Nova Scotia Health

CardioVascular HEALTH NOVA SCOTIA

Clinical Guidelines

IMPROVING CARDIOVASCULAR HEALTH OF NOVA SCOTIANS

Nova Scotia Guidelines for Acute Coronary Syndromes

May 2008

Updates 2014

Antiplatelet Section Updates:

NSTEACS:http://novascotia.ca/DHW/cvhns/docs/NSTEACS-Antiplatetlet-Guidelines-only-May-2014.pdf

STEMI:http://novascotia.ca/DHW/cvhns/docs/STEMI%20Antiplatelet%20Guidelines %20only-May%202014.pdf

Diabetes Section Updates:

NSTEACS:http://novascotia.ca/DHW/cvhns/docs/NSTEACS-Diabetes-Guidelines-October-2014.pdf

STEMI:http://novascotia.ca/DHW/cvhns/docs/STEMI-diabetes-update-October-2014.pdf

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Where guidelines are modified for local circumstances, significant departures from the provincial guidelines should be fully documented and the reasons for the differences explicitly detailed.

If you develop tools and forms within your district to support the guidelines, please share them with us and we will post them in the toolbox on our website. If you wish to obtain sample tools, forms and protocols, please visit the Cardiovascular Health Nova Scotia website at http://www.gov.ns.ca/health/cvhns/ or contact us by telephone (902) 473-7834, fax (902) 473-8616 or e-mail: cvhns@cdha.nshealth.ca.

Recommended Citation

Nova Scotia Guidelines for Acute Coronary Syndromes. Halifax, NS: Cardiovascular Health Nova Scotia; 2008.

ACKNOWLEDGEMENTS

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In addition to the Acute Coronary Syndrome Working Group, Consensus Panel Members and other contributors, Cardiovascular Health Nova Scotia acknowledges the many healthcare professionals from the nine District Health Authorities who gave so generously of their time to review the draft documents or portions of the documents.

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NOVA SCOTIA GUIDELINES
FOR
ACUTE CORONARY SYNDROMES

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PREVALENCE AND BURDEN OF ACS IN NOVA SCOTIA

Heart disease is the leading cause of death in Canada. Acute coronary syndrome (ACS) is an umbrella term used to cover any group of clinical symptoms compatible with acute myocardial ischemia. ACS includes an array of clinical conditions, from unstable angina to non-ST elevation myocardial infarction (NSTEMI) and ST elevation myocardial infarction (STEMI). These disorders are a major indication for emergency medical care and cause of hospitalization in Canada.

- Cardiovascular disease (CVD) is the leading cause of death in Canada with wide, unexplained regional variations in mortality.[1,2]
- CVD is a major disease burden with respect to mortality and health-related quality of life.[1]
- Of the approximately 4000 Nova Scotians treated for ACS each year; 38% are for unstable angina, 43% for non-ST elevation MI and 19% for ST elevation MI.[3]
- Although national and provincial rates of evidence-based pharmacotherapy for AMI have increased over time, there remains room for improvement.[4]
- Thirty-six percent of deaths in Nova Scotia are attributable to CVD.[5]
- Nova Scotia has one of the highest 30-day in-hospital mortality rates in the country.[5,6]
- Circulatory diseases – particularly heart disease, stroke and hypertension – cost the Nova Scotia healthcare system an estimated $252 million each year in direct medical (e.g., hospital, physician) and drug costs.[7]

Research continues to advance knowledge regarding effective strategies for the treatment and prevention of heart disease. Cardiovascular Health Nova Scotia (CVHNS) has made management of ACS a priority and established the Acute Coronary Syndrome Working Group to develop the Nova Scotia Acute Coronary Syndrome Guidelines and related implementation strategies.

GUIDELINE DEVELOPMENT

Mandate of the Working Group

The mandate of the Acute Coronary Syndrome Working Group was to recommend evidence-based standards of care, related targets and strategies for implementation/uptake of standards for the management of ACS.

The work of this group was aligned with the mission, vision and values of CVHNS, a provincial program of the Nova Scotia Department of Health that aims to improve the CV health and care of Nova Scotians. The Program's scope includes cardiac disease and stroke. CVHNS is responsible for:

- developing guidelines and service delivery models,
- working with District Health Authorities (DHAs) to improve CV health,
- monitoring and reporting CV health outcomes,
- facilitating professional development opportunities for health providers, and
- working with others to reduce the risk and burden of CVD.

CVHNS is accountable to the Acute and Tertiary Care Branch of the Nova Scotia Department of Health and receives advice from a Provincial Advisory Council. The Council advises the Program and subsequently the Department of Health on pertinent health care issues and priorities related to the mandate of CVHNS. The Advisory Council consists of physicians, senior leaders from the DHAs, researchers, health professionals, and nongovernmental organizations.

The working group included representation from key decision makers from DHAs, primary care representatives, emergency room physicians, Emergency Health Services (EHS) Nova Scotia, internists, cardiologists and healthcare professionals with expertise in the management of ACS.

Process

The Acute Coronary Syndrome Guidelines were developed by CVHNS over the past 24 months. The process was guided by the Acute Coronary Syndrome Working Group and included the review of existing guidelines (up to 2007) from the American College of Cardiology/American Heart Association, Canadian Cardiovascular Society and the European Society of Cardiology. The NSTEACS and STEMI guidelines were informed and developed through the collection and review of best practices in the provision of ACS care, including the following:

- American College of Cardiology/American Heart Association (ACC/AHA) 2007 Guidelines for the Management of Patients with Unstable Angina/Non-ST Elevation MI[8]
- European Society of Cardiology (ESC) 2007 Guidelines for the Diagnosis and Treatment of Non-ST Segment Elevation Acute Coronary Syndrome[9]
- 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial infarction[10]

- 2004 ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction[11]
- 2003 ESC Management of Acute Myocardial Infarction in Patients Presenting With ST-Segment Elevation Guidelines[12]
- 2004 Canadian Cardiovascular Society Guidelines – The 2004 ACC/AHA Guidelines: A Perspective and Adaptation for Canada by the Canadian Cardiovascular Society Working Group[13]

The definitions for levels of evidence reported in this document are summarized in Appendix A of each document (i.e. the STEMI and NSTEACS guidelines). The levels of evidence are reported where available; if the guidelines offer a different grading for a similar statement, each grading will be listed. The levels of evidence presented in this document are those used in the source documents (i.e. the levels were not re-examined or re-evaluated by the ACS Working Group.

In instances where a recommendation is based on the expert consensus, the notation "Consensus Nova Scotia 2006 or 2007" has been indicated. Literature/citations that were used to inform the Consensus Groups as they came to consensus are referenced. Statements that reflect routine medical care or practices are not graded. Two expert forums (one for NSTEACS (2006) and one for STEMI (2007)) were held to achieve consensus on issues requiring regional input due to limited evidence.

After these forums were held, two cardiologists took the lead in writing the NSTEACS (Dr. Michael Love) and STEMI (Dr. Iqbal Bata) guidelines with the assistance of CVHNS staff and Michael Callaghan, QEII pharmacist. The first draft of the guidelines was circulated to CVHNS Acute Coronary Syndrome Working Group members for input and advice regarding the stakeholder review process. A review template was designed and sent to clinician members of CVHNS' Advisory Council and the Acute Coronary Syndrome Working Group, as well as those who attended the expert forums. This review focused on ascertaining the clarity of the recommendations in the guidelines and any potential issues related to implementation of the guidelines in the DHAs. Representatives from eight of the nine DHAs participated (one DHA was unable to send a representative) in the first review and provided valuable feedback to the Acute Coronary Syndrome Working Group. The reviewers included EHS personnel, cardiologists, internists, nurses and pharmacists.

The first draft of the guidelines was revised based on the feedback received; the revised document was distributed to a wider group of stakeholders in the province for subsequent review in October 2007. The focus of this secondary review was to determine the systems implications for the guidelines, and to request strategies by DHAs for dissemination and implementation. More than 100 people participated in the final review and feedback was obtained from all nine DHAs.

Aims of the Guidelines

Evidence-based best practice guidelines are produced to help healthcare professionals, managers and consumers make decisions about healthcare in specific clinical circumstances. Research has shown that, if properly developed, communicated and implemented, guidelines can improve care.[14,15]

The aims of the guidelines are to:

- Provide explicit recommendations for practicing clinicians, managers, administrators, patients and caregivers about the management of non-ST elevation and ST-elevation ACS, covering the continuum from the acute event to the secondary prevention in the community.
- Provide recommendations based on best available evidence, contextualized to the situation in Nova Scotia.
- Provide consensus statements from the consensus forum participants for important areas of clinical practice where evidence is lacking.

Principles

The principles of the guidelines are that they should:

- Address key issues in ACS management.
- Indicate areas of uncertainty or controversy.

Scope

These guidelines address the management of ACS in adults (>16 years of age) from onset of symptoms through to secondary prevention. The scope of these guidelines includes the management of NSTEACS and STEMI. Areas not covered in these guidelines include primary (population-based) prevention, management of the patient who has not had a myocardial infarction and surgical management.

Context and Use

These guidelines should be taken as recommendations, not as rigid rules. Guidelines cannot cover every eventuality; new evidence is published every day. Furthermore, these guidelines should not be used as a legal resource, as the general nature cannot provide individualized guidance for all patients in all circumstances.[15]

These guidelines relate particularly to the management of ACS care. It is assumed that they will be used within the context of the services available in each DHA, and clinicians and others will be operating within professionally recognized standards of practice.

Feedback is most welcome, as these guidelines will be updated on a regular basis to keep abreast of new evidence.

Supports for Local Adaptation

The Acute Coronary Syndrome Working Group acknowledges that local adaptation of these guidelines will create unique challenges for each of the DHAs. Diversity in ACS statistics, resources and geographical location will influence local adaptation of the guidelines.

When implementing the Nova Scotia Guidelines for Acute Coronary Syndrome Care at the DHA level, the following issues should be considered:

- Improving access to education and training for healthcare practitioners involved in delivering ACS care.
- Developing and sharing protocols, care paths and algorithms.
- Improving access to, and linkages with, other related specialist services.
- Sharing services between neighboring DHAs (re: critical mass).
- Involving local champions and leaders in ACS care to support and liaise regarding business and implementation planning.
- Using telemedicine and other clinical-decision support tools.

As a provincial program of the Department of Health, Cardiovascular Health Nova Scotia can play a role in guidelines dissemination and uptake by:

- Providing support for implementation of these guidelines through education and training initiatives.
- Providing implementation-planning consultation.
- Providing communication and clinical decision support tool development and dissemination.
- Monitoring and evaluating implementation.

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Nova Scotia Health

CardioVascular HEALTH NOVA SCOTIA

Clinical Guidelines

IMPROVING CARDIOVASCULAR HEALTH OF NOVA SCOTIANS

Nova Scotia Guidelines for Non-ST Elevation Acute Coronary Syndromes (NSTEACS)

May 2008

NOVA SCOTIA Health

Your Health Matters

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Diagnosis of NSTEACS	
1.	**Clinical history and physical examination** • Obtain a clinical history and perform a physical examination immediately. *[Class I, Level C[1]]*
2 **2a** **2b**	**ECG monitoring** • Establish continuous electrocardiogram (ECG) monitoring and secure venous access during initial assessment, to facilitate rapid detection and treatment of arrhythmias. *[Class I, Level C[1]]* • Obtain a standard 12-lead ECG within 10 minutes of first medical contact. *[Class I, Level B;[1] Class I, Level C[2]]* Additional leads (e.g. posterior or right-sided leads) should be considered as indicated. Patients with definite ACS and ST elevation should be triaged for urgent reperfusion therapy, i.e. thrombolytic therapy or primary percutaneous coronary intervention (PCI). A repeat ECG should be obtained in the event of recurrent symptoms and at approximately 6 hours and 24 hours after admission.
3	**Troponin measurement** • Obtain blood for troponin measurement on presentation, and other key blood work (e.g. blood glucose [BG], creatinine, complete blood count [CBC]) as soon as possible after ECG is obtained. *[Class I, Level B[1]]* If initial troponin is not elevated then measurement should be repeated 6–12 hours later, as levels may not rise for several hours after onset of symptoms. *[Class I, Level A[2]]*
4	**Imaging investigations** • A chest X-Ray should be performed in the majority of patients, and other investigations considered as appropriate to the clinical circumstances (e.g. computed tomography (CT) imaging, echocardiography). **Additional imaging investigations should not unnecessarily delay treatment for definite ACS.** *[Consensus Nova Scotia 2006]*
5 **5a**	**Definitions** • If non-ST elevation acute coronary syndrome (NSTEACS) is suspected, once troponin result is available, determine whether appropriate diagnostic label is unstable angina (normal troponin) or non-ST elevation myocardial infarction (non-STEMI) (elevated troponin).

5b	• The definition of MI should be according to the diagnostic criteria proposed by the American College of Cardiology and the European Society of Cardiology (ESC).[3] (See *Appendix B*.)
6	**Risk stratification** • Perform risk stratification early based upon history, physical findings and investigation results and repeat as clinical situation evolves. *[Class I, Level C;[1] Class I, Level B[2]]* (See *Triage for cardiac catheterization and revascularization*, page 9.)

Immediate Treatment of Suspected NSTEACS	
7	**Oxygen** • Oxygen (O_2) should be administered immediately (2–6 L/min) to patients with suspected ACS who have evidence of respiratory distress or hypoxemia (O_2 saturation <90%). *[Class I, Level B[4]]*
8 **8a** **8b**	**Antiplatelet therapy** • Acetylsalicylic acid (ASA) (160–325 mg non-enteric coated oral loading dose) should be administered immediately to all patients with suspected ACS who do not have contraindications and who have not been taking ASA previously. *[Class I, Level B;[1] Class I, Level C[2]]* • Patients with contraindications to ASA, regardless of age, should be treated immediately with clopidogrel (300-mg oral loading dose). *[Class I, Level A;[1] Class I, Level B[2]]*
9 **9a** **9b**	**Nitroglycerin** • Nitroglycerin (0.3–0.6 mg every 5 minutes; total of 3 doses) should be administered sublingually (spray or tablet) to hemodynamically stable patients with suspected ACS and continuing symptoms. *[Class I, Level C[1]]* • Intravenous (IV) nitroglycerin (10–200 µg/min infusion) can be considered in patients with continuing symptoms, despite administration of O_2, sublingual nitroglycerin and a beta blocker. *[Class I, Level B[1]]*
10	**Beta blocker therapy** Immediate administration of a beta blocker should be considered in hemodynamically stable patients with suspected ACS, particularly if they have continuing symptoms. Oral treatment is recommended in most cases, but IV therapy (e.g. IV metoprolol 5 mg every 5 minutes, up to 3 times) can be considered in hemodynamically stable patients with continuing symptoms despite administration of O_2 and nitroglycerin. • Oral beta blocker therapy should be continued throughout the hospital stay and after discharge in the majority of definite NSTEACS patients without contraindications. *[Class I, Level B[1]]* (See *Beta blocker therapy*, page 13.)

11	**Calcium channel antagonist therapy** • Consider oral or IV administration of a non-dihydropyridine calcium channel antagonist (e.g. verapamil or diltiazem) in hemodynamically stable patients with suspected ACS who have continuing symptoms **and contraindications to beta blocker therapy**. *[Class I, Level B[1]]* Acute administration of short-acting dihydropyridines (e.g. nifedipine) should be avoided. *[Class III, Level A[1]]*
12	**Morphine** • Morphine (2–4 mg IV or subcutaneously [SC]) or other opiate analgesics can be considered in hemodynamically stable patients with suspected ACS and continuing severe symptoms despite administration of O_2, nitroglycerin and a beta blocker. *[Class I, Level C[1]]*

Additional Immediate and Subsequent Inpatient Treatment of Definite NSTEACS	
13	**Antiplatelet therapy**
13a	***ASA*** • ASA (81–325 mg once daily [OD]) should be continued throughout the hospital stay in all patients with definite NSTEACS and no contraindications. The dose of ASA should be minimized (81 mg daily) in patients also taking clopidogrel or warfarin, to help reduce the risk of bleeding complications. *[Class I, Level A[1]]*
13b	***Clopidogrel*** • Clopidogrel (300-mg oral loading dose) should be administered In addition to ASA as soon as possible to patients with definite NSTEACS who do not have bleeding or other contraindications. *[Class I, Level A[1]]*
13c	• At the discretion of the on-call interventional cardiologist. a higher loading dose of clopidogrel may be considered in high-risk patients being triaged immediately to the cardiac catheterization laboratory. *[Class II, Level B[2]]*
13d	• Clopidogrel can increase the risk of major bleeding in patients who subsequently go on to have cardiac surgery. However, clopidogrel should not be withheld unless there are clinical features or a background history suggesting that urgent cardiac surgery is very likely to be required, e.g. patients with cardiogenic shock or who are already known to have coronary artery disease (CAD) likely to benefit more from surgical revascularization (e.g. >50% left main stem stenosis or triple vessel coronary disease with poor left ventricular systolic function). *[Class I, Level B[1]]*
13e	• Clopidogrel (75 mg OD) should be continued throughout the hospital stay in patients with definite NSTEACS who do not have bleeding or other contraindications, and who are not scheduled to undergo early (within 5 days) coronary artery bypass surgery. *[Class I, Level A[1]]* (See *Antiplatelet therapy*, page 13, for recommended duration of clopidogrel following hospital discharge.)

13f	***Glycoprotein IIb/IIIa receptor inhibitor therapy*** • For patients with definite NSTEACS and refractory ischemia or other high-risk features, IV infusion of a small molecule platelet glycoprotein IIb/IIIa receptor inhibitor (eptifibatide or tirofiban) should be considered in patients without bleeding or other contraindications. *[Class I, Level B[1]]* Early triage to the cardiac catheterization laboratory should be discussed with the on-call interventional cardiologist. (See *Triage for cardiac catheterization and revascularization*, page 9.)
14	**Antithrombin therapy**
14a	***Fondaparinux*** • The factor Xa inhibitor fondaparinux is the **preferred** antithrombin drug for definite NSTEACS in Nova Scotia on the basis of its equivalent efficacy and superior safety to enoxaparin. *[Consensus Nova Scotia 2006]*
14b	• Fondaparinux (2.5 mg SC on the day of admission, followed by 2.5 mg OD thereafter) should be administered immediately to the majority of patients with definite NSTEACS who do not have bleeding or other contraindications. *[Class I, Level B;[1] Class I, Level A[2]]*
14c	• In fondaparinux-treated patients who go on to PCI, fondaparinux can be discontinued after the procedure in the majority of patients. (See *Appendix C*.) In patients managed with a conservative strategy, fondaparinux can be continued until hospital discharge if necessary, to a maximum of 8 days. *[Class I, Level A;[1] Class I, Level B[2]]*
14d	***Unfractionated heparin*** • Unfractionated heparin (UFH) should be used instead of fondaparinux in patients with definite NSTEACS under the following circumstances: *[Class I, Level A;[1] Class I, Level B[2]]* – severe renal impairment (creatinine clearance <30 mL/minute) (See *Appendix D*.) – patients with mechanical heart valves – patients with very high-risk features mandating urgent (within 12 hours) cardiac catheterization, PCI or coronary artery bypass surgery

14e	• Dosing of UFH should be as follows: (See *Appendix E*.) IV loading dose of 60 IU/kg (maximum 4000 IU) – subsequent IV infusion of 12 IU/kg/hour (maximum 1000 IU/hour) – dosage adjustments of the nomograms to correspond to a therapeutic range equivalent to heparin levels of 0.3 to 0.7 U/mL by anti-factor Xa determinations, which correlates with aPTT values between 60 and 80 seconds.[1] – The aPTT range may differ due to variation in laboratory methods used to determine aPTT. A locally approved nomogram for dosing adjustment should be followed.
14f	• In UFH-treated patients undergoing PCI, UFH should be stopped immediately after the procedure in the majority of patients. *[Class I, Level B[1]]* In patients managed with a conservative strategy, UFH should be continued for at least 48 hours, and longer at the discretion of their attending physician. *[Class I, Level A[1]]* (See *Appendix E*.)
15	**Triage for cardiac catheterization and revascularization** As recommended by the Canadian Cardiovascular Society (CCS) Access to Care Working Group,[4] access to cardiac catheterization and revascularization should be prioritized according to risk. *[Consensus Nova Scotia 2006]*
15a	• NSTEMI patients are typically at significantly higher risk of death and recurrent MI than patients with unstable angina. The majority of NSTEMI patients should therefore be considered for early cardiac catheterization, provided the benefits of invasive assessment and revascularization are felt to outweigh the risks. Conversely, lower-risk unstable angina patients need not necessarily undergo early cardiac catheterization, provided that non-invasive testing rules out easily inducible or widespread myocardial ischemia. *[Consensus Nova Scotia 2006]*

15b	• Important considerations when weighing the benefits and risks of cardiac catheterization and revascularization include *[Consensus Nova Scotia 2006]*: – presence of peripheral arterial disease that might affect arterial access – renal function and anticipated risk of contrast nephropathy/renal failure – bleeding risk – ability to tolerate and comply with prolonged dual antiplatelet therapy in the event of drug-eluting stent insertion – patient frailty and fitness/willingness to undergo an invasive procedure – cognitive issues that might affect ability to provide procedure consent – other major life-threatening illness
15c	• The following features should be considered in determining the need for and timing of cardiac catheterization: *[Consensus Nova Scotia 2006]* ***High-risk features*** *(catheterization ± PCI within 24–48 hours)* – hypotension[a] or definite evidence of heart failure – recurrent ventricular arrhythmias – transient ST elevation – new ST depression ≥2 mm in ≥3 leads – recurrent or refractory ischemia despite initial therapy[b] – thrombolysis in myocardial infarction (TIMI) risk score 5–7 (See *Appendix F*.) [a] *with other supportive evidence of ischemia* [b] *definite new or dynamic ST segment changes required to justify urgent status in patients with unstable angina (normal troponin level)* ***Intermediate-risk features*** *(catheterization within 3–5 days)* – NSTEMI with no high-risk features, but known left ventricular ejection fraction (LVEF) <40% – TIMI risk score 3–4 (See *Appendix F*.)

	Low-risk features *(catheterization within 5–7 days)* – NSTEMI with no high- or intermediate-risk features[c] – suspected unstable angina with recurrent symptoms but no ECG changes – unstable angina with easily inducible (<3 METs) or widespread ischemia on non-invasive testing, or some other marker of increased risk[d] – TIMI risk score 1–2 (See *Appendix F*.)[e] [c] *low-risk NSTEMI patients can have invasive assessment deferred to an early outpatient setting (<2 weeks) provided that non-invasive testing does not indicate easily inducible (<3 METs) or widespread ischemia or some other marker of increased risk* [d] [d] *e.g. hypotensive response, sustained ST depression, exercise-induced ventricular tachycardia, large territory of reversible ischemia, multiple perfusion defects, low LVEF <40%* [e] *low-risk unstable angina patients with a TIMI risk score of 1–2 need not necessarily undergo early invasive assessment if non-invasive testing rules out easily inducible or widespread ischemia*
16	**Role of CABG surgery** • In NSTEACS patients found to have disease that requires coronary artery bypass grafting (CABG), surgery should be prioritized according to the same three risk categories (high, intermediate and low) as for patients undergoing PCI. The timing of CABG should be according to the timelines proposed by the CCS Access to Care Working Group:[4] – **high risk: within 3–5 days** – **intermediate risk: within 2–3 weeks** – **low risk: within 6–8 weeks**
17	**Mode of revascularization** • In general, the factors influencing the most appropriate mode of revascularization (PCI or CABG) in patients with NSTEACS should be the same as for patients with stable coronary disease. PCI is usually preferred in patients with single- and double-vessel CAD not involving the left main stem. CABG is strongly preferred in patients with left main stem disease and usually preferable in patients with multi-vessel disease, especially when associated with poor left ventricular systolic function and/or diabetes.
18 **18a**	**Treatment of hyperglycemia/diabetes** • Tight glycemic control is advised for all NSTEACS patients who present with hyperglycemia (random BG >11.0, or fasting BG >7.0 mmol/L).[5,6] *[Consensus Nova Scotia 2006]*

18b	• During the first 48 hours there should be a low threshold for use of insulin to maintain a BG of 7.0–10.0 mmol/L. After 48 hours, standard diabetes management is recommended including oral antihyperglycemic agents and/or insulin as appropriate.[6]
18c	• Caution is recommended in considering the use of thiazolidinediones in patients with cardiovascular disease.[7]
18d	• The long-term therapy goals should conform to the current Canadian Diabetes Association guidelines:[8] fasting BG 4.0–7.0 mmol/L and A1C ≤7.0%, if achievable safely. *[Consensus Nova Scotia 2006]*

Pharmacologic Secondary Preventive Therapy

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19a

Antiplatelet therapy

- ASA (81–325 mg daily) should be continued indefinitely in all NSTEACS patients without contraindications. *[Class I, Level B*;[1] *Class I, Level A*[2]*]* The dose of ASA should be minimized (81 mg daily) in patients also taking clopidogrel or warfarin to help reduce the risk of bleeding complications.

19b

- Clopidogrel (75 mg OD), in addition to ASA, is recommended on discharge for all definite NSTEACS patients in the absence of contraindications. The duration of clopidogrel therapy should be tailored according to patient risk and the type of stent inserted in those who undergo PCI.[9] (See *Table 1*, below.) *[Consensus Nova Scotia 2006]*

Table 1. Recommended duration of clopidogrel therapy

Recommended clopidogrel duration	Patients not undergoing PCI	Patients undergoing PCI
3 months	Patients at low risk of recurrent events	Patients at low risk of recurrent events treated only with BMS
12 months	Patients at increased risk of recurrent events[a]	Patients receiving ≥1 DES or who are at increased risk of recurrent events[a] regardless of stent type
>12 months	Patients at very high risk of recurrent events[b]	Some patients receiving multiple (≥3) DES or undergoing complex PCI[c] or patients at very high risk of recurrent events[b] regardless of stent type

[a] *e.g. second ACS within 12 months, complex or extensive CAD (especially if not amenable to revascularization), associated peripheral arterial or cerebrovascular disease*
[b] *e.g. patients with degenerate saphenous vein bypass grafts or who also have peripheral vascular and cerebrovascular disease*
[c] *DES implanted in left main stem or bifurcation configuration*

20
20a

Beta blocker therapy

- Beta blocker therapy should be initiated early and continued throughout hospitalization in all patients with definite NSTEACS and no contraindications. *[Class I, Level B*[2]*]* (See *Immediate treatment of suspected NSTEACS*, page 5.)

20b	• Although evidence of benefit is limited, the majority of patients with definite NSTEACS should be considered for long-term beta blocker therapy in the absence of contraindications or side effects. *[Class I, Level B[2]]* Long-term therapy may not be necessary or appropriate in low-risk patients (e.g. normotensive patients with preserved left ventricular systolic function who have been completely revascularized). *[Consensus Nova Scotia 2006]*
20c	• Use of cardioselective beta blockers is generally recommended in NSTEACS patients with preserved left ventricular function. *[Class IIa, Level B[1]]* Preferred agents in patients with left ventricular systolic dysfunction are bisoprolol and carvedilol. (*See Appendix G*.)
20d	• In patients with ongoing symptoms, with contraindications to beta blockade, treatment with a calcium channel blocker can be considered. *[Class I, Level C;[1] Class I, Level B[2]]* Short-acting dihydropyridines should be avoided. Non-dihydropyridines (verapamil and diltiazem) should be avoided in patients with a LVEF <40%. *[Class III, Level A[1]]*
21	**Lipid-lowering therapy**
21a	• HMG co-A reductase inhibitors (statins) are recommended for the majority of patients with definite NSTEACS in the absence of contraindications, irrespective of baseline lipid values. *[Class I, Level A;[1] Class I, Level B[2]]*
21b	• A moderate dose of statin should be initiated early after admission. *[Class I, Level A;[1] Class I, Level B[2]]*
21c	• The choice of statin and the dose initiated should take into consideration the long-term lipid targets for patients with established CAD recommended by the Canadian Cardiovascular Society.[10] *[Consensus Nova Scotia 2006]* (See *Appendix G*.) – *Primary target*: LDL-C <2.0 mmol/L – *Secondary targets*: TC to HDL-C ratio <4; in patients with established atherosclerosis, treatment to lower LDL-C by at least 50% is generally appropriate
21d	• Fasting lipid values and liver function tests should be checked 1–2 months after discharge and the dose of statin titrated accordingly in the absence of side effects or other evidence of drug toxicity.
21e	• Some patients may require combination therapy with other agents, such as ezetimibe, niacin or fibrates to achieve their target lipid values. *[Class IIa, Level B[1]]*

22	**ACE inhibitor therapy**
22a	• No randomized clinical trials have specifically tested the safety and efficacy of angiotensin-converting enzyme (ACE) inhibitors in patients with NSTEACS. These agents should be used selectively in patients with definite NSTEACS who are felt to be at specifically increased risk of adverse cardiac events. *[Consensus Nova Scotia 2006]*
22b	• In the absence of contraindications, long-term treatment with an ACE inhibitor is recommended in NSTEACS patients with: *[Consensus Nova Scotia 2006]* – CHF during hospitalization or LVEF <40% – diabetes mellitus – hypertension – extensive CAD – definite peripheral arterial or cerebrovascular disease
22c	• Long-term ACE inhibitor therapy may not be appropriate or necessary in low-risk patients, e.g. normotensive, non-diabetic patients with preserved left ventricular systolic function and minor CAD. *[Consensus Nova Scotia 2006]*
22d	• When ACE inhibitor therapy is indicated, treatment should be initiated as soon as possible after patients are clinically stable with subsequent inpatient or post-discharge titration to target dose.
22e	• The choice and dose of ACE inhibitor should be evidence-based. (See *Appendix G*.)
22f	• NSTEACS patients with contraindications to, or who are intolerant of, ACE inhibitors and who are felt to be at increased risk of adverse events can be considered for treatment with an angiotensin receptor antagonist. *[Class I, Level A;[1] Class I, Level B[2]]*

Non-pharmacologic Secondary Preventive Therapy	
23 **23a** **23b**	**Smoking cessation** • Cigarette smokers should be urged to quit to reduce their risk of recurrent cardiac events and death. Exposure to second hand smoke should also be avoided. Active counselling ("the 5 A's": Ask, Advise, Assess, Assist, Arrange) regarding quitting strategies, and information about local smoking cessation programs and adjunctive pharmacologic interventions should be provided. *[Class I, Level B[1]]* • Referral to a local smoking cessation program should be arranged: – The Canadian Cancer Society's help line (toll-free 1-877-513-5333) provides information about smoking cessation and available community services. – The Nova Scotia Lung Association's Quit4good contact number is 1-888-566-5864. – The website www.addictionservices.ns.ca contains a map of District Health Authorities (DHAs) that offer smoking cessation programs.
24 **24a** **24b**	**Diabetes education** • NSTEACS patients with diabetes should be offered initial and ongoing needs-based diabetes education in a timely manner to enhance self-care practices and behaviours.[8] *[Consensus Nova Scotia 2006]* • Referral to a Diabetes Education Centre (DEC) for ongoing education and management of diabetes and cardiac risk factors is recommended. Visit www.diabetescareprogram.ns.ca for DEC locations in Nova Scotia.
25	**BP control** • Lifestyle changes, in particular weight loss and regular exercise, are an important component of blood pressure (BP) management. As per current Canadian Hypertension Education Program recommendations,[11] target BP is <140/90 mm Hg, except in patients with diabetes or chronic kidney disease, in whom target BP is ideally <130/80 mm Hg. *[Consensus Nova Scotia 2006]*

26	**Nutrition intervention**
26a	• A heart-healthy diet is recommended. Such a diet is limited in sodium (<2.4 g/day), cholesterol (<200 mg/day) fat (<25-35% of total energy intake), saturated and trans fats (<7%), increased in monounsaturated (up to 20%) and polyunsaturated fats (up to 10%), increased in fruits and vegetables and limited in carbohydrates. *[Class I, Level B [1,2]]* Other therapeutic diet modifications may be needed according to comorbidities; written nutrition information to this effect should be provided.
26b	• Patients should be encouraged to achieve and maintain a healthy weight (body mass index [BMI] 18.5–24.9 kg/m^2) and waist circumference (<102 cm men; <88 cm women). Overweight and obese patients should be offered support and advice. Dietary energy content should be aimed at reducing body weight by ~10% from baseline. *[Class I, Level B [1]]* With success, further weight loss can be attempted to achieve a BMI of <27 kg/m^2 and ideally <25 kg/m^2.
26c	• A clinical dietitian should be consulted for a comprehensive nutrition assessment in nutritionally compromised patients requiring nutrition support/intervention.
27	**Exercise**
27a	• Assessment of functional capacity and ability to return to normal activities and employment is recommended 4–6 weeks post-discharge. *[Class I, Level C[2]]* A treadmill exercise test or equivalent non-invasive test should be considered within this time frame, especially in patients known to have residual obstructive coronary disease. *[Class I, Level B[1]; Class IIa, Level C[2]]*
27b	• Regular, moderate-intensity aerobic exercise for 30–60 minutes most days of the week is recommended. Exercise training in a medically supervised environment should be considered for moderate- and high-risk patients.[12] *[Consensus Nova Scotia 2006]*
28	**Secondary prevention programs for cardiovascular disease**
28a	• DHAs are encouraged to explore integrated, chronic disease management programs consistent with Nova Scotia's Chronic Disease Management Strategy. *[Consensus Nova Scotia 2006]*
28b	• Secondary prevention programs are recommended, particularly for patients with multiple modifiable risk factors and for moderate- to high-risk patients in whom supervised exercise training is warranted. *[Class I, Level B[1]]*

28c	• Referral to secondary prevention programs should be arranged prior to hospital discharge. Program entry should be within the recommended time frame of 30 days.[13] *[Consensus Nova Scotia 2006]*

Other Aspects of Management and Follow-Up	
29	**Analgesic therapy** • In patients with chronic musculoskeletal or other pain, the requirement for analgesic therapy should be assessed prior to discharge. Acetaminophen, ASA and small doses of narcotics are the preferred analgesic options. *[Class I, Level C[1]]* Nonsteroidal anti-inflammatory drugs (NSAIDs) with increasing degrees of COX-2 selectivity should be avoided. *[Class III, Level C[1]]*
30	**Patient education about activities of daily living** • Patients should be given specific instructions about physical and sexual activity, driving and return to work before discharge. *[Class I, Level C[1]]*
31	**Role of the family physician** • It is anticipated that family physicians will play a central role in long-term risk factor modification by ensuring that ACS patients receive appropriate lifestyle counselling and evidence-based secondary preventive drug therapy. Family physicians should ensure that drug doses are evidence-based and titrated when appropriate, in pursuit of recommended glycemic, BP and lipid targets. (See *Appendix G*.) *[Class I, Level C[1]]*
32	**Screening for depression** • Depression is common, frequently under-recognized and correlates with a poorer prognosis in ACS patients. Specialists and family physicians should screen for depression and refer/treat accordingly. *[Class IIa, Level B [1]]*
33	**Influenza vaccination** • As recommended by Health Canada,[14] the majority of patients with CAD should receive annual influenza vaccination. *[Consensus Nova Scotia 2006]*
34 **34a**	**Indications for automatic implantable cardioverter defibrillators** • Patients who develop spontaneous ventricular fibrillation or sustained ventricular tachycardia in the absence of ischemia >48 hours after their ACS presentation should be referred for consideration for automatic implantable cardioverter defibrillator (AICD) implantation. *[Class I, Level A[15]]*

34b	• Patients with markedly reduced left ventricular systolic function (EF <30%) >1 month after a MI should be referred for consideration for AICD implantation. *[Class IIa, Level A[16]]*
34c	• Patients with EF 31–35% at least 1 month after MI may also be considered for AICD implantation, although the benefit in this population is less well established. *[Class IIa, Level B[15]]*

ABBREVIATIONS

AICD	automatic implantable cardioverter defibrillator
A1C	glycated hemoglobin / hemoglobin A1C
ACC	American College of Cardiology
ACE inhibitor	angiotensin-converting enzyme inhibitor
ACS	acute coronary syndrome
AHA	American Heart Association
aPTT	activated partial thromboplastin time
ARB	angiotensin receptor II agonist
ASA	acetylsalicylic acid (aspirin)
BID	twice daily
BMI	body mass index
CABG	coronary artery bypass graft
CAD	coronary artery disease
CBC	complete blood count
CCU	chronic care unit
CHF	congestive heart failure
COX-2	cyclooxygenase 2
CPR	cardiopulmonary resuscitation
CrCl	creatinine clearance
CT imaging	computed tomography imaging
DEC	Diabetes Education Centre
DHAs	District Health Authorities
DOB	date of birth
EC	enteric coated
ECG	electrocardiogram
ED	emergency department
EHS	Emergency Health Services
ESC	European Society of Cardiology
HDL-C	high-density lipoprotein cholesterol
HIT	heparin-induced thrombocytopenia
ICH	intracranial hemorrhage
ICU	intensive care unit
INR	International Normalized Ratio
IV	intravenous
LDL-C	low-density lipoprotein cholesterol
LVEF	left ventricular ejection fraction
MI	myocardial infarction
NSAIDs	nonsteroidal anti-inflammatory drugs
O_2	oxygen
OD	once daily
PAD	peripheral arterial disease
PCI	percutaneous coronary intervention
PO	per os (by mouth, orally)

PTT/PT	partial thromboplastin time/prothombin test
PVD	peripheral vascular disease
SC	subcutaneous
SR	sustained release
STEMI	ST elevation myocardial infarction
TC	total cholesterol
TID	three times daily
TNK	tenecteplase
UFH	unfractionated heparin

TRIAL/STUDY ACRONYMS

4-S[17]	Scandinavian Simvastatin Survival Study
AIRE[18]	Acute Infarction Ramipril Efficacy
ASCOT[19]	Anglo-Scandinavian Cardiac Outcomes Trial
ATLAS[20]	Assessment of Treatment with Lisinopril and Survival
A to Z[21]	Aggrastat To Zocor
CARE[22]	Cholesterol and Recurrent Events
CONSENSUS[23]	Cooperative North Scandinavian Enalapril Survival Study
EUROPA[24]	European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease
Extract TIMI 25[25]	Enoxaparin Versus Unfractionated Heparin with Fibrinolysis for ST Elevation MI
GISSI-3[26]	Gruppo Italiano per lo Studio della Sopravivenza nell'Infarto Miocardico
HOPE[27]	Heart Outcomes Prevention Evaluation Study
HPS[28]	Heart Protection Study
LIPID[29]	Long-term Intervention with Pravastatin in Ischaemic Disease
MIRACL[30]	Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering
PROSPER[31]	A Prospective Study of Pravastatin in the Elderly at Risk
PROVE-IT[32]	Pravastatin or Atorvastatin Evaluation and Infection Therapy – Thrombolysis in Myocardial Infarction
SAVE[33]	The Survival and Ventricular Enlargement Study
SOLVD[34]	Studies of Left Ventricular Dysfunction
TNT[35]	Treating to New Targets
TRACE (LVSD)[36]	Trandolapril Cardiac Evaluation (Left Ventricular Systolic Dysfunction)
VALIANT[37]	The Valsartan in Acute Myocardial Infarction Study

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Appendix A. Grading of Evidence: Class and Level

Class	ACC/AHA (2007)[1]	ESC (2007)[2]
I	Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective	Evidence and or general agreement that a given diagnostic procedure/treatment is beneficial, useful and effective
II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the treatment
IIa	Weight of evidence/opinion is in favour of usefulness/efficacy	Weight of evidence/opinion is in favour of usefulness/efficacy
IIb	Usefulness/efficacy is less well established by evidence/opinion	Usefulness/efficacy is less well established by evidence/opinion
Class III	Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful	Category does not exist

Level	ACC/AHA (2007)[1]	ESC (2007)[2]
A	Data derived from multiple randomized clinical trials or meta-analyses	Data derived from multiple randomized clinical trials or meta-analyses
B	Data derived from a single randomized trial or nonrandomized studies	Data derived from a single randomized trial or large nonrandomized studies
C	Only consensus opinion of experts, case studies or standard of care	Consensus of opinion of the experts and/or small studies, retrospective studies, registries

The notification "Consensus Nova Scotia 2006" is used to indicate those recommendations based on the decisions of the provincial expert consensus panel. Literature/citations that informed the panel as they came to consensus are referenced. Statements that reflect routine medical care or practices are not graded.

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Appendix B. Criteria for Definition of MI[1]

Acute, evolving or recent MI

Either one of the following satisfies the diagnosis for an acute, evolving or recent MI:

A. Typical rise and gradual fall in troponin associated with at least one of the following:
   - ischemic symptoms;
   - development of pathological Q waves on the ECG;
   - ECG changes indicative of ischemia; or
   - coronary artery intervention e.g. coronary stenting.

B. Pathologic findings of an acute MI.

Established MI

Either one of the following satisfies the diagnosis for established MI:

A. Development of new pathological Q waves on serial ECGs. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized depending on the length of time that has passed since the infarct developed.

B. Pathologic findings of a healed or healing MI.

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Appendix C. Fondaparinux Cardiac Catheterization Laboratory Protocol

Fondaparinux dosing before PCI

- In NSTEACS patients undergoing definite or possible PCI who have been receiving maintenance fondaparinux therapy ***in the AM***:
  - *Stable patients*[a]
    Hold morning dose of fondaparinux on day of procedure and use UFH or bivalirudin as per usual protocols during PCI
  - *Unstable patients*[b]
    Give usual AM dose of fondaparinux on day of procedure and use UFH 50–70 IU/kg[c] or bivalirudin as per usual protocol during PCI

- In NSTEACS patients undergoing definite or possible PCI who have been receiving maintenance fondaparinux therapy ***in the PM***:
  - *Stable and unstable patients*
    Give usual PM dose of fondaparinux the day before procedure and use IV UFH or bivalirudin as per usual protocols during PCI

[a] *no recurrent ischemia within 24 hours of procedure*
[b] *recurrent ischemia within 24 hours of procedure*
[c] *if >12 hours have elapsed since AM dose of fondaparinux was given, standard dose UFH (70– 100 IU/kg) should be used rather than 50–70 IU/kg*

Femoral arterial sheath removal after fondaparinux administration

- In NSTEACS patients who undergo cardiac catheterization only:
  - Arterial sheath should not be removed until at least 6 hours after the last dose of fondaparinux
  - If fondaparinux needs to be restarted after cardiac catheterization, wait at least 2 hours after sheath removal and at least 18 hours since last dose before administration

- In NSTEACS patients who undergo PCI:
  - Arterial sheath can be removed according to usual protocols governing use of UFH or bivalirudin

If fondaparinux needs to be restarted after PCI, wait at least 2 hours after sheath removal and at least 18 hours since last dose before administration

Appendix D. CrCl Calculations

- IBW (kg) = 0.9 (Ht [cm] – 150) (+50, male; +45, female)
- Estimate CrCl (mL/min):

Male: $\frac{(140 - \text{age}) (\text{IBW kg}) (60)}{(\text{Serum creatinine } \mu\text{mol/L}) (50)}$

Female: 0.85 x male CrCl value

<30 mL/min is equivalent to severe renal insufficiency

Appendix E. Heparin Infusion Protocol for NSTEACS

Patient: _____ Weight: _____ kg Height: _____ cm
Allergies (describe reaction): _____
Time: _____ Estimated CrCl: _____ mL/min

N.B: For patients with NSTEACS, consider using fondaparinux as a first-line antithrombotic.

1. Initial blood work
CBC, PT (INR), aPTT, prior to starting heparin.

2. Heparin orders
The following orders should be administered using heparin 25,000 units in 500 mL of D5W (other solutions require a separate order).

□ Loading (bolus) dose:
60 units/kg X _____ kg (patient weight) = _____ units IV over 20 minutes **(maximum 4000 units), then**

□ Maintenance IV infusion: to begin immediately after the bolus (if given).
12 units/kg/hr x _____kg (patient weight) = _____units/hr **(maximum 1000 units/hr)**

3. Repeat blood work
- CBC daily. Notify physician if platelet count is <100 x 10^9/L
- aPTT in 3 hours

4.0 Adjust heparin infusion according to the following nomogram:*
The therapeutic aPTT range should be calibrated specifically for each reagent lot/coagulometer by determining the aPTT values that correlate with therapeutic heparin levels (equivalent to 0.3 to 0.7 IU/mL) by factor Xa inhibition for the treatment of venous thrombosis.[1]

*aPTT targets will depend on local lab reagents; **it is important that a heparin infusion nomogram be developed by your local laboratory.**

Prescriber's Signature: _____ Date:(yyyy/mm/dd): _____
Prescriber's Name: _____ Reg. No.:_____

REFERENCE
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APPENDIX F. TIMI Risk Score[1]

One point each for:

- ≥65 years of age
- at least 3 risk factors for CAD [a]
- significant coronary stenosis [b]
- ST deviation on presentation
- severe anginal symptoms [c]
- use of ASA in last 7 days
- elevated serum cardiac markers [d]

Total number of points = TIMI risk score

[a] family history of coronary disease, hypertension, dyslipidemia, diabetes or current smoking
[b] prior coronary stenosis ≥50%
[c] ≥2 anginal episodes in last 24 hours
[d] troponin or creatine kinase MB

CCS risk category[2]	TIMI risk score[1]	Recommended timing of cardiac catheterization[2]
Low risk	1–2	5–7 days
Intermediate risk	3–4	3–5 days
High risk	5–7	24–48 hours

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Appendix G. Pharmacotherapy Dosages and Costs: Beta Blockers, Statins and ACE Inhibitors

BETA BLOCKER DOSAGES AND COSTS			
Generic name [a]	*Dosage*	*Dosage frequency*	*Cost/month* [b]
Metoprolol [c]	25 mg	BID	$3.86
	50 mg	BID	$8.45
	100 mg	BID	$15.34
	100 mg SR	OD	$6.97
	200 mg SR	OD	$12.65
Atenolol [c]	50 mg	OD	$12.14
	100 mg	OD	$19.93
Bisoprolol [c]	5 mg	OD	$7.61
	10 mg	OD	$12.61
Carvedilol	3.125 mg	BID	$55.21
	6.25 mg	BID	$55.21
	12.5 mg	BID	$55.21
	25 mg	BID	$55.21
Nadolol	40 mg	OD	$8.51
	80 mg	OD	$12.13
	160 mg	OD	$19.79

[a] Beta adrenergic blockers with intrinsic sympathomimetic activity have not been included, as they are relatively contraindicated in ACS settings

[b] Costs in table were calculated using the January 2008 Atlantic Pharmaceutical Services Incorporated regional price guide and are subject to change. Costs are based on the target dose defined by clinical trials and do not include pharmacist professional fees.

[c] cardioselective agents

Appendix G. Pharmacotherapy Dosages and Costs: Beta Blockers, Statins and ACE Inhibitors (cont'd)

STATIN DOSAGES AND COSTS			
Generic name	*Trial evidence*	*Dosage* [a]	*Cost/month* [b]
Atorvastatin	ASCOT[1]	10 mg	$57.40
		20 mg	$71.76
		40 mg	$77.14
	PROVE-IT,[2] TNT,[3] MIRACL[4]	80 mg	$77.14
Lovastatin		20 mg	$37.63
		40 mg	$69.40
Fluvastatin		20 mg	$28.50
		40 mg	$40.02
		80 mg XL	$48.51
Pravastatin		10 mg	$32.88
		20 mg	$38.79
	CARE,[5] LIPID,[6] PROSPER[7]	40 mg	$46.72
Simvastatin		10 mg	$38.69
		20 mg	$47.82
	4S,[8] HPS[9]	40 mg	$47.82
	A to Z[10]	80 mg [c]	$47.82
Rosuvastatin		10 mg	$40.80
		20 mg	$51.00
		40 mg [d]	$59.70

[a] **Doses in shaded blocks provide at least a 40% reduction in LDL-C**

[b] Costs in table were calculated using the January 2008 Atlantic Pharmaceutical Services Incorporated regional price guide and are subject to change. Costs are based on the target dose defined by clinical trials and do not include pharmacist professional fees

[c] Simvastatin 80 mg was associated with more cases of rhabdomyolysis in the A to Z trial

[d] Specialist supervision is recommended when initiating rosuvastatin 40 mg

Appendix G. Pharmacotherapy Dosages and Costs: Beta Blockers, Statins and ACE Inhibitors (cont'd)

ACE INHIBITOR DOSAGES AND COSTS				
Generic name	*Trial evidence*	*Starting dosage*	*Target dosage*	*Cost/month* [a]
Captopril	SAVE[11] VALIANT[12]	6.25 mg	50 mg TID	$54.85
Lisinopril	GISSI-3[13]	2.5–5 mg OD	10 mg OD	$22.37
	ATLAS[14]		40 mg OD	$53.60 [b]
Ramipril	HOPE[15] (vascular protection)	2.5 mg OD	10 mg OD	$22.94
	AIRE[16] (LVSD)	2.5 mg BID	5 mg BID	$36.22
Perindopril	EUROPA[17] (vascular protection)	2 mg OD	8 mg OD [c]	$30.80
Trandolopril	TRACE[18] (LVSD post MI)	1 mg OD	4 mg OD	$33.76
Enalapril	CONSENSUS,[19] SOLVD[20]	2.5 mg BID	10 mg BID	$53.21

[a] Costs in table were calculated using the January 2008 Atlantic Pharmaceutical Services Incorporated regional price guide and are subject to change. Costs are based on the target dose defined by clinical trials and do not include pharmacist professional fees.

[b] The cost of lisinopril 40 mg is based on taking two 20-mg tablets, as it is not available in a 40-mg tablet.

[c] Generic perindopril is only available in the 8-mg strength (tablets not scored)

Appendix G. Pharmacotherapy Dosages and Costs: Beta Blockers, Statins and ACE Inhibitors (cont'd)

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Appendix H. Glycemic, BP and Lipid Targets

Parameter	Target
A1C[1]	≤7.0%
BP (mm Hg)[2] Patients without diabetes Patients with diabetes or chronic kidney disease	<140/90 mm Hg <130/80 mm Hg
LDL-C*[3]	<2.0 mmol/L
TC to HDL-C ratio**	<4.0
LDL-C lowering**	≥50%

* Primary target
** Secondary target

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Nova Scotia Health

CardioVascular HEALTH NOVA SCOTIA

Clinical Guidelines

IMPROVING CARDIOVASCULAR HEALTH OF NOVA SCOTIANS

Nova Scotia Guidelines for Acute ST Elevation Myocardial Infarction (STEMI)

May 2008

NOVA SCOTIA Health

Your Health Matters

TABLE OF CONTENTS

INTRODUCTION

The definition of myocardial infarction (MI) used in these guidelines is according to the diagnostic criteria proposed by the American College of Cardiology (ACC) and the European Society of Cardiology (ESC).[1] (See *Appendix B*.)

A diagnosis of acute ST elevation myocardial infarction (STEMI) should be considered in patients presenting with ischemic symptoms lasting at least 20 minutes within the past 12 hours and: ECG evidence of ≥1 mm ST elevation in ≥2 contiguous limb leads; or evidence of ≥2 mm ST elevation in ≥2 contiguous pre-cordial leads; or new left bundle branch block. This clinical presentation is sufficient to initiate prompt assessment and management as described in this document (N.B. confirmation of troponin elevation is not required before initiation of treatment, including reperfusion therapy).

Pre-Hospital STEMI Care	
1	• The Canadian Cardiovascular Working group[2] recently recommended that pre-hospital care of STEMI patients should be enhanced. In the setting of the Nova Scotia Emergency Health Services (EHS), paramedics are trained to perform protocol-based clinical assessment as well as pre-hospital ECGs. ECGS and reperfusion checklists (see *Appendix B*) should then be faxed or delivered to a designated emergency department physician for over-read. *[Class IIa, Level B[3]]*
2	• The emergency department physician should then direct further management of the STEMI patient as per District Health Authority (DHA)/EHS protocols. If the time from first medical contact to balloon inflation for primary percutaneous coronary intervention (PCI) is estimated to be >90 minutes, prompt thrombolysis is the preferred reperfusion strategy, provided there are no contraindications. *[Class I, Level B[3]]*
3	• Strategies to improve time to reperfusion in acute STEMI patients should be ongoing, including pre-hospital thrombolysis *[Class IIa, Level B]*[3] or direct activation of cardiac catheterization laboratory by EHS personnel where feasible.[4] *[Consensus Nova Scotia 2007]*

Diagnosis of STEMI	
4	**Clinical history and physical examination** • Obtain a clinical history and perform a physical examination immediately. The time of symptom onset and first medical contact should be documented. *[Class I, Level C[3]]*
5 **5a** **5b**	**ECG monitoring** • Establish continuous electrocardiogram (ECG) monitoring and secure venous access during initial assessment to facilitate rapid detection and treatment of arrhythmias. *[Class I, Level C[3]]* • Obtain a standard 12-lead ECG within 10 minutes of first medical contact. *[Class I, Level C[3]]* Additional leads, e.g. posterior or right-sided leads, should be considered as indicated. **Patients diagnosed with acute STEMI should be triaged for urgent treatment, including reperfusion therapy (i.e. thrombolytic therapy or PCI)**. (See *Reperfusion therapy*, page 7.) A repeat ECG should be obtained 90 minutes after thrombolysis to assess success of thrombolysis. Additional ECG assessments should be obtained at approximately 6 hours and 24 hours after admission, or as indicated based on symptoms. *[Consensus Nova Scotia 2007]*
6	**Troponin measurement** • Obtain blood for troponin measurement on presentation, and other key blood work (e.g. glucose, creatinine, complete blood count) as soon as possible after ECG is obtained. If the initial troponin is not elevated then the measurement should be repeated 6–12 hours later, as levels may not rise for several hours after onset of symptoms. **Confirmation of troponin elevation is not required before initiation of reperfusion therapy.** *[Class I, Level C[3]]*
7	**Imaging investigations** • A chest X-Ray should be performed in the majority of patients and other investigations considered as appropriate to the clinical circumstances (e.g. computed tomography (CT) imaging, echocardiography). **Additional imaging investigations should not delay treatment, including reperfusion.** *[Consensus Nova Scotia 2007]*

Immediate Treatment of Suspected STEMI	
8	**Oxygen** • Oxygen (O_2) should be administered immediately (2–6 L/min) to patients with suspected STEMI who have evidence of respiratory distress or hypoxemia (O_2 saturation <90%). *[Class I, Level B[3]]*
9 **9a** **9b**	**Antiplatelet therapy** • Acetylsalicylic acid (ASA) (160–325 mg non-enteric coated (EC) oral loading dose, followed by 81 mg once daily [OD]) should be administered immediately to all patients with suspected STEMI who do not have contraindications to ASA therapy and who have not been taking aspirin previously. *[Class I, Level C[3]]* Patients with contraindications to ASA, regardless of age, should be treated immediately with clopidogrel (300-mg oral loading dose). *[Class IIa, Level C[3]]* • In addition to ASA, all STEMI patients undergoing primary PCI *[Class I, Level A[3]]* and STEMI patients <75 years of age receiving thrombolysis *[Class IIa, Level C[5]]* should receive an immediate 300 mg loading dose of clopidogrel. STEMI patients >75 years of age receiving thrombolysis should receive an immediate dose of 75 mg of clopidogrel.[6] *[Consensus Nova Scotia 2007]*
10	**Nitroglycerin** • Nitroglycerin (0.3–0.6 mg every 5 minutes; total of 3 doses) should be administered sublingually (spray or tablet) to hemodynamically stable patients (i.e. in those with stable blood pressure [BP]) with suspected STEMI and continuing symptoms, in the absence of contraindications. Intravenous (IV) nitroglycerin (10–200 µg/min infusion) can be considered in patients with continuing symptoms, despite administration of O_2, sublingual nitroglycerin and a beta blocker. *[Class I, Level C[3]]*

11	**Beta blocker therapy** • Oral beta blocker therapy should be initiated within 24 hours for most STEMI patients who have no evidence of heart failure, low output state or other relative contraindication to using beta blocker therapy, and continued throughout the hospital stay and after discharge in the majority of definite STEMI patients without contraindications. *[Class I, Level B[5]]* (See *Beta blocker therapy*, page 15.) Administration of an IV beta blocker should be considered in patients with suspected STEMI who are hypertensive or have ongoing chest discomfort and who do not have contraindications to such treatment. *[Class IIa, Level B[5]]*
12	**Morphine** • Morphine (2–4 mg IV or subcutaneously [SC]) or other opiate analgesics (e.g. meperidine) can be considered in hemodynamically stable patients with suspected STEMI and continuing severe symptoms despite administration of O_2, nitroglycerin and a beta blocker. *[Class I, Level C[3]]*

Additional Immediate and Subsequent Inpatient Treatment of STEMI	
13	**Reperfusion therapy**
13a	• All patients with acute STEMI should be assessed promptly for reperfusion therapy. *[Class I, Level A[3,7]]* Assuming no contraindications exist, options for reperfusion therapy include **primary PCI or thrombolytic therapy**. (See *Table 1*, page 10.)
13b	• All DHAs should have a written protocol that guides EHS system personnel in determining where to take patients with suspected or confirmed STEMI to facilitate timely delivery of reperfusion therapy. *[Class I, Level C[3]]* (See *Appendix D* and *Appendix E.*)
13c	***PCI therapy*** • **Primary PCI** should be considered in the following situations in the absence of procedural contraindications (See *Table 1*, page 10): – Primary PCI is the option of choice for acute STEMI patients with cardiogenic shock presenting *[Class I, Level A[5]; Class I, Level C[7]]* anywhere in Nova Scotia. **In cases of cardiogenic shock associated with STEMI, notify the Ventricular Assist Device Team directly by telephone: 902-223-0715** – Primary PCI should be considered for all STEMI patients who have contraindications to thrombolytic therapy *[Class I, Level B[3]; Class I, Level C[7]]* and should ideally be carried out within 12 hours of symptom onset. – Primary PCI should be considered for other acute STEMI patients, provided there is a high likelihood of balloon inflation within 90 minutes of first medical contact and within 12 hours of symptom onset. *[Class I, Level B[3,7]]* For patients who require transportation, the maximum time from first medical contact to arrival at the cardiac catheterization laboratory should ideally not exceed 60 minutes. *[Consensus Nova Scotia 2007]* (See *Appendix E.*) **How to arrange a primary PCI** Day: Call the cath lab: 902/473-6532 / 473-6633 Evening: Page the interventional cardiologist on call: 902-473-2222 (See *Appendix E*)

13d	***Thrombolytic therapy*** • Thrombolytic therapy should be considered in the following situations, in the absence of contraindications (See *Table 1*, page 10): – **Acute STEMI patients** who present to a facility without access to primary PCI within 90 minutes of first diagnostic ECG should receive thrombolytic therapy with a target door to needle time of ≤30 minutes unless contraindicated. *[Class I, Level B[5]; Class I, Level A[7]]* – A repeat ECG 90 minutes after administration of thrombolytic therapy is recommended to assess the adequacy of reperfusion. – Patients given thrombolytic therapy should be treated promptly with an antithrombin agent and continued on the agent for a minimum of 48 hours. *[Class1, Level C[5]]* (See *Antithrombin therapy*, page 11.) – **Recurrent ST-segment elevation after successful thrombolysis:** If after initially successful thrombolysis, a STEMI patient has recurrent ischemic symptoms lasting ≥15–30 minutes associated with recurrent ST-segment elevation, the treatment of choice is emergent referral for possible **rescue PCI**. o In this situation, page the interventional cardiologist on-call at the QEII Health Sciences Centre (telephone: 902-473-2222) for further advice on management. o However, if rescue PCI is not available within 60–90 minutes, then repeat thrombolysis is a reasonable alternative; in this situation a fibrin-specific agent is preferred (e.g. tenecteplase [TNK]). ▪ It should be noted that low-risk (e.g. uncomplicated inferior) STEMI patients may not benefit from rescue PCI or repeat thrombolysis. There is no role for routine use of glycoprotein IIb/IIIa inhibitors in STEMI patients with recurrent ST-segment elevation unless the patient is being referred for cardiac catheterization and an interventional cardiologist directs its use.[8,9] *[Consensus Nova Scotia 2007]*

	– **Persistent ST-segment elevation after thrombolysis***:* There is no role for repeat thrombolysis in acute STEMI patients with <50% resolution of ST-segment elevation 90 minutes after initial thrombolytic therapy. o In this situation the treatment of choice is emergent referral for possible rescue PCI, provided that initial symptom onset to balloon time is predicted to be <12 hours. *[Class IIa, Level B[5,7]]* It should be noted that low-risk patients – e.g. uncomplicated inferior STEMI patients – may not benefit from rescue PCI. The on-call interventional cardiologist at the QEII Health Sciences Centre should be paged (telephone: 902-473-2222) for further advice on management of failed thrombolysis. (See *Appendix G*.)

KEY TELEPHONE NUMBERS

- **To call the cath lab (day):** 902-473-6532 or 473-6633
- **To page the interventional cardiologist on call:** 902-473-2222
- **To call the Ventricular Assist Device Team:** 902-223-0715

Table 1. Contraindications to primary PCI and thrombolytic therapy

Relative contraindications to primary PCI

- Known terminal co-morbidity/ies expected to limit lifespan <1 year (i.e. lung disease, malignancy)
- Unable to obtain consent from patient or family member
- Moderate to severe dementia
- Known creatinine >200 umol/L or on dialysis
- Prior coronary artery bypass graft (CABG) – unless contraindication to thrombolysis
- Known peripheral arterial disease (PAD) – unless contraindication to thrombolysis **with** palpable femoral pulse

Contraindications to thrombolytic therapy[3]

Absolute contraindications

- Any prior intracranial hemorrhage
- Known structural cerebral vascular lesion (e.g. arteriovenous malformation)
- Known malignant intracranial neoplasm (primary or metastasic)
- Ischemic stroke within 3 months, **except** acute ischemic stroke within 3 hours
- Suspected aortic dissection
- Active bleeding or bleeding diathesis (excluding menses)
- Significant closed head or facial trauma within 3 months

Relative contraindications

- History of chronic severe poorly controlled hypertension
- Severe uncontrolled hypertension on presentation (systolic BP >180 or diastolic BP >110 mm Hg)
- History of prior ischemic stroke >3 months ago, dementia, or known intracranial pathology not covered in contraindications
- Traumatic or prolonged (>10 minutes) cardiopulmonary resuscitation (CPR) or major surgery (within 3 weeks)
- Recent (within 2–4 weeks) internal bleeding
- Noncompressible vascular punctures
- For streptokinase/anistreplase: prior exposure (>5 days ago) or prior allergic reaction to these agents
- Pregnancy
- Active peptic ulcer
- Current use of anticoagulants: higher international normalized ratio (INR) confers a higher risk of bleeding

14	**Antiplatelet therapy**
14a	• ASA (81 mg/day) should be continued throughout the hospital stay and indefinitely post discharge in all patients with definite STEMI and no contraindications. *[Consensus Nova Scotia 2007]*
14b	• Clopidogrel should be administered in addition to ASA in all STEMI patients undergoing primary PCI (300-mg minimal oral loading dose, followed by 75 mg OD). *[Class I, Level A[3]]* The subsequent duration of treatment will depend on the type of stent used and patient risk profile:[10] minimum 1 month post bare metal stent; minimum 12 months post drug-eluting stent. *[Consensus Nova Scotia 2007]*
14c	• Clopidogrel should be administered in addition to ASA in all STEMI patients treated with thrombolysis (300-mg oral loading dose, followed by 75 mg OD for the duration of hospitalization up to a maximum of 28 days. **Note: 300-mg loading dose should be omitted in patients >75 years**[6] *[Consensus Nova Scotia 2007]*
14d	• In patients who subsequently undergo PCI, the duration of clopidogrel treatment will depend on the type of stent used (as above).[10] *[Consensus Nova Scotia 2007]*
15	**Antithrombin therapy**
15a	• For patients treated with thrombolytic therapy, antithrombin agents should be continued for a minimum of 48 hours. *[Class I, Level C[5]]* For patients undergoing primary PCI, antithrombin therapy should be given at the discretion of the interventional cardiologist.
15b	• **Enoxaparin** should be the antithrombin therapy of choice in STEMI patients with normal renal function treated with thrombolysis, in the absence of contraindications. *[Consensus Nova Scotia 2007]* (See *Appendix H* and *Appendix I*.)
15c	• The dose of enoxaparin should be adjusted according to patient age (as per EXTRACT-TIMI 25).[11] In patients undergoing primary PCI, an additional IV dose of enoxaparin may be required at the discretion of the interventional cardiologist: – **In patients <75 years of age**: administer a fixed 30-mg IV bolus, followed by SC injection of enoxaparin 1 mg/kg twice daily (BID). *[Class IIb, Level B[3]]* For the first 2 SC injections, the recommended maximum is 100 mg/dose.

	– **In patients ≥75 years of age**: omit IV bolus of enoxaparin; provide only an SC injection of enoxaparin of 0.75 mg/kg BID.[12] *[Consensus Nova Scotia 2007]* For the first 2 SC injections, the recommended maximum is 75 mg/dose.[12] *[Consensus Nova Scotia 2007]* – After patients have received the first 2 doses of enoxaparin, subsequent doses should not exceed 140 mg/dose based on actual body weight.
15d	• **Unfractionated heparin (UFH**): For patients with severe renal dysfunction (creatinine clearance [CrCl] <30 mL/minute) or concern about bleeding, UFH is a reasonable alternative to enoxaparin. *[Consensus Nova Scotia 2007]*
15e	• Dosing of UFH should be as follows: – IV loading dose of 60 IU/kg (maximum 4000 IU) – subsequent IV infusion of 12 IU/kg/hour (maximum 1000 IU/hour) *[Class I, Level C[3]]* – dosage adjustments of the nomograms to correspond to a therapeutic range equivalent to heparin levels of 0.2 to 0.5 U/mL by anti-factor Xa determinations, which correlate with activated partial thromboplastin time (aPTT) values between 50 and 70 seconds *[Class I, Level C[3]]* – The aPTT range may differ due to variation in laboratory methods used to determine aPTT. A locally approved nomogram for dosing adjustment should be followed. (See *Appendix J*.)
16	**Referral for cardiac catheterization in patients initially treated with thrombolysis**
16a	• Rescue PCI: Patients with acute STEMI who have either recurrent ST elevation after initially successful thrombolysis or incomplete (<50%) resolution of ST elevation 90 minutes after thrombolysis should be considered for emergent rescue PCI. *[Class IIa, Level B[5,7]]* (See *Appendix K*.)
16b	• Emergent cardiac catheterization is recommended after STEMI for patients with acute mechanical complications (e.g. papillary muscle rupture or ischemic ventricular septal defect) and those with recurrent ischemia, ventricular fibrillation/tachycardia, persistent bradycardia resistant to atropine, overt heart failure, or persistent hypotension. *[Class I, Level B[3]]* (See *Appendix K*.) **In cases of hypotension or severe refractory heart failure, notify the Ventricular Assist Device Team by telephone: 902-223-0715.**

16c **16d**	• Patients with high risk STEMI (e.g. extensive MI involving 2 territories [anterolateral, inferolateral, inferoposterior]) and who have responded well to the initial thrombolytic treatment may be considered for referral for cardiac catheterization **during the current hospitalization** without undergoing non-invasive risk stratification. *[Class I, Level B[3]]* • Patients with low-risk STEMI (e.g. isolated uncomplicated inferior STEMI) who have responded well to thrombolysis should undergo a non-invasive risk stratification test, such as an exercise tolerance test, prior to discharge to determine the requirement for cardiac catheterization. *[Class III, Level A[3]]*
17 **17a** **17b** **17c** **17d**	**Role of CABG surgery after STEMI** • Patients with STEMI and cardiogenic shock who have multi-vessel disease should be considered for emergent CABG and possibly left ventricular assist device implantation. *[Class IIa, Level B[3]]* (See *Appendix K*.) **Notify the Ventricular Assist Device team by telephone: 902-223-0715.** • Patients who undergo coronary angiography after STEMI and have anatomy suitable for CABG should be referred promptly for consideration for surgery. In particular, patients with critical left main or left main equivalent disease and multi-vessel disease with a reduced left ventricular ejection fraction (LVEF) should be considered for CABG. *[Class I, Level A[3]]* • Patients with mechanical complications after STEMI (i.e. papillary muscle rupture, ischemic ventricular septal defect) should be referred emergently for surgical management. *[Class IIa Level B[3]]* (See *Appendix K*.) • Clopidogrel should be withheld to reduce the risk of bleeding in patients who are deemed to require urgent bypass surgery. *[Class I, Level B[3]]*

18	**Treatment of hyperglycemia/diabetes**
18a	• Tight glycemic control is recommended for all STEMI patients presenting with hyperglycemia (random glucose >11.0 mmol/L or fasting blood glucose >7.0 mmol/L). During the first 48 hours there should be a low threshold for use of insulin to maintain a blood glucose of 7.0–10.0 mmol/L. After 48 hours, standard diabetes management is recommended, including oral antihyperglycemic agents and/or insulin as appropriate.[13,14] *[Consensus Nova Scotia 2007]*
18b	• Caution is recommended regarding the use of thiazolidinediones in patients with cardiovascular disease.[15]
18c	• Goals of long-term therapy should conform with the current Canadian Diabetes Association guidelines:[16] fasting blood glucose 4.0–7.0 mmol/L and glycated hemoglobin (A1C) ≤7.0%, if achievable safely. *[Consensus Nova Scotia 2007]*

Pharmacologic Secondary Preventive Therapy	
19 **19a**	**Antiplatelet therapy** • ASA (81–325 mg daily) should be continued indefinitely in all STEMI patients without contraindications. *[Class I, Level B[3]; Class I, Level A[3]]* The dose of ASA should be minimized (81 mg daily) in patients also taking clopidogrel or warfarin, to help reduce the risk of bleeding complications.
19b	• Clopidogrel (75 mg OD), in addition to ASA, is recommended on discharge in the absence of contraindications for all STEMI patients who undergo PCI with stent implantation. The duration of clopidogrel therapy should be tailored according to the type of stent used: minimum 1 month post bare metal stent; minimum 12 months post drug-eluting stent.[10] *[Consensus Nova Scotia 2007]*
20	**Beta blocker therapy** • Beta blocker therapy should be initiated early (see *Immediate Treatment of Suspected STEMI*, page 5) and continued long term, unless contraindicated. *[Class I, Level A[3,7]]* (See *Appendix L*.)
21 **21a**	**Lipid-lowering therapy** • HMG co-A reductase inhibitors (statins) are recommended in the majority of STEMI patients. *[Class I, Level A[3,7]]* A baseline fasting lipid panel should be obtained in all STEMI patients within 24 hours of admission. *[Class I, Level A[3]]*
21b	• Moderate statin therapy should be started within 24 hours of admission.[17] *[Consensus Nova Scotia 2007]*
21c	• The choice of statin and the dose initiated *(*see *Appendix L)* should take into consideration the long-term lipid targets for patients with established coronary artery disease (CAD) recommended by the Canadian Cardiovascular Society in its 2006 Dyslipidemia Position Statement[18] *[Consensus Nova Scotia 2007]:* – *Primary target*: low-density lipoprotein cholesterol (LDL-C) <2.0 mmol/L. – *Secondary targets*: Total cholesterol (TC) to high-density lipoprotein cholesterol (HDL-C) ratio <4; in patients with established atherosclerosis, treatment to lower LDL-C by at least 50% is generally appropriate.

21d	• Fasting lipid values and liver function tests should be checked 1–2 months after discharge, and the dose of statin titrated accordingly in the absence of side effects or other evidence of drug toxicity. Some patients may require combination therapy with other agents, such as ezetimibe, niacin, or fibrates to achieve their target lipid values.
22	**ACE inhibitor or ARB therapy**
22a	• Multiple studies have confirmed the beneficial effect of angiotensin-converting enzyme (ACE) inhibitors in patients with acute STEMI. Only one study has demonstrated equivalency of the angiotensin receptor II agonist (ARB) valsartan and the ACE inhibitor captopril in acute STEMI. Consequently, ACE inhibitors should generally be favoured over ARBs unless contraindications exist or side effects occur. *[Consensus Nova Scotia 2007]*
22b	• All STEMI patients should have an ACE inhibitor started orally within 24 hours if hemodynamically stable and no contraindications. *[Class I, Level A[3,7]]* The choice and dose of ACE inhibitor should be evidence-based. (See *Appendix L*.)
22c	• In the absence of contraindications, long-term treatment with an ACE inhibitor is recommended in STEMI patients with: – congestive heart failure (CHF) during hospitalization or LVEF <40% – diabetes – hypertension – extensive CAD – definite PAD or cerebrovascular disease
22d	• Long-term ACE inhibitor therapy may not be appropriate or necessary in low-risk patients, e.g. normotensive, non-diabetic patients with preserved LVEF (i.e. LVEF >40%) and minor CAD.[19] *[Consensus Nova Scotia 2007]*
22e	• STEMI patients with contraindications to, or who are intolerant of, ACE inhibitors, and who are felt to be at increased risk of adverse events, can be considered for treatment with an ARB. There is evidence that valsartan at a target dose of 160 mg BID is as effective as captopril 50 mg three times daily (TID).[20] *[Consensus Nova Scotia 2007]* (See *Appendix L*.)

23	**Other pharmacologic therapies** • In patients with chronic musculoskeletal or other pain, the requirement for analgesic therapy should be assessed prior to discharge. Acetaminophen, ASA and small doses of narcotics are the preferred analgesic options *[Class I, Level C[5]]* but nonsteroidal anti-inflammatory drugs (NSAIDs) with increasing degrees of cyclooxygenase 2 (COX-2) selectivity should be avoided. *[Class III, Level C[5]]*

Non-pharmacologic Secondary Preventive Therapy	
24 **24a**	**Smoking cessation** • Cigarette smokers should be urged to quit to reduce their risk of recurrent cardiac events and death. Exposure to second-hand smoke should also be avoided. *[Class I, Level B[3]; Class I, Level C[7]]* Active counselling (the "5 A's": Ask, Advise, Assess, Assist, Arrange) regarding quitting strategies, and local smoking cessation program information and adjunctive pharmacologic interventions should be provided.
24b	• Referral to a local smoking cessation program should be arranged: – The Canadian Cancer Society's help line (toll-free 1-877-513-5333) provides information about smoking cessation and available community services. – The Nova Scotia Lung Association's Quit4good contact number is 1-888-566-5864. – The website www.addictionservices.ns.ca contains a map of DHAs that offer smoking cessation programs.
25 **25a**	**Diabetes education** • STEMI patients with diabetes should be offered initial and ongoing needs-based diabetes education in a timely manner to enhance self-care practices and behaviours.[16] *[Consensus Nova Scotia 2007]*
25b	• Referral to a Diabetes Education Centre (DEC) for ongoing education and management of diabetes and cardiac risk factors is recommended. Visit www.diabetescareprogram.ns.ca for DEC locations in Nova Scotia.
26	**BP control** • Lifestyle changes, in particular weight loss and regular exercise, are an important component of BP management. *[Class I, Level B[3]]* Target BP is <140/90 mm Hg, except in patients with diabetes or chronic kidney disease, in whom the target BP is ideally <130/80 mm Hg.

27	**Nutrition intervention**
27a	• A heart-healthy diet is recommended. Such a diet is limited in sodium (<2.4 grams/day), cholesterol (<200 mg/day) fat (<25–35% of total energy intake), saturated and trans fats (<7%), increased in monounsaturated (up to 20%) and polyunsaturated fats (up to 10%), increased in fruits and vegetables and limited in carbohydrates. *[Class I, Level B[3,7]]* Other therapeutic diet modifications may be needed according to comorbidities; written nutrition information to this effect should be provided.
27b	• Patients should be encouraged to achieve and maintain a healthy weight (body mass index [BMI] 18.5–24.9 kg/m^2) and waist circumference (<102 cm men; <88 cm women). Overweight and obese patients should be offered support and advice. Dietary energy content should be aimed at reducing body weight by ~10% from baseline. *[Class I, Level B[3]]* With success, further weight loss can be attempted to achieve a BMI of <27 kg/m^2 and ideally<25 kg/m^2.
27c	• A clinical dietitian should be consulted for a comprehensive nutrition assessment in nutritionally compromised patients requiring nutrition support/intervention.
28	**Exercise**
28a	• Assessment of functional capacity and ability to return to normal activities and employment is recommended 4–6 weeks post-discharge. A treadmill exercise test or equivalent non-invasive test should be considered within this time frame in the majority of patients.
28b	• Regular, moderate-intensity aerobic exercise (e.g. brisk walking) for 30–60 minutes most days of the week is recommended. *[Class I, Level B[3]]* Exercise training in a medically supervised environment should be considered for moderate- and high-risk patients.[21] *[Consensus Nova Scotia 2007]*
29	**Secondary prevention programs for cardiovascular disease**
29a	• DHAs are encouraged to explore integrated, chronic disease management programs consistent with Nova Scotia's Chronic Disease Management Strategy. *[Consensus Nova Scotia 2007]*
29b	• Secondary prevention programs are recommended, particularly for patients with multiple modifiable risk factors and for moderate- to high-risk patients in whom supervised exercise training is warranted. *[Class I, Level C[3]]*

29c	• Referral to secondary prevention programs should be arranged prior to hospital discharge. Program entry should be within the preferable recommended time frame of 30 days.[22] *[Consensus Nova Scotia 2007]*

Other Aspects of Treatment Follow-Up	
30	**Role of the family physician** • It is anticipated that family physicians will play a central role in long-term follow up: – Promoting risk factor modification by ensuring that acute coronary syndrome (ACS) patients receive appropriate lifestyle counselling. – Providing evidence-based secondary preventive drug therapy. Family physicians should ensure that drug doses are evidence-based and titrated when appropriate, in pursuit of recommended glycemic, BP and lipid targets. *[Class I, Level C[3]]*(See *Appendix M.*)
31	**Education regarding activities of daily living** • Patients should be given specific instruction about daily activities that are permissible and those that should be avoided. Specific recommendations should be made regarding driving, return to work and sexual activity. *[Class I, Level C[5]]*
32	**Screening for depression** • Depression is common, frequently under-recognized and correlates with a poorer prognosis in ACS patients. Specialists and family physicians should screen for depression and refer/treat accordingly. *[Class I, Level C[3]]*
33	**Influenza vaccination** • As recommended by Health Canada,[23] the majority of patients with CAD should receive annual influenza vaccination. *[Consensus Nova Scotia 2007]*
34 **34a** **34b**	**Indications for automatic implantable cardioverter defibrillators** • Patients who develop spontaneous ventricular fibrillation or sustained ventricular tachycardia in the absence of ischemia 48 hours after their acute STEMI should be referred for consideration of automatic implantable cardioverter defibrillator (AICD) implantation. *[Class I, Level A[3]]* • Patients with markedly reduced LVEF (LVEF<30%) >1 month after a MI should be referred for assessment of AICD implantation. *[Class IIa, Level A]*[24] Patients with EF 31–35% at least 1 month after MI may also be considered for AICD implantation, although its benefit is less well demonstrated in this population. *[Class IIa, Level B[3]]*

ABBREVIATIONS

AICD	automatic implantable cardioverter defibrillator
A1C	glycated hemoglobin / hemoglobin A1C
ACC	American College of Cardiology
ACE inhibitor	angiotensin-converting enzyme inhibitor
ACS	acute coronary syndrome
AHA	American Heart Association
aPTT	activated partial thromboplastin time
ARB	angiotensin receptor II agonist
ASA	acetylsalicylic acid (aspirin)
BID	twice daily
BMI	body mass index
CABG	coronary artery bypass graft
CAD	coronary artery disease
CBC	complete blood count
CCU	chronic care unit
CHF	congestive heart failure
COX-2	cyclooxygenase 2
CPR	cardiopulmonary resuscitation
CrCl	creatinine clearance
CT imaging	computed tomography imaging
DEC	Diabetes Education Centre
DHAs	District Health Authorities
DOB	date of birth
EC	enteric coated
ECG	electrocardiogram
ED	emergency department
EHS	Emergency Health Services
ESC	European Society of Cardiology
HDL-C	high-density lipoprotein cholesterol
HIT	heparin-induced thrombocytopenia
ICH	intracranial hemorrhage
ICU	intensive care unit
INR	International Normalized Ratio
IV	intravenous
LDL-C	low-density lipoprotein cholesterol
LVEF	left ventricular ejection fraction
MI	myocardial infarction
NSAIDs	nonsteroidal anti-inflammatory drugs
O_2	oxygen
OD	once daily
PAD	peripheral arterial disease
PCI	percutaneous coronary intervention
PO	per os (by mouth, orally)

PTT/PT	partial thromboplastin time/prothombin test
PVD	peripheral vascular disease
SC	subcutaneous
SR	sustained release
STEMI	ST elevation myocardial infarction
TC	total cholesterol
TID	three times daily
TNK	tenecteplase
UFH	unfractionated heparin

TRIAL/STUDY ACRONYMS

4-S[25]	Scandinavian Simvastatin Survival Study
AIRE[26]	Acute Infarction Ramipril Efficacy
ASCOT[27]	Anglo-Scandinavian Cardiac Outcomes Trial
ATLAS[28]	Assessment of Treatment with Lisinopril and survival
A to Z[29]	Aggrastat To Zocor
CARE [30]	Cholesterol and Recurrent Events
CONSENSUS[31]	Cooperative North Scandinavian Enalapril Survival Study
EUROPA[32]	European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease
Extract TIMI 25[11]	Enoxaparin Versus Unfractionated Heparin with Fibrinolysis for ST Elevation MI
GISSI-3[33]	Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico
HOPE[34]	Heart Outcomes Prevention Evaluation Study

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Appendix A. Grading of Evidence: Class and Level

Class	ACC/AHA (2004)[1] ACC/AHA (2007)[2]	ESC STEMI (2003)[3]	CCS (2004)[4]
I	Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective	Evidence and or general agreement that a given diagnostic procedure/ treatment is beneficial, useful and effective	Evidence and/or general agreement that a given diagnostic procedure or treatment is beneficial, useful and effective
II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the treatment	Conflicting evidence and/or a divergence of opinion about the usefulness and/or efficacy of the treatment
IIa	Weight of evidence/ opinion in favour of usefulness/efficacy	Weight of evidence/ opinion is in favour of usefulness/efficacy	Weight of evidence in favour
IIb	Usefulness/efficacy is less well established by evidence/opinion	Usefulness/efficacy is less well established by evidence/opinion	Usefulness and/or efficacy less well established
III	Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful	Category does not exist	Evidence that the treatment is not useful and, in some cases, may be harmful
Level	**ACC/AHA (2004)[1] ACC/AHA (2007)[2]**	**ESC (2003)[3]**	**CCS (2004)[4]**
A	Data derived from multiple randomized clinical trials or meta-analyses	Data derived from multiple randomized clinical trials or meta-analyses	Data derived from multiple randomized controlled trials or meta-analyses
B	Data derived from a single randomized trial or nonrandomized studies	Data derived from a single randomized trial or large nonrandomized studies	Data derived from a single randomized controlled trial or large, nonrandomized studies
C	Only consensus opinion of experts, case studies or standard of care	Consensus of opinion of the experts and/or small studies, retrospective studies, registries	Consensus of opinion by experts and/or small studies, retrospective studies or registries

The notification "Consensus Nova Scotia 2007" is used to indicate those recommendations based on the decisions of the provincial expert consensus panel. Literature/citations that informed the panel as they came to consensus are referenced. Statements that reflect routine medical care or practices are not graded.

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Appendix B. Criteria for Definition of MI[1]

Acute, evolving or recent MI

Either one of the following satisfies the diagnosis for an acute, evolving or recent MI:

A. Typical rise and gradual fall in troponin associated with at least one of the following:
   - ischemic symptoms;
   - development of pathological Q waves on the ECG;
   - ECG changes indicative of ischemia; or
   - coronary artery intervention e.g. coronary stenting.

B. Pathologic findings of an acute MI.

Established MI

Either one of the following satisfies the diagnosis for established MI:

A. Development of new pathological Q waves on serial ECGs. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized depending on the length of time that has passed since the infarct developed.

B. Pathologic findings of a healed or healing MI.

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Appendix C. Emergency Health Services Reperfusion Checklist

Age	PCR No.

MM DD YY	PATIENT SURNAME	FIRST NAME AND MIDDLE INITIAL

*Please complete and sign for all male and non-pregnant female patients presenting with signs and symptoms of acute coronary syndrome. For patients to be considered all inclusion criteria must be marked as a **"YES"** and all exclusion criteria must be marked as a **"NO"***

SYMPTOM ONSET		**(place X)**
TIMES OF ONSET _____ : _____	(hours) 0....1....2....	3...4...5...6...7...8....9...10...11...12...

ECG	**(circle one)**	
1. ECG transmission attempted	YES	NO
2. ECG transmission successful	YES	NO
3. Number of attempts	1	2+
HIGH RISK IDENTIFIED	**(circle one)**	
1. Pulmonary edema (Killip III) or cardiogenic shock (Killip IV)	YES	NO
2. HR >100 or SBP <100 mm Hg	YES	NO
3. Inferior MI with bradycardia (HR <50)	YES	NO
4. Anterior MI with ST elevation in ≥4 leads or >4 mm ST elevation in any anterior lead	YES	NO
INCLUSION CRITERIA	**(circle one)**	
1. Symptoms lasting longer than 20 minutes with last 12 hours	YES	NO
2. a. 2 mm of ST elevation in ≥2 contiguous precordial leads; or b. 1 mm ST elevation in ≥2 limb leads; or c. A presumably new LBBB?	YES	NO
EXCLUSION CRITERIA Fibrinolysis	**(circle one)**	
1. Active bleeding or known bleeding/clotting disorder or on blood thinners (warfarin?)	YES	
2. Recent (within 6 weeks) major trauma, surgery (including laser eye surgery), GI/GU bleed	YES	NO
3. History of stroke, TIA, severe dementia or structural CNS damage (tumour, AV malformation or aneurysm)?	YES	NO
4. Significant closed head/facial trauma within the last three (3) months?	YES	NO
5. Significant hypertension (SBP >180 or DsBP >110 mm Hg) at any time from presentation	YES	NO
6. Right arm vs. Left arm SBP difference of 15 mm Hg	YES	NO
7. Prolonged (>10 minutes) CPR?	YES	NO
8. Serious systemic disease/terminal comorbidity that will limit lifespan <1 year	YES	NO
EXCLUSION CRITERIA PCI	**(circle one)**	
1. Serious systemic disease/terminal comorbidity	YES	NO
2. Severe dementia	YES	NO
3. On dialysis	YES	NO
4. Prior CABG – unless contraindication to thrombolysis	YES	NO
5. Known PVD. However, if patient is contraindicated for thrombolysis and has adequate arterial access/femoral pulse – Answer No	YES	NO

SIGNATURE OF ATTENDING PARAMEDIC	REG. NUMBER	NAME OF ATTENDING PARAMEDIC (PLEASE PRINT)	SIGNATURE OF SUPPORTING PARAMEDIC	REG. NUMBER	NAME OF SUPPORTING PARAMEDIC (PLEASE PRINT)

ATTACH AN EKG STRIP ON THE REVERSE OF EACH COPY (WHITE, PINK, YELLOW)

White – billing Yellow – Hospital Pink – Auditors

Form Rev. 01/06

Appendix D. Principles for Non-cath Lab Districts to Consider Regarding Primary PCI Reperfusion Protocol Development

Transport conditions to support local facility bypass:
Reasonable assurance that patients will be transported to QEII Health Science Centre by EHS charter in ≤60 minutes.

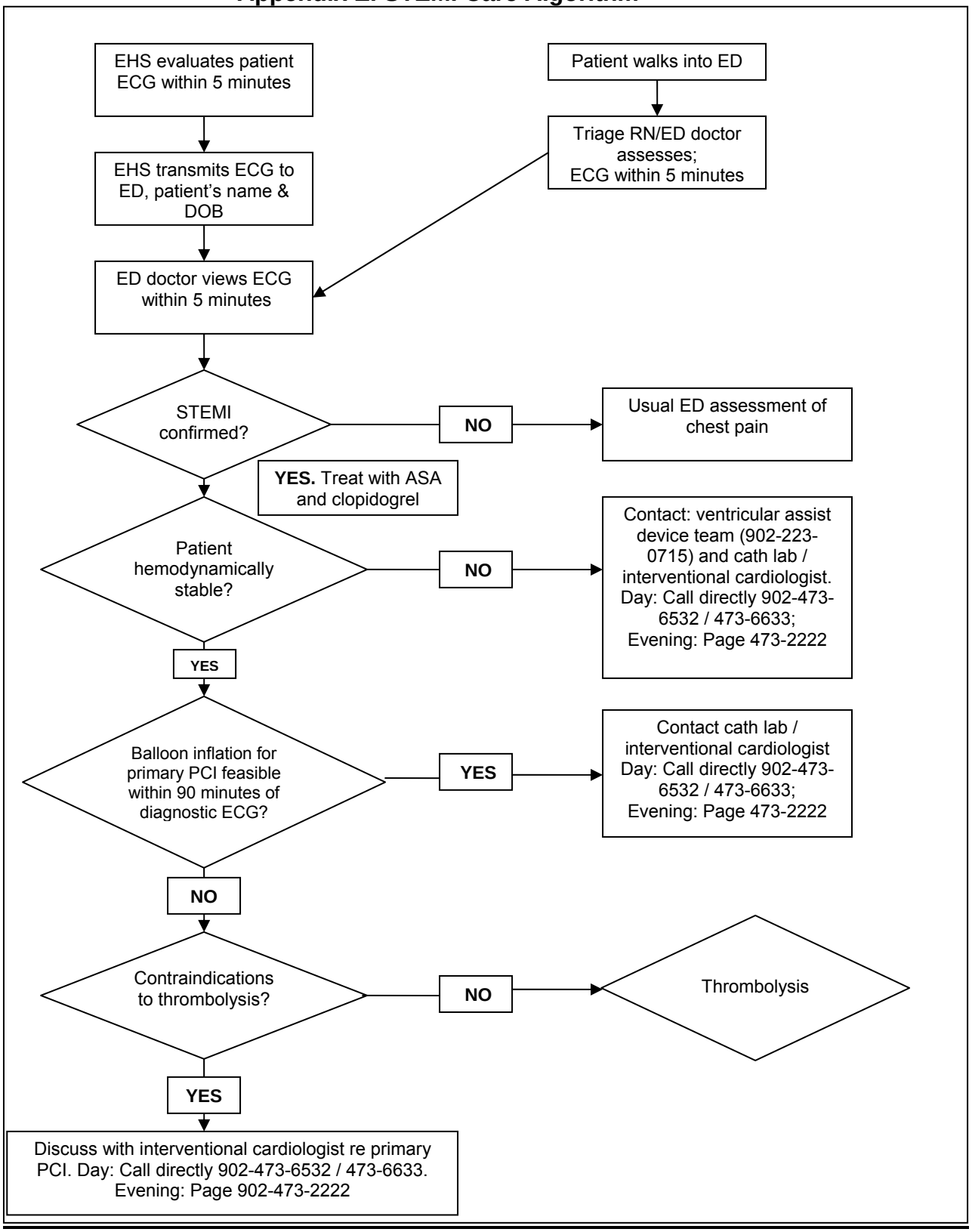
Policy to deal with weather conditions:
For example, if weather affects ability to get to PCI centre on time, thrombolysis may have to be considered.

Repatriation policy to support a local primary PCI strategy:
Guaranteed repatriation policy for uncomplicated STEMI patients within 24 hours.

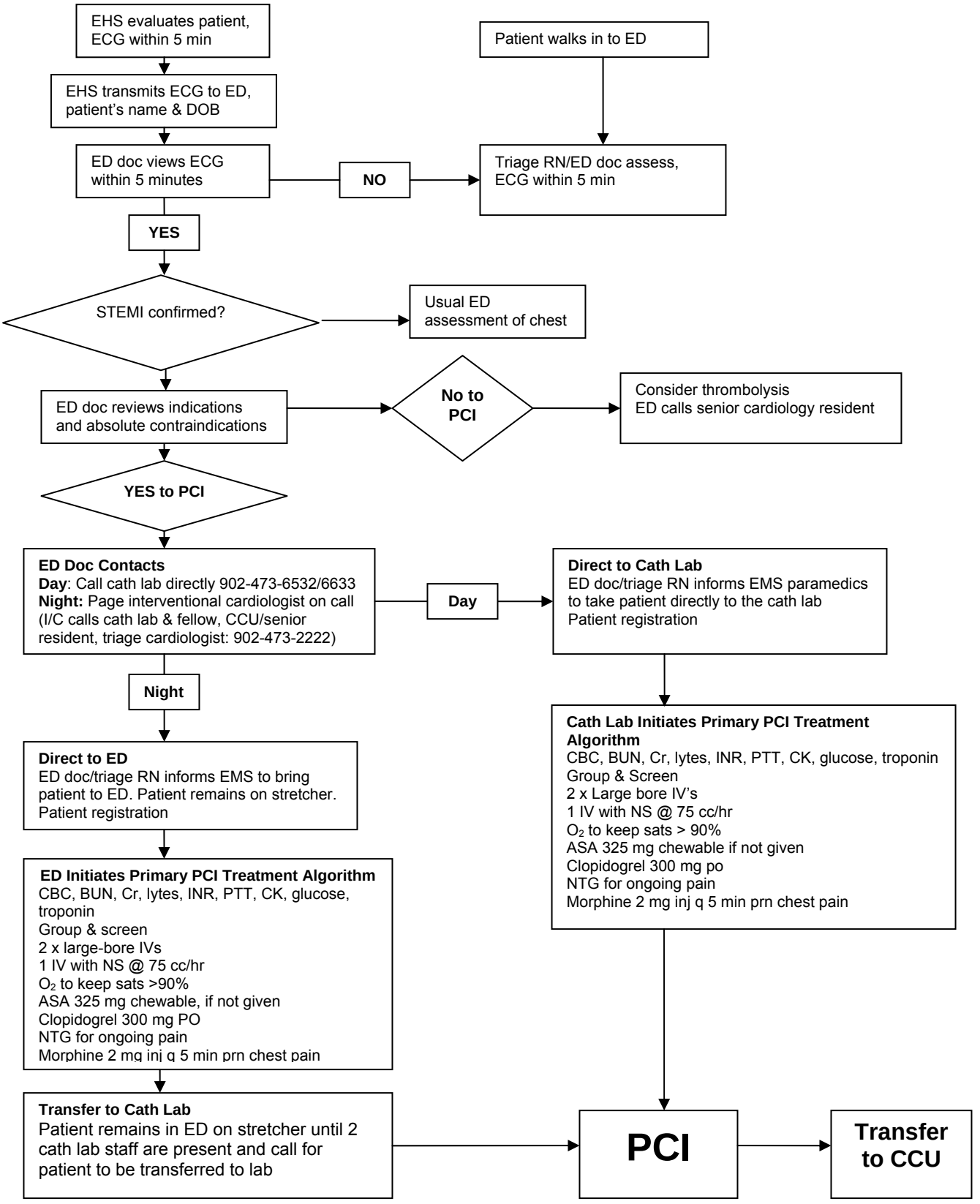
Post-MI access to secondary prevention/chronic disease management programs:
Access to secondary prevention program in view of short hospital stay at the QEII and no in-hospital education at the QEII.

EHS capacity to confirm STEMI through ECGs, activate cath lab, and bypass local facilities.

Appendix E. STEMI Care Algorithm



Appendix F. QEII Health Sciences Centre STEMI Primary PCI Care Map, Hours: 24/7



Appendix G. Sample TNK Protocol for STEMI

Contraindications to thrombolytic therapy

Absolute contraindications

- ❒ Any prior intercranial hemorrhage (ICH)
- ❒ Known structural cerebral vascular lesion (e.g. arteriovenous malformation)
- ❒ Known malignant intracranial neoplasm (primary or metastasic)
- ❒ Ischemic stroke within 3 months **except** acute ischemic stroke within 3 hours
- ❒ Suspected aortic dissection
- ❒ Active bleeding or bleeding diathesis (excluding menses)
- ❒ Significant closed head or facial trauma within 3 months

Relative contraindications

- ❒ History of chronic severe poorly controlled hypertension
- ❒ Severe uncontrolled hypertension on presentation (SBP >180 or DBP >110 mm Hg)
- ❒ History of prior ischemic stroke greater than 3 months, dementia, or known intracranial pathology not covered in contraindications
- ❒ Recent (within 2–4 weeks) internal bleeding
- ❒ Noncompressible vascular punctures
- ❒ Pregnancy
- ❒ Active peptic ulcer
- ❒ Current use of anticoagulants: the higher the INR, the higher the risk of bleeding

The following orders:

1. May be used on Cardiology Unit/Chronic Care Unit (CCU)/Intensive Care Unit (ICU) or Emergency Department and will be carried out by a qualified health professional **only on the authority of a physician**.
2. All orders to be carried out must be **checked/completed** as appropriate.
3. All dates must be written **yyyy/mm/dd.** All times must be on the 24-hour clock **(hh/mm)**.

1. Vital signs

- ❒ Baseline, then q15 min x 3h after initiation of TNK, then q30 min x 2h, then, q1h x 24h

2. Neurological signs

- ❒ Baseline and q4h x 24h
- ❒ Stated height ____ (cm) and weight ___ (kg) prior to TNK administration

3. ECG

- ❒ pre-nitroglycerin ❒ post-nitroglycerin ❒ continuous ECG monitoring

4. Blood work

- ❒ BC stat ❒ PT, INR, PTT stat ❒ Creatinine stat
- ❒ CK stat ❒ Group and screen ❒ Electrolytes stat
- ❒ Glucose stat ❒ Troponin stat

5. IV sites

Start 2 IV sites (do not delay TNK administration while awaiting second IV site access):

❒ normal saline TKVO

❒ saline lock opposite arm, flush 1 mL normal saline q12h IV and after medications

6. ASA

mg (160–325 mg) by mouth (PO) chew stat, then EC ASA _____ mg PO daily

7. O_2

❒ O_2 40% face mask ❒ O_2 100% face mask or ❒ _____

8. Administer TNK as follows:

❒ Reconstitute 50 mg vial of TNK with 10 mL sterile water (5 mg/mL). Swirl slowly; do not shake.

❒ TNK dose _____ mg to be given IV push over 5 seconds using weight-based dosing chart (**maximum dose = 50 mg);** follow with 10 mL saline flush.

TNK dosing		
Patient weight (kg)	*TNK (mg)*	*Volume TNK to be administered (mL)*
<60	30	6
60 to 69	35	7
70 to 79	40	8
80 to 89	45	9
≥90	50	10

N.B. TNK Is not compatible with dextrose. IV line to be flushed with saline prior to and after administration of TNK.

9. Anticoagulation

❒ Discontinue previous heparin/warfarin orders

AND

❒ Preferred antithrombin for patients with estimated CrCl ≥30 mL/min or weight ≤140 kg is enoxaparin. Use post-thrombolysis enoxaparin protocol (See *Appendix H*.)

OR

❒ For patients with estimated CrCl <30 mL/min or weight >140 kg use post-thrombolysis heparin infusion protocol (See *Appendix I*) for STEMI

Physician's Signature: _____ Date (YYYY/MM/DD): _____

Physician's Name: _____ CPSNS No. _____

Appendix H. CrCl Calculations

- Ideal body weight (IBW) (kg) = 0.9 (Ht [cm] – 150) (+50, male; +45, female)
- Estimate CrCl (mL/min):

Male: $\frac{(140 - \text{age}) (\text{IBW kg}) (60)}{(\text{Serum creatinine } \mu\text{mol/L}) (50)}$

Female: 0.85 x male CrCl value

<30 mL/min is equivalent to severe renal insufficiency

Appendix I. Sample Post-thrombolysis Enoxaparin Protocol for STEMI

Patient: _____ Weight: _____ kg Height: _____ cm

Allergies (describe reaction): _____

Estimated CrCl: _____ mL/min

N.B: Enoxaparin is contraindicated if **any** of the following apply (please check):

- ❒ Estimated CrCl is <30 mL/min;
- ❒ Actual body weight is >140 kg;
- ❒ Patient has contraindications to systemic anticoagulation therapy; and
- ❒ Patient has previously documented heparin-induced thrombocytopenia (HIT)

1. Blood work

Complete blood count (CBC), INR and aPTT prior to administration of first dose of enoxaparin. CBC daily while receiving enoxaparin.

2. Enoxaparin orders (please check one):

❒ *For patients <75 years of age:*

Bolus: Enoxaparin 30 mg IV followed immediately by:

Enoxaparin 1 mg/kg x _____ kg (patient weight) = ____ mg SC BID x 2 doses **(maximum 100 mg/dose)**

then provide 1 mg/kg x _____ kg (patient weight) = ____ mg SC BID **(maximum 140 mg/dose)**

❒ For patients ≥*75 years of age:*

Enoxaparin 0.75 mg/kg x _____kg (patient weight) = ____ mg SC BID x 2 doses **(maximum 75 mg/dose)**

then provide 0.75 mg/kg x _____kg (patient weight) = ____ mg SC BID **(maximum 140 mg/dose)**

N.B:

- Enoxaparin should be continued for a minimum of 48 hours then can be reassessed
- Enoxaparin dose should be withheld if due to be given within 12 hours of a cardiac catheterization/PCI procedure
- Enoxaparin should be re-assessed if patient post PCI.
- If enoxaparin dose is given on the morning of catheterization, the angiography sheath should remain in place for 6-8 hours following the dose of enoxaparin in order to reduce the risk of groin hematoma; **and**
- **Enoxaparin has minimum effect on ACT and should not be relied upon for degree of anticoagulation in patients undergoing cardiac procedures.**

Prescriber's Signature: _____ Date:(yyyy/mm/dd): _____

Prescriber's Name: _____ Reg. No.:_____

Appendix J. Sample Heparin Infusion Protocol for STEMI

Patient: _____ Weight: _____ kg Height: _____ cm
Allergies (describe reaction): _____
Time: _____ Estimated CrCl: _____ mL/min

N.B: For patients with STEMI, consider using enoxaparin as the first line antithrombotic..

1. Initial blood work
CBC, PT (INR), aPTT, prior to starting heparin.

2. Heparin orders
The following orders should be administered using heparin 25,000 units in 500 mL of D5W (other solutions require a separate order).

□ Loading (bolus) dose:
60 units/kg X _____ kg (patient weight) = _____ units IV over 20 minutes **(maximum 4,000 units), then**

□ Maintenance IV Infusion: to begin immediately after the bolus (if given).
12 units/kg/hr x _____kg (patient weight) = _____units/hr **(maximum 1000 units per hr)**

3. Repeat blood work
- CBC daily. Notify physician if platelet count is <100 x 10^9/ L.
- Check first aPTT at 3 hours

4. Adjust heparin infusion according to nomogram *

The therapeutic aPTT range should be calibrated specifically for each reagent lot/coagulometer by determining the aPTT values that correlates with therapeutic heparin levels (equivalent to 0.2 to 0.5 IU/mL) by factor Xa inhibition for the treatment of venous thrombosis.

*aPTT targets will depend on local lab reagents; **it is important that a heparin infusion nomogram be developed by your local laboratory.**

Prescriber's Signature: _____ Date:(yyyy/mm/dd): _____

Prescriber's Name: _____ Reg. No.:_____

APPENDIX K. CCS[1] Proposed Upper Limit for Wait Time Benchmarks for Procedures After STEMI

Category/indication	PCI	Diagnostic catheterization
Emergent	Immediate	Immediate to 24 hours
Urgent	Immediate	3 days
Semi-urgent	Immediate	7 days

REFERENCE

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Appendix L. Evidence for Medication Use for Secondary Prevention of ACS: Cost and Normal Starting Dose (Beta Blockers, Statins, and ACE Inhibitors)

BETA BLOCKER DOSAGES AND COSTS			
Generic name [a]	*Dose*	*Dose frequency*	*Cost/month* [b]
Metoprolol [c]	25 mg	BID	$3.86
	50 mg	BID	$8.45
	100 mg	BID	$15.34
	100 mg SR	OD	$6.97
	200 mg SR	OD	$12.65
Atenolol [c]	50 mg	OD	$12.14
	100 mg	OD	$19.93
Bisoprolol [c]	5 mg	OD	$7.61
	10 mg	OD	$12.61
Carvedilol	3.125 mg	BID	$55.21
	6.25 mg	BID	$55.21
	12.5 mg	BID	$55.21
	25 mg	BID	$55.21
Nadolol	40 mg	OD	$8.51
	80 mg	OD	$12.13
	160 mg	OD	$19.79

[a] Beta adrenergic blockers with intrinsic sympathomimetic activity have not been included, as they are relatively contraindicated in ACS settings

[b] Costs in table were calculated using the January 2008 Atlantic Pharmaceutical Services Incorporated regional price guide and are subject to change. Costs are based on the target dose defined by clinical trials and do not include pharmacist professional fees.

[c] cardioselective agents

Appendix L. Evidence for Medication Use for Secondary Prevention of ACS: Cost and Normal Starting Dose (Beta Blockers, Statins, and ACE Inhibitors) *(cont'd)*

STATIN DOSAGES AND COSTS			
Generic name	*Trial evidence*	*Dose* [a]	*Cost/month* [b]
Atorvastatin	ASCOT[1]	10 mg	$57.40
		20 mg	$71.76
		40 mg	$77.14
	PROVE-IT,[2] TNT,[3] MIRACL[4]	80 mg	$77.14
Lovastatin		20 mg	$37.63
		40 mg	$69.40
Fluvastatin		20 mg	$28.50
		40 mg	$40.02
		80 mg XL	$48.51
Pravastatin		10 mg	$32.88
		20 mg	$38.79
	CARE,[5] LIPID,[6] PROSPER[7]	40 mg	$46.72
Simvastatin		10 mg	$38.69
		20 mg	$47.82
	4S,[8] HPS[9	40 mg	$47.82
	A to Z[10]	80 mg [c]	$47.82
Rosuvastatin		10 mg	$40.80
		20 mg	$51.00
		40 mg [d]	$59.70

[a] **Doses in shaded blocks provide at least a 40% reduction in LDL-C**

[b] Costs in table were calculated using the January 2008 Atlantic Pharmaceutical Services Incorporated regional price guide and are subject to change. Costs are based on the target dose defined by clinical trials and do not include pharmacist professional fees

[c] Simvastatin 80 mg was associated with more cases of rhabdomyolysis in the A to Z trial

[d] Specialist supervision is recommended when initiating rosuvastatin 40 mg

Appendix L. Evidence for Medication Use for Secondary Prevention of ACS: Cost and Normal Starting Dose (Beta Blockers, Statins, and ACE Inhibitors) *(cont'd)*

ACE INHIBITOR DOSAGES AND COSTS				
Generic name	*Trial evidence*	*Starting dosage*	*Target dosage*	*Cost/month* [a]
Captopril	SAVE[11] VALIANT[12]	6.25 mg	50 mg TID	$54.85
Lisinopril	GISSI-3[13]	2.5–5 mg OD	10 mg OD	$22.37
	ATLAS[14]		40 mg OD	$53.60 [b]
Ramipril	HOPE[15] (vascular protection)	2.5 mg OD	10 mg OD	$22.94
	AIRE[16] (LVSD)	2.5 mg BID	5 mg BID	$36.22
Perindopril	EUROPA[17] (vascular protection)	2 mg OD	8 mg OD [c]	$30.80
Trandolopril	TRACE[18] (LVSD post MI)	1 mg OD	4 mg OD	$33.76
Enalapril	CONSENSUS,[19] SOLVD[20]	2.5 mg BID	10 mg BID	$53.21

[a] Costs in table were calculated using the January 2008 Atlantic Pharmaceutical Services Incorporated regional price guide and are subject to change. Costs are based on the target dose defined by clinical trials and do not include pharmacist professional fees.

[b] The cost of lisinopril 40 mg is based on taking two 20-mg tablets, as it is not available in a 40-mg tablet.

[c] Generic perindopril is only available in the 8-mg strength (tablets not scored)

Appendix L. Evidence for Medication Use for Secondary Prevention of ACS: Cost and Normal Starting Dose (Beta Blockers, Statins, and ACE Inhibitors) *(cont'd)*

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Appendix M. Glycemic, BP and Lipid Targets

Parameter	Target
A1C[1]	≤7.0%
BP (mm Hg)[2] Patient without diabetes Patients with diabetes or chronic kidney disease	 <140/90 mm Hg <130/80 mm Hg
LDL-C*[3]	<2.0 mmol/L
TC to HDL-C ratio**	<4.0
LDL-C lowering**	≥50%

* Primary target
** Secondary target

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Duality of Interest Declaration							
Name	**Employment**	**Stock shareholder**	**Honoraria/consulting fee**	**Grant/research support**	**Member of advisory panel/standing committee**	**Member board of directors**	**Nothing to Disclose**
Allen, Michael							√
Al-Mane, Faisal							√
Bata, Iqbal			• Biovail • Boehringer Ingelheim • sanofi-aventis				
Bowen, Scott			• AstraZeneca • Merck Frosst • Pfizer • sanofi-aventis				
Callaghan, Michael			• AstraZeneca • sanofi-aventis • Schering-Plough				
Clarke, Adam			• Abbott • AstraZeneca • Bayer • Biovail • Merck Frosst • Novartis • Pfizer • sanofi-aventis • Servier				

Name	Employment	Stock shareholder	Honoraria/consulting fee	Grant/research support	Member of advisory panel/standing committee	Member board of directors	Nothing to Disclose
Cox, Jafna			• Bristol-Myers Squibb • GlaxoSmithKline • Merck Frosst • Pfizer • sanofi-aventis	• Merck Frosst • Pfizer • sanofi-aventis	• Astellas • Bristol-Myers Squibb • sanofi-aventis		
Currie, Thomas							√
Downey, Faye							√
Fort, Stephen			• AstraZeneca • Bristol-Myers Squibb • sanofi-aventis • Schering-Plough	• Boston Scientific • Schering-Plough			
Harrigan, Lynne							√
Hatcher, Nancy							√
Hatheway, Ron			• Merck Frosst		• AstraZeneca		
Kelly, Kim							√
Love, Michael			• Abbott Vascular • AstraZeneca • Boston Scientific • Bristol-Meyers Squibb • Medtronic • sanofi-aventis	• Cordis Canada			

MacDonald, Paul				• AstraZeneca • Schering-Plough			
Nestel, Mada							√
O'Brien, James Michael							√
O'Neill, Blair			• AstraZeneca • Pfizer Canada	• Abbott Laboratories • AstraZeneca • Novartis • Pfizer Canada	• AstraZeneca • Pfizer Canada		
Perk, Masis							√
Seviour, Paul							√
Travers, Andrew			• Hoffmann-La Roche				
Yung, Jason			• AstraZeneca • Aventis • Bristol-Myers Squibb • Novartis • Pfizer Canada				