

## **SUPPLEMENTAL MATERIAL**

**Table S1. Medication Use from Hospital Discharge Through 2 Years According to Diabetes Status**

|                              | No diabetes (n=6153) | All diabetes (n=2429) | Insulin-treated diabetes (n=998) | Non-insulin-treated diabetes (n=1431) | p Value* | p Value† |
|------------------------------|----------------------|-----------------------|----------------------------------|---------------------------------------|----------|----------|
| <b>Statin</b>                |                      |                       |                                  |                                       |          |          |
| Pre-hospital admission       | 58.6% (3605/6153)    | 74.8% (1817/2429)     | 76.1% (759/998)                  | 73.9% (1058/1431)                     | <0.0001  | 0.24     |
| Discharge                    | 92.5% (5690/6152)    | 90.6% (2201/2429)     | 89.9% (897/998)                  | 91.1% (1304/1431)                     | 0.004    | 0.30     |
| 1 year                       | 87.1% (5199/5970)    | 84.5% (1977/2340)     | 83.8% (802/957)                  | 85.0% (1175/1383)                     | 0.002    | 0.45     |
| 2 years                      | 84.4% (4816/5705)    | 83.0% (1816/2188)     | 82.4% (725/880)                  | 83.4% (1091/1308)                     | 0.12     | 0.53     |
| <b>Proton pump inhibitor</b> |                      |                       |                                  |                                       |          |          |
| Pre-hospital admission       | 24.0% (1475/6153)    | 27.5% (668/2429)      | 29.7% (296/998)                  | 26.0% (372/1431)                      | 0.0007   | 0.05     |
| Discharge                    | 25.4% (1563/6152)    | 24.7% (599/2429)      | 27.3% (272/998)                  | 22.9% (327/1431)                      | 0.47     | 0.01     |
| 1 year                       | 22.1% (1317/5968)    | 24.7% (577/2339)      | 26.9% (257/956)                  | 23.1% (320/1383)                      | 0.01     | 0.04     |
| 2 years                      | 21.7% (1238/5704)    | 24.6% (538/2188)      | 27.5% (242/880)                  | 22.6% (296/1308)                      | 0.006    | 0.009    |
| <b>ACE inhibitor or ARB</b>  |                      |                       |                                  |                                       |          |          |
| Pre-hospital admission       | 50.3% (3098/6153)    | 73.0% (1772/2429)     | 76.5% (763/998)                  | 70.5% (1009/1431)                     | <0.0001  | 0.001    |
| Discharge                    | 69.9% (4298/6152)    | 81.2% (1973/2429)     | 82.3% (821/998)                  | 80.5% (1152/1431)                     | <0.0001  | 0.27     |
| 1 year                       | 65.8% (3929/5970)    | 73.5% (1720/2340)     | 74.3% (711/957)                  | 73.0% (1009/1383)                     | <0.0001  | 0.47     |
| 2 years                      | 64.1% (3656/5706)    | 71.7% (1569/2188)     | 71.4% (628/880)                  | 71.9% (941/1308)                      | <0.0001  | 0.77     |
| <b>Beta blockers</b>         |                      |                       |                                  |                                       |          |          |
| Pre-hospital admission       | 57.4% (3534/6153)    | 69.5% (1688/2429)     | 70.5% (704/998)                  | 68.8% (984/1431)                      | <0.0001  | 0.35     |
| Discharge                    | 83.2% (5121/6152)    | 83.3% (2024/2429)     | 83.3% (831/998)                  | 83.4% (1193/1431)                     | 0.92     | 0.95     |
| 1 year                       | 78.1% (4662/5968)    | 79.1% (1850/2339)     | 81.1% (775/956)                  | 77.7% (1075/1383)                     | 0.33     | 0.051    |
| 2 years                      | 74.8% (4270/5705)    | 77.1% (1688/2188)     | 79.0% (695/880)                  | 75.9% (993/1308)                      | 0.03     | 0.09     |
| <b>Calcium blockers</b>      |                      |                       |                                  |                                       |          |          |
| Pre-hospital admission       | 18.5% (1139/6153)    | 28.6% (695/2429)      | 30.4% (303/998)                  | 27.4% (392/1431)                      | <0.0001  | 0.11     |
| Discharge                    | 17.6% (1083/6152)    | 28.3% (687/2429)      | 29.9% (298/998)                  | 27.2% (389/1431)                      | <0.0001  | 0.15     |
| 1 year                       | 17.9% (1066/5968)    | 25.9% (605/2339)      | 26.7% (255/956)                  | 25.3% (350/1383)                      | <0.0001  | 0.46     |
| 2 years                      | 19.3% (1102/5706)    | 25.9% (567/2188)      | 26.5% (233/880)                  | 25.5% (334/1308)                      | <0.0001  | 0.62     |
| <b>Diuretics</b>             |                      |                       |                                  |                                       |          |          |
| Pre-hospital admission       | 28.3% (1740/6153)    | 45.7% (1110/2429)     | 51.9% (518/998)                  | 41.4% (592/1431)                      | <0.0001  | <0.0001  |
| Discharge                    | 32.1% (1977/6152)    | 47.7% (1159/2429)     | 53.3% (532/998)                  | 43.8% (627/1431)                      | <0.0001  | <0.0001  |
| 1 year                       | 29.0% (1729/5968)    | 43.2% (1010/2339)     | 50.8% (486/956)                  | 37.9% (524/1383)                      | <0.0001  | <0.0001  |
| 2 years                      | 28.8% (1641/5706)    | 42.8% (936/2187)      | 49.3% (434/880)                  | 38.4% (502/1307)                      | <0.0001  | <0.0001  |
| <b>Warfarin</b>              |                      |                       |                                  |                                       |          |          |
| Pre-hospital admission       | 4.1% (254/6153)      | 5.8% (140/2429)       | 7.1% (71/998)                    | 4.8% (69/1431)                        | 0.001    | 0.02     |
| Discharge                    | 5.2% (320/6152)      | 6.3% (154/2429)       | 7.8% (78/998)                    | 5.3% (76/1431)                        | 0.04     | 0.01     |
| 1 year                       | 5.0% (297/5968)      | 7.7% (181/2339)       | 8.9% (85/956)                    | 6.9% (96/1383)                        | <0.0001  | 0.08     |
| 2 years                      | 5.6% (319/5706)      | 9.0% (197/2187)       | 11.0% (97/880)                   | 7.7% (100/1307)                       | <0.0001  | 0.007    |

\*No diabetes versus diabetes; †insulin-treated versus non-insulin-treated diabetes. ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker.

**Table S2. Unadjusted 2-Year Outcomes According to Diabetes Status**

|                                                 | <b>No diabetes<br/>(n=6153)</b> | <b>All diabetes<br/>(n=2429)</b> | <b>Insulin-treated<br/>diabetes<br/>(n=998)</b> | <b>Non-insulin-<br/>treated diabetes<br/>(n=1431)</b> | <b>p Value*</b> | <b>p Value†</b> |
|-------------------------------------------------|---------------------------------|----------------------------------|-------------------------------------------------|-------------------------------------------------------|-----------------|-----------------|
| Major adverse cardiac events                    | 5.4% (318)                      | 9.2% (213)                       | 13.2% (124)                                     | 6.5% (89)                                             | <0.0001         | <0.0001         |
| Stent thrombosis                                | 0.9% (49)                       | 1.7% (40)                        | 2.2% (21)                                       | 1.4% (19)                                             | 0.03            | 0.41            |
| Ischemia-driven target vessel revascularization | 8.6% (498)                      | 12.9% (291)                      | 16.7% (151)                                     | 10.3% (140)                                           | <0.0001         | <0.0001         |
| Clinically relevant bleeding                    | 8.6% (509)                      | 10.1% (230)                      | 11.4% (106)                                     | 9.1% (124)                                            | 0.054           | 0.08            |
| Death                                           | 3.2% (186)                      | 5.7% (130)                       | 8.0% (74)                                       | 4.1% (56)                                             | <0.0001         | 0.0001          |
| Cardiovascular                                  | 1.9% (110)                      | 3.9% (87)                        | 5.1% (47)                                       | 3.0% (40)                                             | <0.0001         | 0.01            |
| Cardiac                                         | 1.6% (96)                       | 3.4% (77)                        | 4.7% (43)                                       | 2.5% (34)                                             | <0.0001         | 0.006           |
| Myocardial infarction                           | 4.0% (237)                      | 6.7% (154)                       | 9.6% (90)                                       | 4.7% (64)                                             | <0.0001         | <0.0001         |

\*No diabetes versus diabetes; †insulin-treated versus non-insulin-treated diabetes.

**Table S3. Unadjusted 2-Year Outcomes According to Diabetes Status\***

|                                                 | <b>No diabetes<br/>(n=5799)</b> | <b>Insulin-treated<br/>diabetes<br/>(n=998)</b> | <b>Non-insulin-<br/>treated diabetes<br/>(n=1785)*</b> | <b>Overall<br/>p Value</b> |
|-------------------------------------------------|---------------------------------|-------------------------------------------------|--------------------------------------------------------|----------------------------|
| Major adverse cardiac events                    | 5.2% (289)                      | 13.2% (124)                                     | 6.8% (118)                                             | <0.0001                    |
| Stent thrombosis                                | 0.9% (48)                       | 2.2% (21)                                       | 1.3% (23)                                              | 0.0007                     |
| Ischemia-driven target vessel revascularization | 8.5% (468)                      | 16.7% (151)                                     | 10.0% (170)                                            | <0.0001                    |
| Clinically relevant bleeding                    | 8.7% (484)                      | 11.4% (106)                                     | 8.8% (149)                                             | 0.04                       |
| Death                                           | 4.1% (56)                       | 5.7% (130)                                      | 8.0% (74)                                              | <0.0001                    |
| Cardiovascular                                  | 3.1% (170)                      | 8.0% (74)                                       | 4.2% (72)                                              | <0.0001                    |
| Cardiac                                         | 1.8% (98)                       | 5.1% (47)                                       | 3.1% (52)                                              | <0.0001                    |
| Myocardial infarction                           | 3.9% (218)                      | 9.6% (90)                                       | 4.9% (83)                                              | <0.0001                    |

\*In this sensitivity analysis, the category “Non-insulin-treated diabetes” included patients with diabetes who were on oral medical treatment, diet only or no treatment.

**Table S4. Adjusted Association Between High Platelet Reactivity on Clopidogrel and the Risk of Adverse Events at 2-Year Follow-up According to Diabetes Status\***

|                                                 | <b>No diabetes</b><br><b>Adjusted HR (95% CI)</b> | <b>Diabetes</b><br><b>Adjusted HR (95% CI)</b> | <b>P<sub>interaction</sub></b> |
|-------------------------------------------------|---------------------------------------------------|------------------------------------------------|--------------------------------|
| Major adverse cardiac events                    | 1.44 (1.16-1.78)                                  | 1.02 (0.73-1.43)                               | 0.09                           |
| Death                                           | 1.45 (1.10-1.92)                                  | 0.89 (0.58-1.38)                               | 0.06                           |
| Cardiac death                                   | 1.37 (0.93-2.02)                                  | 0.94 (0.53-1.66)                               | 0.27                           |
| Myocardial infarction                           | 1.42 (1.11-1.82)                                  | 1.14 (0.77-1.69)                               | 0.35                           |
| Stent thrombosis                                | 1.70 (1.20-2.40)                                  | 1.01 (0.58-1.74)                               | 0.11                           |
| Myocardial infarction or stent thrombosis       | 1.45 (1.17-1.80)                                  | 1.07 (0.76-1.51)                               | 0.14                           |
| Ischemia-driven target vessel revascularization | 1.17 (0.99-1.39)                                  | 0.96 (0.71-1.30)                               | 0.26                           |
| Clinically relevant bleeding                    | 0.87 (0.74-1.04)                                  | 0.72 (0.51-1.03)                               | 0.35                           |

\*In this sensitivity analysis, the category “Non-insulin-treated diabetes” included patients with diabetes who were on oral medical treatment, diet only or no treatment. The multivariable model also included age, sex, body mass index, hypertension, hyperlipidemia, current smoker, renal insufficiency, previous coronary artery bypass grafting, previous percutaneous coronary intervention, anemia, white blood counts, platelet counts, aspirin reaction units, ST-elevation myocardial infarction (STEMI) or non-STEMI as clinical presentation, degree of coronary artery disease (single vessel versus multivessel), small vessel disease, target vessel location in the left anterior descending coronary artery, peripheral arterial disease, and total stent length.

**Table S5. Time-Varying Effect of High Platelet Reactivity on the Risk of Major Adverse Cardiac Events in Non-Insulin Treated Diabetes (NITDM) and Insulin-Treated Diabetes (ITDM)**

| Time Interval                                    | P <sup>interaction</sup>     |                             |
|--------------------------------------------------|------------------------------|-----------------------------|
|                                                  | HPR Versus Time<br>for NITDM | HPR Versus Time<br>for ITDM |
| 0-30 days versus 30 days - 2 years               | 0.75                         | 0.73                        |
| 0-1 year versus 1-2 years                        | 0.66                         | 0.36                        |
| 0-30 days versus 30 days-1 year versus 1-2 years | 0.80                         | 0.51                        |
| Time as a continuous variable                    | 0.57                         | 0.44                        |

HPR = high platelet reactivity; ITDM = insulin-treated diabetes mellitus; NITDM = non-insulin-treated diabetes mellitus.

**Table S6. Adjusted Association Between High Platelet Reactivity on Clopidogrel and the Risk of Adverse Events At 2-Year Follow-up Among Patients with Diabetes\* According to Insulin Treatment Status**

|                                                 | <b>Non-insulin-treated<br/>diabetes mellitus<br/>Adjusted HR (95% CI)</b> | <b>Insulin-treated<br/>diabetes mellitus<br/>Adjusted HR (95% CI)</b> | <b>P<sub>interaction</sub></b> |
|-------------------------------------------------|---------------------------------------------------------------------------|-----------------------------------------------------------------------|--------------------------------|
| Major adverse cardiac events                    | 1.65 (1.12-2.45)                                                          | 1.04 (0.71-1.51)                                                      | 0.09                           |
| Death                                           | 2.09 (1.22-3.57)                                                          | 0.74 (0.46-1.21)                                                      | 0.005                          |
| Cardiac death                                   | 2.41 (1.19-4.85)                                                          | 0.78 (0.40-1.52)                                                      | 0.02                           |
| Myocardial infarction                           | 1.55 (0.98-2.46)                                                          | 1.19 (0.76-1.86)                                                      | 0.41                           |
| Stent thrombosis                                | 2.17 (1.13-4.17)                                                          | 1.00 (0.54-1.85)                                                      | 0.09                           |
| Myocardial infarction or stent thrombosis       | 1.16 (0.85-1.58)                                                          | 0.92 (0.66-1.28)                                                      | 0.31                           |
| Ischemia-driven target vessel revascularization | 1.11 (0.79-1.56)                                                          | 0.66 (0.44-0.98)                                                      | 0.049                          |
| Clinically relevant bleeding                    | 1.65 (1.12-2.45)                                                          | 1.04 (0.71-1.51)                                                      | 0.09                           |

\*In this sensitivity analysis, the category “Non-insulin-treated diabetes” included patients with diabetes who were on oral medical treatment, diet only or no treatment. The multivariable model also included age, sex, body mass index, hypertension, hyperlipidemia, current smoker, renal insufficiency, previous coronary artery bypass grafting, previous percutaneous coronary intervention, anemia, white blood counts, platelet counts, aspirin reaction units, ST-elevation myocardial infarction (STEMI) or non-STEMI as clinical presentation, degree of coronary artery disease (single vessel versus multivessel), small vessel disease, target vessel location in the left anterior descending coronary artery, peripheral arterial disease, and total stent length.

**Table S7. Time-Varying Effect of High Platelet Reactivity on the Risk of Major Adverse Cardiac Events in Non-Insulin Treated Diabetes (NITDM)\* and Insulin-Treated Diabetes (ITDM)**

| <b>Time Interval</b>                             | <b>P<sub>interaction</sub></b>   |                                 |
|--------------------------------------------------|----------------------------------|---------------------------------|
|                                                  | <b>HPR Versus Time for NITDM</b> | <b>HPR Versus Time for ITDM</b> |
| 0-30 days versus 30 days - 2 years               | 0.71                             | 0.73                            |
| 0-1 year versus 1-2 years                        | 0.28                             | 0.36                            |
| 0-30 days versus 30 days-1 year versus 1-2 years | 0.56                             | 0.51                            |
| Time as a continuous variable                    | 0.45                             | 0.44                            |

\*In this sensitivity analysis, the category “Non-insulin-treated diabetes” included patients with diabetes who were on oral medical treatment, diet only or no treatment. HPR = high platelet reactivity; ITDM = insulin-treated diabetes mellitus; NITDM = non-insulin-treated diabetes mellitus.