

BACKGROUND

- Aspirin is widely used for cardioprotection with its antiplatelet effects due to blocking of the production of thromboxane (TX) A₂ from activated platelets.
- 11-dehydro-TXB₂ (TXM) is a major stable end-product of TXA₂ measurable in urine that reflects the whole-body rate of biosynthesis of TXA₂.
- Daily low dose aspirin reduces TXM by 70-80% and cardiovascular event incidence by about 10% in primary prevention.

PURPOSE

- The ASCEND (A Study of Cardiovascular Events in Diabetes) study randomised people with DM and no manifest cardiovascular disease at trial entry to receive daily low-dose aspirin or placebo. This TXM sub-study aimed to investigate the association between baseline urinary TXM and future serious vascular events or revascularization (SVE-R), major bleeds and incident cancer independent of other risk factors and treatment..

PATIENTS AND METHODS

- Urinary TXM was measured in 6,487 participants with eligible baseline samples (after excluding 539 participants using NSAIDs).
- TXM appeared log-normally distributed, so analyses were by quintiles and per SD (=0.622) of continuous log_e TXM with adjustment for basic factors (age, sex, sample volume and randomized treatment allocation) and for the predictors of log TXM (smoking, insulin or oral hypoglycaemics, HDL cholesterol, BMI, urinary albumin/creatinine ratio, eGFR).
- During a mean of 6.6 years follow-up there were 618 SVE-Rs, 206 bleeds and 700 cancers.

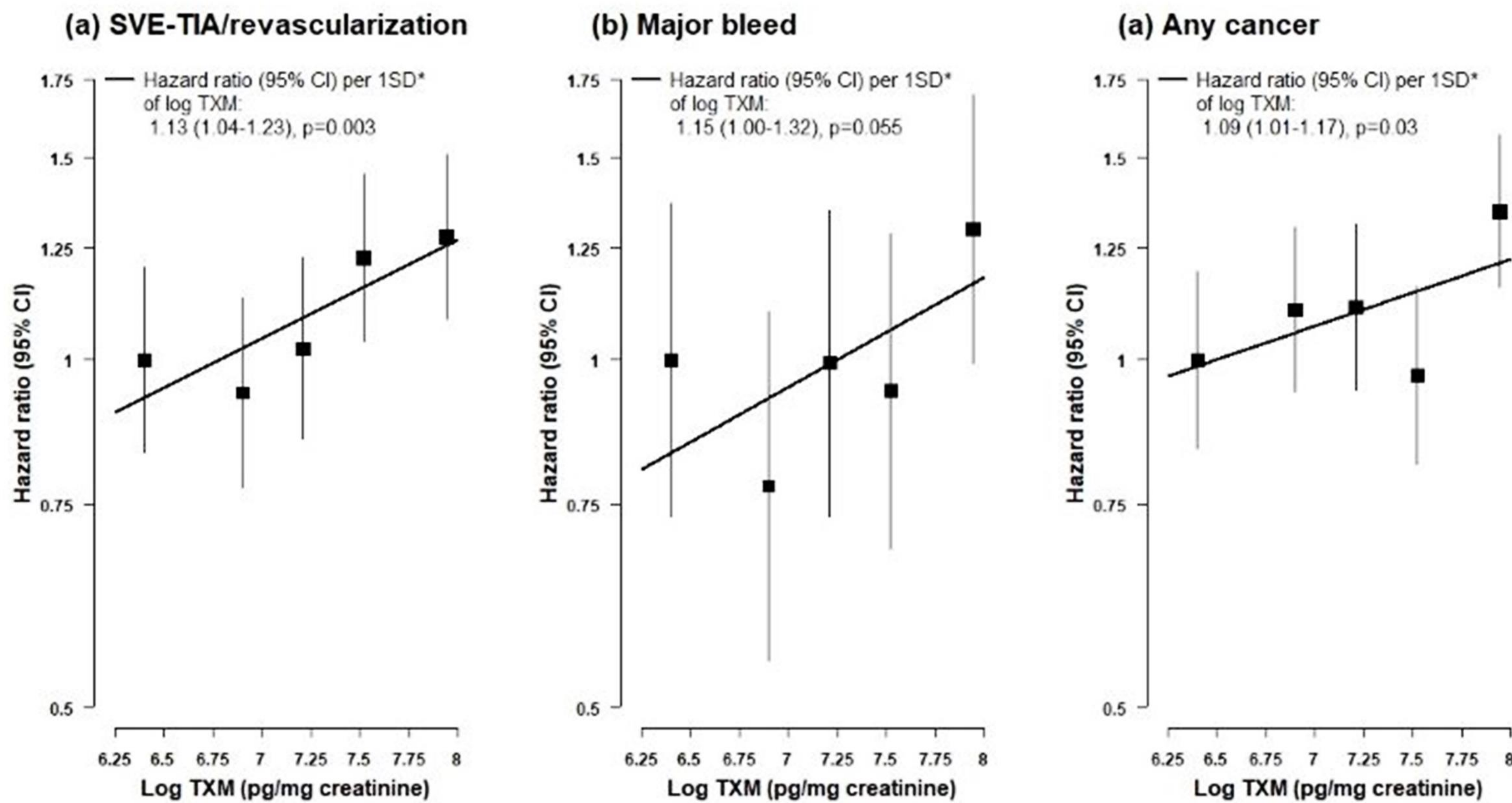


Figure 1. Associations of log TXM with outcomes in placebo allocated participants.

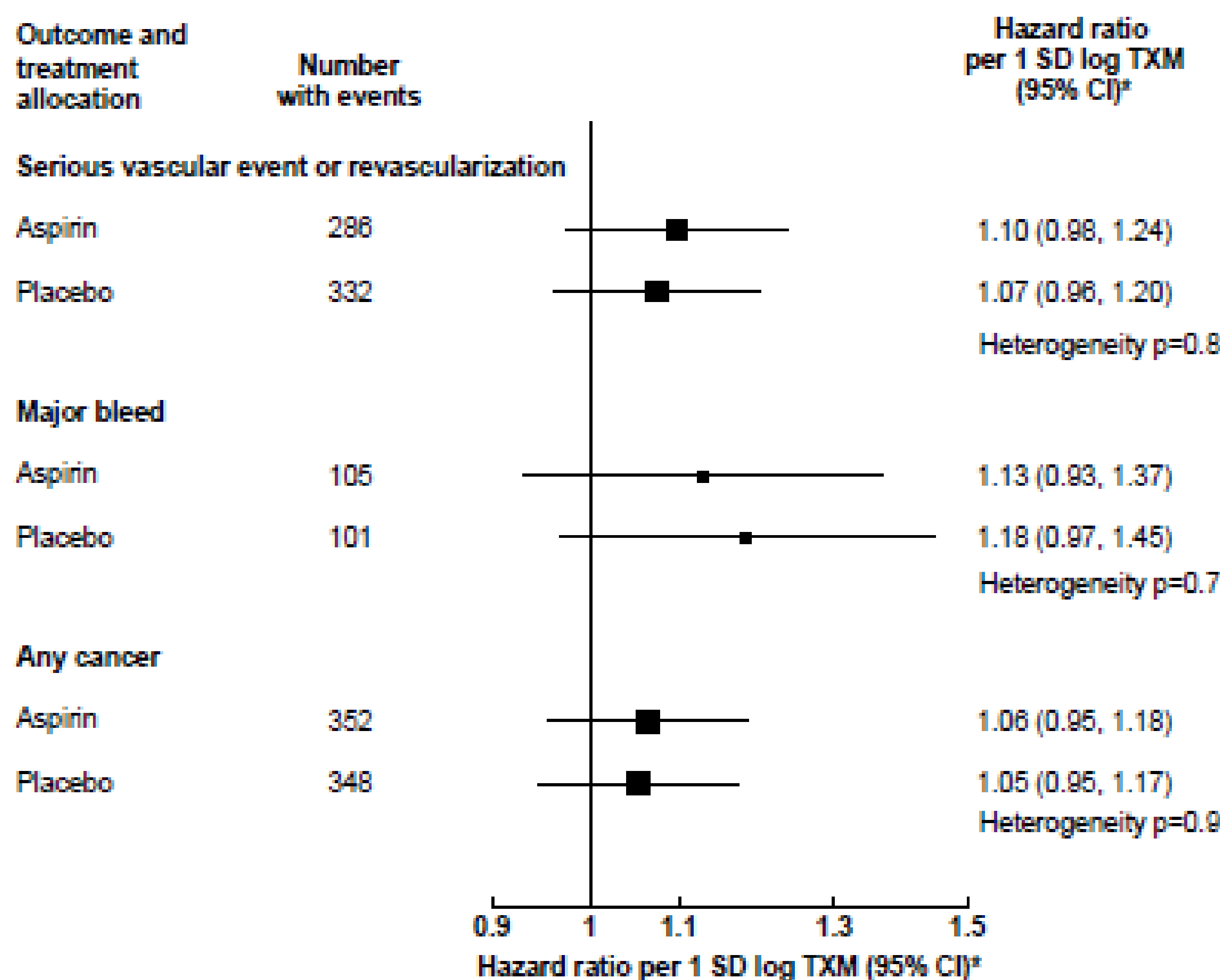


Figure 2. Linear associations of log TXM with outcomes in aspirin and placebo allocated participants.

RESULTS

- Among placebo allocated participants, log TXM was positively, but not statistically significantly, associated with: SVE-R (hazard ratio (HR) per 1 SD of log TXM: 1.07 95% confidence interval [CI], 0.96-1.02), major bleeds (1.18, 0.97-1.45) and cancer (1.05, 0.95-1.17) (Figure 1).
- Similar linear trends were seen in the aspirin allocated participants (Figure 2) where follow-up levels of log TXM would be expected to be 70-80% (ie ~ 2SD log TXM) lower.
- Stronger positive trends were seen with only basic adjustment (data not shown).

Conclusion

- Prior evidence from the effects of aspirin on log TXM and on cardiovascular event reduction in randomized trials suggests about a 5% proportional reduction in events per 1 SD lower log TXM.
- The observational associations between log TXM and SVE-R in this sub-study in both the placebo and aspirin arms were not statistically significant but the CIs encompassed the suggested level of association from the randomized trial effects.
- However, the observed relationships may also reflect residual confounding.
- Further data are needed to confirm whether the TXM levels are a useful predictor of cardiovascular risk.

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