

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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## **SUPPLEMENTARY APPENDIX**

### **ADDITIONAL METHODS**

#### **Myocardial Infarction Ascertainment and Definition**

The BARI 2D protocol required that each patient have a 12-lead ECG at baseline, before the initial revascularization procedure, post procedure generally before hospital discharge, 3 months after randomization, and annually thereafter. Additional ECGs were required in patients who underwent subsequent coronary revascularization procedures (before and after the procedure) and in cases of suspected ischemic events.

All ECGs were interpreted at the Saint Louis University Central ECG and Myocardial Infarction Classification Laboratory. With the use of the Minnesota code criteria, each ECG was coded independently by trained central laboratory staff blinded to the patient's clinical history and treatment assignment. Serial comparison of sequential tracings was performed with the use of a modified Novacode system to identify patients with new ECG changes in the Minnesota Code.<sup>1,2</sup> The modified Novacode adjusts for nonsignificant Minnesota Code Q-wave changes that result from minimal biological or technical procedural variations in the QRS waveform.

Acute coronary syndrome events requiring hospitalization were classified as Q-wave MI, non-Q-wave MI, unstable angina with new ECG changes, or none of the above. The MI criteria used were modified from the universal MI definition in that a two fold elevation of abnormal biomarker profile above the upper limits of normal was used rather than the 99<sup>th</sup> percentile. This modification enhances specificity but reduces sensitivity. When cardiac troponin and CKMB were simultaneously acquired, cardiac troponin took precedence over CKMB in establishing the diagnosis. Myocardial infarction was confirmed if abnormal cardiac biomarkers occurred and there was evidence of angina or angina equivalent symptoms, or ECG or imaging evidence of

new myocardial ischemia. Cardiac biomarkers were not routinely collected after coronary revascularization. When they were collected, a 3 fold elevation in CKMB following a PCI procedure and a 10 fold increase in CKMB following coronary bypass surgery were used as the cut-points to define abnormality.

Q-wave MI required the development of new pathologic Q waves as defined above or the new occurrence of a left bundle branch block in addition to abnormal biomarkers. Silent Q-wave MI was recorded when new pathologic Q waves were detected during a regularly scheduled follow-up ECG and were counted as a new Q wave MI, as were the presence of new pathologic Q waves following a coronary revascularization procedure. A non Q-wave MI met the MI criteria minus new pathologic Q waves. Unstable angina was defined by the presence of angina or angina equivalent symptoms accompanied by hospitalization and new ECG changes.

#### **References Cited in Supplementary Appendix:**

1. Chaitman BR, Zhou SH, Tamesis B, et al. Methodology of serial ECG classification using an adaptation of the NOVACODE for Q wave myocardial infarction in the Bypass Angioplasty Revascularization Investigation (BARI). *J Electrocardiol* 1996;29:265-77.
2. Rautaharju PM, Calhoun HP, Chaitman BR. NOVACODE serial ECG classification system for clinical trials and epidemiologic studies. *J Electrocardiol* 1992;24 Suppl:179-87.

**Table 1 Appendix: Baseline Characteristics of BARI 2D Patients by Randomized Treatment Groups and Intended Method of Revascularization Strata**

Characteristic	BARI 2D Patients N=2368	Randomized Treatment Groups				Revascularization Strata	
		Prompt Revasc N=1176	Intensive Medical N=1192	Insulin Sensitization N=1183	Insulin Provision N=1185	PCI Intended Stratum N=1605	CABG Intended Stratum N=763
Age at study entry, mean, SD	62.4, 8.9	62.3, 8.8	62.4, 9.0	62.3 9.2	62.5, 8.7	62.0, 9.1	63.2, 8.4,
Male, %	70.4	70.4	70.3	70.1	70.6	67.8	75.8
Race/Ethnicity, %							
White non-Hispanic	65.9	65.1	66.6	66.0	65.7	63.6	70.6
Black non-Hispanic	16.8	17.3	16.3	16.7	17.0	19.8	10.5
Hispanic	12.5	12.8	12.3	12.1	13.0	11.7	14.3
Asian non-Hispanic / Other	4.8	4.8	4.8	5.2	4.3	4.9	4.6
Geographic region, %							
USA	63.3	63.2	63.4	63.1	63.5	73.7	41.4
Canada	14.9	14.9	14.9	15.0	14.9	13.6	17.6
Brazil	15.0	15.1	14.9	15.0	15.0	7.9	30.0
Mexico	3.6	3.6	3.6	3.6	3.6	2.1	6.8
Czech Republic/Austria	3.2	3.2	3.1	3.3	3.0	2.7	4.2
HbA1c, % mean, SD	7.7, 1.6	7.6,1.6	7.7,1.6	7.6,1.6	7.7, 1.6	7.6, 1.6	7.7, 1.7
Duration of diabetes, years mean, SD	10.4, 8.7	10.2,8.5	10.7,8.8	10.1, 8.4	10.8, 8.9	10.4, 8.8	10.5, 8.4
Currently taking insulin, %	27.9	27.1	28.7	27.4	28.3	30.5	22.4
History of myocardial infarction, %	32.0	31.7	32.4	32.6	31.5	30.1	36.0
History of congestive heart failure, %	6.6	7.1	6.2	6.7	6.6	7.7	4.5
Cerebrovascular accident TIA, %	9.8	9.5	10.0	9.9	9.6	10.5	8.2
Peripheral artery disease, %	23.7	23.7	23.7	23.9	23.5	23.9	23.5
Angina category (within 6 weeks),%*							
Stable Angina 1, 2	42.5	40.8	44.2	42.8	42.3	41.3	45.0
Stable Angina 3, 4	8.6	10.2	7.1	8.6	8.6	7.9	10.1
Unstable Angina	9.5	11.3	7.7	9.7	9.4	10.7	7.0
Angina equivalents and no angina	21.4	21.5	21.3	20.8	22.0	22.3	19.6
No angina nor angina equivalents	17.9	16.1	19.7	18.1	17.8	17.7	18.4
Prior revascularization, %	23.6	22.9	24.2	23.1	24.1	28.6	13.0
Triple Vessel Disease, %	30.7	31.0	30.4	30.7	30.7	20.3	52.4
Proximal LAD Disease, %	13.2	13.2	13.3	12.1	14.4	10.3	19.4
LV Ejection Fraction,% mean, SD	57.2, 11.0	57.0, 11.3	57.3, 10.7	56.9, 11.0	57.4, 10.9	57.1, 11.0	57.3, 10.9
Abnormal LV Ejection Fraction (< 50%), %	17.5	17.4	17.6	18.4	16.6	17.5	17.5

\* Angina category comparison between Prompt Revasc / Intense Medical group, p=0.0003

**Table 2 Appendix: Event Counts and Percent of Patients with Events by Randomized Treatment and Intended Revascularization Strata**

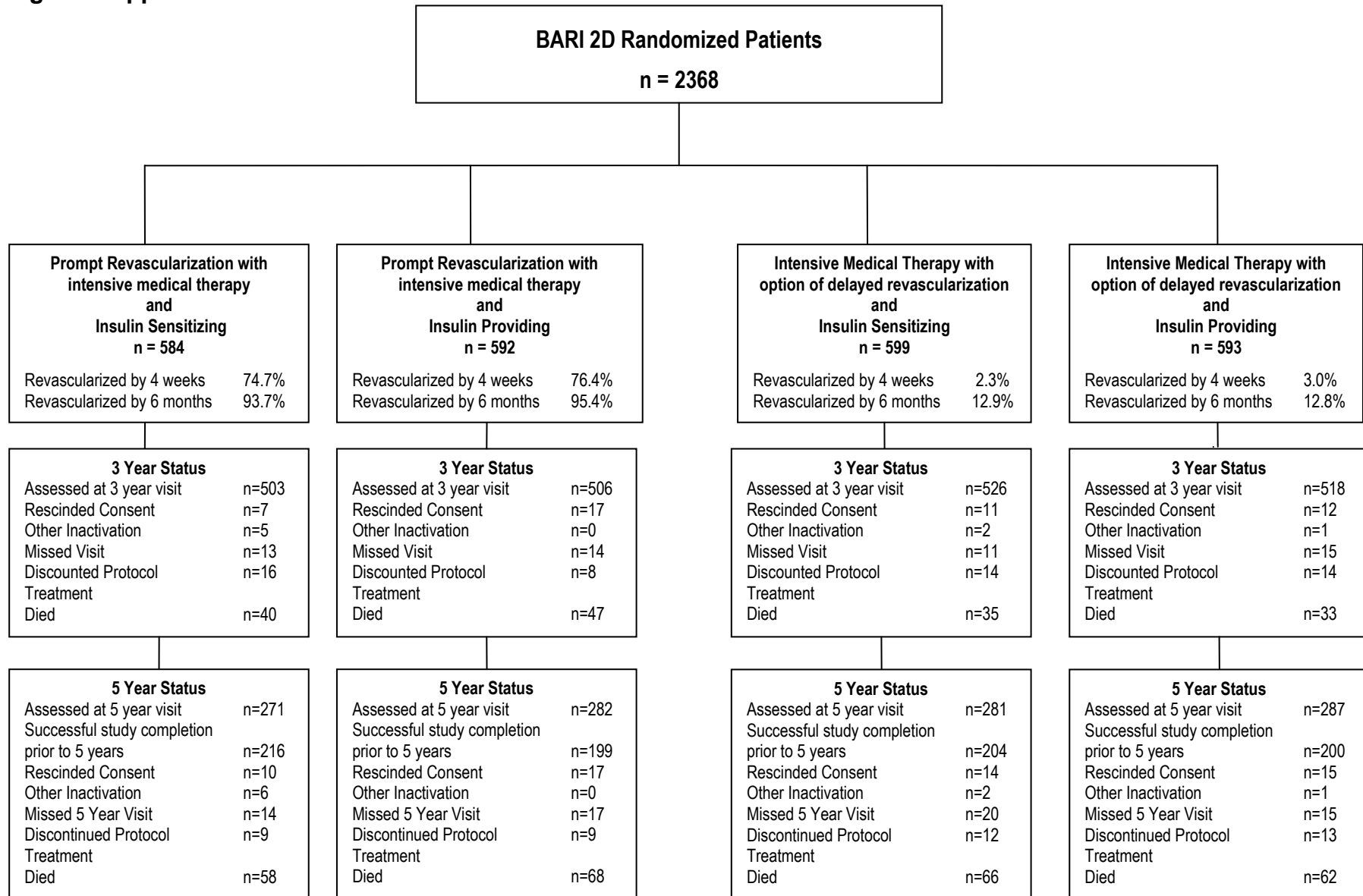
	<b>Prompt Revasc</b>	<b>Intensive Medical</b>	<b>Insulin Sensitization</b>	<b>Insulin Provision</b>	<b>Rev-IS</b>	<b>Med-IS</b>	<b>Rev-IP</b>	<b>Med-IP</b>
<b>All Patients</b>	N=1176	N=1192	N=1183	N=1185	N=584	N=599	N=592	N=593
Death	155(13.2%)	161(13.5%)	156(13.2%)	160(13.5%)	75(12.8%)	81(13.5%)	80(13.5%)	80(13.5%)
MI	118(10.0%)	138(11.6%)	118(10.0%)	138(11.7%)	51(8.7%)	67(11.2%)	67(11.3%)	71(12.0%)
Stroke	30 (2.6%)	33 (2.8%)	27(2.3%)	36 (3.0%)	13(2.2%)	14(2.3%)	17(2.9%)	19(3.2%)
Death/MI/Stroke	266(22.6%)	283(23.7%)	261(22.1%)	288(24.3%)	121(20.7%)	140(23.4%)	145(24.5%)	143(24.1%)
<b>PCI Stratum</b>	N=798	N=807	N=804	N=801	N=396	N=408	N=402	N=399
Death	102(12.8%)	96(11.9%)	97(12.1%)	101(12.6%)	49(12.4%)	48(11.8%)	53(13.2%)	48(12.0%)
MI	90(11.3%)	82(10.2%)	81 (10.1%)	91(11.4%)	42(10.6%)	39(9.6%)	48(11.9%)	43(10.8%)
Stroke	23(2.9%)	23(2.9%)	19(2.4%)	27 (3.4%)	9 (2.3%)	10(2.5%)	14(3.5%)	13(3.3%)
Death/MI/Stroke	187(23.4%)	168(20.8%)	169(21.0%)	186(23.2%)	88(22.2%)	81(19.9%)	99(24.6%)	87(21.8%)
<b>CABG Stratum</b>	N=378	N=385	N=379	N=384	N=188	N=191	N=190	N=194
Death	53(14.0%)	65(16.9%)	59(15.6%)	59(15.4%)	26(13.8%)	33(17.3%)	27(14.2%)	32(16.5%)
MI	28(7.4%)	56(14.6%)	37(9.8%)	47(12.2%)	9(4.8%)	28(14.7%)	19(10.0%)	28(14.4%)
Stroke	7(1.9%)	10(2.6%)	8(2.1%)	9(2.3%)	4(2.1%)	4(2.1%)	3(1.6%)	6(3.1%)
Death/MI/Stroke	79(20.9%)	115(29.9%)	92(24.3%)	102(26.6%)	33(17.6%)	59(30.9%)	46(24.2%)	56(28.9%)

## Figure Legends

Figure 1 Appendix: The Consort diagram depicting the number of patients randomly assigned to each of the four mutually exclusive treatment groups. For the 3 year and the 5 year follow-up clinic visit, patients are categorized as having completed the appropriate visit or according to the reason that the visit was not completed.

Figure 2 Appendix: The estimated percent of patients who underwent revascularization in the prompt revascularization (Panel A solid line) and the intensive medical (Panel A dashed line) randomized treatment groups over five years of follow-up. The percent of active patients receiving any insulin sensitization drug (blue bars) and any insulin providing drug (red bars) at the baseline, 1, 3, and 5 year visits for the insulin sensitization (Panel B) and the insulin provision (Panel C) randomized treatment groups. For each group and time, the mean HbA1c is presented below the bars.

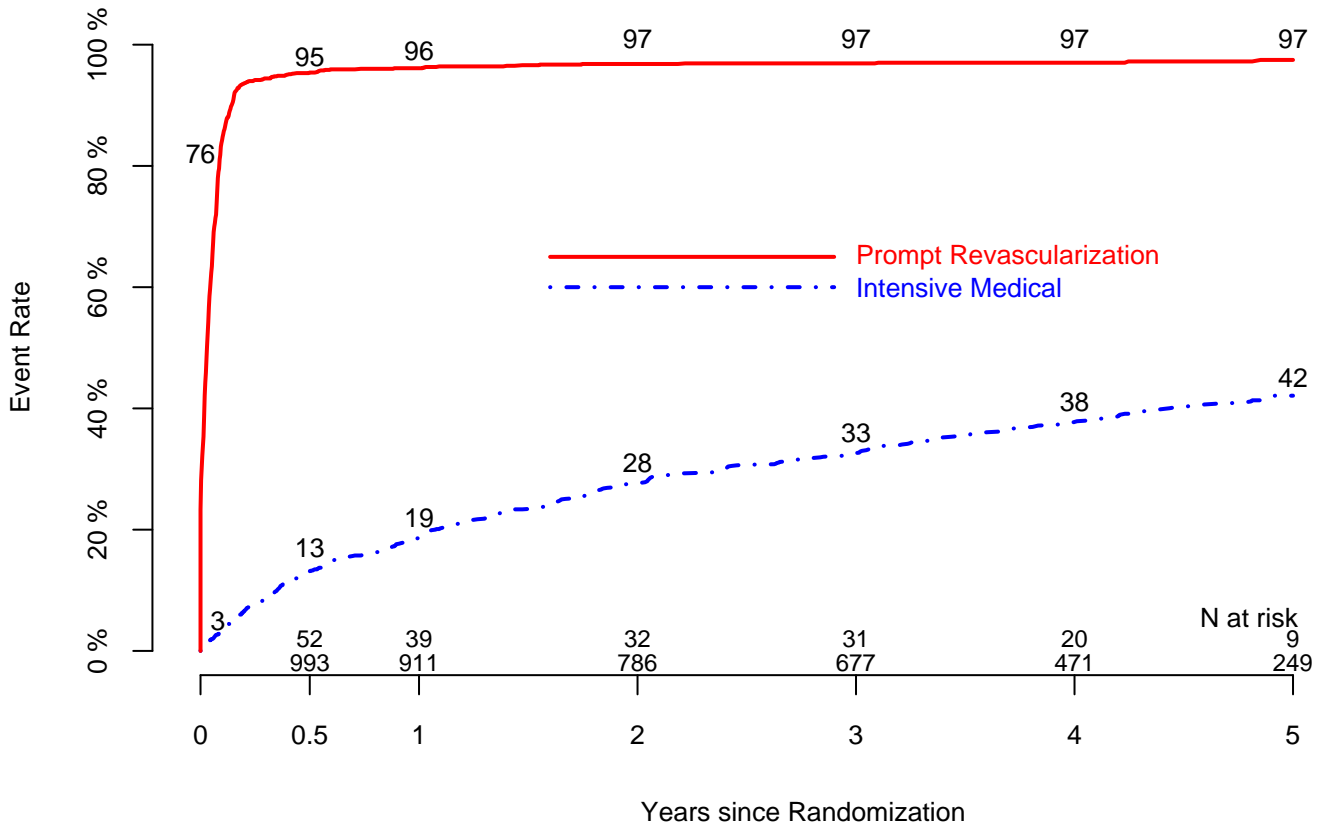
**Figure 1 Appendix**



**Figure 2 Appendix**

**A**

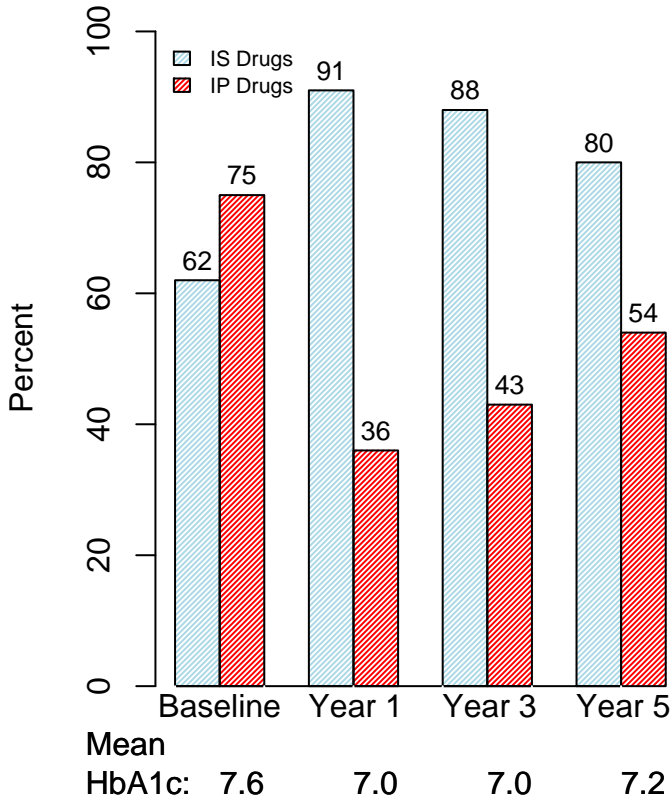
**Cumulative Rate of the First Revascularization**



**Drug use by Randomized Treatment Assignment**

**B**

**Insulin Sensitization Group**



**C**

**Insulin Provision Group**

