Testosterone Supplementation and Sexual Function: A Meta-Analysis Study

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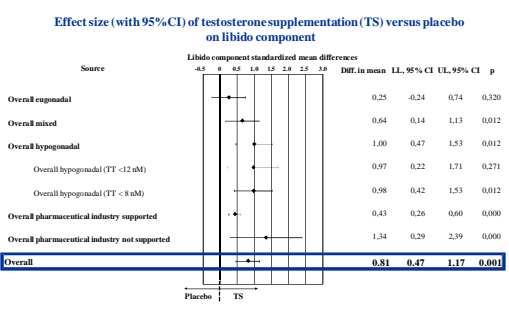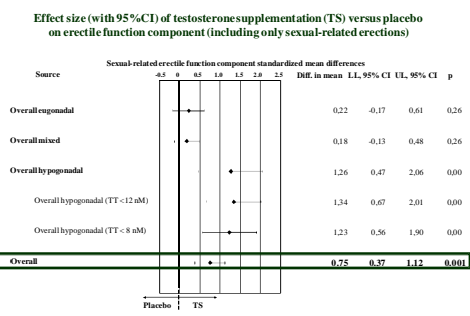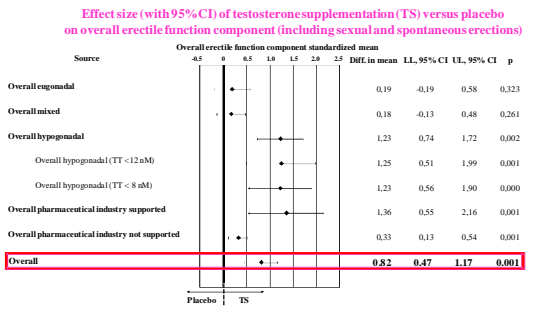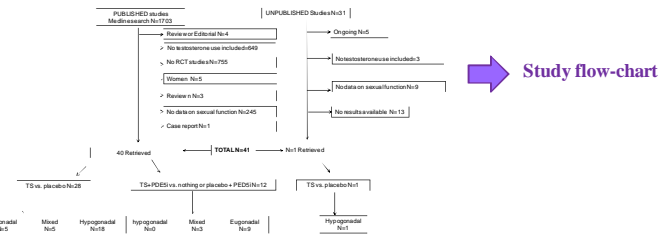
Introduction. The role of testosterone supplementation (TS) as a treatment for male sexual dysfunction remains questionable.
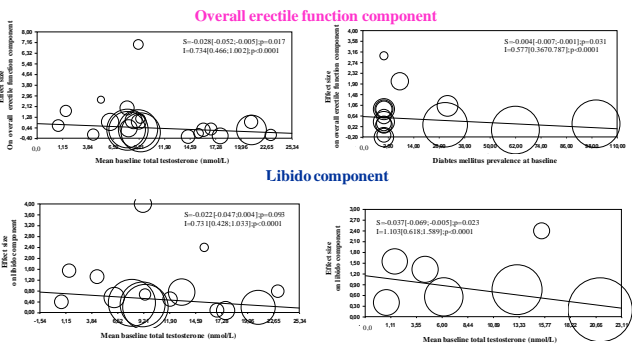
The **aim** of this study was to attempt a meta-analysis on the effect of TS on male sexual function and its synergism with the use of phosphodiesterase type 5 inhibitor (PDE5i).

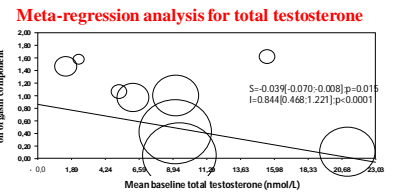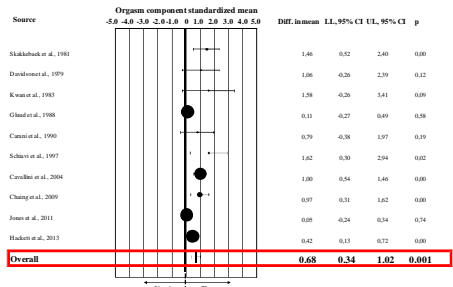**Methods.** An extensive Medline, Embase, and Cochrane search was performed.

Main Outcome Measures. All randomized controlled trials (RCTs) comparing the effect of TS vs. placebo or the effect of TS as add on to PDE5is on sexual function were included. Data extraction was performed independently by two of the authors (A. M. Isidori and G. Corona), and conflicts resolved by the third investigator (M. Maggi).
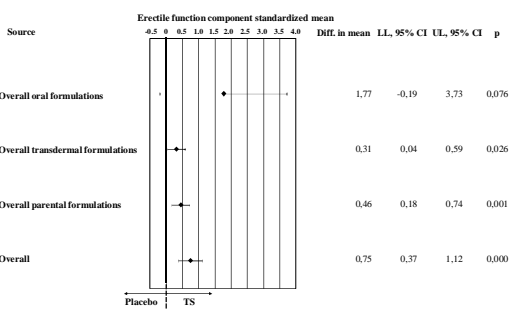
Study flow-chart

Effect size (with 95%CI) of testosterone supplementation (TS) versus placebo on overall erectile function component (including sexual and spontaneous erections)

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

Effect size (with 95%CI) of testosterone supplementation (TS) versus placebo on erectile function component (including only sexual-related erections)

Source	Diff. in mean	LL, 95% CI	UL, 95% CI	p
Overall eugonadal	0,22	-0,17	0,61	0,26
Overall mixed	0,18	-0,13	0,48	0,26
Overall hypogonadal	1,26	0,47	2,06	0,00
Overall hypogonadal (TT <12 nM)	1,34	0,67	2,01	0,00
Overall hypogonadal (TT < 8 nM)	1,23	0,56	1,90	0,00
Overall	0,75	0,37	1,12	0,001

Effect size (with 95%CI) of testosterone supplementation (TS) versus placebo on libido component

Source	Diff. in mean	LL, 95% CI	UL, 95% CI	p
Overall eugonadal	0,25	-0,24	0,74	0,320
Overall mixed	0,64	0,14	1,13	0,012
Overall hypogonadal	1,00	0,47	1,53	0,012
Overall hypogonadal (TT <12 nM)	0,97	0,22	1,71	0,271
Overall hypogonadal (TT < 8 nM)	0,98	0,42	1,53	0,012
Overall pharmaceutical industry supported	0,43	0,26	0,60	0,012
Overall pharmaceutical industry not supported	1,34	0,29	2,39	0,000
Overall	0,81	0,47	1,17	0,001

Meta-regression analysis for total testosterone

Overall erectile function component

Libido component

Effect size (with 95%CI) of testosterone supplementation (TS) versus placebo on orgasm component

Source	Diff. in mean	LL, 95% CI	UL, 95% CI	p
Skakkebaek et al., 1981	1,46	0,52	2,40	0,00
Davidson et al., 1979	1,06	-0,26	2,39	0,12
Kwan et al., 1983	1,58	-0,26	3,41	0,09
Gluud et al., 1988	0,11	-0,27	0,49	0,58
Canini et al., 1990	0,79	-0,38	1,97	0,19
Schiavi et al., 1997	1,62	0,30	2,94	0,02
Cavallini et al., 2004	1,00	0,54	1,46	0,00
Chiang et al., 2009	0,97	0,31	1,62	0,00
Jones et al., 2011	0,05	-0,24	0,34	0,74
Hackett et al., 2013	0,42	0,13	0,72	0,00
Overall	0,68	0,34	1,02	0,001

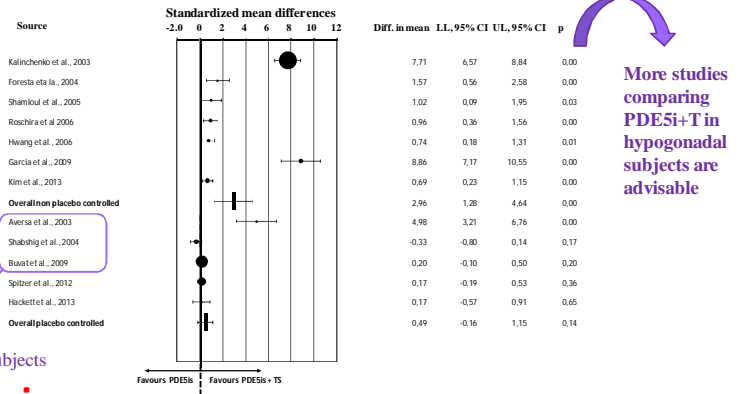**Meta-regression analysis for total testosterone**

Effect size (with 95%CI) of testosterone supplementation (TS) versus placebo on erectile function component (including only sexual-related erections)

Erectile function component standardized mean

Source	Diff. in mean	LL, 95% CI	UL, 95% CI	p
Overall oral formulations	1,77	-0,19	3,73	0,076
Overall transdermal formulations	0,31	0,04	0,59	0,026
Overall parental formulations	0,46	0,18	0,74	0,001
Overall	0,75	0,37	1,12	0,000

No differences between transdermal and parental formulations

Mixed eugonadal/hypogonadal subjects

Effect size (with 95% CI) of testosterone supplementation (TS) vs. placebo as add on to phosphodiesterase type 5 inhibitors (PDE5is) on sexual function in placebo controlled or uncontrolled trials

Standardized mean differences

Source	Diff. in mean	LL, 95% CI	UL, 95% CI	p
Kalinchenko et al., 2003	7,71	6,57	8,84	0,00
Foresta et al., 2004	1,57	0,56	2,58	0,00
Shamloul et al., 2005	1,02	0,09	1,95	0,03
Roschira et al. 2006	0,96	0,36	1,56	0,00
Hwang et al., 2006	0,74	0,18	1,31	0,01
Garcia et al., 2009	8,86	7,17	10,55	0,00
Kim et al., 2013	0,69	0,23	1,15	0,00
Overall non placebo controlled	2,96	1,28	4,64	0,00
Aversa et al., 2003	4,98	3,21	6,76	0,00
Shabshig et al., 2004	-0,33	-0,80	0,14	0,17
Buvat et al., 2009	0,20	-0,10	0,50	0,20
Spitzer et al., 2012	0,17	-0,19	0,53	0,36
Hackett et al., 2013	0,17	-0,57	0,91	0,65
Overall placebo controlled	0,49	-0,16	1,15	0,14

Favours PDE5is — Favours PDE5is + TS

More studies comparing PDE5i+T in hypogonadal subjects are advisable

Conclusions

TS plays positive effects on male sexual function in hypogonadal subjects. The role of TS is uncertain in men who are not clearly hypogonadal. The apparent difference between industry-supported and independent studies could depend on trial design more than on publication bias. New RCTs exploring the effect of TS in selected cases of PDE5i failure that persistently retain low testosterone levels are advisable