

Data Supplement

Oral and intravenous steroids for Multiple Sclerosis relapse.

A systematic review and meta-analysis

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Table e-1. Characteristics of study participants

Reference Study (year)	Study Arm	Subjects (no.)	Male (%)	Age (years)	Disease Duration (years)	MS course	EDSS Score at Study Entry
Alam et al. (1993) [11]	Oral	15	26.7	41.3 (13.6)	3.8 (3.5)	NA	4.80 (1.90)
	IV	20	20.0	41.6 (12.8)	6.5 (7.4)		4.85 (1.90)
Barnes et al. (1997) [12]	Oral	42	42.9	38.0 (9.6)	6.6 (3.1-10.9)	NA	5.0 (3.5-6.5)
	IV	38	28.9	37.0 (11.1)	6.3 (3.6-13.6)		6.0 (3.5-7.5)
Morrow et al. (2004) [13]	Oral	8	25.0	39	5.7	RR (87.5%)	4.0 (2.0-6.5)
	IV	8		(range 24-61)	(range 0.6-38)		
Martinelli et al. (2009) [14]	Oral	20	31.6	36.0 (8.0)	9.8 (6.3)	RR	3.5 (2.0-5.5)
	IV	20	30.0	31.0 (7.0)	7.2 (6.0)		3.0 (2.0-6.0)
Ramo-Tello et al. (2014) [15]	Oral	25	23.0	39.5 (7.9)	-	RR	3.0 (2.5-4.0)
	IV	24	17.0	37.7 (7.8)	-		4.0 (2.5-4.5)
Le Page et al. (2015) [16]	Oral	100	26.0	35.0 (18.2-62.6)	6.2 (3.4-11.9)	RR	3.5 (3.0-4.0)
	IV	99	25.3	34.7 (18.3-58.7)	5.7 (3.0-10.7)		3.5 (3.0-4.0)

Data are mean (SD) or median (IQR), unless otherwise stated

Abbreviations: EDSS= Kurtzke's Expanded Disability Status Scale; IQR=interquartile range;

MS=Multiple Sclerosis; RR=relapsing-remitting; SD=standard deviation

Table e-2 Risk of bias summary table

Bias	Study	Alam et al. (1993) [11]	Barnes et al. (1997) [12]	Morrow et al. (2004) [13]	Martinelli et al. (2009) [14]	Ramo-Tello et al. (2014) [15]	Le Page et al. (2015) [16]
Random sequence generation (Selection Bias)		Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Allocation concealment (Selection Bias)		Unclear risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk
Blinding of participants and personnel (Performance Bias)		Low risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk
Blinding of outcome assessment (Detection Bias)		Unclear risk	Low risk	Unclear risk	Unclear risk	Low risk	Low risk
Incomplete outcome data (Attrition Bias)		Unclear risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Selective reporting (Reporting Bias)		Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Low risk
Non-inferiority design		High risk	High risk	High risk	Low risk	Low risk	Low risk

e-Appendix I

PubMed search strategy^{e-1}

((((((((((random* OR placebo OR trial* OR group* [Title/Abstract]))) OR "drug therapy"[Subheading]) OR "Randomized Controlled Trial"[Publication Type]) OR "Controlled Clinical Trial"[Publication Type]) OR "Comparative Study"[Publication Type])) NOT ("Animals"[Mesh] NOT "Humans"[Mesh]))) AND (((("multiple sclerosis" [Title/Abstract]) AND ("relapse" OR "recurrence" OR "attack" [Title/Abstract]))) AND (("glucocorticoid" OR "corticosteroid" OR "methylprednisolone" OR "methyl prednisolone" OR "methyl-prednisolone" OR "prednisone" OR "high-dose" OR "high dose" OR "oral" OR "intravenous" OR "prednisolone" OR "steroid*" [Title/Abstract])))

CENTRAL search strategy

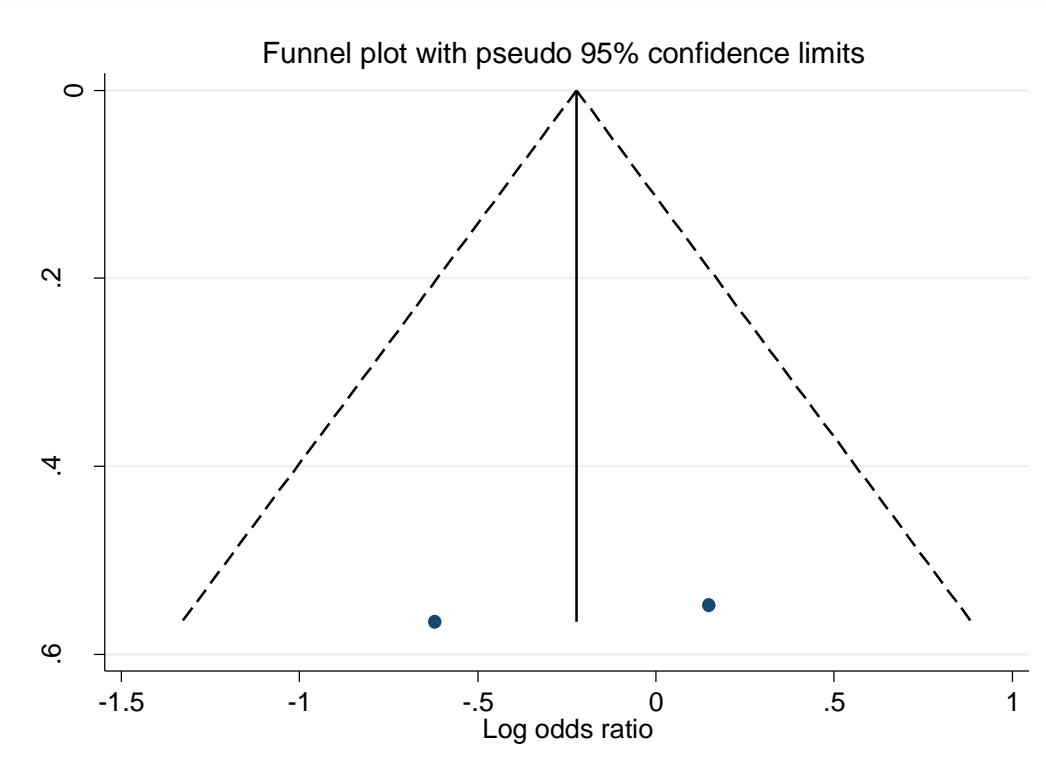
multiple sclerosis AND (relapse OR recurrence) AND (glucocorticoid OR corticosteroid OR steroid OR methylprednisolone OR methyl prednisolone OR methyl-prednisolone OR prednisone OR prednisolone OR high-dose OR high dose) AND (oral OR intravenous) | Title, Abstract, Keywords in Trials

ClinicalTrials.gov search strategy

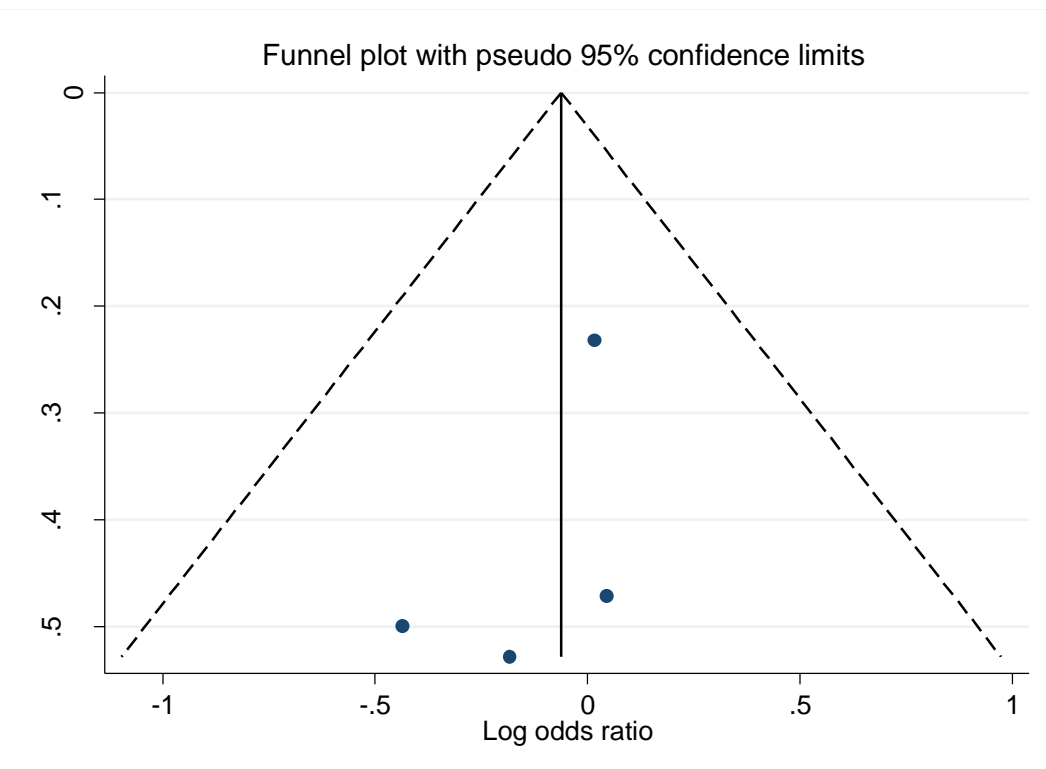
multiple sclerosis AND (relapse OR recurrence) AND (glucocorticoid OR corticosteroid OR steroid OR methylprednisolone OR methyl prednisolone OR methyl-prednisolone OR prednisone OR prednisolone OR high-dose OR high dose) AND (oral OR intravenous) | Interventional Studies

e-Appendix II

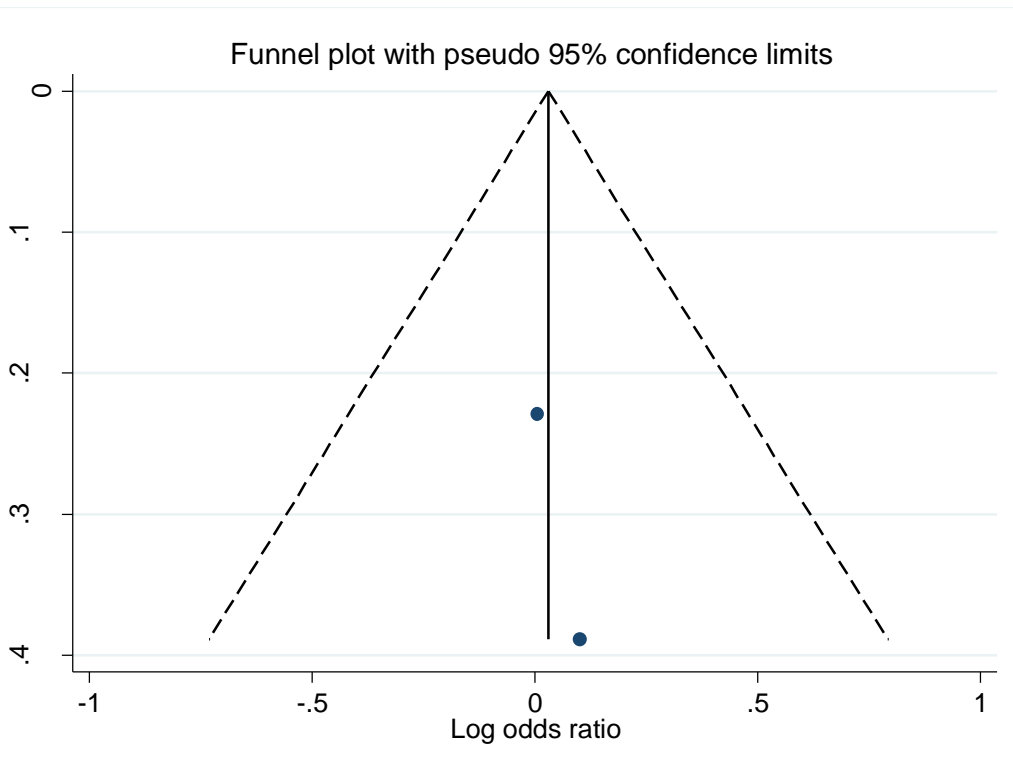
Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: improvement on EDSS at week 1



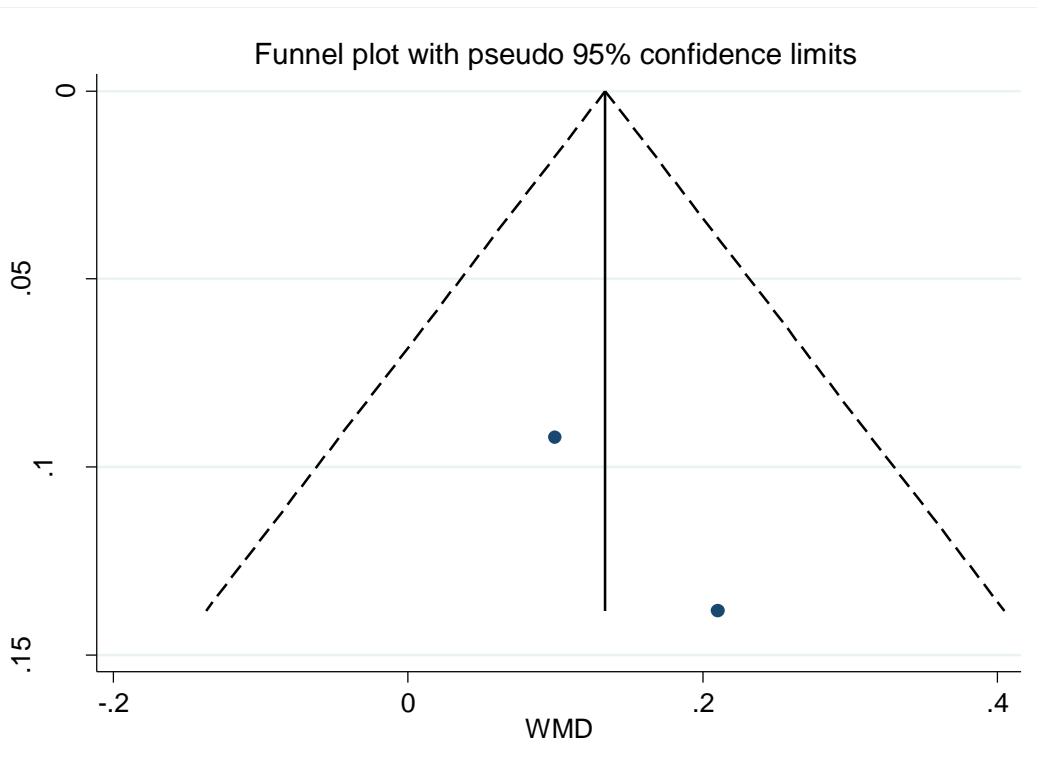
Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: improvement on EDSS at week 4



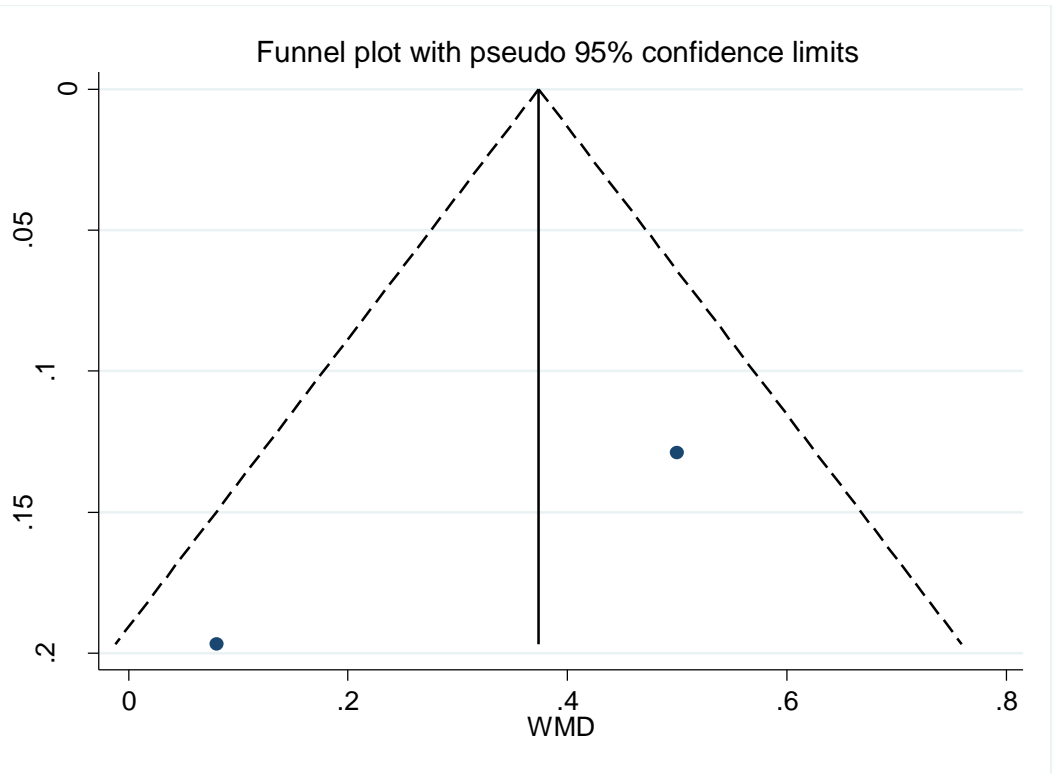
Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: improvement of the most affected functional system at week 4



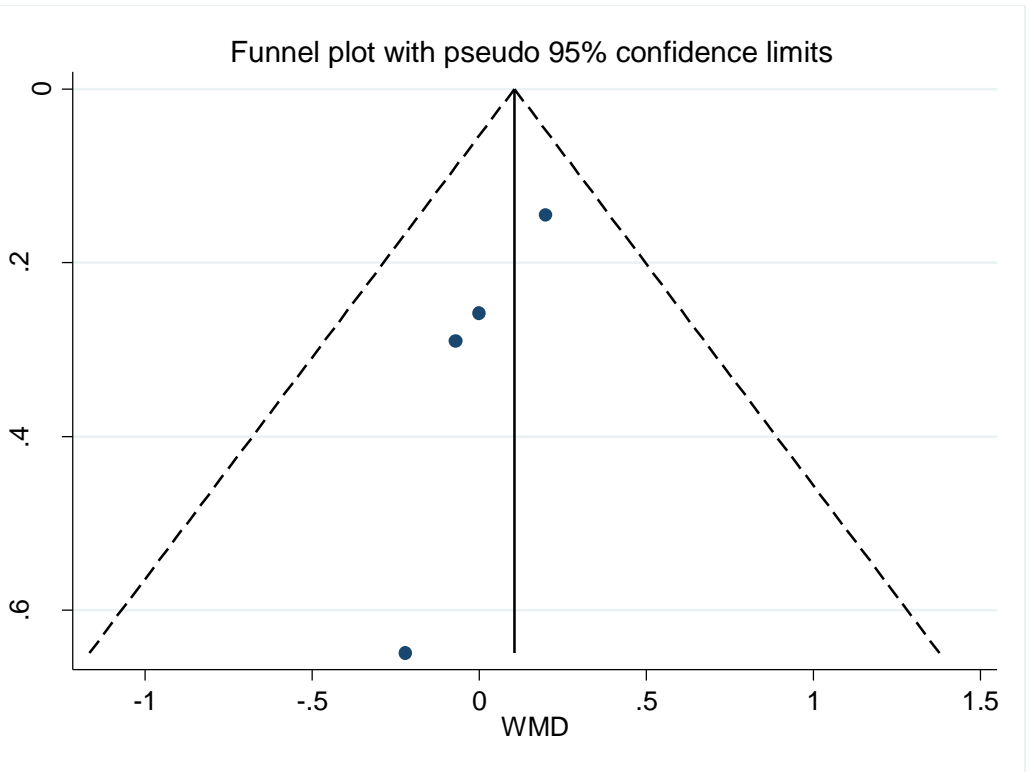
Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: 6-month relapse rate



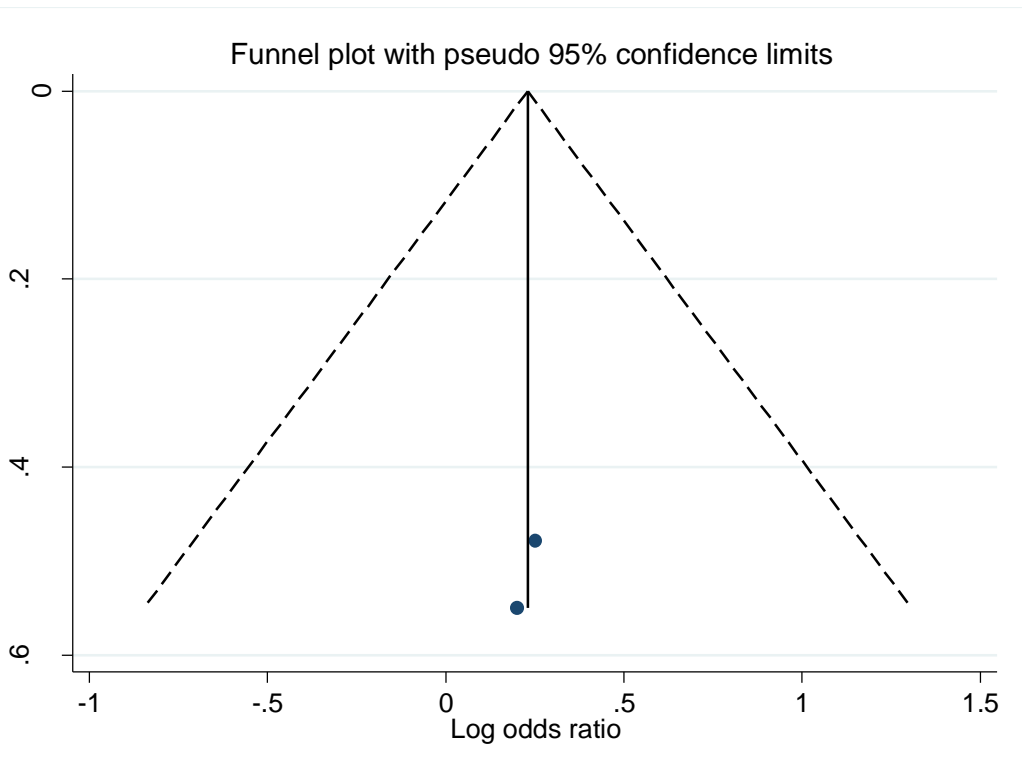
Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: EDSS score change at week 1



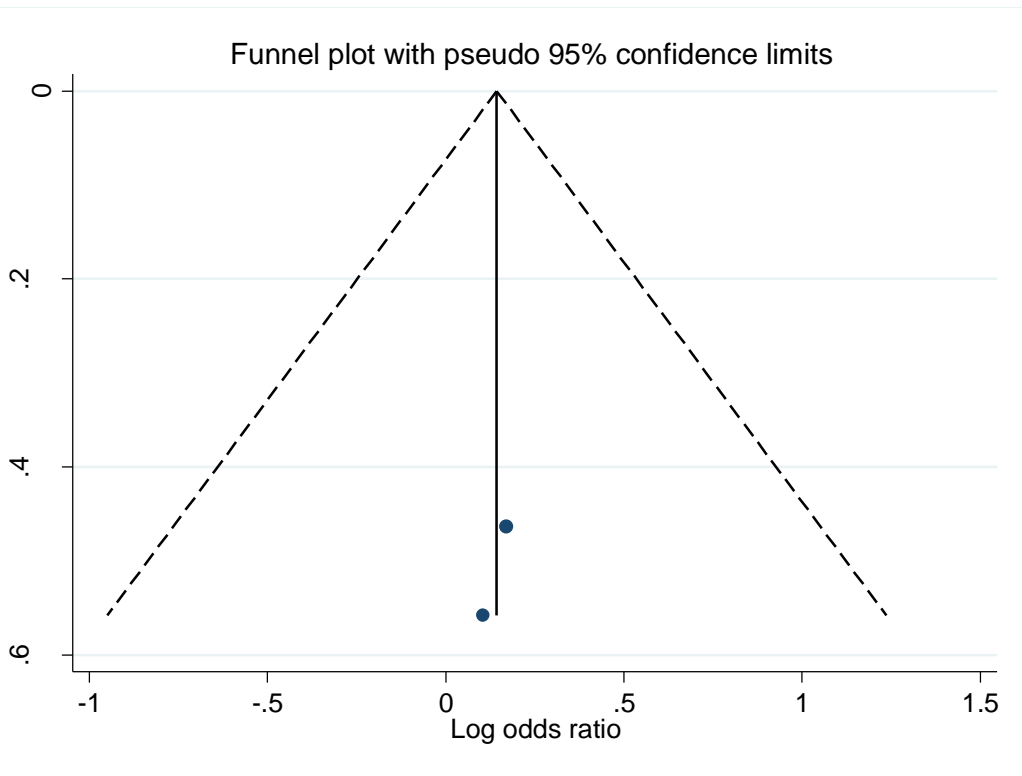
Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: EDSS score change at week 4



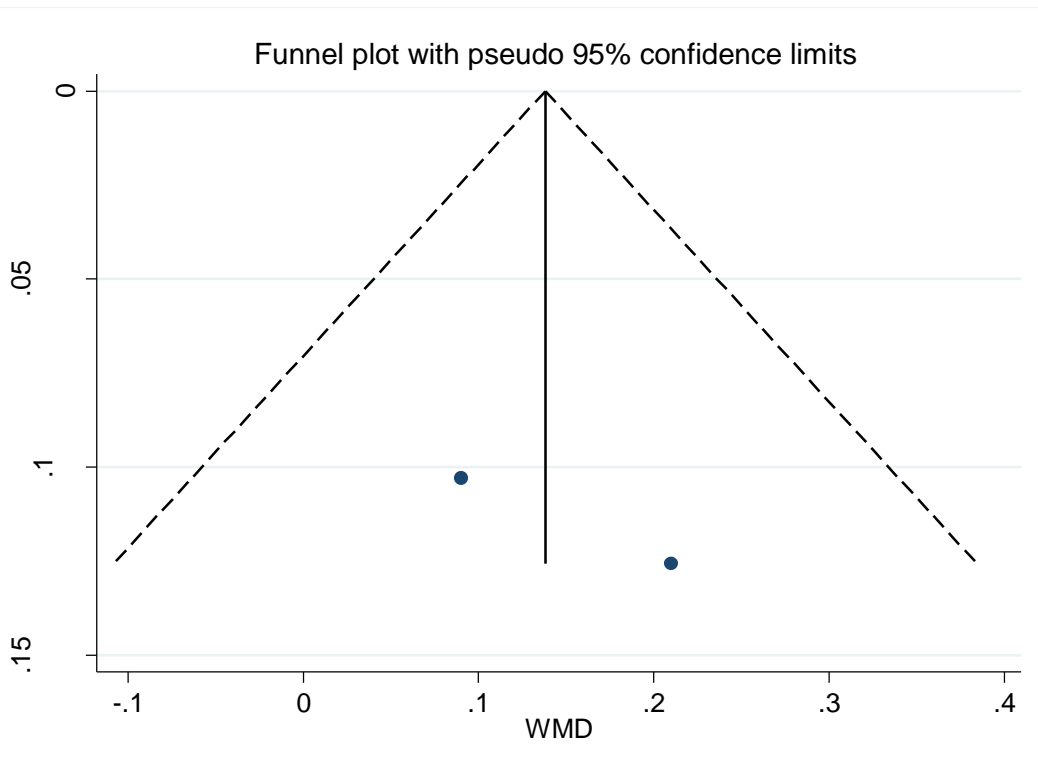
Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: absence of Gadolinium-enhancing lesions at week 1



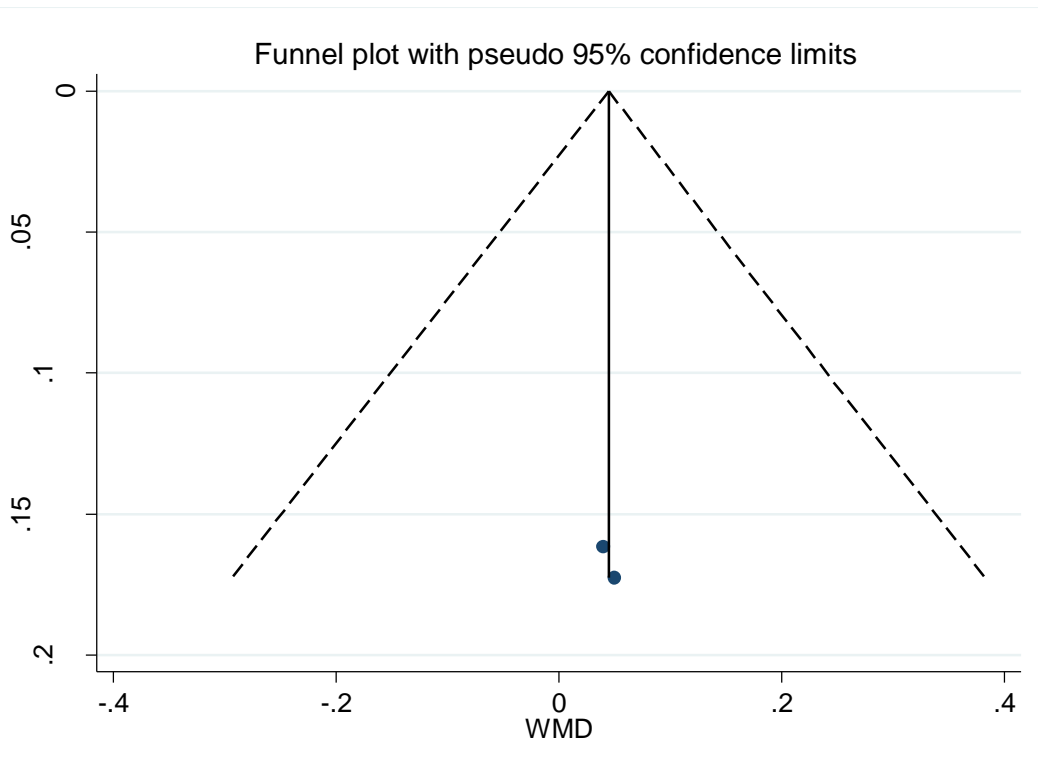
Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: absence of Gadolinium-enhancing lesions at week 4



Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: mean change in Gadolinium-enhancing lesions at week 1



Funnel plot of comparison: Oral versus intravenous steroid treatment, outcome: mean change in Gadolinium-enhancing lesions at week 4



e-Reference

e-1 Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2* (updated September 2009). The Cochrane Collaboration, 2009. Available from www.cochranehandbook.org.