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UMI
Comparing Angiographic Coronary Revascularization Strategies: A ‘Natural’ Experiment

A thesis submitted in conformity with the requirements for the degree of Masters in Clinical Epidemiology and Health Care Research. Graduate Department of Community Health in the University of Toronto

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Abstract

Comparing Angiographic Revascularization Strategies: A ‘Natural’ Experiment, Masters of Clinical Epidemiology and Health Care Research, 1998. Saleem Kassam, Graduate Department of Community Health at the University of Toronto

Objective: To compare rates of clinical restenosis between routine angioplasty and coronary stenting in the real world.

Design: A retrospective cohort analysis comparing markers of clinical restenosis between patients exposed to liberal and conservative coronary stenting policies.

Setting: At a tertiary care, high-volume Canadian institution, patients who underwent percutaneous coronary interventions were captured in a database.

Patients: Individuals undergoing angiographic revascularization during a period of economic restraint (the ‘conservative’ group [C]) from January 1 to February 28 1996, were compared to a before and after cohort, where coronary stent use was at ‘usual’, higher levels (the liberal group [L], November 1 to Nov 30, 1995 (L1), and April 1 to May 31 (L2) 1996)

Follow up: Data was gathered retrospectively. The endpoint was the first of any of the following within nine months: death, MI, CABG, repeat PTCA, or repeat coronary angiography.

Results: There was no difference in clinical restenosis rates between conservative (N= 147) and liberal (N= 232) groups: 34.7% vs 37.9% respectively, p = 0.524 (OR C/L = 0.915, 95% CI [0.694 - 1.206]).

Conclusions: At our institution, a conservative stenting policy did not result a higher clinical restenosis rate than that of a liberal policy.
Acknowledgements

This research undertaking originated in the minds of a few individuals, however its form, spirit and completion are the result of selfless efforts provided by a number of people. Here are just a few whom I'd like to recognize:

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Initially, Nick Dofatikos supplied the database containing the study population at The Toronto Hospital (TTH). Chris Boule helped me extract important information. As the Angioplasty Database Manager at TTH, Karen Mackie provided invaluable information and assistance throughout the project. Both Keith O’Rourke and George Tomlinson helped plan and chart the statistical analyses. Desiree Chanderbhan was constantly available for administrative aid.

The spirit associated with this project would not have been the same without the untiring enthusiasm and dedication of five summer students who got on-board in May 1997 and followed the course of the project to its completion. Their names are: Jeff Myers and Adam Cheng (University of Toronto) and Marcus Bernardini, Matthew Crystal and Matt Winton (University of Western Ontario).

This project could not have been undertaken without the advice and consent of Interventional Cardiologists at The Toronto Hospital. They were both candid and supportive, and shared both their time and their thoughts to make this project a pleasure to work through. Similarly, Eric Cohen, Chris
Morgan, and the Cardiology group at Sunnybrook Health Science Centre lent their support and shared their insights with me.

Finally, I’d like to thank Don Redelmeier and John Parker for serving as internal and external reviewers, as well as the group who provided feedback at the weekly Clinical Epidemiology Rounds at The Toronto Hospital.
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(1) Introduction

Coronary artery disease (CAD) remains the leading cause of mortality and morbidity in Canada. It accounts for more deaths, disability and economic loss in industrialised nations than any other group of diseases.

Treatment modalities to combat progressive CAD include risk factor modification, medical treatment and mechanical revascularization. Evidence supports the role of aggressive risk management for both primary and secondary prevention. Aorto-coronary bypass grafting (ACB) has been established as superior to medical therapy, with regards to symptom management and survival, for individuals with several patterns of coronary disease. This includes those with Left Main Coronary Artery disease, multi-vessel disease with proximal Left Anterior Descending Artery involvement, and three vessel disease and poor ventricular function. Other patients, however, with different favourable coronary anatomy or important co-morbid disease derived less benefit with this strategy.

(1a) The Evolution of Balloon Angioplasty and Coronary Stents:

Balloon angioplasty was introduced as a percutaneous alternative to traditional ACB in 1977. Through a peripheral artery, a balloon catheter is guided across the site of a coronary stenosis and inflated, thus disrupting the plaque and enlarging the luminal diameter to provide enhanced flow. Since its development, percutaneous transluminal coronary angioplasty (PTCA) has become accepted therapy for a variety of clinical scenarios. Recent randomised trials have shown
PTCA to be a leading therapeutic option in the setting of acute myocardial infarction $^{24,41}$, and chronic single and multi-vessel coronary disease, with mortality rates comparable to ACB $^{51,59}$.

Although improvements in angiographic techniques broadened the applications of PTCA, two major limitations to this technique remained: The first was acute closure of the vessel following balloon dilatation, often necessitating emergent bypass surgery in 2-3% of cases $^{36,16}$. The second was re-narrowing of the dilated segment within six months of the procedure. Known as restenosis, this phenomenon occurs in 20 to 50% of manipulated lesions, dependent on their site and angiographic characteristics, and results in repeat dilations and ultimately surgery in a significant number of cases $^{16,26}$.

In an effort to avoid these complications, several other techniques have been employed without convincing improvement $^{1,60}$. In a large Canadian study, directional atherectomy was found to be of no added benefit when compared to standard PTCA $^{1}$.

The use of coronary artery stents has emerged as a potential solution to major drawbacks associated with PTCA. First implanted in 1986, these metal scaffolds are inserted via an inflatable balloon catheter. Once placed over a stenotic lesion, they are expanded until embedded in the vessel wall. In theory, these devices attenuate vessel recoil following balloon dilatation and have been demonstrated to reduce acute closure. This gain in post-procedural lumen size is thought to offset the enhanced local smooth muscle proliferation that occurs around a newly placed stent, resulting in a larger lumen $^{18,33,42}$.
Evidence for the Role of Stents:

Two randomised trials have compared routine intra-coronary stent use to standard balloon angioplasty. In combination, 1100 patients were randomised to PTCA or stent insertion, followed by conventional anti-thrombotic therapy. While 5.1 and 6.9% of patients crossed-over from the PTCA to the stent arm in each study, the angiographic restenosis rates at six months were significantly lower in the stent group compared to the PTCA group (39.9% to 26.1%), with benefits maintained at one year. Combined clinical endpoints of restenosis displayed a trend in the same direction. Importantly, target vessel revascularization rates were significantly lower in the stented patients (19.3% vs. 9.9%), translating into 10 fewer repeat interventions per 100 lesions treated with stents.

Several design features limit the generalizability of these results: Both studies limited inclusion to those lesions most favourable for stent usage (American Heart Association/American College of Cardiology lesion subtype ‘A’ and ‘B1’: see appendix), and enrolled more than half of their cohorts with stable symptomatology; factors defining a minority of patients presenting for angiographic revascularization today.

Some studies have examined the value of stent insertion amongst other lesion subsets, including restenotic lesions, chronic occlusions, left anterior descending artery stenoses, saphenous vein grafts and aorto-ostial atheromas. While some have been prospective in nature, most publications involving more complex anatomy are of poorer methodologic rigour. Importantly,
a large set of lesion sub-types encountered in usual interventional practice (type B2 and C lesions) lack convincing evidence to support routine stent use (fig 1-1).

(1c) Scope of the Problem:

Despite this lack of data, the practice of intra-coronary stenting has found a stronghold amongst the interventional cardiology community. The value of stents following balloon angioplasty catastrophes is uncontested, and is intuitively justified. These events however, occur in a small fraction of angioplasty cases. Their role in routine mechanical revascularization has expanded enormously in the face of poorly defined indications.

Nationally, Canadian rates of stent use have grown rapidly over the last few years, across all regions. In Ontario, the frequency of stent use during angioplasty was greater than 50% in 1996, yet amongst the lowest in the country. Today, this figure is greater than 75% of all procedures. From an institutional perspective, The Toronto Hospital (TTH) has been above the provincial average with respect to frequency of stent use (fig 1-2, 1-3).

In-hospital costs prove stenting to be an expensive alternative to PTCA. At one year, an additional $800 per patient was incurred compared to the angioplasty arm according to data from the STRESS investigators. Several factors make this conclusion less relevant today: Lower stent prices and simpler adjuvant therapy have lowered up-front costs. The extension of their use to more severely diseased anatomy in more symptomatic individuals may provide a much larger clinical benefit. It is estimated that a 10% reduction in restenosis is economically attractive.
If in the ‘real world’, stents result in even greater clinical benefit and lower costs than estimated from randomized studies, they would translate into smaller incremental cost per effect ratios compared to angioplasty.

Stents have profoundly changed the way cardiology is practised today. Economically, their use has underlined the need to critically examine their benefit. In the Canadian environment, an accepted stenting policy has only recently been developed. It comes after enormous growth in stent use has occurred, and their frequent use is now firmly entrenched in cardiology practice. Under these circumstances, randomised studies may be difficult to conduct.

1d) The Stent Shortage: An Opportunity

At our institution, a unique opportunity to examine this issue arose: Due to budget constraints, The Toronto Hospital had to curtail expenditures for coronary stents as of January 1996. As a result, the use of these devices was significantly limited. Two months subsequently, funding for intra- coronary stents was reinstated, however a committee had been struck to develop guidelines for their use. The rate of stent usage returned to the pre-shortage level; at par with other local centre rates (fig 1-4).

In routine practice, strong beliefs exist with regards to the value of coronary stents for many indications. Convincing physicians to allow their patients to participate in a prospective study with random assignment to stent vs standard PTCA would be difficult. As such, this economic constraint may have served to force cardiologists to adhere to more conservative, established
indications for stent use, and employ routine angioplasty otherwise, despite their preferences. By comparing this cohort of patients to another exposed to ‘usual’ practice, the impact of stents may be inferred. The cohort of patients undergoing revascularization when stents were in short supply, will have been exposed to a different set of ‘criteria’ for stent usage compared to cohorts from before and after the shortage. We measured the rate of clinical restenosis between the ‘conservative’ and the ‘usual practice’ cohorts over nine months of follow-up. Using this ‘natural experiment’ we hypothesized that the beneficial effect of stents employed in a liberal fashion, would translate into a significantly lower rate of clinical restenosis over nine months, when compared to the patients revascularized during the shortage.

(2) Conceptual Framework- Research and Design Methods:

Two cohorts of patients were assessed retrospectively 9 months after an angiographic revascularization procedure at The Toronto Hospital. The first group, was subject to a ‘conservative’ policy regarding stent use, employed in an open fashion over January and February, 1996. The second group, presented in months before (November 1995) or after (April and May 1996) the conservative period and was exposed to a less discriminate or ‘liberal’ revascularization approach, as per usual practice at The Toronto Hospital at that time.

The primary outcome was a combined endpoint of the first of the following: All-cause death, myocardial infarction, or the need for a repeat revascularization procedure or repeat angiography over the ensuing 9 months (fig 2-1).
(2a) **Objective**

This study was a retrospective cohort analysis comparing patients exposed to different strategies of revascularization, with respect to clinical events indicative of restenosis.

(2b) **Hypothesis:**

A conservative stenting policy results in more clinical restenosis than usual practice, over the short term, at The Toronto Hospital.

(2c) **Study Population:**

The sample population consisted of all patients who underwent angiographic coronary revascularization procedures at The Toronto Hospital during the specified time periods. This group was made of proportions of patients referred from other hospital patient-care services including the emergency department, local primary-care providers, and suburban and rural communities for which TTH serves as a specialised referral centre.

During January 1 to February 28, 1996, the stent supply at The Toronto Hospital was restricted. This group will hereafter be referred to as the ‘conservative’ (C) cohort. Stents were available in usual supply in the months immediately preceding and following this period. This ‘liberal’ period (denoted L) was composed of two subgroups: The first ‘liberal’ time period was
comprised of patients presenting for interventional revascularization between November 1 and
30, 1995 (denoted L1). The second 'liberal' time period consisted of patients presenting
between April 1 and May 31, 1996 (denoted L2).

Patients who presented on a second occasion within a subsequent time-period retained their
original assignment and were considered to have reached an endpoint. For example, patients who
required a second procedure in April 1996 following revascularization in January 1996 were
considered to have reached an endpoint and could not form part of the April 1996 cohort. We
excluded patients presenting in December 1995 and March 1996 to provide a 'wash-out' period
for the transition to the liberal-to-conservative periods and conservative-to-liberal periods
respectively. In December 1995, cardiologists may have dealt with higher risk patients than is
usual practice in anticipation of budget limitations for stent use. Similarly, many higher risk
patients may have postponed until March in anticipation of re-instated funding for stent use.
Presumably, both these periods would represent periods of exposure that would be considered
'in-between' a 'liberal' and 'conservative' strategy.

(2d) Inclusions:

All patients who underwent coronary angiographic revascularization at TTH during the specified
time periods.
(2e) **Exclusions:**

Those patients whose revascularization strategy (with regards to stent vs PTCA) and follow up angiography was determined for the purpose of another study were excluded. For example, patients who underwent repeat angiography as part of a retrospective study of stent effectiveness in the left anterior descending artery (LAD) were excluded.

(2f) **Ethics:**

Approval was obtained from The Toronto Hospital’s Medical Research Directorate Ethics Review Board prior to commencement. Given that this was a retrospective review, the associated risks and benefits to the patient were minimal. All interventionalists were informed of the study and agreed to allow contact with their patients and assess their hospital information. After informing patients regarding the nature of the study, telephone interviews were conducted, and when appropriate, written consent for access to health data from the patients’ family physician or other health institution was requested. All data, once entered, was identified by unique study number only.

(2g) **Exposure:**

Patients entered the study population in one of 3 ways; 1)in-hospital referrals from the emergency room, acute care beds or general wards, 2) inter-hospital urgent transfer referrals, or 3) elective referrals from TTH or the community. With the exception of primary PTCA (during acute
myocardial infarction), most angiographic interventions occur in two-stages and require a
diagnostic coronary angiogram from the TTH catheterization suite (as an out-patient or
emergently during the same hospital admission) before the interventional procedure. The cine-
mfilms are reviewed by the responsible cardiologist, and therapeutic decisions involve combining
patient preferences with medically acceptable options. Angioplasty is only offered if endorsed
by two interventionalists at TTH.

Recognised, standard angioplasty and stent deployment techniques were used at TTH throughout
the periods in question and will not be detailed further. The protocol for angiographic
revascularization at TTH was similar to that of other hospitals, and did not change over the time
periods in question: Routine cases were admitted one day prior and generally discharged the day
after revascularization. Patients were counselled regarding activity limitations and lifestyle
modification and a follow-up stress-test was recommended at 4 to 6 weeks and at six months
through their primary cardiologist. Risk factors for CAD were treated aggressively. Adjunctive
treatment including post-procedural heparin, short and long-term anti-platelet regimens were
widely accepted and constituted routine interventional care.

As was standard across Ontario databases, a procedure was recorded once a guidewire entered the
patients coronary arterial system, regardless of whether balloon angioplasty had been performed
or the lesion in question had been manipulated. Multiple lesion angioplasty during a single
catheterization constituted one procedure. At this point, two data sheets, addressing clinical and
angiographic factors surrounding a case, were routinely completed by a member of the
interventional team. The need for a second intervention after this step constituted a second case
and separate angiographic data sheets were required. Such events constituted a second event in this study.

(2h) **Outcome Description:**

The primary outcome of interest was evidence for clinical restenosis. This involved a combined outcome of the first of cardiac death, myocardial infarction or the need for repeat revascularization (in the form of PTCA, stent or aorto-coronary bypass surgery) or repeat coronary angiography (without immediate concomitant angioplasty) within 9 months. Differentiation between events involving the culprit lesion and those from other CAD pathology was not be made.

Conceptually, clinical restenosis (CRS) is the clinical correlate of same-site angiographic re-narrowing that occurs within 12 months of a previous mechanical dilatation. Approximately half of all angiographic restenoses do not present clinically and, it can be argued, are of little consequence. The other half of patients however, present with a range of ischemic syndromes, from recurrent angina to sudden death \(^{10}\). In the literature, CRS has been defined in various ways, one of which includes any of; cardiac death, myocardial infarction or repeat revascularization within a time period following the original intervention \(^{22,56}\). Methods for quantifying CRS from clinical trial data rely heavily on such ‘hard’, objective endpoints. Examples include the STRESS and BENESTENT studies comparing angioplasty to stent insertion in terms of angiographic and clinical endpoints \(^{22,56}\). Repeat diagnostic angiography, when not accompanied by same-procedure angioplasty, is both costly and invasive and therefore
constitutes an important outcome among patients undergoing revascularization. It is indicated in patients presenting with refractory angina and so represents an undesirable result of a revascularization procedure. As such, it was included as part of the composite endpoint.

(2i) Data Collection:

All patients subject to angiographic revascularization procedures are captured through the TTH interventional database. Demographic data, case status and angiographic anatomy as well as procedural outcome are recorded. Baseline patient data was obtained from the TTH interventional database. Its reliability was assessed, by comparing a convenience sample of 20 patient entries to interventional data sheets and patient charts (fig 2-2). Among relevant data points, the database was adequate in describing characteristics at time of index procedure. The reproducibility of two angiographic characteristics listed in the database was tested (lesion type by modified AHA/ACC classification and lesion location as high vs low risk). A blinded interventionalist re-assigned a sample of lesions from 15 angioplasty films. We found modest agreement between re-assignment and database designations (Kappa = 0.59 and 0.67 for each characteristic) (fig 2-3).

Outcome data was obtained retrospectively using a combination of telephone-administered questionnaires, TTH hospital patient-care database and physician corroboration. The TTH database was not reliable nor complete in this regard (as patients can have procedures done elsewhere).
The questionnaire consisted of an introductory statement, a set of questions, response choices, and instructions for 4 student administrators (all of whom were in health science fields) (appendix 2).

Compared to face to face interviews, this approach takes advantage of lower costs, while improving the response rate as more subjects can be reached for questioning. Although more labour-intensive than mailed surveys, phone interviews allow for clarification of ambiguous or complex material and allow data gatherers to vaguely characterize non-respondents. By employing hired health students (as opposed to professional interviewers), one may gain the trust of the interviewee, through their familiarity with medicine. The potential for interviewer bias exists, however, both in terms of posing the questions and coding the responses. Also, the lack of anonymity in this method can introduce social desirability bias, as patients true opinions or recollection of the events may be influenced by the perceived response.

A protocol for questionnaire administration and data gathering was developed following pilot testing on both a group of peers and a representative sample of non-study patients (appendix 3). Standardized prompts were employed for anticipated clarification. Yarnell has shown in retrospective interviews for the diagnosis of acute myocardial infarction, that errors can be avoided by using lay-terms that specifically address the severity of symptoms (in this case, chest pain), and whether or not a physician was seen and how he/she referred to it (ie; a “heart attack”).

A specific, standardized introductory statement was included, briefly describing the interviewer and the purpose and nature of the questionnaire. This has been shown to increase compliance
A schedule of contact attempts was kept and a protocol for follow-up calls and leaving messages was followed. Also, a preferred list of responders was issued, such as; patient, followed by spouse, then first relative, and so on.

**(2j) Data Handling:**

Both demographic information and clinical event data was collected and referred to by unique study number. The source and type of corroborative information to be accepted, in order of preference, was pre-specified using explicit criteria. For example, a positive response to 'repeat PTCA' will require TTH database corroboration or a copy of a discharge summary following the procedure to be counted as such. Primary care physicians were contacted for such information after written patient consent.

It is well recognized that substantial discrepancies may exist between medical record data and patient-generated information. In one study that reviewed death certificate diagnoses (traditionally considered the most standardized), 91% of deaths coded as 'definite' or 'possible' coronary heart disease actually met the ICD-9 criteria. Other studies have found sensitivities of 97% but positive predictive values have been considerably lower (70%).

Data was collected on duplicate forms and the student interviewers entered the information in duplicate at a separate stage into a database. Reliability of data entry was tested on two occasions before the majority of data entry occurred.
A blinded test-retest method was applied using all interviewers at different times on the same patients to assess inter-rater reliability, expressed as an unweighted Kappa statistic (using a sample of 45 patients, test-retest mean K = .87 between three interviewers) (fig 2-4).

Specifically for coronary disease, authors have reported that the diagnostic accuracy of patient reported-events improves as the time from the event decreases and the complexity and ambiguity of the diagnosis diminishes. Pagani-hill et al found that the accuracy of recall was significantly lower for acute myocardial infarction, than for cancer or hip fracture. The 40% false-positive rate for the former primarily involved closely related cardiovascular diagnoses. Similar results were found in the Minnesota Heart Survey.

This combination top-down and bottom-up approach was chosen in order to combine getting the most accurate information without compromising breadth. In a recent study at our institution, a similar method achieved near-complete follow-up (personal communication; Dr. W. Cantor).

(2k) Statistical Analysis:

The frequency of pre-defined, baseline demographic and angiographic characteristics were tabulated and the mean age for each cohort was noted. The proportion of patients in each group reaching an endpoint was compared using a Chi-squared test. Subgroup analyses involving individual endpoints, time period sub-groups, and lesion characteristics were performed as secondary analyses. Results are reported without adjustments for multiple comparisons.
Several prospective studies have shown that clinical restenosis event rates for percutaneous balloon angioplasty range from 25% to 45% \(^{22,56,26,16}\). From randomised trials of stent use, clinical event rates have been between 10 to 30% \(^{22,56,26,16}\). Using clinical restenosis as defined for our study (including repeat angiography alone), we estimated that event rates for the conservative and liberal cohort would be 40% and 20% respectively. Choosing one month as ‘before’ the shortage and one month ‘after’ the shortage as our comparison of ‘routine’ stent use, we expected to recruit at least 160 patients per cohort.

During the design phase (before data collection), we chose to include two months as our L2 comparison, to increase the power of the study. During January and February 1996, approximately 160 cases were performed. The ‘before’ and ‘after’ liberal periods (a total of 3 months) involved more than 250 patients (see results). We chose a two-sided alpha level of significance of .05 and accepted a beta error of 0.2.

From a post-hoc perspective, given the relative number of patients stented in each of the liberal and conservative periods was 45.3% and 23.5% respectively, we estimated that the difference in restenosis rates between each would be 4.2%. As such, our study had a 23.4% chance of detecting such a theoretical difference (figs 2-5, 2-6). Since the power is relatively low, the results are reported with calculated 95% confidence intervals around observed differences.

We reported our results using odds ratios as a measure of effect. As such, with respect to clinical restenosis (CRS), a value less than 1 means that the conservative cohort was observed to have a
lower rate of CRS than the liberal group, while a value greater than 1 means that the conservative group had a higher rate of CRS than the liberal group.
(3) Results:

Patient interviews were conducted from June 9, 1997 and corroborating information was collected until September 6, 1997. 280 and 163 procedures were performed in the liberal and conservative periods respectively, on 264 and 160 patients. From these, 232 (71 from L1 and 161 from L2) and 147 patients were eligible for participation (fig 3-1).

Complete data was obtained on 357 of 379 patients. Reasons for lack of complete follow up information included inability to obtain corroborative information regarding clinical restenosis (5 cases), refusal to participate in the interview (2) and inability to contact individuals (15). Both patients who refused to participate allowed us to access their hospital chart and database information. Where no contact was made, we obtained approval form the responsible cardiologists (see appendix 4). The analysis was conducted using this collected information for all 379 patients.

Central to the rationale for our study was the fact that the two periods of interest were clearly different with regards to the rate of stent use (fig 3-1). During the conservative period, 23.5% of eligible patients revascularized received at least one stent, while during the liberal period (L1 and L2), 45.3% of patients received stents, a statistically significant difference (P<.0001). As well, the rates of stent use between the two liberal subgroups (L1 and L2) were different. During November 1995, 49.3% of patients received stents, compared to 42.3% during April and May 1996 comparable (p value for the difference = 0.268, Odds Ratio = 0.907 with 95% CI = [0.762 - 1.081]).
(3a) **Baseline Characteristics:**

Demographic factors for those with complete follow-up are compared to those with incomplete information in fig. 3-2. The frequencies of descriptive variables were generally similar between the two groups. More patients with incomplete data had a history of myocardial infarction or angioplasty before their index procedure, compared to patients with complete follow-up information.

Demographic and angiographic characteristics of all patients by revascularization time period (including the two liberal subgroups L1 and L2) are listed in fig. 3-3. A larger proportion of patients in the L1 cohort had class 4 angina before their procedure compared to C and L2 periods. None of the pre-determined coronary lesion variables clearly distinguishes the subjects in the chosen periods of study into higher and lower risk groups. The distribution of patients with different numbers of diseased vessels and symptom burden is similar to published databases of PTCA \(^{16,19}\).
(3b) **Primary Outcome:**

**Results according to Conservative vs Liberal periods (C / L):**

Patients undergoing revascularization during the conservative period had a 9 month clinical restenosis rate of 34.7%, while those who underwent their index procedure during the liberal periods had a rate of 37.9%. The observed difference in CRS of 3.2% was not statistically significant (p = 0.5). The odds ratio for CRS for the conservative cohort vs the liberal one was 0.915, with lower and upper 95% confidence intervals of 0.694 and 1.206 respectively. This result is graphically depicted in figures 3-4 and 3-5.
(3c) **Other Analyses:**

**Individual endpoints:**

The main results are consistent across each endpoint of the primary outcome with the exception of repeat cardiac catheterization: the liberal group underwent repeat angiography 29.7% of the time while the rate for the conservative group was 19.7%. This difference of 10.0% yielded a p value of 0.030, with an odds ratio between L and C groups of 1.722 and 95% confidence intervals of 1.051 to 2.823 (fig 3-6, 3-7).

**Results according to month of revascularization (C / L1 / L2):**

The rationale for analysing L1 and L2 as one group hinged on the restenosis rates between these two subgroups being similar. Figure 3-4 indicates that they were, in fact, different. The primary endpoint was reached in 49.3% of patients exposed during November 1995 (L1) and 32.9% of patients revascularized during April and May 1996 (L2). The p value for this difference of 16.4% was p = 0.018, and the odds ratio for CRS for L1 patients compared to L2 patients was 1.497 with 95% confidence intervals of 1.084 to 2.068.

The patients exposed to a procedure during the conservative period had CRS rates quite different from L1 and similar to L2. The rate at which the primary endpoint was reached in patients revascularized in January and February 1996 (period C) was 34.7%. This value was statistically different than the rates from L1, with a p value (for the risk difference of 14.6%) of 0.039 and an odds ratio for C vs L1 of 0.704 with 95% confidence intervals of 0.509 to 0.973. It was similar
to rates observed from L2, however, with a significance value for the 1.8% difference of \( p = 0.742 \) and an odds ratio of C vs L2 of 1.054 with 95% confidence intervals of 0.771 to 1.441.

Figure 3-7 describes individual endpoints from within the composite primary outcome by treatment period. Comparing L1 and L2, rates of repeat angioplasty, bypass surgery, admission for myocardial infarction and death were similar. It appears that patients revascularized during the first liberal period underwent repeat angiography more often than those from the second period (42.3% vs 24.2%, \( p = .006 \), odds ratio 1.744 with 95% confidence intervals of 1.186 to 2.565).

The rates of individual endpoints reached in the conservative group were statistically no different than those of the second liberal group. The rate of repeat angiography was, however, different than that of the L1 group (19.7% [C] vs 42.3% [L1], \( p < .001 \), odds ratio 0.467 with 95% confidence intervals of 0.305 to 0.714).

**Clinical Restenosis Without Repeat Angiography:**

Rates of clinical restenosis were tabulated excluding those patients whose only manifestation following index angioplasty was repeat angiography alone (clinical restenosis without angiography) (fig 3-5). The event rates between the liberal and conservative groups were comparable (22.4% and 17.7% respectively, \( p = 0.253 \), odds ratio with 95% confidence interval 1.27 [0.844 – 1.912]). Similarly, the event rates between individual time periods were similar.
Angiographic Restenosis Without Clinical Sequelae:

Amongst the subset of patients who underwent only repeat angiography (without repeat angioplasty, bypass surgery MI or death within 9 months of their index angioplasty), we compared the rates of angiographic restenosis. This endpoint was considered to have been reached whenever the interventionalist documented a lesion dilated during the index procedure as being 'restenotic'. The conservative and liberal groups incurred events in 48.1% and 37.0% of patients respectively (fig 3-5). This difference of 11.1% was not statistically significant (p = 0.376). The difference between time periods (L1, C and L2) with regards to angiographic restenosis are listed in fig 3-4 as well. The conservative and second liberal time periods have similar rates of angiographic restenosis (48.1% and 46.8% respectively). These values are contrasted with that of the first liberal period (22.7%), although this difference of approximately 25% did not reach statistical significance.

Figure 3-8 lists the number of patients with angiographic restenosis in the absence of clinical events by interventionalist. Also, the frequency of repeat catheterization in the absence of clinical event (including repeat angioplasty) is listed. The variability in frequency of repeat catheterization between operators is relatively wide.
**Angiographic subgroups:**

Factors inherent in coronary anatomy determine the suitability of a patient for angiographic revascularization. Combinations of characteristics are classified in the ACC/AHA lesion score. Angiographic characteristics are recognised as strong determinants of restenosis. We stratified patients based on the presence of high risk vs low risk lesions. Figure 3-9 reveals that patients with high risk lesions had a rate of CRS similar to that of those with lower risk lesions.

Coronary stents have been shown to decrease restenosis rates for lesions of the proximal left anterior descending artery. Dissections of left main coronary artery lesions are also particularly life-threatening, and the wide-spread use of stents as an adjunct to PTCA in this setting is undisputed. Patients with either of these high risk lesion subsets demonstrated a rate of CRS no different than those without (fig 3-6).

Several patients in these cohorts had multiple lesions dilated during one catheterization. We compared the rate of CRS between those undergoing multi-lesion angioplasty (with or without stent insertion), to those subjected to a single-lesion procedure (fig 3-6). The rate of CRS for the former was 46.1%, while the latter was 33.7%. This risk difference of 12.4% yielded a p value of 0.031 with an odds ratio (multi-lesion vs single lesion) for CRS of 1.688 and 95% confidence intervals of 1.045 to 2.725.

**Clinical Restenosis By Use of Stent:**

Finally, we examined whether intra-coronary stent insertion during angioplasty was associated with an improved outcome (fig 3-10). Patients who received at least one stent had a clinical
restenosis rate of 39.4%, while those who underwent conventional angioplasty without stent insertion had a rate of 34.8%. The observed difference of 4.6% was not statistically significant (p= 0.368) and the odds ratio for CRS without stents compared to with stents was 1.13 with 95% confidence intervals of 0.87 to 1.44.

**The Environment for Catheter-Based Revascularization:**

An attempt to describe of how the use other clinical modalities for treating CAD were employed around the time periods in question was made. Figure 3-12 tabulates the number of cardiac catheterizations, coronary angioplasties and coronary bypass procedures performed at TTH over the periods in question. Figures 3-13 to 3-15 list the time to angioplasty, as well as the absolute number of angioplasties (with and without stents) performed in the periods of interest and corresponding months 1 year before and after.
(4) Discussion:

This study was a retrospective cohort analysis comparing groups of patients exposed to different strategies for catheter-based coronary revascularization with regards to clinical outcomes. A 'conservative' group consisted of patients exposed to angioplasty during a period when stents were in short supply, while a 'liberal' cohort of patients were exposed to periods of 'usual' stent use, both before and after the shortage. The primary endpoint was a composite measure of death, myocardial infarction or repeated need for procedures indicating suspected restenosis (coronary angiography, angioplasty or coronary bypass). All outcomes were assessed retrospectively in a blinded fashion through a combination of patient interviews, database review and physician corroboration.

Clinical Restenosis:

We found no differences between cohorts C and L with respect to the composite outcome of clinical restenosis. This result was consistent across most individual markers of clinical restenosis between the group of patients revascularized during the conservative period vs those exposed to the liberal period.

The literature reflects a decreasing target vessel restenosis rate (requiring repeat intervention) over time; from approximately 22% in the pre-stent era to 15.5% recently \(^{26,40}\). Several therapeutic advances have contributed to this shift, one of which is the use of intra-coronary stents. The 'negative' result may indicate that in conjunction with other modalities, stents incur no incremental benefit, and in the modern environment, the two strategies may be equivalent.
The value of stents in the ‘real world’ may be quite different than that found in randomized studies. Indeed, a recent database report compared the restenosis rates among stented lesions currently excluded from trials to those equivalent to lesions from the STRESS and BENESTENT studies \(^{54}\). Although ‘trial-equivalent’ lesions had restenosis rates comparable to those stented from STRESS and BENESTENT, ‘less favorable’ lesions had much higher angiographic restenosis rates, comparable to those found in PTCA registries. Similarly, when stent insertion was compared to conventional angioplasty in small vessels (then than 2.75 mm), the clinical restenosis rate was similar (31.0% for PTCA vs 34.4% for stents) and higher than that found in the above randomized studies (31%) \(^{62}\). Melby has recently shown in a retrospective cohort study that when patients were matched according to degree of residual angiographic stenosis post-dilation, clinical outcomes were the same whether angioplasty or stent-insertion was employed \(^{40}\). Finally, Rodriguez has shown that lumen re-narrowing and restenosis does not necessarily result in adverse clinical outcome \(^{52}\). This argument then, would imply that from a resource point of view, the most appropriate rate of stent use may be at least as low as the conservative rate.

Any differences in clinical events signifying restenosis was diluted by the mix of patients (those with stents and those without) in each time period. Had our estimate that the use of stents would decrease CRS from 40% to 20% been true, the difference in CRS rates between cohorts would have been only 4%. The lack of power to find this difference may explain the observed equality of the two strategies with respect to primary outcome.
Subgroup Analyses:

The results of several subgroup analyses from this study deserve mention. We compared restenosis rates among patients with clinical markers of restenosis excluding that of repeat angiography. This endpoint is similar to that used in large, randomized trials of clinical restenosis with stent insertion, and may be remove some influence on the composite outcome held by those controlling the decision to offer repeat angiography (a 'hard' outcome). There was a trend towards more frequent events marking clinical restenosis in the conservative arm when compared to the liberal group as a whole, and when compared to each liberal period separately.

Among patients undergoing repeat catheterization as their only clinical event, rates of angiographically documented restenosis were compared between cohorts. Although the number of subjects was small, there was a strong trend towards lower rates of restenosis in the L1 cohort than in the C and L2 groups. Coincident with the stent shortage, the two cohorts from the later time periods acted similarly. Two explanations come to mind: First, the period of constraint made interventionalists and other cardiologists better at picking out those who really had restenosis, and so their efficiency improved in the later periods. Secondly, because of the shortage, interventionalists were less likely to treat angiographic narrowings in the absence of clinical events.

Patients undergoing multi-lesion angioplasty had higher rates of CRS. This finding intuitively reflects the largely additive risk of restenosis per lesion manipulated. We did not find statistical differences between most angiographic subsets with respect to CRS, however trends favoured traditionally lower-risk lesion subsets. Several studies have shown that angiographic lesion
morphology and location predict the occurrence of clinical events reflecting restenosis\textsuperscript{29,19,9,10}, and the direction of the observed trends in this study concur. A more insightful look at this issue would require adjustment for many co-variables, an exercise that would be under-powered given the size of this study. Also, the relevance of differences through such exercises would be unclear given the number of comparisons already made.

Importantly, the use of coronary stents was not associated with a difference in rates of restenosis between cohorts. This finding may signify that the benefit in their use (if it exists), when applied outside the realm of a clinical trial, is smaller than that found in randomized studies. Alternatively, it may suggest physicians can keep clinical restenosis rates low when faced with a shortage of intracoronary stents. Once again, this observation would argue that with respect to clinical events following balloon angioplasty, the more appropriate strategy for stent use may be the more conservative one.

The observed difference in clinical restenosis rates between the L1 period and the C/ L2 period suggests that these groups behaved differently. Over time, the reported rate of clinical restenosis changed from the ‘before’ liberal period, to the conservative and ‘after’ liberal periods. Following the unforeseen shortage, the rate was no different for the second liberal group. The primary difference between the L1 and C/ L2 groups was the rate of repeat angiography. This may represent a chance distribution found when making multiple comparisons. It may, however, represent something else.
Over time, the improvement in CR rate between L1 and C periods may reflect a change in practice. Other reports describe evolutions in practice over time contributing to a shift in the distribution of clinical endpoints. Singer and colleagues have demonstrated that in response to rationing of medical intensive care unit beds, physicians were better at discriminating chest pain syndromes, without compromising mortality rates \(^1\). Examining before and after cohorts must take this effect over time into consideration. It is certain that physicians learned something from the unforeseen economic constraint on stent use. Alterations in their practice, both on an individual level and from a general triage process perspective, may have been conspicuous or subtle, and will have been directed at keeping restenosis rates low.

The difference was largely a result of differences in restenosis rates between L1 and the other two groups, the majority of which can be accounted for by more frequent repeat angiography in the earlier time period (L1). Physicians may have had less faith in the prevention of restenosis in November 1995, explained by higher risk patients, poorer technology or less expertise in the procedure. As a result, they may have had a lower threshold to repeat angiography in this earlier group than in months that followed, when they were armed with knowledge gained (or lessons learned) from the shortage.

As a result of economic restraint, cost- conscious interventionalists may have tightened their criteria for repeating angiography, given that the test is expensive, and one may be forced to act on the findings. This might imply that the C and L2 groups, although differing in the rate of stent use, may both be considered ‘conservative’ with respect to repeat angiography, relative to the L1 group. Along these lines, a more appropriate study comparison may have compared
periods before the shortage (so called ‘liberal’ periods), with any period within and following the stent shortage (those of ‘conservative’ resource use, including repeat angiography).

The magnitude of a shift in management strategy can be postulated by exploring physicians attitudes towards the imposed stent shortage, and their reaction to it. Interventionalists are responsible, to a large degree, for deciding the therapy best suited for a patient who has anatomy amenable to a catheter-based procedure. Before the onset of this study, interventional cardiologists at TTH were asked about the effect the stent shortage had on patient care. Interviewees offered the full range of responses; some describing a drastic change in their practice style, while others admitted to little impact of the stent shortage. The effect of these reactions to the stent shortage, must be regarded as important and potentially far-reaching, influencing many aspects, from patient selection to the decision to repeat angiography.

The circumstance defining the ‘conservative’ cohort in this study was unique. The effect that rationing of stent use had on cardiovascular surgeons, referring physicians and patients is difficult to ascertain. The possible reactions range from delaying procedures on the part of the cardiologists, to performing less ‘strongly’ indicated procedures by CV surgeons, to agreeing less often to pursue coronary angiography on behalf of the referring physicians and patients. Insights as to how each group dealt with the shortage can be made by comparing the use of other services in and around this period.

The decision to refer for angiography is generally based on the belief that if suitable anatomy is found, revascularization will compare favourably to medical management for a give patient-
symptom complex. Ideally this decision is made independently of the relative availability of different types of procedures (i.e., PTCA, stent insertion or CABG). If the stent shortage lead physicians to feel that revascularization was 'less good', then angiography should be chosen less often. To explore this, we compared the number of cardiac catheterizations performed in each time period, as well as the corresponding months before and after (fig 3-12). There were fewer angiograms performed in March 96 following the shortage, however given the baseline month-to-month variability, the significance of this is unknown. Many factors could, in part or in whole, account for this finding.

It is presumed that patients whose circumstances would normally justify the use of coronary stents will have been offered routine angioplasty as an alternative (not coronary bypass surgery), during the 'conservative' period. To examine this point, we examined the rates of referral for coronary bypass at TTH around each time period (fig 3-12). Apart from an expected lower volume during December, an increase in bypass procedures did not occur around the conservative period. Also, we compared the rates of referral for angioplasty to number actually performed for each period and the corresponding months before and after (fig 3-13). Given the month-to-month variability in referral rates, a clear decrease in the ratio of angioplasty procedures performed vs those referred cannot be found.

Once committed to a catheter-based intervention, choosing when and how to act on anatomically correctable disease may be influenced by the availability of these resources. The time to intervention may have been delayed during the stringent period, in the hopes that lesions cardiologists believed would be better served by stenting could be tackled when stents were more
readily available. We examined this possibility by comparing the time from referral for angioplasty (following diagnostic catheterization) to the index intervention for each cohort (fig 3-14). Referral during November 1996 seems somewhat accelerated than during other periods, however, there is no clear pattern of delay during the conservative period.
(5) Limitations

(5a) Internal Validity

Experimental trials of stent use have demonstrated an advantage over conventional angioplasty for a variety of angiographic and clinical settings with respect to CRS. Within a highly controlled environment, co-determinants of restenosis are dealt with through randomisation. The disadvantage of this design is the inability to accurately represent conditions in the 'real world'. Retrospective analyses such as this one reflect the environment, at the expense of examining groups that are not wholly comparable.

More sophisticated statistical adjustments for other recognised factors that were unevenly distributed between groups (ignoring those that are unknown, but certainly important), would require a much larger sample size. For example, other factors known to influence restenosis rates were not examined in this study including vessel size, the presence of diabetes, and the distinction of new vs restenotic lesions.

The relative use of stents between cohorts as well as their absolute number limited our study sample. As a result, we had relatively little power to detect modest differences in clinical restenosis rates between cohorts.

When small differences in outcome are expected, incomplete follow up decreases the ability to draw inferences from the results. This study failed to obtain complete information on 22 of 357
patients (6.2%). Although measured baseline factors were relatively similar between groups, they may have had importantly different outcomes. This lack of data lends uncertainty our observations and weakens the conclusion that patients from each time period had similar rates of restenosis.

By counting only index procedures (ie; counting only the patients first angioplasty and excluding second presentations from being re-entered as an index intervention) we hope to have minimised contamination between groups. Although patients undergoing index coronary angiography at TTH are unlikely to have been revascularized elsewhere, it is theoretically possible that patients who restenosed had repeat procedures elsewhere (at other hospitals) and so co-intervention could not be ruled out.

The assessors of outcome were four students not blinded to the time period of a patients revascularisation. This may have introduced systematic bias. Raters were, however, blinded to the use of coronary stents among patient procedures. A standardised instrument of measurement was used and tested to improve strengthen accuracy and inter-rater reliability.

The method of outcome assessment in this study involved an element of patient recall. Systematic bias could have occurred here in several ways. Firstly, acute closure of dilated vessels represents an endpoint that may have been less accurately remembered by patients, and poorly documented in hospital charts and physician records. Since stents have been shown to prevent such occurrences, the benefit of their increased use in liberal cohorts may have been missed.
(5b) **Generalizability:**

Although TTH is a tertiary referral centre, and hosts congenital heart disease and cardiac transplant populations unique to the area, it is one of only three institutions performing PTCA in the city. As such, the volume and spectrum of case-load is similar to that of other major centres in the city and across Canada, and we expect the procedural success rate to be generalizable. The rates of clinical restenosis excluding repeat angiography were similar to published results from randomized trials of stent use \(^{22,56}\).

Randomised studies that dictated a specific angiographic procedure (standard PTCA or stent) were ongoing throughout both time periods, and together would have excluded approximately 80 patients from our study. The differential effect of this on restenosis rates in our study periods is unknown.

The procedure for patient referral, triage and specific intervention is similar to that of other Toronto hospitals, and is representative of the practice at TTH in recent years. Between-year variations for each cohort (the effect of evolving technology) are depicted in Figure 3-15. With the exception of our 'conservative' period of economic restraint, the average rate of stent use has increased over time. The months selected for our study appear to follow this trend.
Catheter-based techniques for treating coronary disease are rapidly evolving. The interpretation of results from studies performed a few years ago are less relevant today. Over the periods in question, no identifiable changes in adjuvant therapy or deployment technique took place at TTH. Certainly, the expertise amongst operators (both staff-members and yearly academic fellows) would be expected to improve over the months in question. By choosing cohorts exposed within a short time intervals of each other, we hope to have diminished this powerful influence on stent usage and patient selection.

As a result of the shortage, a committee was set up to better define the role of coronary stents in angioplasty procedures, consisting of clinical epidemiologists, ethicists, economists and interventionalists. Subsequent recommendations, as well as those from a related Cardiac Care Network for Ontario authority, certainly affected the practice of interventional cardiology, however, they were made after the time periods in question.
(6) **Further Research:**

This ‘natural experiment’ examined the effect of stent-usage strategies amongst patients presenting in the real world. In this un-controlled environment, the benefit of intra-coronary stents on restenosis could not be demonstrated. The Cardiac Care Network for Ontario has published guidelines for stent use based on available evidence. It is estimated that 40% of all lesions undergoing angioplasty are considered to have unfavourable angiographic characteristics, which, for the most part, the optimal strategy (stent vs conventional PTCA) is unclear. Prospective studies randomising these patients to stent use vs conventional PTCA would shed light on this issue.

Also, large scale prospective series of patients revascularized during the stent era may be compared to historical controls. Although many therapeutic aspects have changed, inferences regarding the contribution of stents to the decreasing restenosis rate can be made if the sample size is large enough to adjust for imbalances across many known prognostic variables.
(7) **Implications:**

The implications of this study are numerous. Firstly, it suggests that a more conservative approach to stent use may be just as effective as the current standard. Given the predicted cost-savings, it may, in fact be more responsible as well. This study demonstrates that extrapolation of study results to other patient populations is not always justified.

This study also highlights the potential impact a resource shortage can have on routine practice. The restenosis rate remained comparable between periods despite restricted stent availability through the adaptation of physicians, including curtailing repeat angiography.

Studying the impact of stents in the ‘real world’ is difficult. The multitude of factors involved in the decision to employ stents, and their predicted success in a given patient, cannot be adjusted for in retrospective analyses. Prospective, randomised studies will overcome many internal validity issues at the expense of generalizability.
(8) **Conclusions:**

We conclude that a conservative stenting policy, did not result in an increased rate of clinical restenosis than that of a liberal stenting policy, when employed in an open fashion, at our institution. Trends from subgroup analysis suggest that our inability to demonstrate a benefit may have been, in part, due to a lack of power.

We also conclude that the rates of clinical restenosis between periods before and those during and after the imposed shortage were different, and this difference was primarily due to more use of repeat angiography in the earlier period.

Once again, the widespread use of something that makes ‘intuitive’ sense and is supported by evidence from randomized controlled trials in selected patients, does not seem to translate into benefit in a small to moderate-sized real world study.
Tables and Figures
**Stent indication amongst PTCA cases-1996 CCN**

![Pie chart showing distribution of stent indications among PTCA cases](chart.png)

**Fig 1-1:** PTCA = Percutaneous Transluminal Angioplasty, CCN = Cardiac Care Network (Ontario), A/B1, B2/C = AHA/ACC Angiographic Lesion Classification, De Novo = not a restenotic lesion, level 1 = prospective, randomized, methodologically sound research as per the CCN
Lesion Subgroups Presenting for PTCA – TTH 1996

Fig 1-2: TTH = The Toronto Hospital, American Heart Association (AHA)/ American College of Cardiology (ACC) lesion classification
1996 Stent Rate as % of Total Angioplasty Cases- Ontario CCN

Average
St. Michael's
Kingston
Ottawa
SHSC
Hamilton
Sudbury
LHSC
TTH

0% 10% 20% 30% 40% 50% 60%

Fig 1-3: SHSC = Sunnybrook Health Science Centre, LHSC = London Health Sciences Centre, TTH = The Toronto Hospital
**Fraction Stent Use Per PTCA - TTH 95/96**

![Bar chart showing fraction stent use per PTCA - TTH 95/96.](image)

**Fig 1-4:** * see text for details, PTCA = Percutaneous Transluminal Coronary Angioplasty
Study Outline

L1 (N= 71) Nov 95  →  9 month F/U  →  C (N= 147) Jan/ Feb 96  →  9 month F/U  →  L2 (N= 161) Apr/ May 96  →  9 month F/U

Outcome =
Clinical Restenosis (CRS)
Any of...
• Death
• MI
• repeat PTCA
• CABG
• Cath alone

Fig 2-1: L1 = First Liberal period, C = Conservative period, L2 = Second Liberal period, F/U = follow up period, MI = myocardial infarction, CABG = coronary artery bypass surgery, Cath alone = repeat coronary angiography alone
Database Discrepancy Rate—Baseline Clinical Characteristics

- No. of disagreements between database sheets and computer file for major and minor variables

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Fig 2-2:

- Case no. refers to the order in which the database was checked, not the study number
- Major variables included: age, date for PTCA (Percutaneous Transluminal Coronary Angioplasty), history of PTCA, history of ACB (Aorto-Coronary Bypass Surgery) or history of MI (Myocardial Infarction)
- Minor Variables included: exercise results, coronary risk factors, scintigraphic imaging results and lesion characteristics
Angiographic Lesion Database – Reliability

Interventional Cardiologist

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<td>Low risk</td>
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Kappa (K) = [(12 + 2) – (10.563 + 0.563)] / [16 - (10.563 + 0.563)] = 0.590

*high risk lesions = ACC/AHA class A/B (refer to text)
low risk lesions = ACC/AHA class B2/C

Interventional Cardiologist

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Kappa (K) = [(3+11) – (0.9375 + 8.9375)] / [16 - (0.9375 + 8.9375)] = 0.673

* risk location = left main or proximal LAD stenosis (refer to text)

- Single, blinded interventional cardiologist was used
- Nb; only culprit lesion were categorized (15 patients, 16 lesions in total)
- Population taken from periods before and after study sample
- PTCA (Percutaneous Transluminal Coronary Angioplasty) cine-grams were used for the evaluation

Fig 2-3:
**Inter-Rater Reliability**

**Interviewer # 2**

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Kappa K = [(14 + 29) - (5 + 20)] / [45 - (5 + 20)] = 18 / 20 = 0.9

**Interviewer # 3**

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Kappa K = [(14 + 28) - (5.33 + 19.33)] / [45 - (5.33 + 19.33)] = 17.34 / 20.34 = 0.85

**Interviewer # 2**

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<tr>
<td>No</td>
<td>1 (9.67)</td>
<td>28 (19.33)</td>
</tr>
</tbody>
</table>

Kappa K = [(14 + 28) - (5.33 + 19.33)] / [45 - (5.33 + 19.33)] = 17.34 / 20.34 = 0.85

Mean Un-weighted Kappa = (.85 + .85 + .9) / 3 = 0.867

Fig 2-4:
**Power Calculation**

\[
\begin{align*}
\text{Stent} &= .24 \\
C &= 147 \\
\text{No Stent} &= .76 \\
\text{Stent} &= .45 \\
L &= 232 \\
\text{No Stent} &= .55 \\
\text{CRS} = .2 &\rightarrow .048 \\
\text{CRS} = .8 &\rightarrow .192 \\
\text{CRS} = .4 &\rightarrow .304 \\
\text{CRS} = .6 &\rightarrow .456 \times 160 \\
\text{CRS} = .2 &\rightarrow .09 \\
\text{CRS} = .8 &\rightarrow .36 \\
\text{CRS} = .4 &\rightarrow .22 \\
\text{CRS} = .6 &\rightarrow .33
\end{align*}
\]

**Assumptions:**
- The rate of clinical restenosis (CRS) among stented vs non-stented patients was 0.2 vs 0.4.
- The rate of at least one stent insertion per patient was 0.25 in the conservative arm and 0.45 in the liberal arm (post-hoc).
- Level of significance desired: two-sided alpha = 0.05

Estimated rate of CRS:
- Conservative arm = 0.048 + 0.304 = 0.352
- Liberal arm = 0.09 + 0.22 = 0.310

Estimated difference: 0.042
Estimated variance: 0.331

\[
\text{Power} = 1 - \left[ \phi \left\{ \frac{1}{2} (0.042)(\sqrt{379}) / (0.331) \right| - Z\alpha/2 \right] = 1 - \left[ \phi \{0.725\} \right] = 1 - 0.766 = .234
\]

**Fig 2-5:**

**C vs L**
- \( \text{delta} = 4.2\% \)
- **power = 23.4\%**
Study Population

Patients receiving at least 1 stent = 45.3%
L1 = 49.3%
L2 = 42.3%

Patients receiving at least 1 stent = 23.5%
P (C vs L) < .0001

Fig 3-1:
### Baseline Characteristics: Complete Vs Incomplete Follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Incomplete (%)</th>
<th>Complete (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 22</td>
<td>N = 357</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>61.2</td>
<td>60.4</td>
</tr>
<tr>
<td>Male</td>
<td>15 (68)</td>
<td>260 (73)</td>
</tr>
<tr>
<td>Interventionalist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 1</td>
<td>3 (14)</td>
<td>68 (19)</td>
</tr>
<tr>
<td>• 2</td>
<td>5 (23)</td>
<td>50 (14)</td>
</tr>
<tr>
<td>• 3</td>
<td>6 (27)</td>
<td>43 (12)</td>
</tr>
<tr>
<td>• 4</td>
<td>1 (5)</td>
<td>61 (17)</td>
</tr>
<tr>
<td>• 5</td>
<td>1 (5)</td>
<td>43 (12)</td>
</tr>
<tr>
<td>• 6</td>
<td>3 (14)</td>
<td>48 (13)</td>
</tr>
<tr>
<td>• 7</td>
<td>3 (14)</td>
<td>44 (12)</td>
</tr>
<tr>
<td>Previous MI</td>
<td>18 (81)</td>
<td>193 (54)</td>
</tr>
<tr>
<td>Previous PTCA</td>
<td>9 (41)</td>
<td>69 (19)</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>5 (23)</td>
<td>70 (20)</td>
</tr>
<tr>
<td>CCS class *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 1</td>
<td>2 (9)</td>
<td>14 (4)</td>
</tr>
<tr>
<td>• 2</td>
<td>1 (5)</td>
<td>78 (22)</td>
</tr>
<tr>
<td>• 3</td>
<td>11 (50)</td>
<td>109 (31)</td>
</tr>
<tr>
<td>• 4</td>
<td>8 (36)</td>
<td>152 (43)</td>
</tr>
<tr>
<td>Lesion total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 1</td>
<td>14 (64)</td>
<td>274 (77)</td>
</tr>
<tr>
<td>• 2</td>
<td>7 (32)</td>
<td>69 (19)</td>
</tr>
<tr>
<td>• 3</td>
<td>1</td>
<td>12 (3)</td>
</tr>
<tr>
<td>• 4</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Lesion type B1/C</td>
<td>10 (45)</td>
<td>149 (42)</td>
</tr>
<tr>
<td>Left main or proximal LAD involvement</td>
<td>7 (9)</td>
<td>60 (17)</td>
</tr>
</tbody>
</table>

CCS class: Canadian Cardiovascular Society class for angina pectoris
MI = Myocardial Infarction, PTCA = Percutaneous Transluminal Coronary Angioplasty, CABG = Coronary Artery Bypass Grafting, CCS class: Canadian Cardiovascular Society class for angina pectoris, B2/C = American Heart Association/ American College of Cardiology Angiographic Lesion Type, LAD = left anterior descending artery

Fig 3-2:
Baseline Characteristics: By Time Period

<table>
<thead>
<tr>
<th>Variable</th>
<th>Liberal 1 L1 (%)</th>
<th>Conservative C (%)</th>
<th>Liberal 2 L2 (%)</th>
<th>P.value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>59.1</td>
<td>61.0</td>
<td>60.4</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>52 (73)</td>
<td>104 (71)</td>
<td>119 (74)</td>
<td>.816</td>
</tr>
<tr>
<td>Interventionalist</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 1</td>
<td>11 (15)</td>
<td>30 (20)</td>
<td>30 (19)</td>
<td></td>
</tr>
<tr>
<td>• 2</td>
<td>11 (15)</td>
<td>21 (14)</td>
<td>23 (14)</td>
<td></td>
</tr>
<tr>
<td>• 3</td>
<td>11 (15)</td>
<td>23 (16)</td>
<td>15 (9)</td>
<td></td>
</tr>
<tr>
<td>• 4</td>
<td>9 (13)</td>
<td>19 (13)</td>
<td>34 (21)</td>
<td>.461</td>
</tr>
<tr>
<td>• 5</td>
<td>5 (7)</td>
<td>18 (12)</td>
<td>21 (13)</td>
<td></td>
</tr>
<tr>
<td>• 6</td>
<td>13 (9)</td>
<td>16 (11)</td>
<td>18 (11)</td>
<td></td>
</tr>
<tr>
<td>• 7</td>
<td>11 (15)</td>
<td>20 (14)</td>
<td>20 (12)</td>
<td></td>
</tr>
<tr>
<td>Previous MI</td>
<td>44 (62)</td>
<td>69 (47)</td>
<td>98 (61)</td>
<td>.059</td>
</tr>
<tr>
<td>Previous PTCA</td>
<td>19 (27)</td>
<td>28 (19)</td>
<td>31 (19)</td>
<td>.360</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>15 (21)</td>
<td>32 (22)</td>
<td>28 (17)</td>
<td>.599</td>
</tr>
<tr>
<td>CCS class *</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 1</td>
<td>2 (3)</td>
<td>5 (3)</td>
<td>9 (6)</td>
<td></td>
</tr>
<tr>
<td>• 2</td>
<td>8 (11)</td>
<td>28 (19)</td>
<td>43 (27)</td>
<td></td>
</tr>
<tr>
<td>• 3</td>
<td>19 (27)</td>
<td>52 (35)</td>
<td>49 (30)</td>
<td>.072</td>
</tr>
<tr>
<td>• 4</td>
<td>41 (58)</td>
<td>61 (41)</td>
<td>58 (36)</td>
<td></td>
</tr>
<tr>
<td>Lesion total</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 1</td>
<td>54 (76)</td>
<td>115 (78)</td>
<td>119 (74)</td>
<td>.304</td>
</tr>
<tr>
<td>• 2</td>
<td>13 (17)</td>
<td>24 (16)</td>
<td>39 (24)</td>
<td></td>
</tr>
<tr>
<td>• 3</td>
<td>4 (6)</td>
<td>7 (5)</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>• 4</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Type B2/C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 0</td>
<td>32 (45)</td>
<td>68 (46)</td>
<td>61 (38)</td>
<td></td>
</tr>
<tr>
<td>• 1</td>
<td>36 (51)</td>
<td>73 (50)</td>
<td>85 (53)</td>
<td></td>
</tr>
<tr>
<td>• 2</td>
<td>2 (3)</td>
<td>8 (5)</td>
<td>15 (9)</td>
<td>.295</td>
</tr>
<tr>
<td>• 3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>• 4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Left main or proximal LAD</td>
<td>9 (13)</td>
<td>26 (18)</td>
<td>32 (20)</td>
<td>.416</td>
</tr>
</tbody>
</table>

* for variables with more than two categories, Chi-squared test for trends was used
MI = Myocardial Infarction, PTCA = Percutaneous Transluminal Coronary Angioplasty, CABG = Coronary Artery Bypass Grafting, CCS = Canadian Cardiovascular Society anginal class, B2/C = American Heart Association/American College of Cardiology angiographic lesion type, LAD = left anterior descending artery

Fig 3-3:
Results: Clinical Restenosis by Revascularization Period

Proportion

<table>
<thead>
<tr>
<th></th>
<th>Conservative (C)</th>
<th>Liberal (L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>147</td>
<td>232</td>
</tr>
</tbody>
</table>

CRS = Clinical Restenosis
Fig 3-4:
Difference in Proportion of Clinical Restenosis between Revascularization periods

Conservative better

Liberal better

Absolute difference

$= .032$

95% CI

$[.102 \text{ to } -.047]$
Main Outcome and Individual Endpoints by Time Periods

Proportion Reaching Endpoint

Clinical Restenosis  repeat Cath  repeat PTCA

P = .018  P = .001

PTCA = Percutaneous Transluminal Coronary Angioplasty

Fig 3-6
### Individual Endpoints by Revascularization and Time Periods

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Conservative (C) N = 147 (%)</th>
<th>Liberal (L) N = 232 (%)</th>
<th>( P ) ( C/L )</th>
<th>L1 N = 71 (%)</th>
<th>( P ) ( L1/L2 )</th>
<th>L2 N = 161 (%)</th>
<th>( P ) ( L2/L1 )</th>
<th>( P ) ( L1/C )</th>
<th>( P ) ( C/L2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Restenosis</td>
<td>51 (34.7)</td>
<td>88 (37.9)</td>
<td>.524</td>
<td>35 (49.3)</td>
<td></td>
<td>53 (32.9)</td>
<td></td>
<td>.018</td>
<td>.039</td>
</tr>
<tr>
<td>Repeat Angiography</td>
<td>29 (19.7)</td>
<td>69 (29.7)</td>
<td>.030</td>
<td>30 (42.3)</td>
<td></td>
<td>39 (24.2)</td>
<td></td>
<td>.006</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Repeat Angioplasty</td>
<td>23 (15.6)</td>
<td>25 (10.8)</td>
<td>.165</td>
<td>9 (12.7)</td>
<td></td>
<td>16 (9.9)</td>
<td></td>
<td>.535</td>
<td>.561</td>
</tr>
<tr>
<td>CABG</td>
<td>5 (3.4)</td>
<td>11 (4.7)</td>
<td>.527</td>
<td>2 (2.8)</td>
<td></td>
<td>9 (5.6)</td>
<td></td>
<td>.360</td>
<td>.561</td>
</tr>
<tr>
<td>MI</td>
<td>0 (0)</td>
<td>3 (1.3)</td>
<td>.166</td>
<td>1 (1.4)</td>
<td></td>
<td>2 (1.2)</td>
<td></td>
<td>.918</td>
<td>.149</td>
</tr>
<tr>
<td>Death</td>
<td>6 (4.1)</td>
<td>5 (2.2)</td>
<td>.276</td>
<td>1 (1.4)</td>
<td></td>
<td>4 (2.5)</td>
<td></td>
<td>.603</td>
<td>.294</td>
</tr>
</tbody>
</table>

- Values obtained using Pearson chi-square without continuity correction
- MI = myocardial infarction
- CABG = coronary artery bypass grafting

Fig 3-7
**Subgroups: Markers of Restenosis**

![Bar Chart](chart.png)

**P = .006**

**Clinical Restenosis without Cath:**
- L1
- L2

**Angiographic restenosis only:**
- C
- L2

---

**Fig 3-8:** Clinical Restenosis without cath = *any* of MI, repeat PTCA, CABG or death *without* repeat angiography alone amongst all patients. Angiographic restenosis only = a lesion listed as 'restenotic' *without* other clinical sequelae (ie: the absence of MI, repeat PTCA, CABG or death within 9 month follow-up) amongst those in whom repeat angiography was carried out. P value compares the trend between all 3 cohorts.
**Results: Rates of Repeat Angiography and Angiographic Restenosis by Interventionalist**

<table>
<thead>
<tr>
<th>Interventional Cardiologist</th>
<th>Angiographic Restenosis</th>
<th>No Angiographic Restenosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4</td>
<td>14</td>
<td>18</td>
</tr>
<tr>
<td>B</td>
<td>4</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>C</td>
<td>6</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>D</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>E</td>
<td>4</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>F</td>
<td>7</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>G</td>
<td>6</td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>50</td>
<td>83</td>
</tr>
</tbody>
</table>

*Among patients who underwent repeat angiography without other clinical sequelae
*Designations A through G are random assignments for interventional cardiologists the Toronto Hospital

Fig 3-9
Clinical Restenosis by Angiographic Lesion

Subgroups

<table>
<thead>
<tr>
<th>Location</th>
<th>Percentage</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/ B1</td>
<td>0.35</td>
<td>0.452</td>
</tr>
<tr>
<td>B2/ C</td>
<td>0.40</td>
<td>0.498</td>
</tr>
<tr>
<td>other</td>
<td>0.30</td>
<td></td>
</tr>
<tr>
<td>p LAD/LM single</td>
<td>0.45</td>
<td>0.031</td>
</tr>
<tr>
<td>p LAD/LM multi-lesion</td>
<td>0.50</td>
<td></td>
</tr>
</tbody>
</table>

Fig 3-10: p LAD/ LM = proximal LAD or Left Main lesion, multi-lesion implies more than 1 lesion dilated during procedure
Clinical Restenosis by Stent Use

<table>
<thead>
<tr>
<th>Proportion</th>
<th>stent (N = 155)</th>
<th>No stent (N = 224)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.394</td>
<td>0.348</td>
</tr>
<tr>
<td>P</td>
<td>0.368</td>
<td></td>
</tr>
</tbody>
</table>

Odds Ratio
(stent/ no stent for CRS)
= 1.13

95% CI
= [0.867 - 1.44]

Fig 3-11
Cardiac Catheterizations, PTCA and CABG per month - TTH

Fig 3-12:
Table: PTCA referrals: procedures completed, by month

<table>
<thead>
<tr>
<th></th>
<th>Nov 94</th>
<th>Nov 95</th>
<th>Nov 96</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referrals</td>
<td></td>
<td>74</td>
<td>97</td>
</tr>
<tr>
<td>PTCA</td>
<td></td>
<td>84</td>
<td>160</td>
</tr>
<tr>
<td>Ratio</td>
<td></td>
<td>0.88</td>
<td>0.61</td>
</tr>
</tbody>
</table>

- 'referrals' refers to only non-Toronto Hospital patients, whereas PTCA refers to all cases done per month

<table>
<thead>
<tr>
<th></th>
<th>Jan/Feb 95</th>
<th>Jan/Feb 96</th>
<th>Jan/Feb 97</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referrals</td>
<td>140</td>
<td>145</td>
<td>224</td>
</tr>
<tr>
<td>PTCA</td>
<td>176</td>
<td>160</td>
<td>185</td>
</tr>
<tr>
<td>Ratio</td>
<td>0.80</td>
<td>0.91</td>
<td>1.21</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>Apr/May 95</th>
<th>Apr/May 96</th>
<th>Apr/May 97</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referrals</td>
<td>99</td>
<td>179</td>
<td>201</td>
</tr>
<tr>
<td>PTCA</td>
<td>156</td>
<td>188</td>
<td>239</td>
</tr>
<tr>
<td>Ratio</td>
<td>0.63</td>
<td>0.95</td>
<td>0.84</td>
</tr>
</tbody>
</table>

Fig 3-13:
Table: PTCA referrals: time from acceptance to procedure completion

<table>
<thead>
<tr>
<th></th>
<th>days</th>
<th></th>
<th>days</th>
<th></th>
<th>days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov 94</td>
<td>13.3</td>
<td>Jan/Feb 95</td>
<td>16.5</td>
<td>Apr/May 95</td>
<td>17.6</td>
</tr>
<tr>
<td>Nov 95</td>
<td>6.8</td>
<td>Jan/Feb 96</td>
<td>14.0</td>
<td>Apr/May 96</td>
<td>16.8</td>
</tr>
<tr>
<td>Nov 96</td>
<td>14.0</td>
<td>Jan/Feb 97</td>
<td>16.0</td>
<td>Apr/May 97</td>
<td>13.1</td>
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</table>

Fig 3-14:
## Procedures Involving Stents Per Month

<table>
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<th>procedures</th>
<th>stented patients</th>
<th>ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nov 94</td>
<td>97</td>
<td>8</td>
<td>.08</td>
</tr>
<tr>
<td>Jan/Feb 95</td>
<td>176</td>
<td>58</td>
<td>.22</td>
</tr>
<tr>
<td>Apr/May 95</td>
<td>156</td>
<td>62</td>
<td>.28</td>
</tr>
<tr>
<td>Nov 95</td>
<td>84</td>
<td>45</td>
<td>.53</td>
</tr>
<tr>
<td>Jan/Feb 96</td>
<td>160</td>
<td>43</td>
<td>.27</td>
</tr>
<tr>
<td>Apr/May 96</td>
<td>188</td>
<td>155</td>
<td>.56</td>
</tr>
<tr>
<td>Nov 96</td>
<td>92</td>
<td>29</td>
<td>.31</td>
</tr>
<tr>
<td>Jan/Feb 97</td>
<td>185</td>
<td>122</td>
<td>.66</td>
</tr>
<tr>
<td>Apr/May 97</td>
<td>239</td>
<td>180</td>
<td>.75</td>
</tr>
</tbody>
</table>

*Fig 3-15*
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### Appendix 1: Classification of Coronary Artery Lesions

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B*</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Length</strong></td>
<td>&lt; 10 mm</td>
<td>10-20 mm</td>
<td>&gt; 20 mm</td>
</tr>
<tr>
<td><strong>Shape</strong></td>
<td>concentric</td>
<td>eccentric</td>
<td></td>
</tr>
<tr>
<td><strong>Angulation</strong></td>
<td>&lt; 45 degrees</td>
<td>&gt;45, &lt;90 degrees</td>
<td>&gt; 90 degrees</td>
</tr>
<tr>
<td><strong>Tortuosity of proximal segment</strong></td>
<td>none or minimal</td>
<td>moderate</td>
<td>excessive</td>
</tr>
<tr>
<td><strong>Calcification</strong></td>
<td>none or minimal</td>
<td>moderate to heavy</td>
<td>moderate to heavy</td>
</tr>
<tr>
<td><strong>Occlusion</strong></td>
<td>non-occlusive</td>
<td>total occlusion&lt; 3 months</td>
<td>total occlusion&gt; 3 months</td>
</tr>
<tr>
<td><strong>Ostial</strong></td>
<td>no</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td><strong>Bifurcation</strong></td>
<td>no</td>
<td>yes protected</td>
<td>yes unable to protect</td>
</tr>
<tr>
<td><strong>Thrombus</strong></td>
<td>none</td>
<td>some</td>
<td>some</td>
</tr>
</tbody>
</table>

Other factors (saphenous vein grafts for type ‘C’ lesions)

- Type B1 lesions have one ‘B” characteristic; type B2 lesions have two or more ‘B” characteristics
Appendix 2

Telephone Questionnaire
Corroborating Information Y N

Patient Information and Consent Form

Date _dd_mm_yy_ Study no._ Interviewer (initials) __

Interventionalist: __________________________

Contact sequence: first _ second _ third _ fourth _ fifth _ sixth _

Introduction:

Good day Mr/Mrs (last name, first name )__________, my name is ________________ and I am calling you regarding a study being conducted through the University of Toronto and The Toronto Hospital for angioplasty patients. Your cardiologist here gave me your name and allowed me to contact you. I have been told that you had angioplasty at TTH on _____________. Could I request a few minutes of your time to ask some questions about how you are doing since your procedure? In total, the entire interview should take less than five minutes.

Call back date dd_mm_yy_ Time __ __

I am a student at the University of Toronto and am working with the department of cardiology. We are interested in finding out what happened to patients after they had angioplasty and/or stent insertion during a certain time period last year. Your name was one of many who are being polled. You are under no obligation to participate and your health care will in no way be compromised if you choose to participate or not. All information we gather will be held in strict confidence, and will report the results of our study without mentioning names.

Do you have any questions at this point?
I would be happy to address any questions you have regarding the study at any point in this interview.

Consent? Yes 1
No 2

Reason for refusal:
Demographic Information:

D.O.B: dd__ mm__ yy__

Contact phone no. (__) ______

Street Address___________________________
City__________________ Province____
Postal Code_____________

Interventional MD_________________________

Relationship to the patient: (circle one)

- self 1
- spouse 2
- mother/father 3
- child 4
- other relative 5
- friend/other 6

name (last, first) ________________
(If its not 'self')

Cardiologist they see most often____________________ Hospital __________________________
(since the index procedure)

Family MD ____________________________
Date of index procedure: Nov (1-30) 95[] Jan 1- Feb 28 96[] Apr1 -May31 96[]

We are concerned with the time nine months following your angioplasty. From the time following this procedure up to and including:

Aug 30 96[] Nov 30 96[] Feb 28 97[]

Have you...

-had a second balloon angioplasty or stent?
(nb; clarify the difference between this and an angiogram)

1 Yes
2 No
3 Don’t Know

If yes;
how many more have you had (within 9mos)?

1
2
3
4
More than three

detail_____________

when was the first one (after the index)?

dd __
mm __
yy __

to which hospital were you admitted (after the index)?

1 TTH
2 SMH
3 SHSC
4 other (detail)_____________
Have you...

had a second coronary angiogram
(without a second balloon angioplasty or coronary stent)?

1. Yes
2. No
3. Don’t Know

If yes; how many more have you had?

1
2
3
4

More than three

detail __________________________

when was the first one (after the index)?

dd __
mm __

yy __

to which hospital were you admitted (after the index)?

1 TTH
2 SMH
3 SHSC
4 other (detail)__________________
Have you had coronary bypass surgery?

1 Yes
2 No
3 Don't Know

If yes, how many more have you had?

1
2
3
More than three 4

detail

when was the first one (after the index)?

dd __
mm __
yy __

to which hospital were you admitted (after the index)?

1 TTH
2 SMH
3 SHSC
4 other (detail)
Have you...

been admitted to the hospital with a heart attack (diagnosed by a doctor)?

1 Yes
2 No
3 Don’t Know

If yes; how many more have you had? 1
2
3
More than three 4

detail_________________________________

when was the first one (after the index)?

dd __
mm __
yy __

to which hospital were you admitted (after the index)?

1 TTH
2 SMH
3 SHSC
4 other (detail)______________________
Have you...

-had to visit the hospital? (admission or ER visit)

1. Yes
2. No
3. Don't Know

If yes; how many more have you had?

1
2
3
More than three

4

detail

when was the first one (after the index)?

dd__

mm__

yy__

to which hospital were you admitted (after the index)?

1 TITH
2 SMH
3 SHSC
4 other (detail)________________
If patients answer "yes" or "don't know" to any of these questions, read them the following:

As part of the study, we have to ask for documentation from your doctor regarding the same events we have just been discussing. This serves as a check to make sure that everyone has the same information. In order to do so, we need to have your written permission. We will send you a short form that will ask for this permission. It would be of great help to us if you could sign and return this form using a pre-paid envelope or a fax machine.

Once again, thank you for your cooperation. If you have any questions, feel free to call us at 340-4932.

Patient-generated Pertinent Information and Details:
Appendix 3

Data Collection Protocol
**Data Collection Protocol**

**Rules For AMI:** Admission (or discharge) for MI

- Discharge summary documenting:
  1. Acute Myocardial Infarction (AMI)
  2. Q-Wave (transmural) MI
  3. Non Q-Wave (sub-endocardial) MI
  4. Acute Coronary Occlusion

ANY TIME after index event (even if it is the same day)

**** If you are unsure either that the patient did or did not have an AMI, go to "Saleem to check"
Study Data Master Sheet

Name: Last_ _ First_ _ Study No_ 
DOB 01 dd 1 mm 2 yy M_ F_ 

Date of PTCA 27 dd 1 mm 95 yy 

Baseline:

Angioplasty CL_ Case Status E_ Hx MI Y_ CCS class 0_ Hx CABG Y_ 
LS_ U_ N_ 1_ 
JR_ MI_ 2_ 
PG_ SA_ 3_ 
JM_ L_ 4_ 
BK_ SH_ 2_ 
AA_ 1_ 

lesion location lesion type A_ B_ 1_ C_ 

vessel no. 1_ O_ 1_ 
2_ 
3_ 
4_ 

Outcome:

1-solo cath Y_ Total = _ _ 1st dd[ ] mm[ ] yy[ ] 
N_ 

2-PTCA Y_ Total = _ _ stent Y_ N_ 1st dd[ ] mm[ ] yy[ ] 
N_ 

2nd Y_ N_ 
3rd Y_ N_ 
4th Y_ N_ 

3- CABG Y_ Total = _ _ 1st dd[ ] mm[ ] yy[ ] 
N_ 

4-admission for MI Y_ Total = _ _ 1st dd[ ] mm[ ] yy[ ] 
N_ 

5-hosp. (include 1-4) Y_ Total = 01 LOS (d) 1 _ ER Y_ N_ 1st dd[ ] mm[ ] yy[ ] 
N_ 

2nd Y_ N_ 
3rd Y_ N_ 
4th Y_ N_ 
5th Y_ N_ 

6-total days in hospital: (1-5) 1 _
Appendix 4

Corroboration Information Consent Form
**VERIFICATION SHEET** (a.k.a V-Sheet)

Date dd__mm__yy__

Interviewer (intials) MC

MRN

Study Number 062

**Question 1**
Discrepency? Y N

Resolved by ulticare? Y N

**Question 2**
Discrepency? Y N

Resolved by ulticare? Y N

**Question 3**
Discrepency? Y N

Resolved by ulticare? Y N

**Question 4**
Discrepency? Y N

Resolved by ulticare? Y N

**Question 5**
Discrepency? Y N

Resolved by ulticare? Y N

Consent? Y N

Permission Letter sent?

DATE: July 28/77

Letter Received? Y N

DATE: Aug. 22/77

Letter sent to Family MD?

DATE: Aug. 22/77

Corrobarting info Received? Y N

D/C Summary Y N
The Toronto Hospital Angioplasty Study Group  
Dr. A. S. Detsky, Dr. C. Lazzam, Dr. S. Kassam

Dear

As per our conversation, we would like to contact your doctor(s) to get some details about your health during the months following your angioplasty. This letter will serve as authorization for this purpose. The information will be used solely for the purposes of this study and strict confidentiality will be observed. Once again, you are under no obligation to participate and we will not inform your doctors if you do not agree at this point.

If you agree to allow us to contact your doctor(s), please sign and witness the form below and return it via the accompanying addressed envelope if a fax machine is unavailable. We will send a copy to your doctor to allow us to review specific information during the time period in question.

If you have further questions, please feel free to contact the trial coordinating centre at (416) 340 4932. Please send any fax replies to Dr. Kassam c/o Dr. Detsky at (416) 595 5826.

Once again, thank you for your time and cooperation.

Sincerely,


Please circle one of the following...

Y  Yes, you may contact my family physician to get specific information.

N  No, you may not contact my family physician with regards to this study.

Name  Signature  
Witness  Signature  

Date: July 28/97

Date: July 15/97