

CORRESPONDENCE

Comment on: 'Effects of Statin Therapy on Abdominal Aortic Aneurysm Growth: A Meta-analysis and Meta-regression of Observational Comparative Studies'

Dear Editor,

We read the meta-analysis by Takagi et al.¹ with interest. Unfortunately, the conclusion that statins reduce AAA expansion is still not justified by the data.

The problem, as with our analysis widely quoted in the paper,² is that the study quality was poor with small patient numbers in individual studies. Study results were open to confounding from multiple comorbidities and polypharmacy in AAA patient groups. Heterogeneity in the authors' analysis was highly significant (adjusted from $P < 0.0001$ to $P = 0.005$), with a significant variation between expansion rate results suggesting bias. Adjusting confounded or biased data and performing meta-regression simply produce further inaccurate results without correcting the underlying problem. Meta-analysis is only as good as the trial data entered.³

For these reasons we based our conclusion on sensitivity analysis rather than the meta-analysis of all trials which found in favour of the statin group.² Adding the 'high quality' trial (Karrowni 2011) published since our analysis pushes our high quality sensitivity analysis result into significance (SMD -0.25 , $P = 0.04$, Heterogeneity $P < 0.0001$) but still gave a non significant result from large volume (>200 patients total) sensitivity analysis (SMD -0.20 , $P = 0.07$, Heterogeneity $P = 0.006$), highlighting how brittle meta-analysis really is when using small individual datasets.

A more definitive attempt to answer this question can only be made by adjusted re-analysis of pooled raw data from these studies or a high quality RCT.

REFERENCES

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Reply to 'Comment on Effects of Statin Therapy on Abdominal Aortic Aneurysm Growth: A Meta-analysis and Meta-regression of Observational Comparative Studies'

Dear Editor,

We would like to greatly acknowledge the comment by Twine and Williams on our recently published meta-analysis.¹ In a more recent (after our performing the meta-analysis¹) meta-analysis by the RESCAN collaborators² of individual data collated from people under follow-up for a small (3.0–5.4 cm in diameter) abdominal aortic aneurysm (AAA), the pooled meta-analysis estimate (4621 patients from 6 studies) was no longer statistically significant for statins/lipid-lowering drugs (effect estimate [mm/year], -0.205 ; standard error, 0.132 ; $P = 0.121$) after adjustment for potential confounding. The most recently, we³ combined adjusted data for growth rates from high-quality observational comparative studies identified by comprehensive search with those from the individual patient data meta-analysis by the RESCAN collaborators.² Pooled analysis of 13 studies (our identifying 7 studies plus the 6 studies included in the meta-analysis by the RESCAN collaborators²) demonstrated a statistically significant 0.63 mm/year reduction in AAA growth rates with statin therapy in the random-effects model (95% confidence interval [CI], -0.98 to -0.29 mm/year; P for effect = 0.0003 ; P for heterogeneity < 0.0001). Significant statistical between-study heterogeneity of the study-specific estimates may be due to the result by Karrowni et al.⁴ demonstrating a probably excess benefit of statin therapy (mean difference [MD] of growth rates, -3.40 mm/year; 95% CI, -4.63 to -2.17 mm/year). Even though the result by Karrowni et al.⁴ was eliminated in sensitivity analyses excluding individual studies one at a time, combining the remaining 12 studies (there was minimal between-study heterogeneity [$P = 0.05$]) generated an attenuated but still statistically significant result favoring statin therapy (random-effects MD, -0.42 mm/year; 95% CI, -0.66 to -0.18 mm/year; P for effect = 0.0007).³ Thus, the evidence of the benefit of statin therapy for AAA growth is likely compelling and robust.

REFERENCES

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