CRITICAL PATH MANAGEMENT FOR ACUTE MYOCARDIAL INFARCTION

by

ANGELA B.K. LO

B.Sc. (Pharm), The University of British Columbia, 1992

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF SCIENCE in THE FACULTY OF GRADUATE STUDIES (Faculty of Pharmaceutical Sciences)

We accept this thesis as conforming to the required standard

THE UNIVERSITY OF BRITISH COLUMBIA

Apr. 25, 1995

© Angela B.K. Lo, 1995
In presenting this thesis in partial fulfilment of the requirements for an advanced degree at the University of British Columbia, I agree that the Library shall make it freely available for reference and study. I further agree that permission for extensive copying of this thesis for scholarly purposes may be granted by the head of my department or by his or her representatives. It is understood that copying or publication of this thesis for financial gain shall not be allowed without my written permission.

Department of **PHARMACY**

The University of British Columbia
Vancouver, Canada

Date **FEB 21 '95**
Atherosclerotic coronary artery disease continues to be the major underlying cause of myocardial infarction and the leading cause of death in Western society. Preliminary data from a number of Canadian hospitals on the treatment of acute myocardial infarction (AMI) indicate a significant gap between knowledge of proven efficacious therapies and their clinical application.

This was a prospective study, with retrospective controls, of 592 AMI patients at Royal Columbian Hospital and Surrey Memorial Hospital, to determine the efficacy of a critical path for management of AMI patients. Critical path, a continuous quality improvement (CQI) tool, involves the development and implementation of pre-printed standard orders for all AMI patients. The critical path for AMI management was created based on benchmark clinical trials. The objective was to increase the utilization of beta-blockers, and ASA, both proven efficacious therapies. Other outcomes of interest include assessments of in-hospital mortality, length of hospital stay, and use of thrombolytics.

The primary endpoints were changes in usage of ASA and beta-blocker after the critical path protocol. The increase in use of ASA was 1.89% (p=0.511) and in the use of beta-blocker was 4.85% (p=0.381). Secondary endpoints of in-hospital mortality and length of hospital stay demonstrated a non-significant decrease for in-hospital mortality, and a 0.98 day increase in length of hospital
stay. In addition, the critical path protocol led to a 2.22% increase in usage for thrombolytics, another proven efficacious therapy, and a 13.3% decrease for calcium channel blockers, and 20.8% decrease for anti-arrhythmics, both unproven and possibly harmful medications for treatment of AMI.

Implementation of the critical path protocol can be a valuable tool in maintaining the utilization of proven efficacious therapies and dissemination of medical knowledge.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>ii</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>vii</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td>viii</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>ix</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>2</td>
</tr>
<tr>
<td>Definition of Acute Myocardial Infarction</td>
<td>2</td>
</tr>
<tr>
<td>Diagnosis of acute myocardial infarction</td>
<td>3</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td>3</td>
</tr>
<tr>
<td>Electrocardiogram</td>
<td>3</td>
</tr>
<tr>
<td>Cardiac enzymes</td>
<td>4</td>
</tr>
<tr>
<td>Proven Efficacious Therapies for Acute Myocardial Infarction</td>
<td>4</td>
</tr>
<tr>
<td>Thrombolytic Therapy</td>
<td>5</td>
</tr>
<tr>
<td>ASA</td>
<td>7</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>7</td>
</tr>
<tr>
<td>Unproven Medications for Acute Myocardial Infarction</td>
<td>8</td>
</tr>
<tr>
<td>Efficacy Versus Effectiveness</td>
<td>11</td>
</tr>
<tr>
<td>Use of Clinical Guidelines</td>
<td>14</td>
</tr>
<tr>
<td>Hurdles in Designing Clinical Guidelines</td>
<td>16</td>
</tr>
<tr>
<td>Applying Critical Path Management to Improve the Treatment of Myocardial Infarction and Improve Patient Outcomes</td>
<td>17</td>
</tr>
<tr>
<td>Importance of Study</td>
<td>19</td>
</tr>
<tr>
<td>Assumption</td>
<td>20</td>
</tr>
<tr>
<td>Clinical Quality Improvement Network</td>
<td>21</td>
</tr>
<tr>
<td>Objectives</td>
<td>22</td>
</tr>
</tbody>
</table>
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Baseline patient characteristics</td>
<td>35</td>
</tr>
<tr>
<td>2.</td>
<td>Baseline patient characteristics reported separately for RCH and SMH</td>
<td>36</td>
</tr>
<tr>
<td>3.</td>
<td>Overall use of ASA and beta blockers</td>
<td>37</td>
</tr>
<tr>
<td>4.</td>
<td>Use of ASA and beta blockers reported separately for RCH and SMH</td>
<td>38</td>
</tr>
<tr>
<td>5.</td>
<td>Overall length of stay in hospital and in-hospital mortality</td>
<td>39</td>
</tr>
<tr>
<td>6.</td>
<td>Use of thrombolytics, calcium channel blockers, and anti-arrhythmics</td>
<td>40</td>
</tr>
</tbody>
</table>
LIST OF FIGURES

1. Time-line of events for data collection at RCH and SMH . 24
2. Effects of critical path management on the usage of medication and in-hospital mortality . . . . . . . . . . . . 41
I want to thank my supervisors Dr. Ross T. Tsuyuki, and Dr. Naseem Amarshi for all their guidance, encouragement, and support.

I am grateful to the members of my committee including Dr. Frank Abbott, Dr. Jack Diamond, and Dr. Bruce Carleton. I am also grateful to Dr. Terry Montague, Ms. Diane Catellier and other the members of the Clinical Quality Improvement Network who have made this project possible.

I acknowledge the efforts of the Health Records Department at both the Royal Columbian and Surrey Memorial Hospital, and the Pharmacy Department at the Royal Columbian Hospital for their cooperation.
INTRODUCTION

Atherosclerotic coronary artery disease is the major underlying cause of acute myocardial infarction (AMI) and is the leading cause of death in Western Society. Over 850,000 Canadians die each year from the sequelae of atherosclerosis, and the economic costs of cardiovascular disease are estimated at $11.6 billion dollars per year (1). Despite current methods of treatment for AMI, there remains an in-hospital mortality rate of 14% (2). Risk of AMI increases with age, and with an aging population, this represents a burgeoning public health problem (3). It is therefore important that we identify problems in the current acute management and treatment of AMI, implement changes based on strong clinical trials evidence, and, ultimately, improve patient outcomes through reductions in patient morbidity and mortality.
Myocardial Infarction

1. Definition of Acute Myocardial Infarction

Atherosclerotic plaque formation along the wall of coronary arteries results in narrowing of lumen diameter. Plaque fissuring, which can result from blood flow under increased pressures in the area of stenosis or other as yet uncharacterized processes, expose the endothelium, inducing platelet aggregation and thrombus formation (4-6). A subendocardial or non-Q-wave AMI involves an area of ischemic necrosis partially through the myocardial wall. A transmural or Q-wave AMI involves an area of ischemic necrosis which penetrates the full thickness of the myocardial wall. Both Q and non-Q represent a spectrum of damage which occurs during AMI and is related to the amount of area served by the infarct-related artery and the use of various disease-modifying therapies.
2. Diagnosis of acute myocardial infarction

a) Clinical presentation

The diagnostic criteria for AMI includes a history compatible with the symptoms of AMI. Patients usually present with a crushing or squeezing substernal chest discomfort, often lasting longer than 30 minutes, and is unrelieved by rest or sublingual nitroglycerin. The pain may radiate to the left or right arm, neck, jaw, back, shoulders, or abdomen and is not sharp in character. This is often also associated with dyspnea, diaphoresis, nausea, or vomiting.

b) Electrocardiogram (ECG) (7)

The ECG helps to establish the diagnosis of an AMI in 60-80% of cases, gives an indication of the location of the infarct, and helps to monitor for ongoing ischemia. Classical ECG findings diagnostic for AMI are ST segment elevation, although ST segment depression and/or T wave inversion may also be present. Pathological Q-waves, indicating transmural infarction, usually develop over 12-36 hours after the onset of chest pain and therefore are of little use in the early hours of AMI.
c) Cardiac enzymes (7)

Damaged necrotic heart muscle releases cardiac enzymes, namely creatine kinase (CK) and lactate dehydrogenase (LDH), into the bloodstream, in amounts that correlate with the size of the infarct. CK release occurs 6-24 hours post-AMI and normalizes after 48-72 hours. LDH release peaks 3-6 days post-AMI and normalizes after 8-14 days. Most laboratories currently use CK enzyme unless the patient presents after 48-72 hours (the "window" for CK) when LDH is used.

Other high energy utilisation tissues such as skeletal muscle and the brain can also release CK enzymes. However, electrophoretic fractionation of the enzymes can specifically measure the CK-MB isoenzyme which is a very sensitive and specific indicator of CK release from cardiac tissue. A CK-MB fraction of $\geq 3-4\%$ of the total CK is diagnostic for AMI.

3. Proven Efficacious Therapies for Acute Myocardial Infarction

Benchmark trials have proven several therapies to be efficacious in the treatment of AMI in terms of decreases in mortality and rate of reinfarction (8) (Appendix A). Several cardiovascular agencies have produced guidelines for the management
of AMI based upon the evidence from these studies (9).

a) Thrombolytic Therapy

In 1980, DeWood et al. demonstrated, through early coronary artery angiography, that the most likely etiology of AMI is an occlusive coronary thrombosis. Spontaneous lysis from the body’s own fibrinolytic system can occur 6-24 hours after the clotting process (10), however, necrosis would have occurred long before blood flow could be re-established via this mechanism. Clot-dissolving or thrombolytic therapies, such as streptokinase (SK) and alteplase (t-PA), are proteolytic enzymes that can speed up the process of thrombolysis, thereby interrupting the course of infarction, restoring coronary blood flow, and reducing myocardial necrosis.

Streptokinase is a protein derived from beta-hemolytic streptococci. It complexes with plasminogen which facilitates the conversion of plasminogen to plasmin. Plasmin lyses fresh thrombi clots and digests clotting factors V and VIII, prothrombin and fibrinogen. Clot lysis in this fashion can occur within 30 minutes. Two large, benchmark clinical trials, GISSI I (11), and ISIS-2 (12), have both conclusively demonstrated that streptokinase results in reduction in mortality. GISSI I, a randomized trial of 11,712 AMI patients, produced a significant 18% relative reduction in the 21 day mortality (p=0.0002), and ISIS-2, a randomized,
double-blind, placebo controlled trial of 17,187 AMI patients, demonstrated a 23% relative mortality reduction at 35 days (p<0.00001). This was an absolute risk reduction of 2.7%, or in terms of numbers needed to treat, 37 patients would be required to be treated to prevent one death.

Alteplase (t-PA) is a human blood product, now commercially manufactured through recombinant DNA technology. It has a higher affinity for plasmin as compared to SK, such that it binds to fibrin-bound plasmin, rather than circulating plasmin, and thus has been called clot-specific. In the ASSET trial (13), 5000 AMI patients were randomized to t-PA or placebo. At 1 month, use of t-PA resulted in a 26% relative mortality reduction as compared to placebo (p=0.0011).

Results of the recent GUSTO (14) trial has demonstrated that use of front-loaded t-PA (ie. administrating the same dose over a shorter period of time) conferred a small advantage over SK with a 14% relative and 1% absolute mortality risk reduction at 30 days post AMI. Since 100 patients are required to be treated with t-PA before 1 death was prevented as compared to SK, the much higher cost of t-PA ($2200 per dose) as compared to SK ($460 per dose) has been the deterring factor in generalised administration of t-PA to all AMI patients despite its somewhat superior efficacy. Optimal guidelines from agencies such as the BC Cardiac Society has stressed that "...a thrombolytic agent be given in a timely fashion is more important than selection of one..." over another (15).
b) ASA

ASA produces an antiplatelet effect through irreversible acetylation of platelet cyclo-oxygenase to decrease the formation of thromboxane A2, a potent vasoconstrictor and platelet aggregator. ASA also serves to enhance heparin therapy. The importance of ASA in the therapy of AMI was first demonstrated in the ISIS-2 trial (12) which studied the effects of ASA usage specifically in patients with AMI. The investigators found that early use of ASA alone can produce a 21% mortality reduction (p<0.0001), and a 44% reduction in non-fatal reinfarction rate (p<0.0001), similar to that of SK alone. This study also found that when SK and ASA were used concurrently, they produced an additive mortality reduction of 39% (p<0.00001). The dose of ASA used in the ISIS-2 trial was 160mg daily. The Physician's Health Study, which also served to emphasize the importance of ASA in primary prevention therapy, resulted in a 44% relative risk reduction for AMI (16).

c) Beta blockers

Beta adrenergic receptor antagonism in the cardiovascular system results in a reduction of infarct size through a decrease in myocardial oxygen demand. This is accomplished through a reduction in heart rate, contractility, and blood pressure (9). Beta blockers also attenuate the myocardial response to circulating
catecholamines, for example during stress.

In the large ISIS-1 (17) trial of 16,027 AMI patients, atenolol therapy produced a 7 day mortality reduction from 4.3% to 3.7% (p<0.02) compared to placebo. A 14% relative mortality difference between treatment group versus placebo was apparent by the end of day 1. Another large placebo controlled trial of 5778 patients using metoprolol therapy demonstrated a significant mortality reduction from 4.9% to 4.3%, with again mortality benefits evident at day 1 of therapy (18).

Early use of beta-blockers have also shown to reduce risk of nonfatal reinfarction by 19% (p<0.01) and, nonfatal cardiac arrests by 16% (p<0.02) (8).

4. Unproven Medications for Acute Myocardial Infarction

The search for efficacious therapies for AMI has also led to the "discovery" of agents which have no effect, or even increase mortality in AMI. Calcium channel blockers, and anti-arrhythmics are commonly prescribed agents post-AMI. Calcium channel blockers are used for their ability to decrease myocardial ischaemia and vasospasm. Anti-arrhythmics are prescribed for their ability to suppress and prevent ventricular ectopy as well as ventricular tachycardia, and ventricular fibrillation.

However, neither has been demonstrated in clinical trials to reduce mortality. Meta-analysis - a systematic overview of
clinical trials - of lidocaine therapy post-AMI suggests an 11% mortality increase, and a 6-10% mortality increase for calcium channel blockers, although neither reached statistical significance (8).

Results of the CAST trial (19) have demonstrated the dangers of using surrogate endpoints as indicators of patient outcomes. This trial, based on the hypothesis that complete arrhythmia suppression could prevent potentially fatal arrhythmias and would therefore decrease mortality, resulted in significantly more deaths in the anti-arrhythmic treatment group as compared to placebo.

Meta-analysis of anti-arrhythmic agents used post-AMI by Teo et al. (20) demonstrate that use of Class I anti-arrhythmics, such as lidocaine, quinidine, have been associated with increased mortality. Conversely, beta-blockers (Class II anti-arrhythmics) were associated with reduced mortality post-AMI.

Thus, without clear evidence of efficacy in mortality reduction, calcium channel blockers or anti-arrhythmics should not be encouraged on a routine basis, and should be left to the discretion of the physician.
Clinical trials are conducted with the intention that the results would influence clinical practice (21). Lamas et al., demonstrated that in the 1950's, despite clinical trials with clear deleterious outcomes, use of diethylstilbestrol continued to be used in pregnant women (22). Similarly he described other therapies which continued to be used despite lack of any evidence for favourable effect on outcomes such as bedrest prescribed for hepatitis patients, and bland diet prescribed for peptic ulcer patients (22).

Trends in the use of thrombolytic agents have also lagged behind clinical trials evidence. A study of thrombolytic use in the whole population of 4.7 million over 1987-92 of the Trent regional health authority in central England (21) revealed that for nearly 2 years after the first publication of the landmark GISSI study (11), thrombolytic use remained insignificant. The authors remarked that "It was only after the publication of the ISIS-2 trial (23), another report from the GISSI trial (24), and 3 full papers from multinational trials in 1988 (12,25), that thrombolytic use rose steadily over the following 2.5 years" (21) (Appendix B).

There was also a significant positive association \((p=0.003)\) between the contribution of districts to multicentre trials of thrombolysis (21). Perhaps an indirect relationship exists such
that physicians who participate in trials seemed to be the most responsive to new knowledge, and participating centers' contribution to collaborative research further facilitates the dissemination of new knowledge (21).

Despite physicians' desire to practice at the forefront of medicine, these new practices must be derived from high quality evidence from randomized clinical trials and meta-analysis where they exist, rather than from expert opinions (26) which may be biased and may even be contrary to the best available clinical trials evidence. In some cases treatments that have no effect on mortality or are potentially harmful continued to be recommended (26).

Efficacy Versus Effectiveness

Efficacy and effectiveness are terms commonly, and often mistakenly interchanged. Efficacy refers to the degree of benefit associated with the use of a particular intervention under ideal conditions, eg. the effect of a new drug on mortality in a clinical trial. Effectiveness refers to the benefit observed when the therapy is applied to a population in the "real world". A proven efficacious therapy would have decreased effectiveness in a population if it has many contraindications to its use, or has many adverse effects, or if it is not used by practitioners. Research
on the patterns of practice for AMI has demonstrated a gap between clinical trials evidence of efficacy and their clinical application (2,27,28). This has been consistently evident in major high risk subgroups such as the elderly and women (2,29). Evidence of the efficacy of many AMI therapies dates back to 1986 (11), 1985 for beta-blockers (30), and 1988 for ASA (12). Yet in one analysis of 2070 patients from 4 cohorts between 1987-1992 (2), use of ASA averaged only 76%; beta blockers 44%; and thrombolytics, 27% (Appendix C). While this relatively low use of proven efficacious therapies may be in part due to the presence of contraindications to the therapies, this does not fully explain the underuse of therapies. In a review of consecutive AMI patients at RCH, Tsuyuki et al. (27) in 1991 found that the early usage of thrombolytics, ASA, and beta-blockers were 100%, 66%, and 18% respectively. This was despite correction by the authors for the presence of contraindications. It is uncertain where the optimum percentage usage of these therapies lies in that further increases in usage produces slight reduction in mortality but increased incidence of intolerable adverse drug reactions.

Univariate analysis of the effect of patient gender and age differences on physician's prescribing habits revealed female patients and patients greater than 70 years as having a significantly higher mortality rate and receiving significantly fewer prescriptions of all proven effective therapies (2) (Appendices D & E). A trial conducted between 1989-90 by Montague et al comparing patient age-related differences in physician
prescribing habits (29) showed therapies proven to be efficacious were prescribed significantly less often to patients aged above 70 years as compared to patients aged below 70: thrombolysis - 20% versus 43% in younger patients, beta-blockers - 41% versus 62%, ASA - 71% versus 87%, and nitrates - 86% versus 97%. However, mortality was significantly reduced from 20% in 1987 to 13% during 1980-90. With parallel increases in the use of proven effective therapies in both age groups, the mortality reduction was attributed entirely to decreases in mortality in patients aged above 70 (Appendix F).

A trial conducted by Wilhelmsson et al. (30) stratified prospectively for postinfarct risk - small versus large infarcts, because the authors suspected that large infarctions may react unfavourably to beta-blocker therapy. In stark contrast to their belief, patients with larger infarct size benefitted most from beta-blockade. Both trials by Montague et al (29), and Wilhelmsson et al (30), strongly suggest that usage of proven effective therapies seem most beneficial in patients with the greatest mortality risk.

Another case for underutilization of proven efficacious therapy in the elderly was one study conducted by the investigators at the University of Massachusetts Medical School (31). Despite the adjustments for clinical variables such as diabetes mellitus or congestive heart failure, which are commonly cited reasons for prescribing a beta-blocker, there exists an inverse relationship between advancing age and receipt of a beta-blocker post AMI: the
odds ratio for receiving a beta-blocker relative to patients less than 55 years of age were 0.61 for those aged between 55-64, 0.52 for aged 65-74, 0.36 for those aged 75-84, and 0.26 for aged 85 or older indicating an age bias in the therapy of AMI.

Excluding patients with clear contraindication to therapy, the quantitative treatment effect may be slightly different in different biological subgroups, but the qualitative effects will be the same; there is little indication that subgroups such as the aged, female, those with concomitant disease, or more serious infarction, behave differently from each other (12). Effects of a particular treatment are best seen when administered to a large population, especially if the effects are small (32). The entire ethical dilemma in the decision to treat should not only take into account the individual, but also the documented value of a treatment for subgroups, such that modest benefits can be conferred to the many (32).

Use of Clinical Guidelines

Government, consumer groups and employers insist upon a high quality of health care, and that health care providers be held accountable for consistent and appropriate delivery of it. Ultimately, providers will be left with the choice of developing their own standards that reflect their own needs, or letting others
with less knowledge of the delivery of health care, to do it for them (33).

Use of clinical guidelines based on continuous quality improvement (CQI) principles are gaining popularity throughout medicine. CQI is a quality management principle which has been adopted in process-based industries for the past 50 years (34). Unlike quality by inspection, or quality assurance which merely separates good from bad (culminating in a vast amount of wastage), CQI focuses on improving quality at the process level thereby shifting the entire production curve towards higher quality, and at the same time reducing waste and inefficiencies. In contrast to the commonly held criticism that guidelines create "cook book medicine" (35,36), by tying the hands of a good clinician, the goal of CQI is to reduce, not eliminate, variations in the process of care (37). Potential benefits of clinical guidelines include dissemination of medical knowledge, enhancement of attitude towards acceptance of new "standards of care", changes in prescriber behaviour to decrease practice variation, and improve patient outcomes, control cost and reduce the length of hospital stay (35). Several studies evaluating the effectiveness of guidelines in affecting patient outcomes have shown improvements in the management of hypotension, hypertension, administration of pneumococcal or influenza vaccination, and burns (38).
1. Hurdles in Designing Clinical Guidelines

Establishing guidelines, even on one procedure or diagnosis, can differ based upon the objectives of the review panel. Although the ultimate outcome is to improve the quality of care, the expectations of clinicians to improve patient outcomes, contrast those of employers to reduce expenditure, or attorneys to prove negligence (35). In addition, creation of guidelines require involves several principles (35):

1. Ensuring recommendations are based on well-designed studies with definitive results. Few medical procedures have undergone the rigorous test of a randomised, blinded, and controlled trials.

2. Analysis of evidence is unbiased. Even consensus guidelines may be based upon expert opinion rather than firm evidence. Unbiased consensus guidelines and/or meta-analytic evidence should be sought.

3. Each patient is treated as an individual. Clinical guidelines have been criticized as robbing the practitioners of individual judgement. However, an effective guideline can be created if the development strategy is internal (38) such that it is developed in conjunction with peers who are intimately aware of the wide variations. This is analogous to how the application of the principles of clinical epidemiology, which
2. Applying Critical Path Management to Improve the Treatment of Myocardial Infarction and Improve Patient Outcomes

Disparities in the use of proven efficacious therapies for the treatment of AMI, are a result of practice variations between physicians, and present an opportunity for improvement. Implementation of a clinical protocol appeared to offer the greatest potential beneficial change in the shortest time, with the benefits of continuing medical education at minimal cost.

Critical path management, a clinical outgrowth of quality improvement, is a tool used to implement these principles. It involves the development and use of pre-printed explicit orders for all AMI patients. Having all proven efficacious therapies and dosages printed on the order form facilitates the prescribing of these therapies and encourages all physicians to prescribe the same therapies to all AMI patients regardless of age, sex, or other variables. This process is not simply to manage all patients similarly, but to ensure that all patients are managed with the optimal use of the "best" medical therapeutic regimen (39). The best therapeutic regimen is the usage of proven efficacious therapy based on randomised, controlled clinical trials: thrombolysis,
beta blockers, and ASA - to decrease morbidity and mortality, with the avoidance of unproven, and possibly detrimental AMI therapy - calcium channel blockers and anti-arrhythmic drugs.
Importance of Study

Prior to this study, no AMI treatment protocol has been developed beyond an administration guidelines for thrombolytics. This study includes the development of explicit treatment guidelines for AMI, information on patterns of practice for AMI before and after the implementation of the protocol. In addition, the effects of co-therapy of thrombolytics, ASA, beta-blockers, and heparin have not been established. Secondary outcomes such as in-hospital mortality and length of hospital stay provide information on the effects of co-therapy.

Despite the surge in development and adoption of guidelines into medical practice, there remains uncertainty in the efficacy of guidelines. Evidence is scarce on the ability of guidelines to realize the potential benefits of improving practitioner knowledge, and attitude (35).
Assumption

It is not the purpose of this trial to prove the efficacy of the targeted AMI therapies. The assumption is that since these proven effective therapies have been shown through benchmark clinical trials to decrease mortality and improve patient outcomes, increased usage of these therapies will have an effect on morbidity and mortality, and improved patient outcomes.
The Clinical Quality Improvement Network (CQIN) is comprised of investigators interested in improving patient outcomes through shared vision in the development and implementation of clinical quality improvement tools. One of a number of projects founded by CQIN is the Critical Path Management of Acute Myocardial Infarction (39). Currently 12 centres across Canada are participating in this study. This multicenter project involves not only assessment of changes in patterns of practice in drug therapy, but also short and 1 year patient outcomes.

This project will encompass the Royal Columbian Hospital (RCH) and the Surrey Memorial Hospital (SMH) sites, and the analysis will be limited to the objectives outlined in the next section.
Objectives

The primary objective was to increase the utilization of proven efficacious therapies using a critical path protocol for AMI by monitoring the administration of proven efficacious therapy and non-proven medication both before and after the implementation of the critical path protocol. Due to the many contra-indications of thrombolytic therapy, it was anticipated that changes in their utilization were unlikely to be seen, that is, that utilization is likely already at optimal levels (27). Therefore, utilization of beta-blockers and ASA were selected as the major indicator of changes in practice patterns upon implementation of the protocol.

The secondary endpoints of interest were to measure patient outcomes in terms of in hospital mortality, and length of hospital stay. In addition, utilization of proven efficacious therapy for RCH and SMH individually were also recorded.

Although nitrates have been suggested in meta-analysis to reduce mortality, they have not undergone the rigorous testing of a randomized, controlled trial. Therefore, nitrates will not be included for analysis as a proven efficacious therapy, although their use will not be discouraged.
METHODOLOGY

This was a longitudinal study involving retrospective patient chart review to compare the patterns of practice for the treatment of AMI for 7 months before the implementation of the critical path protocol with the prospective analysis patterns of practice for 7 months after the implementation of the protocol. Retrospective data collection was conducted from Feb. 27, 1993 to September 27, 1993 for RCH, and from Apr. 23, 1993 to Nov. 23, 1993 for SMH. Implementation of the protocol began on Sept. 27, 1993 for RCH, and Nov. 23, 1993 for SMH. Prospective data collection was conducted from Sept. 27, 1993 to Apr. 26, 1994 for RCH and from Nov. 23, 1993 to June 22, 1994 for SMH.
Figure 1 Time-line of events for data collection at RCH and SMH
Participant Eligibility

Inclusion criteria

All patients admitted to RCH or SMH with a discharge diagnosis of AMI between Feb. 27, 1993 - Apr. 26, 1994 for RCH, and Apr. 23, 1993 - June 22, 1994 for SMH, were included in the trial. No AMI patients were excluded from analysis. Patients who were admitted more than once for an AMI during either the retrospective or prospective period were included into analysis as separate cases. Patients admitted with one or more diagnosis in addition to AMI, were also included in the study. Diagnosis of AMI was defined as having two of the following present: 1) an acute history of cardiac-type pain or other recognizable symptoms compatible with AMI, 2) elevated creatine kinase enzyme levels (greater than twice the upper limits of normal limits), 3) diagnostic depolarization or repolarization changes on their electrocardiograms.

Exclusion criteria

In the setting of clinical uncertainty about any of the diagnostic criteria, for example, atypical chest pain or CK elevation without an abnormality of the MB fraction, such that patients were classified as uncertain or possible AMI, these
patients were excluded from analysis.

Development and Implementation of the Critical Path

The treatment of AMI was selected for improvement based on: 1) the opportunity for improvement, as described by several analyses of current practice patterns in AMI, 2) the scope of the problem in terms of the prevalence of the disease in the Western society. Upon selection of this project, a development team was appointed consisting of members from nursing, pharmacy, emergency medicine, and cardiogology, thereby "fulfilling" the multidisciplinary approach criteria. Examination of the current practice patterns revealed an opportunity to increase the utilization of proven efficacious therapies, and to discourage the use of unproven medications. A consensus was reached with regards to implementation of a Critical Path for AMI in the form of standard orders, as the fastest and most cost-effective way of improving the drug treatment of AMI (Appendix G). The standard orders were designed such that orders for all non-cardiac drug therapy and other treatments or procedures remain unchanged. All proven efficacious therapy, i.e. thrombolytics, ASA, and beta-blocker, would be written based on the most current clinical evidence in terms of dosages, frequency of administration, route of administration (Appendices H & I). For thrombolytic therapy,
streptokinase was written as "Streptokinase 750,000 units in 50mL D5W over 10 minutes iv, followed by 750,000 units in 50mL D5W over 50 minutes iv", and t-PA was written as "Alteplase (t-PA) 15mg iv over 2 minutes by physician then 0.75 mg/kg (not > 50mg) iv over 30 minutes then 0.5 mg/kg (not > 35mg) iv over 60 minutes" as per the GUSTO trial (14). ASA in accordance to the studies was administered 160 mg daily (12). However, ASA is most commonly available both in hospital and community as the 325 mg per tablet dose. Therefore, the aspirin order was written as "325 mg plain ASA po stat (chewed), then enteric-coated ASA 325 mg po once daily thereafter". Beta blocker therapy was to be given as "metoprolol 5 mg iv over 2 minutes q2min x 3 doses (15mg total dose) administered by physician, then metoprolol 50 mg po 15 minutes later, followed by metoprolol 50 mg q6h for 48 hours, then metoprolol 100 mg po bid thereafter" as per the MIAMI trial (18). Physicians were required to check and initial therapies they wished to prescribed for their patient. They were also at liberty to prescribe other types of therapies which fall under the same drug family, for example, acebutolol instead of metoprolol. Calcium channel blockers were not included in the standard orders, and a guideline for emergency lidocaine administration was included in the "PRN" section. The staff of both RCH and SMH were informed of the content and rationale for implementing the critical path, and were instructed on the use of the order form. The units most involved in the critical path were the emergency department, the intensive care unit, and the coronary care unit. Prospective data
was then collected after implementation of the critical path.

Data Collection

Data collection was conducted through patient chart reviews provided by the RCH and SMH health records department. Charts were pulled for the period from Feb. 27, 1993 to Apr. 26, 1994 for RCH, and from Apr. 23, 1993 to June 22, 1994 for SMH with ICD9 code of 411, (40).

Types of data collected of pertinence to this thesis included patient's name, chart number, age, sex, admission and discharge dates. The remaining data were collected in binomial form denoted by yes or no. The data included past history of AMI, Q-wave AMI (versus non-Q-wave), the use of the following therapies: thrombolytics, beta-blockers, calcium channel blockers, heparin, nitrates, ASA, anti-arrhythmics and angiotensin converting enzyme inhibitors, and in-hospital mortality (Appendix J).
Statistical Analysis

1. Sample Size

The null hypothesis was that the critical path management for AMI would have no effect on the use of proven and unproven therapy between retrospective and prospective patients. Other outcomes of interest included in-hospital mortality, and length of hospital stay.

Sample size calculation was derived from the independent groups proportions equation (41) using data from retrospective analysis (2). The calculation was based on the assumption of a 25% increase or decrease in the use of proven therapy and unproven medications, using two tailed test with (alpha < 0.05 $Z_a = 1.96$), and a 80% power (beta = 0.2, $Z_b = -0.84$) in testing the principal hypothesis.

Calculations

Based on equation for comparing two proportions:

\[ n_{/\text{group}} = \left\{ \frac{Z_a \sqrt{2 \pi_c (1 - \pi_c)} - Z_b \sqrt{\pi_t (1 - \pi_t) + \pi_c (1 - \pi_c)}}{\pi_t - \pi_c} \right\}^2 \]

where $\pi_c = \text{current drug utilization}$

$\pi_t = \text{drug utilization with the critical path}$
Example calculation to see a 25% increase in beta blocker usage, the sample size per group required:

\[ n = \left\{ \frac{1.96 \sqrt{2 \times 0.48 \times 0.52} + (-0.84) \sqrt{(0.60 \times 0.40) + (0.48 \times 0.52)}}{0.60 - 0.48} \right\}^2 \]

= 270 patients per group

<table>
<thead>
<tr>
<th>Therapy</th>
<th>current % usage</th>
<th>% with 25% increase/decrease</th>
<th>sample size required per usage group</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>76</td>
<td>99/59</td>
<td>55</td>
</tr>
<tr>
<td>BB</td>
<td>48</td>
<td>60/36</td>
<td>270</td>
</tr>
<tr>
<td>TT</td>
<td>28</td>
<td>35/21</td>
<td>657</td>
</tr>
</tbody>
</table>

BB = beta-blockers
TT = thrombolytic therapy

Changes in thrombolytic use would unlikely to be seen due to earlier efforts to increase thrombolysis use at many hospitals. Therefore changes in beta-blocker and/or ASA utilization would be the measure of the efficacy of the Critical Path. Using beta-blockers as the major indicator of changes in practice patterns
upon implementation of the critical path protocol, a sample size of 270 patients per group was required to detect a 25% increase/decrease in the usage of all proven effective therapies for the retrospective analysis prior to critical path protocol implementation, and for the prospective analysis after critical path protocol implementation. To protect against unexpectedly lower AMI admission rates, the study size was inflated to 300 patients per group or 600 patients total. Based upon a retrospective survey of the number of patients admitted with a diagnosis of AMI at RCH (approximately 305/yr), and SMH (approximately 296/yr), recruitment of 600 patients was anticipated.

2. Justification for statistical decisions

Previous analyses of the trends in usage of proven efficacious therapy seemed to indicate an increase of 33% in utilization even without active intervention (29). However, it was decided to err on the side of conservativeness and hypothesize a change in 25% utilization to ensure smaller changes may be detected. Although it is highly unlikely that our intervention would result in lower use of proven therapies, a two-tailed-test was chosen again out of conservativeness.
3. Analytical Methods

Nominal data, such as use of efficacious therapy, were evaluated by the Chi square test, and interval data, such as mean length of hospital stay, were evaluated by the Student's t-test. An alpha level of 0.05 was considered significant.

Evaluation of Efficacy

The primary endpoint of interest was the change in the proportion of patients being prescribed proven efficacious therapies, beta-blockers and ASA. Secondary endpoints of interest were unproven medications such as usage of calcium channel blockers and anti-arrhythmics, in-hospital mortality and length of hospital stay.
RESULTS

A total of 591 patients were eligible for analysis for both RCH between Feb. 27, 1993 to Apr. 26, 1994, and SMH between Apr 23, 1993 to June 22, 1994. The baseline demographics of the patients for Royal Columbian and Surrey Memorial Hospitals combined and individually are presented in Tables 1 and 2, respectively. More patients were transferred from another facility to RCH as compared to SMH (Table 2). There were no other clinically important or statistically significant differences in baseline characteristics between baseline and intervention patients.

The primary endpoints of the study were changes in usage of ASA and beta blocker after the implementation of the critical path protocol. The relative increase in use of ASA was 1.9% (absolute increase, 1.7%, p=0.51) and in the use of beta blocker was 4.8% (absolute increase, 3.3%, p=0.38) (Table 3 & Figure 2).

Utilization of ASA and beta blockers was also determined for RCH and SMH individually, and are presented in Table 4. The use of ASA at RCH at baseline was 84.2%, and 85.7% after our intervention. At SMH, similar modest changes in ASA use were observed from 93.9% to 95.6% in the baseline and intervention cohorts, respectively. Beta blocker use at RCH changed from 59.7% to 58.9% as a result of
the critical path intervention, while the change was from 82.7% to 91.2% at SMH (an absolute change of -0.8% for RCH and +8.5% for SMH).

Secondary outcomes of in-hospital mortality and length of hospital stay were also assessed and are presented in Table 5. There was a trend towards decreased in-hospital mortality from 13.6% to 12.7% (p=0.74 for difference) for the 2 institutions combined. The average length of hospital stay showed a statistically non-significant increase of 0.98 day (p=0.41) (Table 5 & Figure 2).

The critical path for AMI physician's order form also encourages the use of thrombolytic therapy in all eligible patients (Table 6). Thrombolytic therapy increased modestly from 44.9% at baseline to 46.1% after our intervention. The utilization of unproven or potentially harmful therapies is similarly discouraged by the critical path. Our intervention resulted in a 13.3% and 20.8% absolute percentage reduction in the use of calcium channel blockers and anti-arrhythmics respectively.
<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>Baseline n = 300</th>
<th>Intervention n = 291</th>
<th>Chi Sq. (df=1)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age range (yrs)</td>
<td>65.22 (SD 13.4)</td>
<td>67.4 (SD 13.6)</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>196 (65.5)</td>
<td>187 (64.2)</td>
<td>0.108</td>
<td>0.742</td>
</tr>
<tr>
<td>Previous MI</td>
<td>56 (18.7)</td>
<td>69 (23.7)</td>
<td>2.192</td>
<td>0.139</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>253 (84.6)</td>
<td>230 (79.0)</td>
<td>3.09</td>
<td>0.078</td>
</tr>
<tr>
<td>Transferred from another facility</td>
<td>27 (9.0)</td>
<td>33 (11.3)</td>
<td>0.861</td>
<td>0.353</td>
</tr>
</tbody>
</table>

Baseline: 7 months prior to implementation of the critical path
Intervention: 7 months after implementation of the critical path
Figures in parentheses indicate percentages unless otherwise indicated
SD: standard deviation
df: degrees of freedom
Table 2  Baseline patient characteristics reported separately for RCH and SMH

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>BASELINE</th>
<th></th>
<th>INTERVENTION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RCH n = 184</td>
<td>SMH n = 115</td>
<td>RCH n = 170</td>
<td>SMH n = 122</td>
</tr>
<tr>
<td>Male sex</td>
<td>121 (65.7)</td>
<td>75 (65.2)</td>
<td>105 (62.1)</td>
<td>82 (67.2)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>29 (15.7)</td>
<td>27 (23.4)</td>
<td>41 (24.2)</td>
<td>28 (22.9)</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>149 (80.9)</td>
<td>104 (90.4)</td>
<td>130 (76.9)</td>
<td>100 (81.9)</td>
</tr>
<tr>
<td>Transferred from another hospital</td>
<td>27 (14.6)</td>
<td>0 (0)</td>
<td>31 (18.3)</td>
<td>2 (1.6)</td>
</tr>
</tbody>
</table>

Baseline: Seven months prior to implementation of the critical path
Intervention: Seven months after implementation of the critical path
Figures in parentheses indicate percentages
Table 3  Overall use of ASA and beta blockers

<table>
<thead>
<tr>
<th></th>
<th>BASELINE</th>
<th>INTERVENTION</th>
<th>Chi sq</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 300</td>
<td>n = 282</td>
<td>(df=1)</td>
<td></td>
</tr>
<tr>
<td>ASA</td>
<td>264 (88.0)</td>
<td>253 (89.7)</td>
<td>0.432</td>
<td>0.511</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>206 (68.6)</td>
<td>203 (71.9)</td>
<td>0.767</td>
<td>0.381</td>
</tr>
</tbody>
</table>

Baseline: Seven months prior to implementation of the critical path
Intervention: Seven months after implementation of the critical path
Figures in parentheses indicate percentages unless otherwise indicated
df: degrees of freedom
### Table 4  Use of ASA and beta blockers reported separately for RCH and SMH

<table>
<thead>
<tr>
<th></th>
<th>BASELINE</th>
<th></th>
<th>INTERVENTION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RCH n = 184</td>
<td>SMH n = 116</td>
<td>RCH n = 168</td>
<td>SMH n = 114</td>
</tr>
<tr>
<td>ASA</td>
<td>155 (84.2)</td>
<td>109 (93.9)</td>
<td>144 (85.7)</td>
<td>109 (95.6)</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>110 (59.7)</td>
<td>96 (82.7)</td>
<td>99 (58.9)</td>
<td>104 (91.2)</td>
</tr>
</tbody>
</table>

Baseline: Seven months prior to implementation of the critical path  
Intervention: Seven months after implementation of the critical path  
Figures in parentheses indicate percentages
Table 5  Overall length of stay in hospital and in-hospital mortality

<table>
<thead>
<tr>
<th></th>
<th>BASELINE</th>
<th>INTERVENTION</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>n = 300</td>
<td>n = 282</td>
<td></td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>41 (13.6)</td>
<td>36 (12.7)</td>
<td>0.75</td>
</tr>
<tr>
<td>LOS (days)</td>
<td>8.2; SD 8.6</td>
<td>9.2; SD 9.0</td>
<td>0.41</td>
</tr>
<tr>
<td>Range (days)</td>
<td>1-116</td>
<td>1-73</td>
<td></td>
</tr>
</tbody>
</table>

Baseline: Seven months prior to implementation of the critical path
Intervention: Seven months after implementation of the critical path
Figures in parentheses indicate percentages
LOS: Length of hospital stay
Table 6  Use of thrombolytics, calcium channel blockers, and anti-arrhythmics

<table>
<thead>
<tr>
<th></th>
<th>BASELINE n = 300</th>
<th>INTERVENTION n = 282</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other proven efficacious therapies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombolytics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q wave MI</td>
<td>135 (44.9)</td>
<td>130 (46.1)</td>
</tr>
<tr>
<td>Non-Q wave MI</td>
<td>125 (41.6)</td>
<td>120 (42.5)</td>
</tr>
<tr>
<td></td>
<td>10 (3.3)</td>
<td>10 (3.5)</td>
</tr>
<tr>
<td>Unproven medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ca channel blocker</td>
<td>113 (37.6)</td>
<td>92 (32.6)</td>
</tr>
<tr>
<td>Anti-arrhythmic</td>
<td>48 (16.0)</td>
<td>36 (12.7)</td>
</tr>
</tbody>
</table>

Baseline: Seven months prior to implementation of the critical path
Intervention: Seven months after implementation of the critical path
Figures in parentheses indicate percentages
Figure 2  Effect of critical path management on the usage of medication and in-hospital mortality
Figure 3 Changes in use of proven efficacious therapy and in-hospital mortality between 1991-1992 and 1993-1994

- ASA $p<0.0001$
- BETA BLOCKER $p<0.0001$
- THROMBOLYTIC $p<0.0001$
- IN-HOSPITAL MORTALITY $p=0.18$
DISCUSSION

Previous patterns of practice studies have shown a marked disparity between the results of clinical trials' evidence and their application in clinical practice (2,21,27,28,29,31). Since AMI is highly prevalent in Western society, and carries a high mortality rate (1), the clinical implications of the present study are clear: improved utilization of efficacious therapies (ie. improving the process of patient care) should lead to better patient outcomes. Improving processes, and therefore quality, frees up hospital resources that can then be used elsewhere. In the long run, improved quality of medical care is less costly (34).

Demographics

The figures in Table 1 demonstrate comparability between baseline and intervention patients with respect to demographic characteristics. A major consideration in using a historical control is advances in medical care which may occur during the study period. To decrease this potentially confounding factor, a relatively short baseline and intervention period was chosen. As well, the clinical trials' evidence of the efficacy of the treatments under study have been available for at least 5 years, thereby ruling out any advances in the treatment of AMI which could have affected practice patterns.
Demographic variables which may affect the utilization of AMI therapies such as age, sex, Q wave versus non-Q wave AMI, or time delay in presentation to hospital (such as those which occur during transfer from another facility), were relatively comparable between the baseline and intervention groups.

Inspection of Table 2 reveals a marked difference between RCH and SMH in the proportion of patients transferred from another institution. This reflects the nature of the 2 institutions studied and is not unexpected. RCH is a tertiary care centre with full diagnostic and invasive cardiovascular facilities, while SMH is a secondary care institution, and therefore would be expected to only receive few referrals. The delays which may occur due to patient transfer could have some effect upon the use of AMI therapies, however, there is no reason that the referring institution could not administer these treatments prior to transfer, or en route.

The incidence of non-Q wave versus Q wave AMI was identified a priori as a possible confounder in the use of proven efficacious therapies. Non-Q wave, or subendocardial infarction occurs when only the inner wall of the myocardium is damaged. Transmural AMI involves the entire wall thickness of the myocardium, and are often signalled by the development of pathologic "Q waves". Typically, transmural AMI is characterized by a larger amount of myocardial damage, and is of greater clinical consequence. The exact contribution of infarct type to patterns of practice represents a complex scenario of the "cart and horse" variety. On one hand,
non-Q wave AMI's have not been conclusively shown to benefit from thrombolysis, beta blockers, or ASA, and therefore physicians may choose not to treat such individuals. However, non-Q wave AMI's may represent the early stages of transmural AMI, and the use of infarct size-limiting therapies may actually halt the progression of what would be destined to be a Q wave AMI to that of "only" a non-Q wave AMI. Furthermore, pathologic Q waves often do not develop until many hours after the infarction has occurred, and for this reason, perhaps should not have a major bearing on treatment decisions. Nevertheless, we observed a fairly even distribution of non-Q and Q wave AMI's among baseline and intervention groups, we feel that non-Q wave AMI's were unlikely to play a major role in the present study in the decision to treat patients with the targeted therapies.

Completeness of follow-up:

Due to missing data from patient charts, data on use of medications, in-hospital mortality and length of hospital stay could not be obtained for 9 patients in the intervention arm. This would not be expected to significantly alter our conclusions.

Primary Endpoints

The implementation of a critical path for the management of AMI had modest beneficial effects on the usage of ASA and beta
blockers. ASA usage increased by 1.7% to 89.7%, and beta blocker usage increased by 3.3% to 71.9%. While these are not statistically significant at conventional levels, they do represent maintenance of the levels of usage which have been achieved through our efforts over the past several years.

The modest success of the critical path process in the present study must be interpreted in the context of our ongoing continuous quality improvement efforts. Much of the lack of a "statistically significant" effect of the critical path process can be ascribed to the unexpectedly high baseline utilization observed in the present study. This may be explained in several ways:

(i) A Hawthorne Effect: Deficiencies in the application of proven efficacious therapies for AMI were first identified at RCH in 1991/92 (27). Since then, efforts had been ongoing at RCH to implement a critical path process. Strong initial resistance from the Emergency Department delayed implementation until September, 1993. During this period, however, the results of the patterns of practice analysis were disseminated and discussed on several occasions in a manner similar to those described by Montague, et al. (29). The phenomenon of improvement of a process by mere observation of it is called the Hawthorne Effect (42). In this case, dissemination of local patterns of practice data by themselves resulted in a marked improvement in utilization of proven therapies for AMI.

The critical path, when finally implemented, then served to continue to improve the patterns of practice, however, only after
they had already improved substantially due to the Hawthorne Effect. Indeed, analysis of the original data from 1991/92 (when this project was first conceived), compared to the current levels of utilization show very marked increases in utilization (Figure 3).

(ii) Utilization of ASA and Beta Blockers Are Already at an Optimal Level: It is possible that the usage of ASA and beta blockers may be already close to, or at, optimal levels. Since both ASA and beta blockers do have some contraindications to their use, it would not be reasonable to expect that their utilization be 100%. For example, it would be inappropriate to administer ASA to a patient with a true ASA allergy, or a beta blocker to an asthmatic patient.

Tsuyuki, et al., reported on patterns of practice in AMI taking into consideration contraindications to these therapies (27). In this study of 372 consecutive AMI patients, it was suggested that approximately 90% of patients are candidates for ASA, and 60% for beta blockers. These estimates were generated retrospectively through chart review, and are likely overly conservative, however, the present study's utilization rates of 89.7% and 71.9% for ASA and beta blockers, respectively, are fairly similar, and therefore do support this hypothesis.

(iii) Beta Error: there remains a possibility that the sample size of the current study may have been too small to reliably detect any small, but real differences attained by the study intervention.
The sample size calculation was based upon an expected 25% change in patterns of practice. In retrospect, this may have been overly optimistic given the baseline patterns of practice. Nevertheless, this issue should be rectified by the larger, multicentre trial of which this study is a part of.
Secondary Endpoints

The Canadian Cardiovascular Society 1991 consensus on Post-myocardial infarction management (43) describes an estimated 15% in-hospital mortality rate. Our results indicate slightly lower, but similar mortality rate of 13%. While this figure seems to be somewhat higher than those reported in several large-scale trials (11,12), it should be noted that many seriously ill patients, such as those in cardiogenic shock or cardiac arrest, were excluded from entry into those trials, thus producing an artificially low mortality rate. In order for our results to be generalizable to that of other facilities, and to reduce selection bias, we felt it important to include all AMI patients in our analysis regardless of prognosis or complications.

A number of variables influence patients' length of stay in hospital. The severity of infarction, presence of concomitant disease, advanced age, the need for surgical and diagnostic procedures, and medications can all affect the length of stay. It was anticipated that the use of proven efficacious therapies in AMI patients could improve the prognosis of these patients, and potentially hasten their recovery. The present study showed a non-significant 0.98 day increase in length of stay. Given the large range of this figure (1 to 116 days), this is not a surprising result. One potentially confounding factor may be that promotion
of the use of proven efficacious therapies for AMI may result in more patients surviving past the first few days of their infarction. This would obviously increase the average length of stay, and suggests the insensitivity of this marker.

Other Endpoints

The use of another proven efficacious AMI treatment, thrombolytic therapy, increased from 44.9% at baseline to 46.1% after the critical path intervention. This is a relatively high usage of thrombolytic therapy, and we would not expect that usage could be much higher because of the presence of numerous contraindications to their use. In the review of 2070 patients by Tsuyuki, et al., thrombolytic usage was found to be as high as 51% in one institution, with an average of 27% over the 4 cohorts studied (2). The increase in the use of thrombolytic therapy observed in the present study can be attributed in part, to the "softening" of many of the criteria for thrombolysis: in particular, a 12 hour time window from onset of chest pain rather than 6 hours, and increased treatment of the elderly. As well, efforts have been directed at both medical staff and the general public to promote the benefits of early thrombolysis.

Another benefit of the use of a critical path tool is to discourage the use of unproven, or potentially harmful therapies. The two most infamous of these therapies are the use of
prophylactic anti-arrhythmic therapy and calcium channel blockers, neither of which have been shown to benefit patient outcomes, and indeed may actually cause harm (8). The statement contained on the critical path order form: "If calcium channel blockers (or anti-arrhythmics) ordered, please state reason" was intended to make physicians think twice about using these medications. It does, however, allow some flexibility for specific situations where these agents may be desirable. The absolute reduction in the use of anti-arrhythmic therapy of 20.8%, and 13.3% for calcium channel blockers can be directly attributed to the critical path process, as the potentially harmful effects of these treatments have been known for many years.

Other Potential Benefits of the Critical Path Process

An attractive feature of the critical path is its ease of use. Physicians are no longer burdened with writing out the same, long orders. All physicians, especially housestaff, are educated on all proven efficacious therapies and optimal dosing at a glance. In effect, a properly designed critical path protocol can give a non-expert all of the therapeutic tools of an expert. The form is a constant reinforcement and a learning tool for all staff involved in the management of AMI as to the best therapeutic regimen, as determined by the best available evidence and a consensus among all local experts.

The critical path is continuously updated based upon the best
available clinical trials' evidence, thus truly embracing the principles of continuous quality improvement and experience-based medicine. Orders pre-printed in this way are more easily read, and may decrease physician and medication errors.

Use of a critical path may also impart legal benefits. Standardizing medication use not only provides physicians with the latest treatment guidelines, but also documentation for future reference, of which and why a medication was used or not used.

Problems Related to Implementation

The use of practice guidelines such as these have been maligned by some physicians as promoting "cookbook" medicine, and that they decrease the "freedom of choice" of physicians. To the latter comment, we must at least partially agree. Previous patterns of practice analyses have conclusively demonstrated that physicians, left up to their own "freedom of choice", consistently do not practice up to the standards created by their own professional organizations (43) or to the clinical trials' evidence in the medical literature (9,21,27,31). In the true spirit of CQI, the goal is to reduce unwarranted practice variations by providing explicit guidelines for the management of AMI patients, based upon methodologically sound clinical trials' evidence. The criticism of promoting cookbook medicine is similarly unwarranted. The critical path ordering form is merely a tool to facilitate patient management; physicians are at liberty to make modifications based
upon their clinical judgement.

One concern that has been expressed is that patients who receive ASA, beta blockers and thrombolytic therapy, could have adverse effects which might complicate the patient's course. For example, we have heard largely unwarranted concerns of worsening heart failure, conduction disturbances, depression, etc. attributed to beta blocker therapy. However, if patients are properly screened for contraindications, and pharmacodynamic and pharmacokinetic variables such as age and concurrent disease are properly considered, adverse reactions should not be a major concern (17). In fact, it has been suggested by meta analysis that patients with heart failure post AMI actually experienced the greatest mortality benefit from beta blockers (44) compared to those without left ventricular dysfunction. This is a variation of the adage that "if a therapy works, it tends to work best in those patients at highest risk" (29,30).

Examination of the data from the individual hospitals reveals that SMH, who have readily embraced the critical path/CQI concept, have a trend towards faring better in their patterns of practice (Table 4) as compared to RCH. A possible explanation for this may be SMH's greater receptiveness and willingness to incorporate new knowledge. In addition, SMH's more unified, and cooperative approach were likely important ingredients to their greater success. This highlights the importance of leadership, teamwork and cooperation in the CQI process, and is well described by Berwick (34).
This was a first attempt at implementing a CQI program at these hospitals, and, as expected, there were problems in its implementation. It is hoped that the experience gained from this project will now facilitate future CQI efforts.
Limitations of the present study

This study relied on a historical control rather than a concurrent control. This method lacks blinding, and lends itself to difficulties in ensuring comparability of baseline patient characteristics and also level of physician knowledge in the treatment of AMI with the progression of time. It was felt that blinding was not possible as physicians would know whether or not they were in the "intervention" arm simply by the presence of the critical path protocol. In addition, it would be impossible to prevent physicians in the "usual care" arm to find out the contents of the critical path protocol and thereby be affected by this knowledge. The use of another hospital to act as a control was also considered but the greater variations in practice and knowledge base between, as opposed to within a site, would be analogous to a comparison between apples and oranges.

Comparability was ensured between the baseline and the intervention group by 1) recruiting consecutive patients in two 7 month blocks, 2) selecting all patients with a discharge diagnosis of AMI. However, since a historical control was used, differences in baseline physician and patient knowledge are inevitable. The impact of the Hawthorne effect (42) on this study is also difficult to separate as described earlier in this paper. Since the object of the critical path tool is not only to improve patterns of practice, but to also disseminate knowledge, then perhaps the two
are intimately connected, with one lending to another, and would not require separation. In the end, all that is really important is that patterns of practice change favourably so that better patient outcomes can be realized.
CONCLUSION

Coronary artery disease remains the leading cause of death in Western society. Despite the availability of efficacious therapies, in-hospital mortality remains high. A critical path protocol for the management of AMI was developed to improve the utilization of proven efficacious therapy and discourage the use of unproven medications. Based upon CQI principles, a critical path for the management of AMI was developed. The efficacy of this critical path was evaluated using a retrospective control, i.e. the patterns of practice prior to its implementation.

Results indicate that the implementation of the critical path for AMI has led to modest increases in the use of proven efficacious therapies and decreases in the use of unproven medications. Repeated observation of the overall changes in the patterns of practice since the conception and development of the critical path have created a large Hawthorne effect, resulting in substantial improvements in use of proven efficacious therapies.

This study represents unprecedented research providing valuable insight and data into the use of a clinical guideline for the pharmacotherapeutic management of AMI patient. An ongoing large scale study involving other community and teaching hospitals could facilitate the assessment and validation of the efficacy of this protocol.
Areas For Future Research

The future will include periodic updating of the contents of the critical path for AMI order forms as new evidence becomes available. Recent clinical trials have established the efficacy of angiotensin converting enzyme inhibitors in the prevention of congestive heart failure in those patients with left ventricular dysfunction post AMI (45,46,47). In the spirit of CQI, these will be added to the critical path ordering forms.

This study is part of a large cooperative effort carried out by the members of CQIN, and represent an important step in the development of the collaborative network. The main study, of which the current study is a part of, should provide further insight into the usage of proven efficacious therapy, short and long term patient outcomes through measures of in-hospital, 35 day, and 1 year mortality, hospital readmission rate, and reason for readmission. As well, the main study will provide further insight into the age and sex bias consistently observed in the previous trials (2,28,29,31).

As an important aspect of continuous quality improvement and continued knowledge dissemination, it would be invaluable to know why physicians "do what they do". Insights from organizational behaviour theory into the barriers to prescribing proven efficacious therapy are required and are also being studied by
CQIN. The reasons why physicians "choose" not to prescribe a proven efficacious therapy, or why they would prescribe a unproven medication will also be captured in a substudy of the main Critical Path Management for AMI protocol (39).

Woolf, in 1993 asked the question, "Do guidelines define optimal care?" (35) The concept of "optimum care" should embrace all aspects of health care - physician practices, patient satisfaction, resource and monetary utilization, and legal implications. For example, in the quest for increasing usage of beta-blockers, suppose that many more patients began experiencing adverse effects such as depression. In this case, the objective of improved physician practices as set out by the guideline may be achieved, but at the expense of other aspects of health and health care. Knowledge regarding the economic benefits of guidelines is limited (35). What are the long and short term monetary costs to enforcement of guideline usage? A long term follow-up to monitor the effects of the guidelines on the above-mentioned, more holistic aspects of health and health care should be undertaken.

Long-standing arguments whether to treat with thrombolytics, or which thrombolytic to use, seem to often overshadow the importance of treating as soon as possible. Evidence from the GISSI trial (11) forms the rationale behind the importance of early therapy: the earlier the treatment is given, the greater the reduction in mortality. The GUSTO substudy (48) supports the existence of a problem in the time delay in treatment of AMI, and identifies several areas of delay. Unpublished data from RCH has
also indicated unexplained delays in thrombolysis, as well as in patients receiving ASA and beta blocker therapy. Perhaps an important adjuvant to the Critical Path for AMI is another protocol for the triage of chest pain patients in the emergency department so that patients can begin the Critical Path for AMI as soon as possible. Such a protocol - Critical Path Management for Chest Pain in the Emergency Department - is currently under development by CQIN (49).

CQI principles through critical paths can also be expanded to other disease states. Opportunities are present in areas such as asthma therapy, treatment of peptic ulcer disease, management of congestive heart failure, atrial fibrillation, and antibiotic use. In fact, opportunities exist wherever there are high quality clinical trials' evidence for efficacy of a given therapy.

Rather than continuing with predominantly drug-focused monitoring activities, such as drug utilization evaluation (DUE), perhaps pharmacy departments should broaden their scope and consider the use of CQI techniques as a complementary activity.

The members of CQIN feel strongly that the use of all proven efficacious therapies can produce optimal patient outcomes, and, in the end, this is less costly to the well-being of the patient and the health care system.
REFERENCES


44. Held P. Effects of beta blockers on ventricular dysfunction after myocardial infarction: tolerability and survival effects. Am J Cardiol 1993; 71:39C-44C.


APPENDIX A: SUMMARY OF CLINICAL TRIALS OF AMI THERAPIES AND THEIR RELATIVE EFFICACY

("NF": non-fatal)

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Relative Effectiveness*</th>
<th>Notable Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA (early)</td>
<td>21% ↓ mortality</td>
<td>ISIS-2</td>
</tr>
<tr>
<td></td>
<td>44% ↓ NF reinfarction</td>
<td></td>
</tr>
<tr>
<td>Thrombolytic therapy</td>
<td>24-26% ↓ mortality</td>
<td>GISSI, TIMI, GUSTO, ISIS-2, ISIS-3, GISSI-2, etc.</td>
</tr>
<tr>
<td>β-blockers (intravenous)</td>
<td>13% ↓ vasc. mortality</td>
<td>MIAMI, ISIS-1</td>
</tr>
<tr>
<td></td>
<td>19% ↓ NF reinfarction</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16% ↓ NF cardiac arrest</td>
<td></td>
</tr>
<tr>
<td>Nitrates</td>
<td>35% ↓ mortality</td>
<td></td>
</tr>
<tr>
<td>β-blockers (oral)</td>
<td>22% ↓ mortality</td>
<td>MIAMI, ISIS-1</td>
</tr>
<tr>
<td>ACE inhibitors (long-term)</td>
<td>0-19% ↓ mortality</td>
<td>SAVE, SOLVD prevention</td>
</tr>
<tr>
<td></td>
<td>37% ↓ development of CHF</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25% ↓ recurrent MI</td>
<td></td>
</tr>
<tr>
<td>Lipid Lowering</td>
<td>1% ↓ cholesterol = 2-3% ↓ CHD events</td>
<td>LRC, etc.</td>
</tr>
<tr>
<td>ASA (long-term)</td>
<td>11% ↓ mortality</td>
<td>Physicians' Health Study, etc.</td>
</tr>
<tr>
<td></td>
<td>44% ↓ MI</td>
<td></td>
</tr>
<tr>
<td>Lidocaine</td>
<td>11% ↑ mortality</td>
<td></td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>6-10% ↑ mortality</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX B: SUPPLY OF THROMBOLYTIC DRUGS IN TRENT REGION FROM DISTRICT PHARMACY SERVICES AND TRIAL ORGANISATIONS
From Figure 1 reference #20

Figure 1: Supply of thrombolytic drugs in Trent region from district pharmacy services and trial organisations
Mean value for districts (bold line) and standard deviation are plotted by financial half-year. Dates of journal publication of the major trial results are also shown.
Table 1 Percent distribution of demographic and clinical variables in 2070 patients with acute myocardial infarction by time and setting

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>71</td>
<td>65</td>
<td>74</td>
<td>73</td>
<td>69</td>
<td>66</td>
<td>66</td>
<td>69</td>
<td>70</td>
</tr>
<tr>
<td>Females</td>
<td>29</td>
<td>35</td>
<td>26</td>
<td>27</td>
<td>31</td>
<td>34</td>
<td>34</td>
<td>31</td>
<td>30</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 70 years</td>
<td>46</td>
<td>51</td>
<td>33</td>
<td>39</td>
<td>37</td>
<td>44</td>
<td>50</td>
<td>39</td>
<td>41</td>
</tr>
<tr>
<td>&lt; 70 years</td>
<td>54</td>
<td>49</td>
<td>67</td>
<td>61</td>
<td>63</td>
<td>57</td>
<td>50</td>
<td>61</td>
<td>59</td>
</tr>
<tr>
<td><strong>Previous AMI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>41</td>
<td>27</td>
<td>29</td>
<td>25</td>
<td>30</td>
<td>33</td>
<td>27</td>
<td>30</td>
</tr>
<tr>
<td><strong>Acetylsalicylic Acid</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>55</td>
<td>34</td>
<td>71</td>
<td>83</td>
<td>92</td>
<td>79</td>
<td>80</td>
<td>77</td>
<td>76</td>
</tr>
<tr>
<td><strong>Beta Blockers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>64</td>
<td>27</td>
<td>41</td>
<td>57</td>
<td>34</td>
<td>35</td>
<td>40</td>
<td>56</td>
<td>44</td>
</tr>
<tr>
<td><strong>Thrombolysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>17</td>
<td>10</td>
<td>15</td>
<td>34</td>
<td>51</td>
<td>24</td>
<td>30</td>
<td>30</td>
<td>27</td>
</tr>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>20</td>
<td>14</td>
<td>13</td>
<td>12</td>
<td>10</td>
<td>18</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
</table>

MIS = Misericordia Hospital, Edmonton AB;
RCH = Royal Columbian Hospital, New Westminster BC;
SMH = Memorial Hospital, Surrey BC;
UAH = University of Alberta Hospitals, Edmonton AB; and
VGH = Victoria General Hospital, Halifax NS
Table 2 Univariate comparison of demographic and clinical variables in 629 females and 1441 males with acute myocardial infarction 1987 to 1992

<table>
<thead>
<tr>
<th></th>
<th>Females (%)</th>
<th>Males (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥70</td>
<td>61</td>
<td>32</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>&lt;70</td>
<td>39</td>
<td>68</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous AMI</td>
<td>27</td>
<td>31</td>
<td>NS</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>69</td>
<td>79</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>36</td>
<td>48</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>20</td>
<td>30</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mortality</td>
<td>18</td>
<td>12</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

NS = not significant
APPENDIX E: UNIVARIATE COMPARISON OF DEMOGRAPHIC AND CLINICAL VARIABLES IN 846 PATIENTS 70 YEARS OF AGE AND OLDER AND 1224 PATIENTS LESS THAN 70 YEARS WITH ACUTE MYOCARDIAL INFARCTION 1987 TO 1992

From Table 3 reference #2

Table 3 Univariate comparison of demographic and clinical variables in 846 patients 70 years of age and older and 1224 patients less than 70 years with acute myocardial infarction 1987 to 1992

<table>
<thead>
<tr>
<th>Variable</th>
<th>≥70 Years (%)</th>
<th>&lt;70 Years (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>55</td>
<td>80</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Females</td>
<td>45</td>
<td>20</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous AMI</td>
<td>26</td>
<td>34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>65</td>
<td>83</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>33</td>
<td>52</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>16</td>
<td>34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mortality</td>
<td>25</td>
<td>7</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

From Table 3 reference #2

Table 3 Univariate comparison of demographic and clinical variables in 846 patients 70 years of age and older and 1224 patients less than 70 years with acute myocardial infarction 1987 to 1992

<table>
<thead>
<tr>
<th>Variable</th>
<th>≥70 Years (%)</th>
<th>&lt;70 Years (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>55</td>
<td>80</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Females</td>
<td>45</td>
<td>20</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Previous AMI</td>
<td>26</td>
<td>34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>65</td>
<td>83</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>33</td>
<td>52</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>16</td>
<td>34</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mortality</td>
<td>25</td>
<td>7</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
APPENDIX F: USE OF PROVEN EFFECTIVE AND UNPROVEN MEDICAL THERAPIES AMONG ACUTE MYOCARDIAL INFARCTION PATIENTS 70 YEARS OR OLDER AND LESS THAN 70 YEARS OVER THREE YEARS.
From Figures 1 & 2 reference #28

Figure 1) Use of proven effective and unproven medical therapies among acute myocardial infarction patients 70 years or older (closed circles) and less than 70 years (open circles) over three years. P values refer to significance of changes with time.

Figure 2) In-hospital mortality rates in acute myocardial infarction patients 70 years or older (closed circles), younger than 70 years (open circles) and both groups combined (squares) over three years. P values refer to significance of changes with time.
APPENDIX G: DEVELOPING AND IMPLEMENTING CRITICAL PATHS

Select Diagnoses/Procedures

Appoint a Development Team

Document Current Process and Causes of Variation

Develop Critical Path; Develop Measures of Conformance and Outcomes

Implement Critical Path

Are Results Acceptable?

Y

Continue Monitoring

N

Improve as Necessary

Note: Use Criteria

Note: Multidisciplinary
# APPENDIX H: STANDARD ORDERS - ACUTE MYOCARDIAL INFARCTION

The Fraser-Burrard Hospital Society

**DOCTOR'S ORDERS**

ALL ORDERS FOR MEDICATIONS SHOULD BE QUALIFIED AS TO LENGTH OF THERAPY OR NUMBER OF DOSES TO BE ADMINISTERED.

"Pharmacy Committee"

MUST BE FILLED IN ON FIRST PAGE OF CHART:

1. ALLERGIES (IF NONE, INDICATE THIS)

2. DIAGNOSIS

---

**STANDARD ORDERS - ACUTE MYOCARDIAL INFARCTION**

<table>
<thead>
<tr>
<th>DATE AND TIME</th>
<th>PHASES</th>
<th>TREATMENTS AND OTHER ORDERS</th>
<th>MEDICATIONS ONLY</th>
<th>DRUG - DOSE - ROUTE - FREQUENCY - DURATION</th>
</tr>
</thead>
</table>

*PLEASE CROSS OUT ANYTHING NOT IN ACCORDANCE WITH YOUR WISHES.*

I. Consider patient for entry into a clinical trial.

II. Notification: Please notify Drs. _______ & _______ of patient's admission and enter on computer and addressograph.

III. Investigations:

- PT, PTT, platelets, CBC (unless already done)
- Electrolytes, BUN, creatinine, glucose
- Serum total cholesterol
- CK, CK-MB stat (if not already done); then bid x 36h
- Urine dipstick, using Chemstrip 5L
- Chest X-Ray (portable)
- 12-lead EKG stat (if not already done), then daily upon admission to CCU, x 3 days
- 12-lead EKG to be done with chest pain (in absence of LBBB or pacemaker)
- Other investigations:

IV. Standard Orders:

- Bedrest with commode
- IV with DSW to KVO or saline lock
- Cardiac diet
- Monitor: EKG
- Pulse oximetry daily
- If SaO₂<85% on room air; give O₂ at 2-4 L/min, via nasal prongs

V. Medications:

1. ASA:
   - ASA PLAIN 325mg po stat (chewed), then
   - ENTERIC-COATED ASA 325mg po once daily thereafter.
   
   * If ASA not ordered, please state reason:

2. Heparin (check one and cross out the other):

   - [ ] HEPARIN INFUSION: as per heparin protocol (fill out pre-printed order form)
   - (a) If patient receiving thrombolytic therapy, do not reduce infusion in first 24h regardless of PTT
   - (b) If hemorrhage occurs, discontinue heparin and call physician
   OR
   - [ ] HEPARIN 5000 units sc q12h
**Absolute Contraindications for Thrombolytic Therapy:**

1. Active internal bleeding
2. Suspected aortic dissection
3. Prolonged or traumatic CPR
4. Recent head trauma or known intracranial neoplasm
5. Recent (<2 weeks) surgery which has potential for rebleeding
6. Diabetic hemorrhagic retinopathy
7. Pregnancy
8. Previous allergic reaction (to streptokinase)
9. Recorded blood pressure >200/120 mmHg
10. History of CVA known to be hemorrhagic

**Relative Contraindications for Thrombolytic Therapy:**

1. Recent trauma or surgery > 2 weeks
2. History of chronic severe hypertension
3. Active peptic ulcer
4. History of CVA
5. Known bleeding diathesis
6. Significant liver dysfunction
7. Previous treatment with streptokinase (for second treatment)

**Absolute Contraindications for IV β-blockers:**

1. Heart rate <60 beats/min
2. Systolic BP <100 mmHg
3. Moderate to severe left ventricular failure
4. Signs of peripheral hypoperfusion
5. AV conduction abnormalities
6. Severe chronic obstructive pulmonary disease

**Relative Contraindications for IV β-blockers:**

1. History of asthma
2. Current use of β-blockers (may require modification of iv dosing)
3. Current use of calcium channel blockers (verapamil and diltiazem: may require modification of iv β-blocker dosing).
4. Severe peripheral vascular disease
5. Poorly controlled insulin dependent diabetes mellitus

*The above are offered as guidelines only, as suggested by the American College of Cardiology/American Heart Association. Circulation 1990;82: 664-707*
**STANDARD ORDERS - ACUTE MYOCARDIAL INFARCTION**

<table>
<thead>
<tr>
<th>DATE AND TIME</th>
<th>NURSES AWARENESS</th>
<th>TREATMENTS AND OTHER ORDERS</th>
<th>NURSES</th>
<th>DRUG DOSE</th>
<th>FREQUENCY</th>
<th>DURATION</th>
</tr>
</thead>
</table>

3. **Thrombolytic Therapy (check one and cross out the other):**
   - [ ] STREPTOKINASE 750,000 units in 50mL DSW over 10 minutes IV, followed by 750,000 units in 50mL DSW over 50 minutes IV (hospital standard).
   - **OR**
   - [ ] ALTEPLASE (t-PA) 15mg IV over 2 minutes by physician, then
     - 0.75mg/kg = _____ (not >50mg) IV over 30 minutes, then
     - 0.5mg/kg = _____ (not >35mg) IV over 60 minutes.
   * If thrombolytic therapy not ordered, please state reason(s):__________________________

4. **Beta blockers (check one and cross out the other):**
   - [ ] -METOPROLOL 5mg IV over 2-5 minutes or 5min. x 3 doses (15mg total dose) given by physician, then:
     - [ ] -METOPROLOL 50mg po 15 minutes later,
     - [ ] -METOPROLOL 50mg po q6h for 48 hours,
     - [ ] -METOPROLOL 100mg po bid thereafter.
   - **OR**
   - [ ] -Other beta blocker:__________________________
   * If beta blocker therapy not ordered, please state reason(s):__________________________

5. **Nitrates (check one and cross out the other):**
   - [ ] NITROGLYCERIN (50mg/250mL D5W): Infuse at 0.1mcg/kg/min. and titrate Q5-10 min. to maintain systolic BP > 100mmHg.
   - **OR**
   - [ ] TRANSDERMAL NITROGLYCERIN PATCH: _____mg/hr.
     - Apply daily in AM, remove at hs.
   * If nitrates not ordered, please state reason(s):__________________________
The Fraser-Burrard Hospital Society

**DOCTOR'S ORDERS**

ALL ORDERS FOR MEDICATIONS SHOULD BE QUALIFIED AS TO LENGTH OF THERAPY OR NUMBER OF DOSES TO BE ADMINISTERED.

"Pharmacy Committee"

**MUST BE FILLED IN ON FIRST PAGE OF CHART:**

1. **ALLERGIES (IF NONE, INDICATE THIS):**

2. **DIAGNOSIS:**

**STANDARD ORDERS - ACUTE MYOCARDIAL INFARCTION**

<table>
<thead>
<tr>
<th>DATE AND TIME</th>
<th>DRUGS AND DOSE</th>
<th>ROUTE</th>
<th>FREQUENCY</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Prn Symptomatic Ventricular Tachycardia:</td>
<td>LIDOCAINE 1.5mg/kg IV over 1-2 minutes, then</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LIDOCAINE 50mg IV over 1-2 minutes Q6min. x 2, and</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LIDOCAINE (1g/250mL) IV infusion at 2-4 mg/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Prn Symptomatic Bradycardias:</td>
<td>ATROPINE 1.0mg IV, may repeat Q5 min, up to 3mg maximum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Prn Sedation:</td>
<td>LORAZEPAM 1-2mg PO/IV q6h pm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Prn Nausea:</td>
<td>DIMENHYDRINATE 25-50mg PO/IV q6h pm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Prn Chest Pain:</td>
<td>12-lead EKG to be done during chest pain.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>NITROGLYCERIN SPRAY 0.4mg sl. May repeat x 3 Q5 min.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>MORPHINE 3-6mg IV prn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>O₂ at 2-4L/min. via nasal prongs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. Prn Constipation:</td>
<td>GLYCERIN SUPPOSITORY pr prn</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>LAXATIVE OF CHOICE pm (caution in renal insufficiency)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. OTHER MEDICATIONS/ORDERS:</td>
<td>DOCUSATE 100mg po bid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACETAMINOPHEN 525-650mg po q6h prn.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*If calcium channel blockers or antidysrhythmics ordered, please state reason(s):*

Signature: __________________________ M.D.
## Allergy

Describe reaction

### Diagnosis

1. Cross out and initial orders not needed.
2. List only those drugs which are currently being administered to the patient. Any drugs ordered that are not listed below, require an explanation.
3. For additional orders, a separate Doctors order sheet must be used.

- Admit to:  
  - [ ] CCU  
  - [ ] ICU
- Attending Physician
- Consulting Physician
- General Practitioner

### Investigations

On admission:
- CBC & diff, CPK, CKMB, electrolytes, BUN, creatinine, PT, PTT
- ECG, Chest X-ray

Follow-up:
- ECG daily x 2 plus PRN as per STAT policy (total of 3)
- CK, CKMB q 12 hrs x 2
- Portable Chest X-ray within 24 hrs (if not done in ER)

- Full fluids x 12 hrs → Cardiac Diet
- Bedrest with commode privileges
- O₂ @ __ Liters per minute by nasal prongs PRN
- EC ASA  
  325 mg p.o. STAT and then daily or __________ p.o. daily.
  If ASA NOT ordered, please state reason.

### Thrombolytics

- [ ] Streptokinase protocol
- [ ] t-PA protocol

If thrombolytics NOT ordered, please state reason.
CRITICAL PATH PATIENT CARE PROTOCOL
ACUTE MYOCARDIAL INFARCTION
CRITICAL CARE ORDERS

- **Beta Blocker**
  - mg I.V. STAT and mg I.V. q
  - mg p.o.
  If beta blocker NOT used, please state reason.

- **Heparin**
  - IV Heparin as per Heparin protocol

- **Nitrates**
  - I.V. nitroglycerine 50 mg in 250 cc D5W
  Start at mcg/min then increase by mcg/min until relief of pain or systolic BP <90 or MAP of 80 mm Hg or a decrease in systolic BP by mmHg.
  If nitrate NOT ordered, please state reason.

- **ACE inhibitor if EF less than 40%**
  - mg p.o.
  If ACE Inhibitor NOT ordered, please state reason.

- **Other Medications**
  - If antidysrhythmics or calcium channel blockers ordered, please state reason.

- **PRN medication**
  - Morphine 2 - 5 mg I.V. PRN for chest pain
  - Gravol 25 - 50 mg I.V. /p.o. q 4 hr PRN
  - Nitroglycerine spray 0.4 mg S/L PRN
  - Colace 100 mg p.o. b.i.d. PRN
  - Magnolax 30cc p.o. o.d. PRN
  - Glycerine suppository x 1 rectally PRN
  - Maalox 30cc p.o. PRN
  - Tylenol 325 mg - 650 mg p.o. q 4 - 6 hrs PRN or
  - Tylenol #3 1- 2 tabs p.o. q 4 hrs PRN
  - Serax 15 - 30 mg p.o. q.h.s. PRN
  - Ativan 1 mg S/L PRN
CRITICAL PATH PATIENT CARE PROTOCOL
ACUTE MYOCARDIAL INFARCTION
TRANSFER ORDERS

1. Cross out and initial orders not needed.
2. List only those drugs which are currently being administered to the patient.
   Any drugs ordered that are not listed below, require an explanation.
3. For additional orders, a separate Doctors order sheet must be used.

- Transfer to Cardiac Step Down Unit on Telemetry - Day _______ Post-myocardial infarction
- Attending Physician
- Consulting Physician
- General Practitioner

- Cardiac Diet or

- Mobilize - Advance as tolerated

- $O_2$ ______ Imp by nasal prongs PRN

- ECG with chest pain as per STAT policy

- Other Laboratory tests:

- Vital signs b.i.d. or

- Myocardial Infarction Teaching - Refer to Cardiac Rehabilitation Partnership Program
Surrey Memorial Hospital

CRITICAL PATH PATIENT CARE PROTOCOL
ACUTE MYOCARDIAL INFARCTION
TRANSFER ORDERS

- Book patient for Low Level Stress Test: Date booked
  Prior to discharge: □ ____________
  6 weeks post discharge: □ ____________

- ASA: Enteric coated ASA: 325 mg p.o. daily or
  If ASA NOT ordered, please state reason______________________________

- Beta blocker
  ____________ ____________ mg p.o.
  If Beta blocker NOT used, please state reason______________________________

- Nitrate:______________________________
  If nitrate NOT ordered, please state reason______________________________

- ACE Inhibitor if ejection fraction less than 40% start on ACE Inhibitor
  ____________ ____________ mg p.o.
  If ACE Inhibitor NOT used please state reason______________________________

- Heparin
  IV Heparin as per Heparin protocol

- PRN medications
  Morphine 2 - 5 mg I.V. PRN for chest pain
  Gravol 25 - 50 mg I.V. /p.o. q 4 hr PRN
  Nitroglycerine spray 0.4 mg S/L PRN
  Colace 100 mg p.o. b.i.d. PRN
  Magnolax 30 cc p.o. o.d. PRN
  Glycerine suppository x 1 rectally PRN
  Maalox 30cc p.o. PRN
  Tylenol 325 mg - 650 mg p.o. q 4 - 6 hrs PRN or ____________________________
  Tylenol #3 1 - 2 tabs p.o. q 4 hrs PRN
  Serax 15 - 30 mg p.o. q.h.s. PRN
  Ativan 1 mg S/L PRN
ANTICOAGULATION (HEPARIN/WARFARIN) ORDERING FORM

1. Allergies (if none, indicate this)
2. Diagnosis

HEPARIN THERAPY:

4. Heparin intravenous bolus dose and initial infusion rates as outlined below (check one).

<table>
<thead>
<tr>
<th>Patients' Wt</th>
<th>Heparin IV Bolus</th>
<th>Initial IV Infusion rates with Heparin 25,000 units in 500 mL D5W</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40 Kg</td>
<td>2,500 units</td>
<td>750 units/h = 15 mL/h</td>
</tr>
<tr>
<td>40-54 Kg</td>
<td>4,000 units</td>
<td>900 units/h = 18 mL/h</td>
</tr>
<tr>
<td>55-69 Kg</td>
<td>5,500 units</td>
<td>1000 units/h = 20 mL/h</td>
</tr>
<tr>
<td>70-84 Kg</td>
<td>7,000 units</td>
<td>1150 units/h = 23 mL/h</td>
</tr>
<tr>
<td>85-99 Kg</td>
<td>8,500 units</td>
<td>1300 units/h = 26 mL/h</td>
</tr>
<tr>
<td>100-120 Kg</td>
<td>10,000 units</td>
<td>1450 units/h = 29 mL/h</td>
</tr>
<tr>
<td>&gt; 120 Kg</td>
<td>12,000 units</td>
<td>1650 units/h = 33 mL/h</td>
</tr>
</tbody>
</table>

5. PTT in 6 hours, then adjust heparin infusion as follows:

<table>
<thead>
<tr>
<th>PTT</th>
<th>Heparin Rate Change</th>
<th>Repeat PTT</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50 sec</td>
<td>5000 unit bolus and increase rate by 150 units (3 mL)/h</td>
<td>in 6 h</td>
</tr>
<tr>
<td>50-59 sec</td>
<td>increase infusion rate by 100 units (2 mL)/h</td>
<td>in 6 h</td>
</tr>
<tr>
<td>60-65 sec</td>
<td>no change</td>
<td>next day</td>
</tr>
<tr>
<td>86-95 sec</td>
<td>decrease infusion rate by 50 units (1 mL)/h</td>
<td>next day</td>
</tr>
<tr>
<td>96-120 sec</td>
<td>stop infusion for 30 min, then decrease rate by</td>
<td>in 6 h</td>
</tr>
<tr>
<td></td>
<td>100 units (2 mL)/h</td>
<td></td>
</tr>
<tr>
<td>&gt; 120 sec</td>
<td>stop infusion for 60 min, then decrease rate by 150 units (3 mL)/h</td>
<td>in 6 h</td>
</tr>
</tbody>
</table>

WARFARIN THERAPY:

6. Please check off and complete if appropriate:

☐ Give warfarin _______ mg daily x 3 days

starting ☐ today

☐ other date: (please specify)

(Warfarin to be ordered on a daily basis after 3 days)

7. Daily PT/INR if when warfarin started. (Call physician with results).

8. Discontinue heparin on the _______ day of warfarin therapy.
   (At least five days of heparin/warfarin overlap are recommended). Signature:
APPENDIX J: CRITICAL PATH FOR AMI DATA COLLECTION FORM

SURREY MEMORIAL HOSPITAL
CRITICAL PATH ANALYSIS OF
ACUTE MYOCARDIAL INFARCTION

Hospital # __________________________
Name ________________________________ Age __________________________
Address _______________________________ Sex __________________________
Phone (res) __________________________ (wk) __________________________
Admission Date ________________________ Discharge Date ____________________

Presentation
Previous MI ___ Pain ___ Transfer ___ Q Wave ___

Medications Received ANYTIME in Hospital
Thrombolysis ___ B-blocker ___ Ca++ blocker ___ Heparin ___
Nitrates ___ ASA ___ Antiarrhythmic ___ ACE-I ___

Medications on Discharge
B-blocker ___ Ca++ blocker ___ Nitrates ___ Antiarrhythmic ___
ACE-I ___ ASA ___

Investigation in Hospital
Stress Test ___ - Treadmill□ EF ___% MUGA ___ Cath ___ Echo ___
- Persantine MIBI□
- Exercise MIBI□

In clinical trial while in hospital? ___

Survival
In hospital ___ 35 days ___ 1 year ___

Readmissions
# in 1 year _______ Indicate reason: Cardiac _______ Non-cardiac _______