

Subclinical Cushing's syndrome and clinical implications in bilateral compared to unilateral adrenal incidentalomas: a meta-analysis

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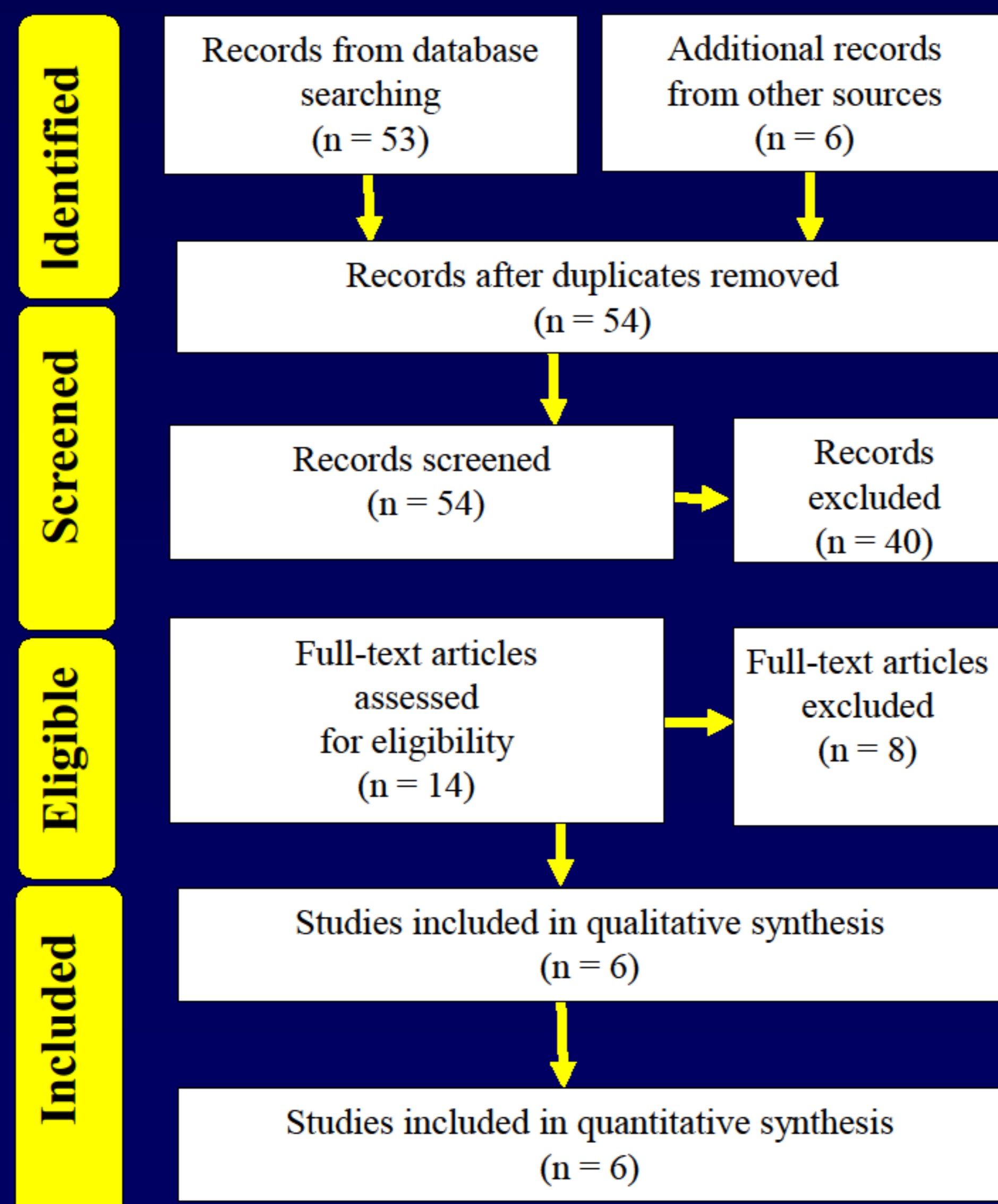
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Introduction: The aim of this study was to systematically review the literature for studies that have investigated possible differences in prevalence of subclinical Cushing's syndrome (SCS) and related clinical implications between patients with unilateral (UAI) and bilateral adrenal incidentalomas (BAI) and to meta-analyze the best evidence available.

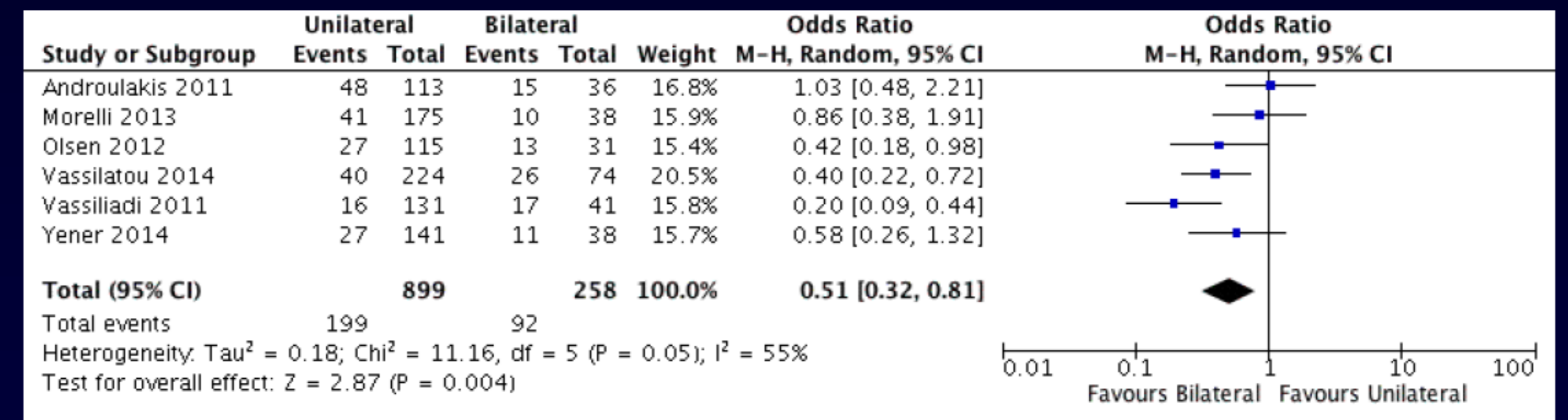
Methods: Electronic databases PubMed, MEDLINE and EMBASE were systematically searched. Main study outcome was the prevalence of SCS in patients with UAI and BAI. Secondary outcomes were the prevalence of obesity, diabetes, glucose intolerance, hypertension, dyslipidemia and osteoporosis in patients with UAI and BAI. Random effects odds ratios (OR) or standardized mean differences (SMD) and 95% confidence intervals (CI) were calculated. Meta-analysis was conducted using Review Manager (RevMan 5.3).

Results:

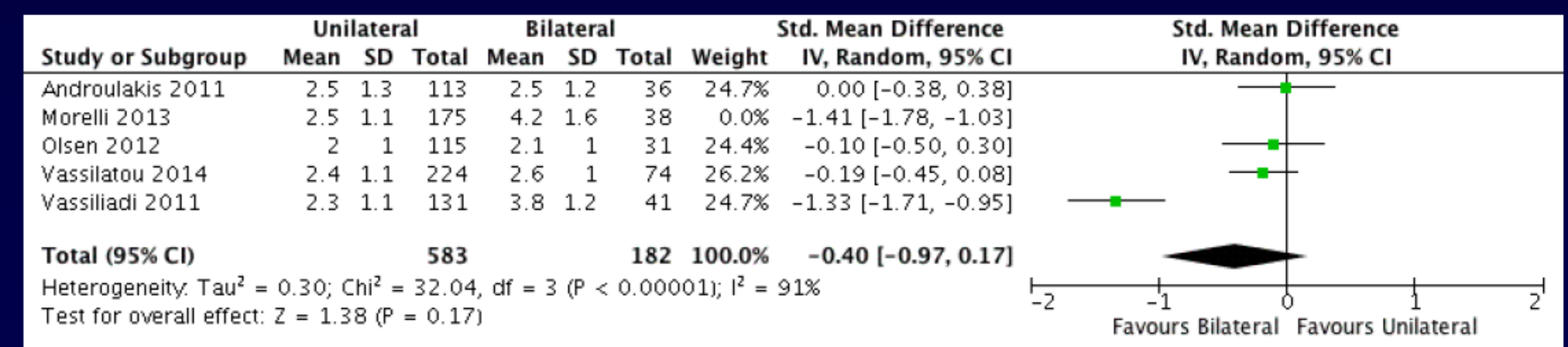
◆ Six studies were included in the meta-analysis involving in total 1239 patients, 968 with UAI and 271 with BAI.



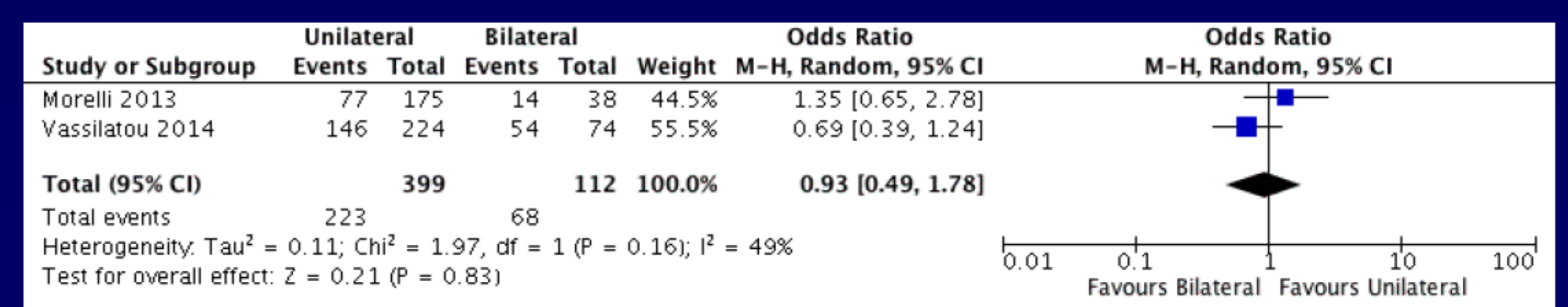
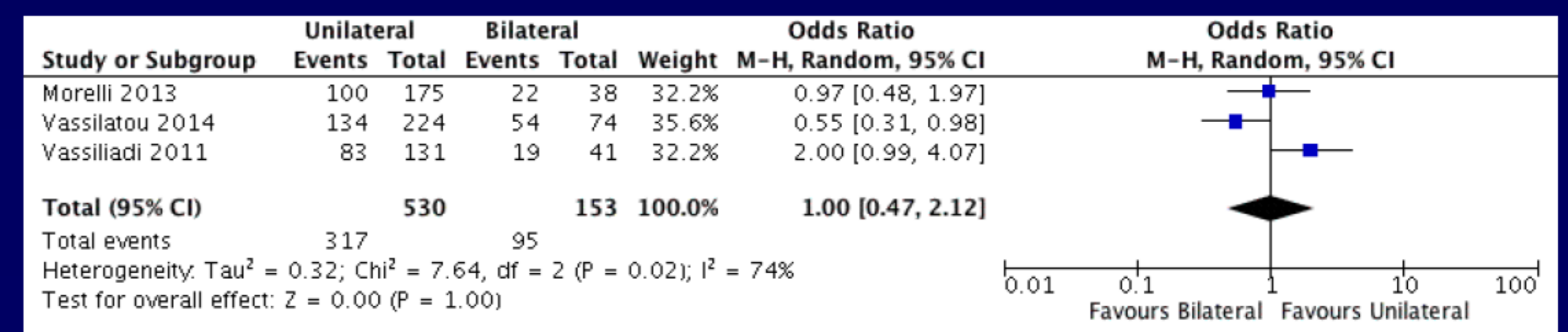
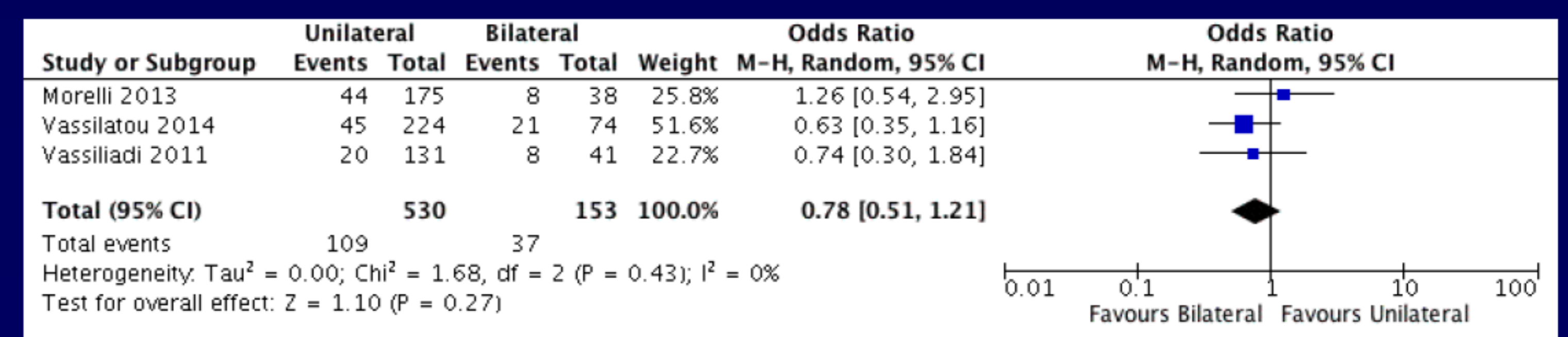
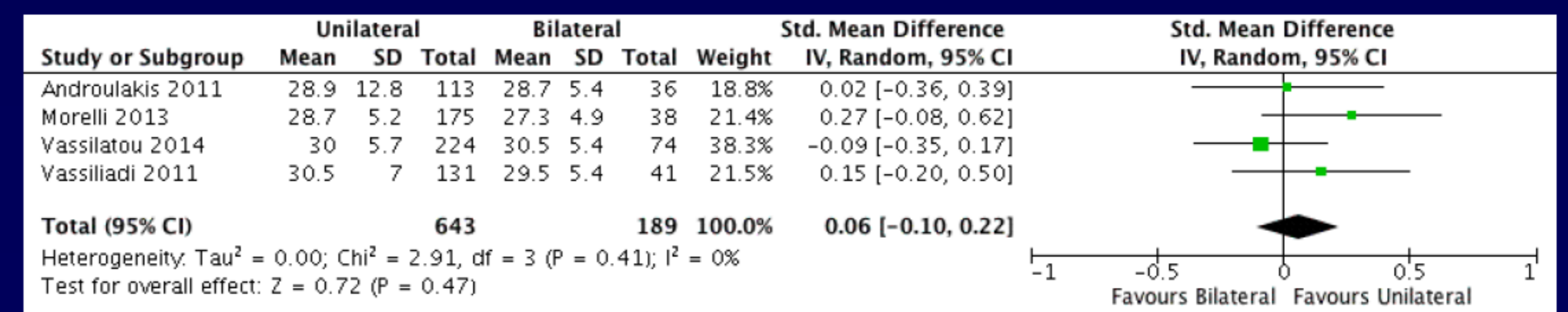
◆ Patients with UAI had lower prevalence of SCS compared with those with BAI [OR (95% CI) 0.51 (0.32; 0.81), I² = 55%].



◆ The mass diameter of UAI did not differ from BAI (the size of the largest lesion) [SMD (95% CI) -0.40 (-0.97; 0.17), I² = 91%].



◆ The prevalence of obesity [SMD (95% CI) 0.06 (-0.10; 0.22), I² = 0%], diabetes [OR (95% CI) 0.78 (0.51; 1.21), I² = 0%], hypertension [OR (95% CI) 1 (0.47; 2.12), I² = 74%] and dyslipidemia [OR (95% CI) 0.93 (0.49; 1.78), I² = 49%] did not differ between UAI and BAI.



Conclusions: Patients with BAI present a higher prevalence of SCS compared to patients with UAI, without any differences in related clinical implications.

ID	Year of publication	First author	Diagnosis of SCS	Patients with SCS n (%)	SCS frequency unilateral n (%)	SCS frequency bilateral n (%)	SCS bilateral vs. unilateral (p value)
1.	2014	Yener	≥2 of the following: Abnormal 1 mg DST, high UFC, low ACTH	38/179 (21.2%)	27/141 (19.1%)	11/38 (28.9%)	0.188
2.	2014	Vassilatou	Abnormal LDDST plus one more: abnormal midnight F, low ACTH, high UFC, low for age DHEA-S	66/298 (22.1%)	40/224 (17.9%)	26/74 (35.1%)	0.003
3.	2013	Morelli	≥2 of the following: Abnormal 1 mg DST, high UFC, low ACTH	51/213 (23.9%)	41/175 (23.4%)	10/38 (26.3%)	0.68
4.	2012	Olsen	Abnormal 1 mg DST and low ACTH	40/146 (27.4%)	27/115 (23.0%)	13/31 (42.0%)	0.041
5.	2011	Androulakis	Abnormal LDDST (cut off based on mean +2 SD values in controls)	63/149 (42.3%)	48/113 (42.5%)	15/36 (41.7%)	> 0.05
6.	2011	Vassiliadi	Abnormal LDDST plus one more: abnormal midnight F, low ACTH, high UFC	33/172 (19.2%)	16/131 (12.2%)	17/41 (41.5%)	0.001

ACTH: adrenocorticotropic hormone; DHEA-S: dehydroepiandrosterone sulphate; DST: dexamethasone suppression test; F: cortisol; LDDST: low-dose dexamethasone suppression test; SCS: subclinical Cushing syndrome; SD: standard deviations; UFC: urinary free cortisol.