

The effectiveness of vitamin D as an alternative to FDA- approved treatment and other therapies for managing vulvovaginal atrophy and sexual inactivity in postmenopausal women.

A systematic review and meta- analysis

The presenting Author: Hala Eldamanhoury,
M.Sc., MRCOG, CIC, CPHQ
Ministry of Health Egypt, New Cairo hospital
hala.md123@gmail.com

Background and Rational

Vulvovaginal atrophy (VVA) and sexual inactivity (SI) are prevalent among postmenopausal women (PMW). While hormonal therapies show significant improvement, non-hormonal therapies are considered the first- line for breast cancer women. However, vaginal hormonal therapies are unavailable in all countries, particularly developing countries such as the middle east, and there are no studies that have tested these therapies in women either with a history of breast cancer or those taking endocrine therapies for their cancer

We conducted this meta- analysis to evaluate the effectiveness of vitamin D (VD), whether alone or in combination with other therapies, in managing VVA and SI in PMW.

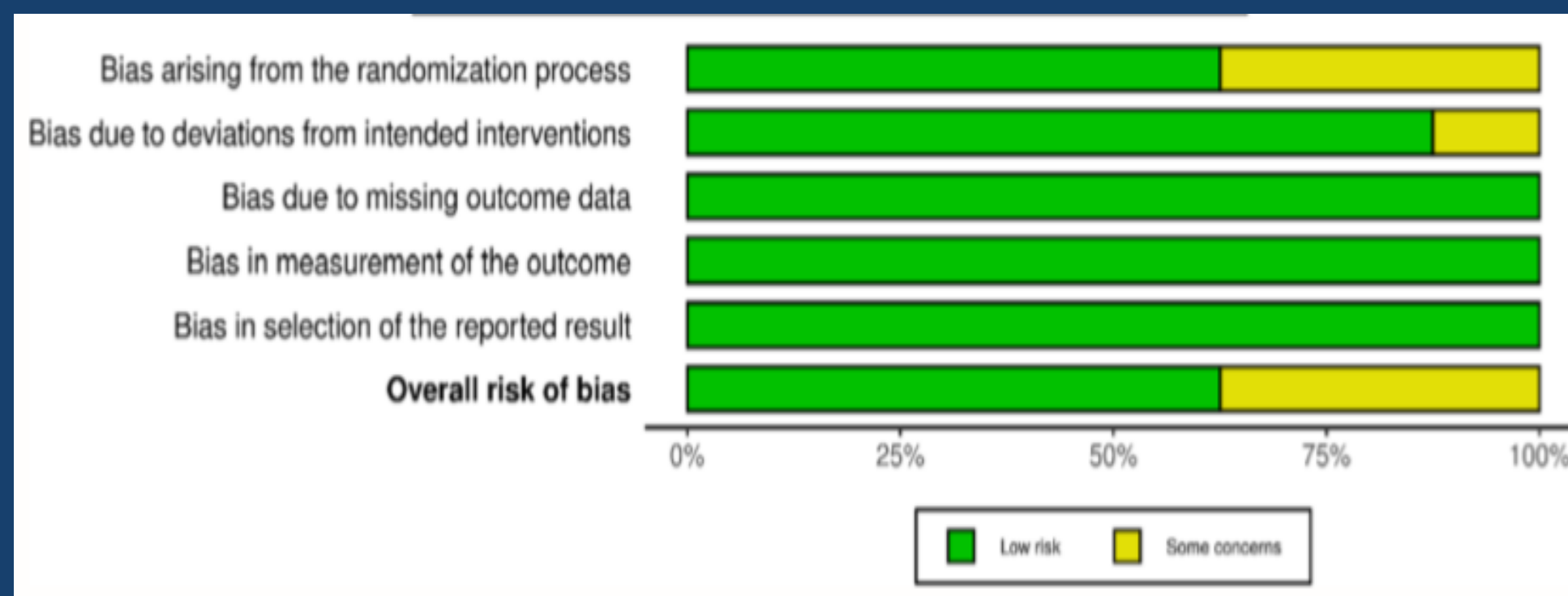
Risk of bias assessment

(a) Cochrane Risk of Bias Tool 2.0 for Randomized Controlled Trials

Study	Risk of bias domains					
	D1	D2	D3	D4	D5	Overall
Kamronrithisorn 2020	+	+	+	+	+	+
Zeyneloglu 2007	-	+	+	+	+	-
Carranza-Lira S 2012	-	-	+	+	+	-
M.A. Checa 2005	-	+	+	+	+	-
Keshavarzi 2019	+	+	+	+	+	+
Rad 2015	+	+	+	+	+	+
Radnia 2023	+	+	+	+	+	+
Zinat Sarebani 2023	+	+	+	+	+	+

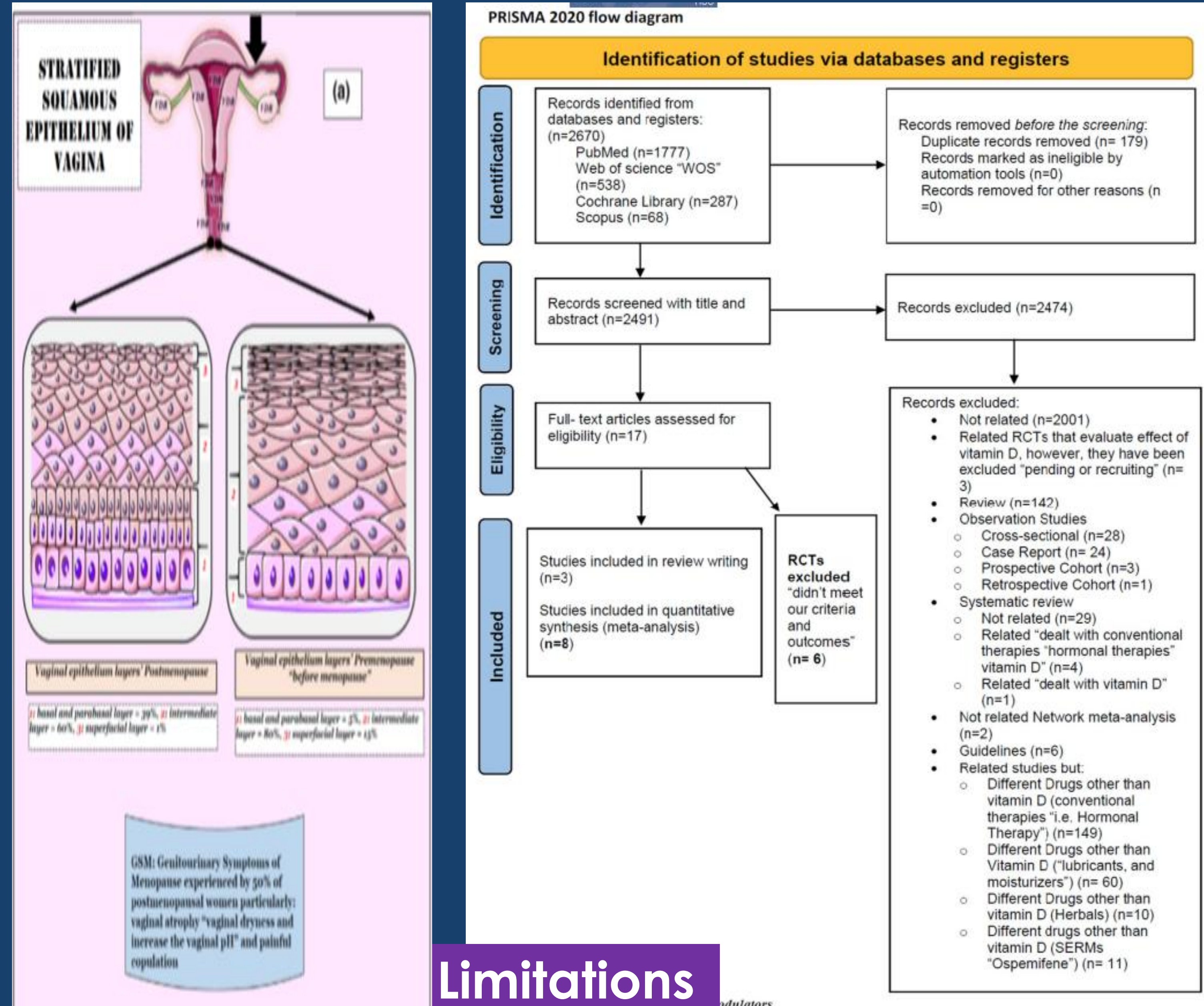
Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
- Some concerns
+ Low



A systematic literature search was undertaken on four electronic databases (Web of Science, PubMed, Cochrane, and Scopus) from inception until June 2023. Selection Criteria: The randomized controlled trials (RCTs) that used the vaginal maturation index (VMI) and vaginal pH to measure VVA and vaginal dryness and the female sexual function index (FSFI) to measure SI were included in the meta- analysis.

Search Strategy

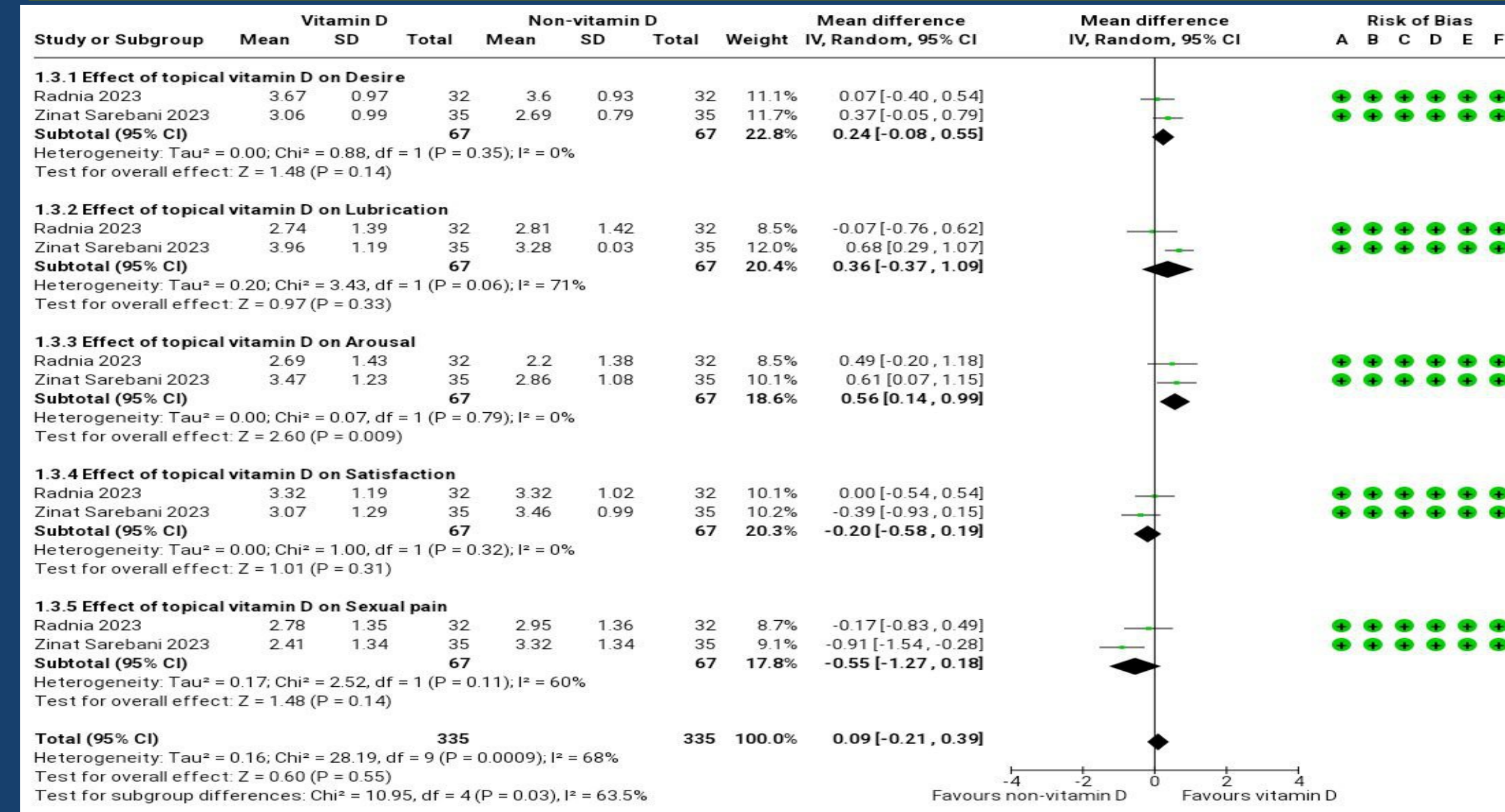


Limitations

The limitations are due to significant heterogeneity in the measures of VMI and FSFI across different subgroups. The sensitivity analysis revealed that removing one study resolved the heterogeneity of the oral subgroup of VMI. However, the inability to resolve the heterogeneity of other subgroups stemmed from the insufficient number of RCTs included in these groups.

Main Results

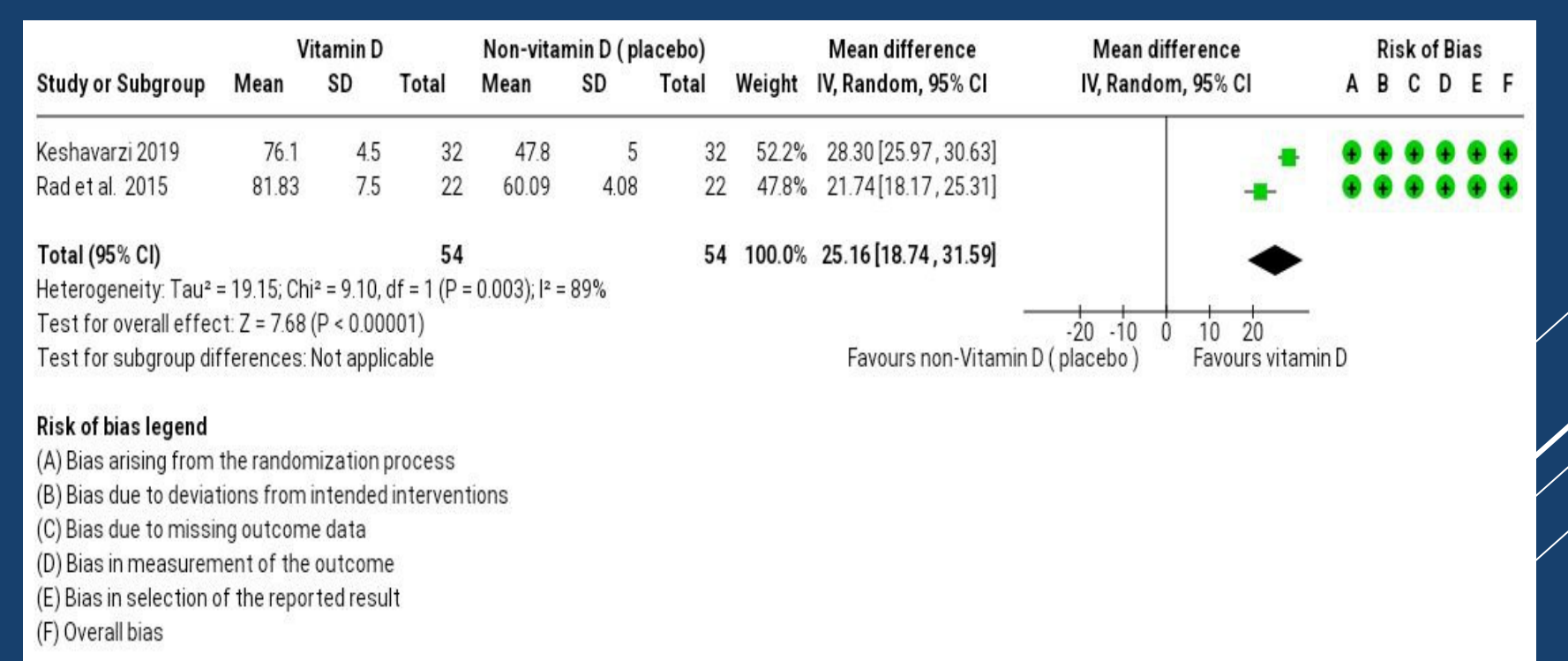
Eight RCTs (608 PMW) were included, and 222 were assigned to the VD arm. For the oral VD subgroup, there was no statistically significant improvement in the mean difference (MD) of VMI (MD -7.62, 95% confidence interval [CI]: -23.84, 8.59). However, VMI's topical VD subgroup was statistically significant (25.16; 95% CI: 18.74, 31.59). For topical form, the total FSFI score (0.24; 95% CI: -1.72, 2.20) and all FSFI domains did not demonstrate statistically significant improvement except arousal (0.56; 95% CI: 0.12, 1.00). Vaginal pH's oral VD subgroup showed statistically significant improvement (-0.27, 95% CI: -0.50, -0.05) compared to the topical VD. Topical VD subgroup (24.45; 95% CI: 7.14, 41.77) showed a statistically significant



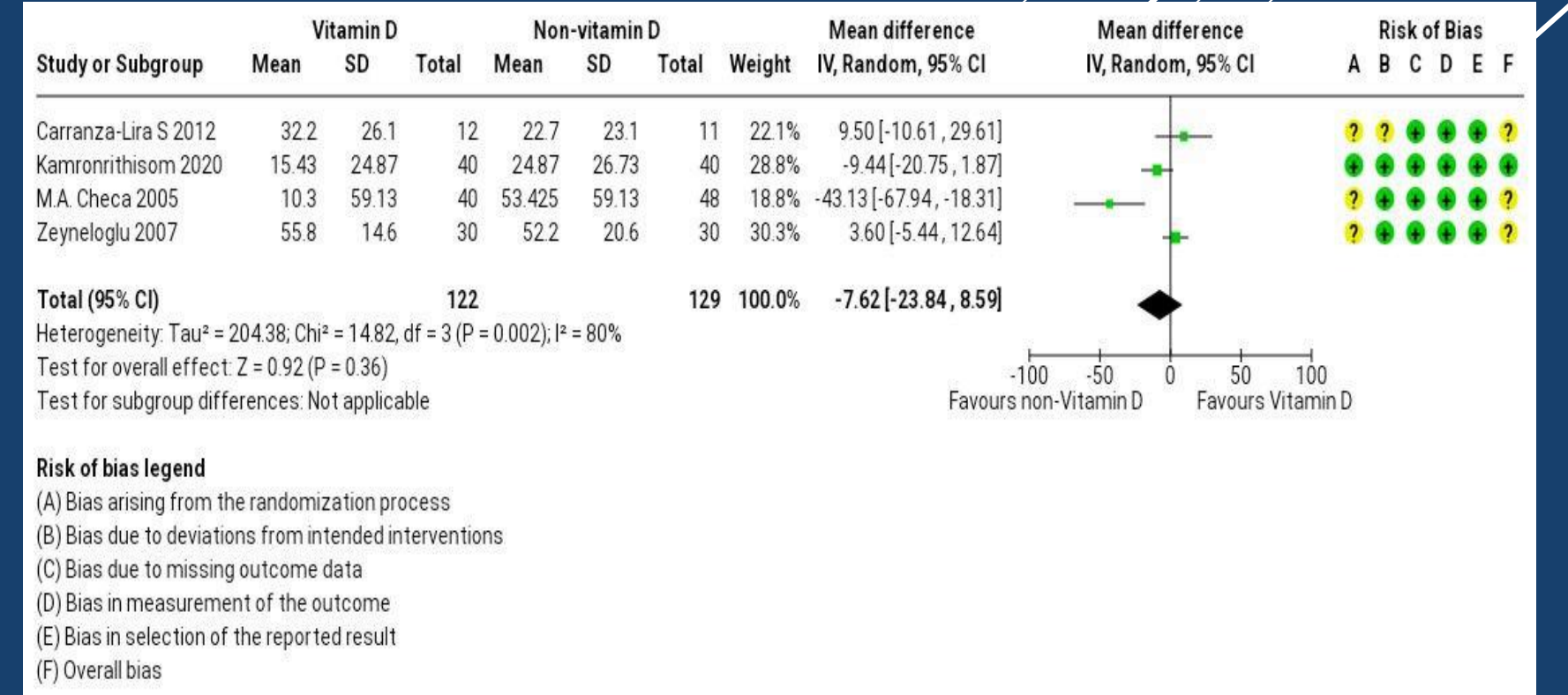
Topical VD measuring FSFI Combined five domains (a) Forest plot showing vaginal maturation index (VMI) in oral versus topical vitamin D subgroup. (b) Forest plot showing vaginal pH in oral vitamin D subgroup. (c) Forest plot showing vaginal pH in topical vitamin D subgroup. (d) Forest plot showing female sexual function index (FSFI) total score in topical vitamin D subgroup. (e) Cumulative forest plot showing female sexual function index (FSFI) five domains in topical vitamin D subgroup. (f) Forest plot showing percentage of superficial cells of vaginal epithelium in oral versus topical vitamin D subgroup.

Conclusion

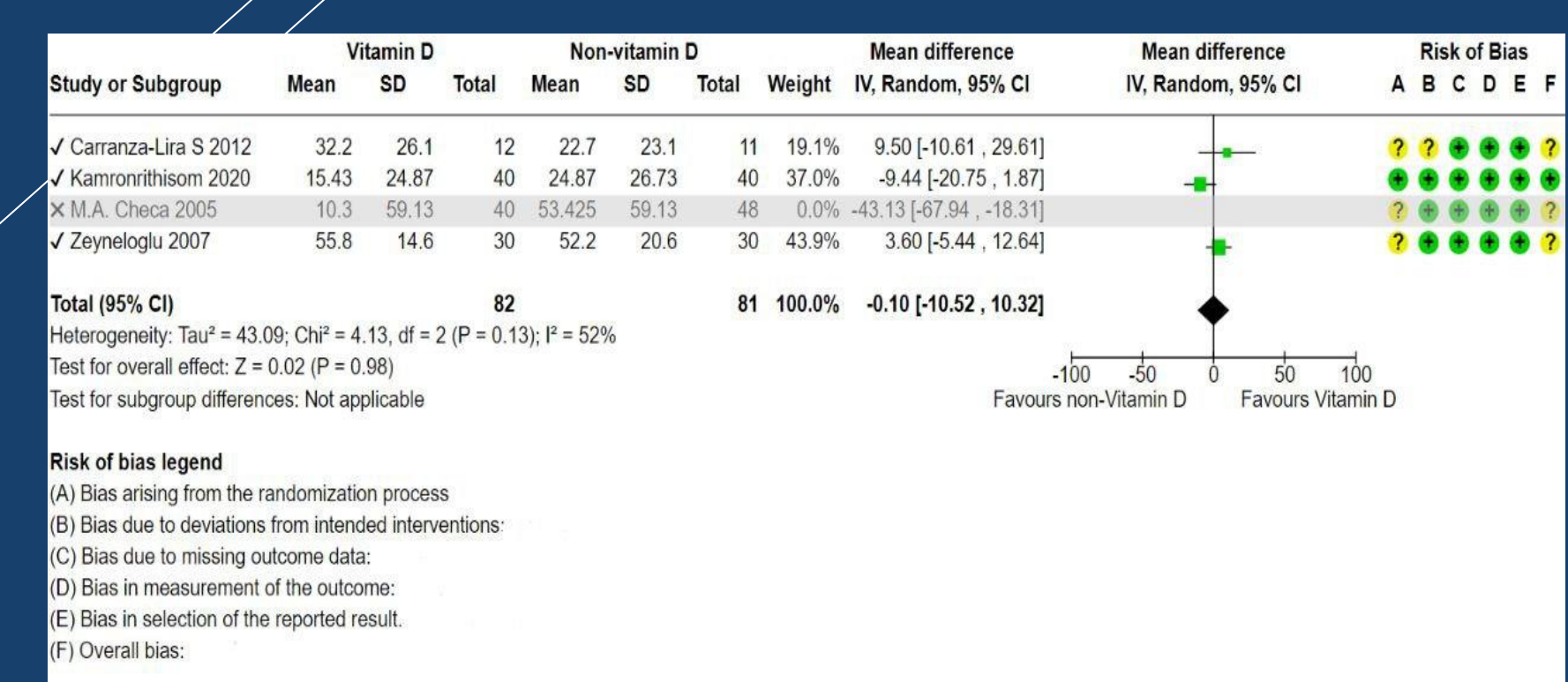
Topical VD showed significant improvements in the percentage of superficial cells, VMI, and the arousal subscale of FSFI, whereas oral VD had no substantial improvement except in vaginal pH. Current information is inadequate; VD alone is not a sufficient alternative to other available treatments, particularly topical estrogen. Further RCTs with larger sample sizes and longer follow- up periods are required to evaluate their effectiveness without any combination with other drugs.



Topical Vit D measuring VMI



Oral Vit D measuring VMI



Sensitivity analysis of the oral vitamin D subgroup showed decreasing in the significant heterogeneity from 74% to 0% by removing the Checa et al. study, which is the source of heterogeneity.