**Supplementary Table 1.** Research Question-Are acute coronary syndrome patients undergoing percutaneous coronary intervention carrying *CYP2C19* loss-of-function alleles treated with clopidogrel at increased risk of major adverse cardiovascular events?

|  |  |
| --- | --- |
| **PICO Model** | **Search terms** |
| **Patient (P)** | Acute Coronary Syndrome [MeSH] OR acute coronary syndrome [tw] OR Percutaneous Coronary Intervention [MeSH] OR percutaneous coronary intervention [tw] OR PCI Patients [MeSH] or pci patients [tw] OR PCI [MeSH] OR Coronary Stenting Patients [MeSH] or coronary stenting patients [tw] OR Stents [MeSH] OR stents [tw] OR Stent Implantation [MeSH] OR stent implantation [tw] OR Myocardial Infarction [MeSH] OR myocardial infarction [tw] OR MI [MeSH] OR mi [tw] OR STEMI [MeSH] OR NSTEMI [MeSH] OR Unstable Angina [MeSH] OR unstable angina [tw] |
| **Intervention (I)** | *CYP2C19* Genotype guided therapy [MeSH] OR cyp2c19 genotype guided therapy [tw] OR *CYP2C19* Genetic Polymorphisms [MeSH] OR *CYP2C19* genetic polymorphisms [tw] OR CYP2C19\*2 Genetic Polymorphism [MeSH] OR CYP2C19\*2 genetic polymorphism [tw] OR cyp2c19\*2 Genetic Polymorphism [MeSH] OR cyp2c19\*2 genetic polymorphism [tw] OR *CYP2C19\*3* Genetic Polymorphism [MeSH] OR *CYP2C19\*3* genetic polymorphism [tw] Or CYP2C19 variants [MeSH] OR cyp2c19 variants [tw] OR *CYP2C19* LoF alleles [MeSH] OR cyp2c19 lof alleles [tw] |
| **Comparison (C)** | Antiplatelets [MeSH] OR antiplatelets [tw] OR P2Y12 inhibitors [MeSH] OR P2Y12 inhibitors [tw] OR [MeSH] OR Clopidogrel [MeSH] OR clopidogrel [tw] OR Plavix [MeSH] OR plavix [tw] |
| **Outcome (O)** | MACE [MeSH] OR mace [tw] OR MI [MeSH] OR mi [tw] OR Recurrent MI [MeSH] OR recurrent mi [tw] OR Recurrent Myocardial Infarction [MeSH] OR recurrent myocardial infarction [tw] OR Death [MeSH] OR death [tw] OR Myocardial Infarction [MeSH] OR myocardial infarction [tw] OR Stroke [MeSH] OR stroke [tw] OR Mortality [MeSH] OR mortality [tw] OR Cardiovascular mortality [MeSH] OR cardiovascular mortality [tw] OR ST elongation [MeSH] OR Stent Thrombosis [MeSH] or stent thrombosis [tw] OR Major Adverse Cardiovascular Events [MeSH] OR major adverse cardiovascular events [tw] OR MACE [MeSH] OR mace [tw] OR Revascularization [MeSH] OR revascularization [tw] OR Urgent revascularization [MeSH] OR urgent revascularization [tw] OR Cardiovascular mortality [MeSH] OR cardiovascular mortality [tw] OR Bleeding [MeSH] OR bleeding [tw] |

**Supplementary Table 2A.** Quality assessment of the included observational studies by NOS

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Year** | **Selection** | | | |  | **Comparability** | |  | **Outcome** | | | **Total Score** |
| 1 | 2 | 3 | 4 |  | 5A | 5B |  | 6 | 7 | 8 |
| Exposed cohort truly/somewhat representative | Nonexposed cohort drawn from the same community | Ascertainment of exposure | Outcome of interest not present at start |  | Cohorts adjusted for age | Cohorts adjusted for other important factor(s) |  | Quality of outcome assessment | Follow-up long enough for outcomes to occur | Adequacy of follow-up of cohorts |
| Arima et al | 2015 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Cavallari et al | 2018 | \* | \* | \* | \* |  |  | \* |  | \* | \* |  | 7 |
| Chen et al | 2015 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Dong et al | 2016 | \* | \* | \* | \* |  |  |  |  | \* | \* |  | 6 |
| Jeong et al | 2011 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Kim et al | 2013 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Lee et al | 2018 | \* | \* | \* | \* |  |  | \* |  | \* | \* | \* | 8 |
| Li et al | 2019 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Liang et al | 2013 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Mahdieh et al | 2018 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Malek et al | 2010 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Marcucci et al | 2012 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Martin et al | 2020 | \* | \* | \* | \* |  |  | \* |  | \* | \* | \* | 8 |
| Tang N et al | 2015 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Tatarunas et al | 2019 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Verschuren et al | 2013 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Wei et al | 2015 | \* | \* | \* | \* |  |  |  |  | \* | \* | \* | 7 |
| Zhang et al | 2021 | \* | \* | \* | \* |  | \* | \* |  | \* | \* | \* | 9 |

NOS score ranges between 0-9 where “0-3” indicates low quality, “4-5” indicates moderate quality and score of ≥6 indicates high quality study

**Supplementary Table 2B.** Assessment of quality of included RCTs by Jadad scale

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Author | Year | 1 | 2 | 3 | 4 | 5 | Score |
| *Was the study described as randomized* | *The method of randomization was described in the paper, and that method was appropriate* | *Was the study described as double blind* | *The method of blinding was described, and it was appropriate* | *Was there a description of withdrawals and dropouts* |
| Mega et al | 2009 | Yes | Yes | Yes | No | Yes | 4 |
| Ogawa et al | 2016 | Yes | Yes | Yes | No | Yes | 4 |
| Tang et al | 2012 | Yes | Yes | Yes | No | Yes | 4 |
| Wallentin et al | 2010 | Yes | Yes | Yes | No | Yes | 4 |

Jadad score ranges from 0-5 where Score “0” indicates very poor trials and score “5” indicates rigorous trials