Table H-3. Subgroup results for KQ 3: antiplatelet and anticoagulant medications in the postdischarge treatment of patients with UA/NSTEMI

| **Study** | **Study Details** | **Subgroup** | **Results Reported by Authors** |
| --- | --- | --- | --- |
| Bonde, 201045 | Observational  Total N: 31,295  Placebo vs. clopidogrel  Fair | Heart failure | Total mortality  HR 0.86 (0.78-0.95) c/w HF no clopidogrel  clop 28.1% vs. 32.2% no clopidogrel |
| Butler, 200946 | Observational  Total N: 2980  Clopidogrel vs. aspirin  Fair | Type of stent | BMS (N=1311)  Total mortality in-hospital  BMS (N=1311): 3.1%  DES (N=1669): 1.4%  p=0.002 |
| Charlot, 201047 | Observational  Total N: 56,406  PPI vs. no PPI  Good | PPI type | PPI + clopidogrel vs. no PPI  Composite outcome (CV death, nonfatal MI, stroke)  Pantoprazole: HR 1.42, 95%CI 1.22-1.67  Omeprazole: HR 1.40, 95%CI 1.10-1.78  Lansoprazole: HR 1.47, 95%CI 1.21-1.81  Esomeprazole: HR 1.29, 95%CI 1.09-1.48 |
|  | PPI vs. No PPI  Composite outcome (CV death, nonfatal MI, stroke)  Pantoprazole: HR 1.5, 95%CI 1.36-1.69  Omeprazole: HR 1.25, 95%CI 1.09-1.41  Lansoprazole: HR 1.45, 95%CI 1.27-1.68  Esomeprazole: HR 1.53, 95%CI 1.39-1.71 |
| Age | Age ≤70 yrs  Composite outcome (CV death, nonfatal MI, stroke)  PPI + clopidogrel vs. No PPI:  HR 1.37, 95%CI 1.19-1.62  PPI vs. No PPI:  HR 1.19, 95%CI 0.99-1.39 |
| Age >70 yrs  Composite outcome (CV death, nonfatal MI, stroke)  PPI + clopidogrel vs. No PPI:  HR 1.30, 95%CI 1.18-1.43  PPI vs. No PPI:  HR 1.33, 95%CI 1.24-1.43 |
| Sex | Male  Composite outcome (CV death, nonfatal MI, stroke)  PPI + clopidogrel vs. No PPI:  HR 1.38, 95%CI 1.23-1.58  PPI vs. No PPI:  HR 1.18, 95%CI 1.004-1.37 |
| Female  Composite outcome (CV death, nonfatal MI, stroke)  PPI + clopidogrel vs. No PPI:  HR 1.34, 95%CI 1.23-1.46  PPI vs. No PPI:  HR 1.32, 95%CI 1.21-1.44 |
| Diabetes | With diabetes  Composite outcome (CV death, nonfatal MI, stroke)  PPI + clopidogrel vs. No PPI:  HR 1.36, 95%CI 1.10-1.70  PPI vs. No PPI:  HR 1.28, 95%CI 1.16-1.43 |
| Without diabetes  Composite outcome (CV death, nonfatal MI, stroke)  PPI + clopidogrel vs. No PPI:  HR 1.25, 95%CI 1.06-1.45  PPI vs. No PPI:  HR 1.35, 95%CI 1.26-1.44 |
| Charlot, 201248 | Observational  Total N: 29,268  Clopidogrel up to 90 days vs. clopidogrel > 90 days  Fair | Type of MI | Death or MI  STEMI  medically treated IRR 0.79 (0.11-5.61; p=0.81)  PCI treated IRR 2.65 (1.25-5.64; p=0.011)  NSTEMI  medically treated IRR 0.99 (0.58-1.69; p=0.97)  PCI treated IRR 1.24 (0.78-1.99; p=0.37) |
| Cheng, 201049  T-ACCORD Registry | Observational  Total N: 1331  Aspirin vs. clopidogrel  Good | Timing of treatment | Survival rate  Aspirin & clopidogrel 0-3 months: 96.5%  Aspirin & clopidogrel 3-6 months: 94.6%  Aspirin & clopidogrel 6-9 months: 100%  Aspirin & clopidogrel 9-12 months: 100% |
| Gwon, 201250 | RCT  Total N: 1443  ASA + clopidogrel 6 months vs. ASA + clopidogrel 12 months  Good | Age | <65 years (n=767)  Primary endpoint  DAPT 6 months vs. 12 months 5.1% vs. 3.2%  HR, 95%CI 1.61 (0.78-3.31) |
| =>65 year (n=676)  Primary Endpoint  DAPT 6 months vs. 12 months 4.5% vs. 5.5%  HR, 95%CI 0.83 (0.42-1.65) |
| ACS | Primary endpoint  DAPT 6 months vs. 12 months 3.6% vs. 4.7%  HR, 95%CI 0.78 (0.38-1.60) |
| Diabetes | primary endpoint  DAPT 6 months vs. 12 months 9.1% vs. 3.0%  HR, 95%CI 3.16 (1.42-7.03) |
| Harjai, 201151 | Observational  Total N: 2604  PPI vs. no PPI  Good | propensity adjusted looking at omeprazole or esomeprazole versus no PPI | omeprazole or esomeprazole vs. no PPI  MACE  HR 0.51, 95%CI 0.28-0.92  NACE  HR 0.59, 95%CI 0.35-1.01  Total mortality  HR 0.49, 95%CI 0.17-1.37  Nonfatal MI  HR 0.65, 95%CI 0.29-1.43  Death/MI  HR 0.52, 95%CI 0.26-1.03  Stent thrombosis  HR 0.59, 95%CI 0.18-1.97  Bleeding  HR 0.59, 95%CI 0.18-1.94 |
| Harjai, 200952 | Observational  Total N: 1859  Aspirin vs. clopidogrel  Good | Diabetes | Composite outcome (all cause death or MI)  DAP > 12 months (N=277): 12%  DAP ≤ 12 months (N=209): 16%  log rank p-value=0.22 between group 1 and 2.  Adjusted HR (95% CI): 0.85 (0.51 - 1.43)  p = 0.55 |
| MI | Composite outcome (all cause death or MI)  DAP > 12 months (N=322): 13%  DAP ≤ 12 months (N=391): 14%  log rank p-value = 0.76  Adjusted HR (95% CI): 0.90 (0.59 - 1.39)  p = 0.63 |
| Harjai, 201153  GHOST | Observational  Total N: 2820  Aspirin 81 mg/day vs. aspirin 162-325 mg/day  Fair | Diabetes | Patients with diabetes  MACE  low dose vs. high dose 12.1% vs. 12.6%  NACE  low dose vs. high dose 17.6% vs. 13.8%  Death/MI  low dose vs. high dose 11.0% vs. 8.3%  Bleeding  low dose vs. high dose 6.6% vs. 2.1%  Stent thrombosis  low dose vs. high dose 2.2% vs. 2.6% |
|  | Patients with DES  MACE  low dose vs. high dose 6.3% vs. 6.7%  NACE  low dose vs. high dose 9.2% 7.5%  Death/MI  low dose vs. high dose 4.66 vs. 5.3%  Bleeding  low dose vs. high dose 3.5% vs. 1.3%  Stent thrombosis  low dose vs. high dose1.7% vs. 1.8% |
| Ho, 200754 | Observational  Total N: 1455  Timing of clopidogrel  Fair | Type of stent | BMS  Total mortality  Continuing vs. discontinuing clopidogrel therapy: discontinuation associated with higher mortality risk  HR (95% CI): 2.65 (1.59 - 4.42)  Nonfatal MI  Continuing vs. discontinuing clopidogrel therapy: discontinuation associated with higher risk for subsequent AMI  HR (95% CI): 1.26 (0.58 - 2.74) |
| DES  Total mortality  Continuing vs. discontinuing clopidogrel therapy: discontinuation associated with higher mortality risk  HR (95% CI): 2.0 (1.06 - 3.75)  Nonfatal MI  Continuing vs. discontinuing clopidogrel therapy: discontinuation associated with higher risk for subsequent AMI  HR (95% CI): 3.57 (1.13 - 11.3) |
| Ho, 200955 | Observational  Total N: 8790  PPI vs. no PPI  Good | PPI use | PPI vs. no PPI at discharge  Composite outcome (death or rehospitalization)  Adjusted HR (95% CI): 1.27 (1.1-1.46) |
| PPI type  Composite outcome (death or rehospitalization)  Omeprazole  Adjusted OR (95% CI): 1.24 (1.08-1.41)  Rabeprazole  Adjusted OR (95% CI): 2.83 (1.96-4.09) |
| Juurlink, 200956 | Observational  Total N: 2791  Timing of clopidogrel  Good | PPI use | Previous vs. remote PPI use  Nonfatal MI  Previous use  HR (95% CI): 0.86 (0.63-1.19)  Remote use  HR (95% CI): 0.81 (0.46-1.41) |
| Pantoprazole vs. other PPI  Nonfatal MI  Pantoprazole  HR (95% CI): 1.02 (0.70-1.47)  Other PPI  HR (95% CI): 1.40 (1.10-1.77) |
| Kreutz, 201057 | Observational  Total N: 16,690  PPI vs. no PPI  Good | PPI use | Prior PPI use (N=12,194)  Major adverse cardiovascular event  No PPI: 17.9%  PPI: 27.8%  HR (95% CI): 1.57 (1.44–1.71)  p<0.0001 |
| No prior PPI use (N=4,499)  Major adverse cardiovascular event  No PPI: 19.2%  PPI: 23.2%  HR (95% CI): 1.24 (0.98–1.71)  p=0.0688 |
| O’Donoghue, 200958  TRITON-TIMI 38 | Observational  Total N: 13,608  PPI vs. no PPI  Good | PPI type | PPI vs. no PPI (clopidogrel arm)  Composite outcome (CV death, nonfatal MI, stroke)  Pantoprazole: Adj HR 0.94 (95% CI, 0.74-1.18)  Omeprazole: Adj HR 0.91 (95% CI, 0.72-1.15)  Lansoprazole: Adj HR 1.00 (95% CI, 0.63-1.59)  Esomeprazole: Adj HR 1.07 (95% CI, 0.75-1.52)  MI  Pantoprazole: Adj HR 0.97 (95% CI, 0.75-1.24)  Omeprazole: Adj HR 0.95 (95% CI, 0.73-1.23)  Lansoprazole: Adj HR 0.86 (95% CI, 0.51-1.46)  Esomeprazole: Adj HR 1.18 (95% CI, 0.81-1.73) |
| PPI vs. no PPI (prasugrel arm)  Composite outcome (CV death, nonfatal MI, stroke)  Pantoprazole: Adj HR 1.09 (95% CI, 0.86-1.39)  Omeprazole: Adj HR 1.04 (95% CI, 0.81-1.34)  Lansoprazole: Adj HR 0.98 (95% CI, 0.61-1.57)  Esomeprazole: Adj HR 0.86 (95% CI, 0.55-1.33)  MI  Pantoprazole: Adj HR 1.09 (95% CI, 0.83-1.43)  Omeprazole: Adj HR 1.02 (95% CI, 0.76-1.36)  Lansoprazole: Adj HR 1.08 (95% CI, 0.66-1.79)  Esomeprazole: Adj HR 0.92 (95% CI, 0.57-1.48) |
| Persson, 201159  (RIKS-HIA) and (SCAAR) | Observational  Total N: 27,972  Warfarin vs. placebo  Good | Clopidogrel use | Oral anticoagulants vs. oral anticoagulants + clopidogrel  Composite outcome (death or MI)  OR (95% CI): 0.93 (0.65-1.3)  Bleeding  OR (95% CI): 1.53 (0.57-4.11)  Total mortality  OR (95% CI): 0.98 (0.50-1.9) |
| Rassen, 200960 | Observational  Total N: 18,565  PPI vs. no PPI  Good | PPI type | Composite outcome (MI or death)  Omeprazole  HR (95% CI): 1.17 (0.68-2.01)  Pantoprazole  HR (95% CI): 1.26 (0.93-1.71) |
| Ray, 201061 | Observational  Total N: 20,596  PPI vs. no PPI  Good | PPI dose | Composite CV events  Low dose  HR (95% CI): 1.0 (0.81-1.22)  High dose  HR (95% CI): 0.94 (0.75-1.17)  Gastroduodenal bleeding  Low dose  HR (95% CI): 0.48 (0.36-0.64)  High dose  HR (95% CI): 0.53 (0.32-0.89) |
| PPI type | Composite CV events  Esomeprazole  HR (95% CI): 0.71 (0.48-1.06)  Omeprazole  HR (95% CI): 0.79 (0.54-1.15)  Pantoprazole  HR (95% CI): 1.08 (0.88-1.32)  Rabeprazole  HR (95% CI): 0.54 (0.30-0.97)  Lansoprazole  HR (95% CI): 1.06 (0.77-1.45)  Gastroduodenal bleeding  Esomeprazole  HR (95% CI): 0.43 (0.18-1.07)  Omeprazole  HR (95% CI): 0.43 (0.16-1.13)  Pantoprazole  HR (95% CI): 0.46 (0.33-0.63)  Rabeprazole  HR (95% CI): 0.25 (0.03-2.01)  Lansoprazole  HR (95% CI): 0.71 (0.43-1.18) |
| New clopidogrel user | Composite CV events  All PPI  HR (95% CI): 0.91 (0.70-1.19)  Pantoprazole  HR (95% CI): 1.02 (0.71-1.46)  Omeprazole  HR (95% CI): 0.79 (0.46-1.36) |
| PCI | Composite CV events  HR (95% CI): 1.01 (0.76-1.34)  Composite outcome (MI or SCD)  HR (95% CI): 1.00 (0.77-1.30)  Stroke  HR (95% CI): 0.97 (0.50-1.90)  CV mortality  HR (95% CI): 1.22 (0.57-2.58) |
| Rossini, 201162 | Observational  Total N: 1346  PPI vs. no PPI  Good | Diabetes | PPI use  Composite outcome (death, MI, rehospitalization, stroke at 1 year)  Diabetes  OR (95% CI): 1.31 (0.379-4.530)  No diabetes  OR (95% CI): 1.723(0.608-4.879)  p interaction 0.368 |
| Age | Age >75 yrs vs. ≤ 75 yrs  Composite outcome (death, MI, rehospitalization, stroke at 1 year)  Age >75  OR (95% CI): 1.609 (0.352-7.369)  Age ≤75  OR (95% CI): 1.46 (0.617-3.459)  p=0.809 |
| ACS and stable CAD | ACS vs. stable CAD  Composite outcome (death, MI, rehospitalization, stroke at 1 year)  ACS  OR (95% CI): 1.454 (0.649-3.26)  Stable CAD  OR (95% CI): 2.106 (0.271-16.37)  p interaction 0.998 |
| CKD | CKD vs. no CKD  Composite outcome (death, MI, rehospitalization, stroke at 1 year)  CKD  OR (95% CI): 0.647 (0.178-2.358)  No CKD  OR (95% CI): 2.48 (0.763-8.056) |
| PPI type | Lansoprazole  MACE in-hospital: 2.2%  MACE at 1 yr: 7.8%  Major bleeding: 1.3%  Minor bleeding: 2.9%  Total mortality at 1 yr: 2.1%  Stent thrombosis: 2.1% |
| Omeprazole  MACE in-hospital: 2.5%  MACE at 1 yr: 4.2%  Major bleeding: 1.6%  Minor bleeding: 7.1%  Total mortality: 0.8%  Stent thrombosis: 1.7% |
| Pantoprazole  MACE in-hospital: 4.1%  MACE at 1 yr: 8.1%  Major bleeding: 1.1%  Minor bleeding: 1.1%  Total mortality: 3.1%  Stent thrombosis: 3.1% |
| Ruiz-Nodar, 201263 | Observational  Total N: 604  Warfarin vs. non-OAC  Fair | Risk of bleeding | low risk of bleeding (HAS-BLED 0-2)  Bleeding  OAC 7.8% vs. non-OAC1.6%; P=0.13 |
| high risk of bleeding (HAS-BLED =>3)  Bleeding  OAC vs. non-OAC  11.8% vs. 4.0%  HR 3.03, 95%CI 1.24-7.38)  Total mortality  OAC vs. non-OAC  9.3% vs. 20.1%  HR 0.45, 95%CI 0.26-0.78)  MACE  OAC vs. non-OAC  13.0% vs. 26.4%  HR 0.48, 95%CI 0.29-0.77) |
| Schmidt, 201264 | Observational  Total N: 13,001  Clopidogrel  Poor | PPI Type | Esomeprazole (Clop+ Eso vs. Clop alone)  Primary composite endpoint  Clop+ Eso vs. Clop alone  153 vs. 108  Nonfatal MI  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.22 (0.19-0.26)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.40 (0.19-0.82)  Revascularization  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.50 (0.43-0.58  PPI no Clop vs. PPI + Clop  HR 95%CI 0.61 (0.31-1.20)  Cardiovascular mortality  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.12 (0.09-0.15)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.27 (0.11-0.69) |
| lansoprazole (Clop+lanso vs. Clop alone)  Primary composite endpoint  Clop+lanso vs. Clop alone  138 vs. 109  Nonfatal MI  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.23 (0.19-0.27)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.28 (0.12-0.67)  Revascularization  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.51 (0.44-0.59)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.28 (0.10-0.82)  Cardiovascular mortality  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.12 (0.09-0.16)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.22 (0.06-0.78) |
| omeprazole (clop +omep vs. clop alone)  Primary composite endpoint  clop +omep vs. clop alone  145 vs110  Nonfatal MI  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.23 (0.19-0.27)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.18 (0.05-0.60)  Revascularization  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.51 (0.44-0.59)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.49 (0.19-1.32)  Cardiovascular mortality  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.12 (0.09-0.16)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.27 (0.06-1.20) |
| pantoprazole (clop+panto vs. clop alone)  Primary composite endpoint  clop+panto vs. clop alone  154 vs. 109  Nonfatal MI  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.22 (0.19-0.26)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.80 (0.25-2.51)  Revascularization  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.50 (0.43-0.58)  PPI no Clop vs. PPI + Clop  HR 95%CI 1.26 (0.42-3.77)  Cardiovascular mortality  no PPI no Clop vs. no PPI +clop  HR 95% CI 0.12 (0.09-0.16)  PPI no Clop vs. PPI + Clop  HR 95%CI 0.16 (0.05-0.54) |
| Simon, 201165  FAST-MI | Observational  Total N: 2744  PPI vs. No PPI  Good | PPI type | Omeprazole (N=993)  Composite outcome (death, MI, or stroke in-hospital)  Adjusted OR (95% CI): 0.92 (0.59-1.43)  Composite outcome (death, MI, or stroke at 1 yr)  Adjusted OR (95% CI): 0.82 (0.54-1.24)  Total mortality  Adjusted OR (95% CI): 1.16 (0.66-2.05)  Nonfatal MI  Adjusted OR (95% CI): 1.18 (0.55-2.52)  Stroke  Adjusted OR (95% CI): 1.18 (0.55-2.52)  Bleeding  Adjusted OR (95% CI): 0.94 (0.44-1.98) |
| Esomeprazole (N=311)  Composite outcome (death, MI, or stroke in-hospital)  Adjusted OR (95% CI): 0.77 (0.41-1.46)  Total mortality  Adjusted OR (95% CI): 0.72 (0.30-1.7)  Nonfatal MI  Adjusted OR (95% CI): 1.20 (0.44-3.30)  Stroke  Adjusted OR (95% CI): 0.54 (0.14-2.16)  Bleeding  Adjusted OR (95% CI): 0.97 (0.33-2.86)  Composite outcome (death, MI, or stroke at 1 yr)  Adjusted OR (95% CI): 1.05 (0.62-1.77) |
| Lansoprazole (N=46)  Composite outcome (death, MI, or stroke in-hospital)  Adjusted OR (95% CI): 0.59 (0.07-4.72)  Total mortality  Adjusted OR (95% CI): 1.30 (0.15-11.5)  Nonfatal MI  0  Stroke  0  Bleeding  Adjusted OR (95% CI): 1.82 (0.22-15.3)  Composite outcome (death, MI, or stroke at 1 yr)  Adjusted OR (95% CI): 0.40 (0.05-2.95) |
| Pantoprazole (N=99)  Composite outcome (death, MI, or stroke in-hospital)  Adjusted OR (95% CI): 1.31 (0.54-3.17)  Total mortality  Adjusted OR (95% CI): 1.00 (0.27-3.68)  Nonfatal MI  Adjusted OR (95% CI): 1.22 (0.26-5.77)  Stroke  Adjusted OR (95% CI): 1.78 (0.36-8.83)  Bleeding  0  Composite outcome (death, MI, or stroke at 1 yr)  Adjusted OR (95% CI): 1.79(0.95-3.37) |
| So, 200966 | Observational  Total N: 1840  ASA dose  Fair | Diabetes | Composite outcome (death or MI)  Low dose ASA (81mg/d):  log OR = -0.0103324 |
| Multivessel disease | Composite outcome (death or MI)  Low dose ASA (81mg/d):  p-value=0.07, compared with diabetes group |
| Type of stent | BMS  Composite outcome (death or MI)  ASA 81 mg/d (N=1120): 5.65%  ASA 325mg/d (N=1120): 3.73%  OR (95% CI): 1.25 (0.67 - 2.33)  Composite outcome (death, MI, or revascularization)  ASA 81 mg/d (N=1120): 12.67%  ASA 325mg/d (N=1120): 8.96%  OR (95% CI): 1.38 (0.92 - 2.06) |
| DES  Composite outcome (death or MI)  ASA 81 mg/d (N=720): 5.21%  ASA 325mg/d (N=720): 4.82%  OR (95% CI): 1.12 (0.53 - 2.34)  Composite outcome (death, MI, or revascularization)  ASA 81 mg/d (N=720): 9.51%  ASA 325mg/d (N=720): 13.20%  OR (95% CI): 0.75 (0.46 - 1.25) |
| Steinhubl, 200228 | RCT  Total N: 2116  Clopidogrel vs. placebo  Good | Diabetes | MACE  RRR 11.2 (46.2 to -46.8) |
| Sex | Men vs. women  MACE  Men  RRR 24.5 (45.5 to -4.6)  Women  RRR 32.1 (58.9 to -12.1) |
| CrCl < 60 ml/min | MACE at 28 days  RRR -57%  clop 11.0% vs. placebo 7.1%  MACE at 1 year  RRR -41%  clop 17.8% vs. placebo 13.1% |
| ACS | MACE  RRR 27.5 (47.8 to -0.6) |
| Stenestrand, 200567  RIKS-HIA | Observational  Total N: 6275  Aspirin vs. OAC  Good | Age | Age ≤75 yrs vs. age >75 yrs  Total mortality  Age ≤75 yrs  RR (95% CI): 0.61 (0.40-0.93)  Age >75  RR (95% CI): 0.71 (0.53-0.96) |
| Sex | Male vs. female  Total mortality  Male  RR (95% CI): 0.60 (0.43-0.82)  Female  RR (95% CI): 0.93 (0.64-1.36) |
| Diabetes | Diabetes vs. no diabetes  Total mortality  Diabetes  RR (95% CI): 0.85 (0.56-1.30)  No diabetes  RR (95% CI): 0.64 (0.47-0.86) |
| Stockl, 201068 | Observational  Total N: 2066  PPI vs. No PPI  Good | Clopidogrel use | Clopidogrel + Pantoprazole vs. clopidogrel alone  Rehospitalization for MI  Adjusted HR (95% CI): 21.8 (0.88-5.39)  Rehospitalization for MI and coronary stent procedure  Adjusted HR (95% CI): 1.91 (1.19-3.06) |
| Valgimigli, 201269  PRODIGY | RCT  Total N: 2013  Clopidogrel dose  Good | Age | Age ≥65 yrs vs. age <65 yrs  Composite outcome (total mortality, nonfatal MI, or stroke)  Age ≥65 yrs  HR (95% CI): 1.12 (0.82-1.51)  Age <65 yrs  HR (95% CI): 0.57 (0.28-1.16) |
| Sex | Male vs. female  Composite outcome (total mortality, nonfatal MI, or stroke)  Male  HR (95% CI): 1.09 (0.77-1.29)  Female  HR (95% CI): 1.00 (0.60-1.68) |
| Diabetes | Diabetes vs. no diabetes  Composite outcome (total mortality, nonfatal MI, or stroke)  Diabetes  HR (95% CI): 0.85 (0.53-1.38)  No diabetes  HR (95% CI): 1.06 (0.76-1.50) |
| Stent type | BMS vs. DES  Composite outcome (total mortality, nonfatal MI, or stroke)  BMS  HR (95% CI): 1.13 (0.68-1.86)  DES  HR (95% CI): 0.93 (0.67-1.30) |
| Renal function | Creatinine clearance >60 mL/min vs. Creatinine clearance ≤60 mL/min  Composite outcome (total mortality, nonfatal MI, or stroke)  CrCl >60 mL/min  HR (95% CI): 0.90 (0.58-1.38)  CrCl ≤60 mL/min  HR (95% CI): 1.14 (0.78-1.65) |
| Valkhoff, 201170 | Observational  Total N: 23,655  PPI vs. No PPI  Poor | PPI timing | Current PPI use vs. past PPI use  Nonfatal MI  OR (95% CI): 0.95 (0.38-2.41) |
| Van Boxel, 201071 | Observational  Total N: 18,139  Clopidogrel dose  Fair | PPI type | Composite outcome (total mortality, nonfatal MI, stroke)  Omeprazole  HR (95% CI): 1.622 (1.379-1.907)  Pantoprazole  HR (95% CI): 1.827 (1.606-2.079)  Esomeprazole  HR (95% CI): 1.833 (1.518-2.214)  Rabeprazole  HR (95% CI): 1.758 (1.073-2.881) |
| Yusuf, 200172  CURE Study | RCT  Total N: 12,562  Clopidogrel vs. placebo  Good | Diabetes | Diabetes (N=2840)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 14.2%  Placebo: 16.7% |
| Age | Age ≤65 yrs (N=6354)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 5.4%  Placebo: 7.6% |
| Age >65 yrs (N=6208)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 13.3%  Placebo: 15.3% |
| Sex | Male (N=7726)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 9.1%  Placebo: 11.9% |
| Female (N=4836)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 9.5%  Placebo: 10.7% |
| NSTEMI | Associated MI (NSTEMI patients) (N=3283)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 11.3%  Placebo: 13.7% |
| No associated MI (UA patients) (N=9279)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 8.6  Placebo: 10.6% |
| Revascularization | Revascularization after randomization (N=4577)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 11.5%  Placebo: 13.9% |
| No revascularization after randomization (N=7985)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 8.1%  Placebo: 10% |
| Chronic kidney disease | Creatinine clearance <64 mL/min (N=4087)  Composite outcome (CV death, nonfatal MI or stroke at 9 months)  Clopidogrel: 13.4%  Placebo: 14.9%  RR (95%CI): 0.89 (0.76-1.05)  CV mortality  Clopidogrel: 8.3%  Placebo: 8.7%  RR (95%CI): 0.95 (0.77-1.17)  Total mortality  Clopidogrel: 9.6%  Placebo: 10%  RR (95%CI): 0.95(0.78-1.16)  Major bleeding  Clopidogrel: 2.3%  Placebo: 1.7%  RR (95%CI): 1.37 (0.89-2.12)  Minor bleeding  Clopidogrel: 5.2%  Placebo: 2.4%  RR (95%CI): 1.5(1.21-1.86) |
| PCI | Patients undergoing PCI  Composite outcome (CV death or nonfatal MI)  Clopidogrel (N= 1313): 79  Placebo (N=1345): 108  RR (95%CI): 0.75(0.56-1.00)  p=0.047  Major bleeding  Clopidogrel (N= 1313): 36  Placebo (N=1345): 32  RR (95%CI): 1.12(0.7-1.78) P=0.64  Minor bleeding  Clopidogrel (N= 1313): 46  Placebo (N=1345): 28  RR (95%CI): 1.68(1.06-2.68) p=0.03 |
| Patients undergoing PCI who received a stent (N= 2172)  Composite outcome (CV death or nonfatal MI)  Clopidogrel: 8.7%  Placebo: 11.7%  RR (95%CI): 0.73(0.56-0.95) |
| Aspirin dose | Aspirin dose ≤100 mg/d (N=5320)  Composite outcome (CV death, nonfatal MI or stroke)  RR (95%CI): 0.81 (0.68-0.97) in favor of clopidogrel  Major bleeding  Clopidogrel: 3%  Placebo: 1.9% |
| Aspirin dose 101-199 mg/d (N=3109)  Composite outcome (CV death, nonfatal MI or stroke)  RR (95%CI): 0.97 (0.77-1.22) in favor of clopidogrel  Major bleeding  Clopidogrel: 3.4%  Placebo: 2.8% |
| Aspirin dose ≥200 mg/d (N=4110)  Composite outcome (CV death, nonfatal MI or stroke)  RR (95%CI): 0.71 (0.59-0.85) in favor of clopidogrel  Major bleeding  Clopidogrel: 4.9%  Placebo: 3.7% |
| Zeymer, 200873  ACOS Registry | Observational  Total N: 4,290  ASA + clopidogrel vs. ASA  Poor | PCI use | PCI  Total mortality  ASA vs. ASA + clopidogrel  OR (95% CI): 0.51 (0.33-0.77)  Composite outcome (death, MI, stroke)  ASA vs. ASA + clopidogrel  OR (95% CI): 0.55 (0.40-0.75) |
| No PCI  Total mortality  ASA vs. ASA + clopidogrel  OR (95% CI): OR 0.90 (0.73-1.11) |

Abbreviations: ASA=aspirin; BMS=bare metal stent; c/w=cases with; CAD=coronary artery disease; CI=confidence interval; CKD=chronic kidney disease; clop=Clopidogrel; CV=cardiovascular; d=day/days; DAP=dual antiplatelet; DAPT=dual antiplatelet therapy; DES=drug-eluting stent; Eso=esomeprazole; HR=hazard ratio; IRR=incidence rate ratio; MACE=major adverse cardiac event; mg=milligram/milligrams; MI=myocardial infarction; min=minute/minutes; mL=milliliter/milliliters; N=number of patients; NACE=net adverse clinical events; NSTEMI=non-ST elevation myocardial infarction; OAC=oral anticoagulation; omep=omeprazole; OR=odds ratio; panto=pantoprazole; PPI=proton pump inhibitor; RCT=randomized controlled trial; RR=relative risk; RRR=relative risk reduction; STEMI=ST elevation myocardial infarction; UA/NSTEMI=unstable angina/non-ST elevation myocardial infarction; vs=versus; yr=year/years