National Heart Foundation of Australia & Cardiac Society of Australia and New Zealand: Australian Clinical Guideline for Diagnosing and Managing Acute Coronary Syndromes 2024

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Disclaimer:
Please note, the experts listed have contributed to the guideline, however, the list and order of authorship is currently being finalised for publication.

Contents

Acknowledgement of Country
We acknowledge the Traditional Owners and custodians of country throughout Australia and their continuing connection to land, waters and community. We pay our respects to them and their cultures, and Elders past, present and future.

Disclaimer
This guideline has been developed by the National Heart Foundation of Australia ABN 98 008 419 761 (**Heart Foundation**) in collaboration with the Cardiac Society of Australia and New Zealand ABN 23 006 63505 (**CSANZ**) to support health professionals in making informed clinical decisions. The content of this guideline is provided for informational purposes only and is not intended to serve as health, medical, or treatment advice. It is based on the best available evidence and expert consensus as of the time of publication. The recommendations are intended to support, not replace, the clinical judgment and shared decision-making process between qualified health professionals and their patients, considering individual patient circumstances and the availability of resources.

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Clinical judgment and decision-making
This guideline should not override the responsibility of health professionals to make appropriate decisions based on the specific circumstances of each patient, including consideration of applicable local regulations and the patient's values and preferences. Health professionals are also responsible for verifying current regulations and recommendations before applying any treatments or interventions referred to in this guideline.

Updates and revisions
Medical knowledge is continually evolving, and guidelines may be updated as new information becomes available. Users are encouraged to consult the latest version of the guideline and to consider any new evidence that may have emerged.

Jurisdictional application
This guideline has been developed in accordance with Australian regulatory and clinical standards and may not be suitable for use in other jurisdictions without appropriate adaptation.

Introduction

This guideline has been developed to assist in the diagnosis and management of people presenting with symptoms suggestive of acute coronary syndromes (ACS), or with confirmed ACS.

The guideline recommendations are based on contemporary evidence and are intended to meet the needs of clinicians caring for the majority of people, recognising that recommendations should inform, but not replace, clinical judgement.

Shared decision-making between people and clinicians is recommended and should be based on an individual's values, preferences, and circumstances.

This guideline was developed in consultation with a broad range of clinical experts and people with lived or living experience, representing different geographic regions, sex, genders, ethnicities, clinical settings and perspectives. Organisations, including those with people with lived or living experience interests and professional expertise, were involved.

What's new in this guideline

Key changes in this guideline

- Introduction of consensus recommendation as a new category of recommendation.
- Dedicated practice points to meet the unique needs of women, older adults, First Nations people, and people living in regional and remote areas.
- Revised definitions of myocardial infarction (see section 1.2).

Assessment and diagnosis

- Guidance on assessing and interpreting electrocardiogram in people with suspected acute coronary occlusion myocardial infarction or myocardial ischaemia (see section 2.2).
- Guidance on using high-sensitivity cardiac troponin testing and interpreting the results to enable more rapid detection or exclusion of myocardial injury (see section 2.3).
- Introduction of high-sensitivity troponin-based clinical decision pathways to risk stratify people with suspected ACS (see section 2.4).
- Recommendations to support management of people with suspected ACS presenting to primary care and regional and remote settings (see section 2.10).

Hospital care and reperfusion

- Updates on recommended timings of reperfusion strategies in people with ST elevation myocardial infarction (see section 3.1).
- Consideration of intravascular imaging to guide percutaneous coronary intervention in people with non-ST-segment elevation ACS who have undergone an invasive approach (see section 3.3.4).
- Revised recommendations on acute phase pharmacotherapies (see sections 3.4 and 3.5).
- New recommendations related to haemodynamic support devices in people with ACS and cardiogenic shock (see section 3.6.2).
- Treatment considerations for people with ACS and multivessel disease without cardiogenic shock (see section 3.7) and spontaneous coronary artery dissection (see section 3.9).

Recovery and secondary prevention

- Revised recommendations on post-ACS pharmacotherapies (see section 4.1).

The guideline update process

This guideline appraises and summarises the available evidence on the clinical care of people with suspected or confirmed ACS. This evidence informs a set of recommendations to guide healthcare professionals in making diagnostic and therapeutic decisions. It replaces the *National Heart Foundation of Australia & Cardiac Society of Australia and New Zealand: Australian clinical guidelines for the management of acute coronary syndromes 2016* [1-3].

The guideline was developed based on the *Grading of recommendations, assessment, development, and evaluation* (GRADE) methodology [4]. It is also informed by the *2016 National Health and Medical Research Council (NHMRC) Standards for Guidelines* [5], adapting them where necessary to meet the specific requirements of this guideline.

Five expert groups with multidisciplinary, clinical and people with lived or living experience input directed and governed the development of this guideline. Members were selected based on their expertise and experience in guideline development. Expertise was sourced across the disciplines of cardiology, emergency medicine, general medicine, general practice, nursing, pharmacy, epidemiology, cardiac rehabilitation and public health. Experts and people with lived or living experience representatives from diverse backgrounds and geographic regions were recruited between the last quarter of 2021 and first quarter of 2022.

Please see the supplementary material for full details on the governance arrangements, processes for establishing the expert groups, literature search and evidence synthesis, developing recommendations using the GRADE methodology, and the public consultation and approvals process [6].

Development of recommendations and using this guideline

Between the second and third quarter of 2022, the Expert Steering Group and Expert Subgroups developed the guideline scope and clinical questions, which were prioritised based on gaps identified in published international guidelines, literature review, priorities and choices faced by health professionals, and values and preferences of people with lived or living experience. The guideline scope was shared with, and feedback received from reference group organisations and the consumer advisory panel. The guideline clinical questions were expressed in patient/population, intervention, comparison, outcome, time, setting (PICOTS) format. In the fourth quarter of 2022, an independent literature reviewer was appointed to conduct the literature review based on these PICOTS questions.

The literature review sought published studies from January 2015 to December 2022. Evidence summaries were completed in the first quarter of 2023. They were supplemented with additional studies identified from conference attendances, searching reference lists, database alerts and relevant international guidelines where the recommendations were adopted or adapted for this guideline. If relevant and pertinent to the recommendations, studies published after the literature search dates were included.

Between the second and fourth quarter of 2023, the expert groups drafted the guideline content and recommendations. Guideline recommendations were developed using GRADE methodology. The GRADE approach offers a transparent and structured process for developing and presenting evidence summaries and recommendations [4].

In the first quarter of 2024, an independent reviewer was commissioned to assess the comprehensiveness and balance of the scientific evidence, certainty of evidence and rationale to inform the wording and strength of the recommendations. A dedicated consumer

advisory panel, representing people with lived or living experience in Australia, was drawn upon to help prioritise peoples' preferences and values.

Table 1 provides a summary of GRADE definitions.

Table 1: GRADE definitions

Certainty of evidence	
The certainty of evidence reflects the extent to which the confidence in the estimates of an effect is adequate to support a particular decision.	
Certainty of evidence	**What it means**
High	The authors are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	The authors are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	The authors' confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low	The authors have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.
Strength of recommendation	
The strength of a recommendation reflects the extent to which the authors are confident that desirable effects of an intervention outweigh undesirable effects, or vice versa, across the range of people for whom the recommendation is intended. It is determined by considering the balance between benefits and harms, certainty of evidence, variability or uncertainty in the values and preferences of the target population, and resource use.	
Strength of recommendation	**What it means**
Strong	The authors are confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects. It implies that most or all individuals will be best served by the recommended course of action.
Weak	The authors concluded that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects but are not certain. It implies that not all individuals will be best served by the recommended course of action.

The GRADE methodology considers the importance of the recommendation. These are recommendations that are not necessarily related to the quality or certainty of the evidence, but that reflect the extent to which the recommendation will impact on the health status or quality of life of the target population. This allows for a strong recommendation to be made even if the certainty of the evidence is low due to the importance of the recommendation.

Recommendations are categorised as ‘consensus’ where there is high certainty that the desirable effects of an intervention clearly outweigh its undesirable effects, but the body of supportive evidence is indirect and the application of the GRADE approach to rate the certainty of evidence or strength of recommendation is inappropriate.

Consensus recommendations were informed by the expert opinion of the Expert Steering Group and expert subgroup members, with consideration of relevant available evidence, values, preferences and resource use at the time of writing. Consensus was established when the majority of the members of the expert groups supported the statement.

Practice points are statements that that may be actionable and often describe the how, who, where, what, and when related to implementing a recommendation. They may contain information supporting elements of a recommendation (e.g. medicine dosing). They may also include information about tools and tips that enhance implementation of the chosen intervention and/or its efficient use. Practice points are not actionable without related recommendations.

Practice points were developed with consideration of the geographical challenges in Australia and availability of resources in Australian healthcare settings. Where there were specific practice points, evidence and/or resources relevant to underserved populations, these were included under a separate heading in the section.

This guideline should be read in conjunction with the *Australian Commission for Safety and Quality in Health Care ACS Clinical Care Standard* which informs quality indicators to drive better outcomes for all people living in Australia [7]. Some sections provide suggested areas for further research.

Further details of the guideline development process can be found in the supplementary material.

Conflicts of interest

Conflicts of interest are considered within a framework of both the relationship (direct or indirect) of the individual to any third party with interests in the guideline topic being considered, and the nature (financial and non-financial) of the potential conflict.

Conflicting interests among the expert groups required appropriate management to ensure recommendations were not compromised. Processes employed by the Heart Foundation aimed to ensure the integrity of guideline developers and to strike an appropriate balance between the existence of interests in a topic under review and the expertise required to make sound and meaningful recommendations.

More information on conflict of interest management and a summary of all disclosures can be found in the supplementary material.

1 Preamble

1.1 Impact of coronary heart disease in Australia

Coronary heart disease (CHD), of which the majority of clinical manifestations are acute myocardial infarction (AMI) and angina, is the leading cause of death in Australia. It accounts for around 10% of all deaths [8]. The prevalence of CHD rises with age, occurring in about 1% of adults aged 45–54 years, increasing to 14% of adults aged 75 years and over [9]. In Australia, from 2020–21, there were approximately 160,000 hospitalisations with CHD as the principal diagnosis [9].

The direct economic impact of CHD to government and non-government sectors (including private health insurance and individual contributions) was 2.5 billion Australian dollars in 2020–21, with the greatest expenditure incurred from public and private inpatient care [9].

The impact of ACS, including prevalence, outcomes and treatment, varies across different population groups. Women with ACS experience delays in presentation to hospital and in timely delivery of life-saving interventions, with longer symptom-to-door and door-to-balloon times, lower intervention rates and lower prescription of secondary prevention medicines compared with men [10-12].

The hospitalisation rate for First Nations people with CHD is twice as high as for non-Indigenous Australians and they are less likely to receive recommended interventions following hospitalisation for an AMI [13].

For people living in regional and remote Australia, the age-standardised rate of CHD hospitalisation is 1.5 times higher than people living in major cities [14].

The assessment and management of older people and/or those with frailty requires consideration of physical and social function, level of frailty, and comorbidities [15].

Specific recommendations to improve outcomes for each of these high-risk populations are therefore incorporated throughout the guideline wherever possible.

1.2 Definitions and terminology

A clear understanding of definitions and terminology is essential for accurate use of this guideline. ACS encompass both AMI and unstable angina (UA).

ACS may also be classified as ST-segment elevation ACS (STEACS) and non-ST-segment elevation ACS (NSTEACS). NSTEACS encompasses both non-ST-segment elevation myocardial infarction (NSTEMI) and UA (see **Figure 1**), with NSTEMI and UA differentiated by the presence or absence of biomarker evidence of cardiomyocyte necrosis respectively.

This guideline has adopted the term acute coronary occlusion myocardial infarction (ACOMI) which includes people presenting with electrocardiogram (ECG) changes of either ST elevation or other changes indicative of major epicardial artery acute coronary occlusion (ACO).

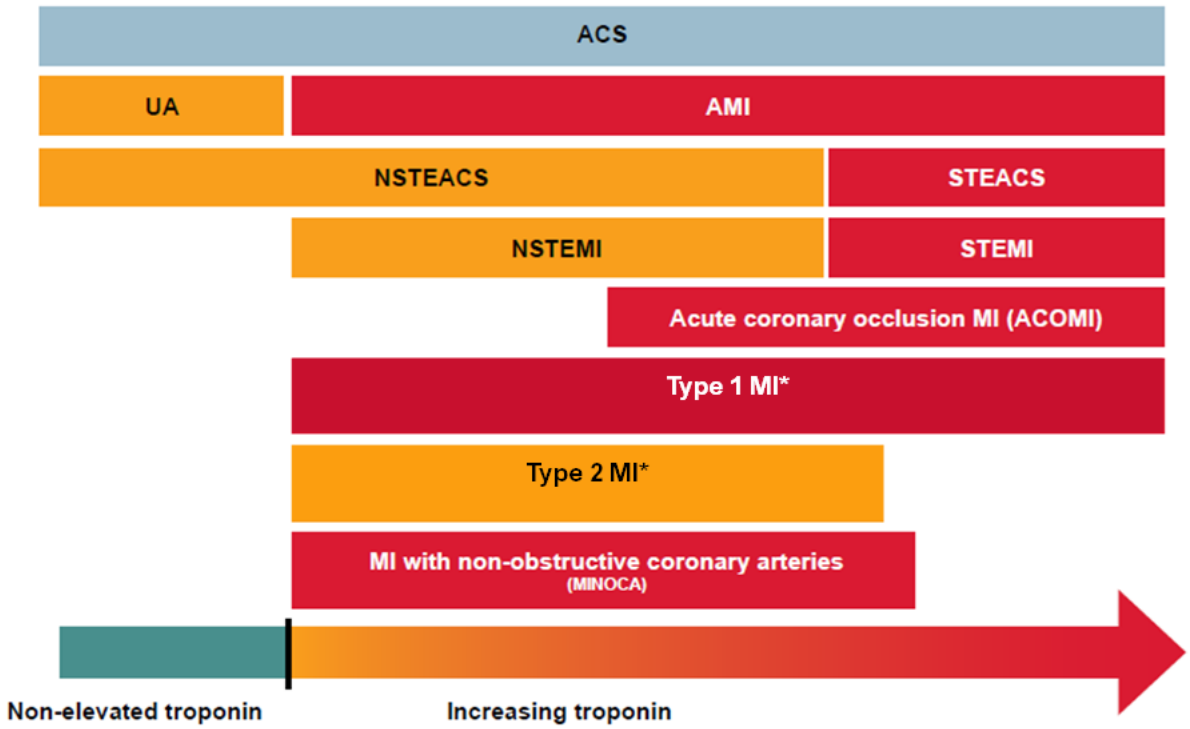


Figure 1: Classifications of conditions associated with ACS. **According to revised Universal definition of myocardial infarction (UDMI) criteria [16, 17]. Abbreviations: ACO, acute coronary occlusion; ACS, acute coronary syndromes; AMI, acute myocardial infarction; MI, myocardial infarction; NSTEACS, non-ST-segment elevation acute coronary syndromes; NSTEMI, non-ST-segment elevation myocardial infarction; STEACS, ST-segment elevation acute coronary syndromes; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina.*

1.2.1 Fourth universal definition of myocardial infarction

The 4th *Universal definition of myocardial infarction* (UDMI) bases the diagnosis of AMI on evidence of cardiomyocyte necrosis as detected by an elevated cardiac biomarker. Preferably a high-sensitivity cardiac troponin (hs-cTn) T or I assay, with at least one value above the 99th percentile of the upper reference limit (URL) [16, 18].

The currently accepted international criteria for diagnosing AMI are the detection of an increase and/or decrease of troponin, with one value above the URL, and at least one of the following [16]:

- symptoms of acute myocardial ischaemia
- new ischaemic ECG changes
- development of pathological Q waves on ECG
- imaging evidence of new loss of viable myocardium, or new regional wall motion abnormality consistent with an ischaemic aetiology
- intracoronary thrombus detected on coronary angiography or autopsy.

Type 1 myocardial infarction (MI) is spontaneous MI with coronary pathology and is characterised by atherosclerotic plaque rupture, ulceration, fissure, or erosion with resulting intraluminal thrombus in one or more coronary arteries leading to decreased myocardial blood flow and/or distal embolisation and subsequent myocardial necrosis [19]. The underlying coronary artery disease (CAD) may be non-obstructive or absent on angiography (myocardial infarction with non-obstructive coronary arteries [MINOCA]) [16].

Type 2 MI occurs when myocardial necrosis is associated with an imbalance between myocardial oxygen supply and demand (usually driven by an increase in the latter) and may be seen in situations associated with hypotension, hypertension, tachyarrhythmia, bradyarrhythmia, anaemia, hypoxaemia, or pulmonary embolism. In contrast to type 1 MI, there is no new anatomical obstruction of the coronary vessels.

Type 3 MI is described as MI resulting in death when biomarkers are not available.

Type 4 and 5 MI represent peri-procedural MI related to percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) respectively.

1.2.2 Revised definition of myocardial infarction

This guideline adopts refined definitions that align more closely with the clinical syndromes that characterise occlusive and nonocclusive MI [16, 17].

In refinements to the 4th UDMI adopted in this guideline, an identical clinical picture to type 1 MI may be caused by non-atherosclerotic mediated coronary occlusion such as spontaneous coronary artery dissection (SCAD), coronary embolism, or coronary vasospasm or microvascular dysfunction (see **Figure 2**), which are all associated with coronary pathology.

Such conditions (classified as type 2 MI in the 4th UDMI) result in a spontaneous reduction in myocardial oxygen supply, with the clinical presentation, investigation findings and early management often indistinguishable from those associated with spontaneous atherosclerotic plaque events. Hence, they are classified as forms of occlusive MI in this guideline (see **Figure 2** and section 2.1.2 History of the presenting complaint) [20-22].

In further refinements to the 4th UDMI, MI due to oxygen supply/demand mismatch without acute coronary obstruction may be further subclassified according to the presence or absence of fixed obstructive CAD.

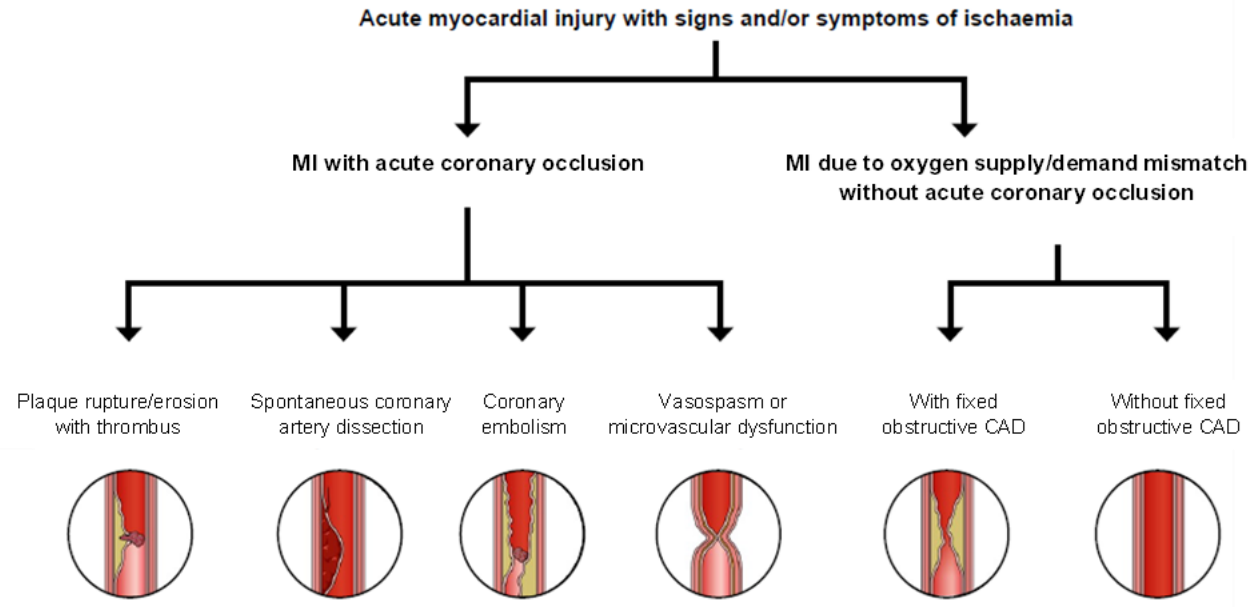


Figure 2: Revised classification of MI. Adapted from [17]. *Both types of MI may present with ECG changes of ST-segment elevation (STEMI) or non-ST-segment elevation (NSTEMI). Abbreviations: CAD, coronary artery disease; MI, myocardial infarction.*

ACO causes downstream MI in the absence of timely reperfusion, that is ACOMI. Importantly, ACOMI may present as ST-segment elevation myocardial infarction (STEMI) or STEMI alternatives (see section 2.2.1 ECG findings of acute coronary occlusion myocardial infarction) [23].

This guideline predominantly focuses on managing people with MI due to atherosclerotic plaque rupture, ulceration, fissure, or erosion with resulting intraluminal thrombus in one or more coronary arteries leading to decreased myocardial blood flow and/or distal embolisation and subsequent myocardial necrosis.

1.2.3 Definition of major adverse cardiovascular events

In assessing people with suspected ACS, the likelihood of diagnosing the index MI and the risk of major adverse cardiovascular events (MACE) over the next 30 days needs to be determined and rated as low, intermediate, or high. In people with confirmed ACS, MACE includes AMI, cardiac death, and stroke. Where there are additional or alternative definitions of MACE, these have been described.

1.2.4 Definition of unstable angina

UA is defined as myocardial ischaemia at rest or on minimal exertion in the absence of acute cardiomyocyte injury/necrosis. This is an important clinical diagnosis based upon symptoms, with or without ECG changes in the absence of elevated troponin concentrations.

Since the introduction of hs-cTn assays, the prevalence of UA has decreased, likely due to greater assay precision allowing detection of low-range changes in troponin concentrations [24-27].

1.2.5 Myocardial infarction with non-obstructive coronary arteries

MINOCA refers to the clinical situation when a person presents with symptoms suggestive of ACS, demonstrates troponin elevation and has non-obstructed coronary arteries at the time of coronary angiography (no coronary artery stenosis ≥50% in any major epicardial vessel) and there is no specific alternate diagnosis for the clinical presentation (e.g. pulmonary embolism or myocarditis) [28, 29].

MINOCA is a working, rather than a final, diagnosis and further investigations are essential to establish the underlying cause. In particular, cardiac magnetic resonance imaging is valuable to establish the presence of MI and to exclude differential diagnoses such as myocarditis. If atherosclerotic heart disease is likely, the person should be treated with appropriate secondary prevention medicines.

2 Assessment and diagnosis

2.1 Assessment of people with suspected ACS

Assessment for ACS is a summative process incorporating the following:

- ECG findings
- clinical findings from history and examination
- results of troponin testing.

These observations are combined to either diagnose or inform risk assessment which will guide the location and timing of further investigations, management, and appropriate follow-up. Rapid identification of people with ACS is crucial as many treatments are time-sensitive and earlier intervention improves outcomes. However, only a minority of people presenting acutely with chest pain to the emergency department (ED) will have a final diagnosis of ACS [30, 31].

Among those presenting with acute chest pain to the ED in whom ACS is suspected, <5% will have STEMI, 5–10% NSTEMI, 5–10% UA, 15–20% other cardiac conditions, and 50–60% non-cardiac diseases [31-34]. While a clear definitive diagnosis may be made at index presentation, most diagnoses will be of a non-cardiac condition or remain unclear and may require further follow-up to complete assessment with primary care physicians as an outpatient [18].

For this reason, risk assessment for ACS is the key focus of investigation and management in the initial assessment, rather than achieving a rule in or rule out diagnosis relating to ACS which may not be possible in many people (see section 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS).

The hierarchy of assessment in suspected ACS is as follows:

1. Identify people with ACOMI (STEMI and STEMI equivalents).
2. Identify people with NSTEMI.
3. Identify people with UA at high risk for 30-day MACE.
4. Identify people with underlying coronary artery disease in whom ACS is not confirmed.

Assessment for people with suspected ACS within an ED setting is described below.

Specific guidance for people presenting in regional and remote, and primary care settings is given in section 2.10 Primary care and regional and remote presentations.

2.1.1 Initial assessment summary

The first steps in the assessment of people presenting to a healthcare setting with symptoms suspicious for ACS include the following (see practice points for setting considerations):

- Prompt identification of people with ACOMI who require consideration for urgent reperfusion therapy.
- An ECG should be obtained and reviewed by a clinician experienced with ECG interpretation, within 10 minutes of presentation, to examine for evidence of ACOMI (see section 2.2 Initial ECG assessment).
- Vital sign measurements including blood pressure, heart rate, respiratory rate and peripheral oxygen saturations should be recorded.
- People without evidence of ACOMI but with ECG evidence of cardiac ischaemia (see section 2.2 Initial ECG assessment), and/or people who are otherwise stratified as

high risk of index MI or 30-day MACE (see section 2.4.1 Clinical decision pathways) should have continuous cardiac monitoring while undergoing further assessment.

- In people with ongoing symptoms, repeated clinical review including ECGs performed at a minimum of every 15 minutes until pain-free should occur. Additional ECGs should be performed if symptoms recur, there are changes in character or a change in clinical condition.
- If there is no evidence of ACOMI on ECG, a targeted history and physical examination should be performed and differential diagnoses considered, with particular focus on other time critical emergencies such as aortic dissection, pulmonary embolism, or pneumothorax to which this guideline does not apply (see **Table 2**) [35, 36].
- If a diagnosis of ACS is considered likely, further investigations including troponin testing should be performed (see section 2.3 Biomarkers and section 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS).
- A chest X-ray may be useful in supporting differential diagnoses according to clinical suspicion, including pneumonia or pneumothorax, and to assess for cardiac size or evidence of cardiac failure. Requesting a chest X-ray should be guided by clinical suspicion of alternate conditions and acquiring a chest X-ray should not delay urgent revascularisation.
- If the ECG is normal, and a person's symptoms are clearly attributable to a non-cardiac cause, this guideline no longer applies. Clear communication with people explaining they do not have ACS is essential and may reduce a person and their carers' anxiety (see section 2.9 Discharge planning and advice).

If ACS is suspected, the following sections describe the subsequent processes of assessment and diagnosis.

Table 2: Differential diagnosis of acute chest pain.

Cardiac: ACS	AMI, unstable angina, stable angina.
Cardiac: Other	Myopericarditis, tachyarrhythmia, hypertensive emergencies, severe aortic stenosis, Takotsubo, cardiac trauma.
Pulmonary	Pulmonary embolism, pneumothorax (including tension), infection (pneumonia, bronchitis), pleuritis.
Vascular	Aortic dissection, expanding aortic aneurysm, sickle cell crisis.
Gastrointestinal	Oesophagitis, reflux, spasm, rupture, peptic ulcer disease, pancreatitis, cholecystitis and biliary disease.
Other	Musculoskeletal disease (including costochondritis, trauma), anxiety disorder, infectious disease (including herpes zoster).

Abbreviations: ACS, acute coronary syndromes; AMI, acute myocardial infarction.

2.1.2 History of the presenting complaint

After assessing for high-risk features on ECG and/or abnormal vital signs, a focused history is required to evaluate for symptoms suggestive of myocardial ischaemia, time of onset, and risk factors for ACS.

As the history is pivotal to assessing potential risk for ACS, barriers to clear clinician-person communication such as cultural issues, language differences, or hearing deficits should be addressed [37]. Engaging with appropriate translator services or culturally appropriate health workers is strongly recommended (see Practice points: First Nations people).

Chest pain, anginal equivalents and associated symptoms

Chest pain due to myocardial ischaemia is more commonly described as substernal discomfort or pressure which may radiate to the neck, arms or jaw and is exacerbated by exertion and relieved with rest after 15 or 20 minutes [38]. While chest pain is the most common symptom of ACS, it is not always present. In addition, many people deny actual chest pain, and refer to discomfort, pressure or heaviness which in this guideline are included under the umbrella term of chest pain.

Descriptions of myocardial ischaemia pain vary considerably, and consideration needs to be given to sex, ethnic background and culture. The description of the pain may help in determining if the person's presentation is consistent with myocardial ischaemia or unlikely to be ACS (see **Figure 3**).

A response or lack of response to treatment (such as nitro-glycerine, standard analgesia or anti-acids) should not be used as a diagnostic criterion for ACS (see section 2.5 Initial therapeutic management) [39].

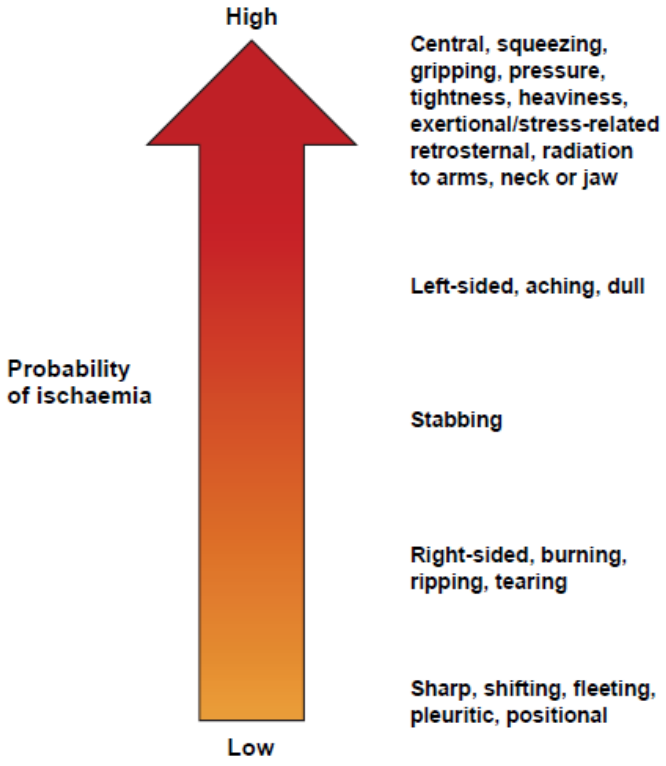


Figure 3: Probability of cardiac ischaemia based on commonly used descriptors of chest pain.

Shortness of breath, fatigue, nausea, diaphoresis or vomiting are not infrequent in people with ACS, with women more likely than men to present with such symptoms (see Practice points: Women). Some people, particularly older adults and those with diabetes, may not describe any chest pain or discomfort but report the features described above (sometimes referred to as anginal or chest pain equivalents).

Although terms such as typical and atypical symptoms of myocardial ischaemia have been used, given their wide variation, cardiac, possible cardiac or non-cardiac symptoms are now recommended terms (see Practice points: Women and Older adults) [18].

Factors associated with myocardial infarction types

An absence of risk factors for CAD does not exclude ACS, which may present as either type 1 or type 2 MI. The risk factors for the different types of AMI are listed in **Table 3**.

Table 3: Factors associated with spontaneous MI with coronary pathology and oxygen supply/demand imbalance.

Factors associated with atherosclerosis [40]:

- Older age (>75 years)
- Diabetes mellitus
- Hypertension
- Hypercholesterolaemia
- Obesity
- Smoking
- Family history of premature atherosclerotic cardiovascular disease (ASCVD) (males, age <55 years; females, age <65 years)

Additional risk for atherosclerosis:

- Chronic inflammatory conditions, such as psoriasis, rheumatoid arthritis, lupus, or HIV/AIDS
- Chronic kidney disease (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- Non-alcoholic fatty liver disease
- High-risk race/ethnicity (e.g. South Asian or First Nations ancestry)
- History of premature menopause (before age 40 years) and history of pregnancy-associated conditions that increase later ASCVD risk, such as hypertensive disorders of pregnancy and gestational diabetes

Factors associated with SCAD [41]:

- Female sex
- Younger age (<50 years)
- Lack of cardiovascular risk factors
- Pregnancy or postpartum
- Fibromuscular dysplasia
- Inherited connective tissue disorders

Factors associated with coronary embolism [42]:

- Aortic or mitral valve, left atrial appendage or left ventricle thrombus, vegetation or neoplasm
- Patent foramen ovale, atrial septal defect or pulmonary arteriovenous malformation and venous source (e.g. deep vein thrombosis)

Factors associated with coronary vasospasm [43]:

- Male sex
- Smoking
- Older age
- Cocaine use

Factors associated with coronary microvascular dysfunction [44]:

- Female sex (especially post-menopausal)
- Atherosclerotic disease
- Chronic inflammation (e.g. systemic lupus erythematosus, rheumatoid arthritis)
- Myocardial diseases
    - Hypertrophic cardiomyopathy
    - Dilated cardiomyopathy
    - Anderson-Fabry's disease
    - Amyloidosis
    - Myocarditis
    - Aortic stenosis

Factors associate with oxygen supply/demand imbalance (+/- atherosclerosis) [16]:

- Severe anaemia
- Hypotension/shock
- Sustained tachycardia or tachyarrhythmia
- Sustained bradycardia or bradyarrhythmia
- Respiratory failure
- Sepsis
- Pulmonary embolism
- Critical illness

Note: Takotsubo cardiomyopathy is not classified as MI and is not discussed in this guideline. Abbreviations: ASCVD, atherosclerotic cardiovascular disease; MI, myocardial infarction; SCAD, spontaneous coronary artery dissection.

Practice points

Women

In women with confirmed ACS, chest pain is the most common presenting symptom, with a frequency equal to men. However, women are more likely to experience and prioritise associated symptoms including jaw, neck, shoulder or back pain, fatigue/tiredness, nausea or vomiting, dizziness, indigestion, shortness of breath/difficulty breathing [45-47]. Women are also more frequently misclassified as having non-cardiac pain due to an under-appreciation of these common associated symptoms being significant [48, 49].

In addition, women are less likely to present directly to hospital and are more likely to experience delays in receiving life-saving procedures once they are in hospital, with higher 30-day mortality (odds ratio [OR] 1.38, 95% confidence interval [CI] 1.06–1.79) [10].

Interpretation of cardiac symptoms by physicians may also be subject to sex bias [50].

- Clinician awareness and recognition of sex differences in presenting symptoms, presentation patterns and management may improve diagnosis and management of women with ACS.
- SCAD needs to be considered as a cause of ACS in young to middle-aged women (see section 3.9 Treatment for spontaneous coronary artery dissection) [41].

Older adults

Older age (>75 years) is an independent risk factor for ACS but also an independent risk factor for other conditions which can present similarly to ACS [51].

Advanced age is also a more potent risk factor for CAD than other traditional factors such as hypertension and hypercholesterolaemia [52, 53].

Chest pain may not be the primary symptom of AMI, including in those with STEMI, with anginal equivalents being commonly seen [52-55].

First Nations people

Coronary heart disease is the leading cause of death in this population. First Nations people with confirmed ACS experience lower intervention rates and poorer outcomes compared with non-Indigenous Australians [13, 56]. First Nations people presenting to EDs with suspected ACS also have a high burden of cardiac risk factors, and those diagnosed with ACS are 10 years younger in age than non-Indigenous people [57].

- Providing access to First Nations healthcare workers, liaison officers, and culturally appropriate interpreter services within hospitals can assist in obtaining an accurate and complete history. Incorporating culture-specific attitudes and values into health promotional tools and providing culturally appropriate pastoral care may also help to bridge cultural gaps [13, 56]. Education focusing on cultural awareness, competency and cultural safety has been shown to improve outcomes as well as minimising the unconscious bias of clinicians [13, 56].

2.2 Initial ECG assessment

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people presenting with chest pain or other symptoms suggestive of ACS, record and assess an ECG for evidence of ACOMI within 10 minutes of first clinical contact.	Consensus	
In people with suspected ACS, record and assess additional ECGs if symptoms persist, change, or recur, or there is diagnostic uncertainty. For those with ongoing ischaemic symptoms and an inconclusive standard 12-lead ECG, record and assess further ECGs with right-sided and/or posterior leads.	Consensus	
In people with ongoing ischaemic symptoms and those with new ischaemic findings on ECG, continuous cardiac monitoring and defibrillator availability is recommended while assessment for ACOMI continues.	Strong	Low

Evidence supporting the recommendations

Identifying people with ACOMI is the priority to expedite initiation of a reperfusion strategy for eligible people to save viable myocardium and reduce morbidity and mortality.

Recording and interpreting the ECG is the most important initial investigation and should be performed within 10 minutes of clinical contact for all people presenting with chest pain or other symptoms of ACS [58]. As ECGs in people with ACOMI can show different patterns (see **Figure 4**), they should be examined by a clinician experienced in ECG interpretation. In remote areas, an established process that enables rapid ECG interpretation is required if an experienced ECG clinician is unavailable [59].

If ACOMI is not initially identified, the ECG should be further examined for features associated with higher likelihood of evolving to ACOMI or signs of myocardial ischaemia (see section 2.2.2 High-risk ECG findings; 2.2.3 Other signs of myocardial ischaemia on ECG; and **Figure 4**). If available, pre-hospital ECGs or ECGs recorded during previous presentations should be compared to assess for new or dynamic changes.

If features of ongoing ischaemia are present or people are stratified as high-risk, close clinical and continuous monitoring of cardiac rate and rhythm with 3–5 lead electrodes of an ECG monitor should be initiated to assist early recognition of arrhythmias or cardiac arrest (see section 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS) [60]. The indications for continued monitoring should be reviewed regularly.

For people with an initial non-ischaemic ECG, resolved symptoms and initial troponin concentration equal to or below the sex-specific 99th percentile, continuous cardiac monitoring is not required (see section 2.3 Biomarkers and 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS). However, repeated ECGs should be performed either at prescribed intervals (e.g. hourly), when repeated troponin samples are collected or as guided by changes in a person's symptoms or clinical condition.

2.2.1 ECG findings of acute coronary occlusion myocardial infarction

ST-segment elevation (STE) is the key ECG criteria required to institute a reperfusion strategy for people with signs or symptoms of myocardial ischaemia (see **Figure 4A**) [61]. STE is not specific to ACOMI and may occur in other disease states, both cardiac and non-cardiac [62]. Cardiac conditions with STE without ACO include pericarditis, left ventricular hypertrophy (LVH), left ventricular aneurysm, left bundle branch block (LBBB), right ventricular pacing, Takotsubo or other cardiomyopathies and Brugada patterns. Non-cardiac STE conditions include normal variant STE (early repolarisation), pulmonary embolism, hyperkalaemia, hypothermia and raised intracranial pressure.

In the clinical context of myocardial ischaemia, STE should be assumed to represent ACOMI until excluded.

Recognised ECG patterns of acute coronary occlusion myocardial infarction

Comparison of ECGs with consequent coronary angiogram results have revealed multiple ECG patterns of ACOMI beyond traditional STE criteria [23, 63, 64]. Recognition of the following patterns improves ECG sensitivity for ACO and should prompt consideration of an ACOMI warranting a reperfusion strategy to ensure all people who can benefit from a reperfusion strategy are identified (see **Figure 4**) [65]. This may require supplemental lead

ECGs to interrogate electrically subtle or silent areas of the heart such as the inferior, basal, posterior and right ventricular walls (see **Table 4**). Notable ECG findings and considerations are:

- High lateral MI manifesting with ST-elevation in non-contiguous leads due to occlusion of the first diagonal branch of the left anterior descending coronary artery (see **Figure 4B**) (referred to as the "South African flag sign") [66, 67].
- STE ≥0.5 mm in leads V1–V3 due to ACOMI of the posterior aspect of the heart should prompt recording of posterior leads (see **Figure 4C**) [68-70].
- STE in lead V1 due to an isolated right ventricular MI should prompt recording of right-sided ECG leads (see **Figure 4D**) [16, 71, 72].
- De Winters pattern (see **Figure 4E**) [73].
- Transient STE, manifesting as STE in ≥2 contiguous leads of ≥0.5 mm that resolves spontaneously, or after aspirin and glyceryl trinitrate (GTN) administration, may represent transient occlusion. These people should continue to be observed with continuous cardiac monitoring and serial ECGs.

Detecting new ST-segment elevation with a baseline abnormal ECG

ECG evidence for ACOMI may be difficult to discern in people with abnormal baseline ECGs, such as LBBB, right ventricular pacing or LVH.

The validated Modified Sgarbossa criteria improves diagnosis of STE in people with LBBB or right ventricular pacing with a specificity of 99% and a sensitivity of 80% (see **Figure 4F**) [74-76]. The modification entails excessively discordant STE with an amplitude >25% of the depth of the preceding S wave in any lead with no scoring required.

There are currently no validated methods to discern STE of ACOMI from STE seen with LVH or hypertrophic cardiomyopathy. In people with LVH, comparison with previous ECGs should be performed but if unavailable, continuous cardiac monitoring with close clinical observation and serial ECGs are required to monitor for development of ACO. Expert consultation should be sought for people with persisting ischaemic symptoms with equivocal ECG findings for ACOMI.

Table 4: ECG leads associated with cardiac regions.

Cardiac region	Leads with STE	Reciprocal STD
Anterior	V3, V4	None
Anterolateral	I, aVL V3–V6	II, III aVF
Anteroseptal	V1–V4	None
Septal	V3, V4	None
Inferior	II, III, aVF	I, aVL
Right ventricular	Right-sided chest leads V3–6	
Posterior	Posterior leads V7–9	V1–V3
Lateral	I, aVL, V5, V6	II, III, aVF
High lateral	I, aVL (V2)	III (II, aVF)

Abbreviations: STE, ST-segment elevation; STD, ST-segment depression.

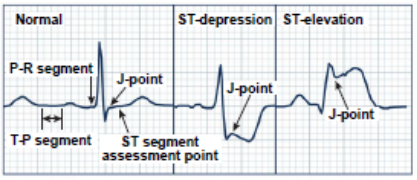
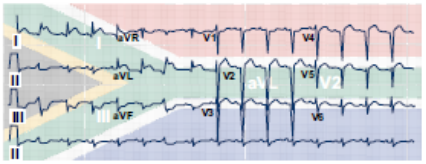
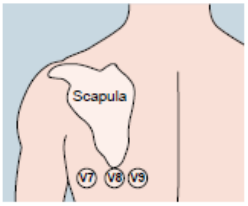
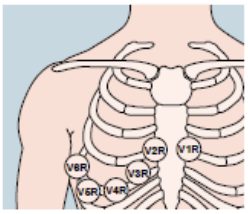
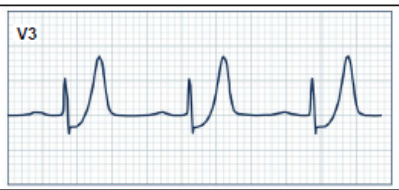
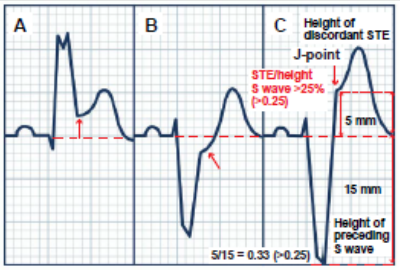
	Criteria	Supporting information and illustration	Recommendation for clinical action
A. Regional STE with reciprocal STD	STE ≥1 mm at the J-point in two contiguous leads in all leads other than V2-4. V2-4 STE criteria: ≥1.5 mm in women ≥2 mm in men >39 years ≥2.5 mm in men <40 years		Activate reperfusion pathway
B. High lateral MI	STE I, aVL, V2 STD III (+/- II, aVF) Subtle STE V5, V6 and reciprocal changes in aVF may be seen.		Activate reperfusion pathway
C. Posterior MI	Precordial STD ≥0.5 mm V1-3 Confirm with posterior leads (V7,8,9) with findings of STE: • ≥0.5 mm in women and men ≥40 years • ≥1 mm in men <40 years	V7, 8, 9 supplementary lead placement 	Activate reperfusion pathway
D. Right Ventricular MI	STE ≥0.5 mm in any right-sided chest lead (V3R-V6R), but particularly V4R. STE ≥1 mm in men <30 years	Right precordial supplementary lead placement 	Activate reperfusion pathway
E. De Winter T waves	J-point depression with up-sloping ST segments and tall, prominent, symmetric T waves in precordial leads, with STE (≥0.5 mm) in aVR and an absence of STE in precordial leads.		Activate reperfusion pathway
F. Modified Sgarbossa Criteria **(LBBB or paced rhythm)**	Any of the following: A) Concordant STE >1 mm in leads with positive QRS complex B) Concordant STD ≥1 mm V1-3 C) STE ≥1 mm in one or more leads at the J-point which is proportionally discordant to the preceding S wave by >25%.		Activate reperfusion pathway

Figure 4: ECG findings consistent with acute coronary occlusion myocardial infarction (ACOMI). *Abbreviations: ECG, electrocardiogram; LBBB, left bundle branch block; MI, myocardial infarction; STE, ST-segment elevation; STD, ST-segment depression.*

2.2.2 High-risk ECG findings

ACO is a dynamic process which may not be evident on the initial ECG. Certain ECG patterns are now recognised as being associated with potential progression to ACOMI which call for prompt and continuous ECG and clinical monitoring to rapidly identify ACOMI.

Wellens T waves: characteristic T wave inversions in precordial leads which in a person in whom symptoms have resolved, may represent a reperfusion syndrome associated with a critical stenosis of the left anterior descending artery, known as Wellens syndrome (see **Figure 5A**) [77]. Avoid provocative testing (e.g. exercise stress testing) and strongly consider invasive coronary angiography. If/when ischaemic symptoms return, the ECG recorded during symptoms will pseudo-normalise with more upright T waves.

Diffuse ST depression across multiple leads with STE in aVR: may represent global ischaemia of various etiologies including a left main occlusion, triple vessel disease or supply/demand mismatch ischaemia seen in type 2 MI (see **Figure 5B**) [78]. People with persisting symptoms with no identifiable alternative causes for ischaemia or who do not respond to treatment of contributors should be considered for coronary angiography [79].

Hyperacute T waves: symmetrical, broad-based T waves disproportionately large to the preceding QRS complex can be the first ECG finding of an evolving MI, although its prognostic significance has been questioned (see **Figure 5C**) [80, 81]. These people should be subject to close clinical and continuous cardiac monitoring and serial 12-lead ECGs to examine for development of signs of ACOMI. An important differential diagnosis is hyperkalaemia (see **Figure 5C**).

2.2.3 Other signs of myocardial ischaemia on ECG

Other ECG findings in a person with suspected myocardial ischaemia which should prompt continuous cardiac monitoring and consideration of treatment for NSTEACS are as follows.

ST-segment depression (STD): ≥0.5 mm at the J-point in ≥2 contiguous leads which is horizontal or down sloping (see **Figure 5D**). The deeper and more widespread the depression, the more severe the ischaemia [82, 83]. STD in contiguous leads should be first considered as reciprocal change of an ACOMI and the ECG examined for corresponding STE as STD secondary to subendocardial ischaemia does not generally localise to a regional coronary territory (see **Figure 4**, **Figure 5** and **Table 4**) [84]. Although STD occurs in other conditions (e.g. LVH, hypokalaemia, digoxin use), a recent systematic review found it to be highly specific (97.2–99.3%) but poorly sensitive (16.6–20.0%) for ischaemia [85].

T wave abnormalities: including dynamic inversion or flattening (see **Figure 5E**). New T wave inversion (TWI) compared to a previous ECG or dynamic T wave changes during serial ECGs may represent ischaemia. Specificity of TWI for ischaemia is higher in the context of other signs of ischaemia on the ECG [86].

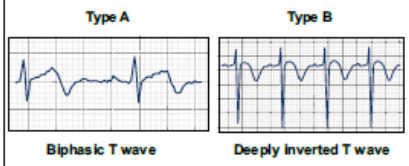
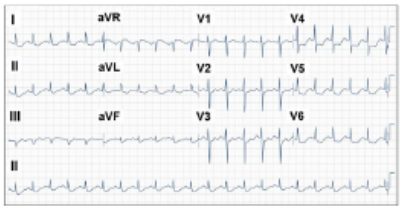
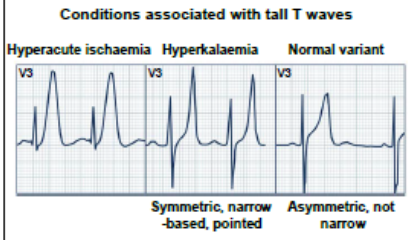
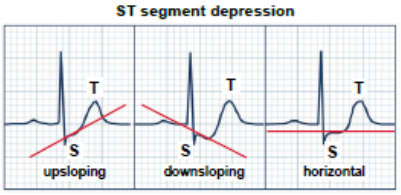
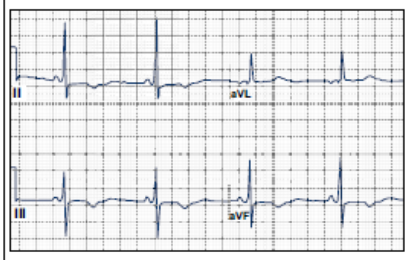
	Criteria	Supporting information and illustration	Recommendation for clinical action
A. Wellens' criteria	Isoelectric or minimally elevated J-point <1 mm AND either biphasic T waves V2, V3 (Type A) or symmetric TWI V2, 3 (sometimes V1, V4, V5, V6) (Type B)	 Pattern appears when pain free. "Pseudonormalisation" of ECG changes with symptoms of ischaemia (e.g., chest pain).	Urgent consultation with cardiology. Continuous cardiac monitoring and serial ECGs. No functional testing. Low threshold for invasive angiography.
B. Diffuse STD in multiple leads and STE in aVR	STE aVR >1 mm Multi-lead STD I, II, aVL and V1-6 Absence of STE other leads		Consider early reperfusion if ECG findings persist despite management of symptoms or seek alternative cause. Correct hypotension, hypoxia, anaemia.
C. Hyperacute T Waves	Large, symmetrical, broad-based T waves. Regional distribution.		Cardiac monitoring and serial ECGs.
D. STD	Horizontal or down-sloping STD ≥0.5 mm at the J-point in ≥2 leads is suggestive of subendo-cardial ischaemia. STD which is sustained for ≥0.08 s in ≥1 lead (except aVR) is most significant.		Continuous monitoring serial ECGs. If persists or worsens treat as per NSTEACS recommendations.
E. TWI	Significant for ischaemia if ≥1 mm deep; present in ≥2 contiguous leads or changing acutely in leads with a normally upright T wave (all except lead III, aVR and V1). Wide differential. If new or dynamic, consistent with ischaemia.		Continuous monitoring, serial ECGs.

Figure 5: High-risk ECG findings for ACS and findings suggestive of cardiac ischaemia.
Abbreviations: ECG, electrocardiogram; NSTEACS, non-ST-segment elevation acute coronary syndromes; STE, ST-segment elevation; STD, ST-segment depression; TWI, T-wave inversion.

Computer-assisted ECG interpretation

No international standardised system for computer interpretation of ECGs currently exists, with different ECG machine manufacturers using different algorithms with varying sensitivity and specificity for diagnosing cardiac conditions. Computer errors specific to ACS and ACOMI diagnosis include attribution of Q waves in LVH, LBBB, and/or dilated or hypertrophic cardiomyopathy to ACOMI; and an inability to discriminate STE of early repolarisation, pericarditis, or LBBBs from ACOMI [87]. A careful evaluation of the ECG by a clinician who can incorporate the clinical context into the assessment is required.

Continuous ECG monitoring, where available, is an exception as it is designed to detect subtle differences over time in ST segments, changing T wave morphology or evolving new Q waves.

2.2.4 Continuous ECG monitoring

In people without ongoing symptoms, normal or non-ischaemic ECG changes and initial normal troponin values, continuous ECG monitoring is not required. High-risk features in people with suspected ACS who require ongoing ECG monitoring are listed in **Table 5**.

Table 5: High-risk clinical features for people with suspected ACS requiring ongoing ECG monitoring.

Haemodynamic instability or cardiogenic shock
Recurrent or ongoing chest pain refractory to medical treatment
Cardiac arrest
Recurrent dynamic ST-T wave changes or other changes consistent with myocardial ischaemia or infarction on ECG
Arrythmias (e.g. sustained ventricular tachycardia, high degree atrioventricular block)
Mechanical complications of MI (e.g. new systolic murmur)
Acute heart failure

Abbreviations: ECG, electrocardiogram; MI, myocardial infarction.

Practice points

- An initial normal ECG does not exclude ACS. If myocardial ischaemia is strongly suspected to exist, record and interpret serial ECGs.
- In people with symptoms of ischaemia with clear evidence of ACOMI on ECG, treatment decisions should not be delayed while waiting for troponin test results.
- When performing serial ECGs, maintain the same placement of leads when possible, to prevent artifactual errors in interpretation.

2.2.5 Future direction

Artificial intelligence (AI) and machine learning applied to ECG interpretation and linked with clinical data are currently being researched with the aim of delivering a more accurate and timely assessment of ACS and ACOMI [88].

2.3 Biomarkers

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with suspected ACS, evaluation with high-sensitivity cardiac troponin assays is recommended.	Strong	High
Elevated cardiac troponin (cTn) values are defined as >99th percentile using assay-specific values.	Consensus	
Apply the assay-specific troponin metrics relevant to the cTn assay being used.	Consensus	
When evaluating changes (deltas) in troponin values, serial results from a single assay must be used.	Consensus	

Evidence supporting the recommendations

Cardiac troponin I (cTnI) or cardiac troponin T (cTnT) is the biomarker of choice in the diagnosis of ACS due to its organ-specific amino acid sequence, parts of which act as targets for assays using monoclonal antibodies [16, 89, 90].

Cardiac troponin assays have evolved from the 1990s to deliver improved sensitivity for detecting troponin. Currently, the most analytically sensitive assays preferred for clinical use are high-sensitivity assays [16, 91]. A high-sensitivity assay is more precise than earlier assays, with measures of imprecision or % coefficient of variation (CV) of ≤10% at the sex-specific 99th percentiles and can detect very low troponin concentrations. These assays can detect troponin in at least 50% of healthy individuals.

Evaluation with hs-cTn assays enable more rapid detection or exclusion of myocardial injury and increase diagnostic accuracy for MI compared to earlier generation of cardiac troponin (cTn) assays called contemporary troponin assays. The ability to detect very low troponin values with accuracy has been used to achieve safe, early rule out of MI and rapid discharge from the ED based on assay-specific metrics lower than the 99th percentile (see section 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS) [92-94].

Contemporary assays are still used in smaller hospitals around Australia, including point-of-care (POC) contemporary troponin assays in many regional and remote settings. Their lower sensitivity mean they should be used in combination with clinical scores when risk stratifying people with suspected ACS (see section 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS). POC assays for hs-cTn have been developed and will likely become increasingly available [95-98].

2.3.1 Analytic properties of cardiac troponin assays

The cut-off threshold used to define an elevated cTn value which is diagnostic of myocardial injury is the 99th percentile of a healthy population and this value is assay-specific [16]. Within Australia, different units are used to report contemporary (µg/L) and highly sensitive troponin assays (ng/L), reflecting the lower sensitivity of the older cTn assays (see **Table 6**). Other metrics of assay performance include limit of detection and limit of blank (see **Figure 6**).

Table 6: Contemporary vs highly sensitive cTn assay features.

Characteristic	**Contemporary troponin assays***	**High-sensitivity troponin assays**
Precision	Variable	≤10% CV at 99th percentile
Detection	~ 20–50% of healthy reference population	≥50% of healthy reference population
Units	Micrograms per litre (µg/L)	Nanogram per litre (ng/L)
Sex-specific 99th percentiles	No. Overall 99th percentile values only.	Yes. Female and male 99th percentiles.
Timing of serial testing for MI using 99th percentile	0 and 6–8 hours	0 and 3 hours
Single low-risk troponin values for MI*	No	Yes
Ability to use in rapid, early assessment strategies	No	Yes
Platform	POC and laboratory-based	POC and laboratory-based

**Using a contemporary assay, if a person presents symptom-free for >6–8 hours only one test needed. If ≤99th percentile, no second test is required. If >99th, a second test is needed. Abbreviations: cTn, cardiac troponin; CV, coefficient of variation; MI, myocardial infarction; POC, point-of-care.*

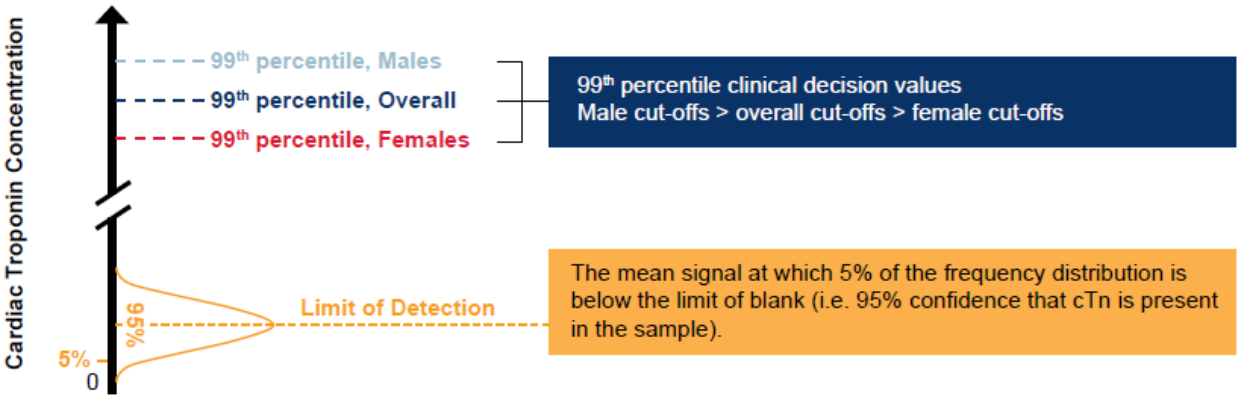


Figure 6: Various analytic definitions for troponin assays. Adapted with permission from Elsevier [99]. *Abbreviations: cTn, cardiac troponin.*

Use of hs-cTn assays has shown that women have lower circulating normal cTn concentrations, resulting in differing values for the 99th percentile between women and men [100]. Consequently, use of single overall cut-off points to determine myocardial injury and potentially MI in women will result in underdiagnosis.

In transgender men and women, the use of sex hormones, rather than sex assigned at birth, may impact on myocardial mass and influence hs-cTn reference ranges [101]. To maintain safety, the reference range should be based upon the lower cut-off points (female), however more research is required [101].

Despite increases in the 99th percentile of cTn being observed in people aged over 60 years, changes to the 99th percentile based upon age are not clinically used [100, 102-104].

2.3.2 Point-of-care troponin assays

POC troponin analyses providing earlier results may result in more expeditious management of people with suspected ACS and comparable safety to laboratory-based assays may be achieved (see **Table 7** in section 2.4.1.1 High sensitivity troponin-based clinical decision pathways2.4.1.1 High sensitivity troponin-based clinical decision) [95, 96, 98, 105]. Using contemporary POC assays, the 99th percentile at serial timepoints over 6–8 hours is needed to assess people with suspected ACS [106]. Recent evaluations support rapid assessment processes using POC hs-cTn assays [96, 107-109]. Knowledge of hs-cTn POC assays is rapidly evolving and use in clinical decision pathways in EDs, outpatient clinics or primary care may be implemented as analytical robustness, clinical safety and cost efficacy of such devices have been demonstrated [105].

2.3.3 Clinical interpretation of troponin values

Careful interpretation of cTn results integrated with all clinical information including ECGs is required (see **Figure 7**) [18]. Serial measurements are required to identify if there is a stable or changing pattern associated with an elevated cTn. Stable elevations are seen with chronic myocardial injury but may also be seen in the plateau phase of troponin release in MI (e.g. in people with delayed presentation). People with changing values (both increasing and decreasing) warrant evaluation for evidence of myocardial ischaemia, noting that acute myocardial injury due to other causes (e.g. acute heart failure, pulmonary embolism) needs

to be considered when clinically appropriate. Differentiation between types of MI also requires careful evaluation, as does differentiation from myocardial injury (see **Figure 7**) [110].

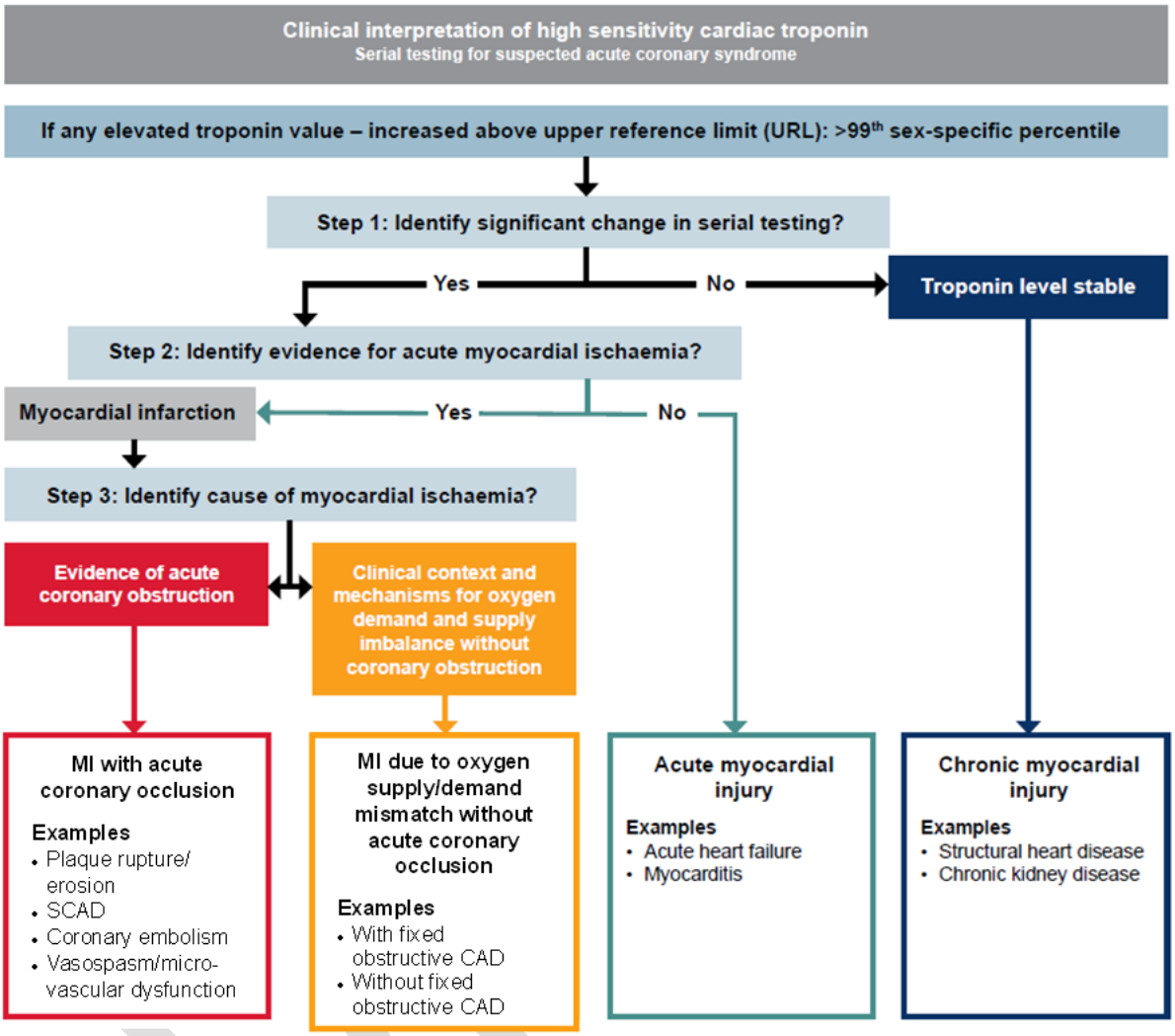


Figure 7: Clinical interpretation of hs-cTn results. Modified from the Accelerated Chest Pain Risk Evaluation (ACRE) Project, Clinical Excellence Queensland, Queensland Health. *For guidance on identifying evidence for acute myocardial ischaemia, refer to section 2.2.2 High-risk ECG findings and 2.2.3 Other signs of myocardial ischaemia on ECG. Abbreviations: CAD, coronary artery disease; hs-cTn, high-sensitivity cardiac troponin; MI, myocardial infarction; SCAD, spontaneous coronary artery dissection.*

The introduction of hs-cTn assays has led to a decrease in the frequency of UA, defined as cTn values ≤99th percentile, whereby better detection of small changes in troponin levels has meant that a proportion of people previously classified as UA have been reclassified as MI [111].

2.3.4 Time from onset of coronary occlusion vs. symptom onset

In the setting of an ACOMI, there may be delays to when cTn levels in blood become elevated although this timeframe has become shorter with the ability of hs-cTn assays to detect lower concentrations of circulating troponin (see **Figure 8**). Repeat troponin testing is required for people with ongoing or recurrent symptoms.

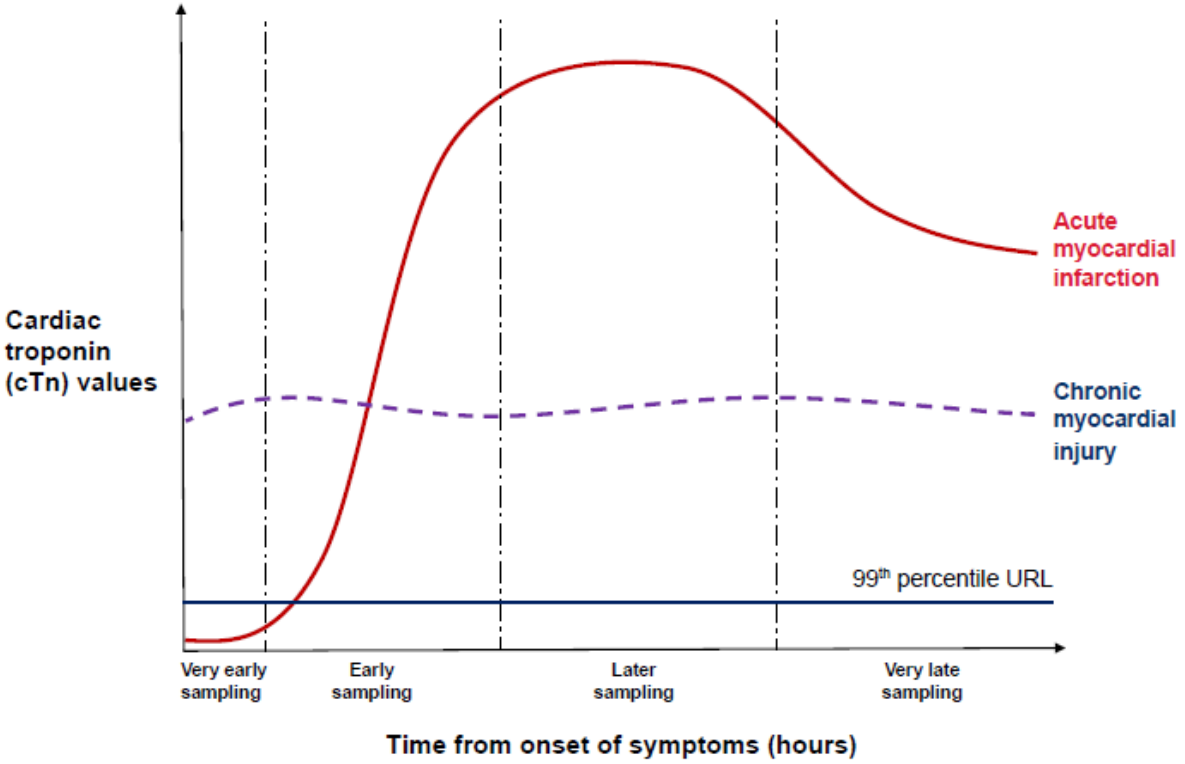


Figure 8: Early troponin kinetics in people with acute myocardial infarction. *Abbreviations: cTn, cardiac troponin; URL, upper reference limit.*

2.3.5 Comparing results from different troponin assays

Cardiac troponin I assays developed by diagnostic companies use different antibody combinations, resulting in differences in numerical results for the same amount of circulating troponin. Significant differences exist in the categorisation of people based on different hs-cTn assays [112]. Results of one assay cannot be interpreted using the reference range of a different assay and serial testing of cTn concentrations can only be interpreted when measured using the same assay.

Differences between troponin T and I assays

Both high-sensitivity cardiac troponin I (hs-cTnI) and high-sensitivity cardiac troponin T (hs-cTnT) provide comparable diagnostic accuracy in the early diagnosis of MI [113]. Troponin T is more likely to be elevated with poor renal function (see Renal disease section) and chronic muscular diseases (e.g. chronic myopathy, myositis). This is possibly due to re-expression of

cTnT in the diseased muscle or due to cross reactivity of the cTnT assay with a fragment of skeletal muscle troponin T [114, 115].

Non-MI causes of troponin elevation

Numerous ischaemic, non-coronary cardiac, and non-cardiac causes of myocardial injury can result in elevated cTn concentrations (see **Figure 9**) [16, 90, 116, 117]. Life-threatening conditions including aortic dissection and pulmonary embolism may result in elevated cTn values. Cardiac troponin elevation indicates myocardial injury but is not specific to the underlying pathophysiology [16]. People without MI who have an elevated cTn value have a worse prognosis than those with MI [118].

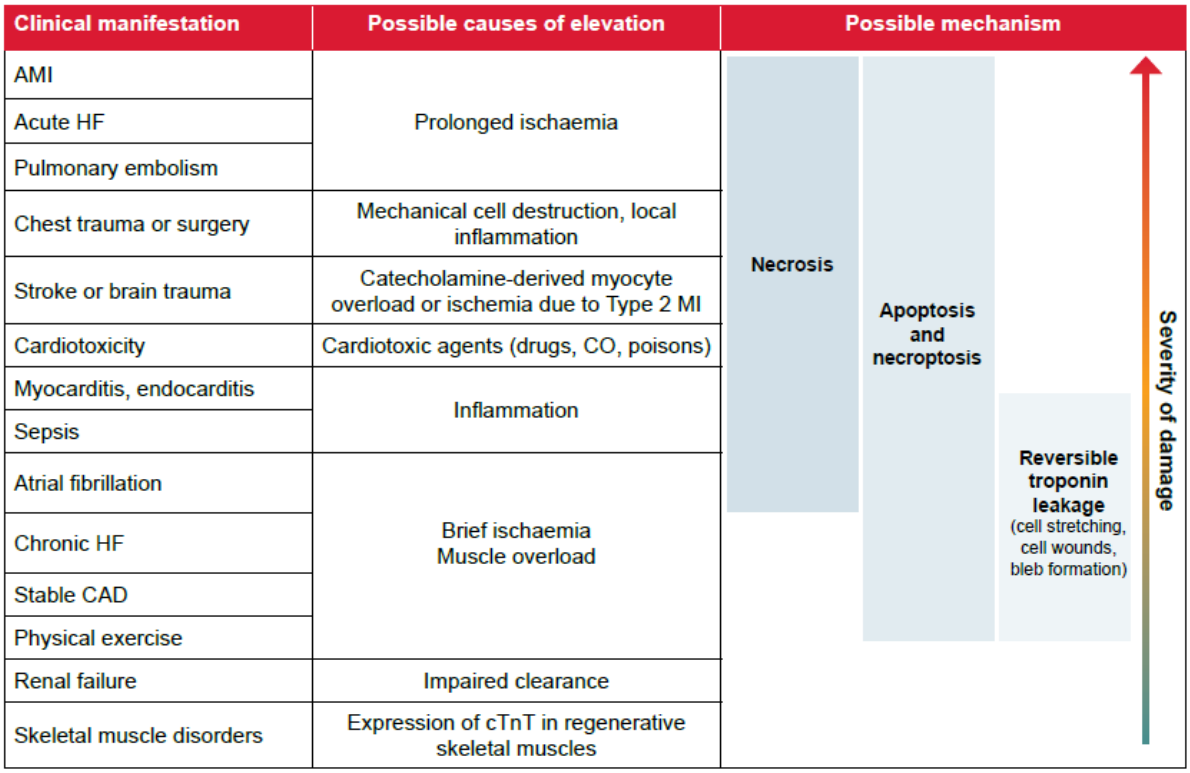


Figure 9: Conditions associated with troponin elevation. Adapted from [90]. *Abbreviations: AMI, acute myocardial infarction; CAD, coronary artery disease; CO, carbon monoxide; cTnT, cardiac troponin T; HF, heart failure; MI, myocardial infarction.*

Renal disease

Chronically elevated cTn concentrations are often reported with decreased renal function, more so with cTnT than cTnI concentrations. Recently published guidelines for MI diagnosis in people undergoing haemodialysis recommend serial cTn measurements, rather than management according to an elevated baseline value [119].

False positive and false negative cardiac troponin results

Analytical false positive results for cTn may occur due to antibody interference from macrotroponins (high-molecular weight complexes of cTn fragments bound to immunoglobulins [autoantibodies to cTn] causing delayed troponin clearance) and heterophilic antibodies which bind to cTn assay antibodies (causing positive signals in the absence of cTn). The causes of heterophile antibodies are largely unknown, however they may be found in people with rheumatoid arthritis, and viral infections such as Epstein Barr and cytomegalovirus [120]. Conversely, severe haemolysis and other substances in plasma, like biotin, may result in false negative results [121, 122].

When cTn results and the clinical presentation are concerningly discordant, the hospital's laboratory should be contacted to consider and exclude rare analytically false-positive cTn test results [121].

Other biomarkers

Additional biomarkers exist but are not used for the diagnosis of MI. There is no role for creatine kinase MB-isoenzyme (CK-MB), including for the identification of reinfarction in people with AMI [123].

Practice points

- Sex-specific 99th percentiles are recommended for use [124-126].

2.4 Risk assessment and clinical diagnostic pathways for suspected ACS

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
People with symptoms and ECG changes consistent with ACOMI require urgent reperfusion. Do not use clinical decision pathway (CDP).	Strong	Very Low
People presenting with acute chest pain or other symptoms suggestive of ACS should receive care guided by an evidence-based CDP that includes assay-specific troponin metrics to categorise people into high-, intermediate-, and low-risk strata.	Consensus	
A high-sensitivity troponin-based risk stratification pathway is recommended, using the 0/1-hour or 0/2-hour strategy, or the High-STEACS algorithm.	Consensus	
When contemporary troponin assays are used, a CDP incorporating formal clinical score-based risk stratification is recommended.	Consensus	

Evidence supporting the recommendations

For people with suspected ACS, a structured assessment process in Australian EDs improves care and health service efficiency by identifying people with MI and those at high risk of MACE within 30 days who require further investigation, treatment or longer periods of observation before discharge [127]. This practice also reduces unnecessary investigations and therapies and decreases avoidable inpatient admissions for people at low risk of 30-day MACE. While older studies report missed MI rates of 1–2%, contemporary evidence suggests missed MI and/or 30-day MACE rates of <1% in people discharged from the ED following structured evaluation incorporating clinical information, cTn and ECG testing [31, 128-130].

For people with ECGs suggestive of ischaemia including those at high risk of progressing to ACOMI, referral for inpatient evaluation should occur (see section 2.2 Initial ECG assessment).

For people in whom ACOMI is initially excluded and those without ischaemic ECG findings, multiple diagnostic approaches have been reported, some focussed on optimum use of hs-cTn results alone (see section 2.4.1.1 High sensitivity troponin-based clinical decision pathways), others using a clinical risk scoring system incorporating cTn values (see section 2.4.1.2 Clinical score-based clinical decision pathways). Use of hs-cTn assays within a validated algorithm enables rapid identification of people with and without myocardial injury and, when combined with clinical and ECG criteria, identifies people likely to be experiencing an MI.

Additional risk assessment using clinical risk scores (e.g. *Emergency department assessment of chest pain score* (EDACS) and *History, ECG, age, risk factors and troponin* (HEART) score) have utility when contemporary cTn assays are in use (as opposed to hs-cTn assays) and may support identification of people at risk of MACE within a short period (usually 30 days from presentation) (see section 2.4.1.2 Clinical score-based clinical decision pathways and Supplementary material) [131].

Urgent revascularisation is not necessarily labelled as an adverse event, however few risk assessment studies have been published using clinically significant endpoints limited to MI and cardiac death, with many including revascularisation as a MACE which has been questioned [132-136].

2.4.1 Clinical decision pathways

Clinical decision pathways (CDPs) for people with suspected ACS define an assessment process that includes ECG and troponin testing intervals and may integrate clinical risk scores. To standardise and make consistent the approach to care and decision-making, CDPs should be implemented at the local institution level based on the local troponin assay-specific performance thresholds. Guidance to operationalise algorithms into clinical practice is provided.

Risk strata

A three-tiered stratification is recommended, grouping people into high, intermediate, or low risk of MACE including MI (see **Figure 10**). In addition to cTn measurement, all strategies involve taking an appropriate history and physical examination, and demonstrating that the ECG is normal, non-ischaemic, or unchanged from previously.

High risk: the probability of an event, most commonly MI, within 30 days is higher than 50–70% (positive predictive value >50–70%) [137]. These people require admission and further cardiac evaluation.

Importantly, as not all high-risk people are ultimately determined to have an MI, explanation about risk (rather than saying this is the diagnosis) to the affected person is essential. Refer to section 3 Hospital care and reperfusion for further evaluation and management of high-risk people.

Intermediate risk: for those people identified as intermediate risk using the hs-cTn-based CDP 0/1 or 0/2-hour protocols, 30-day MACE rates vary between 2–22%, and additional evaluation is required [34, 138, 139]. Intermediate-risk people will have either normal (≤99th percentile) or elevated (>99th percentile) cTn values, with the latter requiring evaluation in an inpatient setting.

For intermediate-risk people with serial cTn results ≤99th percentile, outpatient testing is acceptable as 30-day MACE rates in such cases are <2% (see section 2.6 Diagnostic testing for people with suspected ACS) [31].

People with elevated but unchanging cTn values consistent with chronic myocardial injury rather than ACS are out of the scope of this guideline (see section 2.3 Biomarkers).

Low risk: the risk of MACE within 30 days is <1% and may be identified with either hs-troponin-based CDP or clinical score-based tools (see **Table 7** and Supplementary material). In general, hs-cTn strategies safely define a larger proportion of people as low-risk than clinical risk scores combined with contemporary cTn assays. When defined as low-risk using a hs-cTn strategy, further testing to exclude AMI is not required [18, 140, 141].

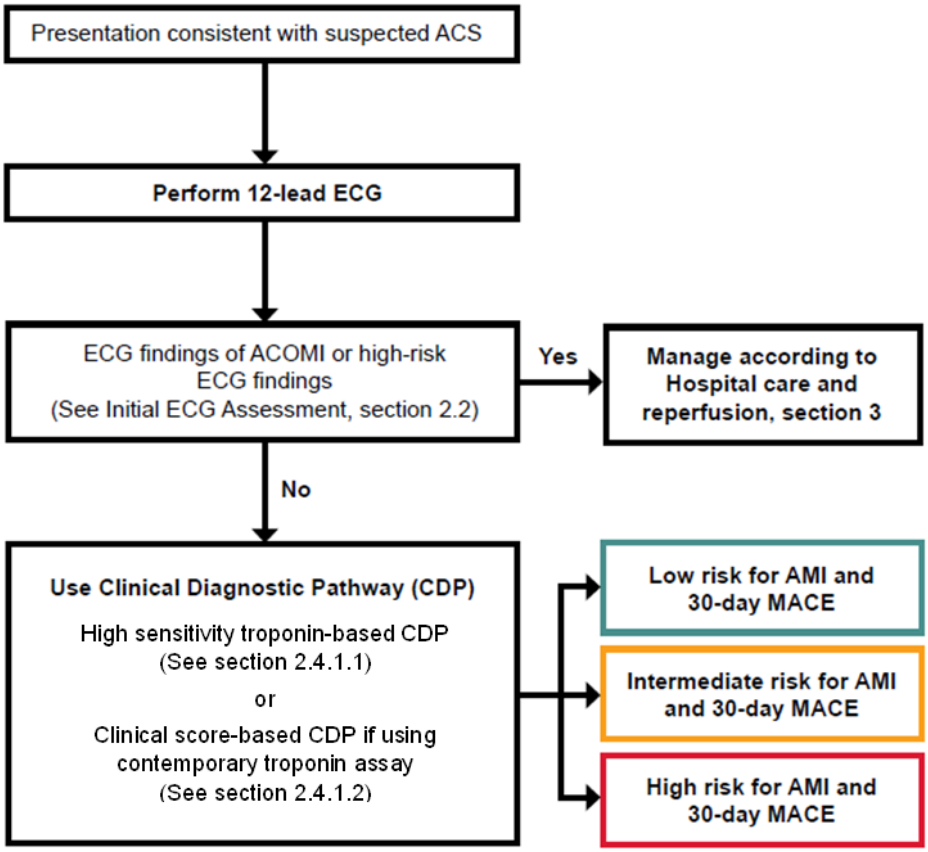


Figure 10: Assessment process for people with suspected ACS. *Abbreviations: ACOMI, acute coronary occlusion myocardial infarction; ACS, acute coronary syndromes; AMI, acute myocardial infarction; ECG, electrocardiogram; MACE, major adverse cardiovascular events.*

Risk stratification for people with suspected ACS: identifying myocardial infarction and unstable angina

For people without findings consistent with ACOMI on the initial ECG, further assessment aims to identify people with NSTEMI and UA through evaluation of clinical features with additional ECG and troponin testing. NSTEMI is associated with significant troponin changes (see below).

People who have ongoing or recurrent symptoms of ischaemia, or new ECG findings suggestive of ischaemia during initial or repeat testing, should be considered at high risk for ACS, even if initial cTn levels are not elevated, which may suggest UA. Serial cTn testing should be pursued if clinical suspicion of ACS remains high, as late increases in cTn have been described in <1% of people with NSTEMI [142].

2.4.1.1 High sensitivity troponin-based clinical decision pathways

Strategies incorporating hs-cTn assay results rather than older contemporary troponin assays are recommended in facilitating safe, rapid disposition planning. Overall, hs-cTn-based risk stratification may identify ~50–65% of people presenting with suspected ACS as low-risk, ~20–30% as intermediate-risk and ~15–25% as high risk for MACE [143, 144]. When used in a validated algorithm combined with non-ischaemic ECG changes, safety and efficacy are achieved without using clinical risk scores [18, 137].

0-, 0/1-, and 0/2-hour strategies have been developed for most hs-cTn assays and the metrics are assay-specific (see **Figure 11**, **Table 7** and Supplementary material) [34, 94, 137, 138, 142, 145-152].

Single hs-cTn measurements

A single hs-cTn measurement is not suitable for people with symptom onset <2 hours who require serial testing [24, 94, 138, 147, 149, 153-155]. In people with symptom onset ≥2 hours combining hs-cTn assay-specific values with non-ischaemic ECG findings, a single cTn measurement can very safely identify 20–50% of people to be low-risk [34, 38, 93, 94, 138, 141, 143-146, 149, 155-162].

A single measurement approach has been extensively validated using both hs-cTnT and hs-cTnI assays with high negative predictive value and sensitivity for excluding index MI and a <1% risk of MI or death during short- and longer-term follow-up [32, 92, 93, 141, 143, 155, 162-165]. Unlike hs-cTn assays, clinical decision-making based on single measurement of conventional cTn has not been validated [166].

0-, 0/1-, and 0/2-hour strategies

For people identified as being at intermediate risk using the 0/1- or 0/2-hour protocols, index or 30-day MACE rates may vary between 2–22%, and additional evaluation is required (see section 2.6 Diagnostic testing for people with suspected ACS) [34, 138, 139]. For people with normal serial cTn values, 30-day MACE rates are ≤2% [31].

While mostly large observational studies have evaluated 0/1- and 0/2-hour protocols, randomised trials of the 0/1-hour protocol have reported 30-day MI and death rates of <1% [34, 148, 167-169]. In addition to metrics being assay-dependent, the change thresholds (deltas) for the 0/1- and 0/2-hour algorithms are time-dependent, so it is crucial blood specimens are collected within the specified windows (see **Table 7**).

In most hospitals, delays in central laboratory assay turnaround times render the 0/1-hour protocol impractical. POC hs-cTn assays may overcome this limitation but are not yet widely available. A 0/2-hour protocol is therefore currently the most practical option in most settings.

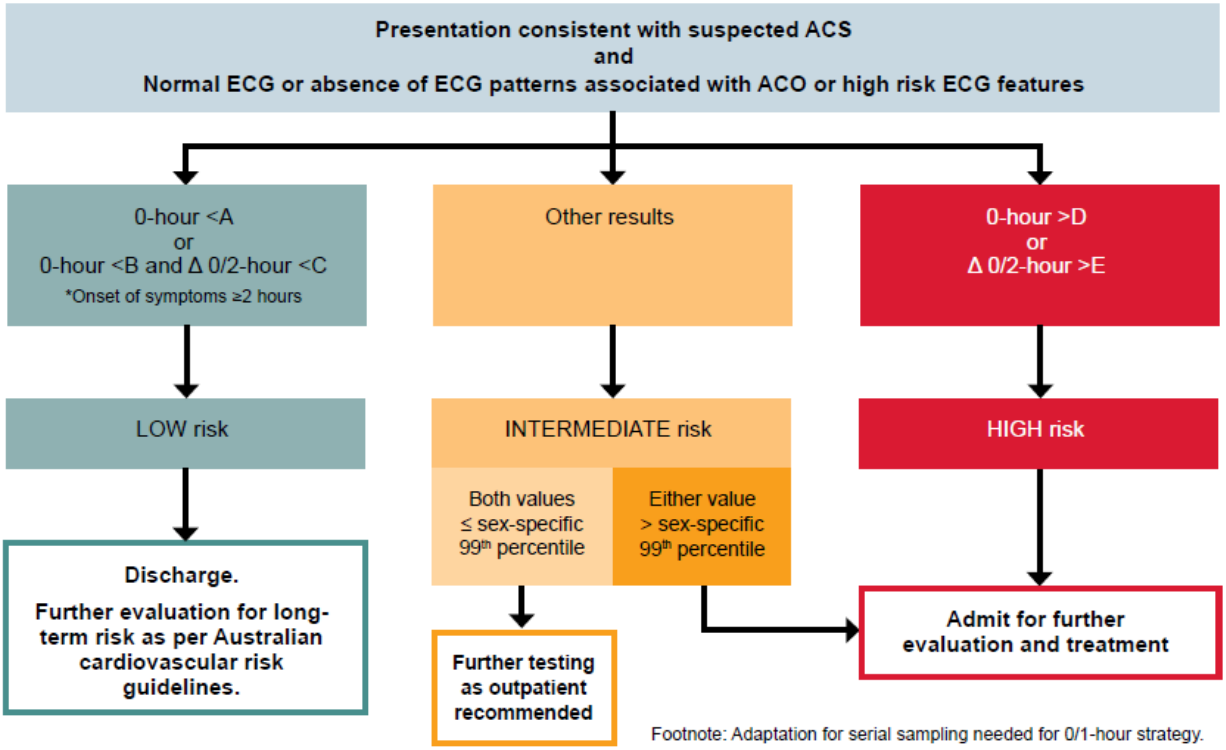


Figure 11: 0/2-hour testing recommendations. *Note: the 0/2-hour time points are shown in this figure. If using a 0/1-hour strategy, change timeframes accordingly. Refer to* ***Table 7*** *for interpretation of cTn assay-specific values and sex-specific 99th percentiles. *All people with symptom onset <2 hours need serial testing. People with ongoing symptoms should be assessed according to high-risk criteria. Abbreviations: ACO, acute coronary occlusion; ACS, acute coronary syndromes; ECG, electrocardiogram.*

Table 7: Troponin assay and metrics for use in 0/1- and 0/2-hour sampling strategies.

Assay	Sampling timepoints	A	B	C	D	E	F Female 99th percentile	G Male 99th percentile
Hs-cTnI (Architect; Abbott)	0/1h	<4	<5	<2	≥64	≥6	16	34
	0/2h	<4	<6	<2	≥64	≥15	16	34
Hs-cTnI (Access; Beckman Coulter)	0/1h	<4	<5	<4	≥50	≥15	11	20
	0/2h	<4	<5	<5	≥50	≥20	11	20
Hs-cTnI (Centaur; Siemens)	0/1h	<3	<6	<3	≥120	≥12	40	58
	0/2h	<3	<8	<7	≥120	≥20	40	58
Hs-cTnI (Atellica; Siemens)	0/1h	<4	<6	<3	≥120	≥12	39	54
	0/2h	NA	NA	NA	NA	NA	NA	NA
Hs-cTnI (Vitros; Clinical Diagnostics)	0/1h	<1	<2	<1	≥40	≥4	9	12
	0/2h	<1	<2	<3	≥40	≥5	9	12
Hs-cTnT (Elecsys; Roche)	0/1h	<5	<12	<3	≥52	≥5	9	17
	0/2h	<5	<14	<4	≥52	≥10	9	17
Hs-cTnI (Pathfast; LSI Medience)*	0/1h	<3	<4	<3	≥90	≥20	20	30
	0/2h	<3	TBD	TBD	≥90	TBD	20	30
Hs-cTnI (Triage True; Quidel)*	0/1h	<4	<5	<3	≥60	≥8	14	26
	0/2h	<4	TBD	TBD	≥60	TBD	14	26
Hs-cTnI (VTLi, Siemens)*	0/1h	<4	TBD	TBD	TBD	TBD	18	27
	0/2h	<4	<6	<5	≥60	≥15	18	27

**Point of care assay. 99th percentiles presented in column F/G are as per the International Federation of Clinical Chemistry tables rounded to the nearest whole number [32, 34, 93, 109, 142, 145, 147-149, 163, 164, 170-179]. Abbreviation: hs-cTnI, high-sensitivity cardiac troponin I; hs-cTnT, high-sensitivity cardiac troponin T.*

High-STEACS strategy

The United Kingdom (UK) *High-sensitivity troponin in the evaluation of patients with acute coronary syndrome* (high-STEACS) algorithm is a well validated, safe and effective

approach using a variety of hs-cTn assays [32, 141, 144, 148, 154]. Further details are described in the Supplementary material.

2.4.1.2 Clinical score-based clinical decision pathways

Sites using contemporary cTn assays

Incorporation of a clinical score-based tool (e.g. EDACS, HEART) in assessing people with suspected ACS is essential if using a conventional cTn assay. EDACS and the HEART score are the most widely validated strategies and have high sensitivity for index AMI and 30-day MACE (see Supplementary material) [157, 159, 180-188]. However, when compared to hs-cTn-based CDP, smaller numbers of people will be identified as low/intermediate risk and additional testing may occur without an improvement in MACE [34, 38, 94, 145, 146, 160, 161, 166, 172, 189, 190]. Furthermore, because sex-specific considerations are not included in all scoring systems, their effectiveness in men and women may not be equal [191]. Further information on these clinical based scores is provided in the Supplementary material.

2.4.2 Implementing a clinical decision pathway for suspected ACS

Accelerated management and disposition by using CDPs can be highly cost-effective. In an Australian randomised controlled trial (RCT) using hs-cTnT, the 0/1-hour algorithm resulted in more frequent ED discharge (45% vs 32%; p <0.001) and a 1-hour shorter ED length of stay (p <0.001). Similar clinical outcomes occurred at 30 days (p=0.001 for noninferiority) compared with a usual care approach using 0/3-hour cTn measurements with an hs-cTnT threshold of ≥30 ng/L [167].

A recent large, randomised trial showed failure to follow recommended management for people defined as low-risk using hs-cTn strategies resulted in substantial increase in resource use in terms of ED stay, hospital stay, non-invasive and invasive tests, with no differences in 30-day MACE [140].

Implementation of CDPs for suspected ACS, especially CDPs using hs-cTn assays rather than clinical risk scores, confers significant benefits for people and health care systems and requires the engagement of multidisciplinary teams [24, 31, 140, 169, 183, 184, 192-196].

Centres choosing to implement an alternate strategy to the recommended CDPs should validate this CDP and include assessment of 30-day mortality and re-presentation with confirmed ACS in all people with chest pain.

Practice points

Women

Risk of ACS in women is often underestimated by clinician assessments and traditional risk tools which lack sex-specific considerations. Often women are misclassified as having non-ischaemic chest pain [33, 37, 191, 197, 198].

- When using hs-cTn-based strategies and the 99th percentile URL, apply sex-specific thresholds (see **Figure 11**) [16, 32, 34, 150, 199, 200].

Older adults

In older people with a higher co-morbidity burden, including renal impairment, the specificity of hs-cTn results for MI is reduced [173, 199, 201, 202].

- Although hs-cTn concentrations increase with age in healthy people, uniform cut-offs are recommended for clinical use which may result in fewer older adults being deemed at low risk for MI [16].

First Nations people

The use of single hs-cTn measurements enables safe identification of people at low risk for MI and 30-day MACE [203].

- The HEART score and IMPACT pathways (see Supplementary material) have both been evaluated in small studies in First Nations populations and can be cautiously considered for use [204].
- All First Nations adults (18 years and over) with suspected ACS should undergo investigation for underlying CAD, due to a high risk of future cardiac events [205, 206].

People with renal impairment

Elevations in cTn are common in this population, leading to their exclusion from many assessment trials [207]. The safety of hs-cTn-based strategies appears to be similar in people with and without renal dysfunction.

- Hs-cTn-based strategies can be used in people with renal dysfunction, however fewer people will be identified as low risk [201, 202].

2.4.3 Future direction

Newer strategies for individualised determination of likelihood of MI

Newer strategies for determination of risk of MI have been developed on large international multicentred datasets using machine learning techniques. These include the MI3 algorithm study (derived in 3,013 people and validated in 7,998 people), the ARTEMIS study (derived in 2,575 people and validated in 23,411 people) and the CoDE-ACS study (derived in 10,038 people and externally validated in 3,035 people) [208-210]. Such strategies use additional information (e.g. specific interval time of cTn testing, biometric measurements) and validation studies suggest large proportions of people can be defined as low risk, with improved specificity for MI in high-risk people.

2.5 Initial therapeutic management

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In all people with suspected or confirmed ACS, give aspirin (300 mg orally, dissolved or chewed) unless contraindicated.	Strong	High
People with suspected or confirmed ACS with oxygen saturation (SpO2) ≥90% do not require oxygen therapy.	Strong	Moderate
In people with suspected or confirmed ACS receiving oxygen therapy, SpO2 should not exceed 96%.	Strong	Moderate
In the presence of ongoing chest pain, give glyceryl trinitrate sublingual tablet or spray every five minutes for up to three doses if no contraindications exist.	Consensus	
In people with chest discomfort and in the absence of contraindications, it is reasonable to administer intravenous fentanyl or morphine boluses.	Consensus	

Evidence supporting the recommendations

Aspirin

Large meta-analyses have confirmed that in people with MI, aspirin reduces the risk of serious vascular events (vascular death, MI and stroke) at a small cost of increase in major bleeding [211, 212]. Although maintenance doses of 100 mg are as effective as larger doses, a loading dose of 150–300 mg is recommended, based on pharmacokinetic data showing that this is required to completely inhibit the thromboxane mediated pathway of platelet activation (see section 3.4 Antiplatelet therapy in the acute phase) [213].

Oxygen therapy

Two large pragmatic randomised trials have shown that the routine use of supplemental oxygen in people with suspected ACS without hypoxaemia does not improve mortality at 30 days or 12 months [214, 215]. In addition, a meta-analysis incorporating one of these and several earlier smaller studies has found that oxygen therapy is associated with a greater incidence of recurrent MI and coronary revascularisation at 6–12 months following an ACS. This study also reported strong evidence of a dose response relationship between oxygen saturation and increased mortality risk in acutely ill people and people in intensive care including those with MI, advocating caution against achieving higher saturations in these people [216].

Practice points

Oxygen therapy

- Routine use of oxygen therapy is recommended below 90% saturation on the premise that hypoxaemia at this level contributes to coronary ischaemia, although whether this therapy improves clinical outcomes is not known [214].
- It is not known whether there is benefit in giving oxygen to people with oxygen saturation between 90–92% although this is common practice [217-219].
- Care should be exercised when administering oxygen to people with chronic obstructive airways disease where the target arterial oxygen saturation (SaO2) is to be 88–92%.

Nitrates

- Contraindications to GTN administration include hypotension, right ventricular infarction, or recent use of a phosphodiesterase 5 inhibitor (sildenafil, vardenafil or tadalafil). If symptoms persist, consider intravenous (IV) GTN and/or alternative therapy.
- In people with acute ischaemia, IV nitrates are more effective than sublingual nitrates for symptom relief but have no impact on prognosis [220, 221].

Opioid analgesia

- Titrate doses of opioid analgesia to resolution of chest pain, as dose requirements differ for people dependent on their age, comorbidities, and concurrent medicine use [222-224].
- Fentanyl is often chosen due to its short time to peak effect, short duration of action, and minimal provocation of histamine release which may cause itching and hypotension.
- Both morphine and fentanyl administration are associated with increased platelet reactivity and decreased antiplatelet effect of P2Y12 inhibitors in the first hours of ACS, and slow absorption of oral medicines including ticagrelor [223, 225-227].

Other medicines

- In people confirmed as having ACS, do not give non-steroidal anti-inflammatory drugs due to the increased risk of MACE [228, 229].
- Additional antiplatelet and anticoagulation therapy or other therapies such as beta blockers should not be given to people without a confirmed or probable diagnosis of ACS (see section 3.4 Antiplatelet therapy in the acute phase and 3.5 Anticoagulant therapy in the acute phase).

2.6 Diagnostic testing for people with suspected ACS

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people at intermediate risk (as defined by a validated CDP) with elevated troponin concentrations (>99th percentile), inpatient investigation is recommended.	Strong	Moderate
In people at intermediate risk without elevated troponin concentrations, consider outpatient investigation with non-invasive testing.	Consensus	
In people at low risk who remain symptom-free, further cardiac testing for CAD is not routinely required.	Consensus	

Evidence supporting the recommendations

In people at intermediate risk of ACS, invasive angiography or non-invasive cardiac testing allows further risk stratification in a population who are presumed to have had an acute episode of coronary instability. These tests additionally may help establish alternative aetiology of chest pain and future risk of ACS beyond 30 days.

Invasive or non-invasive inpatient testing should be considered for people at intermediate risk with elevated troponin concentrations above the sex-specific 99th percentile (see **Figure 11**) because of their relatively high risk of a cardiac event within 30 days (5–22%, see section 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS) [230, 231]. Outpatient non-invasive testing can be considered (ideally within 30 days) for people at intermediate risk with serial values ≤ sex-specific 99th percentile, in whom the 30-day event rate is substantially lower (<2%) [31].

Non-invasive testing is not routinely recommended in people classified as low-risk although the criteria used to define low-risk people in whom further investigation is not warranted have varied [18, 140, 141, 232, 233]. In people stratified as low-risk using CDPs recommended in this guideline (see section 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS) the likelihood of a cardiac event over the next two years is low, suggesting that further cardiac anatomic or functional investigations are unnecessary, at least in the short-term [34, 95, 143, 154, 163, 234].

Primary care physician follow-up is recommended to ensure resolution and appropriate treatment of the symptoms that prompted ED presentation and, if appropriate, assess their long-term risk of a cardiovascular event as per the *Australian guideline for assessing and managing cardiovascular disease risk* (cvdcheck.org.au).

Practice points

Non-invasive test selection – anatomical versus functional

- In people without known CAD, computed tomography coronary angiography (CTCA) may be considered as first line investigation in the absence of contraindications (see **Table 8**). A normal CTCA (ruling out both obstructive and non-obstructive plaque) has a high negative predictive value in excluding ACS and is associated with an extremely low risk of ACS for at least 4–5 years [235-240]. Identification of non-obstructive plaque can also guide preventative medical therapies, such as statin therapy.
- In people with known CAD, previous stents or extensive coronary calcification, interpretation of CTCA can be more challenging, and functional testing may be favoured. Functional testing can help determine whether symptoms are due to obstructive plaque, define ischaemic burden and thereby short-term prognosis. Functional testing can include stress imaging (e.g. stress echocardiography, stress cardiac magnetic resonance [CMR], stress/rest single-photon emission computed tomography [SPECT] and stress/rest positron emission tomography [PET]), or exercise ECG (see **Table 8**). Stress CMR and echocardiography, can provide additional useful diagnostic and prognostic information on left ventricular function, regional wall motion abnormalities, valvular function and exclude differential diagnoses of myopericarditis and Takotsubo syndrome.
- A person's cardiovascular risk factors, clinician expertise and health service facilities, particularly in regional and remote areas, may all impact selection of cardiac investigation [18, 241-243].
- In people classified as low-risk including First Nations people with symptoms of suspected ACS and those with sociodemographic factors that limit their access to timely and adequate follow-up, or ability to re-present to the ED should the symptoms recur or risk levels change, consider inpatient non-invasive testing [205].

Table 8: Clinical considerations for the use of non-invasive testing for people at intermediate risk. Adapted with permission from Elsevier [244].

Ischaemic test modality	Strengths	Limitations	Considerations for use
Exercise stress ECG	• Low cost • Wide availability • Assessment of exercise symptoms, capacity • No ionising radiation	• Decreased accuracy compared with anatomical and stress-imaging tests • Requires interpretable ECG and ability to exercise sufficiently • Higher false positive rate in females	• Rarely recommended as a stand-alone test due to known CAD, inability to exercise, or significant arrhythmias • Contraindication in severe symptomatic aortic stenosis or severe hypertension
Stress echocardiography	• Wide availability • High diagnostic specificity • Assessment of ventricular and valvular function	• Decreased sensitivity compared with anatomical and other stress-imaging tests • Dependent on good image quality	• Known good image quality and ability to exercise • Consider use of an ultrasound-enhancing agent to improve

	• No ionising radiation	• Requires dobutamine in people unable to exercise	endocardial visualisation • Known moderate or severe valvular disease
Stress/rest SPECT	• Wide availability • Relatively high diagnostic sensitivity • Assessment of ventricular function	• Increased artifacts resulting in non-diagnostic results and decreased diagnostic accuracy compared with stress/rest PET • Radiation exposure	• Known CAD or high coronary artery calcification burden on chest computed tomography (CT) imaging • Preferred over stress echocardiography in people who cannot exercise or who have significant exercise-induced bronchospasm
Stress/rest PET	• High diagnostic accuracy • Lower radiation exposure than SPECT • Measures myocardial blood flow and flow reserve • Assessment of ventricular function	• Limited availability • Relatively higher cost • Lack of exercise assessment	• Known CAD or high coronary artery calcification burden on chest CT imaging • Preferred over SPECT due to higher diagnostic accuracy and lower rate of nondiagnostic test results
Stress CMR	• High diagnostic accuracy • Accurate assessment of chamber sizes, ventricular and valvular function • Diagnosis of prior infarction, scar, fibrosis • Measurement of myocardial blood flow and flow reserve is possible but not widely available currently • No ionising radiation	• Limited availability • Relatively higher cost • Lack of exercise assessment • Long scan acquisition times • Claustrophobia • Often not immediately available to people with pacemakers or ICDs • Contraindicated in people with significant renal dysfunction	• Known CAD and/or cardiomyopathy • Elevated troponin not thought to be secondary to ACS • Known moderate or severe valvular disease • No significant renal dysfunction
CTCA	• High diagnostic accuracy • Does not require exercise • Identifies non-obstructive CAD	• Radiation exposure • Lack of exercise assessment • Contraindicated in people with significant renal dysfunction	• No known CAD • Absence of severe coronary calcification • Prior normal, mildly abnormal, or inconclusive stress test results

		• Blooming artifacts when significant coronary calcification present • Atrial fibrillation or other arrhythmias • May require beta blockers • Incidental non-cardiac findings	• No known iodinated contrast medium allergy or significant renal dysfunction • Low likelihood of high-quality stress testing or lack of timely access

Abbreviations: ACS, acute coronary syndromes; ECG, electrocardiogram; CAD, coronary artery disease; CMR, cardiac magnetic resonance imaging; CT, computed tomography; CTCA, CT coronary angiogram; ICD, implantable cardioverter-defibrillator; PET, positron emission tomography; SPECT, single photon emission computed tomography.

2.6.1 Cost-effectiveness

Reducing unnecessary testing has benefits for both people and health services. The overall reductions in hospital admission and length of stay impacted population estimates for cost savings from an Australian ED registry of 30,769 people presenting before and 23,699 people presenting after implementation of an accelerated diagnostic pathway that included cessation of testing of people at low risk resulted in an annual total cost reduction of $13.5 million [184]. Improved efficiency of assessment and discharge of people at low-risk results in overall cost reductions.

2.6.2 Considerations for regional, remote and First Nations people

Regional, remote and First Nations people are disproportionately affected by reduced access to services, longer wait times and greater travel distances to access diagnostic services. Definitive early identification of CAD through the use of CTCA may be of significant benefit in this group [245].

Implementation of an Australian telemedicine program supporting remote exercise stress testing with cardiology specialist support at a metropolitan location has been shown to reduce waiting times for tests to be conducted and enabled a significant proportion of people to be managed in local health facilities [246].

Assigning a warranty period following a negative CTCA should be done with some caution in First Nations people due to limited evidence for this population.

2.7 Role of rapid access chest pain clinics

Rapid access chest pain clinics (RACPCs) may assist with choice of further investigations including non-invasive testing or management in selected people discharged following an ACS [247]. Multiple UK studies have found this model to be safe, efficient and cost-effective compared to hospital admission [248].

Various RACPC models have been trialled throughout Australia and regardless of referral patterns or investigations used, seem to deliver similar results to the UK system [247]. These include more efficient access to testing and diagnosis; cost savings compared to hospital

admission; greater individual satisfaction; and most importantly, equal or improved safety compared to traditional hospital-based care [249-253].

Other benefits demonstrated in Australia include reduced invasive investigations; lower rates of ED re-presentation; and a clear mechanism for timely follow-up of people with their test results, which can be difficult when they are discharged from ED directly to the community.

The recommendation is to prioritise access to these clinics for selected intermediate-risk people with cTn levels <99th percentile where protocolised assessment guidelines are not available.

2.8 Re-presentation with symptoms

People who re-present to ED with possible symptoms of ACS within 30 days and who have not already undergone non-invasive testing for CAD and/or coronary ischaemia may warrant consideration of functional or anatomical testing, as well as a detailed re-appraisal for alternate diagnoses. If re-presentation has occurred after prior negative exercise ECG testing, use of investigations with greater sensitivity and specificity, or an anatomic test should be considered if suspicion of ACS remains high.

2.9 Discharge planning and advice

Following comprehensive and structured assessment of people with suspected ACS as detailed in this guideline, people who do not require admission for further assessment and/or management or transfer to another facility can be discharged. The outcome of ED assessment for suspected ACS will determine the guidance to be provided to the person (and support people) prior to discharge.

Many people will not have a definitive diagnosis for their symptoms, but acute, life-threatening diagnoses including AMI and UA will have been deemed to be of very low probability [254]. Specific discharge advice for non-ACS presentations is not within the scope of this guideline.

2.9.1 Discharge advice for primary care physicians

To support ongoing management of people post-discharge, concise information in the form of a discharge summary should be provided for a persons' primary care physician.

2.9.2 Discharge advice for people at low risk for ACS

Discharge advice for people identified as low risk for ACS should follow evidence-based recommendations for the condition(s) diagnosed and should include clear verbal and written communication that the person has been comprehensively assessed, AMI was excluded, and UA is deemed unlikely. It is important to highlight that CAD has not been excluded, and that follow-up with their primary care physician is recommended for assessment and management according to the *Australian guideline for assessing and managing cardiovascular disease risk* (cvdcheck.org.au). Information about a person's actions if there are recurrent symptoms is recommended. Clinicians should take the opportunity to briefly educate the person on cardiovascular health and cardiovascular causes of chest pain and

other key symptoms. This can be supported by recommendations for quality sources of online health information and telephone-based triage services.

The use of a shared decision instrument may assist in conveying risks of heart disease and of the lack of benefit, and possible harm of further testing in low-risk people (see Supplementary material) [140].

2.9.3 Discharge advice for people at intermediate risk for ACS

This should include reassurance to the person and their support people that they have been comprehensively assessed as safe to be discharged. Clear verbal and written information on management of existing and/or new symptoms including when to call an ambulance, re-present to the ED, or contact their usual point of primary care should be included.

There should be clear verbal and written information on referral for outpatient assessment and management which should include advice on the clinician/clinic that the person is referred to for outpatient follow-up and whether the person or support people will need to arrange an appointment or if this has already been arranged by the facility. If the person or support person is to arrange for this follow-up, then a clear timeline and contact details for doing so should be provided in the written discharge advice.

Education on cardiovascular risk and steps that the person can take to reduce cardiovascular risk should be provided. Guidance for quality sources of online cardiovascular health information is also recommended.

2.9.4 Discharge advice for people with a prior history of coronary artery disease who are assessed as having a chronic or stable coronary syndrome

A small number of people presenting to the ED who present with a prior diagnosis of CAD may be discharged with probable chronic or stable CAD presentation. The advice given needs to balance:

1) Reassurance that the person has been comprehensively assessed and is deemed safe to be discharged at this time, notwithstanding a probable cardiac cause for their symptoms and presentation.
2) A clear plan for further follow-up for assessment and management.
3) A clear plan for managing existing or new symptoms.
4) Education on their cardiovascular health and reiteration on when to call an ambulance or present to an ED.

Discharge planning and advice supports reduced ED presentations and better outcomes. Clinicians, including registered nurses and nurse practitioners, should be supported to undertake comprehensive pre-discharge assessment and discharge planning. This is important to help manage a person's anxiety; high levels of anxiety are associated with an increased likelihood of symptom recurrence and re-presentation to hospital [255, 256].

Shared decision-making is encouraged in cardiovascular disease treatment. It is recognised that more work is needed around how to best implement shared-decision making to achieve the goals of people at risk of or living with cardiovascular disease (see Supplementary material) [257-261].

2.10 Primary care and regional and remote presentations

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
Health services should establish centralised support systems to facilitate prompt assistance with ECG interpretation and access to troponin results when on-site access is not available	Strong	Low
Health services should establish centralised support systems to facilitate clinical advice to health practitioners working in regional and remote settings.	Strong	Low
Health services should establish centralised support systems to facilitate access to cardiac investigations if required for people in regional and remote settings.	Strong	Low
For people with suspected ACS initially evaluated in the primary care setting, prompt transfer to a facility where definitive risk assessment can occur (e.g. emergency department) is recommended.	Consensus	

Evidence supporting the recommendations

Optimising management for all people with symptoms of suspected ACS is the aim of health care irrespective of the person's location. Given the geographic challenges within Australia, coordinated centralised systems of care are needed. Telehealth models allow prompt access to specialist services for clinicians outside major tertiary centers.

An Australian state-based model has demonstrated that access to early cardiologist support for ECG interpretation, POC troponin results and cardiology-assisted decision-making is associated with mortality reduction [262]. In addition, a recent Australian cluster-randomised trial of in-hours, routine tertiary level support versus usual care for people in hospitals without emergency physicians showed fewer missed STEMIs [59].

Health services should evaluate the need and ability to facilitate and support specialised services to practitioners in non-tertiary centers including primary care and regional and remote settings.

2.10.1 Considerations for primary care presentation

Initial assessment

As outlined previously, assessment for ACS is a summative process incorporating the following:

- ECG findings

- clinical findings of history and examination
- results of cTn testing.

The ability for a health practitioner to reliably diagnose or, just as importantly, exclude ACS is determined by their ability to perform and interpret these aspects of the clinical assessment. If the clinician determines a person has suspected ACS, facilitation of transfer to the nearest medical facility where definitive assessment for ACS can occur is mandatory.

Initial ECG assessment

People presenting with suspected ACS require prompt access to an ECG (within 10 minutes) and interpretation by a suitably trained clinician (see section 2.2 Initial ECG assessment). However, if ACS is suspected, ECG acquisition should not delay transfer to a facility that can perform serial troponin testing and provide revascularisation, as delays are associated with harm in people with ACOMI [263-268].

If an ECG cannot be performed within 10 minutes, prompt transfer via ambulance to a location where an ECG can be performed is required. This may mean the first ECG is evaluated by trained paramedics.

If an ECG is non-ischaemic and the clinical presentation does not align with ACS as the likely diagnosis, it is reasonable to continue assessment in the primary care setting.

Troponin testing

If ACS remains a possible diagnosis after initial history and ECG assessment, and cTn testing is required in a metropolitan primary care setting, transfer to the nearest facility (usually an ED) where definitive risk assessment can occur should be facilitated [18, 30, 269].

For contemporary POC troponin assays available in Australia, there are no single test strategies to exclude AMI [106]. Hence, serial testing is required, which is often not feasible in the primary care setting (see section 2.3 Biomarkers and 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS). Hs-cTn POC assays are available, but not widely distributed, and currently limited evidence exists around single test strategies for exclusion of MI in primary care settings [96].

Risk assessment and clinical diagnostic pathways

In a systematic review of older risk assessment rules for use in the primary care setting without cTn results, no difference was seen between use of a risk score or primary care physician's clinical judgement in the ability to rule out ACS [270]. As such, risk scores such as the Marburg Heart Score, Grijseels and Bruins Slot rules are not recommended for exclusion of ACS in a primary care setting [271].

2.10.2 Considerations for regional and remote presentations

Presentations to regional and remote settings impose challenges from limited human and technical resources and potentially prolonged anticipated transfer times [272]. Roughly one quarter of people presenting with chest pain (1,138/4,398) require transfer to at least one other hospital and as a result, median times to angiography and overall length of stay are prolonged [273].

Geographical location also affects clinical outcomes, with greater mortality observed at 18 months post-event amongst people having presented with ACS to non-PCI capable centres, most of which are in regional or remote locations [274, 275].

While the initial assessment phase for people with suspected ACS remains unchanged, key points in deciding transfer of people with suspected ACS include knowledge of local service capabilities and support available in regional and remote settings, especially availability of relevant investigations including chest X-rays, cTn testing and/or other cardiac tests (e.g. CTCA, exercise stress testing, echocardiography) and the health practitioner's clinical judgement.

Initial ECG assessment

If the ECG can be performed but not interpreted, it is reasonable for it to be done and urgent remote evaluation should be sought (e.g. via telehealth) [59].

When the clinical and ECG assessment supports a diagnosis of ACOMI, consideration of urgent reperfusion therapy is required and urgent transfer of the person to the nearest facility where this management can occur is needed (see section 3 Hospital care and reperfusion).

Troponin testing

Many regional and remote settings are reliant on contemporary cTn assays, including POC platforms [127]. Clinicians must be aware of the type of troponin assay in use locally and ensure results are used in an evidence-based CDP (see section 2.3 Biomarkers and 2.4 Risk assessment and clinical diagnostic pathways for suspected ACS).

Where contemporary cTn assays are in use, UA should be considered in the presence of normal cTn results if clinical suspicion for ACS is high based on ECG interpretation and/or clinical history, and further serial cTn testing over 6–8 hours should occur [30]. Management may include initial treatment for presumed ACS, a period of continuous cardiac monitoring and/or transfer to a PCI-capable centre.

Risk scores and clinical assessment pathways

Evidence supporting the use of clinical risk scores without incorporating troponin values is limited. In the absence of hs-cTn assays, incorporation of cTn results with risk tools within a validated CDP is crucial (see section 2.4.1.2 Clinical score-based clinical decision pathways and Supplementary material). In a rural New Zealand setting, use of the EDACS accelerated diagnostic pathway with serial POC contemporary cTn measurements safely risk stratified people with suspected ACS (see Supplementary material) [276].

Non-invasive diagnostic testing

For people in whom further diagnostic testing is deemed necessary, arrangements for investigations and clinician follow-up are required (see section 2.6 Diagnostic testing for people with suspected ACS). Understanding of availability and access to investigations (functional or anatomical) available in the region should help inform the decision. However, should a particular investigation be determined to be superior for a specific person but is unavailable in a person's region, transfer to another facility should be considered.

Support in facilitating appropriate testing in areas with more resources (especially metropolitan settings) for people from regional and remote areas is an obligation of tertiary centers. Decisions around further diagnostic testing can be informed by consultation with cardiac teams or, when available, rapid access chest pain clinics. Remote access to rapid access chest pain clinics may help improve diagnostic pathways for people in regional and remote settings.

Shared decision-making

Given the complexity around clinical decision-making, including both the possibility of ongoing management in resource-poor settings or transfer away from community for ongoing care, shared decision-making is vital (see section 2.9 Discharge planning and advice and Supplementary material).

3 Hospital care and reperfusion

3.1 Acute management of STEMI – reperfusion for STEMI

3.1.1 Eligibility for reperfusion

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with STEMI within 12 hours of symptom onset, perform emergency reperfusion with either primary PCI or fibrinolytic therapy.	Strong	Moderate
In people with STEMI, symptom onset over 12 hours before presentation and evidence of continuing myocardial ischaemia (persistent ischaemic symptoms, haemodynamic compromise, and/or life-threatening arrhythmias), perform emergency reperfusion with primary PCI.	Strong	Moderate

Evidence supporting the recommendations

Timely reperfusion limits the extent of MI and reduces mortality by minimising total ischaemic time [277-280]. The impact on mortality is greatest in the first hour after symptom onset and diminishes with time, virtually dissipating by 12 hours [281].

Routine emergency reperfusion in people who present greater than 12 hours after symptom onset is not recommended. However, a primary PCI strategy may be considered in the presence of ongoing ischaemia, as observational studies support a survival benefit and two small, randomised trials have reported reductions in infarct size and four-year mortality [282-285].

For people with STE and multivessel disease (MVD), complete revascularisation should be the goal (see section 3.7 Treatment for ACS with multivessel disease without cardiogenic shock).

Practice points

- When deciding on eligibility for reperfusion, consider cognitive function, comorbidities and frailty that influence a person's overall survival. The superiority of PCI over fibrinolysis appears to extend to older people, although trials have been small, with few very elderly (>90 years), and have not included evaluation of frailty or co-morbidity.

3.1.2 Choice of reperfusion strategy

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with STEMI within 12 hours of symptom onset, primary PCI is the preferred reperfusion strategy over fibrinolysis, if it can be performed within 120 minutes of first medical contact.	Strong	High
In people with STEMI within 12 hours of symptom onset, perform fibrinolysis if primary PCI cannot be delivered within 120 minutes of first medical contact.	Strong	Moderate

Evidence supporting the recommendations

Currently, the options for reperfusion for STEMI are primary PCI or fibrinolytic therapy, with the choice dependent on several factors (see **Figure 12**). Fibrinolytic therapy, compared with control, reduced overall mortality at 35 days with a relative risk of 0.82 (95% CI 0.77–0.87) based on data from nine trials conducted during the 1980s and 1990s involving 58,600 people [286].

In a meta-analysis of 23 trials including 7,739 people with STEMI comparing primary PCI to fibrinolytic therapy, primary PCI was found to be better at reducing the combined end-point of short term death, non-fatal reinfarction and stroke (8% vs 14%, p<0.0001), benefits that persisted in the longer term [278].

An observational analysis from the National Registry of Myocardial Infarction in the United States demonstrated the relative benefit of primary PCI over fibrinolysis was lost after a delay to PCI of 121 minutes [287].

Importantly, the trials comparing primary PCI and fibrinolysis did not include routine early angiography in the fibrinolytic arms. There is evidence that an early fibrinolysis strategy followed by routine early angiography may be non-inferior to PCI (see section 3.2 Ongoing management of fibrinolytic-treated people). Also, very early administration of fibrinolysis in the pre-hospital setting may confer superior outcomes to PCI, especially among people presenting within two hours of symptom onset [288].

Efficacy of fibrinolysis is not demonstrated in people presenting 12 or more hours after onset of symptoms. Given the lower efficacy and persistent bleeding risks associated with fibrinolysis in such people, reperfusion with PCI is preferred in people with continued myocardial ischaemia (see above) [284, 285, 289-292].

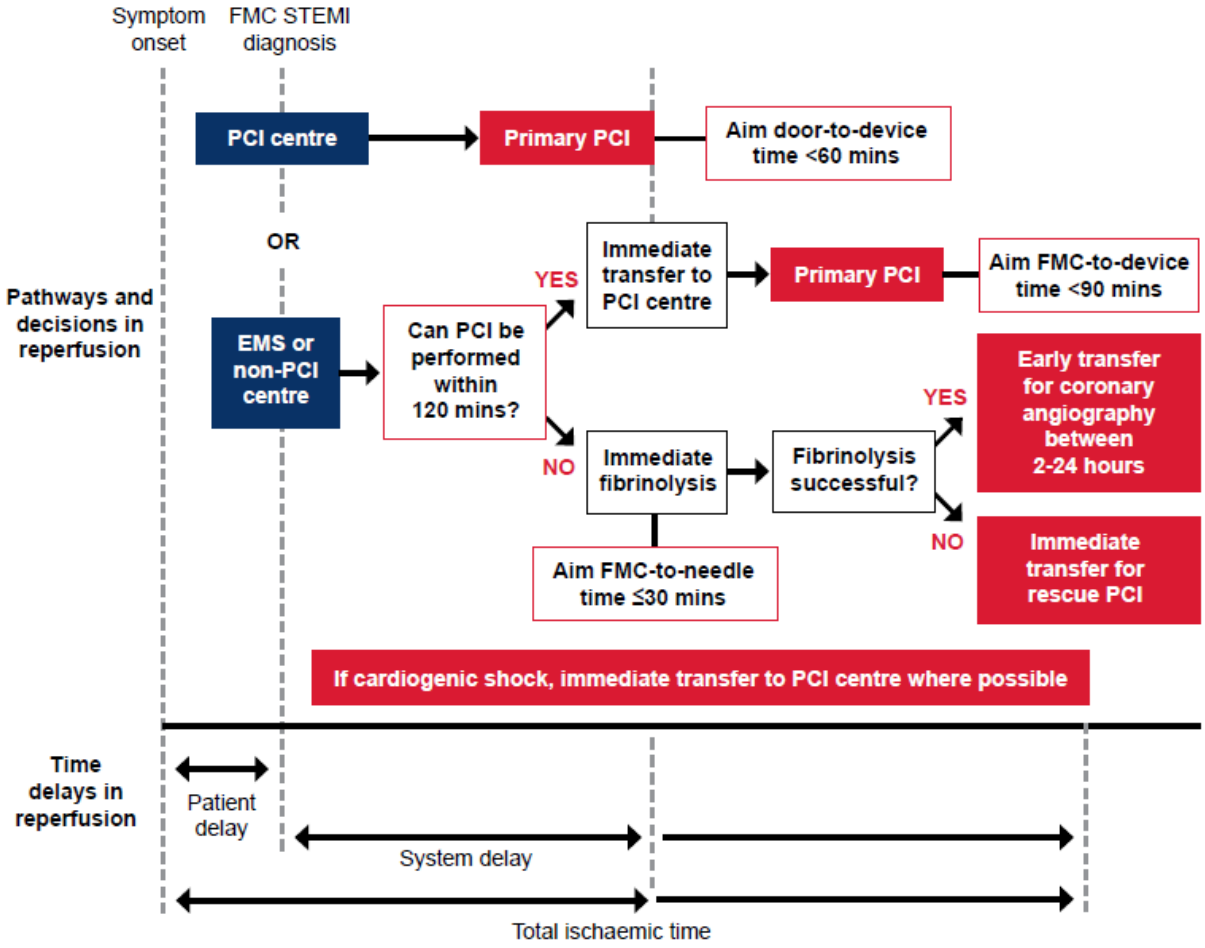


Figure 12: Decision-making and organisation of reperfusion strategies within first 12 hours of medical contact. Adapted from [30]. *Abbreviations: EMS, emergency medical service; FMC, first medical contact; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.*

Practice points

Effective service models are critical for achieving appropriate reperfusion times and should incorporate ambulance, primary health, emergency, cardiology and regional and remote health care services.

- Specific measures to reduce time to reperfusion may include: pre-hospital ECG and single-call catheter laboratory activation; pre-hospital fibrinolysis by suitably trained clinicians (e.g. paramedics, nurses, First Nations health practitioners); direct transfer to PCI-capable hospitals and direct transfer to the catheterisation laboratory on hospital arrival [19].

3.1.3 Administration of fibrinolytic therapy

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with STEMI for whom fibrinolysis is the preferred reperfusion strategy, it should be delivered within 30 minutes of first medical contact. Consider pre-hospital administration.	Strong	Moderate
In people aged ≥70 years, half the standard dose of tenecteplase is recommended as part of a pharmaco-invasive strategy.	Strong	Moderate

Evidence supporting the recommendations

Timing of fibrinolytic therapy

Fibrinolytic therapy should be considered when the delay to primary PCI is >120 minutes and there are no absolute contraindications to fibrinolysis. Fibrinolysis should be delivered as soon as possible after the establishment of the diagnosis, ideally within 30 minutes of first medical contact and pre-hospital if possible [19, 293-295].

People with an absolute contraindication should be transferred for PCI (see **Table 9**). People with a relative contraindication need to have the risks and benefits of treatment considered.

Dosing fibrinolytic therapy in older people

The STREAM study (n=1,892) compared pre-hospital fibrinolytic therapy and routine angiography 6–24 hours later against primary PCI in people unable to receive the latter within 60 minutes. Among people aged 75 years and over receiving full dose tenecteplase, higher rates of intracranial haemorrhage were seen, an effect reduced by halving the tenecteplase dose with no change in efficacy [296].

The subsequent STREAM-2 study (n=602) restricted enrolment to older people (>60 years, mean age 70 years) and compared half dose tenecteplase and routine angiography 6–24 hours afterwards against primary PCI [297]. There was no difference between groups in the primary efficacy endpoint and while major intracranial haemorrhage was higher in the pharmaco-invasive arm (6/400 vs 0/203), half of these events were associated with dosing protocol deviations.

Table 9: Contraindications for fibrinolysis. Adapted with permission from Wolters Kluwer Health, Inc. [268].

Absolute contraindications

- Any prior intracerebral haemorrhage
- Known structural cerebral vascular lesion (e.g. arteriovenous malformation)
- Known malignant intracranial neoplasm (primary or metastatic)
- Ischaemic stroke within 3 months
  - EXCEPT acute ischaemic stroke within 4.5 hours
- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed-head or facial trauma within 3 months
- Intracranial or intraspinal surgery within 2 months

Relative contraindications

- History of chronic, severe, poorly controlled hypertension
- Significant hypertension on presentation (SBP >180 mm Hg or DBP >110 mm Hg)
- History of prior ischaemic stroke >3 months
- Known intracranial pathology not covered in absolute contraindications
- Dementia
- Traumatic or prolonged (>10 min) CPR
- Major surgery (<3 weeks)
- Recent (within 2 to 4 weeks) internal bleeding
- Non-compressible vascular punctures
- Pregnancy
- Active peptic ulcer
- Oral anticoagulant therapy

Abbreviations: CPR, cardiopulmonary resuscitation; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Practice points

- An easily administrable fibrinolytic agent that can be given as a bolus dose, such as Tenecteplase, is advisable especially in the pre-hospital setting.

- Currently available fibrinolytics include tenecteplase (weight adjusted [30–50 mg] IV bolus); reteplase (10 units IV followed by 10 units IV, 30 minutes later); alteplase (weight adjusted accelerated bolus and infusion regimen).

3.1.4 Procedural recommendations in primary percutaneous coronary intervention

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
For people with STEMI at a PCI-capable centre, deliver primary PCI within 60 minutes of arrival. For people with STEMI transferred from a non-PCI centre, deliver primary PCI within 90 minutes of first hospital arrival.	Consensus	
Use radial access over femoral access when performing primary PCI, unless contraindicated.	Strong	High
In people undergoing primary PCI, do not perform routine thrombectomy.	Strong	Moderate
In people who are asymptomatic and stable for more than 48 hours following occlusion of an infarct-related artery, do not perform routine PCI to this artery.	Strong	Moderate

Evidence supporting the recommendations

Time targets for primary PCI

For people with a diagnosis of STEMI, it is important to limit system delay (time from first medical contact or arrival at a healthcare system to reperfusion), as this is a predictor of mortality [298]. Targets for delivery of primary PCI include within 60 minutes of a person arriving at a PCI-capable centre, or within 90 minutes if transferred from a non-PCI capable centre [293]. Pre-activation of the catheterisation laboratory when the diagnosis is made in the pre-hospital setting and bypassing the ED on arrival to the PCI-capable centre, reduces treatment delays [299, 300].

Radial versus femoral access

Multiple RCTs and an individual person-level data meta-analysis (n=21,600) have shown a benefit of radial over femoral access in people with STEMI with a reduction in total mortality (1.6% vs 2.1%, hazard ratio [HR] 0.77, 95% CI 0.63–0.95) and major bleeding (1.5% vs 2.7%, OR 0.55, 95% CI 0.45–0.67) [301-305]. A radial-first approach is therefore recommended for primary PCI, unless precluded by contraindications [137, 294, 301, 306].

Treatment of the infarct-related artery

Routine thrombus aspiration of the infarct-related artery (IRA) has been associated with a small but significantly increased risk of stroke without a survival benefit, compared with routine stenting [307-309]. Thrombus aspiration may be considered in people with high thrombus burden with careful attention to technical strategies to avoid embolisation.

When stenting is required, meta-analyses show that currently available drug-eluting stents have better efficacy and safety than bare metal stents, with lower restenosis and stent thrombosis [293, 310-315]. This includes people at high bleeding risk (HBR), people who require triple antithrombotic therapy or short duration dual antiplatelet therapy (DAPT).

Routine deferred stenting of the IRA is not recommended due to an increased risk of target vessel revascularisation without a survival benefit [316, 317]. Deferred stenting could be considered in select people, for example, residual large thrombus burden where immediate PCI is unlikely to be successful [318, 319].

Routine PCI of a completely occluded IRA in asymptomatic stable people who are >48 hours from symptom onset has been associated with an increased risk of recurrent MI, with no survival or major cardiovascular outcome benefit, compared to medical therapy [290, 320].

Practice points

- Where stenting is required, drug eluting stents are preferred over bare metal stents.
- Routine deferred stenting of the IRA is not recommended. However, in people with STEMI and risk factors for slow or no reflow, such as high thrombus burden, consider deferred stent implantation.
- In people with STEMI where primary PCI of the IRA is not feasible (e.g. severe left main CAD or an uncrossable coronary lesion), CABG may be an appropriate primary reperfusion strategy. CABG may be particularly appropriate if there is a large area of myocardium at risk and surgery is available in a timely manner (see section 3.8 Coronary artery bypass graft surgery in ACS) [321, 322].

3.2 Ongoing management of fibrinolytic-treated people

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
People successfully treated with fibrinolytic therapy should be transferred to a PCI-capable centre as soon as possible with a plan for angiography between 2 and 24 hours.	Strong	Moderate
Consider transferring people with unsuccessful reperfusion after fibrinolytic therapy to a PCI-capable centre as soon as possible for PCI.	Weak	Moderate

Evidence supporting the recommendations

A network meta-analysis of 31 RCTs compared outcomes of people randomised to fibrinolytic therapy (n=4,212), primary PCI (n=6,139), or fibrinolysis followed by routine early PCI (n=5,006), categorised as facilitated PCI when the median time interval between fibrinolysis to PCI was <2 hours (n=2,259) and as a pharmaco-invasive approach when this interval was ≥2 hours (n=2,747) [323]. Primary PCI was associated with the lowest risk of mortality (OR 0.73, 95% CI 0.61–0.89) when compared with fibrinolysis alone. However, among strategies in people receiving initial fibrinolysis, the pharmaco-invasive approach was associated with a trend towards lower mortality (OR 0.79, 95% CI 0.59–1.08) and showed significantly less revascularisation (OR 0.52, 95% CI 0.37–0.75) in comparison to fibrinolysis alone. Furthermore, in comparison to a facilitated approach, a Bayesian model showed the probability of adverse outcomes was lower with a pharmaco-invasive approach [323].

Another meta-analysis of seven studies comparing only early routine PCI after fibrinolysis versus standard therapy (i.e. fibrinolysis alone or rescue PCI where indicated) found no significant difference in 30-day mortality (OR 0.87, 95% CI 0.59–1.30, p=0.51) but did find a significant reduction in re-infarction (OR 0.55, 95% CI 0.36–0.82, p=0.003) and the composite of death and re-infarction (OR 0.65, 95% CI 0.49–0.88, p=0.004) at 30 days, without a significant increase in major bleeding (OR 0.93, 95% CI 0.67–1.34). These benefits were sustained out to 12 months [324].

Once a pharmaco-invasive approach is chosen, post-hoc analyses suggest the benefit is greatest the sooner PCI is achieved from symptom onset or administration of fibrinolysis (without transitioning to a facilitated approach). A meta-analysis of six randomised trials (n=1,238), demonstrated reduced 30-day recurrent ischaemia where angiography was achieved within two or four hours in comparison to beyond four hours (3.7% vs 3.7% vs 7.9%, p=0.02), but no reduction in 30-day mortality or re-infarction [325].

In a meta-analysis of eight RCTS (n=1,177), rescue PCI for failed fibrinolysis compared with conservative treatment was associated with a significant reduction in re-infarction (risk ratio [RR] 0.58, 95% CI 0.35–0.97), but no reduction in mortality [326]. Systems of care should be developed to provide advice and enable, when appropriate, immediate or early transfer for angiography for people being treated with fibrinolytics who are not in a PCI-capable hospital (see **Figure 12**) [327].

Practice points

- Following fibrinolytic therapy, perform ECGs regularly as per local protocols until the person is pain-free. Continue until at least 60–90 minutes post-fibrinolysis.
- In people being treated with fibrinolytic therapy, failed reperfusion is indicated by ongoing ischaemic chest pain, ≤50% ST recovery on an ECG performed 60–90 minutes after fibrinolysis, or ongoing haemodynamic instability.

First Nations people

- Ensure ongoing management education is culturally appropriate to the person, including the recommendation to transfer to a PCI-capable centre.

People living in regional and remote areas

- Establish specific, formal care pathways to facilitate transfer between non-PCI capable centres and PCI-capable centres (often metropolitan).
- In the event of failed fibrinolysis and haemodynamic instability without the possibility of timely transfer for PCI, consider an additional half-dose of fibrinolytics with caution. Clinical benefit has not been shown and the person's individual circumstances and bleeding risk should be carefully considered [328].

3.3 Acute management of NSTEACS

3.3.1 Risk stratification for people with confirmed NSTEACS

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with NSTEACS, consider using the GRACE risk score to determine short- and long-term cardiovascular prognosis.	Weak	High
In people with ACS undergoing coronary angiography, consider using bleeding risk scores to determine short-term bleeding risk.	Weak	Moderate

Evidence supporting the recommendations

Assessment of the short- and longer-term risk of death or recurrent ischaemic and bleeding events in people admitted with an ACS may provide guidance regarding requirement for and timing of invasive management as well as selection and duration of antithrombotic therapy. Clinical assessment, objective tools and hs-cTn-based CDPs may all contribute to risk stratification in people with NSTEACS.

Clinical risk assessment

A subset of people present with criteria that are associated with a high risk of short-term mortality. These include people with haemodynamic instability/cardiogenic shock, life-threatening arrhythmias, mechanical complications of MI, acute heart failure clearly related to NSTEACS, and/or ongoing symptoms in the presence of high-risk ECG criteria such as STD >1 mm in >6 leads additional to STE in aVR and/or V1, Wellens criteria on ECG or recurrent intermittent ST elevation (see section 2.2 Initial ECG assessment). An early invasive management strategy is recommended for these people (see section 3.3.3 Timing of invasive management for NSTEACS).

In the absence of these very high-risk criteria, clinical assessment has been shown to perform poorly in the determination of prognosis when compared to objective risk tools.

Objective risk prediction for ischaemic outcomes

In people admitted with NSTEACS, prognosis is well predicted by *Global Registry of Acute Coronary Events* (GRACE) risk score which performs better than *Thrombolysis in myocardial infarction* (TIMI) risk and subjective clinical assessment [273, 329-331]. Observational analyses have shown guideline-directed care is associated with greater survival gains in higher risk people, but that the intensity of delivered care is often inversely proportionate to the level of objectively determined individual risk [332-334].

While it is intuitive that objective risk scores may help identify people with ACS who would benefit from risk-concordant delivery of care, two prospective cluster randomised trials have failed to demonstrate an effect of routine GRACE risk score implementation on guideline-indicated treatments and clinical outcomes in people hospitalised with ACS [335, 336]. Baseline levels of hs-cTn have been shown to be strongly associated with death or MI at 30 days [337].

Risk prediction for bleeding outcomes

Major bleeding in hospital is associated with increased mortality and a range of scores have been developed to predict this outcome among people presenting with an ACS (see **Table 10**).

Table 10: Parameters of bleeding risk scores. Adapted with permission from Elsevier [338].

Parameter	CRUSADE	ACUITY	ACTION	GRACE	HAS-BLED
Sex	x	x	x		
Renal function	x	x	x	x	x
Haematocrit/Anaemia	x	x			
Heart rate	x		x	x	
Blood pressure	x		x	x	
Congestive heart failure	x				
Vascular disease	x				
Diabetes	x		x		
Age		x	x	x	x
Antithrombic medicine		x	x		x
Presentation		x			
White blood cell count		x			

Weight	x		
Cardiac arrest		x	
ECG ST changes		x	
Abnormal biomarkers		x	
Killip class		x	
Stroke			x
Hypertension			x
Liver disease			x
Bleeding history			x
Labile INR			x
Alcohol use			x

Abbreviations: ACTION, Acute coronary treatment and intervention outcomes network; ACUITY, Acute catheterization and urgent intervention triage strategy; CRUSADE, Can rapid risk stratification of unstable angina patients suppress adverse outcomes with early implementation of the ACC/AHA guidelines; ECG, electrocardiogram; GRACE, Global Registry of Acute Coronary Events; HAS-BLED, Hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly, drugs/alcohol concomitantly; INR, international normalised ratio.

A recent comparison of scoring systems reported that *Acute coronary treatment and intervention outcomes network* (ACTION) had the highest discrimination [C statistic 0.767 (0.737–0.797), three studies], followed by *Can rapid risk stratification of unstable angina patients Suppress Adverse outcomes with Early implementation of the ACC/AHA guidelines* (CRUSADE) [C statistic 0.714 (0.659–0.779), 12 studies] and *Acute catheterization and urgent intervention triage strategy* (ACUITY) [C statistic 0.711 (0.626–0.797), seven studies] [338]. The *Academic Research Consortium high bleeding risk* (ARC-HBR) score is an alternative pragmatic approach recommended by European guidelines [339].

These scores have been developed in populations with a high prevalence of coronary angiography and receipt of DAPT. While they may be considered when choosing procedural and antiplatelet strategies, the impact of their implementation on outcomes when implemented prospectively has not been evaluated.

Practice points

GRACE risk scores were developed before the use of hs-cTn. The majority of people identified as high-risk by the GRACE risk score are also determined to be high-risk using hs-cTn testing alone.

- Many people are at risk of both increased bleeding and ischaemic events. Observational data suggest that bleeding, more than ischaemic risk, should inform decision-making, primarily focussed on the duration of DAPT (see section 3.4

Antiplatelet therapy in the acute phase and 3.5 Anticoagulant therapy in the acute phase) [340].

Women

- The commonly used GRACE 2.0 score underestimates mortality in women with NSTEACS. The latest GRACE 3.0 score performs better in women and reduces sex inequalities in risk stratification [341].

Older adults

The GRACE risk score is heavily age-weighted and does not take account of characteristics highly prevalent in older adults such as frailty, multimorbidity, polypharmacy and cognitive dysfunction leading to higher scores in older adults [342]. The relationship between frailty and risk of adverse outcomes has been demonstrated in multiple studies using different frailty assessment tools [343-346]. The baseline risk of bleeding is also increased compared with younger people [347].

- A conservative management approach may be appropriate in older adults despite their high risk on objective risk scoring.

3.3.2 Routine versus selective invasive management for NSTEACS

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with NSTEACS at high or very high-risk of adverse cardiovascular events, perform routine invasive coronary angiography, with coronary revascularisation (PCI or CABG) where appropriate.	Strong	High
In people with NSTEACS not at high or very high risk of adverse cardiovascular events, testing for inducible ischaemia (e.g. stress testing) may guide the need for invasive coronary angiography.	Weak	Moderate

Evidence supporting the recommendations

People with confirmed NSTEACS at high risk of adverse cardiovascular events or death include those with:

- confirmed diagnosis of NSTEMI according to the 4th UDMI
- high risk according to hs-cTn algorithms (see section 2.4.1.1 High sensitivity troponin-based clinical decision pathways)

- dynamic ST-segment or T wave changes
- transient ST elevation
- GRACE risk score >140.

People with confirmed NSTEACS at very high risk of adverse cardiovascular events or death include those with:

- haemodynamic instability or cardiogenic shock
- life-threatening arrhythmias
- mechanical complications of MI
- ongoing symptoms in the presence of ECG criteria such as STD >1 mm in >6 leads additional to STE in aVR and/or V1, or Wellens criteria on ECG (see section 2.2 Initial ECG assessment)
- recurrent intermittent STE.

A routine invasive approach (coronary angiography) with subsequent revascularisation (PCI or CABG as indicated) in people with NSTEACS has been studied in systematic reviews, meta-analyses and RCTs, in the context of evolving adjunctive pharmacotherapies and interventional practices [348-350]. Overall, a routine invasive approach in people with NSTEACS has net benefits in reducing the composite endpoints of death, recurrent MI and re-hospitalisation for ischaemia, though the majority of this benefit is in non-fatal events and only seen in people at high risk [351, 352].

A 2016 meta-analysis of 12 RCTs (n=9,650) of people with NSTEACS, found that routine invasive angiography reduced the composite endpoint of MI and death (OR 0.86, 95% CI 0.77–0.96) at mean 39-month follow-up, compared to a selective invasive approach [352]. Consistent with past meta-analyses, this reduction was driven by lower recurrent MIs (RR 0.78, 95% CI 0.68–0.88) with non-significant total mortality (RR 0.88, 95% CI 0.77–1.01) [135].

The benefit of a routine invasive approach is greater in people with high-risk features with absolute risk reductions in MI and cardiovascular death of 2%, 4% and 11% in people at low, intermediate- and high-risk respectively, as determined by GRACE risk score [350]. In addition, RCTs investigating routine versus invasive strategies pre-dated the use of high-sensitivity troponin.

In admitted non high-risk people with NSTEACS, invasive management may be guided by non-invasive anatomic or functional testing, which may reduce the need for invasive angiography and is predictive of excellent short- and mid-term prognosis (see section 2.6 Diagnostic testing for people with suspected ACS) [353-356].

Practice points

- Goals of therapy, people's preferences, impact of other major co-morbidities and geriatric syndromes affecting life expectancy should be factored into the decision for a routine invasive approach.
- In people with NSTEACS not at high or very-high risk of adverse cardiovascular events and without known CAD, anatomical imaging with CTCA instead of functional testing may be appropriate to exclude CAD, particularly in the context of unclear NSTEACS diagnosis (see section 2.6 Diagnostic testing for people with suspected ACS) [357, 358].

3.3.3 Timing of invasive management for NSTEACS

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with NSTEACS with very high-risk criteria, an immediate invasive strategy within 2 hours of diagnosis is recommended.	Consensus	
In people with NSTEACS and high-risk criteria, consider an early invasive strategy within 24 hours of diagnosis.	Weak	High

Evidence supporting the recommendations

Multiple RCTs (the largest being TIMACS and VERDICT) and meta-analyses have investigated the timing of invasive coronary angiography in people with NSTEACS [359, 360]. An early invasive strategy was usually defined as within 24 hours (e.g. median of 14 hours after randomisation in TIMACS), while a delayed invasive strategy was usually defined as within 2–3 days (median 50 hours and 62 hours in the TIMACS and VERDICT trials, respectively). Overall, these studies found that an early invasive strategy did not confer a benefit in mortality, MI and stroke, compared with a delayed invasive strategy, when performed in all people with NSTEACS without consideration of individual risk [361]. Therefore, the timing for invasive management of NSTEACS must take a person's risk into account.

Unstable or very high-risk people with NSTEACS have largely been excluded from RCTs investigating an early versus delayed invasive approach. In these people an immediate (i.e. within two hours from hospital admission) invasive strategy is recommended due to their presumed poor prognosis in the absence of invasive management, based on expert opinion, rather than strong randomised data (see **Figure 13**).

In high-risk people with NSTEACS, the TIMACS trial found a reduction in death, MI and stroke at 6 months associated with early versus delayed (median time 50 hours) intervention (14% vs 21%, p=0.005) in the subgroup of people with a GRACE risk score >140, with no increase in major bleeding [359]. An individual meta-analysis on timing of invasive strategy (eight RCTs, n=5,324 people) found lower mortality with an early invasive strategy in people with elevated cardiac biomarkers at baseline (HR 0.76, 95% CI 0.581–0.996), diabetes (HR 0.67, 95% CI 0.45–0.99), a GRACE risk score >140 (HR 0.70, 95% CI 0.52–0.95), and aged 75 years and older (HR 0.65, 95% CI 0.46–0.93) although tests for interaction were inconclusive [362]. However, the GRACE scores calculated in these trials used CK-MB and earlier troponin assays, with no contemporary data to guide early angiography in people with elevated GRACE scores on the basis of high-sensitivity troponin assays.

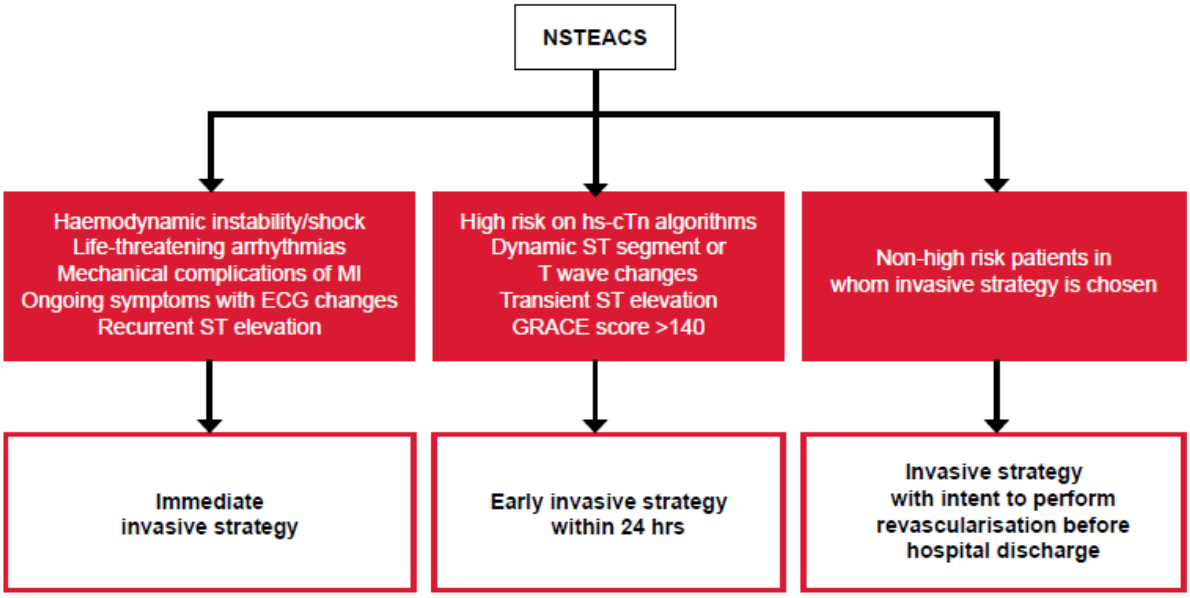


Figure 13: Timing of invasive management for NSTEACS. *Abbreviations: ECG, electrocardiogram; GRACE, Global Registry of Acute Coronary Events; hs-cTn, high-sensitivity cardiac troponin; MI, myocardial infarction; NSTEACS, non-ST-segment elevation acute coronary syndromes.*

3.3.4 Procedural considerations in NSTEACS

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with NSTEACS who have undergone an invasive approach, radial access is preferred to femoral access, unless contraindicated.	Strong	High
In people with NSTEACS who have undergone an invasive approach, consider intravascular imaging to guide PCI.	Weak	High

Evidence supporting the recommendations

Radial access

Multiple RCTs and meta-analyses have shown a reduction in mortality (1.6% vs 2.1%, HR 0.77, 95% CI 0.63–0.95) and major bleeding (1.5% vs 2.7%, OR 0.55, 95% CI 0.45–0.67) with radial instead of femoral access in people with NSTEACS [301-305]. Therefore, unless precluded due to a lack of operator experience or other related contraindications, a radial first approach is recommended over femoral access.

Intravascular-imaging-guided PCI

An intravascular imaging (IVI)-guided approach to PCI over standard angiography-guided PCI has been tested in multiple RCTs and meta-analyses, with a range of different complex person- and lesion-specific characteristics. A 2024 meta-analysis (22 RCTs, n=15,964) found that IVI-guided PCI (optical coherence tomography (OCT) and intravascular ultrasound (IVUS)), compared to angiography-guided PCI, reduced target lesion failure (RR 0.71, 95% CI 0.63–0.80, p<0001), driven by reductions in risks of cardiac death (RR 0.55, 95% CI 0.41–0.75, p=0.001), target vessel-MI (RR 0.82, 95% CI 0.68–0.98; p=0.030) and target lesion revascularisation (RR 0.72, 95% CI 0.60–0.86, p=0.0002) [363]. IVI-guided PCI also reduced the risks of all MI (RR 0.83, 95% CI 0.71–0.99; p=0.033) and all-cause death (RR 0.75, 95% CI 0.60–0.93; p=0.0091). Outcomes for OCT-guided procedures were similar to IVUS-guided procedures.

From a 2023 meta-analysis of 32 RCTs, 19 were categorised as ACS trials and subgroup analysis found the benefit of IVI-guided over angiography-guided PCI was of similar or greater magnitude in peoples with ACS [364]. Of note, RCTs included in both meta-analyses had different inclusion criteria, and largely included more complex lesions (e.g. bifurcations, presence of calcification and/or long segment of disease), and people at higher risk (e.g. people with diabetes). Therefore, the recommendation for intracoronary imaging over angiography alone cannot be applied to every PCI procedure.

Practice points

Women

A benefit of routine over selective invasive approach has been seen in women with NSTEACS. In contrast, observational studies have shown that women with NSTEACS are less likely to receive an invasive strategy, or radial access compared to men [352, 365]. Women with STEMI also have documented delays to reperfusion, lower rates of invasive angiography, lower rates of radial access and poorer outcomes, compared to men [10-12, 365].

- Clinician awareness and recognition of sex differences in presenting symptoms, ECG diagnostic criteria and underlying MI aetiologies (e.g. an increased proportion of SCAD and MINOCA in women) may improve outcomes.
- A radial-first approach is recommended for women and men.
- In pregnant women with STEMI not found to be caused by SCAD, it is reasonable to perform primary PCI as the preferred revascularisation strategy with appropriate shielding to protect the foetus against radiation [306].

Older adults

To date, of the five randomised trials specific to invasive management in older people (mostly ≥75 years), four have found no benefit in the primary endpoints, and the fifth showed reduced MI and urgent repeat revascularisation with a routine invasive versus a selective invasive strategy [366-371]. More recently, the FIRE study recruited older participants with MI and MVD (median age 80 years) and found a benefit with physiology-guided complete revascularisation. Of note, this trial did not report frailty [372, 373].

Meta-analyses of mixed designs have shown a likely reduction in MI and recurrent revascularisation with an invasive strategy versus a conservative (medical management) approach. In addition, there is a survival benefit in observational studies and a strong trend

towards survival benefit in randomised trials, at the cost of a higher risk of bleeding relative to a conservative strategy in older people with NSTEACS [373-375].

A small multicentre RCT of people over 70 years (mean age 86, n=167) with NSTEACS and objective signs of frailty, did not find a benefit from an initial invasive approach [376].

- Consider an invasive strategy over an initial conservative approach in older adults in the absence of frailty, multimorbidity and cognitive dysfunction.

First Nations people

- Information regarding transfers or invasive management should be provided with support from First Nations health practitioners or liaison officers and, where required, in the person's preferred language.
- Once transferred, First Nations people from regional areas are less likely to receive angiography than non-Indigenous counterparts [377]. Clinicians should be mindful of potential barriers to equitable care including inadequate cultural competency, perceptions of medicine compliance, delayed transfers to PCI-capable hospitals, and inadequate family and community engagement by clinicians [56].

3.4 Antiplatelet therapy in the acute phase

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with STEMI treated with fibrinolytic therapy, give dual antiplatelet therapy with aspirin and clopidogrel.	Strong	Moderate
In people with STEMI undergoing primary PCI and people with NSTEACS undergoing a routine invasive strategy, give dual antiplatelet therapy with aspirin and a potent P2Y12 inhibitor (ticagrelor or prasugrel).	Strong	High
In people with STEMI undergoing primary PCI and people with NSTEACS undergoing a routine invasive strategy for whom ticagrelor or prasugrel are contraindicated, and those receiving oral anticoagulation, give clopidogrel.	Strong	High
In people with NSTEACS for whom a selective invasive strategy is planned, give ticagrelor or clopidogrel.	Strong	High
In people with NSTEACS, consider routine genotypic or platelet function guidance of P2Y12 therapy.	Weak	Moderate
In people with NSTEACS, consider de-escalation from potent P2Y12 inhibitor to clopidogrel, but not during the first 30 days following an ACS event.	Weak	Moderate
In people with ACS with concomitant non-valvular atrial fibrillation and CHADS2VA score >1, give aspirin and clopidogrel, together with a non–vitamin K oral anticoagulant.	Strong	High
In people with STEMI undergoing primary PCI or those with NSTEACS undergoing an invasive strategy, routine glycoprotein IIa/IIIb inhibitor is not recommended.	Consensus	

Evidence supporting the recommendations

Aspirin

The benefit of aspirin on outcomes following STEMI independently and synergistically with fibrinolytic therapy was originally shown in the ISIS 2 study (n=17,187) [378]. A meta-analysis incorporating broader populations of people with MI (15 RCTs conducted before 1997; n=19,302) found that, compared with placebo, aspirin reduces the risk of serious vascular events (vascular death, MI and stroke; OR 0.70, 95% CI 0.64–0.77) [211]. The risk of haemorrhagic stroke is increased, while that of ischaemic stroke decreased, giving an overall reduction in all-stroke risk (OR 0.62, 95% CI 0.33–0.91).

An RCT (n=25,086 with ACS) comparing high-dose aspirin (300–325 mg daily) with low-dose aspirin (75–100 mg daily) showed no significant difference in cardiovascular death, MI, stroke or major bleeding between groups at 30 days [379].

Platelet P2Y12 inhibitor treatment with fibrinolytic therapy

In a large study enrolling 45,852 people with STEMI, clopidogrel added to aspirin reduced death, reinfarction or stroke by 9% (95% CI 3–14) when compared to aspirin alone [380]. In a trial of 3,491 people with STEMI randomised to clopidogrel or placebo at the time of fibrinolysis, coronary patency improved and ischaemic endpoints were reduced among people receiving clopidogrel [381]. The loading dose has not been studied in older people and is therefore not recommended in people over 75 years.

One small prospective open-label randomised trial (n=335) comparing ticagrelor and clopidogrel at the time of fibrinolysis found no difference in ischaemic MACE events but more minor bleeds with ticagrelor [382].

There was no difference in ischaemic or bleeding events in an RCT of 3,799 people randomised to ticagrelor or clopidogrel beyond 24 hours from fibrinolysis [383].

Platelet P2Y12 inhibitor therapy in people with STEMI undergoing primary PCI

The preferred P2Y12 inhibitors are ticagrelor or prasugrel as they have more rapid onset of action, greater potency and are superior to clopidogrel in clinical outcomes [384, 385]. Prasugrel is contraindicated if the person is <60 kg, ≥75 years and/or has had a previous stroke/transient ischaemic attack. Clopidogrel should be given as the preferred P2Y12 inhibitor in people with previous haemorrhagic stroke, on oral anticoagulants (OACs) or with moderate-to-severe liver disease.

The timing of P2Y12 inhibitor administration in people with STEMI undergoing primary PCI has been studied in a recent meta-analysis (three RCTs, 14 observational studies, n=70,465) [386]. Pretreatment (P2Y12 inhibitor administration before angiography) compared to no pretreatment (P2Y12 administration during or immediately after PCI) did not result in reductions in all-cause mortality or major bleeding. Subgroup analysis found that P2Y12 inhibitor pretreatment in the pre-hospital setting was associated with a reduction in MI, compared to no pretreatment (RR 0.73, 95% CI 0.56–0.91, p<0.01). Therefore, in people with a working diagnosis of STEMI undergoing primary PCI, pretreatment with a P2Y12 inhibitor may be considered. If pretreatment is not given, all people should receive a P2Y12 inhibitor loading dose at the time of PCI (see Supplementary table 5).

Platelet P2Y12 inhibitor treatment in NSTEACS

Clopidogrel with aspirin reduced the composite of cardiovascular death, MI or stroke when compared to aspirin alone in 12,562 people with NSTEMI (RR 0.80, 95% CI 0.72–0.90) [387]. As for people with STEMI, subsequent trials have shown that potent P2Y12 inhibition with ticagrelor or prasugrel is preferred over clopidogrel in people with NSTEACS undergoing a routine invasive strategy [384, 385]. Two RCTs have found that pretreatment with prasugrel at the time of diagnosis (before angiography) compared with treatment at the time of PCI following angiography did not reduce ischaemic events but did increase bleeding [388]. Similar results were reported from an analysis of the SWEDEHEART registry that

included ticagrelor and clopidogrel in NSTEACS [389]. Therefore, P2Y12 inhibitors can be withheld until the coronary anatomy is known if coronary angiography can be performed within the time recommendations (see section 2.6 Diagnostic testing for people with suspected ACS).

Ticagrelor, but not prasugrel, was found to be superior to clopidogrel in people with NSTEACS managed without PCI. Therefore, prasugrel is not recommended in people who do not undergo PCI [385, 390].

In the CURRENT-OASIS trial (n=25,086), a loading dose of 600 mg of clopidogrel followed by maintenance of 150 mg showed no difference in ischaemic endpoints and a significant increase in major bleeding (HR 1.24, 95% CI 1.05–1.46) when compared against 300 mg loading and 75 mg maintenance [379]. There was, however, a benefit in the sub-group of people who received PCI (HR 0.85, p=0.04) and double-dose clopidogrel may be considered in these people [379].

An RCT of 4,018 people with ACS (ISAR REACT 5) randomised to either ticagrelor or prasugrel, of which 83% received PCI, demonstrated an increase in death, recurrent MI and stroke, in people randomised to ticagrelor (HR 1.36, 95% CI 1.09–1.70) with no significant differences in bleeding [391].

Guiding therapy based on genetic or platelet function testing

Approximately 30% of people do not respond to clopidogrel which is thought to be the reason for the improved efficacy and increased bleeding of the more potent P2Y12 antagonists when compared to clopidogrel. Selection of therapy on the basis of response to clopidogrel based on either genotyping or platelet function testing has not shown a consistent benefit, likely because these strategies do not provide a comprehensive assessment of platelet responsiveness, together with differences in trial design and lack of power [392-394].

A network meta-analysis of 15 RCTs including 61,898 people with ACS demonstrated that therapy guided by genotyping of clopidogrel resistance compared to potent P2Y12 inhibitor therapy appeared to provide the best balance between less bleeding with clopidogrel and fewer ischaemic events with potent P2Y12 inhibitors ticagrelor and prasugrel [392, 395, 396]. However, while hypothesis-generating, genotyping is not readily available in Australia, and when platelet function guided escalation is used, people need to be on clopidogrel initially to demonstrate non-responsiveness which may place these people at increased risk in the ACS setting.

De-escalation of potent P2Y12 inhibitor therapy

Three major RCTs investigated the safety and efficacy of intentional de-escalation of potent P2Y12 inhibitor therapy following an ACS [397-399]. One single centre study compared the impacts of de-escalation from ticagrelor or prasugrel to clopidogrel, to no switching of therapies (n=646), with a primary composite outcome of cardiovascular death, urgent revascularisation, stroke and bleeding (Bleeding Academic Research Consortium Scale [BARC] ≥2) [399]. There was net benefit in the de-escalated group (HR 95% CI 0.48 (0.34–0.68)), driven by lower bleeding risk and no difference in ischaemic endpoints.

A multi-centre trial randomised people to ticagrelor and aspirin or intentional de-escalation to clopidogrel and aspirin after one month (n=2,697). The primary endpoint was a composite of cardiovascular death, MI, stroke, or bleeding (BARC ≥2) at 12 months. There was a

demonstrated 4.6% absolute risk benefit (HR 95% CI 0.55 (0.40–0.76)) in people undergoing de-escalation, also driven by reductions in bleeding risk [397].

Similar results were observed in another multi-centre trial using prasugrel 10 mg daily for the first month, followed by randomisation to either reduced dose prasugrel (5 mg daily) or standard dosing (n=2,338); (HR 95% CI 0.70 (0.52–0.92)) [398].

In all three studies, de-escalation did not occur until more than one month following discharge, and therefore earlier de-escalation cannot be recommended at this time [29]. Additionally, de-escalation occurred without giving a loading dose of clopidogrel upon switching.

Two of the studies were conducted in primarily east Asian populations, in whom ethnic differences in both response to clopidogrel and outcomes following PCI have been identified when compared to Caucasian populations [397, 398, 400].

Combining oral antiplatelet and oral anticoagulant therapy in ACS

In people with ACS requiring anticoagulation for non-valvular atrial fibrillation, studies with direct oral anticoagulants (DOACs) have shown that after an initial period (1–4 weeks) of triple therapy (aspirin in addition to a P2Y12 antagonist and an OAC), lower bleeding rates are seen with DOACs and clopidogrel compared to warfarin with continued DAPT (see section 4 Recovery and secondary prevention and **Figure 16**) [401-403].

Discontinuing P2Y12 inhibition prior to cardiac surgery for ACS

Based on pharmacokinetic data, the safe windows for cessation of P2Y12 inhibitors prior to non-emergency cardiac surgery are five days for clopidogrel, three days for ticagrelor and seven days for prasugrel [404].

Intravenous glycoprotein IIb/IIIa inhibitors

Routine use of intravenous glycoprotein IIb/IIIa inhibitors (GPI) in people undergoing primary PCI confers no benefit and significantly increases bleeding risk [405, 406]. A small RCT (n=162) of tirofiban versus heparin alone in select people with STEMI who had TIMI <3 following post-dilation showed significantly greater reperfusion (32% vs 10%, p=0.001), and reduction of in-hospital in-stent thrombosis and non-fatal MI [407]. Intracoronary GPI has not been found to be superior to IV administration [408].

Trials using GPI in people with NSTEACS showed a reduction in ischaemic events at a cost of increased bleeding when compared to heparin alone. However, all were conducted prior to the routine use of potent P2Y12 inhibitors and later generation stenting [409, 410]. Contemporary studies have shown that upstream use of GPI increases bleeding and transfusion requirements without offering clinical benefit [410]. In people not undergoing an invasive strategy, GPIs were not shown to reduce death or recurrent MI compared to placebo [411].

Practice points

- **Aspirin:** In the event of aspirin sensitivity, risk assessment and consideration of desensitisation should be made using a standardised protocol to achieve adequate antithrombotic therapy [412].
- **Selection of platelet P2Y12 inhibitor therapy:** Prasugrel has Therapeutic Goods Administration (TGA) approval but is not currently available in Australia. Exercise care regarding timing and dosing of P2Y12 inhibitors when switching between these agents to ensure maintenance of effectiveness and minimisation of bleeding risk. For guidance on switching strategies, see Supplementary figure 3.
- **Timing of platelet P2Y12 inhibitor administration in STEMI:** Administration of the P2Y12 inhibitor after the coronary anatomy is known is reasonable when the diagnosis of STEMI is uncertain or if there is a clinical suspicion of need for urgent cardiothoracic surgery (e.g. left main ischaemia pattern on ECG).
- **Timing of P2Y12 inhibitor initiation in NSTEACS:** Decisions regarding timing of initiation of P2Y12 inhibitor in relation to invasive angiography may be institution-dependent and need to be clearly defined and communicated effectively between emergency and inpatient services.
- **Combining P2Y12 inhibition with anticoagulation:** In people with ACS with an indication for vitamin K agonist (e.g. mechanical heart valve), use aspirin with clopidogrel rather than ticagrelor or prasugrel to reduce the risk of bleeding. Target international normalised ratios (INRs) should be at the lower therapeutic range (e.g. 2.5–3 for mechanical mitral valves).
- **Intravenous GPI administration:** Bailout GPI may be considered in people at high ischaemic risk such as high thrombus burden, no-flow or slow-flow.
- **Discontinuing P2Y12 inhibitor prior to CABG:** In people with NSTEACS for whom non-emergent CABG is planned, do not administer P2Y12 inhibitor within three days of surgery for ticagrelor, five days for clopidogrel or seven days for prasugrel.
- **Discontinuing intravenous GPI in thrombocytopenia:** Tirofiban is the only GPI marketed in Australia, while eptifibatide and abciximab can be obtained through the TGA's Special Access Scheme. Glycoprotein IIb/IIIa inhibition is not recommended in people with thrombocytopenia (platelet count <150,000/mL) and should be suspended immediately if platelet count falls below this level or drops by 50% or more from baseline.
- **Discontinuing intravenous GPI prior to CABG:** In people undergoing CABG, discontinuation of short-acting GPI (eptifibatide and tirofiban) for four hours and abciximab for 12 hours before surgery is recommended to reduce the risk of bleeding and transfusion [413-415].

3.5 Anticoagulant therapy in the acute phase

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
People treated with fibrinolytic therapy should receive anticoagulation (unfractionated heparin or enoxaparin).	Strong	Moderate
People undergoing primary PCI should receive anticoagulation (unfractionated heparin or bivalirudin).	Strong	Moderate
People with NSTEACS should receive anticoagulation (unfractionated heparin, enoxaparin, or fondaparinux).	Strong	Low

Evidence supporting the recommendations

Anticoagulant treatment with fibrinolytic therapy

The GUSTO trial (n=40,021) of people with STEMI receiving fibrinolysis with tissue plasminogen activator (tPA) and IV heparin, or streptokinase and either IV or subcutaneous heparin, or combination of both fibrinolytic agents and IV heparin showed the lowest mortality among those receiving tPA and IV heparin [416]. In the ASSENT-3 trial, of people with STEMI receiving fibrinolysis with tenecteplase, enoxaparin, 30 mg IV followed by 1 mg/kg twice daily (n=2,040) resulted in fewer ischaemic endpoints than IV heparin (n=2,038) (RR 0.74, 95% CI 0.63–0.87) [417].

Anticoagulant therapy with primary PCI

Unfractionated heparin (UFH) (in combination with DAPT) has been the standard of care for many decades in people undergoing primary PCI. RCTs comparing bivalirudin and heparin prior to 2022 reported no difference in ischaemic endpoints but less bleeding with bivalirudin [310, 418, 419]. However, these RCTs are difficult to interpret in today's clinical practice due to heparin historically being combined with routine (instead of bailout) GPI and low rates of radial access.

The unblinded BRIGHT-4 RCT (n=6,016) published in 2022 demonstrated a benefit of bivalirudin over UFH (0.7 units/kg) in primary PCI, with a reduction in 30-day total mortality (89 vs 118 people, p=0.04) and major bleeding (5 vs 24 people, p=0.001), with high (93%) radial access use and bailout (not routine) GPI [420]. Bivalirudin can therefore be considered instead of UFH in people undergoing primary PCI for STEMI, factoring in differences in cost and experience with administration. Bivalirudin should be used instead of UFH in people with heparin-induced thrombocytopenia.

Anticoagulant therapy in NSTEACS

Three small studies enrolling a total of 847 people showed that UFH was associated with a 62% reduction in trial-defined MACE (OR 0.38, 95% CI 0.15–0.97) with no increase in major bleeding at five days when compared to placebo [421-423]. Although these trials precede

the use of early invasive management and availability of troponin assays, they form the basis for recommending anticoagulation therapy in people with high- and intermediate-risk of ACS.

A meta-analysis of five RCTs comparing heparin with low molecular weight heparin (LMWH) on background therapy with aspirin (n=11,838) showed LMWH to be associated with a reduction in trial-defined MACE (OR 0.81, 95% CI 0.69–0.95) with no significant increase in bleeding [424]. These studies were conducted before the availability of troponin assays, with very low rates of coronary angiography. This meta-analysis did not include the largest trial comparing heparin to LMWH (n=9,978) which enrolled people on a background of DAPT with high rates of early coronary angiography [425]. There was no difference in the ischaemic endpoint of death and MI, but a significant increase in major bleeding in people receiving LMWH (HR 1.21, 95% CI 1.05–1.40) which was commonly femoral access-related.

Contemporary meta-analyses of UFH with bivalirudin have shown no significant benefit for ischaemic outcomes, especially with the emergence of preference for radial access and fewer bleeding events [426].

A pooled analysis of two trials (n=20,378) comparing fondaparinux with LMWH in people on DAPT showed a halving of major bleeding at nine days (HR 0.52, 95% CI 0.44–0.62) with no difference in trial-defined MACE. There were high rates of angiography in these trials, but the median time to angiography was long (2.5 days in the larger OASIS-5 trial) [424, 427].

Practice points

Anticoagulant treatment with fibrinolytic therapy

- Omit IV bolus of enoxaparin in people >75 years receiving fibrinolysis and enoxaparin.
- Enoxaparin is recommended over UFH unless there is severe kidney impairment (eGFR <30 ml/min) [428, 429].

Anticoagulant therapy with primary PCI

- In people requiring PCI with a history of heparin-induced thrombocytopenia, consider bivalirudin as an alternative to UFH. Outcomes with bivalirudin are optimised when followed by a high dose post-PCI infusion (1.75 mg/kg/hr) for 2–4 hours [430].

Anticoagulant therapy in NSTEACS

- In people treated with fondaparinux undergoing coronary angiography and/or PCI, standard dose heparin is recommended at the time of the procedure to reduce the risk of guiding-catheter thrombosis [387, 427].
- In people receiving LMWH in whom femoral access for coronary angiography is planned, it is common practice to omit the morning dose of enoxaparin to minimise access-related bleeding complications [431].

Anticoagulant use in people already receiving warfarin or DOACs

There are no randomised studies evaluating strategies for early anticoagulation in people with ACS who are already taking warfarin or DOACs. Guidance for these people is derived from expert opinion [432].

- In people with continued indications for oral anticoagulants (atrial fibrillation and CHADS2VA score (>1), mechanical heart valves, or recurrent venous thromboembolism), do not cease this treatment.
- In people with NSTEACS undergoing invasive management, wherever possible a brief washout period from the effects of OACs is desirable to reduce the risk of potential bleeding complications among those who may require femoral vascular access or resulting from additional anticoagulation during the procedure. This can be 24 hours for people on DOACs with normal renal function and 48 hours for those with impaired renal function. For people on warfarin, an INR of <2.0 is recommended when using the radial approach and <1.5 when using the femoral approach.

3.6 Acute management of ACS with cardiac arrest and/or cardiogenic shock

3.6.1 ACS with cardiac arrest

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with return of spontaneous circulation after resuscitated cardiac arrest and persistent ST elevation on ECG, perform emergency reperfusion.	Strong	Low
In haemodynamically stable people with resuscitated cardiac arrest and no ST elevation on ECG, do not perform routine emergency coronary angiography.	Strong	Moderate

Evidence supporting the recommendations

Cardiac arrest in the context of STEMI is a common cause of early death and usually occurs out-of-hospital [433]. In people with resuscitated cardiac arrest and an ECG consistent with STEMI, reperfusion with primary PCI improves survival [434-436].

In the absence of ST elevation on ECG, a meta-analysis of seven RCTs (n=1,544) found no survival or neurological benefit of early or immediate angiography over a delayed angiography strategy in people with resuscitated cardiac arrest [437]. It is important to note that people with cardiogenic shock were excluded from these trials, hence emergency angiography in the presence of haemodynamic instability may be considered.

Practice points

- In people with STEMI and resuscitated cardiac arrest, primary PCI is the preferred reperfusion strategy. Fibrinolysis may be considered if primary PCI is unavailable, however supportive evidence is lacking with potential for harm in cardiac arrest that is refractory, prolonged and/or traumatic [19, 293, 438].
- In people with STEMI and resuscitated cardiac arrest, the decision for primary PCI should factor in treatment futility. For instance, advanced age, presence of severe metabolic acidosis and/or no return of spontaneous circulation for an extended period of time, is associated with a low likelihood of meaningful long-term survival [439].

3.6.2 ACS with cardiogenic shock

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with ACS and cardiogenic shock, perform PCI of the IRA only.	Strong	Moderate
In people with ACS and cardiogenic shock, routine insertion of an intra-aortic balloon pump is not recommended.	Strong	High
In people with ACS and cardiogenic shock, routine venoarterial extracorporeal membrane oxygenation is not recommended.	Strong	Moderate
In select people with STEMI and cardiogenic shock, consider left ventricular assist devices.	Weak	Moderate

Evidence supporting the recommendations

Treatment of MVD in ACS with cardiogenic shock

In people with NSTEACS, MVD and cardiogenic shock, RCTs have studied the benefit of culprit-only PCI versus routine PCI of culprit and non-culprit lesions at the time of initial angiography. The CULPRIT-SHOCK trial included approximately 40% of enrolled people with a NSTEMI (n=706). At 30 days, the composite primary endpoint of death or renal replacement therapy occurred in 45.9% of the culprit-only PCI group versus 55.4% of the multivessel PCI group (RR 0.83, 95% CI 0.71–0.96) [440]. The difference was driven by significantly lower mortality in the culprit-only PCI group.

In people with STEMI complicated by cardiogenic shock, a single RCT and observational studies have found that routine PCI of non-IRAs at the time of primary PCI was associated with increased risk of death and renal failure [440-442]. Therefore, in the presence of cardiogenic shock, PCI of non-IRAs should not be performed at the time of the index procedure, but staged PCI should be considered for complete revascularisation.

Haemodynamic support devices in MI and cardiogenic shock

In people with MI and cardiogenic shock, routine insertion of an intra-aortic balloon pump (IABP) has been associated with an increased risk of bleeding with no impact on survival or infarct size [443-445].

In the ECLS-SHOCK trial (n=417 people with AMI and cardiogenic shock, planned for urgent revascularisation), early venoarterial extracorporeal membrane oxygenation (VA-ECMO) did not reduce 30-day mortality compared to usual care (RR 0.98, 95% CI 0.80–1.19, p=0.81) [446]. Early VA-ECMO was associated with higher rates of peripheral vascular complications requiring interventions (RR 2.86, 95% CI 1.31–6.25), compared to usual care.

A meta-analysis (four RCTs, n=567) did not find a reduction of 30-day mortality with the early use of VA-ECMO (OR 0.93; 95% CI 0.66–1.29), with higher major bleeding (OR 2.44, 95% CI 1.55–3.84) and peripheral ischaemic vascular complications (OR 3.53, 95% CI 1.70–7.34), compared to standard care [447]. There were no prespecified subgroups where any benefit for VA-ECMO could be seen.

The DanGer Shock trial recruited people with STEMI and cardiogenic shock (n=360) and found that percutaneous left ventricular assist devices (LVADs) (the microaxial-flow-pump, or Impella) reduced all-cause death compared to standard care (45.8% vs 58.5%, HR 0.74, 95% CI 0.55–0.99, p=0.04) [448]. The survival benefit came at a cost of increased bleeding and vascular complications (24% vs 6.2%, HR 4.74, 95% CI 2.36–9.55). In addition to haemodynamic evidence of shock, people enrolled had left ventricular impairment (<45%, median left ventricular ejection fraction [LVEF] 25%) and elevated arterial lactate (>2.5 mmol/l, median 4.6 mmol/L). People with right ventricular impairment and those with resuscitated out-of-hospital cardiac arrest who were comatose (Glascow coma scale ≤8) were excluded.

Practice points

- Consider IABP in select cases, for example, where there are mechanical complications (ventricular septal rupture, mitral regurgitation or free ventricular wall rupture) and/or as bridging to heart transplant or LVAD.
- Consider mechanical support including VA-ECMO on a case-by-case basis, as rescue or bridging therapy, or for treatment of intractable ventricular tachyarrhythmias, in consultation with a multidisciplinary team.
- Consider LVADs in people with STEMI and cardiogenic shock on a case-by-case basis, given the selected population enrolled and the complication rate in the DanGer Shock trial.
- In people with ACOMI and cardiogenic shock, where PCI is unavailable, consider lysis with a plan for subsequent angiography (see recommendations in section 3.2 Ongoing management of fibrinolytic-treated people) [449].

3.7 Treatment for ACS with multivessel disease without cardiogenic shock

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In haemodynamically stable people with STEMI and MVD, perform PCI of suitable non-IRA(s).	Strong	High
Consider performing PCI of the non-IRA at the time of primary PCI or within 19 days of the index procedure.	Weak	Moderate
In people with STEMI and MVD, routine invasive physiology assessment (e.g. FFR) to evaluate non-IRA severity is not recommended.	Consensus	
In people with NSTEACS and non-complex MVD, consider routine PCI of non-IRA in the same setting.	Weak	Low
In people with NSTEACS and MVD, consider invasive physiology assessment (e.g. FFR) to evaluate non-IRA severity.	Weak	Low

Evidence supporting the recommendations

Treatment of MVD in STEMI

In people with STEMI, MVD and without cardiogenic shock, RCTs have shown a benefit of complete revascularisation over culprit-only PCI with a reduction in cardiac death, recurrent MI and repeat revascularisation [318, 450-463].

The MULTISTARS-AMI trial recruited people with STEMI and MVD to undergo immediate (at the time of index procedure, n=418) versus staged (19–45 days after index procedure, n=422) PCI of the non-IRA. Immediate revascularisation was superior to staged PCI with lower death, non-fatal MI, stroke, unplanned ischaemia-driven revascularisation and heart failure hospitalisation (RR 0.52, 95% CI 0.38–0.72, p<0.001) [464]. This trial suggests that complete revascularisation during the index procedure is both safe and superior to outpatient staged PCI. It is unknown if immediate non-IRA PCI is superior to inpatient staged PCI (or PCI performed within 19 days).

It should be noted that only a third of people in the above trials had triple-vessel disease and people with left main disease, chronic total occlusions or planned for surgical revascularisation, were largely excluded. Therefore, in people with complex MVD, CABG may be the appropriate complete revascularisation strategy.

Treatment of MVD in NSTEACS

While complete revascularisation in STEMI is beneficial, currently there has been no dedicated trial comparing complete revascularisation versus PCI of the IRA only in all-

comers with NSTEACS. NSTEACS presents unique clinical challenges for management of MVD, including difficulty identifying the culprit lesion and a heterogenous pathophysiology.

A meta-analysis of observational studies in people with NSTEACS (15 studies, n=171,279) found people who underwent multivessel revascularisation had higher short-term risk, but lower long-term MACE (OR 0.76, 95% CI 0.61–0.93), all-cause death (OR 0.83, 95% CI 0.71–0.97) and repeat revascularisation (OR 0.62, 95% CI 0.42–0.90) [465].

Invasive physiology to evaluate the non-IRA in STEMI or NSTEACS and MVD

Several RCTs have compared a physiology-guided approach (mostly using fractional flow reserve, FFR) to angiography-alone approach in people with STEMI and MVD. Meta-analyses have not shown an overall benefit to FFR-guided complete revascularisation in STEMI with MVD, and some have shown that angiography-guided complete revascularisation is associated with a lower risk of all-cause death and new MI compared to FFR-guided PCI [463, 466, 467]. The COMPLETE RCT demonstrated a clear benefit of complete revascularisation in people with STEMI and MVD, even without a physiology-guided approach in most cases [452]. Therefore, in people with STEMI and MVD, the decision to undertake PCI of the non-IRA can be based on angiographic severity alone.

In people with NSTEACS and MVD, physiology may be of more value. Several RCTs have specifically compared a physiology-guided approach to an angiography-guided approach in treatment of the non-IRA. The overall evidence supports physiology or FFR as being reliable for non-culprit lesion estimation in NSTEACS and that FFR-guided PCI results in more people being treated medically, compared to angiography-guided PCI [468, 469]. However, the results have been conflicting regarding outcomes. The FLOWER-MI trial (n=1,171) showed no difference in clinical outcomes of FFR-guided versus angiography-guided PCI of the non-IRA [470]. The FRAME-AMI trial showed a reduction in MACE with FFR-guided versus angiography guided non-IRA PCI, with the limitation that the trial was terminated early due to slow recruitment with only 43% (n=562) of the planned sample size enrolled [471].

In older people with MI and MVD, physiology assessment may be of benefit. The FIRE trial (n=1,445), of people ≥75 years with MI and MVD (median age 80 years, 65% NSTEMI, 35% STEMI) showed FFR or angiography derived quantitative flow ratio guided complete revascularisation versus infarct-artery only PCI resulted in a significant reduction in the composite endpoint of death, MI, stroke or revascularisation at one year (HR 0.73, 95% CI 0.57–0.93, p=0.01), driven by reductions in cardiovascular death and MI (HR 0.64, 95% CI 0.47–0.88), with no difference in safety outcome and similar efficacy in STEMI and NSTEMI [372].

Practice points

Treatment of non-IRAs

- In people with STEMI and MVD, with unknown renal function, inpatient PCI as a staged rather than immediate procedure, may be preferable if complex MVD is present or operator fatigue precludes same-setting multivessel PCI.
- In people with NSTEMI and MVD, timing for complete revascularisation should consider factors such as the presence of cardiogenic shock, lesion complexity and risk of contrast nephropathy.

- While a benefit of FFR-guided over angiography-guided complete revascularisation has not been conclusively shown, it is reasonable to use FFR in intermediate (50–69%) non-infarct related stenoses [467].
- In people with ACS and complex MVD, a multidisciplinary heart team approach to revascularisation strategy is recommended. Management of people with ACS and complex MVD should be guided by multidisciplinary heart team discussions incorporating person-based (e.g. age, frailty, infarct size, personal preference) and lesion-based (e.g. anatomical considerations such as location, severity and complexity) factors.

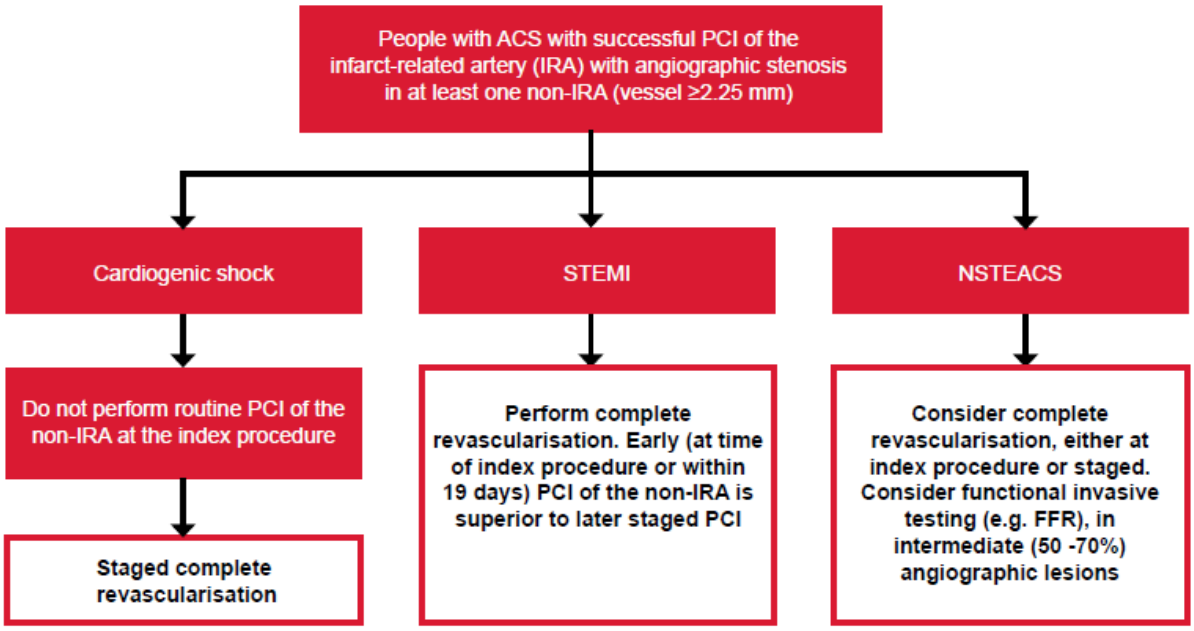


Figure 14: Management of multivessel disease in people with ACS. *Abbreviations: ACS, acute coronary syndromes; FFR, fractional flow reserve; IRA, infarct-related artery; NSTEACS, non-ST-segment elevation acute coronary syndromes; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.*

3.8 Coronary artery bypass graft surgery in ACS

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with STEMI, mechanical complications and mitral valve disease (e.g. ventricular septal rupture, mitral valve insufficiency because of papillary muscle infarction or rupture, or free wall rupture), perform CABG at the time of surgery.	Strong	Low

Evidence supporting the recommendations

Peri-operative mortality after mechanical complications of STEMI remains high [472]. Few percutaneous or medical treatments are available and urgent surgery most often remains the best option. A haemodynamically unstable person may require interim mechanical circulatory support. Performing CABG at the time of surgery for a mechanical complication of STEMI is based on small retrospective series with no randomised trial data [473].

Practice points

- In people with STEMI where PCI cannot be performed, consider emergency CABG if there is ongoing ischaemia and a large area of jeopardised myocardium.
- Overall, 4–10% of people with NSTEACS will require CABG [474]. Factors that should be considered when deciding between PCI and CABG are the same as for people presenting electively, including assessing comorbidities, fitness for major surgery, and coronary anatomy.
- In people with ACS and MVD where CABG has been chosen as the complete revascularisation strategy, performing CABG at day one to seven (compared to day 0 or >7 days) after diagnosis has lowest risk of mortality [475].
- In people with ongoing ischaemia or haemodynamic instability with an indication for CABG, do not delay urgent surgery due to antiplatelet exposure.

3.9 Treatment for spontaneous coronary artery dissection

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with ACS due to SCAD but who are otherwise stable, routine revascularisation is not recommended.	Consensus	
In people with SCAD and haemodynamic instability and/or ongoing ischaemia, consider selective revascularisation.	Weak	Very Low

Evidence supporting the recommendations

As there are no RCTs to guide therapy, recommendations in SCAD are based on observational studies or expert opinion [476]. Intervention is challenging and routine revascularisation is not recommended as it has been associated with complications such as iatrogenic dissection, wiring of the false lumen, propagation of the intramural haematoma, acute vessel closure and stent or graft failure [477-479]. However, in a subgroup of people with SCAD who have significant ongoing ischaemia and haemodynamic compromise, urgent revascularisation with PCI or CABG may be required [480-483].

3.10 Myocardial infarction with non-obstructive coronary arteries

In people with NSTEACS and MINOCA, it is important to exclude alternative diagnoses [484]. Consider CMR imaging in all people with MINOCA where the underlying cause is not obvious. Manage people with MINOCA where the underlying cause has been established according to the relevant disease-specific guidelines. If no underlying cause is found, treat according to secondary prevention guidelines for atherosclerotic disease.

3.11 Type 2 myocardial infarction

No trials have examined the benefits of a routine invasive strategy in people with type 2 MI [485]. Whether competing risks from non-cardiac conditions obscure the benefits of invasive management – and at what level of competing risk this occurs – remains uncertain. All available evidence demonstrates that people with type 2 MI experience higher all-cause mortality than people with type 1 MI, in part related to associated non-coronary competing risks [485].

In the absence of any trial evidence, angiography with a view to revascularisation may be considered if there is ongoing ischaemia or haemodynamic compromise despite adequate treatment of the underlying acute stressors which provoked the type 2 MI (see section 3.1.3 Administration of fibrinolytic therapy and **Table 9**).

3.12 Duration of cardiac monitoring

Cardiac monitoring plays a pivotal role as an adjunct therapy in the management of ACS. Continuous cardiac monitoring has become a firmly embedded standard of practice but in the absence of evidence from RCTs [486]. Clinical assessment for the risk of life-threatening arrhythmias should be individualised based on known associated risk factors: arrhythmias, ongoing symptoms, reduced left ventricular (LV) function (LVEF <40%), failed coronary reperfusion, haemodynamic instability, and complications of PCI (side branch occlusion, unsealed dissection, embolisation).

Practice points

- In people with NSTEACS or STEMI, initiate cardiac monitoring immediately, with ST-segment ischaemia monitoring where available. Continue uninterrupted for a minimum of 24 hours.
- People with ACS post-PCI should be monitored, with ST-segment ischaemia monitoring where available, continuously and uninterrupted for 24 hours.
- Reevaluate the need for continuous ECG monitoring every 24 hours.
- Educate staff regarding proper skin preparation, assessment of skin turgor and ECG electrode replacement every 24 hours, as this reduces inappropriate alarms [487, 488].
- Further guidance regarding cardiac monitoring can be found on the Agency for Clinical Innovation website (aci.health.nsw.gov.au/cardiac) [486].

4 Recovery and secondary prevention

Participation in exercise-based cardiac rehabilitation and person-centred, secondary prevention (collectively termed cardiovascular risk management) programs is integral to the overall management of people discharged following ACS to reduce future clinical events, improve quality of life and prognosis [489].

All people with ACS, including women, older adults, regional and remote residents, First Nations people, and people from culturally and linguistically diverse communities benefit from risk management programs to prevent recurrent events [55, 489].

Whilst the person is in hospital, arrange an early, post-discharge review by the treating team and a system-generated referral to a flexible, inclusive risk management program to enable effective transition of care, and an accelerated resumption of daily and work responsibilities in the community.

These risk management programs target adherence to medicines and behavioural change that include:

- Supporting people to manage their recovery post-ACS and adopt healthy behaviours (e.g. quitting smoking and/or drug and alcohol abuse, being physically active, eating healthily and maintaining good mental health), together with scheduled reviews by their cardiologist, primary care physician and/or specialist cardiac nurse.
- Intensive clinical risk factor education and modification (e.g. controlling hypertension, lowering blood lipids, and optimally managing diabetes).
- Filling prescriptions, reaffirming adherence to guideline-indicated medicines and facilitating review for actual and potential medicine-related harm, when suspected.
- Taking actions to protect against influenza and other pathogens, exposure to climate extremes, severe air pollution and cardiac toxicity where applicable.
- Empowering people and their carers towards greater self-care and management of their underlying cardiac status and comorbidities.

4.1 Post-ACS pharmacotherapy

4.1.1 Antiplatelet therapy

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people discharged following an ACS who are at high ischaemic and/or low bleeding risk, prescribe DAPT with aspirin and a P2Y12 inhibitor for 6 to 12 months.	Strong	High
In people discharged following an ACS who are at low ischaemic and/or high bleeding risk, cease DAPT at 1 to 3 months following an ACS and continue single antiplatelet therapy.	Strong	High
In people discharged following an ACS who have completed a course of DAPT (i.e. 1–12 months), prescribe long-term P2Y12 inhibitor over aspirin.	Strong	Moderate
In people discharged following an ACS who remain at high ischaemic and low bleeding risk, consider long-term DAPT (>12 months).	Weak	Moderate
In people discharged following an ACS with an indication for long-term OAC therapy, continue OAC and DAPT (preferentially aspirin and clopidogrel) for 1 week to 1 month, then cease aspirin.	Strong	High
In people discharged following an ACS with an indication for long-term OAC therapy, cease antiplatelet therapy at 6 to 12 months and continue anticoagulation alone.	Strong	Moderate

Evidence supporting the recommendations

The landmark P2Y12 inhibitor trials in people with ACS undergoing PCI reported primary outcomes following 9–12 months of DAPT which became the standard duration of therapy [384, 385]. However, these trials were designed in the era of early generation drug eluting stents when late stent thrombosis was more common than is seen in current practice.

More recent studies regard long duration therapy as being up to six months, particularly among people that have been stented, based on the observation that the incidence of ischaemic events plateaus by this time while cumulative bleeding risk continues to rise [490].

Studies on DAPT are dominated by people undergoing PCI, with those managed by CABG or medical treatment alone confined to subgroup analyses. Therefore, the above-mentioned recommendations may not apply to these non-PCI groups.

Short-term vs standard duration of DAPT in people with ACS

Improved ischaemic outcomes attributable to developments in stent technologies and secondary prevention strategies have prompted a number of studies exploring outcomes following shorter duration DAPT, driven principally by the desire to reduce bleeding risk. These trials have compared short-term (1–3 months) DAPT against standard term (6–12 months) DAPT after which aspirin or the P2Y12 inhibitor is ceased, leaving the other as single antiplatelet therapy (SAPT).

A meta-analysis of RCTs in people with ACS undergoing PCI (n=25,907) compared 1–3 months with 6–12 months of DAPT followed by SAPT. It found a significant reduction in bleeding events in the 1–3 month treatment group (HR 0.47, 95% CI 0.47–0.62) with no significant differences in MACE [404]. This study also reported a trend towards increased MACE with short-term DAPT in people with STEMI, left main or left anterior descending artery disease (i.e. high ischaemic risk) [404].

In short duration DAPT studies, the antiplatelet selected for continuation as SAPT has most commonly been a P2Y12 inhibitor (clopidogrel or ticagrelor). A network meta-analysis of people with ACS (24,838 patient-years of follow-up) and stable counterparts (85,221 patient-years) undergoing stenting showed continuation of P2Y12 rather than aspirin appears to provide the best trade off to reduce risk of both major bleeding and MI [491, 492].

People at high bleeding risk

A number of scores are available to predict HBR in people receiving DAPT following PCI. The PRECISE-DAPT score was developed to provide a standardised tool for predicting mid-term (1-year) bleeding events during DAPT in an all-comers PCI population and shows similar discriminative capacity for bleeding when compared with the older CRUSADE and ACUITY scores [493, 494]. The ARC-HBR is an alternative pragmatic approach recommended in European guidelines [137].

A meta-analysis in people at HBR (n=9,006) found that 1–3 months DAPT significantly reduced major or clinically relevant non-major bleeding (RR 0.76, 95% CI 0.61–0.94) with no difference in MACE (all-cause death, MI and stroke) [495]. There was no difference in outcomes when aspirin or P2Y12 was used for continuing SAPT.

Another meta-analysis in people at HBR (n=16,848, including people receiving OAC therapy), compared short-term DAPT (≤3 months) followed by aspirin or P2Y12 inhibitor SAPT against standard DAPT (6–12 months) after PCI [496]. Compared with standard DAPT, major bleeding was lower with short-term DAPT (OR 0.68, 95% CI 0.51–0.89) whereas incidence of MI, all-cause death, cardiovascular death, stroke, or stent thrombosis was not statistically different. Similar findings have been reported in people with HBR undergoing complex PCI [340].

Long-term SAPT

A network meta-analysis of people after PCI (n=73,126; consistent findings in ACS sensitivity analysis) found compared with DAPT (from 1–18 months duration), P2Y12 inhibitor and aspirin monotherapies reduced bleeding, whereas the risk for MI was similar with P2Y12 inhibitor and increased by aspirin monotherapy [497].

A meta-analysis of people with established vascular disease (n=61,623, 30% with ACS) found that P2Y12 inhibitor monotherapy reduced the risk of MACE (composite of stroke, MI, or death in the majority of studies) by 11% compared with aspirin monotherapy (RR 0.89,

95% CI 0.84–0.95) [498]. This finding was consistent irrespective of the P2Y12 inhibitor used (clopidogrel or ticagrelor, p=0.83). There was also no significant difference in the risk of major bleeding with P2Y12 inhibitor monotherapy compared with aspirin (RR 0.94, 95% CI 0.72–1.22).

These findings also align with those from a recent meta-analysis (seven RCTs) in 24,325 people with CAD, including 12,178 people receiving P2Y12 inhibitor monotherapy (clopidogrel 7,545 [62%]; ticagrelor 4,633 [38%]) and 12,147 people assigned to receive aspirin [499].

Prolonged (>12 months) duration of DAPT

A study of 21,162 people who had previous MI (1–3 years earlier), found that DAPT with ticagrelor and aspirin was associated with a reduction in the composite outcome of cardiovascular death, MI or stroke compared with aspirin alone (HR 0.85, 95% CI 0.75–0.96), which was balanced by an increase in major bleeding (HR 2.69, 95% CI 1.96–3.7) [500].

A meta-analysis (n=25,985, 42.4% ACS) comparing prolonged DAPT (>12 months) with standard DAPT (6–12 months) following PCI found that prolonged DAPT reduced the risk of MI and stent thrombosis, but increased the risk of bleeding, compared with standard DAPT, with no difference in the risk of all-cause death or cardiovascular death [501]. People with a prior MI, with ACS at presentation, without diabetes, or younger than 75 years may derive the most ischaemic benefit from extended DAPT.

In a pooled post-hoc analysis of eight RCTs, n=14,963 people treated with PCI, stratified by PCI complexity and bleeding risk, long-term DAPT reduced ischaemic events in non-HBR people in both complex (absolute risk difference: −3.86%; 95% CI −7.71–0.06) and noncomplex PCI (absolute risk difference: −1.14%; 95% CI −2.26– −0.02). There was no benefit of prolonged DAPT seen in people with HBR. Results in people with ACS were consistent with the whole cohort [502].

People with atrial fibrillation requiring long-term anticoagulation

A meta-analysis of the four DOAC-based RCTs comparing dual antithrombotic therapy with triple antithrombotic therapy in people with atrial fibrillation undergoing PCI (n=10,234, >50% ACS) found significantly less bleeding with dual therapy (clopidogrel + DOAC) (RR 0.66, 95% CI 0.56–0.78), with no difference in the composite of ischaemic events, but a significant increase in stent thrombosis (RR 1.59, 95% CI 1.01–2.5) [503]. This translates into a reduction in major bleeding events of 2.3% and an absolute increase in stent thrombosis of 0.4%. In each of these studies, aspirin was administered peri-procedurally and was ceased from one day to one week following PCI in the dual antithrombotic arms.

A subsequent network meta-analysis of five RCTs (n=11,542) comparing different double and triple antithrombotic regimens found that non-vitamin K OAC plus P2Y12 inhibitor without aspirin had the best safety profile, when compared to treatments that included aspirin (as a component of triple therapy) or vitamin K antagonists [504].

Additional secondary and pooled analyses of these studies have found that stent thrombosis was highest in the first 30 days after randomisation, with higher rates in the non-aspirin group [505]. This suggested the potential for increased thrombotic complications among people receiving dual therapy (i.e. no aspirin) within the first month [503, 506]. It may therefore be reasonable to continue aspirin for up to one month following PCI in people

who are not at HBR, although this recommendation is based on consensus opinion and has not been specifically addressed in any of the randomised trials [432].

A recent trial evaluating longer term antithrombotic therapy in people requiring anticoagulation found that ceasing SAPT at six months and continuing with a DOAC for more than one year following stenting had no effect on ischaemic or bleeding events in people with HBR [507]. Another trial of DOAC-containing regimens showed that concomitant treatment with aspirin compared with DOAC monotherapy for more than one year following stenting was associated with increased mortality with event rates of 4% and 6% per patient-year, respectively (HR 0.72, 95% CI 0.55–0.95) [508]. Antiplatelet therapy should be ceased and the DOAC continued at 12 months in people following an ACS with an indication for long-term OAC.

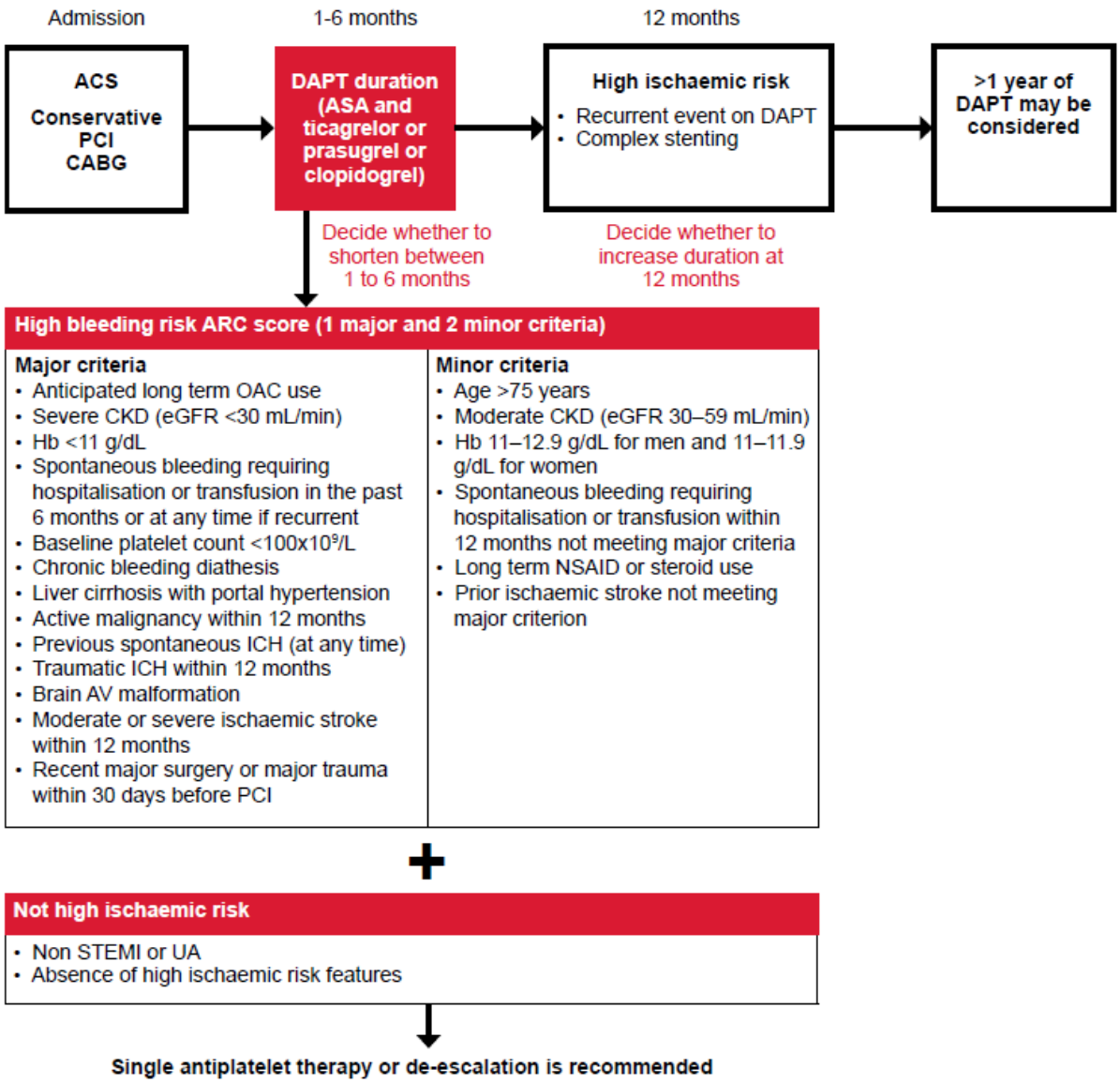


Figure 15: Considerations for dual antiplatelet therapy (DAPT) in people with ACS.
Abbreviations: ACS, acute coronary syndromes; ARC, Academic Research Consortium; ASA, acetylsalicylic acid; AV, atrioventricular; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; DAPT, dual antiplatelet therapy; eGFR, estimated glomerular filtration rate; Hb, haemoglobin; ICH, intracranial haemorrhage; NSAID, nonsteroidal anti-inflammatory drug; OAC, oral anticoagulant; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina.

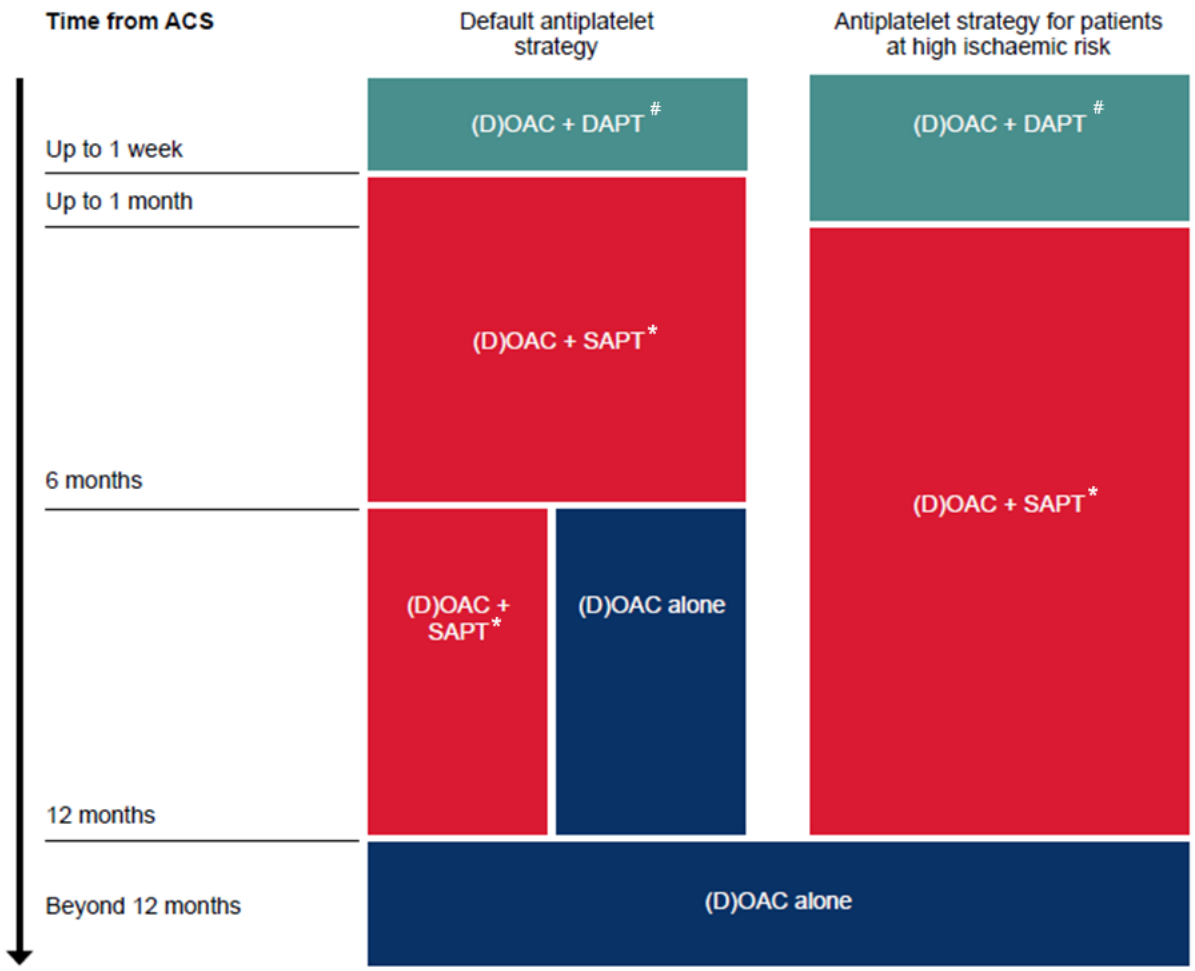


Figure 16: Recommended antiplatelet treatment strategies for patients with ACS requiring long-term (D)OAC for atrial fibrillation. *#DAPT: aspirin plus clopidogrel preferred. *SAPT: clopidogrel preferred. Note: People receiving triple therapy should be given a proton pump inhibitor. Abbreviations: ACS, acute coronary syndromes; DAPT, dual antiplatelet therapy; (D)OAC, direct oral anticoagulant; SAPT, single antiplatelet therapy.*

Practice points

Short-term vs standard duration of DAPT in people with ACS

- In older people (e.g. ≥70 years) with ACS, particularly if HBR, consider clopidogrel as the P2Y12 receptor inhibitor [29].

People at high bleeding risk

- A mobile phone-based application has been developed to assist with decision-making for people at HBR (see http://www.cerc-europe.org/arc-hbr-high-bleeding-risk-evaluator/). This is based on an algorithm that predicts risk of major ischaemic and bleeding events [509].
- In people receiving DAPT with high risk of gastrointestinal bleeding, a proton pump inhibitor is recommended.

People requiring long-term anticoagulation

- In people with ACS undergoing PCI with other conditions, that require long-term anticoagulation (e.g. mechanical heart valves), recommendations cannot currently be made due to lack of trial evidence in these groups.
- The recommendations in this section can be applied to people with ACS and MI undergoing medical management [403]. This is based on results from the AUGUSTUS trial, which showed consistent findings irrespective of management strategy [510].
- In people who have undergone PCI and are at HBR, de-escalating therapy to anticoagulation alone after six months may be reasonable. This recommendation is based on consensus opinion and is consistent with recommendations for people who do not require an anticoagulant [432].
- In people receiving triple therapy, a proton pump inhibitor is recommended.

4.1.2 Statin therapy

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with an ACS, initiate and continue indefinitely, the highest tolerated dose of HMG-CoA reductase inhibitors (statins), unless contraindicated or completely statin intolerant.	Strong	High
In people with initial or partial intolerance to statin, consider using a different statin, dose or dosing frequency to achieve person-specific therapeutic objectives, following an ACS.	Weak	Low
In people discharged following an ACS with suboptimal low density lipoprotein cholesterol (LDL-C) levels despite statin therapy or who are statin intolerant, consider adding ezetimibe.	Weak	Moderate
In people discharged following an ACS at high ischaemic risk with suboptimal LDL-C levels despite maximally tolerated statin therapy and ezetimibe, give PCSK9 inhibitors.	Strong	High

Evidence supporting the recommendations

In a meta-analysis of statin therapy versus controls in the subset of people with pre-existing vascular disease (n=64,443; 45% ACS) the composite endpoint of MI, stroke, coronary revascularisation or vascular death was reduced by 20% for every 1.0mmol/L reduction in low-density lipoprotein-cholesterol (LDL-C) [511]. Similar benefits occur in meta-analysis of high versus lower dose statin therapy [512]. These randomised trials of statin therapy before or after PCI in people with ACS (n=6,743) found high-dose versus no- or low-dose statins

reduced the combined outcomes of death, recurrent MI and stroke by 28% (OR 0.82, 95% CI 0.70–0.95) beyond 30 days. This aligned with the lower risk of MI and MACE at 30 days. The later benefit occurs within the first six months after ACS [511].

A meta-analysis of placebo-controlled RCTs (n=123,940, 16.4% ACS) found almost half (48%) reported at least one episode of muscle pain or weakness during a median of 4.3 years corresponding to a 3% relative increase in those taking statins compared with placebo (RR 1.03, 95% CI 1.01–1.06) [511]. Up to 70% of people reporting statin intolerance may tolerate reduced dose regimens or substitution of a hydrophilic statin [513].

The IMPROVE-IT randomised trial in people with ACS (n=18,144) found a modest reduction in study-specific MACE, in statin-ezetimibe group versus statin-monotherapy (HR 0.936, 95% CI 0.89–0.99) [514].

Monoclonal antibodies to PCSK9, known as PCSK9 inhibitors, are very effective at significantly lowering LDL-C in people already receiving intensive lipid-lowering therapy. In a randomised trial of 18,924 people with a recent ACS on maximally tolerated statins and LDL-C of at least 1.8 mmol/L, the PCSK9 inhibitor alirocumab reduced the composite cardiovascular endpoint over a median follow up of 2.8 years (HR 0.85 95% CI 0.78–0.93) compared with placebo. There was also a lower risk of all-cause mortality favouring active treatment over placebo [515].

Practice points

- Initiate high-potency statin therapy (e.g. atorvastatin or rosuvastatin) early during the ACS admission, irrespective of baseline LDL-C level [512].
- Re-evaluate total and LDL-C level approximately three months after initiating treatment and adjust statin therapy or add non-statin therapy according to whether levels are at target values.
- An initial target LDL-C level of <1.4 mmol/L is suggested within the context of an individualised care plan. There is additional benefit from progressively lowering cholesterol levels with no lower limit.
- In men <50 years and women <60 years who have had an ACS event, consider diagnostic genetic testing for predisposing factors such as familial hypercholesterolaemia. If genetic predisposition is confirmed, consider cascade testing, genetic counselling, and initiating statins in family members [516].

Women

Women are less likely to receive a statin post-ACS. In a large Australian cohort treated with PCI for MI (n=14,140), female sex was associated with a lower prescription rate of statin therapy at discharge from hospital (adjusted HR 0.58, 95% CI 0.41–0.84) [517].

- In women at risk of a major vascular event, commence statin therapy. There is no difference in event reduction between men and women of equivalent baseline risk of vascular disease following statin treatment [518].

Older adults

In people older than 75 years with evidence of occlusive vascular disease (such as prior MI), statin therapy produces comparable significant reductions in major vascular events to those seen in younger people [519].

4.1.3 Beta blocker therapy

Recommendations

Recommendation	Strength of recommendation	Certainty of Evidence
In people with ACS and left ventricular impairment, beta blockers are recommended.	Consensus	
In people with ACS and preserved left ventricular systolic function who have undergone coronary revascularisation and are receiving optimal medical therapy, consider withholding beta blockers.	Weak	Moderate

Evidence supporting the recommendations

In a meta-analysis of RCTs (n=102,003 people post-MI), beta blockers lowered all-cause mortality in the pre-reperfusion era (incidence rate ratio (IRR) 0.86, 95% CI 0.79–0.94), but not in the reperfusion era (IRR 0.98, 95% CI 0.92–1.05), ($P_{interaction}$=0.02) [520]. However, significant reductions in recurrent MI occurred in both the pre-reperfusion and reperfusion eras, respectively (IRR 0.78, 95% CI 0.78–0.98 and IRR 0.72, 95% CI 0.62–0.83). The reduced effect on mortality in the reperfusion era likely reflects a reduction in the frequency and severity of LV dysfunction, as the benefits of beta blockers in people with LV dysfunction are well established [521, 522].

Consistent with the hypothesis that beta blockers are of limited value in the absence of LV dysfunction, the recent REDUCE-AMI randomised registry-based trial enrolling 5,020 people with AMI and preserved ejection fraction, undergoing early angiography, showed that long-term use of beta blockers did not reduce the composite endpoint of all-cause death and MI at 3.5 years of follow-up [523].

Practice points

- In people with MI and risk factors for cardiogenic shock, exercise caution when initiating beta blockers as they may be at increased risk of early mortality [524].
- IV beta blockade in STEMI prior to PCI has not been shown to reduce death or MI at one year [525, 526].
- In people with confirmed LV dysfunction, consider using a beta blocker of proven benefit in heart failure with reduced ejection fraction (specifically bisoprolol, carvedilol, metoprolol (controlled or extended release), or nebivolol). See the *Guidelines for the prevention, detection, and management of heart failure in Australia* for further details including other recommended therapies [527].

- In people with preserved LV function, no benefit in continuing beta blockers beyond 12 months has been seen [528, 529]. A number of ongoing randomised trials are evaluating this prospectively [530-532].
- The cessation of beta blockers at the time of hospital discharge or at later times post-MI in people with preserved LVEF are also being addressed in ongoing randomised trials.
- In asymptomatic people discharged following an episode of UA (i.e. without MI) and with normal LVEF, there is paucity of evidence for protection against MACE from beta blocker therapy in the absence of other indications.

4.1.4 Renin-angiotensin antagonist therapies

Recommendations

Recommendation	Strength of recommendation	Certainty of Evidence
In people with ACS and heart failure symptoms, LVEF ≤40%, diabetes, hypertension and/or chronic kidney disease, initiate and continue angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers if ACE inhibitors not tolerated.	Strong	High
In people with ACS and LVEF ≤40% and heart failure with or without diabetes, initiate and continue mineralocorticoid receptor antagonists.	Strong	High
In people with ACS, use of an angiotensin receptor–neprilysin inhibitor is not recommended.	Strong	High

Evidence supporting the recommendations

A meta-analysis of randomised trials in AMI (n=98,496), indicated angiotensin converting enzyme (ACE) inhibitors results in a 7% decrease in mortality at 30 days, with the greatest benefit in people with heart failure or anterior MI [533].

The evidence for long-term benefit comes from a meta-analysis of randomised trials of people with stable vascular disease (n=29,805; >50% with prior MI) where long-term use of ACE inhibitors significantly reduced cardiovascular mortality, non-fatal MI and stroke in the context of long-term secondary prevention (OR 0.82, 95% CI 0.76–0.88) [534]. However, a more recent meta-analysis of ACE inhibition or angiotensin receptor blocker (ARB) treatment in people with coronary disease (n=61,961) has shown that this benefit is not seen in people receiving active antihypertensive therapy, or those with low anticipated event rates [535]. The recommendations, then, are for the long-term use of these medicines in people with anticipated high event rates, particularly those with conditions shown to benefit from ACE inhibition such as diabetes, hypertension or chronic kidney disease.

ARBs have been shown to have a comparable effect to ACE inhibitors in people post-MI with reduced LVEF [536].

In an RCT of people with recent MI and LV dysfunction and symptoms of either heart failure or a diagnosis of diabetes (n=6,632), the mineralocorticoid receptor antagonist, eplerenone,

in combination with standard therapy within 3–14 days of an AMI reduced mortality and cardiovascular hospitalisations (RR 0.87, 95% CI 0.79–0.95) [537].

A recent randomised trial (n=5,661, post-MI with LVEF ≤40% or transient pulmonary congestion) to either angiotensin receptor-neprilysin inhibitor or ACE inhibitor before hospital discharge, showed no difference in cardiovascular death or incident heart failure at 22 months [538]. Therefore, angiotensin receptor-neprilysin inhibitors are not recommended in this context.

Practice points

- In people with ACS and LVEF ≥40% or without clinical heart failure, consider use of ACE inhibitors or ARBs if ACE inhibitors not tolerated to improve survival [535].
- For people with ACS and concurrent hypertension, ACE inhibitors and ARBs are indicated as first-line agents for hypertension management. Current blood pressure management and targets are provided in the Heart Foundation's *Guideline for the diagnosis and management of hypertension in adults* [539].

4.1.5 Colchicine therapy

Recommendation

Recommendation	Strength of recommendation	Certainty of evidence
In people discharged following an ACS, consider initiating colchicine (0.5 mg daily) and continuing long-term unless contraindicated or colchicine intolerant.	Weak	High

Evidence supporting the recommendations

Residual inflammation in the coronary vasculature after ACS may contribute to subsequent reinfarction. Anti-inflammatory medicines such as colchicine have the potential to directly address such an inflammatory environment, thereby minimising the risk of recurrent MACE.

A recent systematic review and meta-analysis (n=7,207) in people with ACS with <1 month to 22.6 months follow-up, found that colchicine resulted in a lower risk of coronary revascularisation (RR 0.46, 95% CI 0.29–0.73) and stroke (RR 0.39, 95% CI 0.18–0.81) [540]. There was no significant difference in all-cause mortality (RR 1.25, 95% CI 0.70–2.24), cardiovascular mortality, or recurrent MI. Colchicine increased the risk of gastrointestinal adverse reactions (RR 1.89, 95% CI 1.25–2.84).

4.2 Vaccination against influenza and other respiratory pathogens

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people discharged following an ACS, annual vaccinations for influenza and other respiratory pathogens are recommended.	Consensus	

Evidence supporting the recommendations

In people with ACS, an international contemporary trial which randomised 2,571 people who had experienced STEMI or NSTEMI to influenza vaccine or placebo, found that influenza vaccine reduced the primary composite outcome of all-cause death, MI, or stent thrombosis (HR 0.72, 95% CI 0.52–0.99) at one year follow-up [541]. The findings are consistent with those from a recent meta-analysis of randomised trials and observational studies comprising almost 240,000 people with cardiovascular disease and a median follow-up of 19.5 months. Influenza vaccination was associated with reduced risk of all-cause and cardiovascular mortality but not MI when compared with the control group [542].

Practice points

- The influenza vaccine can be safely administered within 72 hours of hospitalisation for AMI, including for an invasive coronary procedure [541].
- The *Australian Immunisation Handbook* (AIH) recommends that people with CAD receive influenza and pneumococcal vaccinations as per recommended schedules, given they are at increased risk of influenza and pneumococcal disease, and severe outcomes from influenza. See the AIH for further vaccination details including eligibility under the National Immunisation Program [543].
- People with chronic cardiac conditions, including ischaemic heart disease, are at increased risk of severe COVID-19 and may benefit from additional doses of COVID-19 vaccine. See the AIH for further details regarding COVID-19 vaccination [543].

4.3 Person-centred non-pharmacological secondary prevention

Recommendations

Recommendation	Strength of recommendation	Certainty of evidence
In people with ACS with or without revascularisation and during hospitalisation, refer to exercise facility-based outpatient cardiac rehabilitation program.	Strong	Moderate
In people with ACS who smoke, advise to stop and refer to a behavioural intervention (such as cognitive behaviour therapy or cessation counselling program), combined with pharmacotherapy where appropriate (nicotine replacement therapies, varenicline and bupropion individually or in combination).	Strong	Moderate

Evidence supporting the recommendations

A contemporary systematic review of 85 trials randomising 23,430 predominately people post-MI and post-revascularisation to either exercise-based cardiac rehabilitation or usual care with a median follow-up of 12 months (range 6 months to 19 years) showed meaningful reductions in MI and all-cause hospital admissions (RR 0.82, 95% CI 0.70–0.96; 22 and 0.77, 95% CI 0.67–0.89, respectively) [489]. Although risk reductions in cardiovascular mortality were reported (RR 0.74, 95% CI 0.64–0.86), the certainty of evidence was downgraded due to imprecision. There was no significant effect on all-cause mortality (RR 0.96, 95% CI 0.89–1.04) and cardiovascular hospitalisation (RR 0.85, 95% CI 0.67–1.08). There is limited evidence on improving health-related quality of life and cardiac rehabilitation cost-effectiveness. The overall effects were independent of cardiac rehabilitation delivery models, exercise doses, duration of follow-up, or risk of bias. A flexible, cardiovascular risk management program is a reasonable alternative [544].

Smoking cessation is strongly associated with decreased risk of subsequent nonfatal and fatal MI [545, 546]. Smoking is prevalent among people hospitalised with ACS. An observational study in 9,375 people with ACS with a mean follow-up of 3.9 years found an 80% higher risk of death among those who continued to smoke compared with lifelong non-smokers and people who quit smoking [547].

Practice points

- In people with ACS where an exercise facility-based cardiac rehabilitation is not available, refer to a flexible, cardiovascular risk management program.
- Cardiac rehabilitation and secondary prevention programs should offer evidence-based aerobic and resistance training in accordance with the current Cardiac Society of Australia and New Zealand Position Statement [548].
- Exercise-induced cardiac events are negligible in comparison to the risk associated with being habitually sedentary [549].

- During ACS admission, initiate relevant disease and lifestyle education; the latter covering smoking cessation, regular exercise, healthy eating, filling prescriptions and adherence to medicine regimen.
- At discharge, provide people with ACS a verbal and written discharge summary detailing diagnosis, treatment, follow-up care and highlighting taking medicines as prescribed, healthy lifestyle choices, and re-present to ED should recurrent ischaemic symptoms arise.
- Embed system-generated referral to a risk management program based on a person's preference, values and the available resources [550-555].
- Adopt effective two-way communication with the primary care physician to support their ongoing care of people with ACS.
- Consider post-discharge comprehensive medicine review, particularly in those with significant medicine changes, polypharmacy and/or multimorbidity, those on high-risk medicines such as anticoagulants, and those at risk of medicine non-adherence [556].
- Consider use of digital health interventions in the delivery of cardiovascular risk management programs post-ACS such as reminders, text messaging, mobile health (mHealth) apps, telehealth consultations, wearable devices and electronic decision support tools [553, 557, 558].
- Where possible, provide access to trained cultural health workers for First Nations people or bilingual educators for people whose first language is not English.
- Harmonising care across clinical domains is important, particularly for older adults with geriatric syndromes including frailty, impaired cognitive function, and polypharmacy [55].
- A person's psychosocial needs should be considered, in particular depression, anxiety and social isolation using a validated tool. When issues are identified and the program lacks the relevant expertise, convey the finding to the person's primary care physician for review and management.

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Abbreviations and acronyms

ACE	angiotensin converting enzyme
ACO	acute coronary occlusion
ACOMI	acute coronary occlusion myocardial infarction
ACS	acute coronary syndromes
AIH	Australian Immunisation Handbook
AMI	acute myocardial infarction
ARB	angiotensin receptor blockers
ARC-HBR	Academic Research Consortium high bleeding risk
ASCVD	atherosclerotic cardiovascular disease
BARC	Bleeding Academic Research Consortium
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CDP	clinical decision pathway
CHD	coronary heart disease
CI	confidence interval
CK-MB	creatine kinase MB-isoenzyme
CMR	cardiac magnetic resonance
CTCA	computed tomography coronary angiography
cTn	cardiac troponin
cTnI	cardiac troponin I
cTnT	cardiac troponin T
CV	coefficient of variation
DAPT	dual antiplatelet therapy
DOAC	direct oral anticoagulants
ECG	electrocardiogram
ED	emergency department
EDACS	Emergency department assessment of chest pain score

eGFR	estimated glomerular filtration rate
FFR	fractional flow reserve
GPI	glycoprotein IIb/IIIa inhibitor
GRACE	Global Registry of Acute Coronary Events
GRADE	Grading of recommendations, assessment, development and evaluation
GTN	glyceryl trinitrate
HBR	high bleeding risk
HEART	History, electrocardiogram, age, risk factors, troponin
high-STEACS	high sensitivity troponin in the evaluation of patients with acute coronary syndrome
HR	hazard ratio
hs-cTn	high-sensitivity cardiac troponin
IABP	intra-aortic balloon pump
INR	international normalised ratio
IRA	infarct-related artery
IRR	incidence rate ratio
IV	intravenous
IVI	intravascular imaging
IVUS	intravascular ultrasound
kg	kilogram
LBBB	left bundle branch block
LDL-C	low density lipoprotein cholesterol
LMWH	low molecular weight heparin
LV	left ventricular
LVAD	left ventricular assist device
LVEF	left ventricular ejection fraction
LVH	left ventricular hypertrophy
MACE	major adverse cardiovascular events

mg	milligram
MI	myocardial infarction
MINOCA	myocardial infarction with non-obstructive coronary arteries
mm	millimetre
mmol/L	millimoles per litre
MVD	multivessel disease
ng/L	nanograms per litre
NSTEACS	non-ST-segment elevation acute coronary syndromes
NSTEMI	non-ST-segment elevation myocardial infarction
OAC	oral anticoagulant
OCT	optical coherence tomography
OR	odds ratio
p	probability
PCI	percutaneous coronary intervention
PET	positron emission tomography
POC	point-of-care
RACPC	rapid access chest pain clinic
RCT	randomised controlled trial
RR	risk ratio
SAPT	single antiplatelet therapy
SCAD	spontaneous coronary artery dissection
SPECT	single-photon emission computed tomography
SpO2	oxygen saturation
STD	ST-segment depression
STE	ST-segment elevation
STEACS	ST-segment elevation acute coronary syndromes
STEMI	ST-segment elevation myocardial infarction
TIMI	Thrombolysis in myocardial infarction

TWI	T-wave inversion
UA	unstable angina
UDMI	Universal definition of myocardial infarction
UFH	unfractionated heparin
UK	United Kingdom
URL	upper reference limit
VA-ECMO	venoarterial extracorporeal membrane oxygenation
µg	microgram
µg/L	microgram per litre

Terminology and definitions

Term	Definition
Chest pain – cardiac	Chest pain due to an underlying cardiac aetiology. Includes classic chest discomfort based on quality, location, radiation, and provoking and relieving factors that make it more likely to be of cardiac ischaemic origin.
Chest pain – non-cardiac	Chest pain symptoms likely due to a non-cardiac cause.
Chest pain – possible cardiac	Chest pain symptoms that suggest a cardiac origin.
Coronary microvascular dysfunction	Epicardial or microvascular endothelial or non-endothelial dysfunction that limits myocardial perfusion, most often detected as reduced coronary flow reserve.
Heart failure	Heart failure is a complex clinical syndrome resulting from any structural or functional impairment of ventricular filling or ejection of blood. The main manifestations of heart failure are dyspnoea and fatigue, which may limit exercise tolerance, and fluid retention. These may lead to pulmonary or splanchnic congestion and/or peripheral oedema. There is no single diagnostic test for heart failure; it is largely a clinical diagnosis based on a careful history and physical examination including 12-lead ECG, chest X-ray, transthoracic echocardiography and laboratory blood testing. When the diagnosis is unclear following initial clinical assessment and an echocardiogram cannot be arranged in a timely fashion, measurement of plasma natriuretic peptide levels is recommended.
Myocardial infarction (MI)	MI is the irreversible necrosis of heart muscle. A common cause for infarction is deprivation in myocardial oxygen supply due to interruption of blood flow in ≥1 coronary artery caused by plaque rupture, erosion, fissure, or coronary dissection. MI can also result from inflammatory, metabolic, or toxic insults to the myocardium. Early and accurate detection of MI is important for initiating and maintaining appropriate therapy. In clinical trials, lack of a uniform MI definition can result in low concurrence between the initial clinical and later adjudicated assessments of MI, which will affect accuracy of primary end points and trial outcomes. Thus, uniform definitions are needed to ensure accurate reporting of MI events across clinical trials and registries.
Myocardial infarction – Type 1	Type 1 MI is characterised by atherosclerotic plaque rupture, ulceration, fissure, or erosion with resulting intraluminal thrombus in one or more coronary arteries leading to decreased myocardial blood flow and/or distal embolisation and subsequent myocardial necrosis. The person may have underlying coronary artery disease (CAD), but non-obstructive coronary atherosclerosis or there may be no angiographic evidence of CAD.

Myocardial infarction – Type 2	Type 2 MI is myocardial necrosis associated with an imbalance between myocardial oxygen supply and demand, and may be associated with hypotension, hypertension, tachy/bradyarrhythmias, anaemia, hypoxaemia, coronary artery spasm, spontaneous coronary artery dissection (SCAD), coronary embolism, and coronary microvascular dysfunction.
Myocardial infarction – Type 3	Type 3 MI is MI resulting in death when biomarkers are not available.
Myocardial infarction – Type 4 and 5	Types 4 and 5 MI relate to percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) respectively
Myocardial infarction with non-obstructive coronary arteries (MINOCA)	The diagnosis of MINOCA is made in people with acute myocardial infarction (AMI) that fulfills all the following criteria: 1. AMI (modified from the Fourth universal definition of myocardial infarction criteria [16]): Detection of a rise or fall of cardiac troponin (cTn) with ≥1 value above the 99th percentile URL and corroborative clinical evidence of infarction evidenced by ≥1 of the following: • symptoms of myocardial ischaemia • new ischaemic electrocardiographic changes • development of pathological Q waves • imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischaemic cause • identification of a coronary thrombus by angiography or autopsy. 2. Non-obstructive coronary arteries on angiography, defined as the absence of obstructive disease on angiography (i.e. no coronary artery stenosis ≥ 50%) in any major epicardial vessel. (Note that additional review of the angiogram may be required to ensure the absence of obstructive disease). This includes people with normal coronary arteries (no angiographic stenosis), mild luminal irregularities (angiographic stenosis <30% stenoses), moderate coronary atherosclerotic lesions (stenoses >30% but <50%). 3. No specific alternate diagnosis for the clinical presentation. Alternate diagnoses include but are not limited to non-ischaemic causes such as sepsis, pulmonary embolism, and myocarditis [28].
Myocardial injury	Myocardial injury, acute versus chronic (or acute-on-chronic), is defined by the presence of an elevated cardiac troponin (cTn) concentration above the 99th percentile of the URL. Myocardial injury is a frequently encountered clinical syndrome and is associated with an adverse prognosis. Myocardial injury is considered acute if there is a rise or fall of cTn concentrations

	over time, and chronic when cTn concentrations are persistently elevated. Clinicians must distinguish between one of the MI subtypes and non-ischaemic myocardial injury. Acute myocardial injury is related to the diagnosis of MI, particularly when accompanied by supportive evidence in the form of symptoms, electrocardiographic abnormalities, or imaging evidence of new regional wall motion abnormalities or new loss of viable myocardium. Non-ischaemic myocardial injury may arise secondary to cardiac or non-cardiac conditions.
Myocarditis	Myocarditis is an inflammatory disease of the myocardium caused by viral infections or post-viral immune-mediated response. Clinical manifestations of myocarditis are varied and include chest pain that is often sharp and reflective of epicardial inflammation involving the pericardium. Myocardial dysfunction often causes fatigue and exercise intolerance. Predominance of heart failure distinguishes myocarditis from pericarditis; cTn is usually elevated.
Non-ST-segment elevation acute coronary syndromes (NSTEACS)	NSTEACS encompasses non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina. NSTEMIs are characterised by the presence of both criteria: 1. Detection of a rise or fall of cardiac biomarker values (preferably cTn) with ≥1 value above the 99th per-centile URL. Electrocardiographic changes or ischaemic symptoms may or may not be present. 2. Absence of electrocardiographic changes that are diagnostic of a ST-segment elevation myocardial infarction (STEMI) (see STEMI). Refer to definition of unstable angina below.
Occlusion myocardial infarction (OMI)	Occlusion MI is acute coronary occlusion or near occlusion with insufficient collateral circulation, such that downstream myocardium will undergo imminent infarction without timely reperfusion. Occlusion MI may not always result in ECG findings of STEMI.
Older adults	Adults older than 75 years old.
Pericarditis	Pericarditis is inflammation of the pericardial layers characterised by chest pain, electrocardiographic changes, and often pericardial effusion. It is often caused by an infectious or non-infectious process but can also be idiopathic. Pericarditis usually presents with sharp pleuritic chest pain, which may be improved by sitting up or leaning forward, although in many instances such findings are not present. A pericardial friction rub may be audible. Widespread ST elevation with PR depression is the electrocardiographic hallmark, although changes are non-specific and may be transient.

Pulmonary embolism (PE)	Intravascular migration of a venous thrombus to the pulmonary arterial circulation. It is diagnosed by a positive pulmonary angiogram, an unequivocally positive helical CT scan, a high-probability ventilation-perfusion scan, or autopsy.
Spontaneous coronary artery dissection (SCAD)	Epicardial coronary artery dissection that is not associated with atherosclerosis or trauma and is not iatrogenic. Predominant mechanism of myocardial injury occurring due to spontaneous coronary artery dissection is coronary artery obstruction caused by an intramural hematoma or intimal disruption rather than atherosclerotic plaque rupture or intraluminal thrombus.
ST-segment elevation myocardial infarction (STEMI)	STEMI are characterised by the presence of both criteria: 1. Electrocardiographic evidence of STEMI: new or presumed new ST-segment elevation at the J-point in 2 contiguous leads with the cut-off point: ≥ 1 mm in all leads other than leads V2–V3 where the following cut points apply: ≥2 mm in men ≥40 years; ≥2–5 mm in men <40 years; or ≥1–5 mm in women regardless of age. When the magnitudes of J-point elevation in leads V2 and V3 are registered from a prior ECG, new J-point elevation ≥1 mm (as compared with the earlier ECG) should be considered an ischaemic response. 2. Detection of a rise or fall of cardiac cTn with ≥1 value above the 99th percentile URL.
Unstable angina (UA)	Myocardial ischaemia at rest or on minimal exertion in the absence of acute cardiomyocyte injury/necrosis. UA is characterised by angina pectoris that occurs without stress or activity, or with decreasing stress or activity compared with stable angina and has been present for <2 weeks. ECG changes of ACOMI and elevated troponin values are not seen in UA.