

### Meta-Analysis of Randomized and Observational Studies and National Registries Shows that the Risk of Peri-Operational Stroke is Higher When Carotid Intervention is Performed Within Less Than 48 Hours from the Index Cerebrovascular Event

We are grateful to Naylor for his careful review of our recently published meta-analysis.<sup>1</sup> He highlighted an error in the number of events in the forest plot of stroke and that most studies reported data on any (rather than ipsilateral) stroke, and also suggested the inclusion of two national registries.<sup>2,3</sup>

Naylor is right about the number of events in the study by Azzini *et al.*<sup>4</sup> We confirm that the correct number of strokes in the very urgent and urgent groups in this study is zero. We subsequently repeated the analysis with the correct figures and

found that the pooled odds ratio (OR) remained unchanged (OR 2.19; 95% confidence interval (CI) 1.43–3.35,  $p < .001$ ).

Scrutiny of the papers included in our meta-analysis showed that most of the authors (9 out of the 13 papers) did not specify whether they reported ipsilateral or any stroke (Table 1). Therefore, the outcome endpoint of our meta-analysis should be any or ipsilateral stroke (rather than ipsilateral stroke).

Although our literature search strategy was comprehensive and two independent authors were involved in the process, we missed two national registries,<sup>2,3</sup> which did not appear in the reports that the applied literature search strategy retrieved. One of them<sup>2</sup> included patients with previous ipsilateral carotid surgery, which was an exclusion criterion of our review. We conducted the meta-analysis

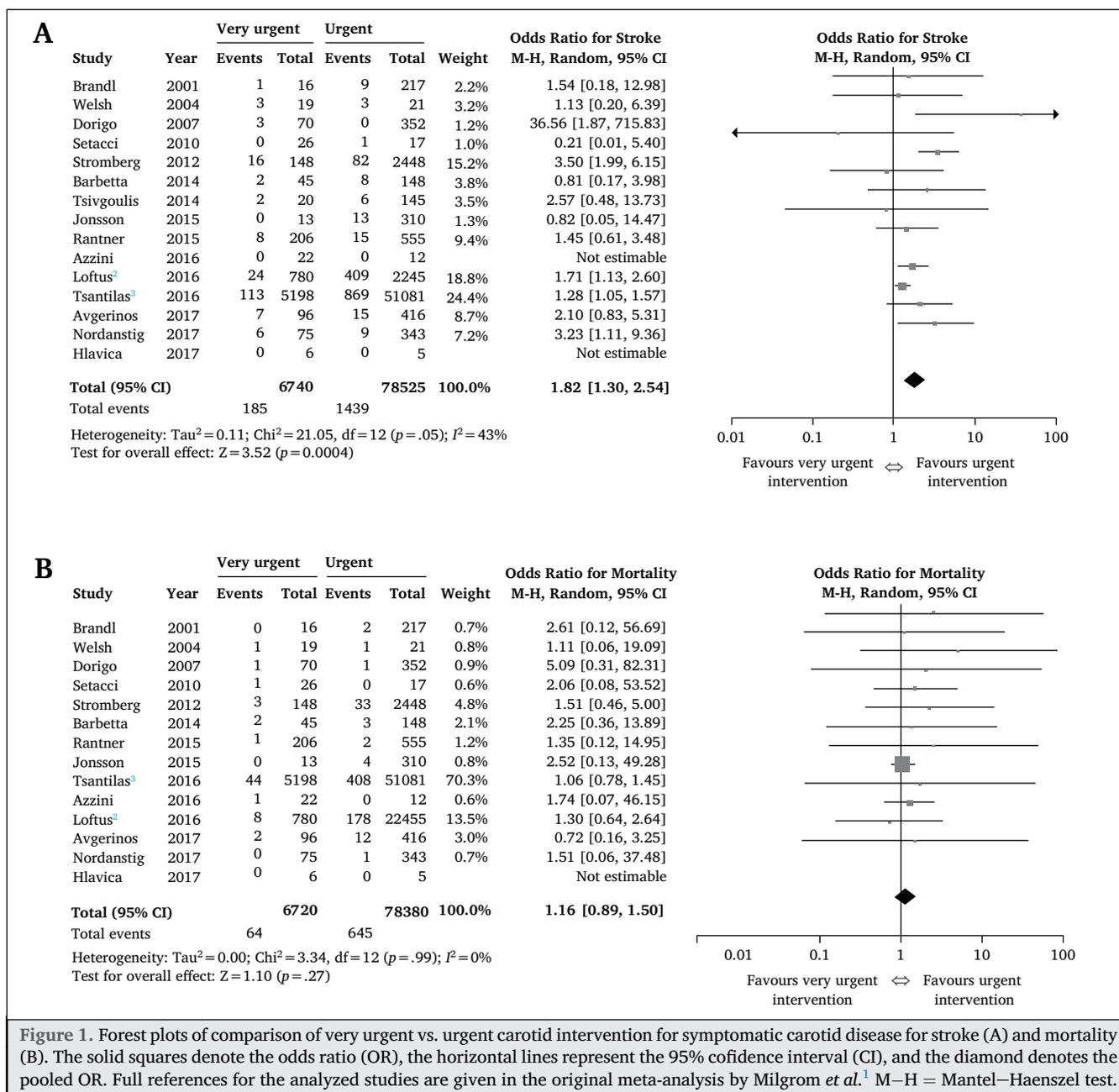


Figure 1. Forest plots of comparison of very urgent vs. urgent carotid intervention for symptomatic carotid disease for stroke (A) and mortality (B). The solid squares denote the odds ratio (OR), the horizontal lines represent the 95% confidence interval (CI), and the diamond denotes the pooled OR. Full references for the analyzed studies are given in the original meta-analysis by Milgrom *et al.*<sup>1</sup> M-H = Mantel-Haenszel test.

Table 1. Laterality of stroke reported by the included studies in the meta-analysis by Milgrom *et al.*<sup>1</sup>

Author	Stroke
Avgerinos <i>et al.</i>	Not specified whether ipsilateral or any stroke, but probably any stroke was considered
Nordanstig <i>et al.</i>	Data on ipsilateral and any stroke provided, but any stroke considered for the meta-analysis
Hlavica <i>et al.</i>	Not specified
Azzini <i>et al.</i>	Not specified whether ipsilateral or any stroke, but probably any stroke was considered
Johnsson <i>et al.</i>	Any stroke
Rantner <i>et al.</i>	Not specified whether ipsilateral or any stroke, but probably any stroke was considered
Tsivgoulis <i>et al.</i>	Any stroke
Barbetta <i>et al.</i>	Not specified whether ipsilateral or any stroke, but probably any stroke was considered
Strömberg <i>et al.</i>	Not specified whether ipsilateral or any stroke, but probably any stroke was considered
Setacci <i>et al.</i>	Not specified whether ipsilateral or any stroke, but probably any stroke was considered
Dorigo <i>et al.</i>	Any stroke
Welsh <i>et al.</i>	Not specified whether ipsilateral or any stroke, but probably any stroke was considered
Brandl <i>et al.</i>	Not specified whether ipsilateral or any stroke, but probably any stroke was considered

including the aforementioned national registries and found that the pooled effect size for stroke remained unchanged in favour of urgent ( $\geq 48$  h) intervention (OR 1.82; 95% CI 1.30–2.54,  $p = .0004$ ). The statistical heterogeneity remained insignificant (Fig. 1A). The direction of pooled effect size in the mortality analysis also remained unchanged (OR 1.16; 95% CI 0.89–1.50,  $p = .27$ ) (Fig. 1B).

We thank Naylor for his valuable comments. Inclusion of two further studies has undoubtedly enhanced the robustness of our results and lends support to our hypothesis that very urgent carotid intervention for symptomatic carotid disease carries a higher stroke risk.

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Available online 31 May 2019

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<https://doi.org/10.1016/j.ejvs.2019.02.022>  
 DOI of original article: <https://doi.org/10.1016/j.ejvs.2019.01.032>