

What is the effect of sildenafil citrate intake on women undergoing assisted reproduction? A systematic review and meta-analysis of randomized controlled trials

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Background

The sildenafil citrate (SC) has been extensively examined in previous clinical trials to gauge its impact on enhancing the success rate of assisted reproductive technology (ART). This is attributed to its well-documented vasodilatory and antithrombotic activities, making it one of the most thoroughly researched medications in this regard. Numerous clinical trials have been carried out and a mounting body of evidence suggest beneficial effect of SC on ART outcomes.

Considering the substantial debate surrounding the effectiveness of SC, we executed a contemporary systematic review and meta-analysis of randomized controlled trials (RCTs) specifically targeted at appraising the influence of SC on various clinical endpoints of ART.

Objectives

The aim of this study was to assess the impact of SC on clinical outcomes in women undergoing ART.

Methods

Five different databases (PubMed, Scopus, Embase, Web of Science, and the Cochrane Central Register) were searched for the available trials from inception to April 2023.

-Patients: infertile women who undergoing ART.

-Intervention: Received SC alone or in combination with other agents.

-Control: Received a placebo, no treatment or an active agent other than SC.

-Outcomes: Our main outcomes were clinical pregnancy and endometrial thickness.

- Study design: Randomized controlled trials.

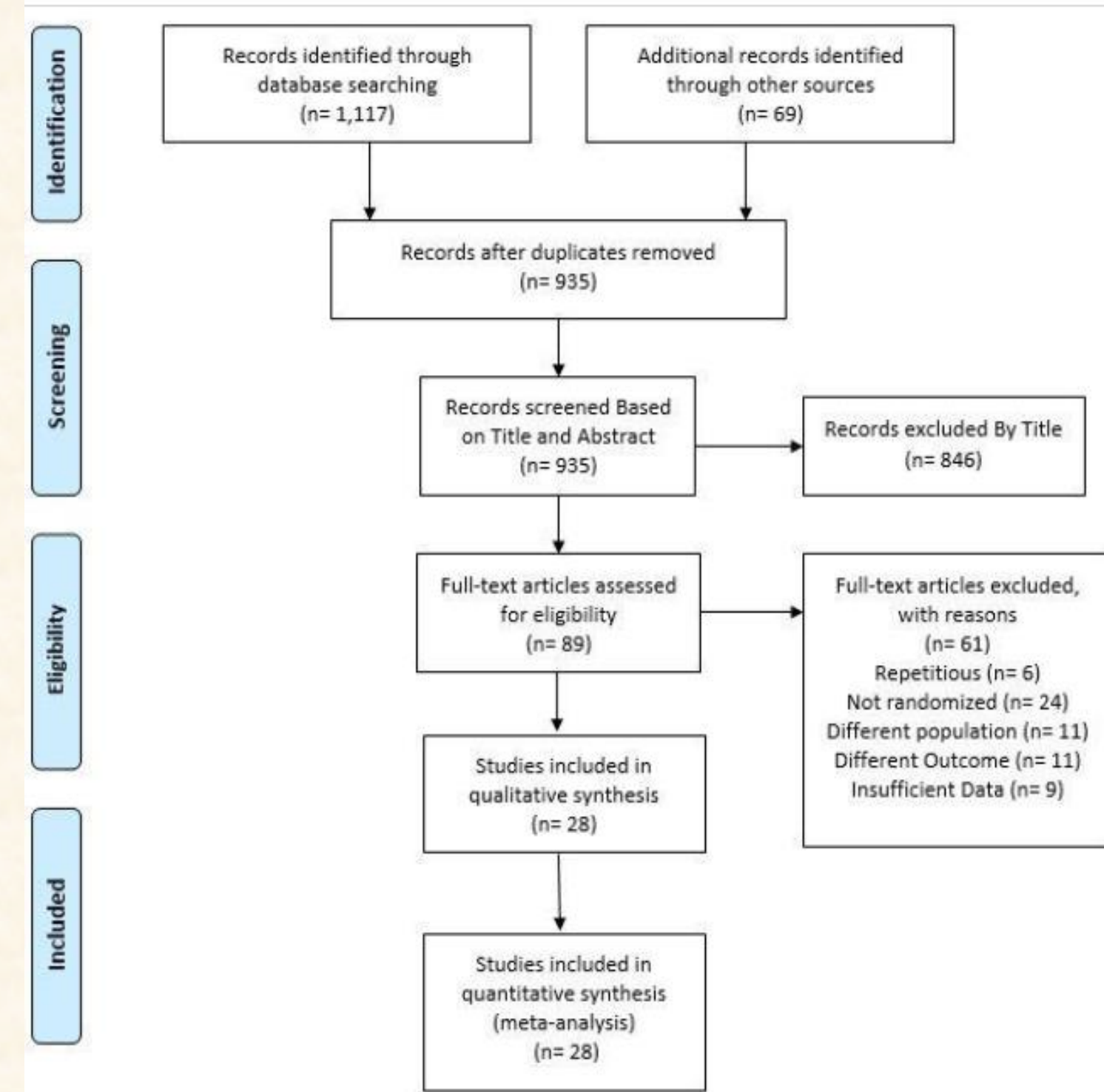


Figure 1. PRISMA flow diagram.

Author, year	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Missing outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Moni et al. ^[17] 2020	?	?	?	?	?	?	?
El-Sayed et al. ^[18] 2017	?	?	?	?	?	?	?
Tehraninejad et al. ^[19] 2018	?	?	?	?	?	?	?
Ataalla et al. ^[20] 2018	?	?	?	?	?	?	?
Wafa et al. ^[21] 2019	?	?	?	?	?	?	?
Korram et al. ^[22] 2018	?	?	?	?	?	?	?
Reddy et al. ^[23] 2016	?	?	?	?	?	?	?
Abdelkader Fahmy et al. ^[24] 2015	?	?	?	?	?	?	?
Ashoush and Abdelshafy ^[25] 2019	?	?	?	?	?	?	?
Abdourouane et al. ^[26] 2020	?	?	?	?	?	?	?
Young et al. ^[27] 2019	?	?	?	?	?	?	?
Vardhan et al. ^[28] 2019	?	?	?	?	?	?	?
Mangal and Mehrishi ^[29] 2019	?	?	?	?	?	?	?
Dehghani Firoozabadi et al. ^[30] 2019	?	?	?	?	?	?	?
Aleeva et al. ^[31] 2012	?	?	?	?	?	?	?
Kim et al. ^[32] 2010	?	?	?	?	?	?	?
Abdullah et al. ^[33] 2021	?	?	?	?	?	?	?
Betapunkar et al. ^[34] 2022	?	?	?	?	?	?	?
Mohammed et al. ^[35] 2023	?	?	?	?	?	?	?
Dawood et al. ^[36] 2020	?	?	?	?	?	?	?
Mohamed et al. ^[37] 2022	?	?	?	?	?	?	?
Gupta et al. ^[38] 2021	?	?	?	?	?	?	?
Abbas et al. ^[39] 2021	?	?	?	?	?	?	?
El-Khouly et al. ^[40] 2022	?	?	?	?	?	?	?
El-Ashaa et al. ^[41] 2021	?	?	?	?	?	?	?
Abdel Hamid et al. ^[42] 2021	?	?	?	?	?	?	?
Wafa et al. ^[43] 2022	?	?	?	?	?	?	?
El-Ghany et al. ^[44] 2022	?	?	?	?	?	?	?

Figure 2. Risk of bias summary.

Results

Twenty-eight RCTs comprising 3,426 women were included in the study.

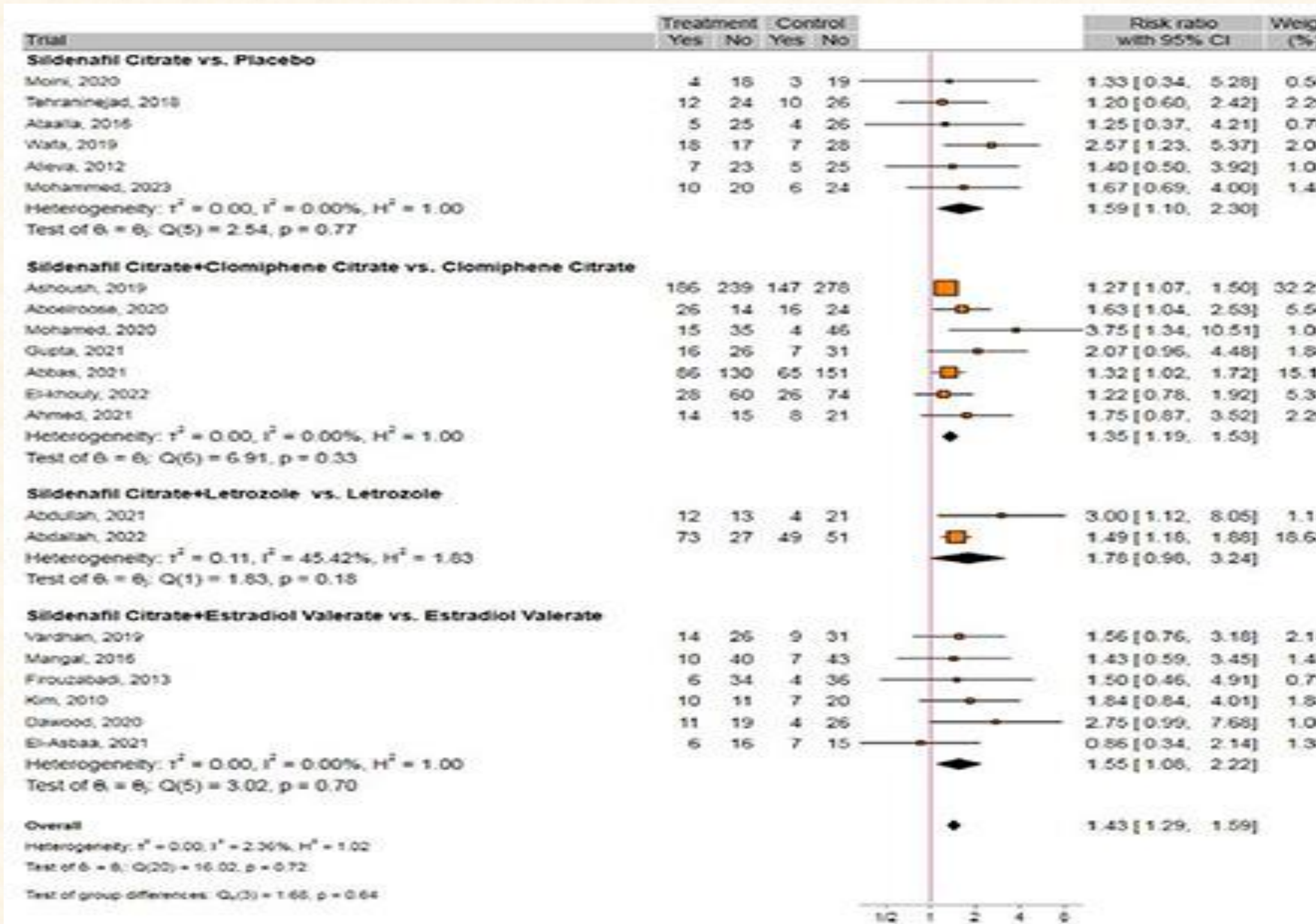


Figure 3. the risk of clinical pregnancy.

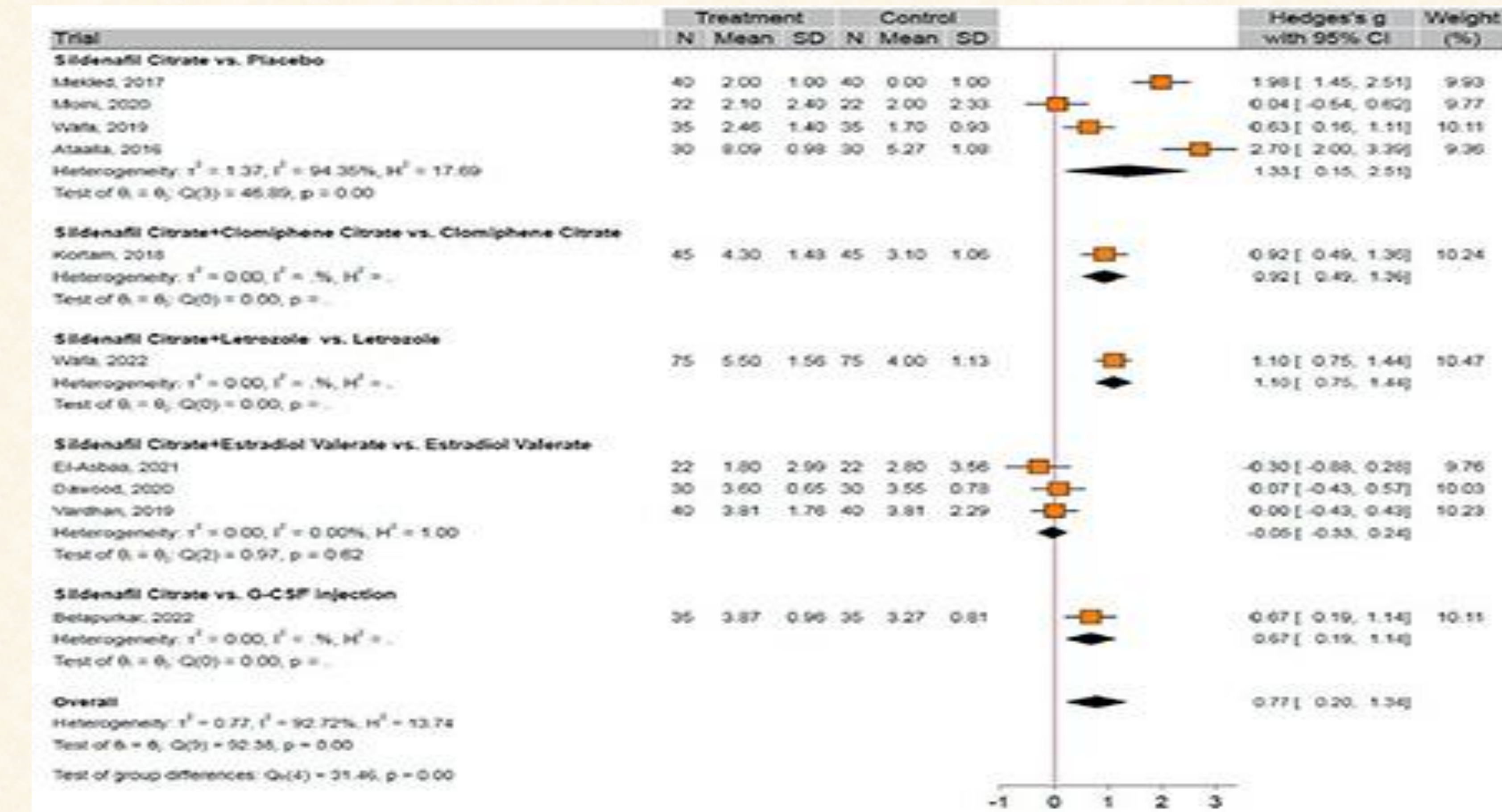


Figure 7. the mean of endometrial thickness.

Conclusion

The findings suggest that luteal supplementation of sildenafil citrate can be considered a beneficial approach to enhance endometrial thickness and improve the clinical pregnancy rate in women undergoing ART.

Limitations of the Study:

The majority of the RCTs we analyzed depicted inadequate methodological quality and harbored a small number of patients. However, we did not perform subgroup analyses to investigate the potential causes of many variability, such as the specific dose of SC, stage of embryo transfer, or type of protocol used. This was because the analyzed studies did not offer sufficient detailed data about their methods.

Reference

- Wafa YA, ALKhouly MM, Mosalam RM. Role of Low Dose Sildenafil in Improvement of Implantation Rate in Case of Recurrent ICSI failure. The Egyptian Journal of Hospital Medicine. 2019;75:2173-2182.
- El-Sayed A, Mekled A, Abd El-Rahim A. Effect of sildenafil citrate on the outcome of in vitro fertilization after multiple IVF failures attributed to poor endometrial development: a randomized controlled trial. The Egyptian Journal of Hospital Medicine. 2017;69:1553-1557.

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