**TITLE:** Semi-systematic review of definitions and diagnostic tests for aspirin resistance: An opportunity to stratify prevention of placental disease.

**INTRODUCTION**: Aspirin is pivotal for prevention of coronary artery disease and cerebrovascular disease worldwide, and confers a 10% risk reduction in pre-eclampsia and fetal growth restriction. However, in the last 15 years evidence has emerged that a significant proportion of individuals exhibit suboptimal response to aspirin, determined clinically and biochemically. We conducted a semi-systematic review of definitions and diagnostic tests for aspirin resistance, and explore the potential relevance of ‘aspirin resistance’ in pregnancy.

**METHODS:** We searched MEDLINE, EMBASE and the Cochrane Library from 1957-28/02/15. Limits; humans and English language. Search terms; ‘aspirin’, ‘acetylsalicylic acid’ appearing adjacent to ‘resistance’, ‘non-responsiveness’, ‘treatment failure’ and pseudoresistance. All original articles were included, review articles and articles describing aspirin plus alternative antiplatelet agents or anticoagulants were excluded.

**RESULTS:** 492 articles, after abstract and full text reviews 135 were included. There is broad experience with platelet activation testing including 4 studies in high-risk obstetrics. We identified thirteen platelet activation assays, PFA 100 Collagen/Epinephrine cartridges were most frequently used. 88 definitions of aspirin resistance have been described, the vast majority (133/135, 98.5%) utilise laboratory-based parameters. 50.4% (68/135) considered the issue of aspirin compliance when defining aspirin resistance.

**CONCLUSION:** Aspirin resistance does not currently have a uniform definition, nor has an adequately sensitive, specific diagnostic test emerged. However, there is evidence of important clinical associations and promising parallels in pregnancy that warrant careful attention. In obstetric research pregnancy-specific reference ranges are crucial and clinical significance of aspirin resistance must be judged against important obstetric and neonatal outcomes.