Appendix Table F7. Assessment of risk of bias for studies of patients selected on the basis of platelet reactivity testing and then randomized into alternative antiplatelet

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author**  **Year**  **Country**  **UID**  **Study name (if available)** | **Q1** | **Q2** | **Q3** | **Q4** | **Q5** | **Q6** | **Q7** | **Q8** | **Q9** | **Q10** | **Q11** | **Q12** | **Q13** | **Q14** | **Q15** | **Q16** | **Q17** |
| Price  2011  Multinational  21406646  GRAVITAS | Unclear | Low | Low | Low | Low  (protocol-specified) | Low | Low | High  (6 mo) | Low | Low | Low  (centralized, interactive voice-response system) | Low  (encrypted reactivity values; central randomization) | Low  (encrypted reactivity values and placebo-controlled design) | Low  (blinded clinical events committee) | Low | Low | Low |
| Palmerini  2010  Italy  19604542  DOUBLE | Unclear | Low | High | Unclear | High  (cut-off for response was based on prior literature; unclear choice of cut-off for selection of patients) | High  (patients with AEs were excluded from analyses of reactivity; no other clinical outcomes assessed) | Unclear | High  (1 mo) | Low | Low | Low  (computer-generated random sequence) | Unclear | Unclear | Unclear | Low | Low | Low |
| Valgimigli  2009  Italy  19528337  3T/2R | Low  (“all patients”) | Low | Low | Low | Low  (threshold based on prior literature) | Low | Low | High  (1 mo) | Low | Low | Low  (block of 6, stratified (stable or unstable CAD; and response status) by a local nurse using sealed envelopes) | High  (local randomization using envelopes) | Low | Low | Low  (uncertainty in estimates was reported) | High  (only limited outcomes were reported in the clopidogrel non-responsive patients) | Low |
| Cuisset 2008  France  19463379 | Unclear | Low | Low | Unclear | Low  (threshold based on prior literature) | Low | Unclear | High  (1 mo) | Low | Low | Unclear | Unclear | Unclear | Unclear | Low | Low | Low |
| Gurbel 2010  Multinational (N. America and Europe)  20194878  RESPOND | Unclear | Low | High  (>5% dropout) | Low | Low  (single threshold used for stratification; unclear rationale) | High  (no clinical outcomes) | Unclear | High  (30 d) | Low | Low | Low  (centralized block randomization) | Unclear | Low | Unclear | Low | Low | Low |

\*Despite including both responders and non-responders, this study was categorized as a study of randomized treatment after test-based selection because patients were assigned to different treatments during the course of the study based on their original response status.  
**Abbreviations:** AE = adverse event; CAD = coronary artery disease; mo = month; PMID = PubMed identification number.

**Quality items**Q1: Consecutive sample of patients enrolled  
Q2: Case-control design avoided  
Q3: Study avoided inappropriate exclusions and post-hoc exclusions were <5%  
Q4: Index test results interpreted without knowledge of outcomes?  
Q5: If a test threshold was used, was it prespecified?  
Q6: Reference standard likely to correctly classify the target condition (low if at least one clinical outcome assessed)?  
Q7: Reference standard results interpreted without knowledge of index test results?  
Q8: Appropriate interval between index test and reference standard (at least 12 mo of followup)?  
Q9: All patients received a reference standard (outcome data for >90% of patients)?  
Q10: All patients received the same reference standard?  
Q11: Random sequence generation  
Q12: Allocation concealment  
Q13: Blinding of participants and personnel  
Q14: Blinding of outcome assessment  
Q15: Incomplete outcome data (do they report enough data to estimate uncertainty for the primary outcome)  
Q16: Selective reporting bias (do they report numerical results on the primary and secondary outcome; and are these identified in the methods)  
Q17: Other bias (e.g., extreme numerical errors and inconsistencies)