An overview of systematic reviews of the prognostic utility of platelet function tests for predicting vascular event rates in patients on aspirin therapy: implications of discrepancies in study identification and selection

Janine Dretzke, Sue Bayliss, Jennifer O’Donnell, Marie Lordkipanidzé, Smriti Raichand, David Fitzmaurice, David Moore
Overview of presentation

• Background/wider project
• Current review and overlap with previous systematic reviews
• Reasons for differences:
  – Review question
  – Search strategies
  – Study selection criteria
  – Reporting issues
  – (Additional factors)
• Implications
The prognostic and diagnostic utility of tests of platelet function for the detection of “aspirin resistance” in patients with established cardiovascular or cerebrovascular disease: A systematic review and economic evaluation


http://www.hta.ac.uk/2468
Background

Current project:
Review of previous systematic reviews
Review of primary studies
OVERLAP WITH PREVIOUS SYSTEMATIC REVIEWS
Previous systematic reviews

- For citation checking purposes
- 12 relevant (systematic) reviews identified with same/similar study question
- Focus on 5 with some systematic/repeatable elements
  - Recent
  - Details of search strategy/study selection criteria
  - Included studies listed
  - Not restricted to a specific type of platelet function test

  - Canivano-Petrenas 2010
  - Krasopoulos 2008
  - Pusch 2008
  - Sofi 2008
  - Snoep 2007

- Overlap between included studies mapped and compared with those included in current review
Overlap of included studies between reviews

No. of publications

Publications up to 2007

Included in current review

Excluded from current review

Canivano Petrenas 2010

Krasopoulous 2008

Pusch 2008

Snoep 2007

Sofi 2008

CURRENT

0

102

9

7

13

16

7

9

19

2

Included in current review

Excluded from current review
Only two primary studies consistently identified/selected for inclusion in all 6 reviews.
Proportions of different tests included

(limited to 2008 for current review)

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>P</th>
<th>K</th>
<th>S8</th>
<th>S7</th>
<th>Current</th>
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</thead>
<tbody>
<tr>
<td>Platelet Function Analyzer-100</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Light Transmission Aggregometry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thromboxane measurement</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>VerifyNow</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole Blood Aggregometry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thromboelastography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than one test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</table>
Reasons for differences?

• Review question

• Search strategies

• Selection criteria

• Reporting issues
Review question
Questions addressed by reviews

“To review the prevalence of aspirin resistance in patients with a high risk of cardiovascular events, and secondly, to investigate its epidemiology and mechanism of action, and the clinical consequences it can provoke” (C-P)

“To determine if there is a relation between aspirin “resistance” and clinical outcomes in patients with cardiovascular disease” (K)

“To systematically assess the relationship between residual platelet activity on acetylic salicylic acid therapy and the occurrence of recurrent events in a meta-analysis of prospective studies” (S8)

“To systematically review all available evidence on whether laboratory aspirin resistance is related to a higher risk of cardiovascular recurrent events” (S7)

“We systematically reviewed all available evidence on prevalence of aspirin resistance and its association with clinical outcome” (P)

“To review systematically the evidence relating PFTs to the risk of adverse clinical outcome(s) in patients on aspirin therapy with established cardiovascular or cerebrovascular disease; more specifically, to determine whether different PFTs have prognostic, diagnostic/predictive or economic utility” (Current)
Search strategies
# Search strategies-sources

<table>
<thead>
<tr>
<th>Systematic review</th>
<th>Search strategies</th>
<th>Number of initial hits</th>
<th>Number included studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canivanos-Petrenas 2010</td>
<td>PubMed (limited to MeSH headings and “clinical trial”, “randomised controlled trial”, meta-analysis”) EMBASE, Cochrane Library, citation checking</td>
<td>190 hits</td>
<td>16</td>
</tr>
<tr>
<td>Pusch 2008</td>
<td>PubMed, MEDLINE, Cochrane Library, citation checking</td>
<td>No details</td>
<td>33</td>
</tr>
<tr>
<td>Sofi 2008</td>
<td>Text and MeSH terms MEDLINE, EMBASE, SciCit Index, Cochrane Library, citation checking</td>
<td>“Search strategies generated 26 potentially relevant studies”</td>
<td>11</td>
</tr>
<tr>
<td>Krasopoulous 2008</td>
<td>MEDLINE, EMBASE, CINAHL, Cochrane Library, citation checking</td>
<td>36,573 hits</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>268 abstracts scanned</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>57 papers reviewed in detail</td>
<td></td>
</tr>
<tr>
<td>Snoep 2007</td>
<td>MEDLINE, EMBASE, Web of Science, Cochrane Library, citation checking, authors contacted</td>
<td>1978 hits</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>232 abstracts scanned</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>104 papers reviewed in detail</td>
<td></td>
</tr>
<tr>
<td>CURRENT (searches 2012)</td>
<td>MEDLINE, EMBASE, Cochrane Library, conference proceedings, ongoing trial registries, citation checking</td>
<td>16,583 hits</td>
<td>(28-2007, 34-2008) 102</td>
</tr>
</tbody>
</table>
Search strategies-terms

Krasopoulos 2008
Terms used:
“acetylsalicylic acid”
“aspirin”
“antiplatelet”
“antiplatelets”
“platelets”
“drug resistance”
“aspirin resistance” (36,573 hits)

Refined to “aspirin resistance” (320 hits)
Refined to “aspirin resistance and clinical outcome” (210 hits)

Pusch 2008
Terms used:
“aspirin”
“acetylsalicylic acid”
“failure”
“resistance”
“platelet aggregation”
“platelet activation”
“clinical outcome”
“hospitalisation”
“acute coronary syndrome”
“myocardial infarction”
“unstable angina”
“stable angina”
“peripheral artery disease”
“TIA”
“stroke”

No details on combining
Search strategies-terms

Sofi 2008
“acetyl salicylic acid”
“aspirin”
“antiplatelet”
“residual platelet reactivity”
“persistent platelet reactivity” in combination with
“resistance”
“failure”
“recurrence” and
“major adverse cardiovascular events”
“cardiovascular disease”
“coronary artery disease”
“coronary heart disease”
“ischemic heart disease”
“myocardial infarction”
“acute coronary syndromes”

Text and MeSH terms used
Search strategies-terms

Canivano –Petrenas 2010

*PubMed*

MeSH terms “aspirin” and “drug resistance”

Limited to human, English and Spanish articles

*After retrieving a high number of articles, two further limits were included:*

(i) “clinical trial” “meta-analysis” “randomized controlled trial”

(ii) “review” “practice guidelines”

*EMBASE*

“aspirin” AND “drug resistance” OR “disease resistance” OR “resistance blood vessel” OR “therapy resistance”
Search strategy current review

- 1  \(((\text{ASA or aspirin or acetylsalicylic} \text{ or anti platelet or anti-platelet}) \text{ adj2 (respons$ or non-respons$ or respond$ or non-respond$ or resistance or resist$)})).mp\)
- 2  \((\text{platelet adj (response or respond$ or reactivity)})).mp.\)
- 3  1 or 2
- 4  \text{exp Aspirin/}\)
- 5  \text{exp Drug Resistance/}\)
- 6  4 and 5
- 7  3 or 6
- 8  \((\text{platelet function adj (analys$ or analyz$)}).mp.\)
- 9  \((\text{platelet function adj (assay$ or test$)}).mp.\)
- 10  \text{Platelet Function Tests/}\)
- 11  \text{PFA-100.mp.}\)
- 12  \text{PlateletWorks.mp.}\)
- 13  \text{Platelet Mapping.mp.}\)
- 14  \text{Impact Cone.mp.}\)
- 15  \text{platelet analyser$.mp.}\)
- 16  \text{platelet analyzer$.mp.}\)
- 17  \text{multiplate.mp.}\)
- 18  \text{aggregometry.mp.}\)
- 19  \text{LTA.mp.}\)
- 20  \text{AA-induced LTA.mp.}\)
- 21  \text{lumiaggregometry.mp.}\)
- 22  \text{WBA.mp.}\)
- 23  \text{ULTEGA assay.mp.}\)
- 24  \text{Impact-R.mp.}\)
- 25  \text{TRAP-6.mp.}\)
- 26  \text{TEG.mp.}\)
- 27  \text{s-TEG.mp.}\)
- 28  \text{thromboelastometry.mp.}\)
- 29  \text{ROTEM.mp.}\)
- 30  \text{VerifyNow.mp.}\)
- 31  \text{Verify-Now.mp.}\)
- 32  \text{VN-RPFA.mp.}\)
- 33  \text{VASP.mp.}\)
- 34  \text{VASP-P.mp.}\)
- 35  \text{platelet reactivity index.mp.}\)
- 36  \text{vasodilator-stimulated phosphoprotein phosphorylation assay$.mp.}\)
- 37  \text{T-Guide.tw.}\)
- 38  \text{T Guide.ti,ab.}\)
- 39  \text{xylum clot signature analyser.mp.}\)
- 40  \text{xylum clot signature analyzer.mp.}\)
- 41  \text{ASA test$.mp.}\)
- 42  \text{ASA assay$.mp.}\)
- 43  \text{AA-induced LTA.mp.}\)
- 44  \text{exp Platelet Count/ or platelet counting.mp.}\)
- 45  \text{thrombelastography.mp. or Thrombelastography/}\)
- 46  \text{thrombotic status analyser$.mp.}\)
- 47  \text{thrombotic status analyzer$.mp.}\)
- 48  \text{or/8-47}\)
- 49  \text{exp Cardiovascular Diseases}\)
- 50  \text{exp Cerebrovascular Disorders/}\)
- 51  \text{exp Diabetes Mellitus/}\)
- 52  \text{or/49-51}\)
- 53  \text{48 and 52}\)
- 54  \text{(predict$ or prognos$).mp.}\)
- 55  \text{48 and 54}\)
- 56  \text{7 or 53}\)
- 57  \text{7 or 55}\)
- 58  \text{56 or 57}\)
- 59  \text{exp animals/ not humans/}\)
- 60  \text{58 not 59}\)
## Comparison of search terms used

<table>
<thead>
<tr>
<th>Terms relating to</th>
<th>Current review</th>
<th>Pusch 2010</th>
<th>Sofi 2008</th>
<th>Krasopoulos 2008</th>
<th>Canivano-Petrenas 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Resistance</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Platelet (function)</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Outcomes/condition</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Names of tests</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prognosis/prediction</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filter for study design</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Examples of restricting searches

Krasopoulos 2008
“The initial search identified 36,573 papers. When we refined our search to aspirin resistance the number of papers was reduced to 320, and 210 remained when we further refined the search to aspirin resistance and clinical outcome.”

Canivano-Petrenas 2010
After retrieving a high number of articles, two further limits were included:
(i) “clinical trial” “meta-analysis” “randomized controlled trial”
(ii) “review” “practice guidelines”
Prognostic filters

• No review used an existing prognostic/predictive filter
• Current review used terms predict$ or prognos$.mp. but not a formal filter only part of search limited by this

test AND condition/outcome AND predict$ or prognos$.mp

OR

Aspirin AND resistance
Prognostic filters

• “Existing published prognosis search filters have lower sensitivity and precision values than their therapy counterparts” Chatterley & Dennett 2012

• Best known are (validated) Haynes filters which are built into Ovid databases and Pubmed Clinical Queries:

  “Prognosis” filter
  incidence.sh. OR exp mortality OR follow-up studies.sh. OR prognos:.tw. OR predict:.tw. OR course:.tw.

  “Clinical prediction guide” filter
  predict:.mp. OR scor:.tw. OR observ:mp.
## Retrieval using different filters
(MEDLINE only)

<table>
<thead>
<tr>
<th></th>
<th>Search strategy for current review (8887 hits)</th>
<th>Restricted by sensitive (broad) Haynes filter “prognosis” (1584 hits)</th>
<th>Restricted by Haynes clinical query “clinical prediction guide” (2498 hits)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of included studies retrieved</td>
<td>66</td>
<td>51 (77%)</td>
<td>41 (62%)</td>
</tr>
</tbody>
</table>
Study selection criteria
## Study selection criteria

<table>
<thead>
<tr>
<th>Review</th>
<th>Patients on mono and dual therapy?</th>
<th>Prospective* and retrospective studies?</th>
<th>Other (selected)</th>
</tr>
</thead>
</table>
| Canivanos-Petrenas 2010 | No details                        | No details                             | Aspirin for secondary prevention  
Definition of aspirin resistance  
Methods of platelet function test defined |
| Pusch 2008            | No details                        | No details                             | No details                                                                      |
| Sofi 2008             | No details                        | Prospective only                       | RR, OR or HR presented (or data to calculate them)                              |
| Krasopoulos 2008      | Both included                      | Prospective and retrospective          | Platelet function test preceding outcome  
Investigators blinded to patients’ aspirin status  
Measure of prospective clinical outcome used in both groups |
| Snoep 2007            | No details                        | No details                             | Clear description of method used to establish effect of aspirin on platelet therapy  
Data reported on recurrence rates of cardiovascular outcomes |
| CURRENT               | Both included                      | Prospective only                       | Any studies where results of platelet function test are linked to clinical outcome (whether numerical or narrative) |

* Sampling for platelet function test preceded outcomes
Reporting issues
Reporting issues-terminology example

• Identified and included in all 6 reviews
  – Gum 2003 and Stejskal 2006
  – “aspirin resistance” in title and abstract

• Identified and included only in current review
  – Payne 2004
    Title: “Beneficial Effects of Clopidogrel Combined With Aspirin in Reducing Cerebral Emboli in Patients Undergoing Carotid Endarterectomy”
  – RCT
  – Focus on clopidogrel, but also measures response to aspirin; only apparent in main body of article
Summary so far
Findings from comparison of systematic reviews

- Differences in included studies not explained by research questions
- Search strategies and selection criteria mostly not reproducible
- Differences could in part be explained by:
  - Differences in search strategies
  - Differences in study selection criteria
  - Poor reporting in published studies
- May lead to misleading results/different conclusions for different platelet function tests
- Reliance on prognostic filters would have led to missed studies in current review
Conclusions I

• Prognostic /predictive studies are difficult to find and extensive searches are needed
• Variable terminology used in primary studies
• Even broad search strategies (no filter) may miss studies
• More than one search strategy may need to be combined
• The prognostic element may not be the main aim of the study (e.g. in an RCT), so relevant information is more ‘hidden’
• Various “levels” of reporting results; whole text often has to be read, study selection process very time consuming
• Retrieval of very large numbers of citations may give rise to ad hoc changes to search strategies (e.g. adding further text words to narrow results) thus potentially biasing results
Additional factor-selective presentation of results

• Inclusion/exclusion from meta-analyses

• Results can be presented by:
  – Different platelet function tests
  – Different outcomes (e.g. death, stroke)
  – Different thresholds
  – Different outcome statistics (adjusted or unadjusted OR, RR, HR)
  – Calculation of thresholds from tertiles
Any test, outcome (except bleeding) or threshold
### PFA-100, MACE

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Patients</th>
<th>Group</th>
<th>Mono</th>
<th>Antigen</th>
<th>Threshold</th>
<th>Within-study</th>
<th>Directly Available?</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addad</td>
<td>2009</td>
<td>Tunisia/France</td>
<td>204</td>
<td>CAD</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>143s</td>
<td>1st tertile vs 2nd &amp; 3rd tertile (MACE)</td>
<td>no</td>
<td>1.84 (0.88, 3.97)</td>
</tr>
<tr>
<td>Addad</td>
<td>2009</td>
<td>Tunisia/France</td>
<td>204</td>
<td>CAD</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>290s</td>
<td>1st &amp; 2nd tertile vs 3rd tertile (RAVE)</td>
<td>no</td>
<td>5.61 (0.00, 47.0e+12)</td>
</tr>
<tr>
<td>Addad</td>
<td>2009</td>
<td>Tunisia/France</td>
<td>204</td>
<td>CAD</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>143s</td>
<td>1st tertile vs 2nd &amp; 3rd tertile (MACE)</td>
<td>no</td>
<td>0.09 (0.23, 30.20)</td>
</tr>
<tr>
<td>Bevilacqua</td>
<td>2009</td>
<td>Italy</td>
<td>202</td>
<td>CAD</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>190s</td>
<td>no</td>
<td>yes</td>
<td>2.11 (1.33, 3.34)</td>
</tr>
<tr>
<td>Christians</td>
<td>2008</td>
<td>France</td>
<td>97</td>
<td>CAD</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>187s</td>
<td>no</td>
<td>no</td>
<td>1.33 (0.45, 3.98)</td>
</tr>
<tr>
<td>Pamukcu</td>
<td>2007</td>
<td>Turkey</td>
<td>234</td>
<td>CAD</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>185s</td>
<td>no</td>
<td>no</td>
<td>1.44 (0.83, 2.67)</td>
</tr>
<tr>
<td>Bonseraglio</td>
<td>2009</td>
<td>Italy</td>
<td>129</td>
<td>CVD/Stroke</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>185s</td>
<td>no</td>
<td>no</td>
<td>1.07 (0.35, 3.30)</td>
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<tr>
<td>Linneman</td>
<td>2009</td>
<td>Germany</td>
<td>57</td>
<td>PAD/PVD</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>192s</td>
<td>no</td>
<td>no</td>
<td>0.01 (0.00, 2782.26)</td>
</tr>
<tr>
<td>Aksu</td>
<td>2009</td>
<td>Turkey</td>
<td>220</td>
<td>UA/ACS</td>
<td>Mono base, f-vp, 13% mono, 27% dual</td>
<td>collagen/epinephrine</td>
<td>170s</td>
<td>no</td>
<td>no</td>
<td>2.07 (1.58, 4.01)</td>
</tr>
<tr>
<td>Fuchs</td>
<td>2006</td>
<td>Austria</td>
<td>206</td>
<td>UA/ACS</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>300s</td>
<td>Recurrence of ACS</td>
<td>yes</td>
<td>2.00 (1.11, 3.52)</td>
</tr>
<tr>
<td>Fuchs</td>
<td>2006</td>
<td>Austria</td>
<td>206</td>
<td>UA/ACS</td>
<td>Mono</td>
<td>collagen/ACP</td>
<td>High vs low quartile</td>
<td>Recurrence of ACS</td>
<td>yes</td>
<td>3.33 (1.44, 7.59)</td>
</tr>
<tr>
<td>Hoboglu</td>
<td>2007</td>
<td>Turkey</td>
<td>140</td>
<td>UA/ACS</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>170s</td>
<td>yes</td>
<td>no</td>
<td>2.32 (1.11, 4.84)</td>
</tr>
<tr>
<td>Modica</td>
<td>2009</td>
<td>Sweden</td>
<td>334</td>
<td>UA/ACS</td>
<td>Mono</td>
<td>epinephrine</td>
<td>quartiles</td>
<td>yes</td>
<td>no</td>
<td>0.80 (0.64, 1.19)</td>
</tr>
<tr>
<td>Poulsen</td>
<td>2007</td>
<td>Denmark</td>
<td>287</td>
<td>UA/ACS</td>
<td>Mono</td>
<td>collagen/ACP</td>
<td>Not clear</td>
<td>death, MI, stroke or revasc</td>
<td>no</td>
<td>0.94 (0.55, 1.62)</td>
</tr>
<tr>
<td>Poulsen</td>
<td>2007</td>
<td>Denmark</td>
<td>287</td>
<td>UA/ACS</td>
<td>Mono</td>
<td>collagen/epinephrine</td>
<td>150s</td>
<td>death, MI, or stroke</td>
<td>no</td>
<td>1.00 (0.55, 2.03)</td>
</tr>
<tr>
<td>Poulsen</td>
<td>2007</td>
<td>Denmark</td>
<td>287</td>
<td>UA/ACS</td>
<td>Mono</td>
<td>collagen/ACP</td>
<td>Not clear</td>
<td>death, MI, stroke or revasc</td>
<td>no</td>
<td>1.02 (0.55, 2.03)</td>
</tr>
</tbody>
</table>

**unadjusted hazard ratio**
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Country</th>
<th>Patients</th>
<th>Group</th>
<th>Mono</th>
<th>Agonist</th>
<th>Threshold</th>
<th>Within-study difference available?</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kemptert</td>
<td>2009</td>
<td>Germany</td>
<td>58</td>
<td>CAD</td>
<td>Mono post-op, 3 pre-op clopidogrel</td>
<td>AA (1mM)</td>
<td>30%</td>
<td>no</td>
<td>9.10 (0.02, 412381.03)</td>
</tr>
<tr>
<td>Cha</td>
<td>2006</td>
<td>South Korea</td>
<td>107</td>
<td>CVD</td>
<td>Mono</td>
<td>ADP (10uM)</td>
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<td>4.67 (1.48, 11.22)</td>
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<tr>
<td>Cha</td>
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<td>ADP (10uM)</td>
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<td>2.39 (0.52, 10.21)</td>
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<tr>
<td>Linnetman</td>
<td>2009</td>
<td>Germany</td>
<td>57</td>
<td>PAD/PVD</td>
<td>Mono</td>
<td>AA (0.5 mg/mL)</td>
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<td>0.11 (0.00, 226495.64)</td>
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<tr>
<td>Spectre</td>
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<td>Israel</td>
<td>54</td>
<td>PPQIACS</td>
<td>Mono before, dual post-PCI</td>
<td>AA (1.8mM)</td>
<td>40%</td>
<td>15 months</td>
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<tr>
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<td>Israel</td>
<td>54</td>
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<td>Mono before, dual post-PCI</td>
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<td>Modica</td>
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<td>LAAVCS</td>
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<td>Epinephrine (0.1 mg) vs 1st quartile</td>
<td>yes</td>
<td>2.00 (1.21, 3.32)</td>
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<td>Gun</td>
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<td>326</td>
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<td>Mono</td>
<td>AA (0.5mg/hr) &amp; ADP(10uM)</td>
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<td>Patients</td>
<td>Group</td>
<td>Monotherapy</td>
<td>Thromboxane</td>
<td>MACE</td>
<td>HR (95% CI)</td>
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<tr>
<td>Frelinger</td>
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<td>USA</td>
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<td>tertiles</td>
<td>MACE</td>
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<td>204</td>
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<td>3261</td>
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<td>quartiles</td>
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<tr>
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<td>quartiles</td>
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<td>Iran</td>
<td>124</td>
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<td>&lt;134, 134-298, &gt;298</td>
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<td>high vs med/low</td>
<td>MACE</td>
<td>1.04 (1.02, 3.68)</td>
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</table>
Implications

• Resources for time consuming searches/study selection process when undertaking systematic reviews of prognostic research

• Caution when interpreting findings from one (systematic) review of prognostic research

• Take heterogeneity into account when planning/undertaking synthesis
Limitations of this work

• Only one clinical area/question considered, may not be generalisable
• Similar issues are being encountered in ongoing work on “Systematic review of prognostic factors and prognostic models for the recurrence of venous thromboembolism (VTE) following treatment for a first idiopathic VTE”
References


• [http://hiru.mcmaster.ca/hiru/HIRU_Hedges_MEDLINE_Strategies.aspx#References](http://hiru.mcmaster.ca/hiru/HIRU_Hedges_MEDLINE_Strategies.aspx#References) (Haynes Filters)
Questions?

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