Review – Sexual Medicine

Comparative Effectiveness and Safety of Oral Phosphodiesterase Type 5 Inhibitors for Erectile Dysfunction: A Systematic Review and Network Meta-analysis

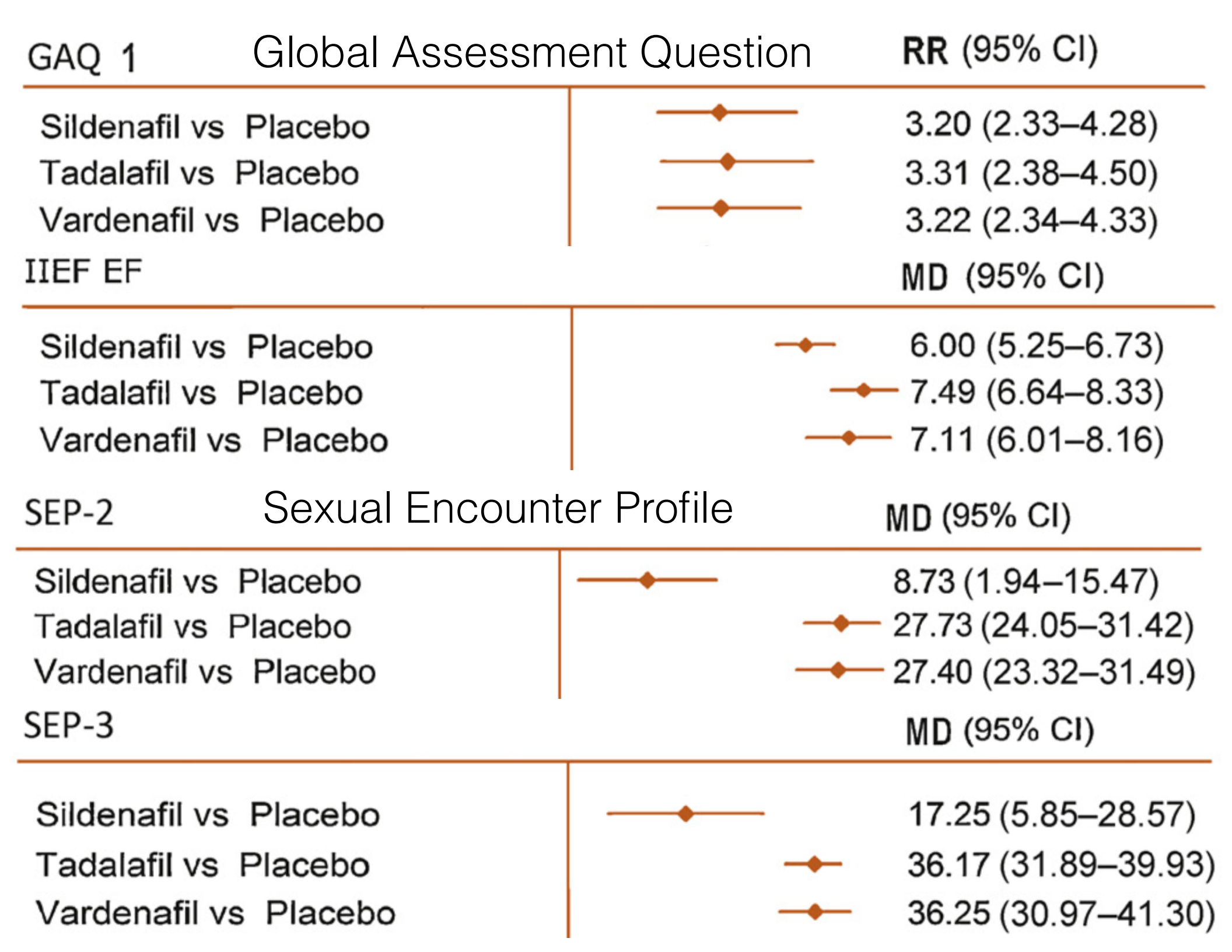
118 trials (31,195 people)

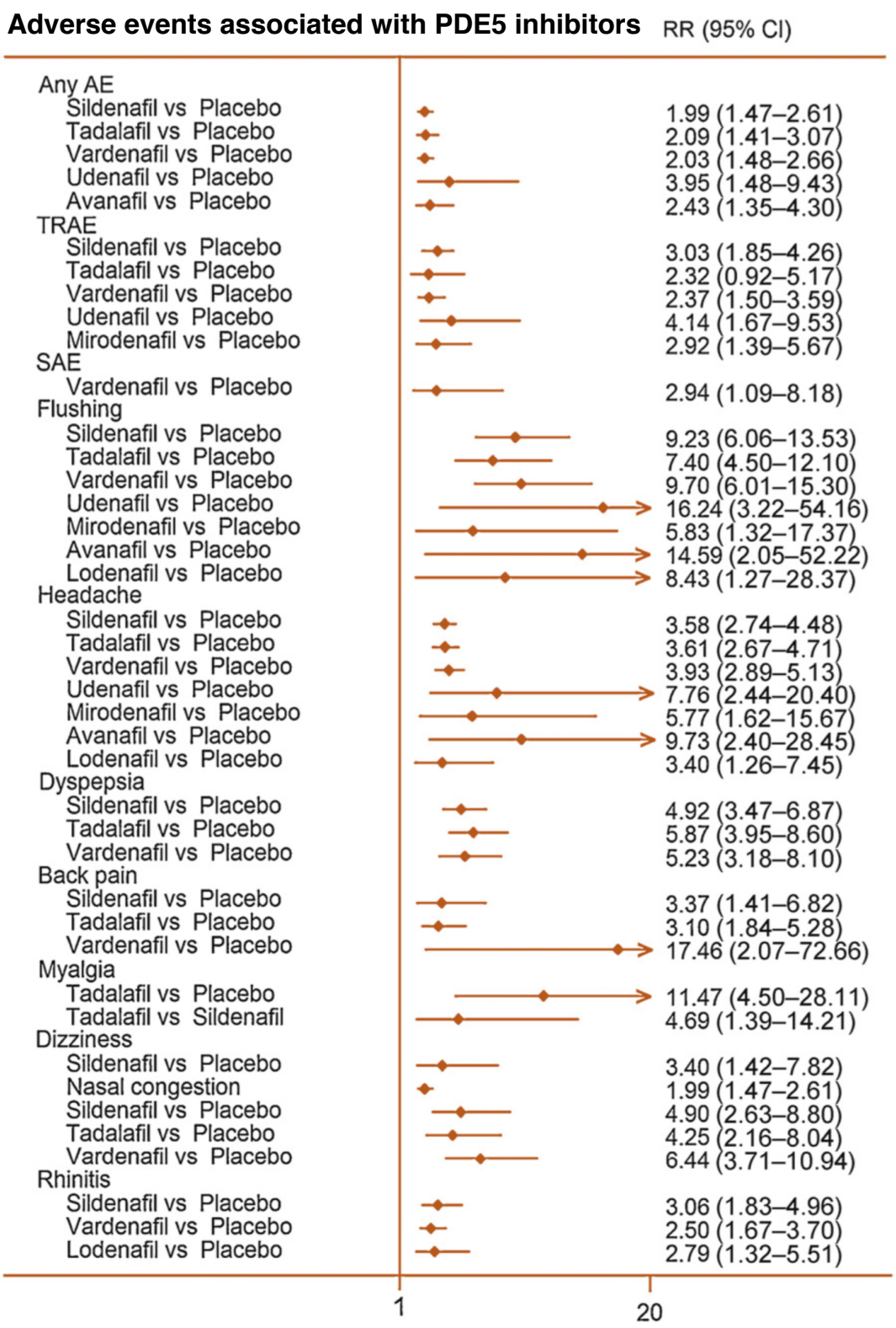
Primary outcome

- Global assessment Questionnaire
- Index of Erectile Function
- Erectile Function domain score

Also sexual encounter profile and adverse events

Euro Urol 2013;63:902–12


GAQ 1
Global Assessment Question
RR (95% CI)
Sildenafil vs Placebo
3.20 (2.33–4.28)
Tadalafil vs Placebo
3.31 (2.38–4.50)
Vardenafil vs Placebo
3.22 (2.34–4.33)
IIEF EF
MD (95% CI)
Sildenafil vs Placebo
6.00 (5.25–6.73)
Tadalafil vs Placebo
7.49 (6.64–8.33)
Vardenafil vs Placebo
7.11 (6.01–8.16)
SEP-2
Sexual Encounter Profile
MD (95% CI)
Sildenafil vs Placebo
8.73 (1.94–15.47)
Tadalafil vs Placebo
27.73 (24.05–31.42)
Vardenafil vs Placebo
27.40 (23.32–31.49)
SEP-3
MD (95% CI)
Sildenafil vs Placebo
17.25 (5.85–28.57)
Tadalafil vs Placebo
36.17 (31.89–39.93)
Vardenafil vs Placebo
36.25 (30.97–41.30)



45% vs 25%

10% vs 1%

10-15% vs 2-4%

5% vs 1%

5% vs 2%

Most likely dose related

Dose Response and Effect

Table 4. Efficacy Outcomes by Dose for Parallel-Group, Fixed-Dose Studies*

Efficacy Measure	25 mg			50 mg			100 mg		
	Sildenafil Citrate Group, %	Placebo Group, %	WMD or RBI† (95% CI)	Sildenafil Citrate Group, %	Placebo Group, %	WMD or RBI† (95% CI)	Sildenafil Citrate Group, %	Placebo Group, %	WMD or RBI† (95% CI)
Successful sexual intercourse, mean % of attempts per participant	43	17	26 (18-35)	50	14	36 (30-42)	51	14	36 (31-42)
Men with ≥1 successful sexual intercourse attempt during treatment	82	53	1.5 (1.2-1.9)	81	43	1.8 (1.5-2.3)	82	43	1.9 (1.2-3.0)
Men with self-reported improvement in erections	66	29	2.2 (1.9-2.6)	76	27	2.8 (2.3-3.4)	82	25	3.2 (2.7-3.8)

*WMD indicates weighted mean difference; RBI, relative benefit increase; and CI, confidence interval.
†WMD is given for the first efficacy measure and RBI is given for the second and third efficacy measures.

Arch Int Med 2002;162:1349-60

Table 5. Discontinuations and Adverse Events by Treatment Dose*

	Sildenafil Group, %	Placebo Group, %	RRI (95% CI)
Discontinuations			
Flexible dose†	7	14	0.6 (0.5-0.9)
Fixed dose, 25 mg‡	10	14	0.8 (0.5-1.1)
Fixed dose, 50 mg	8	13	0.6 (0.4-0.96)
Fixed dose, 100 mg	9	14	0.7 (0.5-0.96)
Any adverse event			
Flexible dose	48	36	1.4 (1.3-1.6)
Fixed dose, 25 mg	61	45	1.4 (1.2-1.6)
Fixed dose, 50 mg	65	48	1.4 (1.2-1.5)
Fixed dose, 100 mg	79	50	1.5 (1.3-1.8)
Headache			
Flexible dose	11	4	2.6 (1.8-3.7)
Fixed dose, 25 mg	18	6	3.0 (2.0-4.6)
Fixed dose, 50 mg	20	7	2.9 (2.1-4.0)
Fixed dose, 100 mg	28	7	4.0 (2.9-5.6)
Vasodilation (flushing)			
Flexible dose	12	2	5.8 (3.4-10.0)
Fixed dose, 25 mg	9	1	7.1 (3.2-15.7)
Fixed dose, 50 mg	17	2	8.0 (4.7-13.9)
Fixed dose, 100 mg	18	2	7.6 (4.3-13.2)
Dyspepsia			
Flexible dose	5	1	3.8 (2.2-6.6)
Fixed dose, 25 mg	5	2	2.5 (1.1-5.6)
Fixed dose, 50 mg	8	2	3.9 (2.2-7.0)
Fixed dose, 100 mg	17	2	8.9 (4.8-16.5)
Abnormal vision			
Flexible dose	3	<1	3.1 (1.8-5.4)
Fixed dose, 25 mg	<1	<1	1.5 (0.2-10.3)
Fixed dose, 50 mg	2	<1	3.3 (0.7-15.5)
Fixed dose, 100 mg	11	<1	11.6 (4.4-30.5)

*RRI indicates relative risk increase; CI, confidence interval.

†In flexible-dose trials, participants began at a 50-mg dose, with adjustment between 25 and 100 mg as determined by treatment response and participant tolerance. Discontinuation and adverse events data are available for 3780 men from these trials.

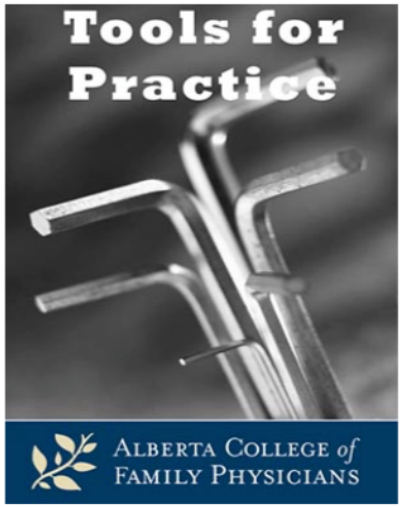
‡Fixed-dose trials compared individuals in the placebo arm with those receiving a fixed sildenafil citrate dose of 25, 50, or 100 mg. For each fixed-dose comparison, discontinuation and adverse events data are available from the following number of men: 25 mg (n = 397) vs placebo (n = 521); 50 mg (n = 605) vs placebo (n = 716); and 100 mg (n = 506) vs placebo (n = 607).

Dose Response and Tolerability

Arch Int Med 2002;162:1349-60

Testosterone - transdermal, IM, oral

April 28, 2014



Testosterone supplementation in men: Let's pause for a moment

<u>Clinical Question</u>: Is testosterone supplementation effective and safe for androgen decline in aging males?

<u>Bottom-line</u>: In older men, testosterone increases some muscle strength by 7%, with moderate improvements in erectile function and libido. There also appears to be an increase of adverse events, particularly cardiovascular in those with higher risk. Many results are inconsistent, at high risk of bias, and difficult to quantify in real world application.

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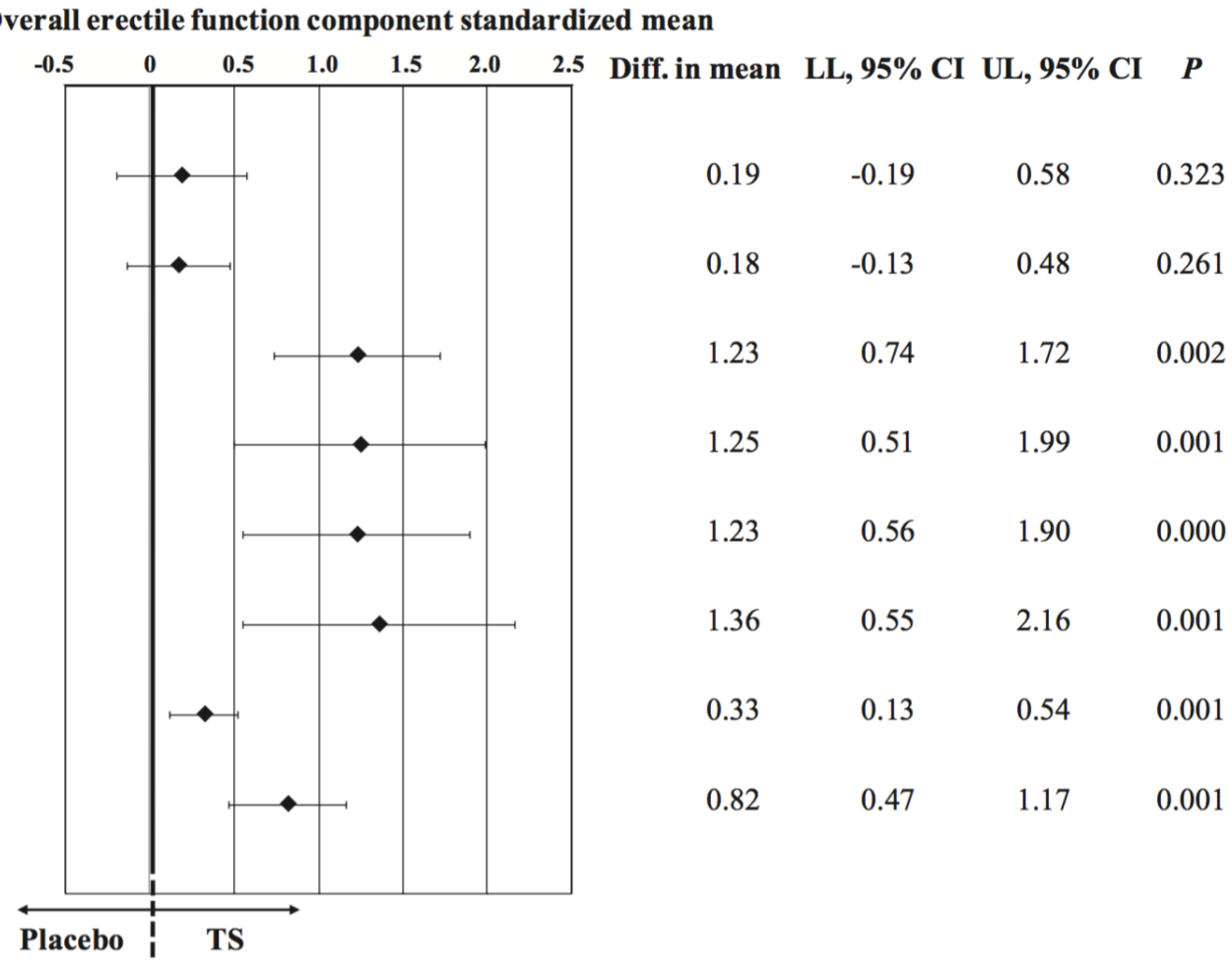

Source	Diff. in mean	LL, 95% CI	UL, 95% CI	*P*
Overall eugonadal	0.19	-0.19	0.58	0.323
Overall mixed	0.18	-0.13	0.48	0.261
Overall hypogonadal	1.23	0.74	1.72	0.002
Overall hypogonadal (TT <12 nM)	1.25	0.51	1.99	0.001
Overall hypogonadal (TT < 8 nM)	1.23	0.56	1.90	0.000
Overall pharmaceutical industry supported	1.36	0.55	2.16	0.001
Overall pharmaceutical industry not supported	0.33	0.13	0.54	0.001
Overall	0.82	0.47	1.17	0.001

J Sex Med 2014;11:1577–92

Current Pharmacological Management of Premature Ejaculation: A Systematic Review and Meta-analysis

22 studies

selective serotonin reuptake inhibitors (SSRIs), topical anesthetic creams, tramadol, and phosphodiesterase type 5 inhibitors are more effective than placebo at increasing IELT (intravaginal ejaculation latency time)

dapoxetine - more homogeneous data - 1.39 minute increase

European Urology 2016;69:904–916

Efficacy and Safety of Flibanserin for the Treatment of Hypoactive Sexual Desire Disorder in Women

A Systematic Review and Meta-analysis

5 published studies, 3 unpublished

one-half additional satisfying sexual event per month

dizziness, somnolence, cause, fatigue all increased

JAMA Intern Med. 2016;176(4):453-462. doi:10.1001/jamainternmed.2015.8565