved by rest or nitroglycerin. Conventionally, the term *angina* is reserved for cases in which the discomfort is due to myocardial ischaemia resulting from atheromatous coronary artery disease (CAD).

Less commonly *anginal-type* chest pain sounding similar, or even identical, to true angina can arise in the absence of CAD due to:

- dynamic coronary artery problems (e.g. coronary spasm, cardiac syndrome X, endothelial dysfunction),
- non-coronary cardiac problems (e.g. aortic stenosis, cardiomyopathy, vasculitis etc),
- non-cardiac causes mimicking angina (e.g. oesophageal, musculo-skeletal or psychogenic problems).

Myocardial ischaemia, which underlies true angina, results from an imbalance between the supply of and demand for myocardial oxygen.

*Myocardial oxygen supply* is essentially the coronary flow and is itself dependent on the luminal cross-sectional area of the coronary artery and coronary arterial tone, both adversely affected by atherosclerotic plaque.

*Myocardial oxygen demand* is determined by heart rate, myocardial contractility (force of contraction) and wall stress, all of which increase with exercise and emotion.

Imbalance, caused by demand exceeding supply, initiates a sequential ischaemic cascade of metabolic abnormalities, perfusion mismatch, contractile dysfunction, ECG changes and then angina. The pain of angina is mediated by the release of adenosine, from ischaemic myocardium, that stimulates A1 receptors on cardiac nerve endings.

The stable angina threshold frequently varies from day to day or even during the same day. This symptom variability, including the occurrence of rest pain, results from dynamic factors, especially the degree of vasoconstriction at the site of underlying fixed atheromatous plaques (dynamic stenosis) or at the distal coronary vessels, and from factors such as ambient temperature, mental stress and neurohumoral influences.
The Canadian Cardiovascular Society (CCS) has produced a classification system which has been widely adopted:

**CCS CLASS I**
Ordinary physical activity such as walking, climbing stairs does not cause angina. Angina occurs with rapid or prolonged exertion at work or recreation.

**CCS CLASS II**
Slight limitation of ordinary activity. Angina occurs on walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold or wind or under emotional stress or only during the few hours after waking. Angina occurs after walking more than two blocks on the level or climbing more than one flight of ordinary stairs at a normal pace and in normal conditions.

**CCS CLASS III**
Marked limitations of ordinary physical activity. Angina occurs on walking one to two blocks on the level and climbing one flight of stairs in normal conditions and at a normal pace.

**CCS CLASS IV**
Inability to carry on any physical activity without discomfort – anginal symptoms may be present at rest.

### 2. Why Is Angina Important?

The main importance of angina is that it is a symptom suggesting that the individual may have underlying CAD. Ischaemic heart disease (IHD) resulting from CAD is common and remains the major cause of death and morbidity in the Western world. The Health Survey for England (2003) reported a standardised prevalence of IHD in informants aged 35 and over in the North West of 9.4% in men and 6.6% in women.

It is important to understand that CAD produces adverse effects either:
- **predictably** – via a gradual increase in arterial obstruction (enlarging plaque), worsening the severity of stable angina, and/or
- **unpredictably** – by sudden and unheralded complications, usually due to plaque erosion or rupture, causing a heart attack (myocardial infarction [MI]), unstable angina or sudden death.

Annual mortality rates in stable angina vary from 0.9 to 1.4%, with an annual incidence of non-fatal MI of 0.55 to 2.6%. However, critically within the stable angina population there can be up to tenfold variation in an individual’s prognosis. A prognostic assessment, termed **risk stratification** is therefore an essential part of the management of patients with stable angina.

### 3. The Need for Guidelines

Despite a decline in the rate of major coronary events in recent years, data from the British Regional Heart Study based on GP records has shown a 2.6% annual increase in new diagnoses of angina in the 20 years of follow up to 2000 in males aged 40–59 at entry.
The National Service Framework (NSF) for CHD, Government targets and financial constraints within the NHS mandate the more rapid identification of patients, the application of evidence-based choices in ensuring best practice and the cost-effective use of scarce resources.

The management of angina is now truly multi-disciplinary. Guidance is thus required to promote seamless, consistent and equitable management across organisational boundaries. The target audience for these guidelines includes all the relevant healthcare professionals but in addition, it is intended to encourage involvement by patients in decisions about their own care.

These guidelines are not meant to be a comprehensive review of all angina-related literature, for which the reader is referred to the following publications that have informed this local guidance:

- American College of Cardiology and American Heart Association (ACC/AHA) 2002 Guideline Update for the Management of Patients with Chronic Stable Angina.¹
- Scottish Intercollegiate Guidelines Network Management of Stable Angina (2007).³

4. Principles Underpinning Guidelines

This is inevitably a consensus document combining the views of a number of multi-disciplinary task groups set up by the Cheshire and Merseyside Cardiac Network (CMCN). Whenever possible guidance is evidence-based and designed to be deliverable within the NHS locally. It is recognised, however, that some parts will currently be aspirational since not all health economies will be able to deliver every aspect within current resource constraints. Therefore, where appropriate, acceptable alternatives to best practice have been identified.

These guidelines have adopted the following principles:

- The guidance addresses not only clinical practice but also relevant models of care, standards of service provision and audit.

- The diagnosis and management of angina usually starts and ends in the primary/community care setting with secondary and tertiary services providing key interventions within the framework of the patient’s long-term care.

- The diagnosis of angina is rarely definitive and the concept of probability or likelihood of disease is used.

- The management of angina requires, in addition to symptomatic relief, the amelioration of adverse events or complications and thus prognostic risk stratification is a central feature.
• In practice, diagnostic and prognostic assessments are conducted in tandem rather than sequentially as the same clinical and investigational tools are used for both. However, for clarity of understanding and presentation, these linked assessments are described separately.

• Modern medical management now includes a number of effective and locally well-developed treatment modalities in addition to drug therapy, including cardiac rehabilitation and refractory angina management. This guidance attempts to define their place in patient management.

• Invasive and interventional approaches carry risks as well as benefits and are not infinitely available. Guidance is given on appropriate indications, treatment choices and patient prioritisation to allow best possible use of local resources compatible with good standards of care.

• Successful implementation of these guidelines will require investment in the ongoing education of a large constituency of relevant healthcare professionals.

Where appropriate the customary ACC/AHA classifications of recommendation have been adopted:

CLASS I Conditions for which there is evidence and/or general agreement that a given procedure/treatment is useful and effective

CLASS II Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy of a procedure/treatment
   IIa Weight of evidence/opinion is in favour of usefulness/efficacy
   IIb Usefulness/efficacy is less well established by evidence/opinion

CLASS III Conditions for which there is evidence and/or general agreement that a given procedure/treatment is not useful/effective and in some cases may be harmful

1ACC/AHA 2002 Guideline Update for the Management of Patients With Chronic Stable Angina. www.acc.org
3www.sign.ac.uk
**Summary**

**Table 2**

<table>
<thead>
<tr>
<th>Reason for referral:</th>
<th>Refer to:</th>
<th>Recommended time frame from referral to patient being seen:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable known angina:</td>
<td>General cardiology outpatient clinic</td>
<td>4-6 weeks</td>
</tr>
<tr>
<td>- further cardiological advice about ongoing management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Worsening known angina:</td>
<td>Rapid access clinic or general cardiology outpatient clinic</td>
<td>14 days</td>
</tr>
<tr>
<td>• Stable angina:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- early assessment and treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Possible or probable unstable angina:</td>
<td>A&amp;E, Acute Medical Assessment Unit (AMU) or Heart Emergency Centre (HEC)</td>
<td>immediate</td>
</tr>
<tr>
<td>- urgent treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>New onset chest pain suspected angina:</td>
<td>Rapid access clinic or reserved slots in general cardiology outpatient clinic</td>
<td>14 days</td>
</tr>
<tr>
<td>- confirmation of diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- risk stratification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- management plan</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1. Patients with Known Stable Angina

This section refers to patients in whom a diagnosis of angina has previously been made and confirmed by specialist assessment either within general practice or more usually within secondary/tertiary care. The principles of management should be:

- GPs should ensure that unless contraindicated by infirmity or co-morbidity, all patients with a diagnosis of angina should have undergone diagnostic testing and risk stratification (see Stages 2 and 3). This should be undertaken within general practice or by referral to a general cardiology clinic in secondary care.

- Long-term management should be delivered in the community on a structured basis, ideally within a multi-disciplinary management programme in primary care. The focus should be on symptomatic anti-anginal treatment; drug treatment as secondary prevention of future events (see Stage 6); and risk factor/lifestyle modification (see Stage 5).

- Specialist advice on specific management issues e.g. in relation to medication, perioperative risk, air travel etc should be obtained via a referral to a general outpatient cardiology clinic, using the local general cardiology referral form. **The patient should be seen within 4-6 weeks.** In some areas, there may be arrangements in place for such advice to be obtained by telephone.

- It is important to identify changes in clinical status indicative of worsening stable angina requiring assessment or re-assessment for revascularisation or of unstable angina mandating admission to hospital. See Section 2 below.

This process will be aided by consideration of the following questions during each primary care follow up:

- Has the patient decreased his or her level of physical activity since the last visit?
- Have the patient’s anginal symptoms increased in frequency and become more severe since the last visit?
- How well is the patient tolerating therapy?
- How successful has the patient been in modifying risk factors and improving knowledge about ischaemic heart disease?
- Has the patient developed any new co-morbid illness or has the severity or treatment of any co-morbid illness worsened the patient’s angina?
2. Patients with Worsening Known Angina

Worsening angina may represent either increasingly symptomatic stable angina or the onset of an acute coronary syndrome (ACS), usually unstable angina but occasionally MI.

Increasingly Symptomatic Stable Angina

This usually occurs gradually over weeks or months. It may be due to:
- progression of underlying atheromatous disease consequently with a reduced angina threshold
- altered patient factors such as increased weight, increased activity demands e.g. change of job; poor compliance with drugs; increased family/work stress etc.
- co-morbidity altering supply/demand balance as a result of either cardiac problems such as worsening aortic stenosis, uncontrolled hypertension or non-cardiac problems such as anaemia, hypoxia due to respiratory disease, thyrotoxicosis etc.

Unless the cause is easily identifiable and managed within the community, such patients should be referred to secondary care to be seen by a medical clinician who is able to make decisions on immediate changes and institute further investigation such as coronary angiography. **It is recommended that such patients should be seen within 14 days of receipt of referral either within a general cardiology clinic or in a designated Rapid Access Chest Pain Clinic (RACPC).** (See Section 3 below)

Unstable Angina

This is characterised by:
- either a sudden (over hours to days) increase in angina frequency/duration/severity,
- or a change to angina occurring on minimal exertion or at rest where this is not the patient’s usual angina pattern,
- or angina recurring within days or a few weeks of discharge post-MI or post-cardiac intervention.

**Such patients should be referred as an emergency to A&E, an Acute Medical Assessment Unit (AMU) or Heart Emergency Centre as per local pathways.** (See CMCN Non-ST Elevation Acute Coronary Syndrome [NSTEMACS] Guidelines)

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1CMCN NSTEACS Guidelines, www.cmcn.nhs.uk
3. New Patients with Recent Onset Chest Pain – Suspected Angina

Patients suspected to have new onset angina should be referred to a dedicated outpatient clinic (RACPC) or reserved rapid access slots within general cardiology clinics and seen within 14 days of receipt of referral in accordance with mandatory national requirements.

The rapid access provision should meet the following standards:

- **RACPCs** should work under protocols set up by a cardiologist. As a minimum staff must be able to call on a consultant cardiologist although he/she does not have to be present at all times.

- Initial assessment of the patient should be performed by practitioners skilled and experienced in assessing patients with chest pain and in the interpretation of an exercise ECG.

- The service should have the following diagnostic facilities with results reported during the patient’s attendance:

  - **Essential**
    - 12 lead resting ECG
    - Exercise ECG

  - **Desirable**
    - Echocardiogram
    - Chest X-Ray – film to be available to cardiologist and reported by radiologist later

- Patients who cannot exercise should be seen within 14 days of referral and if indicated, referred for alternative investigations e.g. perfusion imaging, stress echo, or coronary angiography. (See Stages 2,3 and 4.)

- Patients who are given a confirmed diagnosis of stable angina require immediate access to an appropriately trained practitioner to commence education and arrange cardiac rehabilitation follow-up. (See Stage 5.)

- The quality of local GPs’ referral practice to rapid access services should be regularly reviewed by PCTs to ensure it continues to be appropriate.
4. Communications

Referral to the rapid access services should be made by the patient’s GP using the designated rapid access form delivered electronically or by fax. See sample at end of chapter.

A response to the patient’s GP via fax/e-mail/patient delivery should be made within 24 hours of the patient being seen. The content of the response should include:

- Diagnosis (where this has been made).
- Results of investigations.
- Follow-up appointments/investigations which have been arranged.
- Information as to what treatment changes have been made by the clinic (e.g. medication changes).
- Treatment changes which the GP is asked to make.
- Information/advice which has been given to the patient.
STAGE 2
DIAGNOSIS

Summary

ALGORITHM 2
DIAGNOSIS

CLINICAL ASSESSMENT
Chest pain features Table 3 History and risk factors Table 4
Physical examination Table 5 12 lead ECG and bloods

PRE-TEST PROBABILITY OF CAD Table 6

<20 %  ≥20 - <30%  ≥30 - <80%  >80%

Unable to exercise/ Exercise ECG using Exercise ECG/ stress imaging
Ex. ECG contra- Bruce protocol for risk contraindicated Table 7 stratification only
indicated Table 7 if appropriate

POST-TEST PROBABILITY OF CAD Table 8

>20% - <50% >50% <20% CAD possible CAD probable CAD unlikely

Stress imaging

Select technique Table 11

CAD unlikely

Contraindicated Table 9 or inconclusive. Consider angiography for diagnosis

RISK STRATIFICATION Tables 12,13,14

Low  Intermediate  High

Manage risk
Exclude other causes - echo
Further cardiac lx - only if exclusion of CAD essential
Consider angiography if revascularisation to be considered for symptoms

Review medical treatment, risk factor modification
Consider angiography if revascularisation to be considered for symptoms

Coronary angiography unless contra-indicated or unlikely to affect management
1. Use of Algorithm 2

Algorithm 2 demonstrates the recommended investigational pathway for diagnosis and risk stratification of patients. In practice, these assessments are conducted in tandem as the same clinical and investigational tools are used for both. However, for clarity of understanding and presentation, they are described sequentially as stages 2 and 3 and coronary angiography which is used for both diagnostic and prognostic purposes is described separately as stage 4.

The algorithm demonstrates the pathways for patients presenting with suspected stable angina without previously known CAD and for patients with known CAD who present with recurrent or worsened stable angina. In this latter group, the diagnosis is rarely in doubt and further diagnostic tests add little since they are a high prevalence population with high pre-test probability. Therefore, the focus of non-invasive testing should be risk stratification and prognosis.

Use of Algorithm 2 will lead to a logical, evidence-based and cost-effective approach. It should be used as the basis for decision-making as to the appropriateness of invasive coronary angiography with a view to interventional treatment by percutaneous coronary intervention (PCI) or coronary arterial bypass graft (CABG).

The algorithm also recognises and endorses as good practice, the direct application of coronary angiography without preliminary non-invasive testing in some patient groups. Thus in many patients with known CAD, or those with a very high (≥ 80%) pre-test probability of CAD who, despite appropriate medical treatment, have severe limiting or worsening typical angina, non-invasive testing is often unnecessary and direct listing for coronary angiography is appropriate.

2. Clinical Assessment

History

This should include consideration of the following aspects:

- **Chest pain** - the initial suspicion or presumptive diagnosis of angina is usually based on the patient’s description of the pain.

<table>
<thead>
<tr>
<th>Table 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CLASSIFICATION OF CHEST PAIN</strong></td>
</tr>
<tr>
<td>Typical angina</td>
</tr>
<tr>
<td>Atypical angina</td>
</tr>
<tr>
<td>Non-cardiac chest pain</td>
</tr>
</tbody>
</table>
• **Patient setting** - the likelihood of a chest pain being angina whatever its features is highly dependent on the patient setting in which it occurs. Evidence of previous/known CVD or the co-existence of vascular risk factors increases the likelihood of angina.

**Table 4**

<table>
<thead>
<tr>
<th>Evidence of CVD</th>
<th>Risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known IHD</td>
<td>Age- M &gt;40 yrs; F &gt;50 yrs</td>
</tr>
<tr>
<td>Previous CVA, TIA</td>
<td>Gender - M &gt; F</td>
</tr>
<tr>
<td>Known PVD</td>
<td>Family IHD history -especially premature M&lt;50 yrs ; F&lt;60 yrs</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
</tr>
<tr>
<td></td>
<td>Dyslipidaemia</td>
</tr>
<tr>
<td></td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td>Diabetes Mellitus</td>
</tr>
</tbody>
</table>

**Examination**

This is usually diagnostically less helpful than the history but signs may exist supporting an ischaemic origin, suggesting an alternative cardiac cause, or pointing positively to a non-cardiac cause.

**Table 5**

<table>
<thead>
<tr>
<th>Ischaemia</th>
<th>Non- ischaemic cardiac</th>
<th>Non-cardiac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usually normal.</td>
<td>Pericardial rub.</td>
<td>Musculo-skeletal</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>Valvular disease -especially AS.</td>
<td>-chest wall tenderness, positive physical manoeuvres.</td>
</tr>
<tr>
<td>-AF, SVT, VT, bradycardia.</td>
<td>Cardiomyopathy -LVH, CCF.</td>
<td>Respiratory</td>
</tr>
<tr>
<td>LV dysfunction-S3, pulmonary oedema.</td>
<td>Aortic dissection -AR, differential arm pulses or BP.</td>
<td>-pleural rub, pneumothorax, consolidation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-pyrexia, rash, epigastric Tenderness</td>
</tr>
</tbody>
</table>

**Baseline Tests**

• **Blood tests** – all patients should have haemoglobin; blood glucose (preferably fasting); lipid profile including total cholesterol, HDL cholesterol and triglycerides; urea and electrolytes. Where appropriate other tests may be necessary including thyroid function, liver function, troponin etc.
• **ECG** – a 12 lead resting ECG should be done in all patients. It will be normal in ≥50% of patients. This does not exclude CAD but does strongly imply normal resting left ventricular (LV) function and hence a favourable prognosis. Evidence of prior Q wave MI, LV hypertrophy (LVH), or ST/T wave changes, consistent with myocardial ischaemia, favour a diagnosis of angina. An ECG done during pain adds greatly to its otherwise poor diagnostic ability.

• **Chest X-ray** – this does not add specific diagnostic or prognostic information and is therefore not a routine test. It should be done in patients with suspected heart failure, valvular disease or pulmonary disease, (including smokers who have not had a chest X-ray in the last year).

• **Echocardiogram** – this is not a routine test for angina assessment. It should only be requested for (a) patients with a systolic murmur suggestive of aortic stenosis, mitral regurgitation or hypertrophic cardiomyopathy or (b) to assess LV function in patients with signs, symptoms or ECG suggestive of heart failure or LV dysfunction.

### 3. Pre-Test Probability of CAD

**Concept of Disease Probability or Likelihood**

The presence of CAD and hence a diagnosis of angina cannot be confirmed or refuted with 100% certainty by non-invasive means i.e. clinical assessment or non-invasive testing. A Bayesian approach to diagnosis that deals with probabilities should therefore be adopted. This approach uses the clinician’s pre-test estimate of disease likelihood and then modifies it on the basis of the results of diagnostic tests to generate individualised post-test disease probabilities for a given patient.

The pre-test probability depends on the prevalence of the disease in the population studied as well as the individual’s clinical features especially age, gender, risk factor profile and chest pain type.

In populations with a low prevalence of CAD e.g. young, female, with no risk factors and atypical pain, a positive test result will have a much higher chance of being a false positive than the same result in a high prevalence population e.g. 60 years old, male, with diabetes and with typical chest pain.

See Table 6.
<table>
<thead>
<tr>
<th>Chest pain type</th>
<th>MEN</th>
<th>WOMEN</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No of risk factors</td>
<td>No of risk factors</td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Non-cardiac chest pain</td>
<td>Atypical chest pain</td>
</tr>
<tr>
<td>40-49</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>50-59</td>
<td>23</td>
<td>35</td>
</tr>
<tr>
<td>60+</td>
<td>49</td>
<td>55</td>
</tr>
</tbody>
</table>

**Definitions**

**Smoking:** > half a pack per day in last five years or 25 pack years

**Hyperlipidaemia:** cholesterol >6.5mmol/l

**ECG**

The above values are for patients with a normal resting ECG. If ST-T wave changes or Q waves are present, the likelihood of CAD will be higher.
4. Non-Invasive Diagnostic Testing to Produce Post-test Probability of CAD

These tests are used to detect signs of myocardial ischaemia during stress and hence to improve the clinically based pre-test estimate of probability of CAD. **Relevant investigations are exercise/stress tolerance testing with ECG recording (exercise ECG), usually using a motorised treadmill or occasionally a bicycle; myocardial perfusion scintigraphy (MPS); stress echo using dobutamine (DSE)**

**Exercise ECG**

For reasons of availability and cost, an exercise ECG using the Bruce protocol is the initial test of choice. It should be performed for diagnostic purposes in all patients in whom the pre-test probability lies in the range ≥ 30-<80% and in whom there are no contra-indications.

*Table 7*

<table>
<thead>
<tr>
<th>CONTRA-INDICATIONS TO DIAGNOSTIC EXERCISE ECG TESTING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absolute contra-indications</strong></td>
</tr>
<tr>
<td>- Uncontrolled hypertension: &gt;200 mmHg systolic and/or &gt;110 mmHg diastolic</td>
</tr>
<tr>
<td>- LBBB on ECG</td>
</tr>
<tr>
<td>- Pre-excitation pattern i.e. delta waves</td>
</tr>
<tr>
<td>- Paced rhythm</td>
</tr>
<tr>
<td>- Uncontrolled arrhythmia</td>
</tr>
<tr>
<td>- Suspected unstable angina</td>
</tr>
<tr>
<td>- More than 2 mm resting ST depression, particularly if the patient is on digoxin</td>
</tr>
<tr>
<td>- Acute myocarditis or pericarditis</td>
</tr>
<tr>
<td>- Uncontrolled, symptomatic heart failure</td>
</tr>
<tr>
<td>- Symptomatic severe aortic stenosis</td>
</tr>
<tr>
<td>- Inability to perform exercise ECG due to co-morbidity or disability</td>
</tr>
</tbody>
</table>

**Relative contra-indications – caution required**

- Suspected significant outflow tract obstruction due to moderate aortic stenosis or hypertrophic obstructive cardiomyopathy
- Other significant valvular disorder e.g. mitral stenosis or aortic regurgitation
- Recent ACS: MI/high risk unstable angina ≤ 3 weeks; known left main stem stenosis
- High degree atrioventricular block

Outside the range ≥ 30% to <80%, the test has little diagnostic accuracy producing excessive false positives in very low prevalence populations and failing to add to the pre-test probability in very high prevalence populations. Within this range, its accuracy is reasonable having an overall sensitivity of 68% and a specificity of 77% for the detection of significant CAD using a diagnostic threshold of 1mm horizontal or down-sloping ST depression.
The degree of ST-depression is the principal diagnostic, as opposed to prognostic, outcome from an exercise ECG. This should be factored into known pre-test clinical variables to obtain a refined and individualised post-exercise ECG probability of CAD as shown in Table 8 below.

**Table 8**

### POST-EXERCISE ECG PROBABILITY OF CAD

#### MEN

<table>
<thead>
<tr>
<th>Age</th>
<th>Non-cardiac chest pain</th>
<th>Atypical chest pain</th>
<th>Typical angina</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ST - depression mm</td>
<td>ST - depression mm</td>
<td>ST - depression mm</td>
</tr>
<tr>
<td>30-39</td>
<td>≤0.4 0.5-0.9 1.5-1.9 2.0-2.4 ≥2.5</td>
<td>≤0.4 0.5-0.9 1.5-1.9 2.0-2.4 ≥2.5</td>
<td>≤0.4 0.5-0.9 1.5-1.9 2.0-2.4 ≥2.5</td>
</tr>
<tr>
<td>40-49</td>
<td>1 10 5 39 68</td>
<td>6 21 38 55 76 92</td>
<td>25 68 83 91 96 99</td>
</tr>
<tr>
<td>50-59</td>
<td>4 26 13 65 87</td>
<td>16 44 64 78 91 97</td>
<td>61 86 94 97 99 &gt;99</td>
</tr>
<tr>
<td>60+</td>
<td>6 45 20 53 91</td>
<td>25 57 75 86 94 98</td>
<td>73 91 96 98 99 &gt;99</td>
</tr>
<tr>
<td></td>
<td>8 19 26 62 81 94</td>
<td>32 65 81 89 96 99</td>
<td>79 94 97 99 99 &gt;99</td>
</tr>
</tbody>
</table>

#### WOMEN

<table>
<thead>
<tr>
<th>Age</th>
<th>Non-cardiac chest pain</th>
<th>Atypical chest pain</th>
<th>Typical angina</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>&lt;1 2 3 8 24</td>
<td>1 4 9 15 33</td>
<td>63 79 93</td>
</tr>
<tr>
<td>40-49</td>
<td>1 11 6 24 53</td>
<td>3 12 25 39 63</td>
<td>86 53 72 84 93 98</td>
</tr>
<tr>
<td>50-59</td>
<td>2 16 8 50 78</td>
<td>10 31 50 67 84 95</td>
<td>47 78 89 94 98 99</td>
</tr>
<tr>
<td>60+</td>
<td>5 49 17 72 90</td>
<td>21 52 72 83 93 98</td>
<td>69 90 95 98 99 99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>[%Probability]</th>
<th>≥ 50</th>
<th>≥ 20 &lt;50</th>
<th>&lt; 20</th>
</tr>
</thead>
</table>
Stress Imaging

Stress imaging should be considered if there are no absolute contra-indications (see Table 9), in the following situations:
- When pre-test probability of CAD is in the range $\geq 20 < 30\%$. (See Table 6)
- When exercise ECG is contra-indicated. (See Table 7)
- When post-exercise ECG probability is in the range $\geq 20 < 50\%$. (See Table 8)

Table 9

<table>
<thead>
<tr>
<th>ABSOLUTE CONTRA-INDICATIONS TO STRESS IMAGING</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Uncontrolled hypertension: $&gt;200$ mmHg systolic and/or $&gt;110$ mmHg diastolic</td>
</tr>
<tr>
<td>- Suspected unstable angina or acute MI</td>
</tr>
<tr>
<td>- Acute myocarditis or pericarditis</td>
</tr>
<tr>
<td>- Uncontrolled, symptomatic heart failure</td>
</tr>
<tr>
<td>- Symptomatic severe aortic stenosis</td>
</tr>
</tbody>
</table>

The two techniques currently appropriate in the CMCN area are:
- Myocardial perfusion scintigraphy (MPS) involving single photon emission computed tomography (SPECT); technetium (sesta) methoxy-isobutyl-isonitrile (MIBI) as the radiotracer; and adenosine, dipyridamole, dobutamine or exercise as the stress agent.
- Stress echocardiography with dobutamine as the stress agent.

There is little difference between the two techniques in terms of accuracy. (Table 10)

Table 10

<table>
<thead>
<tr>
<th>PHYSICAL EXAMINATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
</tr>
<tr>
<td>Exercise MPS</td>
</tr>
<tr>
<td>Vasodilator stress MPS</td>
</tr>
<tr>
<td>Dobutamine stress echo</td>
</tr>
</tbody>
</table>

In the majority of cases, the choice of technique should be based on local availability, including waiting times, and expertise. In some clinical scenarios, however, one or other test is to be preferred. (See Table 11)
Table 11

<table>
<thead>
<tr>
<th>Indication</th>
<th>MPS with SPECT</th>
<th>Stress Echocardiography</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Suitability Comment</td>
<td>Suitability Comment</td>
</tr>
<tr>
<td>Diagnosis of ischaemia</td>
<td>Yes</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>More sensitive</td>
<td>More specific</td>
</tr>
<tr>
<td>Assessment of myocardial viability</td>
<td>Yes</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>More sensitive</td>
<td>More specific</td>
</tr>
<tr>
<td>Patients with paced rhythm/LBBB</td>
<td>Yes</td>
<td>no</td>
</tr>
<tr>
<td>Poor echo subject</td>
<td>Yes</td>
<td>yes with limitations</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contrast may overcome limitation</td>
</tr>
<tr>
<td>Patients with asthma/COPD</td>
<td>yes with limitations</td>
<td>yes with limitations</td>
</tr>
<tr>
<td></td>
<td>Use dobutamine in pharmacologic</td>
<td>Reduced image quality likely</td>
</tr>
<tr>
<td></td>
<td>stress imaging since adenosine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>and dipyridamole are contra-indicated</td>
<td></td>
</tr>
<tr>
<td>More comprehensive cardiac examination required</td>
<td>No</td>
<td>yes</td>
</tr>
<tr>
<td>Assessment of valvular lesions (low-grade AS with</td>
<td>No</td>
<td>yes</td>
</tr>
<tr>
<td>LV dysfunction, MS/MR)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If there is a lengthy delay in the local waiting time for stress imaging the clinician may consider in individual cases that it is in the patient's interest to proceed directly to coronary angiography.
Other Imaging Techniques

Cardiac magnetic resonance is rapidly emerging as a technique capable of providing highly accurate diagnostic information regarding myocardial ischaemia and myocardial viability as well as cardiac anatomy and function. It is currently limited by availability and cost and should be reserved for special cases after discussion with the appropriate provider.

The spatial and temporal resolutions of computed tomography (CT) have improved enormously. Multi-detector or multi-slice CT (MDCT) shows great promise for non-invasive coronary imaging – 90-94% sensitivity, 95-97% specificity, 93-99% negative predictive accuracy for 64 detector scanners. At present, its place in the investigational hierarchy for angina is unknown. A cardiac MDCT service is currently unavailable locally.

STAGE 3
RISK STRATIFICATION

STAGE 3
RISK STRATIFICATION
STAGE 2
RISK STRATIFICATION

Summary

ALGORITHM 2
RISK STRATIFICATION

- No known CAD-suspected angina
- Known CAD

CLINICAL ASSESSMENT
Chest pain features Table 3
History and risk factors Table 4
Physical examination Table 5
12 lead ECG and bloods

PRE-TEST PROBABILITY OF CAD Table 6

- < 20%
- ≥ 20 - < 30%
- ≥ 30 - < 80%
- ≥ 80%

Unable to exercise/
Ex. ECG contraindicated Table 7

Exercise ECG using
Bruce protocol

POST-TEST PROBABILITY
OF CAD Table 8

- Stress imaging
- ≥ 20 - < 50%
  CAD possible
- > 50%
  CAD probable
- < 20%
  CAD unlikely

Select technique
Table 11
Contraindicated Table 9 or inconclusive.
Consider angiography for diagnosis

RISK STRATIFICATION Tables 12, 13, 14

- Normal
- Abnormal
- Inconclusive

CAD unlikely

- Low
- Intermediate
- High

Manage risk
Exclude other causes - echo
Further cardiac inv - only if
exclusion of CAD essential
Consider angiography if
revascularisation to be
considered for symptoms

Review medical treatment,
risk factor modification
Consider angiography if
revascularisation to be
considered for symptoms

Coronary angiography
unless contra-indicated
or unlikely to affect
management

Consider angiography if
revascularisation to be
considered for symptoms
The long-term prognosis of stable angina varies widely from individual to individual, perhaps up to tenfold. The assessment of risk helps to determine the optimum treatment regime for an individual and in these guidelines risk is defined in terms of annual CV mortality as:

- **high** $>3\%$
- **intermediate** $1-3\%$
- **low** $<1\%$

A reasonable estimate of risk can be obtained simply from clinical evaluation (history and ECG) or from invasive coronary angiography. **However, it is recommended that initially a quantitative estimate be obtained wherever possible from the results of the same non-invasive tests used for diagnostic purposes.**

Table 12 outlines the use of the Duke Treadmill Score for risk stratification by exercise ECG whilst Tables 13 and 14 give prognostic stratification criteria for MPS and stress echocardiography respectively.

**Table 12**

<table>
<thead>
<tr>
<th>Duke Treadmill Score</th>
<th>Risk Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\leq -11$</td>
<td>High</td>
</tr>
<tr>
<td>-10 to +4</td>
<td>Intermediate</td>
</tr>
<tr>
<td>$\geq +5$</td>
<td>Low</td>
</tr>
</tbody>
</table>

**RISK STRATIFICATION: EXERCISE ECG**

Duke Treadmill Score calculation
Total score = time in minutes on Bruce protocol – $5 \times$ maximum ST-deviation in any lead in mm – $4 \times$ angina index ($0 =$ no angina, $1 =$ angina not limiting, $2 =$ limiting angina)
### Table 13

<table>
<thead>
<tr>
<th>Finding</th>
<th>Risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress-induced large perfusion defect (particularly if anterior)</td>
<td>High</td>
</tr>
<tr>
<td>Stress-induced multiple perfusion defects of moderate size</td>
<td></td>
</tr>
<tr>
<td>Large fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)</td>
<td></td>
</tr>
<tr>
<td>Stress induced moderate perfusion defect with LV dilation or increased lung uptake (thallium-201)</td>
<td></td>
</tr>
<tr>
<td>Mild/moderate resting LV dysfunction (LVEF = 35% - 49%)</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Stress induced moderate perfusion defect without LV dilation or increased lung intake (thallium-201)</td>
<td></td>
</tr>
<tr>
<td>Normal or small myocardial perfusion defect at rest or with stress**</td>
<td>Low</td>
</tr>
</tbody>
</table>

**Patient with these findings will probably not be at low risk in the presence of either a high risk treadmill score or severe resting left ventricular dysfunction (LVEF<35%).**

### Table 14

<table>
<thead>
<tr>
<th>Finding</th>
<th>Risk group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extensive ischaemia with wall motion abnormality involving &gt;2 segments developing at low dose of dobutamine (≤ 10mg/kg/min) or at a low heart rate (&lt;120 beats/min)</td>
<td>High</td>
</tr>
<tr>
<td>Mild/moderate resting LV dysfunction (LVEF 35% - 49%)</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Limited ischaemia with a wall motion abnormality involving &lt; 2 segments only at higher doses of dobutamine</td>
<td></td>
</tr>
<tr>
<td>Normal wall motion or no change of limited resting wall motion abnormalities during stress**</td>
<td>Low</td>
</tr>
</tbody>
</table>

**Patient with these findings will probably not be at low risk in the presence of either a high risk treadmill score or severe resting left ventricular dysfunction (LVEF<35%).**
STAGE 4
CORONARY ANGIOGRAPHY
STAGE 4
CORONARY ANGIOGRAPHY

Summary

ALGORITHM 2
CORONARY ANGIOGRAPHY

CLINICAL ASSESSMENT
Chest pain features Table 3
History and risk factors Table 4
Physical examination Table 5
12 lead ECG and bloods

PRE-TEST PROBABILITY OF CAD Table 6

< 20%
≥ 20 - < 30%
≥ 30 - < 80%
≥ 80%

Unable to exercise/
Ex. ECG contraindicated Table 7

Exercise ECG using
Bruce protocol

Exercise ECG/ stress imaging
for risk stratification only
if appropriate

STRESS IMAGING

≥ 20 - < 50%
≥ 50%
< 20%

CAD possible
CAD probable
CAD unlikely

RISK STRATIFICATION Tables 12, 13, 14

Low
Intermediate
High

Manage risk
Exclude other causes - echo
Further cardiac tests - only if exclusion of CAD essential

Contraindicated Table 9 or inconclusive. Consider angiography for diagnosis

Select technique Table 11

Contraindicated Table 10 or inconclusive. Consider angiography for diagnosis

Consider angiography if revascularisation to be considered for symptoms

Review medical treatment, risk factor modification

Coronary angiography unless contra-indicated or unlikely to affect management

No known CAD-suspected angina
Known CAD

Normal
Abnormal
Inconclusive

CAD unlikely

Consider angiography if revascularisation to be considered for symptoms
Coronary angiography holds a fundamental position in the investigation of patients with stable angina. It provides reliable anatomical information to identify the presence or absence of coronary lumen stenosis; defines therapeutic options including the suitability of medical treatment or myocardial revascularisation and determines prognosis by defining the extent and severity of coronary artery stenosis. This allows classification into one-two-three vessel disease or left main stem CAD.

However, it is important to recognise its limitations which include the following:
- It does not diagnose coronary atheroma since vessel wall disease may be present when the lumen is normal.
- It does not give information on myocardial ischaemia since it does not assess the functional importance of any anatomical stenosis.
- It is insensitive in detection of a thrombus.
- It is ineffective in determining which plaques have characteristics likely to lead to acute coronary events. Plaques resulting in unstable angina and MI commonly produce less than 50% stenosis before the acute event and will therefore be angiographically "silent".

Complications and Consent

In the vast majority of cases, coronary angiography for stable angina should be a day case procedure. It can be carried out with adequate quality and safety in either a tertiary or DGH setting. However, it is an invasive investigation and as such has inherent risks and complications. The composite rate of death, MI or stroke associated with routine diagnostic catheterisation in patients is of the order of 0.1% to 0.2%. The composite rate of major complications is about 1%. Where possible the complication rate of the relevant hospital should be known and quoted. In making the decision to proceed to invasive coronary angiography, it is important to take into account the patient’s willingness to accept the risks of the procedure and his/her willingness to proceed to any therapeutic intervention that might arise. Obviously, it is important to consider the patient’s suitability on the basis of comorbidity and frailty.
Recommendations for Angiography

Algorithm 2 indicates the group of patients identified as high risk on clinical assessment or after non-invasive investigation who should undergo coronary angiography on **prognostic** grounds unless contra-indicated or unlikely to affect management. (ACC/AHA Class I recommendation)

The algorithm also identifies patients at low or intermediate risk for whom revascularisation might be considered for **symptom control**. (ACC/AHA Class I recommendation for patients with CCS Class III and IV angina despite medical therapy.)

Table 15 lists the above indications and identifies additional patient groups who may benefit from angiography:

**Table 15**

<table>
<thead>
<tr>
<th>RECOMMENDATIONS FOR CORONARY ANGIOGRAPHY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient groups</td>
</tr>
<tr>
<td>Identified as high risk (annual CV mortality &gt;3%)</td>
</tr>
<tr>
<td>Patients with CCS Class III and IV for whom revascularisation might be considered for symptom control</td>
</tr>
<tr>
<td>Patients with angina who have survived sudden cardiac death or serious ventricular arrhythmia</td>
</tr>
<tr>
<td>Patients with angina and symptoms and signs of congestive cardiac failure</td>
</tr>
<tr>
<td>Patients with an uncertain diagnosis after non-invasive testing in whom the benefit of a more certain diagnosis outweighs the risk of coronary angiography</td>
</tr>
<tr>
<td>Patients who cannot undergo non-invasive testing due to disability, illness or morbid obesity</td>
</tr>
<tr>
<td>Patients with an occupational requirement for a definitive diagnosis</td>
</tr>
<tr>
<td>Patients with inadequate prognostic information</td>
</tr>
</tbody>
</table>

**Audit**

Each institution should make adequate provision for quality assurance and audit of its catheter laboratory procedures. Quality assurance requires that angiography be carried out by practitioners competent in the procedure or by trainees under adequate supervision and that operators carry out sufficient cases per year to maintain competence. In addition, CMCN has established a data set for coronary angiography which will aid quality assurance, allow bench marking and underpin audit.
Summary

Comprehensive angina management requires, in addition to drug therapy (see Stage 6) and revascularisation (see Stage 7), close attention to:

- **Lifestyle issues** including advice on smoking, diet, weight reduction, alcohol consumption, driving, sexual intercourse and physical activity/exercise.
- **Modifiable risk factors** for atherosclerosis including hypertension, diabetes and dyslipidaemia.
- **Psychosocial factors** including depression, anxiety, misconceptions, negative behaviour patterns and poor coping mechanisms.
- **Education** of patient's family and carers.

Whilst all relevant healthcare professionals should deal with aspects of these issues during the patient's multiple contacts in primary care and hospital, they are most effectively and comprehensively addressed by cardiac rehabilitation practitioners. **Provision should be made locally for all patients with newly diagnosed stable angina to have at least an initial consultation with a cardiac rehabilitation practitioner.** Local resource constraints may mean that it is not possible to offer all patients follow-up in a comprehensive programme tailored to their needs. However, the initial consultation will as a minimum, enable the practitioner to assess the patient, provide him/her with a personal plan and identify any major areas of concern which will require specific professional intervention.

Continuing physical or psychosocial issues not resolved by treatment (drugs or revascularisation), or by standard rehabilitation should lead to referral to a refractory angina service.
1. Cardiac Rehabilitation

Comprehensive cardiac rehabilitation consists of exercise training together with education and psychological support. The purpose of these interventions is to facilitate a return to normal living and to encourage patients to make lifestyle changes in order to prevent further events. It has much in common with, and links to, the provision of long-term secondary prevention co-ordinated in general practice but takes the opportunity, following a significant cardiac event to provide a patient and his/her family with more intensive support. The support is given over a relatively short period, through a programme delivered in a group or individually that should be tailored to meet the patient’s particular needs.

Several meta-analyses of randomised controlled trials (RCTs) in exercise based cardiac rehabilitation programmes since the 1980’s have demonstrated that these programmes reduce all cause and cardiac mortality in patients with coronary artery disease.\(^1\) Although most of the trials have been in patients post-MI, the presence of the same underlying pathology in patients with stable angina means that the likely benefit to this group should not be ignored.

A more recent meta-analysis of 63 RCTs demonstrated that benefit was not restricted to exercise based programmes.\(^2\) It covered three types of programme delivered individually or in a group: (a) combined education, risk factor counselling and supervised exercise; (b) combined education and risk factor counselling with no supervised exercise; and (c) supervised exercise alone. All types of programme were found to improve processes of care, coronary risk factor profiles, functional status and quality of life. In all types, a reduction in all cause mortality was absent at 12 months but was demonstrable at two years and sustained at five years.

Effective cardiac rehabilitation recognises the need to design services that take account of the diverse needs of the population in terms of age, gender, impairment, literacy, ethnicity, religious practice, cultural diversity, income, employment, dependents, and carers. Failure to design services appropriately has been shown to lead to inequality of patient access and poor compliance.

The design of trials has been such that the optimal mix of interventions, including frequency and duration and the incremental benefit of the various components, remains unclear. The detail described below reflects the local consensus view informed by current international guidelines.

All cardiac rehabilitation services should use the national data set\(^3\) to ensure consistent record keeping of the patient’s ongoing management, effective monitoring of patient outcomes to inform future service development and comprehensive audit.
Priorities for Referral

In addition to the NSF requirements of post-MI and post-revascularisation, it is recommended that the following cohorts of patients with stable CAD be offered cardiac rehabilitation in the priority order indicated:

1. All patients newly diagnosed with stable angina.

2. Patients previously diagnosed with stable angina who are experiencing severe adaptation problems such as issues with activity levels, weight control, adherence to medication etc.

3. Patients waiting for coronary revascularisation who will benefit from input to prepare for the procedure (‘pre-hab’) and afterwards to aid recovery.

Pathway at Point of Diagnosis

The practitioner initially informing the patient of his/her diagnosis of angina should ensure that the steps indicated in Table 16 have been taken.

Table 16

<table>
<thead>
<tr>
<th>PATHWAY AT POINT OF DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• A clear easily understood explanation about what will happen next should be given.</td>
</tr>
<tr>
<td>• A leaflet/booklet explaining about angina, such as a British Heart Foundation advice booklet or locally developed version should be provided. (With appropriate alternatives for non-English speakers and patients with vision or reading difficulties.)</td>
</tr>
<tr>
<td>• A referral should be made to the local Cardiac Rehabilitation Service and contact details of the service should be provided to the patient.</td>
</tr>
<tr>
<td>• Patients should be encouraged to continue normal daily activities, unless there are compelling reasons to the contrary. To advise against activity can be unhelpful to the patient’s future rehabilitation prospects and can cause undue distress.</td>
</tr>
</tbody>
</table>

Initial Consultation

The initial consultation should include:

- **Assessment of psychological well being**
  A psychological tool for assessment should be used to identify problems. It is important to recognise that psychological factors can often act as a barrier to the rehabilitation process. Concerns related to living with angina can influence mood, degree of disability and quality of life. Beliefs and misconceptions about heart disease have been shown to influence outcome, as has presence of depression and anxiety. If serious or pre-existing psychological problems are identified, see relevant sub-section below.
• Risk factor profile assessment and individual advice on management
Lifestyle intervention to discontinue smoking, make healthier food choices, increase aerobic physical activity, achieve optimal weight, and weight distribution is central to CVD prevention. These lifestyle issues and the control of blood pressure, cholesterol and glucose can be addressed more intensively in a comprehensive rehabilitation programme. However, the consultation at least provides an opportunity to set goals with patients in relation to their modifiable risk factors.

• Fitness assessment and advice
This will be informed by the cardiologist’s/GP’s assessment, exercise ECG results and the patient’s pre-morbid and current fitness/activity levels. Recognised fitness assessment tools may be used, for example the Shuttle Walk test. The assessment is primarily intended to plan the supervised exercise element of a comprehensive programme that will be carried out in a group or individually at home. However, it will also provide useful information about safe levels of exercise during daily activities.

• Patient education
This will include advice about medication, angina, symptoms, how to recognise chest pain, how to treat it and when to call for help. It is important to dispel myths around angina and promote the importance of adherence to medication.

Advice should also be given about social, cultural, family and carer needs, and issues such as returning to work, travel, driving, insurance cover and sexual relationships.

Choice of Programme

Following this consultation and in discussion with the patient, an agreed decision will be made on the appropriate individualised cardiac rehabilitation pathway to be followed. Outcomes from the consultation may also reveal a need for referral onto specialist services such as smoking cessation, diabetic and psychology.

Comprehensive Rehabilitation Programme

The optimal provision for patients with newly diagnosed stable angina is an individualised programme based on the needs identified at the initial consultation and which includes the following:

• Lifestyle advice e.g. healthy eating, smoking cessation, weight reduction
• Goal setting and targeting
• Medication advice to ensure adherence
• Stress management
• Relaxation
• Education about the heart, its function and the disease process.
• Individually tailored exercise programme
• Monitoring and evaluation of outcomes

The principles of adult learning should be adopted in order to improve patients’ understanding.
Exercise programmes should include a mixture of warm-up, pulse-raising activities, strength work and cool-down exercises (as outlined in British Association Cardiac Rehabilitation [BACR]/American College of Sports Medicine [ACSM] guidelines). They should be delivered by appropriately trained cardiac rehabilitation practitioners or by suitably qualified exercise professionals (BACR Level IV), working, for example, in leisure centres.

There is no current evidence on the most effective length of a supervised exercise programme. The NSF for CHD suggests that cardiac rehabilitation services should aim to provide around two supervised exercise sessions per week for at least six weeks. It is therefore reasonable to expect that angina programmes work towards this level.

**Home-Based Programme**

Where a centre-based comprehensive programme is unavailable or unsuitable, or when a patient decides against this approach due to personal preference, a home-based programme such as The Angina Plan\(^5\) or equivalent locally-devised programme should be provided. For some patients, the greater flexibility and familiarity of a home-based programme will improve their compliance.

The patient should be assessed by a cardiac rehabilitation practitioner and a management plan agreed. The plan requires professional review and monitoring through regular contact, usually by telephone. Patients will have a copy of the plan that will be evaluated upon completion. Where patient goals have not been met, a reassessment should take place.

The Angina Plan can be delivered by a variety of health professionals who have undergone the required training and assessment.

**Serious Pre-existing Psychological Problems**

Patients identified as having serious or pre-existing psychological problems at assessment should be referred in consultation with their GP to local specialised services. If there is a significant delay between referral and consultation, regular contact should be maintained with the patient by the Cardiac Rehabilitation Service wherever possible.

**Continuing Angina**

Cardiac rehabilitation practitioners should consider referring those patients who continue to have adaptation/coping difficulties, despite intervention from the local service, to the National Refractory Angina Centre (NRAC) for further management including motivational psychotherapy and multidisciplinary cognitive behavioural therapy (CBT).

For further details about refractory angina and sample NRAC referral form, see Section 2.
Communication with Primary Care

Clear communication with primary care should take place for all patients at the following key points:

- Following initial diagnosis.
- After initial consultation with cardiac rehabilitation practitioner, outlining the next steps which will have taken account of the patient’s preferences and the services available locally.
- Following the patient’s completion of the rehabilitation programme.

Long Term Management

The patient’s GP practice should ensure that the patient is placed on the heart disease register and offered regular follow-ups. These follow-ups will include checks on blood pressure and cholesterol, weight management and medication review. It is an opportunity to assess angina status and reinforce positive lifestyle choices.

In order to help patients maintain the beneficial changes achieved by cardiac rehabilitation, referral to an exercise programme run in the patient’s local community should be made. Usually described as Phase IV cardiac rehabilitation, these programmes are often provided by local authority and voluntary organisations such as heart support groups. Personnel delivering these programmes should be qualified to BACR IV trainer level and should be in regular contact with the local Cardiac Rehabilitation Service. This will help ensure continuity of care.

Staffing

Cardiac rehabilitation practitioners will have a variety of professional backgrounds but should be trained and experienced in line with the competencies identified in the NHS Knowledge and Skills Framework. In particular, they should be assessed as possessing the following:

Specialist knowledge
- Cardiopulmonary anatomy and physiology.
- Cardiovascular disease process, major diagnoses, the implications of modifiable risk factors, frequently used drugs and their complications.
- Research-based evidence of the impact of environmental, social, lifestyle and behavioural factors on the incidence of CVD and of the impact of CVD on individuals and their families.
- Principles and practice of adult learning.

Specialist skills
- Cardiac risk stratification
- Assessment of psychological, social and emotional needs
- Assessment of cardiopulmonary capacity
- Monitoring cardiovascular and pulmonary responses to exercise
- Methods of monitoring to ensure patient safety
2. Refractory Angina

Definition and Epidemiology of Refractory Angina

Chronic refractory angina pectoris (CRA) is a clinical diagnosis. It is based on the presence of symptoms of stable angina due to myocardial ischaemia resulting from advanced CAD which persists despite optimal anti-anginal therapy. Such patients therefore present with continuing angina which significantly impairs the quality of their lives and which is not responding to optimal anti-anginal drug therapy and is not amenable to any form of coronary intervention such as PCI or CABG.

It is a distressing chronic pain condition that causes severe reduction in the quality of life of both patients and their families. Typically such patients complain of a myriad of problems causing repeat and often protracted hospital admissions. These problems can be exacerbated by lack of support and understanding of their condition that in turn adds to their continuing general deterioration.

Patients attending a refractory angina clinic are a heterogeneous cohort made up of sub-groups whose angina is refractory to conventional medical therapy for one or more of the following reasons:

- PCI and CABG are not technically feasible e.g. because of severe distal disease.
- PCI and/or CABG have already been carried out on one or more occasion and further intervention is deemed to carry unjustifiable risks.
- Comorbidity precludes coronary intervention.
- Patient choice not to undergo further coronary intervention.

The current prevalence of CRA is said to be one in ten thousand and its incidence one in twenty thousand with both rates increasing year on year. The average age is sixty three years and 70% are male. Generally, there is a long history of CAD (>8 years) which is usually three vessel disease (>68%) and often in association with some LV impairment.

It has been estimated that there will be approximately 1800 patients with recurrent moderate to severe angina post-CABG in the North West region within the next ten years. Two thirds of this group (1200 patients) will not be amenable to further revascularisation and hence will become CRA patients. In addition, within the same period an approximately equal number of patients will have CRA without prior CABG due to unrevascularisable disease.
Refractory Angina Management at National Refractory Angina Centre (NRAC)

Treatment aims and the treatment contract

The primary aim of therapy is to maximise the patient’s quality of life by ameliorating the effects of the condition without jeopardising quantity of life. The patient and their carers need time and help to define how angina impairs their quality of life and what level of recovery would be acceptable. These are difficult concepts in the present care system which is a largely pathology or disease-based medical treatment paradigm.

The ideal doctor/patient relationship exists when the patient, their carers and doctor can openly 'negotiate' a treatment contract with clearly stated aims and objectives. In this way the choice of therapy becomes simplified for the doctor and it enables the patient to make more rational decisions about which therapy is most appropriate to his/her particular needs.

Core Programme

•  Patient Education

Education to promote both the patient’s and carer’s understanding of their condition and the available treatments is a core component of the NRAC care model in line with internationally accepted best practice guideline recommendations.

The programme consists of an initial three-hour multi-disciplinary assessment and diagnostic day case clinic. On entry into the programme, patients are invited to define their objectives. All patients are given the Angina Plan, the NRAC angina manual and other relevant material including information on each of the treatment modalities offered.
• **Therapeutic options for pain management**

A broad menu of available therapeutic options has been developed for pain management. There is a hierarchy with patients starting with the simplest and moving upwards in order to try to achieve adequate pain control.

- **TENS (transcutaneous electrical nerve stimulation)** – This is the application and stimulation of electrically conducted pads to the skin resulting in activation of the large diameter nerve fibres which in turn inhibit the onward transmission of painful stimuli to the brain.

- **Temporary sympathectomy** – This is carried out using local anaesthetic infiltrated around the left stellate ganglion at level C5/6 of the cervical vertebra and in the para-vertebral region of T3/4. Usually stellate blockade is tried first with three attempts at four to six week intervals. This is the average period of remission gained by a successful blockade. If this fails then a series of three para-vertebral blocks again at four to six week intervals is used.

- **Opioids** – Although there is limited evidence for the effectiveness of opioids in CRA, in clinical practice oral and transdermal opioids can be effective. Furthermore, epidural or intrathecal opioids are sometimes beneficial.

- **Enhanced external counter pulsation therapy (EECP)** – This modality is used for patients suffering from debilitating effects of CRA or heart failure. It consists of diastolic gated sequential leg compression which is a non-invasive and low-risk outpatient procedure enhancing coronary blood flow by diastolic augmentation. EECP is safe and there is some evidence base for its efficacy.

- **Spinal Cord Stimulation** – This is a form of neuro-modulation in which suppression of pain is induced by application of an electronic device to modify nervous system function. The underlying principles are based on the gate theory of pain control i.e. that non-destructive stimuli can interfere with the transmission of pain within the central nervous system and thereby prevent the pain messages from reaching the brain.

- **Intrathecal pumps** – These are used for the suppression of pain by the infusion of prescribed medication such as hydromorphone directly into the intrathecal space. However, dose related side effects are common and many patients find these intolerable.
Psychological Support Modalities

- Group cognitive behavioural therapy (CBT) – This format of CBT is felt to optimise patient empowerment and is designed to address a number of issues including demystifying angina; graduated exercise using goal setting and pacing; relaxation and stress management; optimization of medication; lifestyle modification; understanding therapeutic alternatives and dealing with setbacks.

- Motivational psychotherapy – Patients in whom an appropriate psychological assessment tool e.g. the Hospital Anxiety and Depression (HAD) score indicates the need, should undergo professional psychological assessment in order to decide whether formal psychotherapy might be beneficial.

- Counselling – This enables a realistic and achievable “treatment contract” to be decided upon so that the patient, their family and the clinical treatment team have an agreed objective.

Patient Referral

Currently, access is limited to referral from consultants within secondary and tertiary cardiological care. It is hoped that access will be expanded in the future to include referral from GPs. Referrals should preferably be made on the designated NRAC referral form Direct referral by letter is also acceptable providing that adequate details are given including cardiac history, clinical features, relevant investigation results, risk factors and current treatment.

3National Audit for Cardiac Rehabilitation. NHS Information Centre for Health and Social Care Central Cardiac Audit Database.
4There are a number of suitable tools but a score using the Hospital Anxiety and Depression Scale (HADs) is currently part of the NACR dataset for cardiac rehabilitation and will therefore provide useful benchmarking information.
## NATIONAL REFRACTORY ANGINA CENTRE REFERRAL FORM

<table>
<thead>
<tr>
<th>Date (dd/mm/yy)</th>
<th>Referrer name</th>
<th>GP: Specialist nurse; matron hospital doctor</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>PATIENT</strong></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td></td>
<td></td>
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<tr>
<td>Address</td>
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<td>Post code</td>
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<td>Email</td>
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<tr>
<td>NHS No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRAC No</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>CLINICAL FEATURES</strong></th>
<th><strong>INVESTIGATION RESULTS</strong></th>
<th><strong>TREATMENTS [NAME &amp; DOSE]</strong></th>
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<tbody>
<tr>
<td>Angina G33</td>
<td>Haemoglobin 423</td>
<td>Aspirin 8B63-plavix</td>
</tr>
<tr>
<td>Prior MI G30</td>
<td>Creatinine 44J3</td>
<td>Betablocker 8B69</td>
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<tr>
<td>Hyperlipid C324</td>
<td>Cholesterol 44P</td>
<td>Statin 8B28</td>
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<tr>
<td>FH CHD</td>
<td>TC:HDL 44PF</td>
<td>Fibrate</td>
</tr>
<tr>
<td>Hypertension G20</td>
<td>K 444</td>
<td>ACE inhibitor 8B6B</td>
</tr>
<tr>
<td>BP 246 /</td>
<td>Glucose 44G</td>
<td>Ca Ch Blocker</td>
</tr>
<tr>
<td>Diabetes C10</td>
<td>HbA1C</td>
<td>K Ch opener</td>
</tr>
<tr>
<td>FH Premature CHD 12CA</td>
<td>TSH 442</td>
<td>Nicorandil</td>
</tr>
<tr>
<td>CABG 792</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTCA 7928</td>
<td></td>
<td></td>
</tr>
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<td>AF G5730</td>
<td>ECG normal 3216</td>
<td>Obesity C380</td>
</tr>
<tr>
<td>PVD G73</td>
<td>ECG abn 3217</td>
<td>Weight 22A</td>
</tr>
<tr>
<td>Smoker 137R</td>
<td>CXR norm 5352</td>
<td>Waist 22NO</td>
</tr>
<tr>
<td>Daily cigarettes 137</td>
<td>CXR abn 5353</td>
<td>Waist-Hip ratio</td>
</tr>
<tr>
<td>Alcohol u/wk 136</td>
<td>TIA G65</td>
<td>PFR 3395</td>
</tr>
<tr>
<td>Most recent angiogram</td>
<td>Date</td>
<td></td>
</tr>
<tr>
<td>Most recent Echo assessment</td>
<td>Date</td>
<td>Normal Mild moderate severe impairment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>PLEASE GIVE YOUR ASSESSMENT IT WILL HELP US PREPARE FOR THE FIRST ASSESSMENT CLINIC</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s understanding of angina</td>
</tr>
<tr>
<td>Carer’s understanding of angina</td>
</tr>
<tr>
<td>Effect of other chronic pain on QoL</td>
</tr>
<tr>
<td>Effect of other chronic illness on QoL</td>
</tr>
<tr>
<td>Effect of fear on QoL</td>
</tr>
<tr>
<td>Effect of frustration on QoL</td>
</tr>
</tbody>
</table>
STAGE 6
DRUG TREATMENT
Summary

In the acute episode, glyceryl trinitrate (GTN) is the drug of choice.

The prophylactic treatment of symptoms requires a strategic approach commencing with monotherapy using a first-line agent in small dosage. If necessary, titrate upwards to maximally tolerated dose and if symptoms continue, add a second-line agent.

The contribution which can be made by drug therapy to the reduction of risk factors for the progression of atherosclerosis and occurrence of acute cardiac adverse events includes anti-platelet therapy, lipid lowering therapy and anti-anginal drugs.
Introduction

This chapter covers the use of drugs to prevent and treat angina and to improve prognosis. Key details about individual drugs will be given in the following sections but full information on dosages, formulations, contraindications, use in pregnancy and during lactation and side effects should be sought from the British National Formulary (BNF) and summaries of product characteristics (SMPCs).

1. Drug Treatment of Acute Episode

Glyceryl trinitrate (GTN) is the drug of choice. It reduces pre-load and after-load and induces coronary vasodilatation. It is effective quickly (usually < five minutes) and lasts 20-30 minutes. It can be repeated as necessary but recurrent chest pain over a short period should raise the question of worsening angina or acute coronary syndrome.

It can be taken in different formulations, tablets, spray and buccal tablets, which should be tailored to suit the patient and context. Attention should be paid to the likelihood of headache on first use when tablets are particularly appropriate.

2. Prophylactic Drug Treatment of Symptoms

Four classes of drug are widely accepted as effective for symptomatic prophylaxis in reducing the frequency and severity of anginal chest pain and/or breathlessness where this is an angina-equivalent due to ischaemia. A fifth class has recently been licensed and others with novel modes of action are in development.

There is no universally acknowledged strategy for the optimal cost effective use of these drugs and the following reflects local consensus. However, individual patients react very differently in terms of benefit and efficacy and so in practice choice is often determined by patient response.

Recommended Strategy

- Commence with monotherapy using a first-line agent in small dosage.
- Titrate dose upwards until the usual dose or maximally-tolerated dose is reached.
- If symptoms continue, add a second-line agent to optimise symptom control, assessed subjectively by clinician and objectively by exercise ECG.
• There is little objective evidence of added benefit from a third or fourth drug although it is acceptable to try with the proviso that they be stopped if the patient does not respond.

• Consider the potential adverse effects on blood pressure (BP), heart rate (HR) and left ventricular function (LVF).

• The failure of a maximally tolerated drug treatment to control symptoms adequately constitutes an indication for consideration of revascularisation even in the absence of other indications.

• Anti-anginal agents, especially beta blockers, when no longer required, should be tailed off rather than stopped abruptly unless they are causing significant side effects.

Table 17 overleaf summarises the agents which are described in detail in the sections that follow.
<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Common Examples</th>
<th>Prophylactic Treatment of Symptoms</th>
<th>Main Uses in Patient</th>
<th>Common Sub-Groups</th>
<th>Main Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Betablocker (BB)</td>
<td>Atenolol</td>
<td>Hypertension, Tachycardia, Atrial fibrillation</td>
<td>Controlled heart failure</td>
<td>Any heart failure</td>
<td>Combined with BB</td>
</tr>
<tr>
<td></td>
<td>Diltiazem</td>
<td>Hypertension, Atrial fibrillation</td>
<td>PVD, Asthma/COPD, Diabetes</td>
<td>Hypotension, Bradycardia</td>
<td>Combined with BB</td>
</tr>
<tr>
<td></td>
<td>Verapamil</td>
<td>Hypertension, Tachycardia</td>
<td>Combined with BB, Mod/severe LV dysfunction</td>
<td>Hypotension, Bradycardia</td>
<td>Combined with BB</td>
</tr>
<tr>
<td></td>
<td>Amlodipine, Felodipine</td>
<td>Hypertension, PVD, Asthma/COPD</td>
<td>Diabetes, Unstable angina, Severe aortic stenosis</td>
<td>Hypotension, Hypotension</td>
<td>Combined with BB</td>
</tr>
<tr>
<td></td>
<td>Nicorandil</td>
<td>Asthma/COPD, PVD</td>
<td>Diabetes, Hypotension, Phosphodiesterase type-5 inhibitors e.g. sildenafil</td>
<td>Hypotension, Hypotension</td>
<td>Combined with BB</td>
</tr>
<tr>
<td></td>
<td>Modified release isosorbide mononitrate (ISMN)</td>
<td>Asthma, COPD, Diabetes</td>
<td>Heart failure, Hypotension, HOCM/AS</td>
<td>Hypotension, Hypotension</td>
<td>Combined with BB</td>
</tr>
<tr>
<td></td>
<td>Ivabradine</td>
<td>In normal sinus rhythm, current inhibitor is effective</td>
<td>Bradycardia, sino-atrial disorder</td>
<td>Bradycardia, Sino-atrial disorder</td>
<td>Combined with BB</td>
</tr>
</tbody>
</table>

**Caution-Indications**

- Combined with BB:
  - Bradycardia, Hypotension
  - Combined with BB:
  - Bradycardia, Hypotension

**Sub-Groups**

- Combined with BB:
  - Bradycardia, Hypotension
  - Combined with BB:
  - Bradycardia, Hypotension

**Main Side Effects**

- Combined with BB:
  - Bradycardia, Hypotension
  - Combined with BB:
  - Bradycardia, Hypotension

**Pharmacologic treatment of symptoms**

- Combined with BB:
  - Bradycardia, Hypotension
  - Combined with BB:
  - Bradycardia, Hypotension

**Main group**

- Combined with BB:
  - Bradycardia, Hypotension
  - Combined with BB:
  - Bradycardia, Hypotension

**Side-Effects**

- Combined with BB:
  - Bradycardia, Hypotension
  - Combined with BB:
  - Bradycardia, Hypotension

**Drug Type**

- Combined with BB:
  - Bradycardia, Hypotension
  - Combined with BB:
  - Bradycardia, Hypotension

**Table 17**
First Line Agents

**Beta Blockers (BBs)**

BBs are the recommended first choice for exercise or emotion induced angina. Whilst no more effective in reducing symptoms than other agents, extrapolation from successful post-MI trials suggests they may also reduce mortality in patients with stable angina although this has not been proved in a placebo controlled trial. See also section 3 ‘Drug Treatment to Improve Prognosis in Stable Angina: Anti-anginal Drugs’.

BBs work by blockade of the $\beta_1$ adrenoceptor, so reducing myocardial oxygen demand (especially on exercise) by slowing the heart rate, lowering the blood pressure and reducing myocardial contractility. Perfusion of ischaemic areas may be improved by prolonging diastole and by ‘reverse coronary steal’ due to increased vascular resistance in non-ischaemic areas.

**Cardio-selective BBs** are recommended because they preferentially block $\beta_1$ adrenoceptors in the heart and blood vessels rather than elsewhere especially in the bronchi.

Some BBs such as oxprenolol, pindolol, acebutolol and celiprolol also have a partial agonist activity. This causes simultaneous $\beta_1$ activation termed *intrinsic sympathomimetic activity (ISA)*. The importance of this is unproven but these drugs cause less bradycardia and may therefore be less efficacious.

In contrast to standard BBs, some newer agents such as carvedilol and nebivolol, have an additional *arteriolar vasodilating action*. Since this reduces the likelihood of cold peripheries and worsened claudication such drugs may be useful where these are concerns.

All BBs are effective in angina but Table 17 will help guide the choice of agent for an individual patient.

**Rate Limiting Calcium-channel Blockers (CCBs)**

CCBs work by interfering with the inward displacement of calcium ions through the slow (L-type) channels of active membranes. The target tissues are therefore the myocardium (reduced contractility), cardiac conducting system (reduced heart rate) and vascular smooth muscle (peripheral vasodilation). However, CCBs are a heterogeneous group of compounds with important differences in pharmacological action due largely to variable effects on the target tissues. CCBs are generally divided into two subgroups with similar but not identical properties.

The rate-limiting CCB group consists of diltiazem and verapamil. These principally reduce myocardial oxygen demand through their major effects on the conducting system (bradycardia, impaired AV conduction) and the myocardium (negative inotropic response) reducing contractility. They also have a moderate effect on vascular smooth muscle causing some coronary and peripheral vasodilation.
They are recommended as **first-line agents** when BBs are contra-indicated or not tolerated, especially when used as monotherapy. They are also safe and effective as second-line agents in combination with other anti-anginal classes but special precautions are necessary with BBs see Table 17.

**Second-Line Agents**

**Non-Rate Limiting CCBs**

The larger non-rate limiting group includes all other CCB agents, the vast majority of which are analogues of the prototype dihydropyridine drug, nifedipine.

These agents have a major effect on the vascular smooth muscle, causing marked coronary and especially peripheral vasodilation and lesser effects on the myocardium and conducting system.

These are therefore second-line agents and ideally combined with a BB because the latter will block the reflex tachycardia often associated with vasodilation.

**Potassium-Channel Activators**

Nicorandil is the only available drug in this group. It has both arterial and venous dilating properties due to its potassium channel activation and an associated nitrate activity. It is licensed for angina treatment and prophylaxis as monotherapy (second-line agent). It is also useful in combination with other drug classes. (Off licence.)

**Nitrates**

Nitrates are veno- and vasodilatory. Their principal benefit in angina derives from reduced preload due to venodilation but also from coronary vasodilation. Three main agents are available: GTN, isosorbide mononitrate (ISMN) and isosorbide dinitrate (ISDN), which is converted to its active metabolite ISMN.

GTN, either sub-lingually or preferably by the buccal route, is valuable for situational **prophylaxis** prior to exertion. (For use in the relief of an acute episode, see above.) For **long-term prophylaxis**, ISMN is preferred to ISDN because it avoids the variability of conversion to ISMN. It is also preferred to GTN (buccal, patch etc) because of its ease of use and patient acceptability.

The problems with nitrates relate to headaches (which can be severe but tend to reduce with continued use) and reduced efficacy (nitrate tolerance) on continuous usage with long-lasting or transdermal preparations. Nitrate tolerance can be avoided by appropriate dosing techniques, which allow 8-12 hour nitrate low or nitrate-free periods. This can be achieved by limiting use of ISMN to a once-daily modified release preparation or to two asymmetrically timed conventional formulations or by removing the patch at night.

The choice between different preparations of ISMN will depend on price and patient preference but in general, a single daily dose of a modified release preparation is preferred.
CURRENT INHIBITORS

Ivabradine is the only currently available drug in this group. It inhibits the cardiac pacemaker If current in the sino-atrial node selectively and specifically resulting in reduced heart rate but not reduced BP. By reducing myocardial oxygen demand, it is as symptomatically effective as atenolol but has no BB related side effects. It is licensed as an alternative agent in patients who cannot tolerate a BB. It is restricted to use in sinus rhythm and has no value in atrial fibrillation. It should be prescribed under specialist supervision only.

3. Drug Treatment to Improve Prognosis in Stable Angina

An essential component of stable angina management is the optimal control of risk factors for progression of atherosclerosis and for the occurrence of acute cardiac adverse events. This involves optimal control of hypertension, dyslipidaemia and diabetes as well as smoking cessation using both non-pharmacological methods and drug therapy. A detailed account of these aspects is outside the scope of these guidelines but this section summarises recommendations on drug therapy for secondary prophylaxis whilst Stage 5 addresses aspects of lifestyle modification and non-pharmacological risk factor management.

Anti-Platelet Therapy

- **Low dose aspirin** is the drug of choice and is the cornerstone of pharmacological prevention of arterial thrombosis. It irreversibly inhibits cyclo-oxygenase-1 (COX-1) in platelets and this prevents thromboxane production. Optimal anti-thrombotic dosage is 75mg since gastro-intestinal side effects, especially bleeding, increase as the dose increases.

- **Clopidogrel** is a thienopyridine, which non-competitively blocks the platelet adenosine diphosphate (ADP) receptor, producing anti-thrombotic effects similar to aspirin. It is not recommended as first-line anti-platelet medication except in patients with contra-indications to low dose aspirin. The combination of clopidogrel with aspirin is not recommended in the management of stable angina unlike its recommended use in management post-NSTEACS or post-PCI. (See CMCN Guidelines on the Use of Clopidogrel in the Management of CAD.)

- **Dipyridamole** and **warfarin** are not recommended for anti-thrombotic prophylaxis in stable angina. As part of treatment for other conditions and under specialist supervision, they may be prescribed with aspirin. (Off licence.)

Lipid-Lowering Therapy

- **Statins** reduce the risk of fatal and non-fatal vascular events in secondary prophylaxis, including stable angina. Reference should be made to the CMCN guidelines Statins in the Secondary Prevention of CVD.
• **Fibrates, nicotinic acid (NIACIN), ezetemibe and resins** may be needed, alone or in combination with statins, to control severe dyslipidaemia especially when low HDL and/or high triglycerides predominate or remain after cholesterol reduction. However, there is no strong evidence to support their routine use and they are not recommended as standard therapy in stable angina.

**Anti-Anginal Drugs**

• **BBs without ISA** in addition to reducing anginal symptoms have also been shown to reduce mortality by 24% during long-term secondary prophylaxis post-MI. Some BBs (metoprolol, bisoprolol, carvedilol) also effectively reduce cardiac events in patients with heart failure, commonly in the setting of CAD.

• **Calcium antagonists** are not recommended for use on prognostic grounds in uncomplicated angina though rate-limiting CCBs may be used post-MI, in the absence of heart failure, as alternatives when BBs are not tolerated.

• **Nitrates** have no beneficial effects on prognosis in stable angina and are therefore not recommended for secondary prophylaxis.

• **Potassium channel openers.** Nicorandil was shown to have some cardio-protective properties in the IONA trial, reducing major coronary events (predominantly the soft endpoint of recurrent hospital admission for chest pain), in stable angina as an add-on to conventional therapy. The size and importance of this effect remains a subject of debate.

**Other Drugs**

• **ACE Inhibitors** are well established for the treatment of hypertension, heart failure and diabetes with microalbuminuria. Three trials (HOPE, EUROPA and PEACE), have studied their effects in secondary prophylaxis in stable CAD or in patients at very high risk of developing it (diabetes with risk factor). Cost efficacy has been shown for the high- and medium-risk cohorts but not proven in the low-risk. Therefore, routine use of ACE inhibitors (ramipril or perindopril in relevant trial doses) is only recommended for stable angina patients with co-existing hypertension, diabetes, heart failure, asymptomatic LV dysfunction or post-MI.

• **Angiotensin receptor blocking drugs (ARBs)** are appropriate treatment for hypertension, heart failure or diabetic renal dysfunction in angina patients only when ACE inhibitors are indicated but not tolerated. They are not recommended as first-line agents especially in non-diabetics with preserved LV function.

• **Hormone Replacement Therapy (HRT).** Although epidemiological evidence supported substantial cardiovascular benefits of HRT in post-menopausal women, subsequent prospective trials have shown no benefit or potential harm. Routine use of HRT is thus not recommended on cardiovascular grounds and current users should discontinue if possible, or taper doses to the minimum required for non-cardiovascular purposes.
• **COX-2 Inhibitors** and **NSAIDS**. COX-2 inhibitors should be avoided in stable angina because, unlike aspirin (a COX-1 inhibitor), they reduce the formation of prostacyclin which has beneficial vasodilatory and platelet inhibiting effects, so predisposing to elevated BP, accelerated atherogenesis, stroke and thrombosis or plaque rupture.

Standard NSAIDS are non-selective, reversible COX inhibitors. Their effects on platelet function and thrombosis are thus unpredictable. Paracetamol should be the preferred analgesic but if NSAIDs are needed they should be used in the lowest dose for shortest time and wherever possible in combination with low-dose aspirin to assure effective platelet inhibition.
## RECOMMENDATIONS FOR PCI AND CABG

Assuming suitable anatomy, appropriate risk stratification and discussion with patient. ACC/AHA class of recommendation in brackets.

<table>
<thead>
<tr>
<th>Indication</th>
<th>For prognosis</th>
<th>For symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina and LM disease</td>
<td>CABG (I)</td>
<td>CABG (I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCI for highly-selected cases or patients unsuitable for CABG</td>
</tr>
<tr>
<td>Angina and three-vessel disease with objective large ischaemia</td>
<td>CABG (I)</td>
<td>CABG (I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCI (I)</td>
</tr>
<tr>
<td>Angina and three-vessel disease with poor ventricular function</td>
<td>CABG (I)</td>
<td>CABG (I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCI where risk of CABG very high or prohibitive</td>
</tr>
<tr>
<td>Angina with two- or three-vessel disease including severe disease of the proximal LAD</td>
<td>CABG (I)</td>
<td>CABG (I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCI (I)</td>
</tr>
<tr>
<td>Angina CCS classes I-IV* with multi-vessel disease (diabetic)</td>
<td>CABG (IIa)</td>
<td>CABG (I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCI could be considered in selected cases</td>
</tr>
<tr>
<td>Angina CCS classes I-IV* despite medical therapy with multi-vessel disease (non-diabetic)</td>
<td>CABG (I)</td>
<td>CABG (I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCI (I)</td>
</tr>
<tr>
<td>Angina CCS classes I-IV* despite medical therapy with one-vessel disease including severe disease of the proximal LAD</td>
<td>CABG (I)</td>
<td>CABG (I)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PCI (I)</td>
</tr>
<tr>
<td>Angina CCS classes I-IV* despite medical therapy with one-vessel disease not including severe disease of the proximal LAD</td>
<td>PCI (I)</td>
<td>CABG (IIb)</td>
</tr>
<tr>
<td>Angina with minimal (CCS Class I) symptoms on medication and one- or two- or three-vessel disease but objective evidence of large ischaemia</td>
<td>CABG (IIb)</td>
<td>PCI (IIb)</td>
</tr>
</tbody>
</table>

*range of symptomatic grades for which evidence is available and should not be construed as directive to perform revascularisation across entire range of symptomatology.
Following coronary angiography and assessment of left ventricular function (either by left ventricular angiography or non-invasively), patients may be considered for coronary revascularisation.

There are two well-established approaches to revascularisation for the treatment of chronic stable angina caused by coronary atherosclerosis: surgical revascularisation (CABG) and percutaneous coronary intervention (PCI). As in the case of pharmacological therapy, the potential objectives of revascularisation are two-fold: firstly to improve survival or survival free of infarction and secondly to diminish or eradicate symptoms. The individual risk of the patient as well as symptomatic status must be a major factor in the decision-making process.

Currently both methods of revascularisation are facing rapid development. Advances in CABG techniques include the greater use of arterial conduits, the introduction of minimally-invasive techniques and the increase in use of off-pump surgery. PCI has seen a rapid development in the movement away from simple balloon angioplasty towards the insertion of metal stents and most recently the increased use of drug–eluting stents (DES), which are metal stents coated with anti-proliferative or anti-mytotic agents, designed to reduce the rate of in-stent restenosis. Current and future guidelines on the practice of PCI and CABG will have a direct bearing on the management of stable angina.

This chapter is based on not only the American and European Guidelines on stable angina referred to in the Introduction but also on the current leading references for PCI and CABG:

- Guidelines for percutaneous coronary interventions. The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology.¹
- ACC/AHA 2004 guideline update for coronary artery bypass graft surgery.²

### 1. Selection of Patients for Revascularisation Therapy

In general, patients who have indications for coronary angiography and in whom catheterisation reveals severe coronary artery stenosis are potential candidates for myocardial revascularisation. The principal indications for revascularisation are:

- To improve prognosis – this relates to effects on mortality or morbidity especially MI. This indication is relevant where coronary angiography has shown anatomy associated with a high risk of adverse events which can be ameliorated by CABG and includes significant stenosis of the left mainstem (LM), significant proximal three vessel disease, and significant two-vessel disease including high grade stenosis of the proximal left anterior descending artery (LAD).
To control symptoms – when maximally tolerated medical treatment has failed to suppress symptoms to the point where the patient is happy with the quality of his/her life. This relates to change in angina class, exercise duration, time to angina on treadmill testing, repeat hospitalisation for angina or other parameters of functional capacity or quality of life.

Where such indications for revascularisation exist, the following should also be considered before deciding on a patient’s eligibility for intervention:

- The patient prefers an interventional rather than a medical approach having been fully informed of the risks and benefits to be expected.
- There is a high likelihood of technical success.
- The risks (mortality and morbidity) of the procedure are acceptable.

An adequate response to therapy must be judged in consultation with the patient. For some, CCS Class 1 symptoms (angina only on strenuous exertion but not during ordinary activity) are acceptable but others may wish for complete abolition of their symptoms. What is an acceptable risk of morbidity and mortality should be considered on an individual basis for each patient. Patients should not be advised to have a procedure for which the procedural mortality exceeds their estimated annual mortality, unless there is evidence of substantial prognostic benefit in the longer term, or symptoms are having a serious impact on their quality of life despite appropriate medical therapy.

2. Recommendations for Revascularisation

The current evidence-based indications for revascularisation fall into the two categories identified above. Specific recommendations are detailed below.

To Improve Prognosis in Patients with Stable Angina

Class I
- CABG for significant LM CAD or its equivalent (i.e. severe stenosis of ostial/proximal segment of left descending and circumflex coronary arteries).
- CABG for significant proximal stenosis of three major vessels, particularly in those patients with abnormal LV function, or with early or extensive reversible ischaemia on functional testing.
- CABG for single or two vessel disease with high grade stenosis of proximal LAD with reversible ischaemia on non-invasive testing.
- CABG for significant disease with impaired LV function and viability demonstrated by non-invasive testing.

Class IIa
- CABG for single- or two-vessel CAD without significant proximal LAD stenosis in patients who have survived sudden cardiac death or sustained ventricular tachycardia.
- CABG for significant three-vessel disease in diabetics with reversible ischaemia on functional testing.
- PCI or CABG for patients with reversible ischaemia on functional testing and evidence of frequent episodes of ischaemia during daily activities.
To Improve Symptoms in Patients with Stable Angina

Class I
• CABG for multi-vessel disease (MVD) technically suitable for surgical revascularisation in patients with moderate to severe symptoms not controlled by medical therapy, in whom risks of surgery do not outweigh potential benefits.
• PCI for single-vessel disease technically suitable for percutaneous revascularisation in patients with moderate to severe symptoms not controlled by medical therapy, in whom procedural risks do not outweigh potential benefits.
• PCI for MVD without high-risk coronary anatomy, technically suitable for percutaneous revascularisation in patients with moderate to severe symptoms not controlled by medical therapy and in whom procedural risks do not outweigh potential benefits.

Class IIa
• PCI for single-vessel disease technically suitable for percutaneous revascularisation in patients with mild to moderate symptoms which are nonetheless unacceptable to the patient, in whom procedural risks do not outweigh potential benefits.
• CABG for single-vessel disease technically suitable for surgical revascularisation in patients with moderate to severe symptoms not controlled by medical therapy, in whom operative risk does not outweigh potential benefit.
• CABG in MVD technically suitable for surgical revascularisation in patients with mild to moderate symptoms, which are nonetheless unacceptable to the patient, in whom operative risk does not outweigh potential benefit.
• PCI for MVD technically suitable for percutaneous revascularisation in patients with mild to moderate symptoms, which are nonetheless unacceptable to the patient, in whom procedural risks do not outweigh potential benefits.

Class IIb
• CABG in single-vessel disease technically suitable for surgical revascularisation in patients with mild to moderate symptoms, which are nonetheless unacceptable to the patient, in whom operative risk is not greater than estimated annual mortality.

3. Selection Of Method Of Revascularisation

Selection of the method of revascularisation should be based on:

• Risk of periprocedural mortality and morbidity.
• Likelihood of success, including factors such as technical suitability of lesions for angioplasty or surgical bypass.
• Risk of re-stenosis or graft occlusion.
• Completeness of revascularisation. If considering PCI for MVD, is there a high probability that PCI will provide complete revascularisation or at least in the same range as CABG?
• Diabetic status.
• Local hospital experience in cardiac surgery and interventional cardiology.
• Patient preference.
4. Contraindications to Myocardial Revascularisation

Contraindications to myocardial revascularisation are described in Table 19 below.

Table 19

<table>
<thead>
<tr>
<th>CONTRAINDICATIONS TO MYOCARDIAL REVASCULARISATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Patients with one- or two-vessel CAD without significant proximal LAD stenosis who have mild or no symptoms and have not received an adequate trial of medical therapy or have no demonstrable ischaemia or only a limited area of ischaemia/viability on non-invasive testing</td>
</tr>
<tr>
<td>• Borderline (50–70%) coronary stenosis in location other than LM and no demonstrable ischaemia on non-invasive testing</td>
</tr>
<tr>
<td>• Non-significant (&lt;50%) coronary stenosis</td>
</tr>
<tr>
<td>• High risk of procedure-related morbidity or mortality (&gt;10–15% mortality risk) unless the risk of the procedure is balanced by an expected significant improvement in survival or the patient's quality-of-life without the procedure is extremely poor</td>
</tr>
</tbody>
</table>

5. Specific Patient and Lesion Subsets

• Patients with severely depressed LV function and/or high surgical risk, patients with LM disease, patients with diabetes and MVD, and patients with previous bypass surgery warrant particular consideration when selecting revascularisation options.

• Patients in whom surgical risk is prohibitively high may benefit from revascularisation by PCI, particularly when residual viability can be demonstrated in the myocardium perfused by the target vessel(s). This issue is currently addressed in two large randomised studies, the STICH³, and the HEART UK⁴ trials.

• Although PCI in LM stem disease is feasible, and good results have been achieved in registries comparing DES and bare metal stents, surgery should remain the preferred approach until the outcome of further trials are known.

• Subgroup analyses of randomised trials have shown reduced mortality with bypass surgery compared with PCI in diabetic patients with MVD. The BARI⁵ trial was the largest of these trials and the only one in which a statistical difference in mortality of patients with diabetes was detected between the treatment groups. A limitation of these trials is that they were conducted before the widespread use of DES stents or adjuvant periprocedural antiplatelet therapy.

Two major trials are underway to address this important issue: BARI 2D⁶, and FREEDOM⁷. However, for the present, due consideration should be given to the evidence available and PCI should be used with reservation in diabetics with MVD until the results of further trials are known.
• There are no randomised controlled trials comparing treatment options in patients with previous bypass surgery. Re-do surgery may be undertaken on symptomatic grounds where the anatomy is suitable. However, the operative risk of re-do bypass surgery is as high as three-fold greater than initial surgery, and for those with a patent internal mammary artery (IMA) graft there is the additional risk of damage to this graft during surgery. On the other hand PCI can be performed following previous surgical revascularisation, either in the vein graft or arterial graft, or the native coronary tree beyond the graft which is not revascularised, and may provide a useful alternative to re-do surgery for symptomatic relief.

• In the case of a chronic total occlusion that cannot be crossed in patients with MVD, failure to treat the chronic total occlusion will result in incomplete revascularisation, which could be avoided if the patient were to be referred for bypass surgery.

3 The Surgical Treatment for Ischemic Heart Failure Trial (STICH).
4 Heart failure revascularisation trial (HEART).
6 BARI 2 Diabetes.
7 Future Revascularisation Evaluation in Patients with Diabetes Mellitus (FREEDOM) Trial.
ALGORITHM 3
ASSESSMENT AND MANAGEMENT OF CVD RISK PRIOR TO ELECTIVE NON-CARDIAC SURGERY

ALL PRE-OP PATIENTS clinically assessed

Patients with known significant heart disease:
- valvular disease especially aortic stenosis
- serious arrhythmia: uncontrolled AF, known VT/AF
- ACS < 90 days
- on waiting list for revascularisation

Patients with suspected valvular disease:
- aged ≥65 with aortic ejection systolic murmur.
- aged < 65 with above murmur and poor exercise tolerance or abnormal ECG

All other patients

Echo (if not done in last 12 months)

Refer to cardiologist

Refer to cardiologist

Assess risk factors using Revised Cardiac Risk Index see Table 20

score 0-1

score 2

score 3-6

Consider beta-blockers (see table 21)

Refer to cardiologist

If not contra-indicated:
prescribe 4 weeks pre-op or asap

If contra-indicated:
- if surgery can be deferred - refer to cardiologist
- if surgery cannot be deferred - proceed*

*If patient has drug-eluting stent take additional precautions as per Table 22
1. Introduction

Emergency and elective surgery differ significantly in terms of logistics, time frame and clinical considerations such as haemodynamic stability, blood volume etc. The CMCN Task Group concluded that the risk assessment for emergency surgery should be undertaken with the anaesthetists on an individual patient basis. Therefore, the following guidelines relate entirely to elective procedures and in this area, the use of Algorithm 3 will allow a logical evidence-based and cost-effective approach.

2. Mechanisms of Perioperative Acute Coronary Syndrome (ACS)

The pathophysiology of ACS perioperatively differs from that in stable CAD. In the setting of pre-existing stable CAD, acute ischaemic syndromes occur because of destabilisation (erosion, rupture) of atheromatous plaques. The pathophysiology of perioperative ischaemic events is less clear but current belief is that half result from plaque destabilisation and half from prolonged imbalance of the supply and demand of myocardial oxygen. This imbalance may result from:

- increased myocardial demand due to increased heart rate and blood pressure often sympathetically mediated via pain, or due to large fluid volume shifts
  or
- reduced coronary supply due to anaemia, hypotension or increased coronary vascular tone (coronary spasm).

Standard non-invasive testing may be of value in assessing pre-existing stable CAD and the propensity to plaque rupture but would be of limited value in predicting prolonged supply-demand imbalance.

3. Accuracy of Non-Invasive Testing in Pre-operative Assessment

Non-invasive cardiac tests (exercise ECG, MPS, DSE) allow a reasonably accurate assessment of prognosis (death, serious cardiac events) during medium- and long-term follow-up i.e. in the setting of chronic CAD. They have proved much less reliable in predicting such events over the ninety-six hour perioperative period which is required for accurate pre-operative assessment.
This inaccuracy results from the following:
- the mechanisms of pre-operative ischaemia/infarction differ from those in stable CAD (see Section 2 above)
- patients who are assessed for non-cardiac surgery are usually a low risk population with only about 2% actually suffering a perioperative cardiac event. In this type of low prevalence population, non-invasive tests have modest sensitivity and very poor specificity (high false positive rates).

The problem is how to identify accurately a small number of high-risk patients in this predominately low-risk population. The high false positive rate of non-invasive testing has often led to unnecessary, further and increasingly invasive investigations that multiply costs, increase delays and expose patients to unnecessary risks.

### 4. Classical Approach

The current standard or classical approach is that advocated in the 2002 ACC/AHA Guidelines\(^1\) and involves pre-operative, non-invasive testing for a large proportion of patients. A brief summary is given below:

- **Step 1** – identification of clinical predictors of perioperative risk, based on history, examination and ECG. Patients are grouped into those having major, intermediate or minor predictors.

- **Step 2** – assessment of the patient's functional capacity in METs based on activities of daily living using the Duke Activity Status Index. Higher perioperative risk is associated with inability to meet four METs demand.

- **Step 3** – classification of the proposed non-cardiac surgical procedure into high, intermediate or low risk operative groups.

- **Step 4** – the results of steps 1-3 determine the most appropriate of three management strategies:
  - High risk - delay or cancel non-cardiac surgery to allow for optimisation of medical therapy, risk factor modification and coronary angiography with a view to revascularisation
  - Intermediate risk – undertake non-invasive investigation(s) and depending on results, coronary angiography.
  - Low risk - proceed to non-cardiac surgery without further investigation or treatment.

Unfortunately the majority of patients fall into the intermediate group requiring non-invasive testing. The CMCN Task Group did not regard this as the optimal approach for the following reasons:

- Heavy burden placed on non-invasive testing resources.
- Poor predictive accuracy of such tests.
- Delays and costs incurred.
- Excessive and unnecessary need for coronary angiography resulting from the inevitable false positive results.
5. Preferred (Modern) Approach

The CMCN Task Group recommends a more modern approach outlined in Algorithm 3. This shifts the emphasis away from pre-operative risk stratification, which uses non-invasive testing, to risk modification with drug therapy aimed at reducing perioperative ischaemia and hence the likelihood of adverse cardiac events.

The principles underlying the preference for this strategy are:

- No evidence exists that non-invasive testing leads to a therapeutic strategy that reduces perioperative risk of MI or death.
- Non-invasive testing has a uniformly low positive predictive accuracy which does not improve on information available from clinical assessment alone.
- The most robust clinical assessment scheme currently available is the Revised Cardiac Risk Index (RCRI)\(^2\) as used by Grayburn and Hillis.\(^3\)
- Beta blockers and to some extent statins, have recently been shown to reduce the risk of perioperative cardiac events whilst routine coronary revascularisation has not.

The approach is easy to use by a range of healthcare professionals and minimises the pressure on non-invasive testing resources by focussing them on patients most likely to accrue benefit from their application. However, it is recognised that the pathway outlined in Algorithm 3 will not cover every possible set of circumstances and clinicians may consider modification is justified in individual cases.

The pathway involves the application of the RCRI, a simple bedside clinical index, to all patients requiring pre-operative assessment who do not have known significant heart disease, including significant valvular disease, especially aortic stenosis, serious arrhythmia (uncontrolled AF, VT/VF), recent ACS (< 90 days), or are on a revascularisation waiting list. The index and scoring system is described in Table 20.

Cardio-pulmonary exercise testing (CPET) consists of exercise testing with simultaneous ECG and gas exchange measurements. It is increasingly used in cardiology to assess objectively functional capacity, stress inducible myocardial ischaemia, the cause of unexplained breathlessness and to risk stratify prior to cardiac transplantation. Recently, it has also been shown to predict patients at high risk of perioperative cardiac complications.

Conclusive evidence of its accuracy and cost-effectiveness in prospective studies pre-operatively is still lacking and in comparison to a standard exercise ECG it is more complex, more time consuming and requires added skills. For these reasons, CPET is not recommended as a routine pre-operative assessment but its value to anaesthetists in certain surgical cases is recognised and where such a service is in existence its use may well add important information.
Pre-operative management with beta blockers

It is recommended that patients with an RCRI score of two should be started on beta blockers, ideally four weeks prior to surgery but if time does not allow then as soon as possible and definitely on admission. It is not known if, or when, they should be stopped but certainly, abrupt withdrawal should be avoided. Consensus advice is given in Table 21.

Table 21

<table>
<thead>
<tr>
<th>BETA BLOCKERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agents</strong> - Bisoprolol, atenolol and metoprolol. Evidence favours the longer acting agents and atenolol has been shown to be superior to metoprolol.</td>
</tr>
<tr>
<td><strong>Contraindications</strong> - asthma, uncontrolled heart failure; hypotension (SBP&gt;100) or cardiogenic shock; bradycardia (&lt;60 bpm); 2° – 3° AV heart block; sino-atrial disorder (sick sinus syndrome); severe peripheral vascular disease (but can be used with caution in stable and non-critical PVD); known coronary artery spasm or phaeochromocytoma.</td>
</tr>
<tr>
<td><strong>Dosage</strong> – Bisoprolol 5-10mg daily; atenolol 25-100mg daily; metoprolol 50-100mg twice daily. Start with the lower dose and increase after 3 days to get resting heart rate to ≤ 60bpm providing SBP ≥ 100 and no side effects.</td>
</tr>
<tr>
<td><strong>Duration</strong> - Start 4 weeks pre-op or if time does not allow as soon as possible and definitely on admission. Continue daily until discharge. No evidence for longer duration of treatment exists except where there are other indications e.g. hypertension, angina.</td>
</tr>
</tbody>
</table>
**Statins**

The situation regarding statins is less clear. A significant number of perioperative events are caused by rupture of vulnerable plaques during the unusual stresses associated with anaesthesia and surgery. A role for rapid plaque stabilisation with statins is therefore logical and is now supported by growing evidence. However, the CMCN Task Group did not consider current evidence was strong enough to recommend routine initiation of pre-operative statins but they should not be withdrawn in patients already taking them.

**Other drugs**

Although other drugs including aspirin, clopidogrel, alpha blockers and calcium-channel blockers have been considered for pre-operative use, the evidence does not support their recommendation.

**CABG**

The routine use of CABG pre-operatively for patients with stable, significant CAD does not reduce risk and is not recommended. However, if irrespective of the non-cardiac surgery, cardiac symptoms are unstable or if CABG would be recommended on standard symptomatic or prognostic grounds, then it is sensible for this to be carried out prior to the non-cardiac procedure if time allows.

Studies have shown a significantly higher risk of death and/or cardiac complications in patients undergoing non-cardiac surgery early after CABG. The optimal safe period to delay non-cardiac surgery after CABG is unknown and will depend on the risk/benefit balance in individual patients. However, for most cases it is prudent to avoid elective non-cardiac surgery for at least one month and, where possible, for six months.

**PCI**

PCI is not recommended for routine prophylactic use prior to non-cardiac surgery and indications for it should be as in the non-operative setting.

After balloon angioplasty, a minimum of one week should be left to allow for healing of the traumatised vessel prior to non-cardiac surgery.

**Patients with pre-existing in-situ stents.** These patients risk either stent thrombosis due to the discontinuation of dual anti-platelet therapy or haemorrhage due to its continuation. With bare metal stents, ideally four to six weeks should elapse to allow for full re-endothelialisation.

The situation with regard to drug-eluting stents (DES) is less clear. DES delay re-endothelialisation and hence patients require a longer period on dual anti-platelet therapy before non-cardiac surgery is undertaken. Recent data has also raised concerns about late thrombosis with DES. No evidence based guidelines exist for the management of DES patients prior to non-cardiac surgery but the following principles have consensus agreement.
### PATIENTS WITH DRUG ELUTING STENTS (DES): PRE- and PERIOPERATIVE ADVICE

| 1. | Whenever possible advice should be sought from the cardiologist who implanted the DES with regard to perioperative management. |
| 2. | Whenever possible, elective PCI should be delayed until after any foreseeable elective, non-cardiac surgery has been undertaken. Obviously, where PCI is for ACS or intractable symptoms it should not be delayed. |
| 3. | **Non-urgent elective** surgery should be postponed for 12 months after DES insertion when clopidogrel can be stopped. Low dose aspirin should be continued unless the surgeon or type of surgery precludes it, when it should be restarted as soon as possible post-operatively. |
| 4. | **Urgent elective surgery** which cannot be delayed until 12 months have elapsed e.g. for cancer, should be undertaken on dual anti-platelet therapy if possible. If the surgeon or type of surgery precludes this, then aspirin alone should be continued (other than in exceptional circumstances) and clopidogrel restarted as soon as possible post-operatively. If the surgery is likely to be delayed for > 5 days and clopidogrel continuation is not acceptable then the following regime has been suggested whilst continuing low dose aspirin throughout:- |
   | - 5 days pre-op: Stop clopidogrel |
   | - 3 days pre-op: Admit to hospital  
   | Commence short acting Gpiib/IIIa inhibitor (tirofiban) infusion  
   | Commence unfractionated heparin infusion  
   | - 6 hours pre-op: Stop tirofiban infusion  
   | Stop heparin infusion  
   | - 1st post-op day: Give oral loading dose of 300mg of clopidogrel  
   | - 2nd post-op day: Start maintenance oral clopidogrel 75mg daily |
| 5. | **Emergency or urgent non-elective surgery** which needs to be undertaken immediately or at very short notice should go ahead when clinically indicated. In these circumstances, the question of pre-operative cessation of anti-platelet agents does not arise. |

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APPENDIX TO STAGE 8
ASSESSMENT AND MANAGEMENT OF CVD RISK OF POTENTIAL CANDIDATES FOR RENAL TRANSPLANTATION

Summary

ALGORITHM 4
CV RISK ASSESSMENT FOR POTENTIAL RENAL TRANSPLANT RECIPIENTS

History, exam, bloods, resting ECG

All other patients

Newcastle risk assessment score
Tables 23 & 24

Patients with known significant heart disease:
- a) valvular disease especially aortic stenosis
- b) serious arrhythmia: uncontrolled AF, known VT/VF
- c) ACS < 90 days
- d) on waiting list for revascularisation

≤8

>13

9-12

Referral to cardiologist
- clinical assessment
- echo
- stress imaging

Low risk

High risk

Tx contraindicated

Cardiac catheter

No prognostic disease

Prognostic disease

Defer Tx, refer to cardiologist on clinical grounds

Advise Tx team to add to waiting list

Defer Tx, reconsider after treatment if appropriate

Advise Tx team not to add to waiting list
For a number of reasons outlined below, the CMCN Task Group considered that assessment prior to renal transplantation (RTx) and pancreatic-renal transplantation (PRTx) constituted special situations not adequately addressed by national or international guidelines. The essential principles of the ‘modern’ approach (known pathology, validated clinical risk tool, proven risk modification by drugs) do not hold in these situations and hence the decision to develop a version of the classical (risk stratification) approach modified to take account of the limited evidence available. The guidance, which is outlined in Algorithm 4 and detailed below, is therefore recommended but not fully validated and constitutes the consensus view of the Task Group.

1. Objectives

The aims of the pre-operative assessment prior to RTx and PRTx are wider than for other non-cardiac surgery.

- To quantify perioperative risk to inform discussion with patients on consent.

- To prioritise the use of a severely limited supply of organs by enabling an assessment of intermediate outcomes to be made. The European Transplant Guidelines recommend that recipients have a pre-transplant life expectancy of more than two years in order to justify organ usage.

- To reduce perioperative risk where possible and initiate specialist cardiovascular follow up where appropriate.

2. Special Considerations (Why RTx and PRTx Differ)

There are a number of major differences from other non-cardiac surgery, which invalidate the strategy hitherto recommended, including the following:

- The surgery, whilst elective, is carried out at very short notice.

- Unlike the usual pre-operative population, which is low risk (low disease prevalence), RTx and PRTx patients are relatively high risk both for perioperative events and for current or future CAD. This and the need to ensure year life expectancy beyond two years, means that the risk to be assessed is not just short term due to surgery but also intermediate and long term.
• Clinical features are modified with a much higher prevalence of silent myocardial ischaemia due to poor exercise tolerance, anaemia and neuropathy. Exercise ECG with Bruce protocol is usually of little value especially in the presence of LVH.

• The RCRI has not been validated in this group of patients. The Newcastle Scoring System for Clinical Risk Assessment (Table 23) has been specifically derived for RTx and validated to some extent. High scores (≥ 13) have been shown prospectively to correlate with longer duration of delayed graft function, poorer glomerular filtration rate at six months, inferior patient and graft survival over five years of follow up, together with an increased relative rate (≥4) of early graft loss within sixty days.

• In this higher prevalence population, non-invasive imaging (MPS, DSE) is more accurate for risk prediction but has a reduced diagnostic predictive accuracy (up to 20% false negatives).

• There is no evidence base for pre-operative risk modification by either drug therapy or revascularisation.

• Coronary angiography, PCI and CABG are inherently more risky in these patients and their therapeutic value lessened.

• Coronary angiography has some value, albeit limited, in predicting future cardiac events. However, it retains its accuracy in identifying patterns of significant CAD, which have been shown to benefit from revascularisation.

3. CMCN Pathway

The CMCN recommended pathway for pre-operative assessment of RTx and PRTx patients is outlined in Algorithm 4. The principles of the pathway are:

• Patients who have significant heart disease including serious arrhythmia (uncontrolled AF, VT/VF), significant valvular disease especially aortic stenosis, recent ACS (≤ 90 days), or are on a revascularisation waiting list should be referred directly to a cardiologist. Specialist assessment will decide whether transplantation should proceed, is completely contraindicated or whether invasive investigation by cardiac catheterisation is necessary to make this decision.

• In all other patients, a relevant health care professional (not a cardiologist) should undertake clinical assessment and risk assessment using the Newcastle scoring tool. The Newcastle score should be used to direct further actions and decision making as indicated in Algorithm 4 and Table 24.
**Table 23**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;45</td>
<td>0</td>
</tr>
<tr>
<td>45-65</td>
<td>2</td>
</tr>
<tr>
<td>65+</td>
<td>4</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>3</td>
</tr>
<tr>
<td><strong>BP assessment</strong></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td></td>
</tr>
<tr>
<td>- Systolic blood pressure &lt;110mm Hg</td>
<td>4</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>- Controlled with drugs (BP ≤ 150/90mm Hg)</td>
<td>2</td>
</tr>
<tr>
<td>- Uncontrolled (BP &gt;150/90mm Hg), with or without medication</td>
<td>3</td>
</tr>
<tr>
<td><strong>Exercising distance</strong></td>
<td></td>
</tr>
<tr>
<td>50-200m or slowing on stairs</td>
<td>3</td>
</tr>
<tr>
<td>&lt;50 m or stops on stairs</td>
<td>4</td>
</tr>
<tr>
<td><strong>Body mass index</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;18 or &gt;30</td>
<td>3</td>
</tr>
<tr>
<td><strong>Cerebrovascular disease</strong></td>
<td></td>
</tr>
<tr>
<td>Previous CVA or TIA</td>
<td>3</td>
</tr>
<tr>
<td><strong>Peripheral vascular disease</strong></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>3</td>
</tr>
<tr>
<td><strong>Angina</strong></td>
<td></td>
</tr>
<tr>
<td>Stable</td>
<td>3</td>
</tr>
<tr>
<td>Variable or on minimal exertion(40-50m)</td>
<td>4</td>
</tr>
<tr>
<td><strong>Coronary vascular surgery and MI</strong></td>
<td></td>
</tr>
<tr>
<td>One MI/CABG/two vessel disease/PCI</td>
<td>3</td>
</tr>
<tr>
<td>Two MI/CABG for triple vessel disease/two surgical procedures including CABG</td>
<td>4</td>
</tr>
<tr>
<td><strong>Cardiac valve disease</strong></td>
<td></td>
</tr>
<tr>
<td>Mitral, tricuspid, pulmonary valve disease or surgery</td>
<td>2</td>
</tr>
<tr>
<td>Aortic valve disease or surgery</td>
<td>3</td>
</tr>
<tr>
<td><strong>Maximum possible score</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>35</td>
</tr>
</tbody>
</table>

**NEWCASTLE SCORING SCHEME², ³**

<table>
<thead>
<tr>
<th>Score</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 8</td>
<td>Patients are low risk for presence of significant CAD and for perioperative events and should proceed to consideration for transplant by the transplant team.</td>
</tr>
</tbody>
</table>
| 9 - 12| Patients require further cardiological assessment. They should be referred to a cardiologist who, on the basis of clinical assessment, echo and stress imaging should decide on the risk/benefit ratio of cardiac catheterisation. When appropriate this will refine the risk estimate (perioperative, intermediate and long term) and lead to three alternative sets of advice to the transplant team:  
  - Accept for Tx consideration.  
  - Defer until treatment (for CAD or valvular heart disease) reduces the risk to acceptable levels.  
  - Do not proceed to Tx consideration. |
| ≥ 13  | Patients have a high perioperative risk and are hence a low priority for organ donation. The expectation is that such patients will not be accepted for transplant but they should be referred to a cardiologist for optimisation of cardiac care. |
4. Re-Assessment of Patients Accepted on Tx Waiting List

Patients may remain on a Tx waiting list for several years whilst awaiting a suitable organ. During this period, there is a significant risk of development or progression of CAD or valvular disease due to the frequent presence of adverse vascular risk factors and the tendency to metastatic calcification. It is therefore recommended that such patients should be re-assessed annually, initially by a non-cardiologist.

Algorithm 5 outlines the management pathways. If the annual assessment shows no new cardiac problems or no significant changes, then further investigation is not required. However, if the Newcastle score, ECG or echo identifies new cardiac problems or deterioration in previously known ones, then the patient should be referred to a cardiologist. Specialist assessment and investigation will inform the decision on the need for cardiac catheterisation and hence whether transplantation should proceed, be deferred or await further cardiac treatment.
ALGORITHM 5
CARDIAC RE-ASSESSMENT OF PATIENTS ON TX WAITING LIST

On Tx waiting list

Annual assessment by non-cardiologist
- Clinical, Newcastle score
- ECG
- echo for valvular disease

New/worsening symptoms or
New/worsening ECG changes or
Worsened echo findings or
Newcastle score increased by >1

Refer to cardiologist
- clinical assessment
- echo
- stress imaging

Significant change

Cardiac catheter

Contraindications

Defer Tx for treatment or remove from Tx waiting list

No significant change

No significant change

No further investigations

Review in 12 months

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1 European Best Practice Guidelines for Renal Transplantation (Part 1). NDT, 2000. 15 s7