

Supplementary Table 1: Sexual function questionnaires used and reported outcomes

Author & Year	Population	Intervention	Concurrent estrogen therapy	Sexual function questionnaire	Outcomes reported
Postmenopausal women					
Barrett-Connor 1999	Surgical menopause	Oral testosterone	Oral estrogen	Modified scale by Sherwin and Kupperman	Vaginal dryness
Floter 2002	Surgical menopause			McCoy's SS	SSE (no SD data), total sexual function, desire, orgasm
de Paula 2007	Natural menopause			McCoy's SS	Desire
Penteado 2009	Natural menopause			SECS	Desire, orgasm
Lobo 2003	Surgical menopause+ Natural menopause			BISF-W SIQ	Total sexual function, desire, orgasm, responsiveness
Braunstein 2005	Surgical menopause	Transdermal patch vs Placebo	Oral estrogen	PFSF	SSE, all sexual function domains
Shifren 2000	Surgical menopause			BISF-W	Total sexual function
Simon 2005	Surgical menopause			PFSF PDS	SSE, all sexual function domains
Buster 2005	Surgical menopause	Transdermal patch vs Placebo	Oral estrogen (80%) Transdermal estrogen (20%)	PFSF PDS	SSE, all sexual function domains
Davis 2006	Surgical menopause	Transdermal patch vs Placebo	Transdermal estrogen	PFSF	SSE, all sexual function domains
Shifren 2006	Natural menopause	Transdermal patch vs Placebo	Oral estrogen	PFSF PDS	SSE, all sexual function domains
Panay 2010	Natural menopause	Transdermal patch vs Placebo	No concurrent estrogen therapy (74%) 26% Oral transdermal	PFSF PDS	SSE, all sexual function domains
Unpublished	Natural menopause	Transdermal patch vs Placebo		PFSF PDS	SSE, all sexual function domains
Davis 2008	Surgical menopause+ Natural menopause	Transdermal patch vs Placebo	No concurrent estrogen therapy	PFSF PDS	SSE, all sexual function domains
Huang 2014	Surgical menopause+ Natural menopause	Intramuscular injections of testosterone enanthate	Intramuscular injections	BISF-W FSDS	Total sexual function, desire, arousal, FSDS
El-Hage 2007	Surgical menopause	Transdermal cream vs Placebo	Transdermal estrogen	BISF-W	Total sexual function, desire, arousal, orgasm
Nathrost-Boos 2006	Natural menopause	Transdermal gel vs Placebo	Oral/Transdermal estrogen	McCoy's SS	SSE (cannot be used as reported median numbers only)
Premenopausal women					

Fooladi 2014*	Women with SSRI/SNRI therapy	Transdermal patch vs Placebo	Not applicable	SSS	SSE, total sexual function, desire, orgasm, pleasure FSDS
Goldstat 2003	Women with low sexual desire	Transdermal cream vs Placebo		SSS	Total sexual function
Davis 2008a	Women with low sexual desire	Transdermal spray vs Placebo		SSS	SSE, total sexual function, desire, orgasm, pleasure

*Some postmenopausal women might be included.

SSE=Satisfactory Sexual Events, FSFS= Female Sexual Distress Scale, McCoy's SS= McCoy's Sexual Satisfaction, SECS= Sexual Energy Change Scale, PFSF=Profile of Female Sexual Function, FSFI= Female sexual function index, PDS= Personal Distress Scale, SSS= Sabbatsberg Sexual Satisfaction, BISF-W= The Brief Index of Sexual Functioning for Women, SIQ= The Sexual Interest Questionnaire, DISF= Derogatis Interview for Sexual Functioning.

Supplementary Table 2: Non-sexual function outcomes reported by included studies

Author & Year	Population	Intervention	Concurrent estrogen therapy	Reported outcomes
Lipid profile				
Barrett-Connor et al. 1999	Surgical menopause	Oral testosterone	Oral estrogen	Lipid profile
Basaria et al. 2002	Surgical menopause+ Natural menopause	Oral testosterone	Oral estrogen	Lipid profile
Dobs et al. 2002	Surgical menopause+ Natural menopause	Oral testosterone	Oral estrogen	Lipid profile
de Paula et al. 2007	Natural menopause	Oral testosterone	Oral estrogen	Lipid profile
Floter et al. 2004	Surgical menopause	Oral testosterone	Oral estrogen	Lipid profile
Hickok et al. 1993	Natural menopause	Oral testosterone	Oral estrogen	Lipid profile
Watts et al. 1995	Surgical menopause	Oral testosterone	Oral estrogen	Lipid profile
Leao et al. 2006	Surgical menopause	Oral testosterone	Oral estrogen	Lipid profile
Lobo et al. 2003	Surgical menopause+ Natural menopause	Oral testosterone	Oral estrogen	Lipid profile
Shifren et al. 2000	Surgical menopause	Oral testosterone+ Transdermal patch	Oral estrogen + Transdermal patch	Lipid profile
El-Hage et al. 2007	Surgical menopause	Transdermal cream vs Placebo	Transdermal estrogen	Lipid profile
Nathrost-Boos et al. 2006	Natural menopause	Transdermal gel vs Placebo	Oral/Transdermal estrogen	Lipid profile
Huang et al. 2014, 2014	Surgical menopause	Intramuscular injections of Testosterone enanthate	Intramuscular injections	Lipid profile
Davis et al. 1995	Surgical menopause+ Natural menopause	Implant	Implant estradiol	Lipid profile
Davis et al. 2008	Surgical menopause+ Natural menopause	Transdermal patch vs Placebo	No concurrent estrogen therapy	Lipid profile
Gruber et al. 1998	Natural menopause	Transdermal gel vs Placebo	No concurrent estrogen therapy	Lipid profile
Musculoskeletal health				
Barrett-Connor et al. 1999	Surgical menopause	Oral testosterone	Oral estrogen	Bone mineral density
Dobs et al. 2002	Surgical menopause+ Natural menopause	Oral testosterone	Oral estrogen	Body composition Muscle strength
Floter et al. 2005	Surgical menopause	Oral testosterone	Oral estrogen	Bone mineral density
Leao et al. 2006	Surgical menopause	Oral testosterone	Oral estrogen	Body composition (visceral fat)

Watts et al. 1995	Surgical menopause	Oral testosterone	Oral estrogen	Bone mineral density
Miller et al. 2000	Surgical menopause+ Natural menopause	Sublingual testosterone	Sublingual estrogen+Progestogen	Bone mineral density Bone metabolism
Gruber et al. 1998	Natural menopause	Transdermal gel vs Placebo	No concurrent estrogen therapy	Bone mineral density
Davis et al. 2000	Surgical menopause+ Natural menopause	Implant	Implant estradiol	Bone mineral density
Davis et al. 1995	Surgical menopause+ Natural menopause	Implant	Implant estradiol	Bone mineral density
Huang et al. 2014, 2014	Surgical menopause+ Natural menopause	Intramuscular injections of Testosterone enanthate	Intramuscular injections	Body composition Muscle strength Abdominal fat volumes
Psychological general wellbeing (PGWB)				
Dias et al. 2006	Natural menopause	Oral testosterone	Oral estrogen	Depression
Floter et al. 2005	Surgical menopause	Oral testosterone	Oral estrogen	PGWB
Moller et al. 2013	Surgical menopause	Oral testosterone	Oral estrogen	PGWB
Davis et al. 2006	Surgical menopause	Transdermal patch vs Placebo	Transdermal estrogen	PGWB
El-Hage et al. 2007	Surgical menopause	Transdermal cream vs Placebo	Transdermal estrogen	DASS POMS
Nathrost-Boos et al. 2006	Natural menopause	Transdermal gel vs Placebo	Oral/Transdermal estrogen	PGWB
Shifren et al. 2000	Surgical menopause	Oral testosterone + Transdermal patch	Oral estrogen + Transdermal patch	PGWB
Davis et al. 2008	Women with low sexual desire	Transdermal spray vs Placebo	No concurrent estrogen therapy	PGWB
Davis et al. 2014	Natural menopause	Transdermal gel vs Placebo	No concurrent estrogen therapy	PGWB
Fooladi et al. 2014*	Women with SSRI/SNRI therapy	Transdermal patch vs Placebo	Not applicable	PGWB, POMS, BDI-II
Goldstat et al. 2003	Women with low sexual desire	Transdermal cream vs Placebo	Not applicable	PGWB, BDI
Cognitive function				
Moller et al. 2010	Surgical menopause	Oral testosterone	Oral estrogen	Memory function: WAIS-R, RBMT
Moller et al. 2013	Surgical menopause	Oral testosterone	Oral estrogen	Cognitive fatigue: WAIS-R
Wisniewski et al. 2002	Surgical menopause+ Natural menopause	Oral testosterone	Oral estrogen	Cognitive task performance

Huang et al. 2015	Surgical menopause	Intramuscular injections of testosterone enanthate	Intramuscular injections	Cognitive function
Davis et al. 2014	Natural menopause	Transdermal gel vs Placebo	No concurrent estrogen therapy	Verbal learning and memory ISLT
Menopausal symptoms				
Barrett-Connor et al. 1999	Surgical menopause	Oral testosterone	Oral estrogen	Vaginal dryness
Liu et al. 2011	Natural menopause	Oral testosterone	Oral estrogen	Hot flashes
Simon et al. 1999	Natural menopause	Oral testosterone	Oral estrogen	Menopausal symptoms
Watts et al. 1995	Surgical menopause	Oral testosterone	Oral estrogen	Hot flashes
Cardiovascular disease				
Kocoska-Maras et al. 2009	Surgical menopause	Oral testosterone	Oral estrogen	Cardiovascular disease; inflammatory markers
Leao et al. 2006	Surgical menopause	Oral testosterone	Oral estrogen	Inflammatory markers Glucose metabolism
Huang et al. 2014	Surgical menopause	Intramuscular injections of testosterone enanthate	Intramuscular injections	Cardiovascular disease risk markers: Lipid Insulin resistance Inflammatory markers BP and hear rate
Breast health				
Hofling et al. 2007, 2007	Natural menopause	Transdermal patch vs Placebo	Oral estrogen	Breast cell proliferation Breast density
Davis et al. 2009	Surgical menopause+ Natural menopause	Transdermal patch vs Placebo	No concurrent estrogen therapy	Brest density
Others				
Hickok et al. 1993	Natural menopause	Oral testosterone	Oral estrogen	Endometrial histology
Huang et al. 2015	Surgical menopause	Intramuscular injections of testosterone enanthate	Intramuscular injections	Voice change
Simon et al. 1999	Natural menopause	Oral testosterone	Oral estrogen	Gonadotropin Endogenous androgen bioavailability
Androgenic and non-androgenic adverse events				
Barrett-Connor et al. 1999	Surgical menopause	Oral testosterone	Oral estrogen	Non-androgenic adverse events: discontinuation rate Androgenic adverse events: Acne, hirsutism
Basaria et al. 2002	Surgical menopause+ Natural menopause	Oral testosterone	Oral estrogen	No adverse events (data not shown)

Liu et al. 2011	Natural menopause	Oral testosterone	Oral estrogen	Vaginal bleeding, breast pain (no test results). None of them were severe judged by the investigators.
Lobo et al. 2003	Surgical menopause+ Natural menopause	Oral testosterone	Oral estrogen	All adverse events Non-androgenic adverse events: Headache, infection, hot flushes, flue, rhinitis, breast pain, acne. Androgenic adverse events: Acne, hirsutism.
Watts et al. 1995	Surgical menopause	Oral testosterone	Oral estrogen	Headache, hot flushes, edema, breast pain, hair disorder, acne.
Braunstein et al. 2005	Surgical menopause	Transdermal patch vs Placebo	Oral estrogen	Any adverse events Serious adverse events Withdrawal Non-androgenic adverse events: Site reaction, respiratory infection breast pain, headache Androgenic adverse events: Acne, hirsutism
Shifren et al. 2006	Natural menopause	Transdermal patch vs Placebo	Oral estrogen	Any adverse events Serious adverse events Withdrawal Non-androgenic adverse events: Site reaction, respiratory infection, facial hair Androgenic adverse events: Acne, alopecia, voice deepening, clitoral enlargement.
Simon et al. 2005	Surgical menopause	Transdermal patch vs Placebo	Oral estrogen	Any adverse events Serious adverse events Withdrawal Non-androgenic adverse events: Site reaction, respiratory infection, headache Androgenic adverse events: Acne, alopecia, voice deepening.
Buster et al. 2005	Surgical menopause			Any adverse events Serious adverse events Withdrawal Non-androgenic adverse events: Site reaction, respiratory infection, facial hair Androgenic adverse events: Acne, alopecia, voice deepening.
Shifren et al. 2000	Surgical menopause	Oral testosterone + Transdermal patch	Oral estrogen + Transdermal patch	Androgenic adverse events: Acne, hirsutism, facial depilation
Davis et al. 2006	Surgical menopause	Transdermal patch vs Placebo	Transdermal estrogen	Any adverse events Serious adverse events

				Withdrawal Non-androgenic adverse events: Site reaction, respiratory infection, breast pain, headache, facial hair Androgenic adverse events: Acne, hirsutism, facial depilation
Huang et al. 2014	Surgical menopause	Intramuscular injections of testosterone enanthate	Intramuscular injections	No serious adverse events
Panay et al. 2010	Natural menopause	Transdermal patch vs Placebo	No concurrent estrogen therapy (74%) 26% Oral transdermal	Any adverse events Serious adverse events Withdrawal Non-androgenic adverse events: Site reaction Androgenic adverse events: Acne, alopecia, hirsutism, voice deepening.
Davis et al. 2008	Surgical menopause+ Natural menopause	Transdermal patch vs Placebo	No concurrent estrogen therapy	Any adverse events Serious adverse events Withdrawal Non-androgenic adverse events: Site reaction, respiratory infection, breast cancer, headache, facial hair Androgenic adverse events: Acne, alopecia, hirsutism, voice deepening.
Davis et al. 2008	Premenopause	Transdermal spray vs Placebo	No applicable	Total adverse events Withdrawal Non-androgenic adverse events: Site reaction, respiratory infection, headache, facial hair, nausea Androgenic adverse events: Acne, voice change, mFG score.
Fooladi et al. 2014*	Women with SSRI/SNRI therapy	Transdermal patch vs Placebo	Not applicable	No adverse events (data not shown)
Goldstat et al. 2003	Premenopause	Transdermal cream vs Placebo	Not applicable	No adverse events (data not shown)

*Some postmenopausal women might be included.

DASS= Depression Anxiety Stress Scale, POMS= the Profile of Mood States, SSRIs= selective serotonin reuptake inhibitors, SNRIs= Serotonin noradrenalin reuptake inhibitors, BDI= Beck Depression Inventory, WAIS-R=Wechsler Adult Intelligence Scale-Revised, RBMT= Rivermead Behavioural Memory Test, ISLT= The International Shopping List Test.

sFigure 1: Forest plot of comparison: Testosterone versus Comparator: Satisfying Sexual Events by Mode of Oestrogen (E) Administration

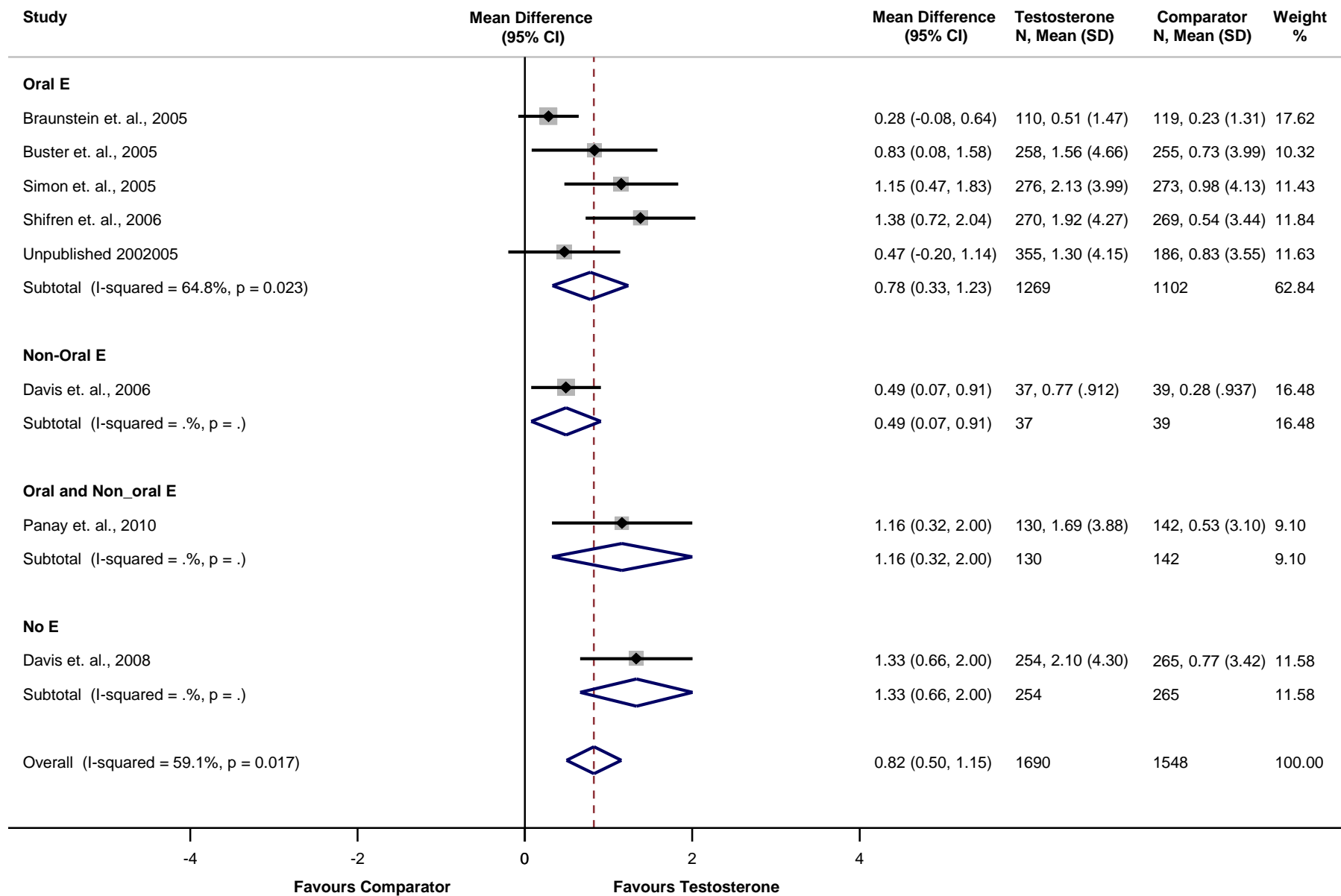
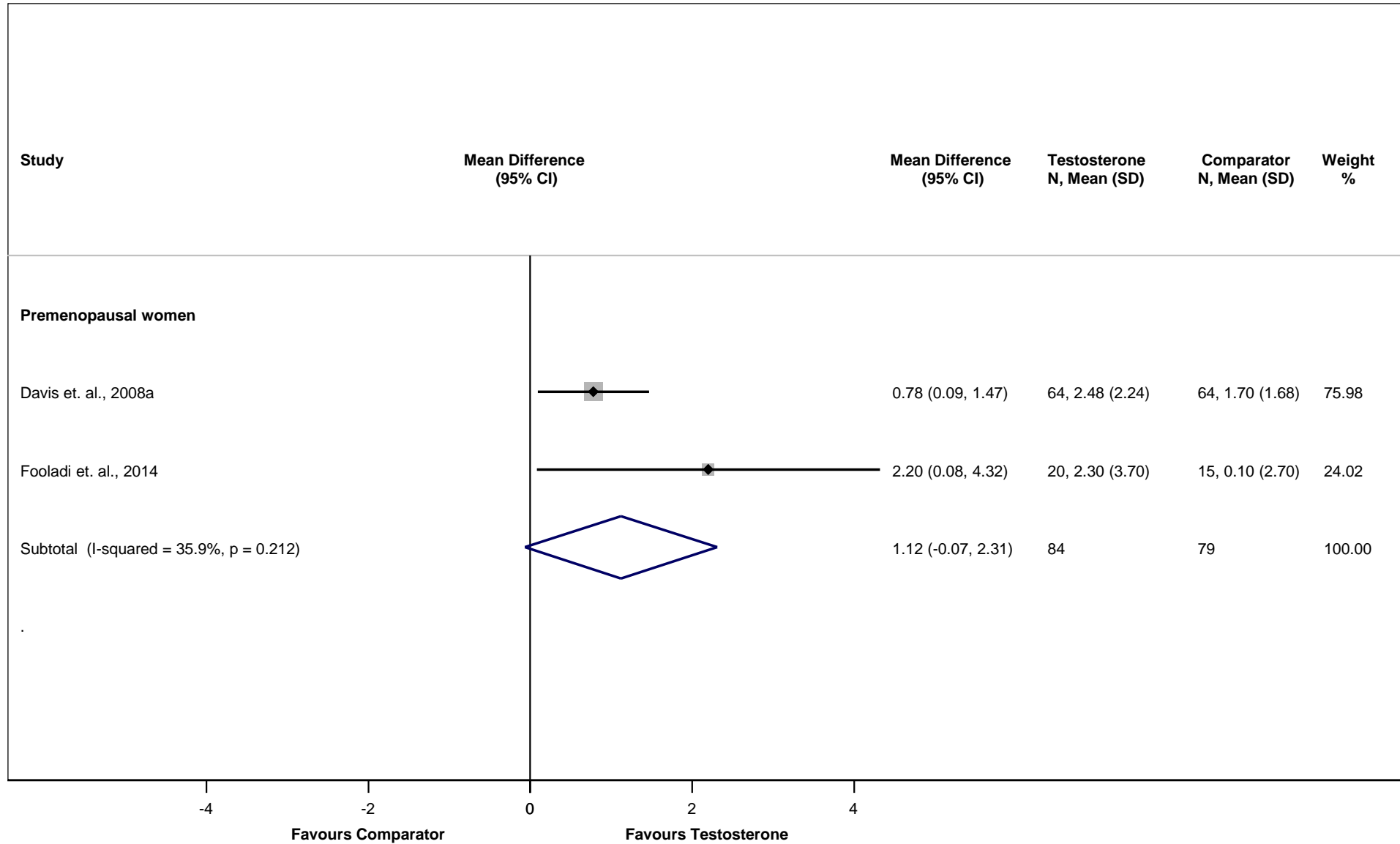


Figure 2: Forest plot of comparison: Testosterone versus Comparator: Satisfying Sexual Events by Menopausal Status



sFigure 3: Forest plot of comparison: Testosterone versus Comparator: Sexual Desire by Menopausal Status

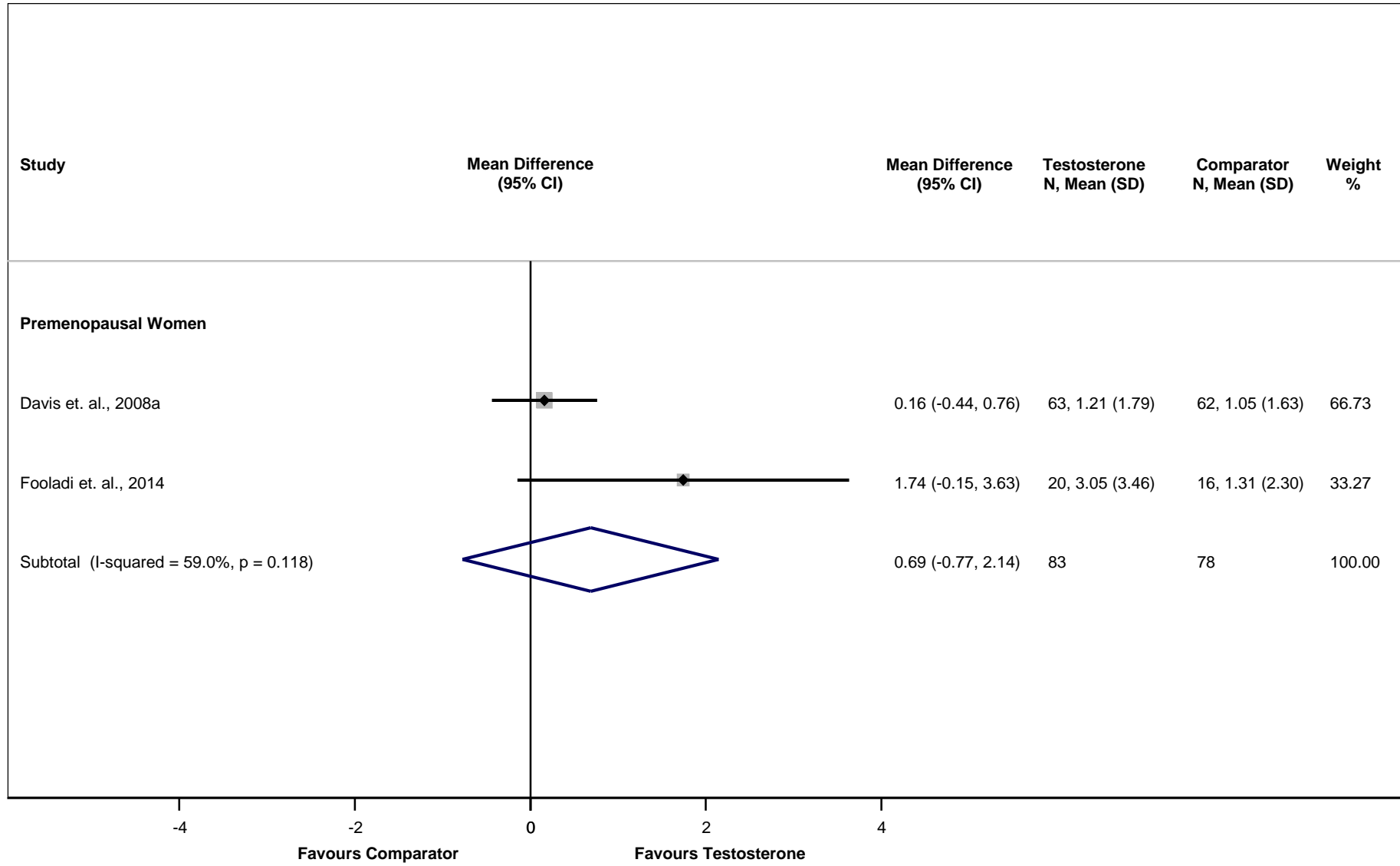
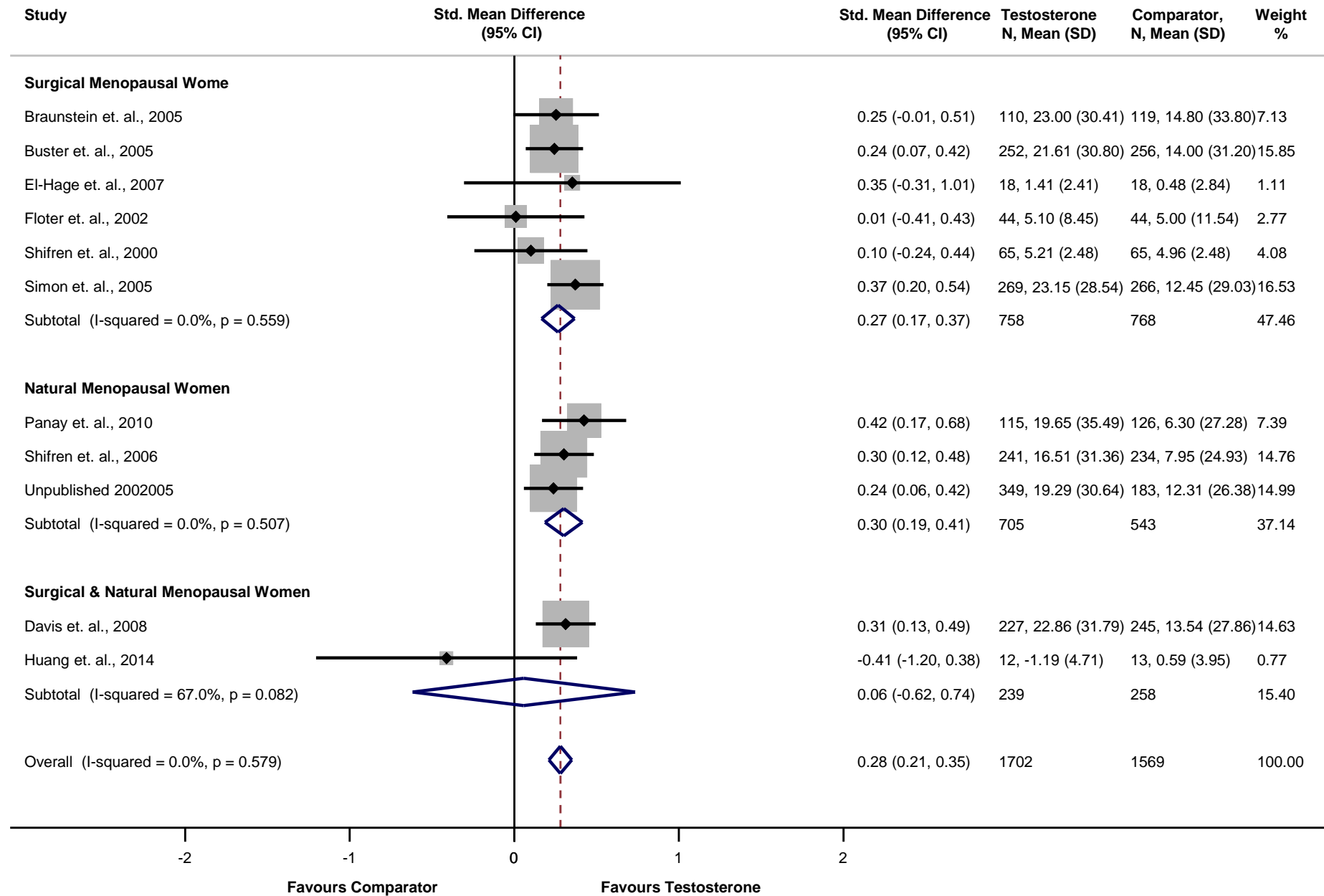
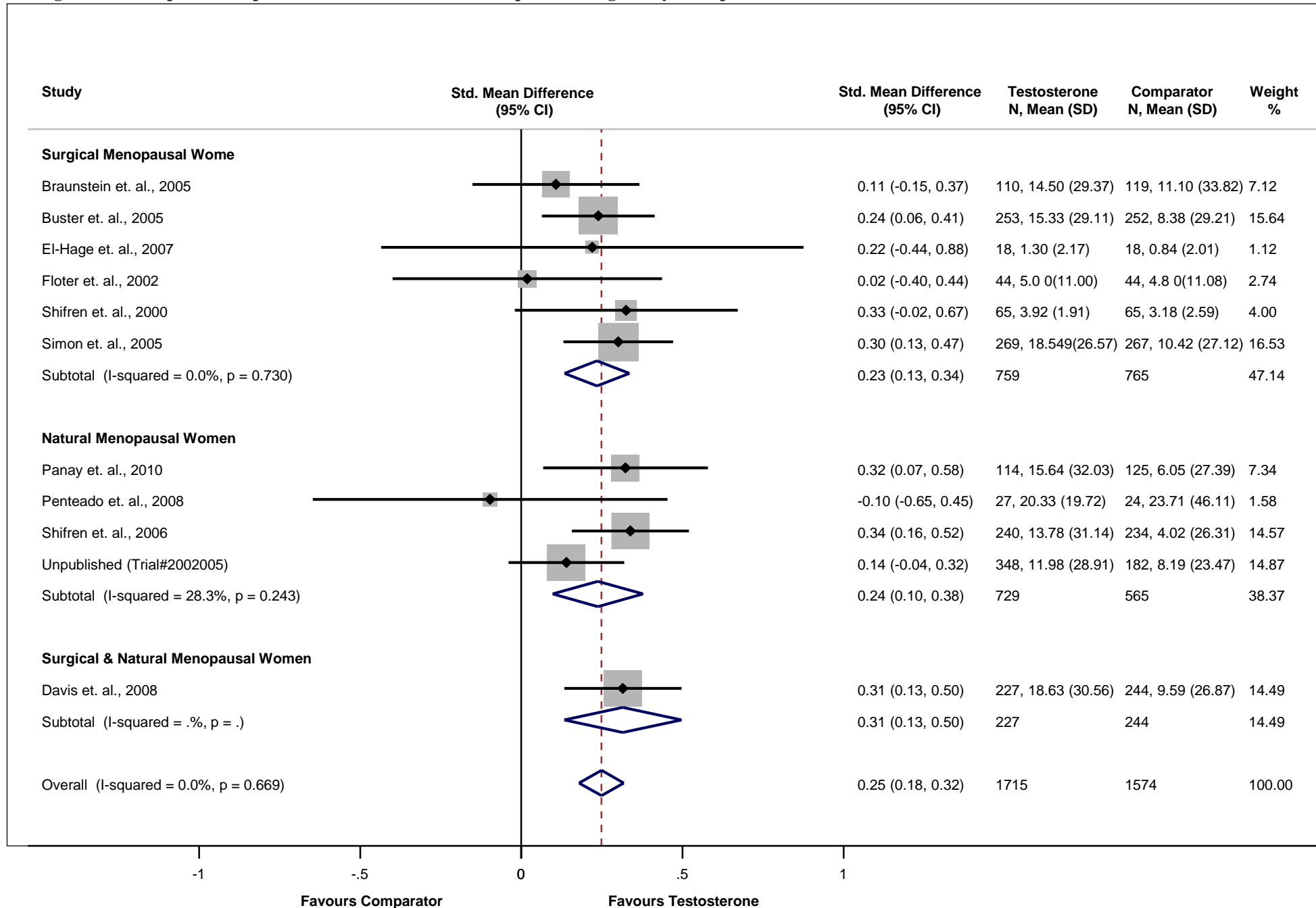


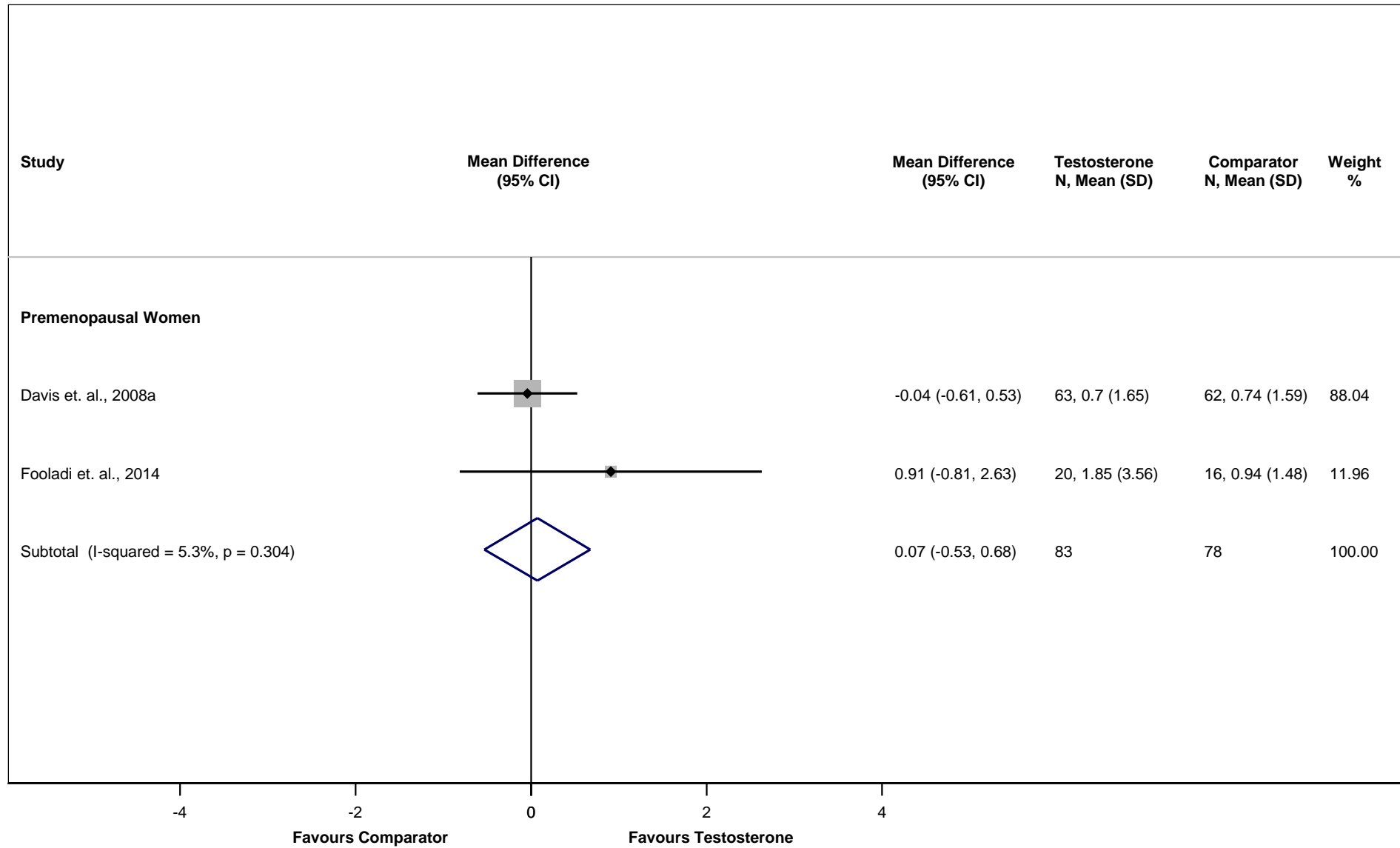
Figure 4: Forest plot of comparison: Testosterone versus Comparator: Arousal by Menopausal Status



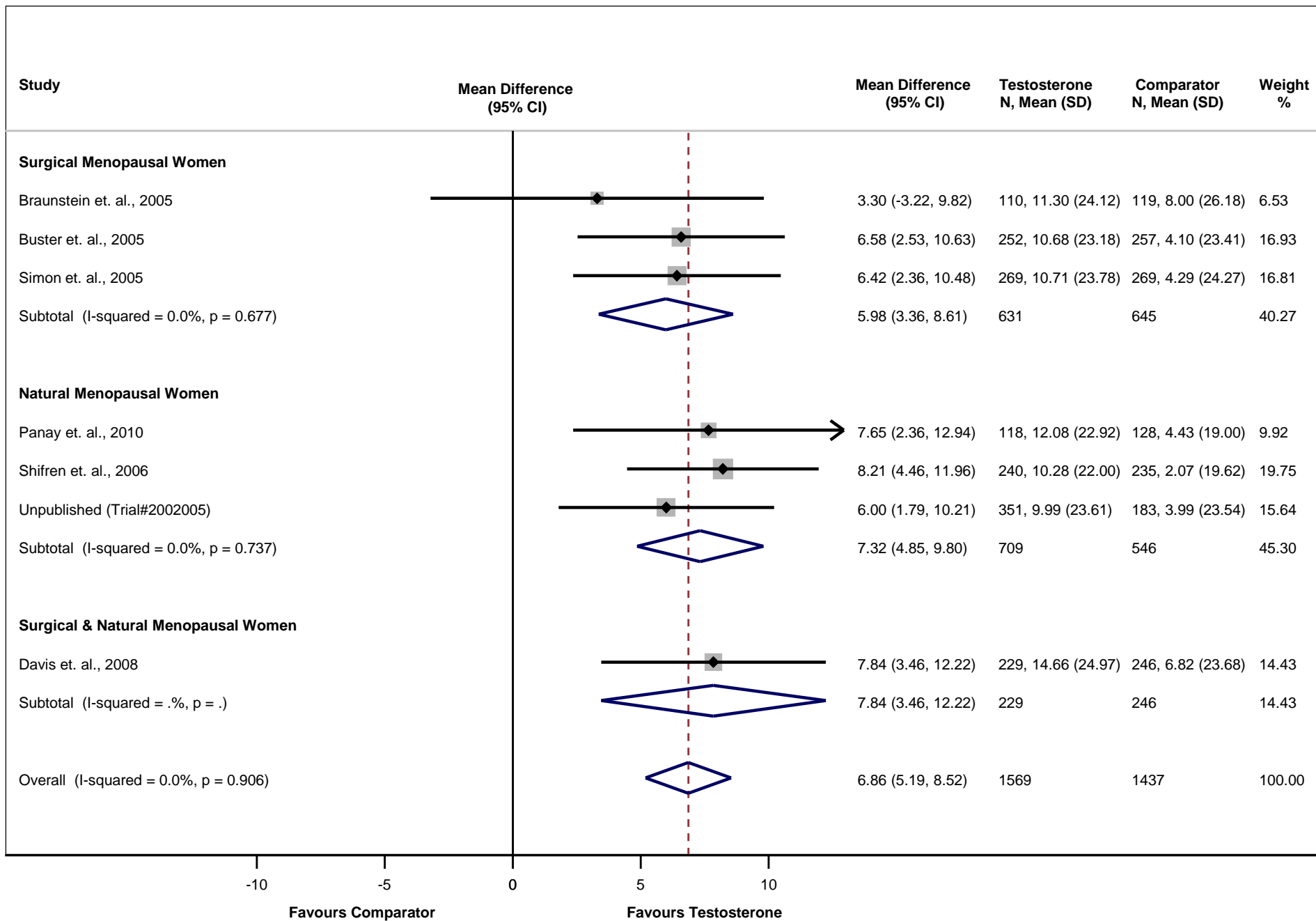
sFigure 5: Forest plot of comparison: Testosterone versus Comparator: Orgasm by Menopausal Status



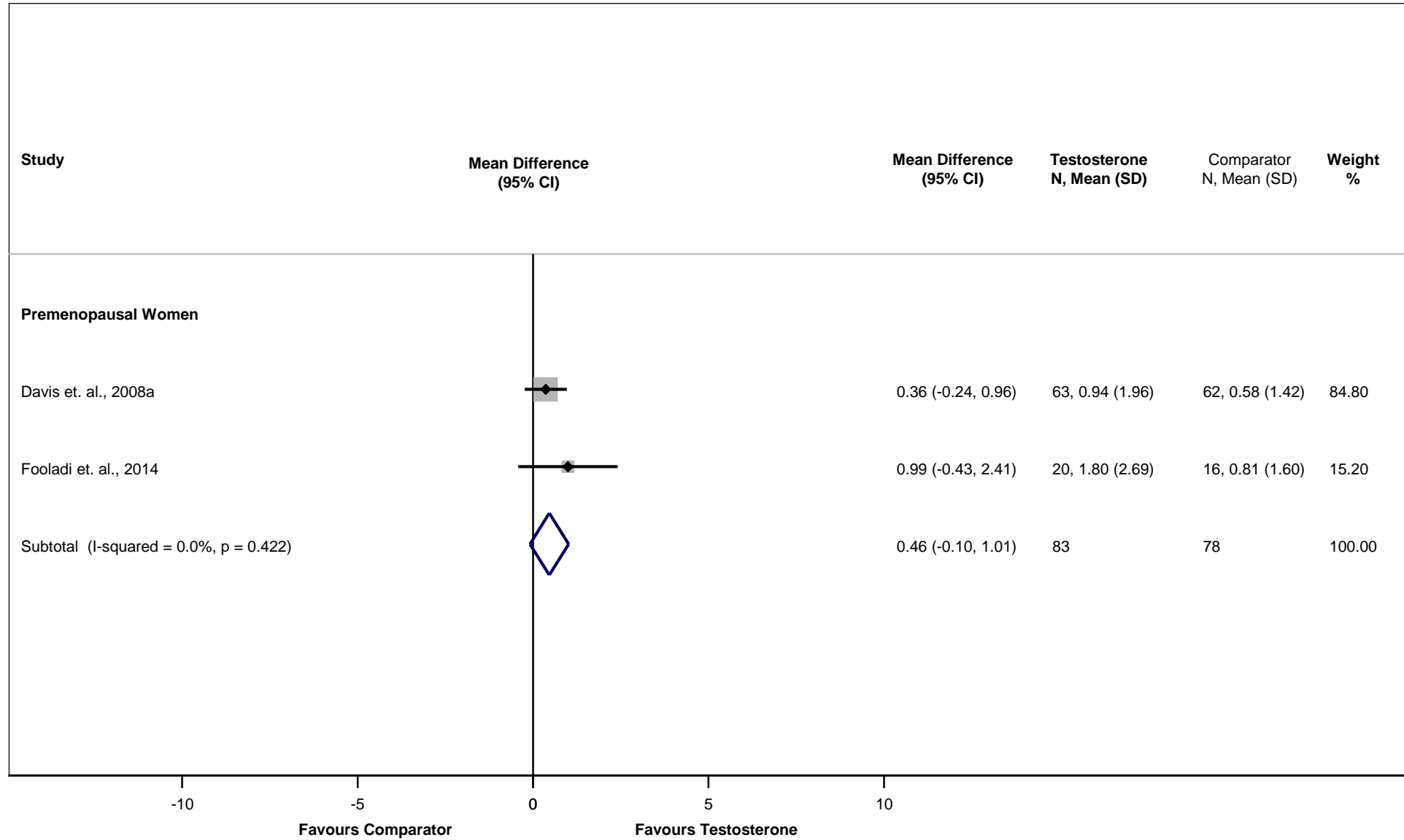
sFigure 6: Forest plot of comparison: Testosterone versus Comparator: Orgasm by Menopausal Status



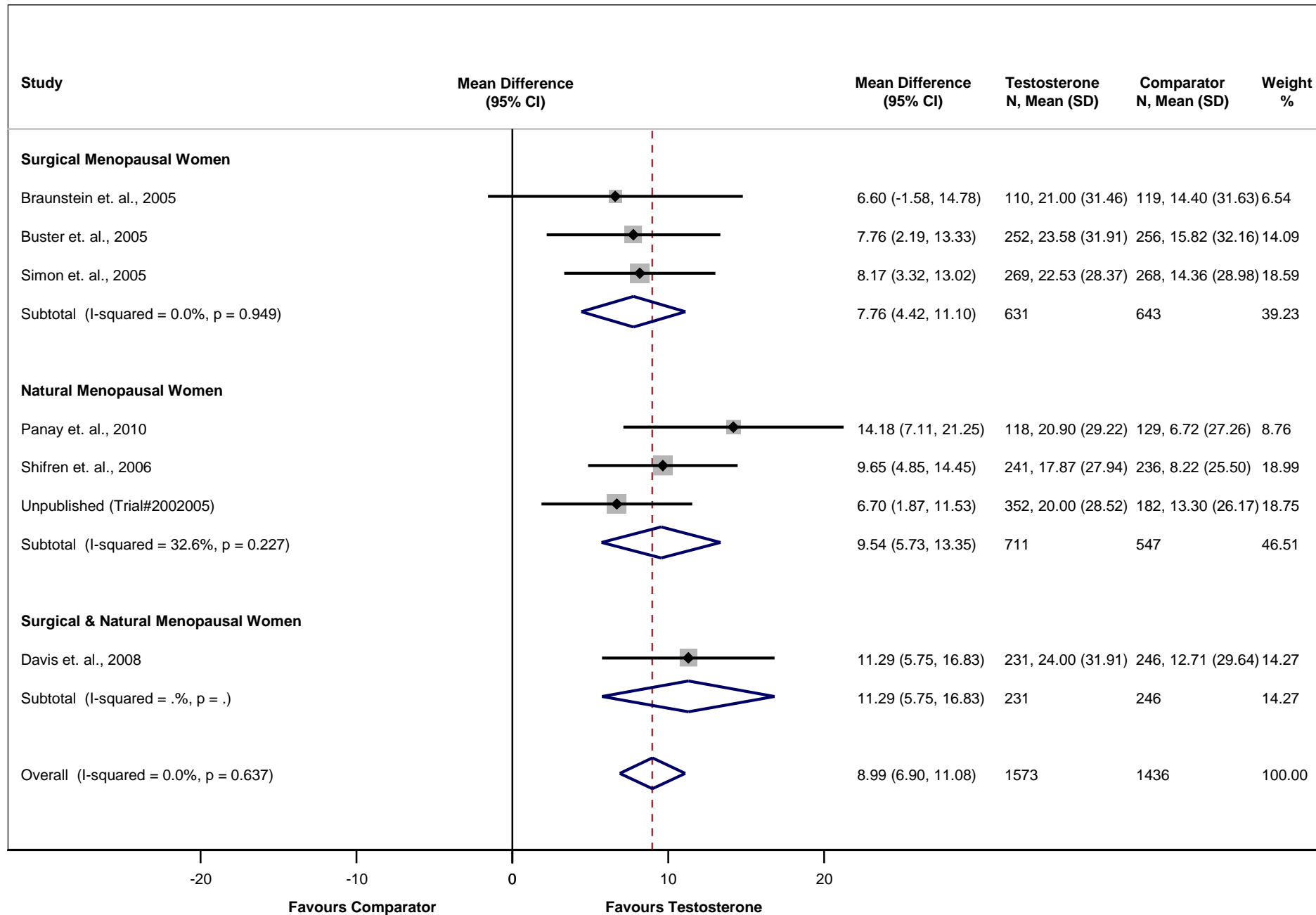
sFigure 7: Forest plot of comparison: Testosterone versus Comparator: Pleasure by Menopausal Status



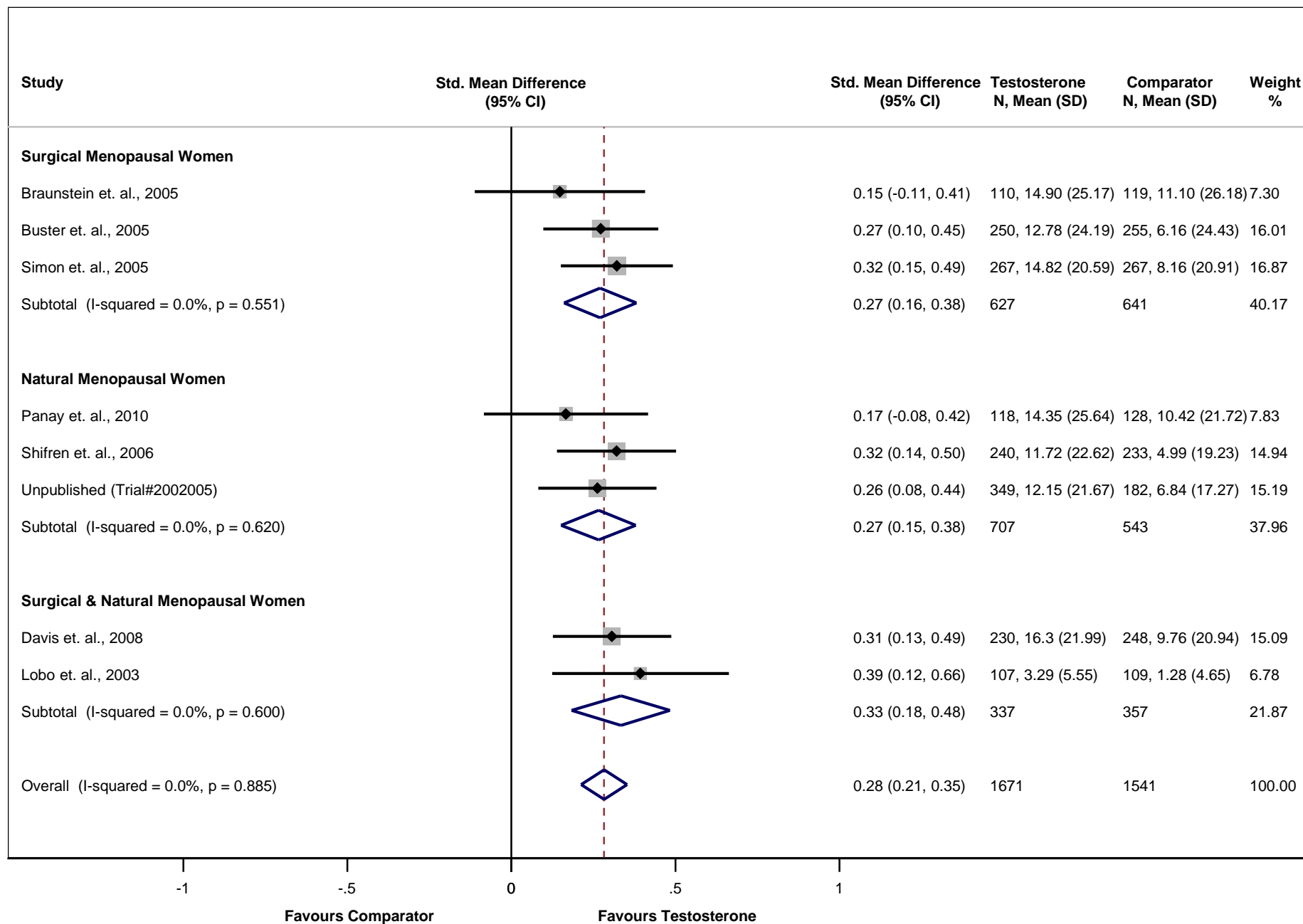
sFigure 8: Forest plot of comparison: Testosterone versus Comparator: Pleasure by Menopausal Status



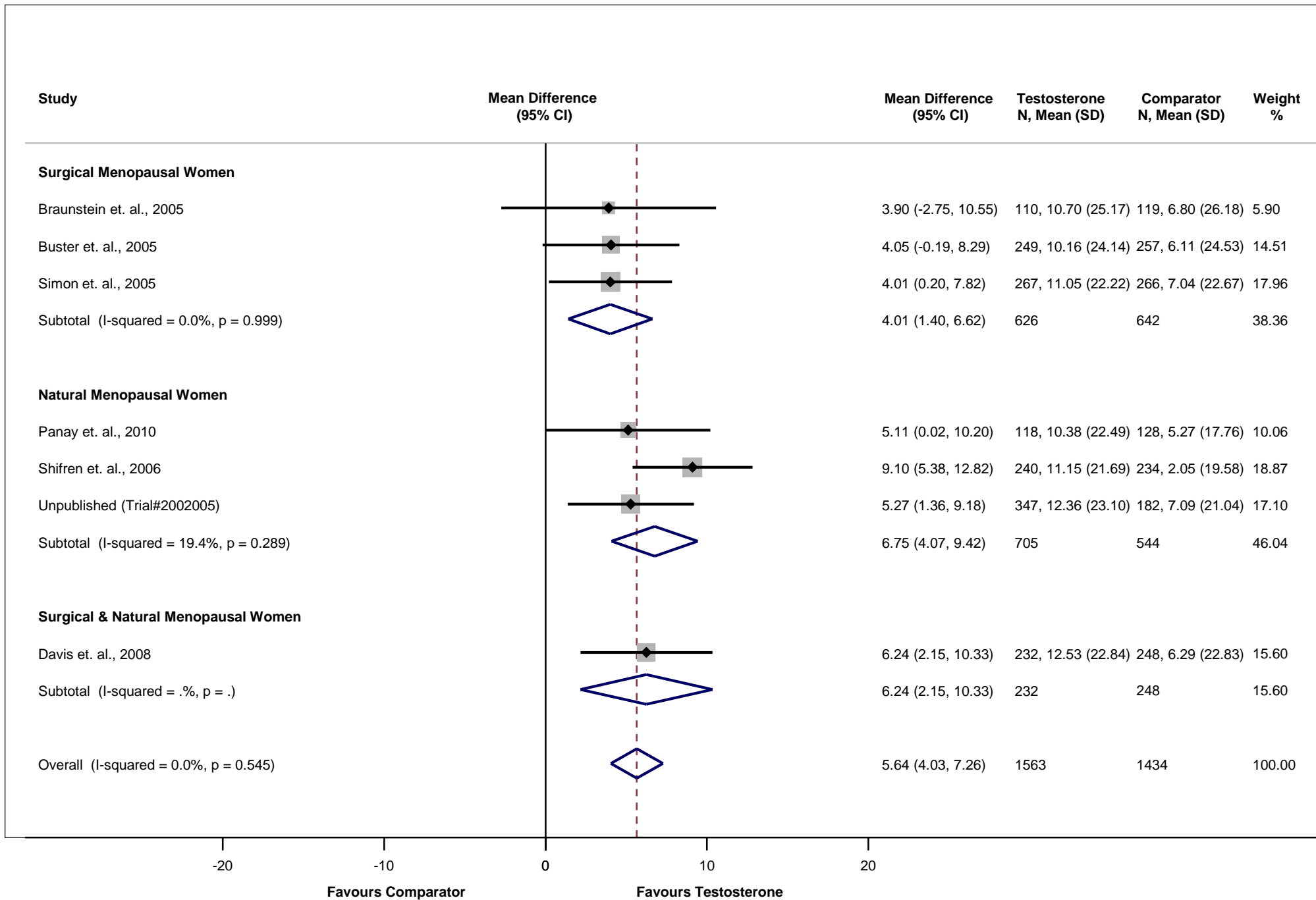
sFigure 9: Forest plot of comparison: Testosterone versus Comparator: Sexual Concerns by Menopausal Status (Higher Score Indicates Less Concern)



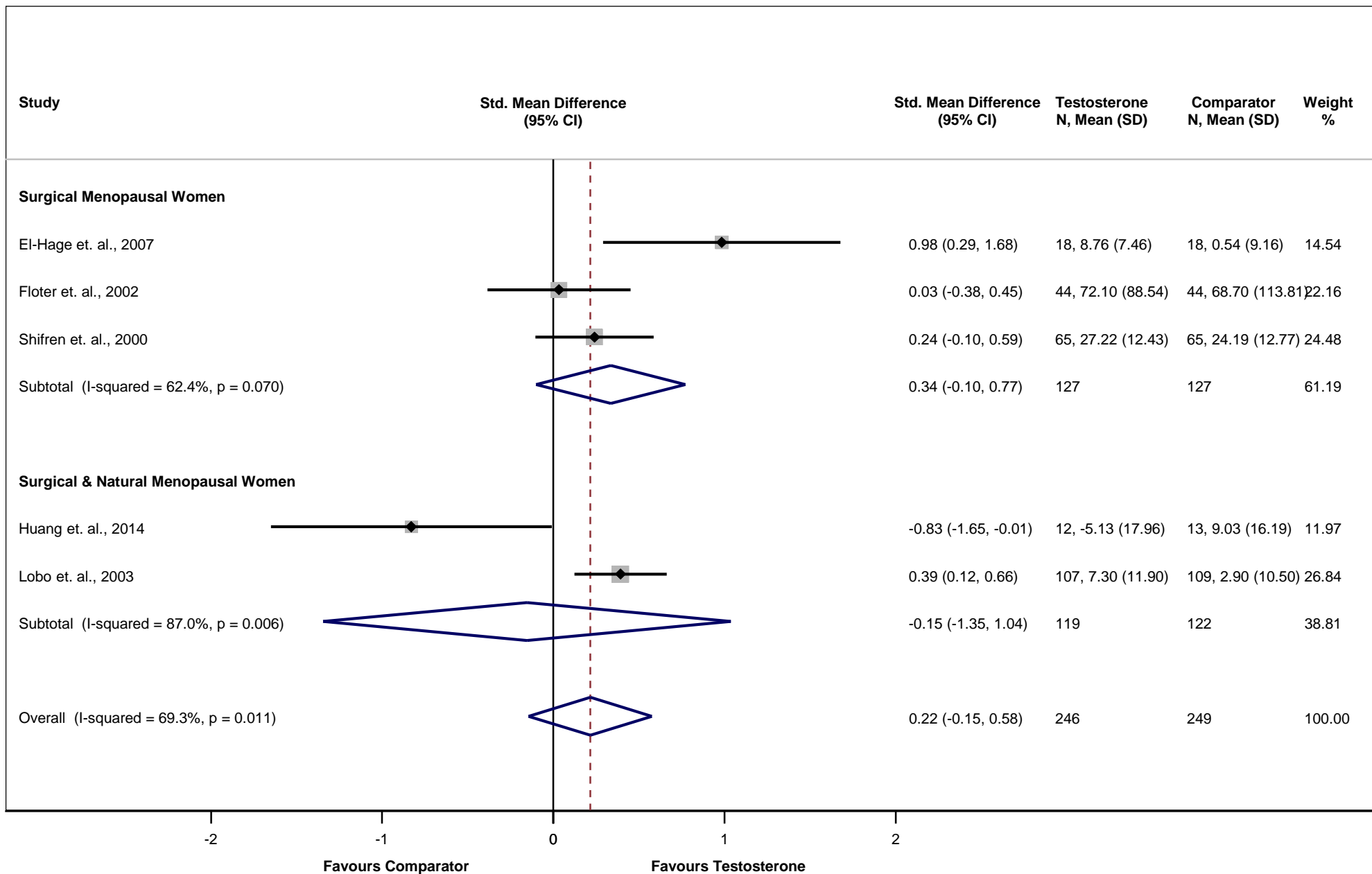
sFigure 10: Forest plot of comparison: Testosterone versus Comparator: Responsiveness by Menopausal Status



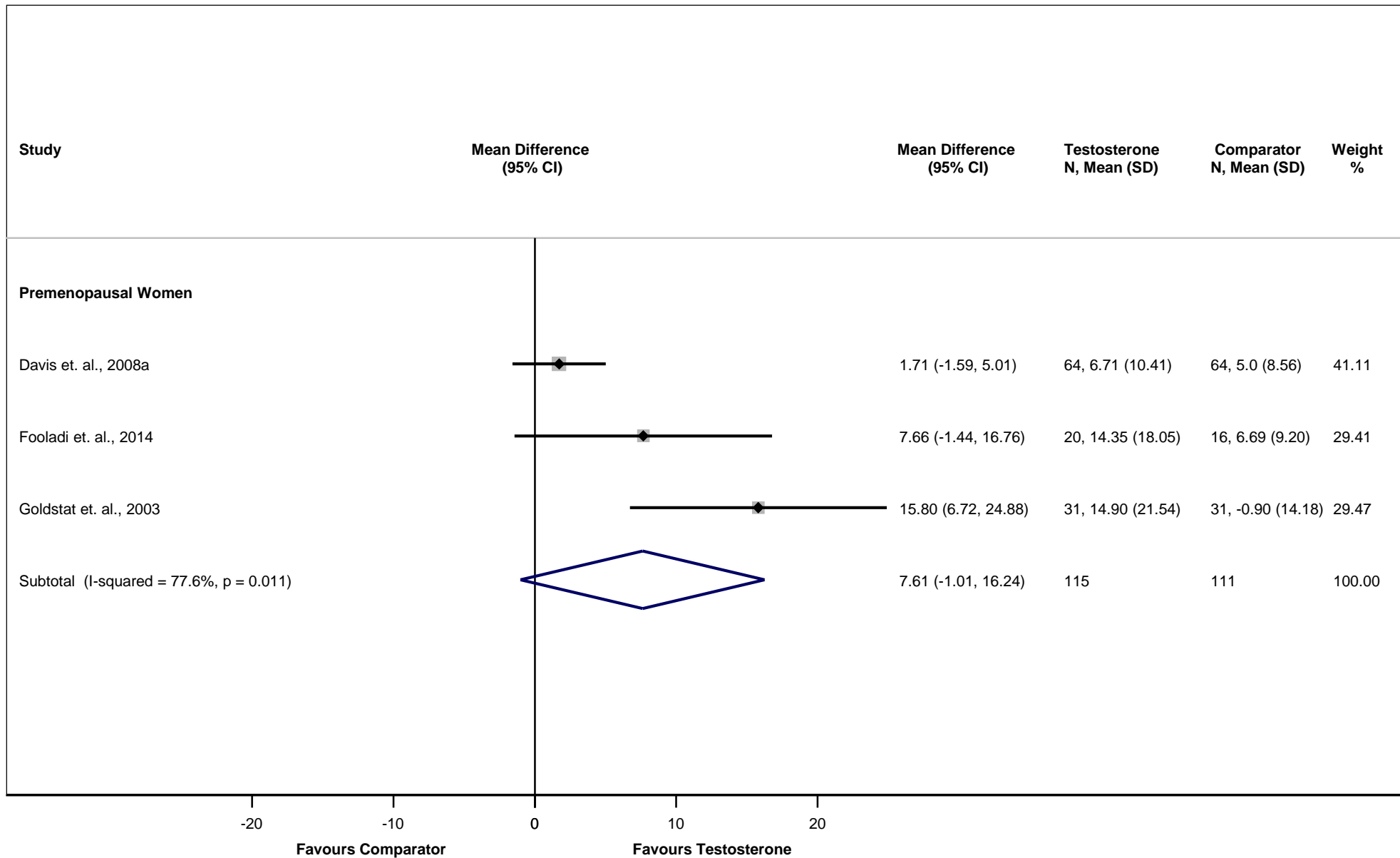
sFigure 11: Forest plot of comparison: Testosterone versus Comparator: Sexual Self-image by Menopausal Status



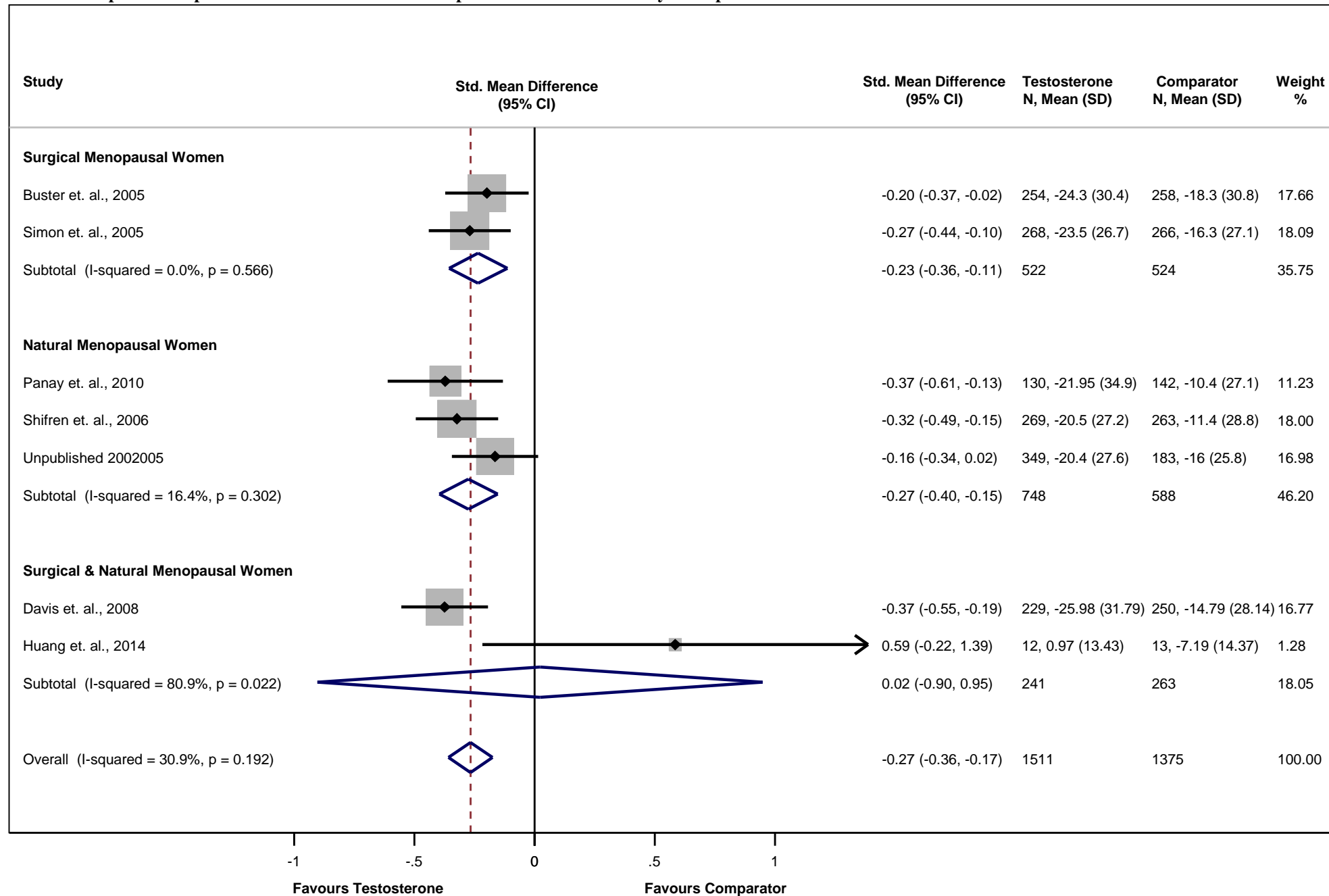
sFigure 12: Forest plot of comparison: Testosterone versus Comparator: Total Sexual Function Score by Menopausal Status



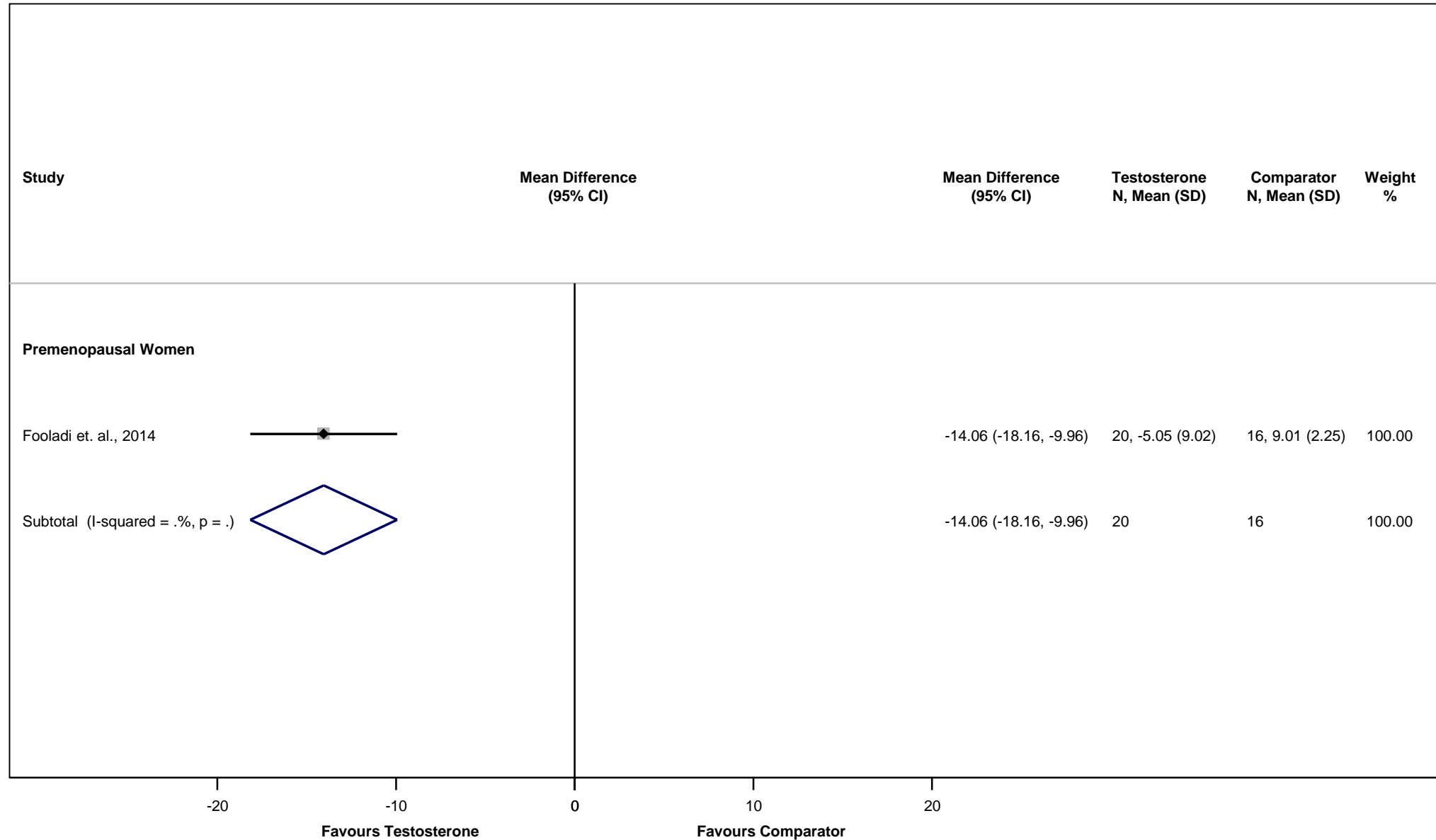
sFigure 13: Forest plot of comparison: Testosterone versus Comparator: Total Sexual Function Score by Menopausal Status



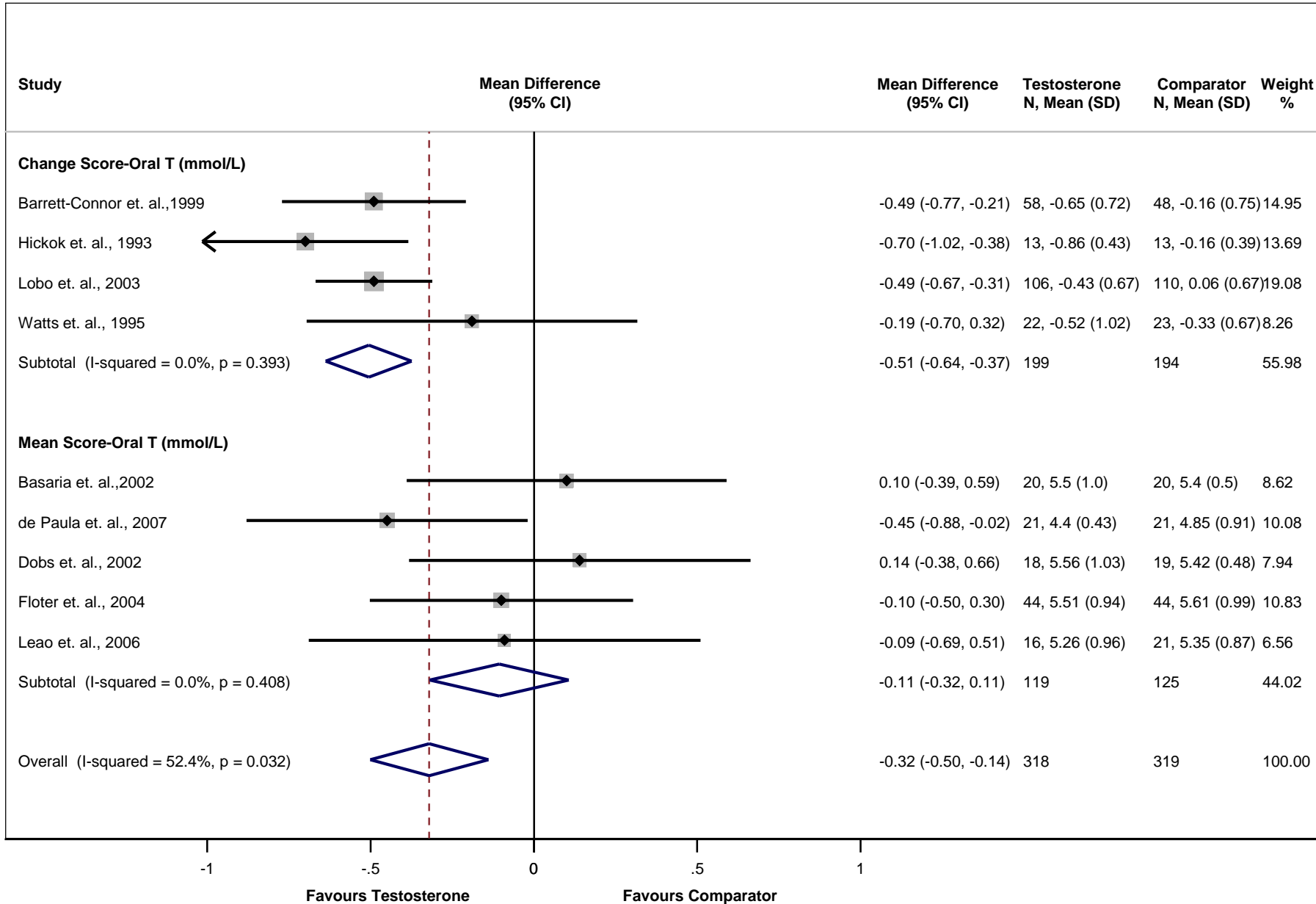
sFigure 14: Forest plot of comparison: Testosterone versus Comparator: Sexual Distress by Menopausal Status



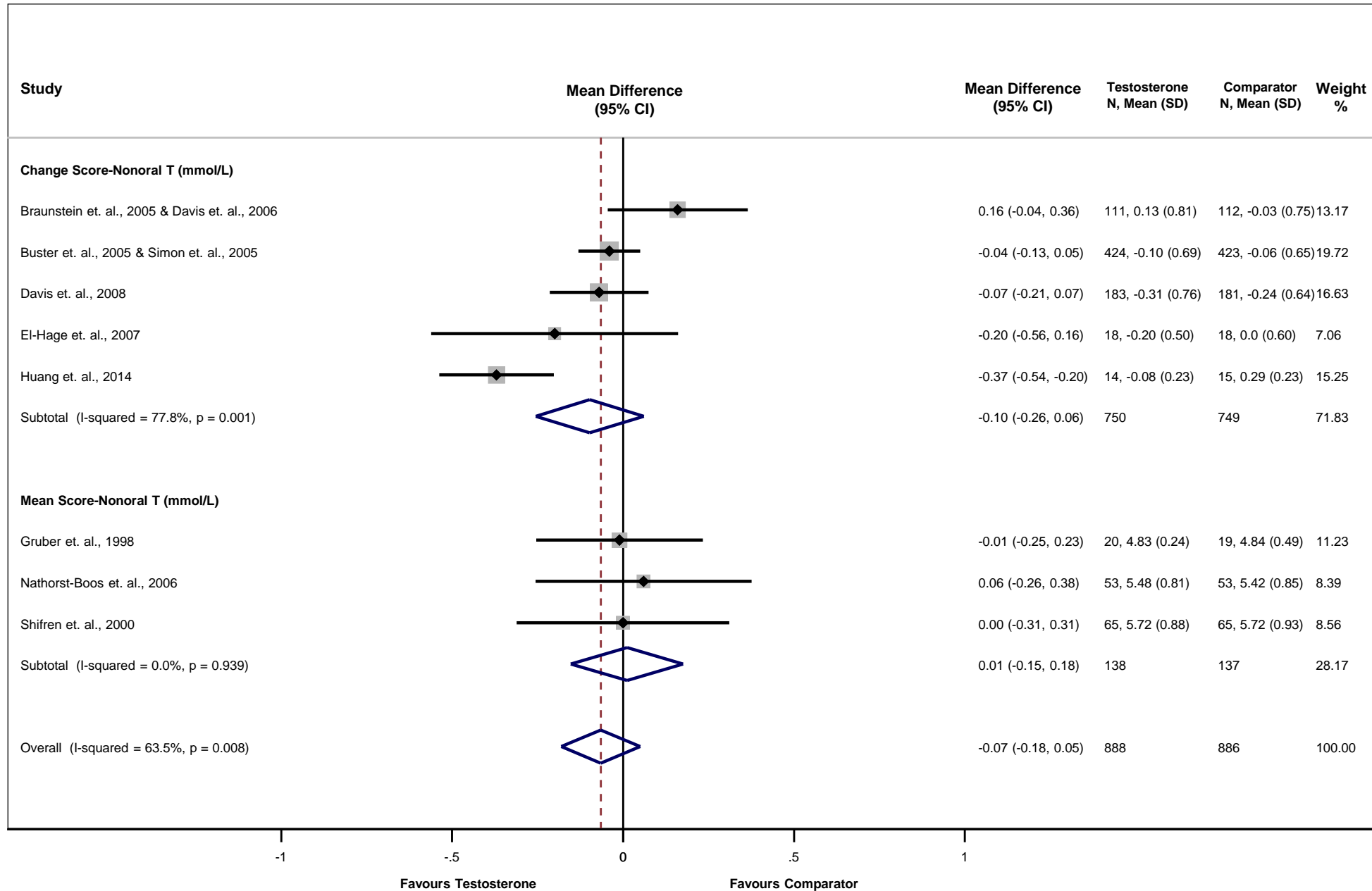
sFigure 15: Forest plot of comparison: Testosterone versus Comparator: Sexual Distress by Menopausal Status



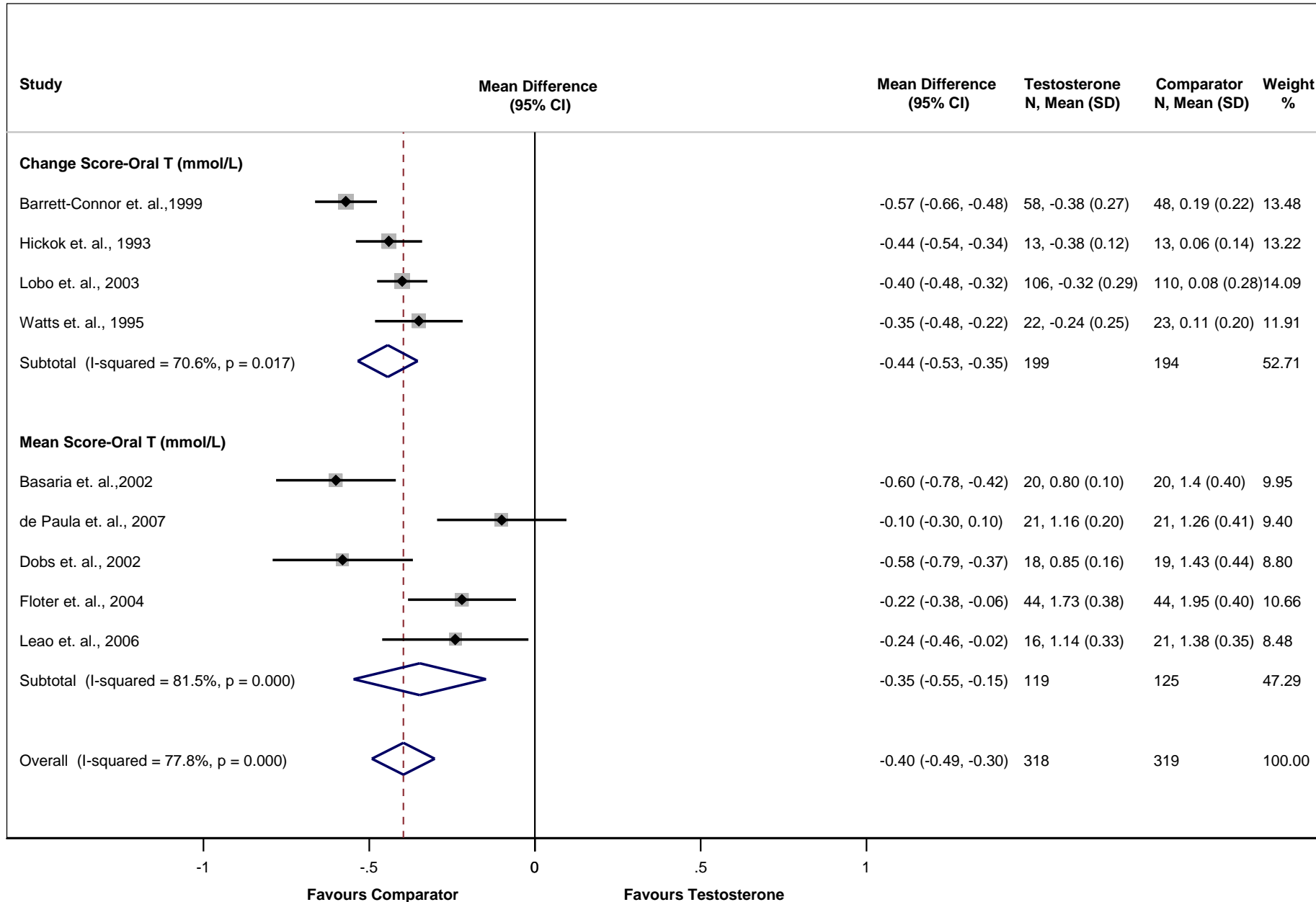
sFigure 16: Forest plot of comparison: Testosterone versus Comparator: Total Cholesterol for Oral T



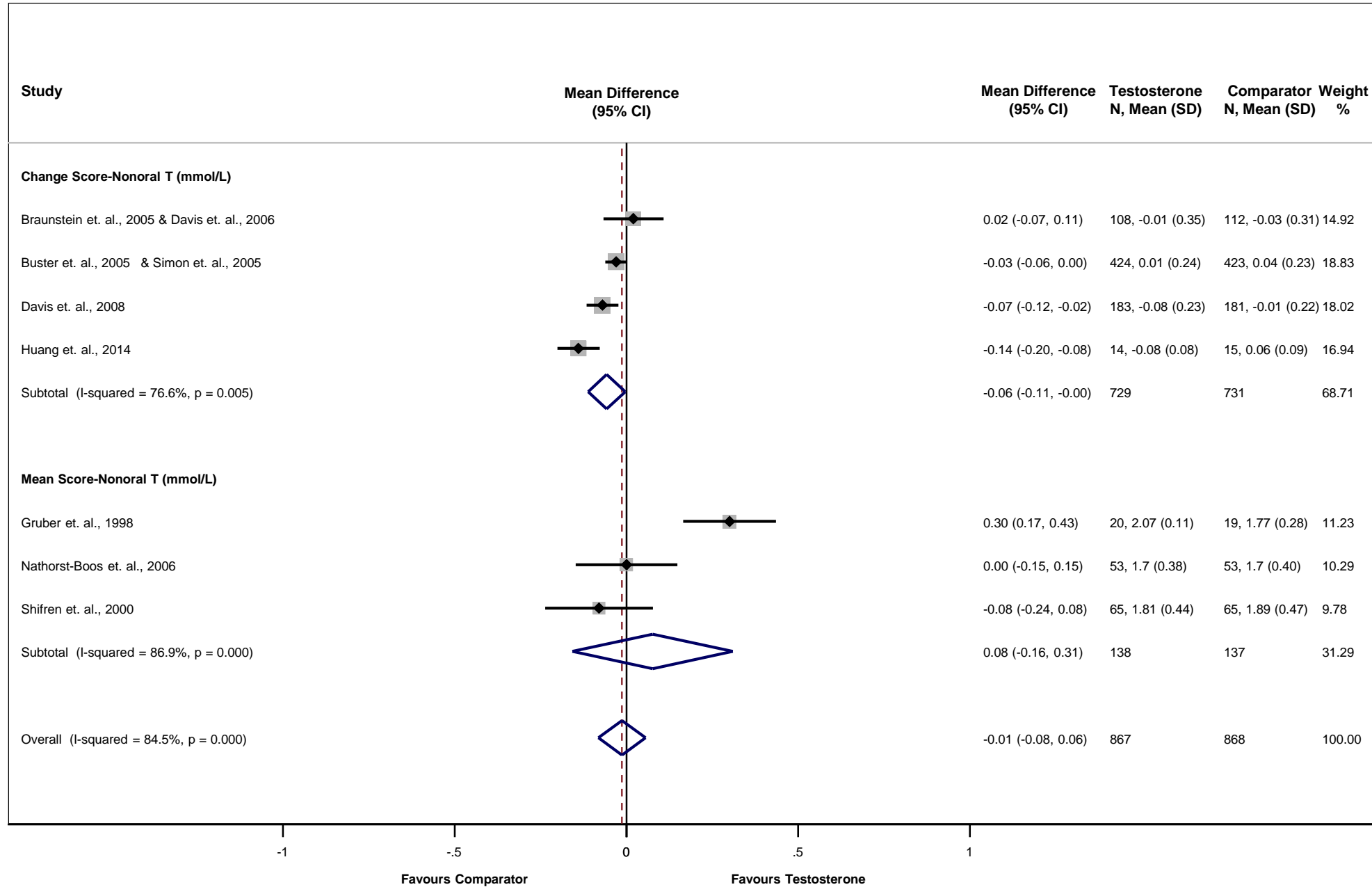
sFigure 17: Forest plot of comparison: Testosterone versus Comparator: Total Cholesterol for Non-oral T



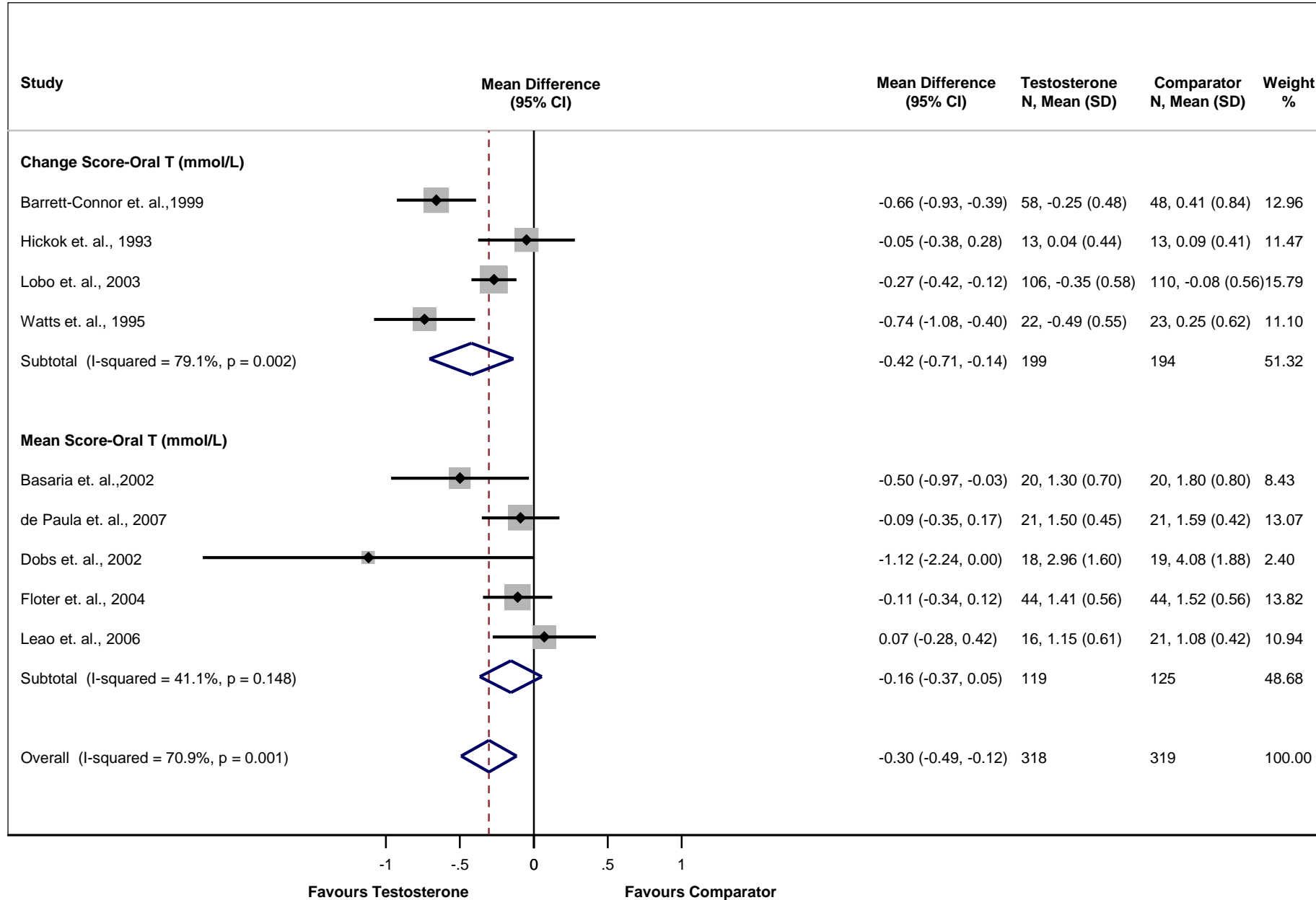
sFigure 18: Forest plot of comparison: Testosterone versus Comparator: HDL Cholesterol for Oral T



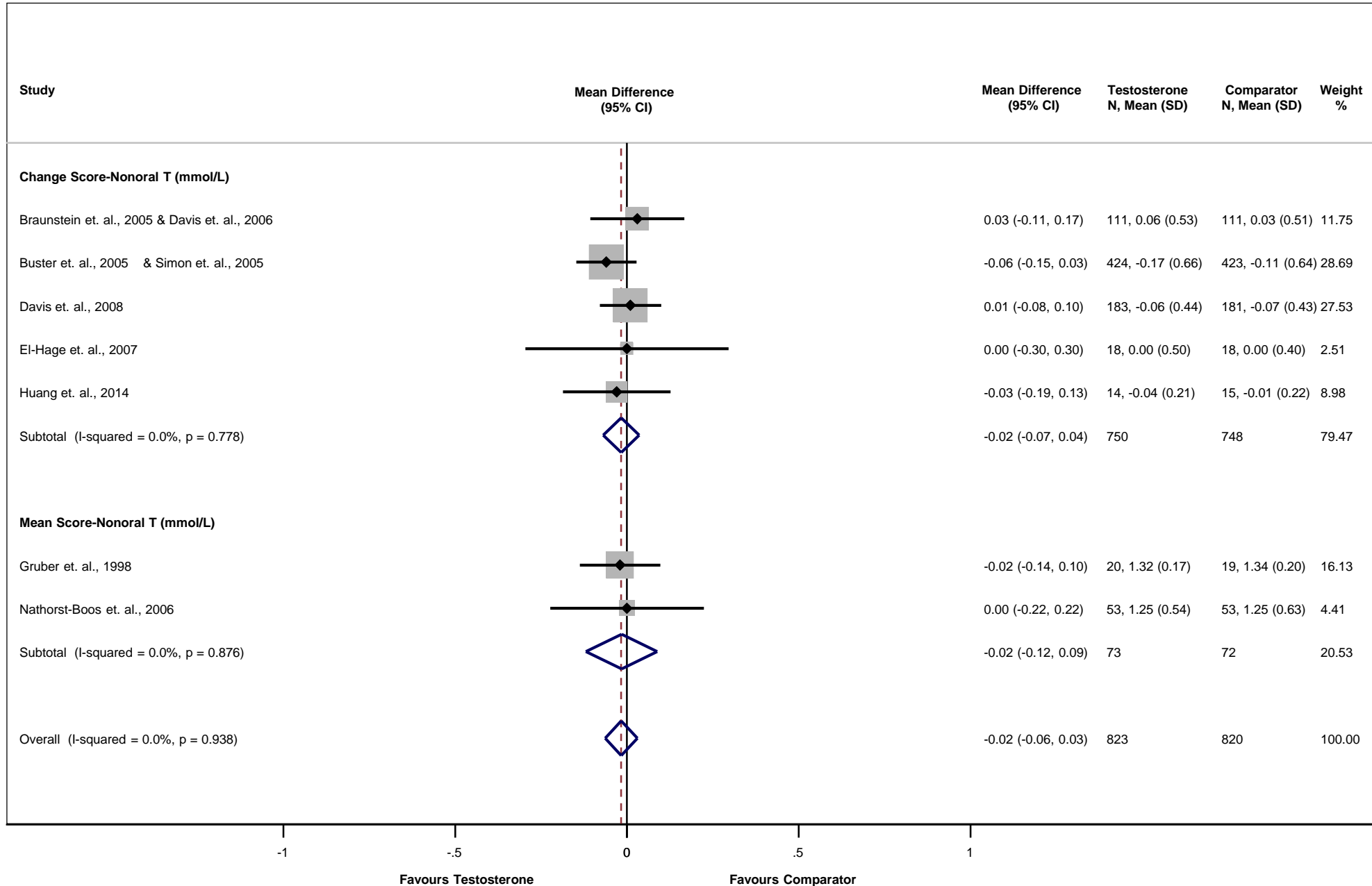
sFigure 19: Forest plot of comparison: Testosterone versus Comparator: HDL Cholesterol for Non-oral T



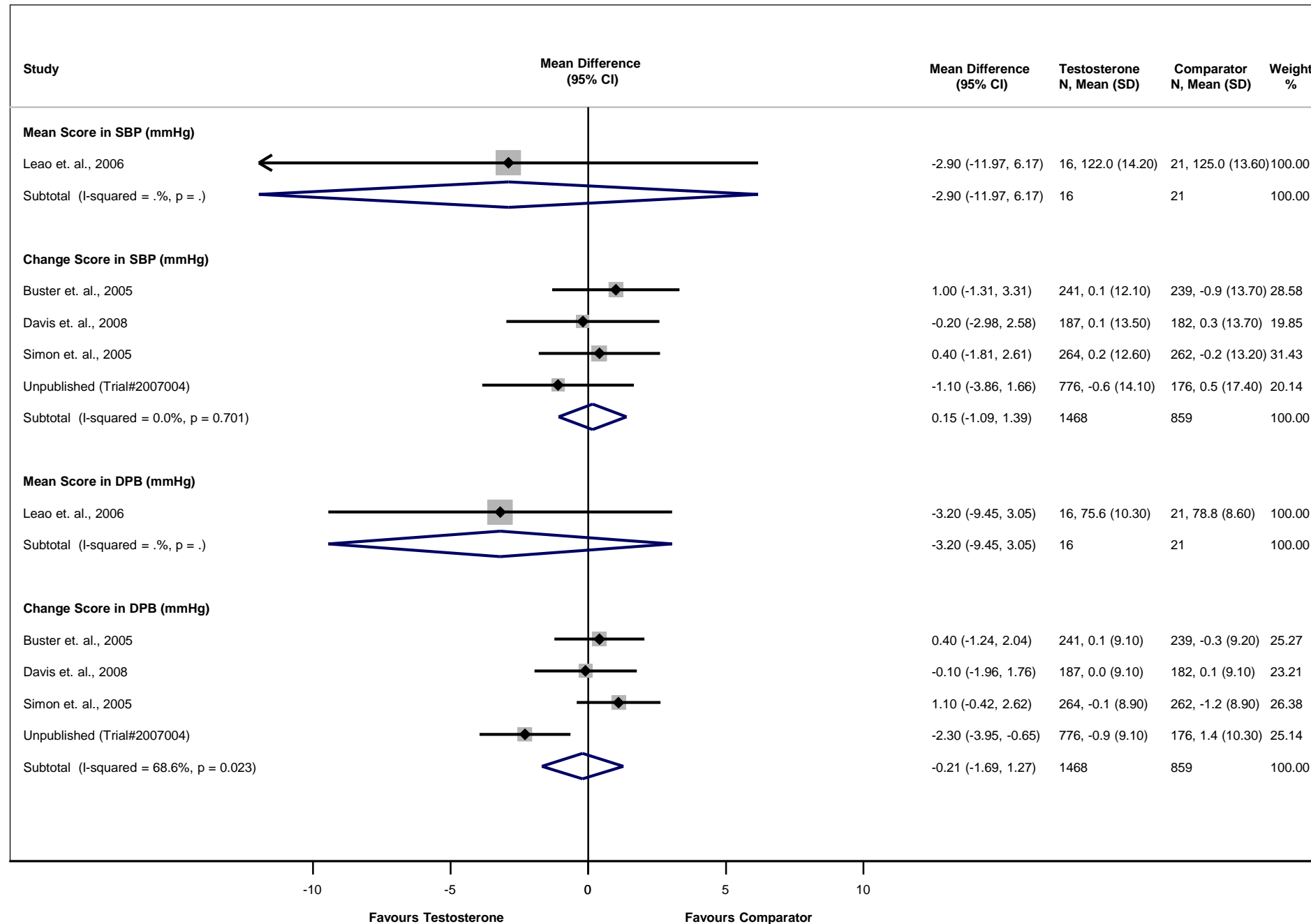
sFigure 20: Forest plot of comparison: Testosterone versus Comparator: Triglyceride Cholesterol for Oral T



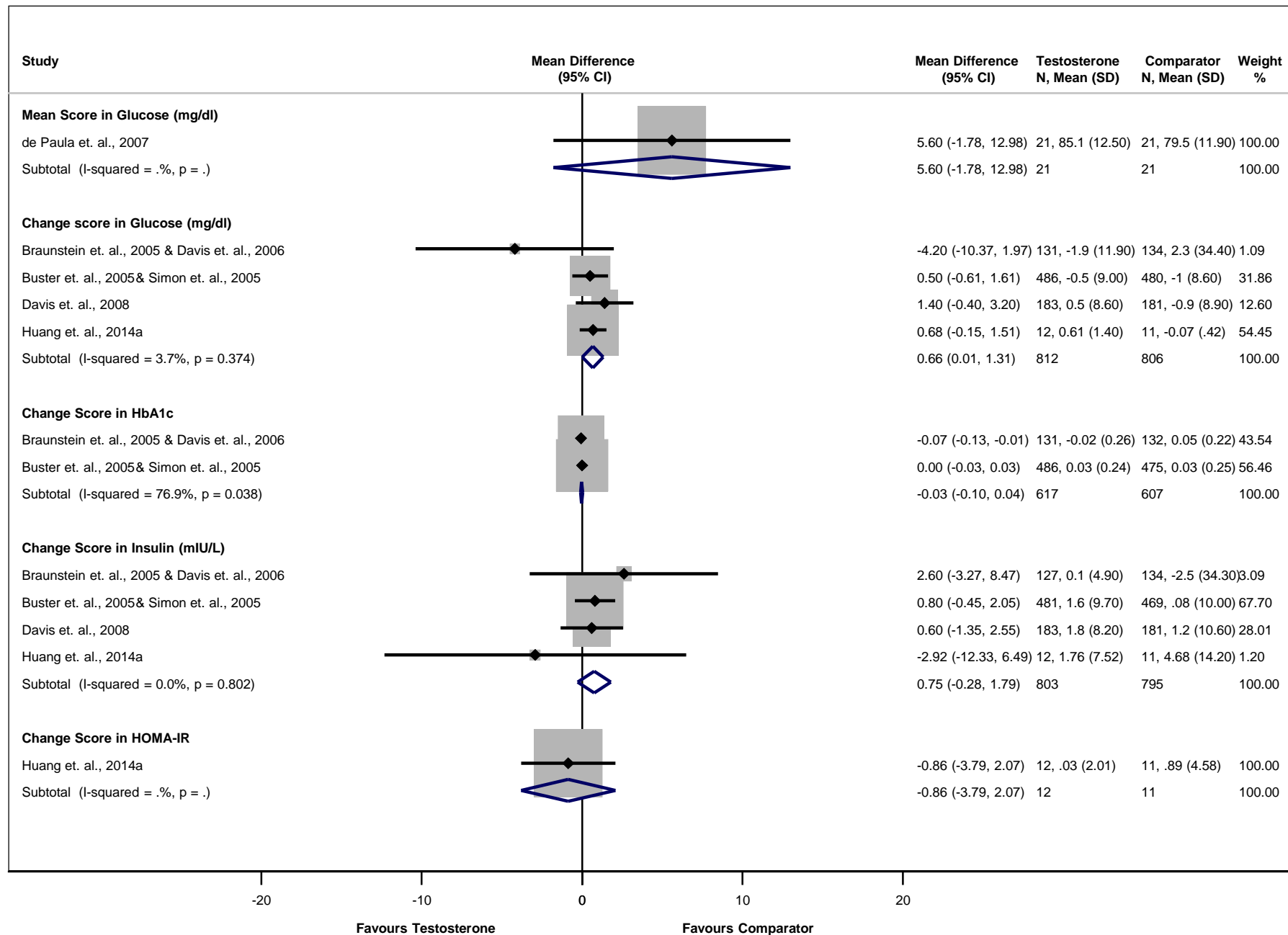
sFigure 21: Forest plot of comparison: Testosterone versus Comparator: Triglyceride Cholesterol for Non-oral T



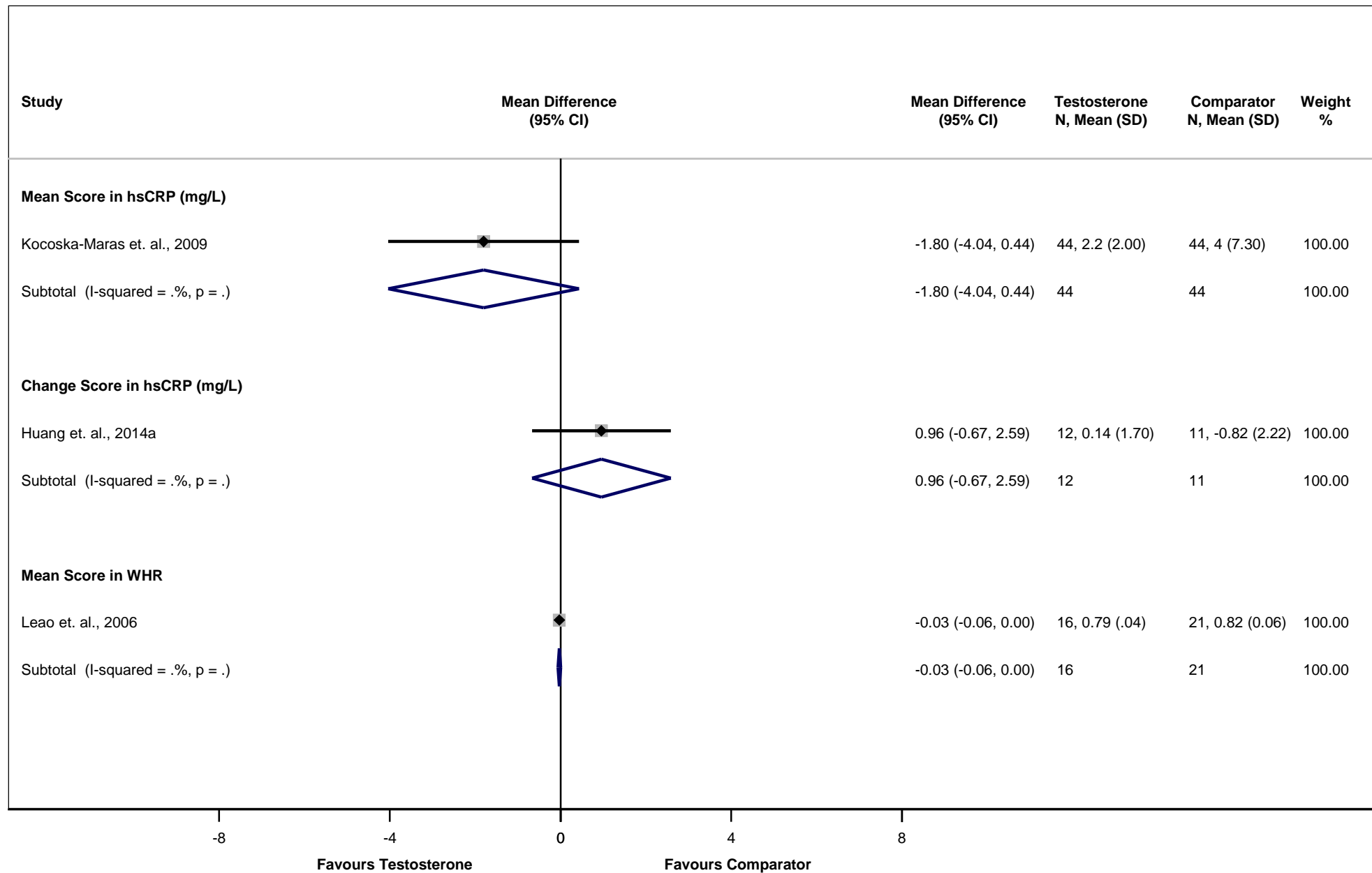
sFigure 22A: Forest plot of comparison: Testosterone versus Comparator: Cardio-metabolic Risk Markers



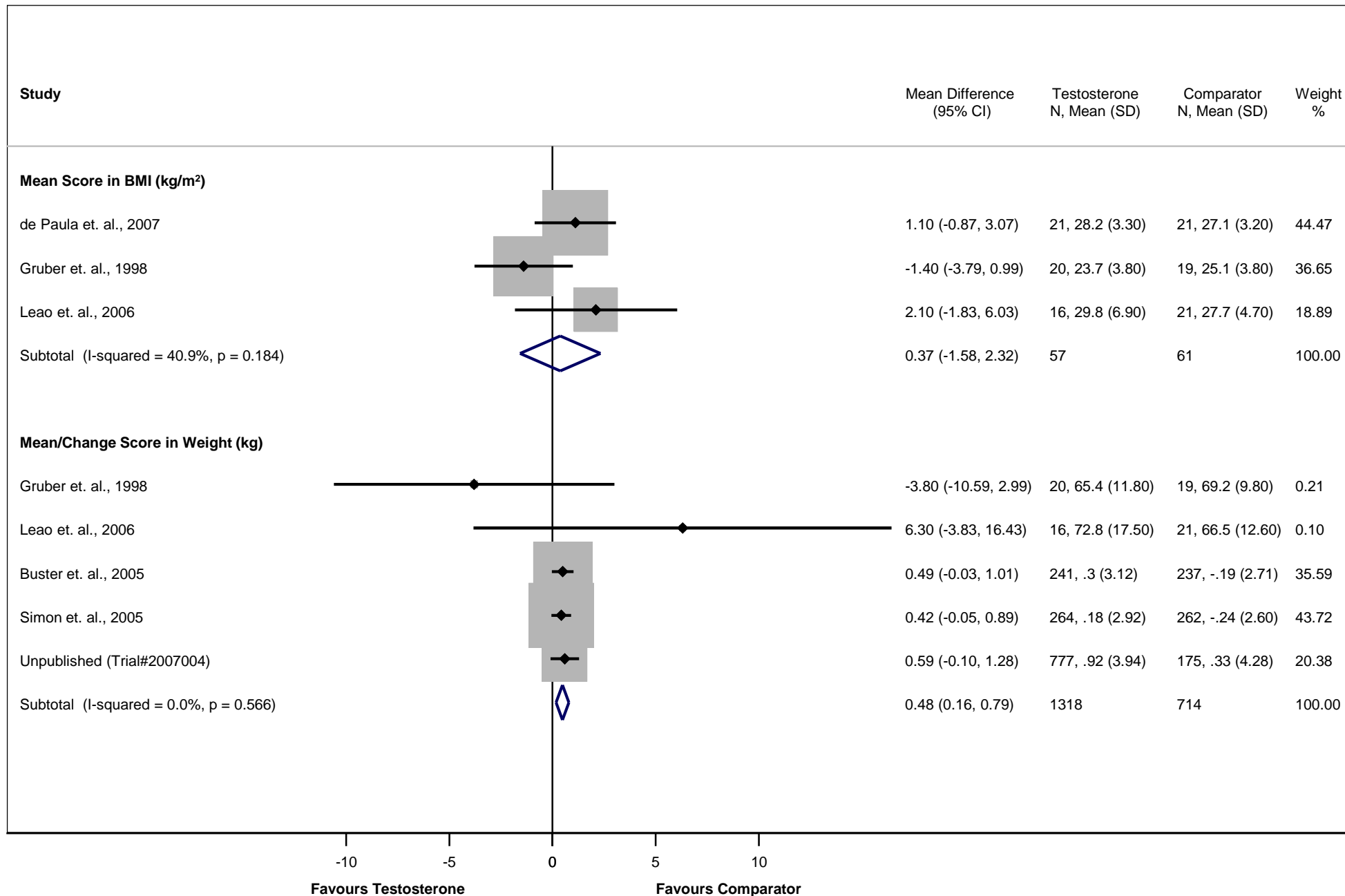
sFigure 22B: Forest plot of comparison: Testosterone versus Comparator: Cardio-metabolic Risk Markers



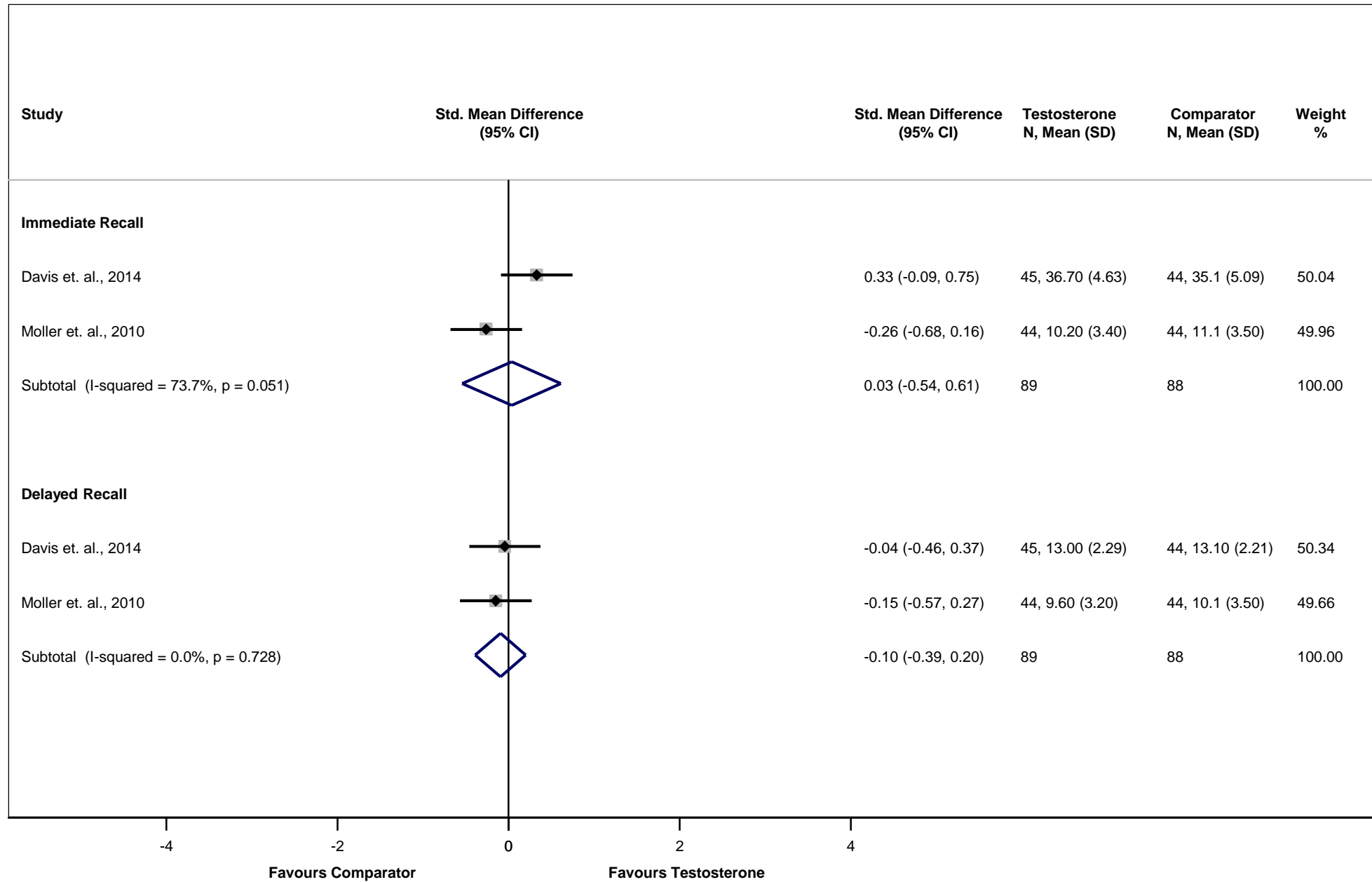
sFigure 22C: Forest plot of comparison: Testosterone versus Comparator: Cardio-metabolic Risk Markers



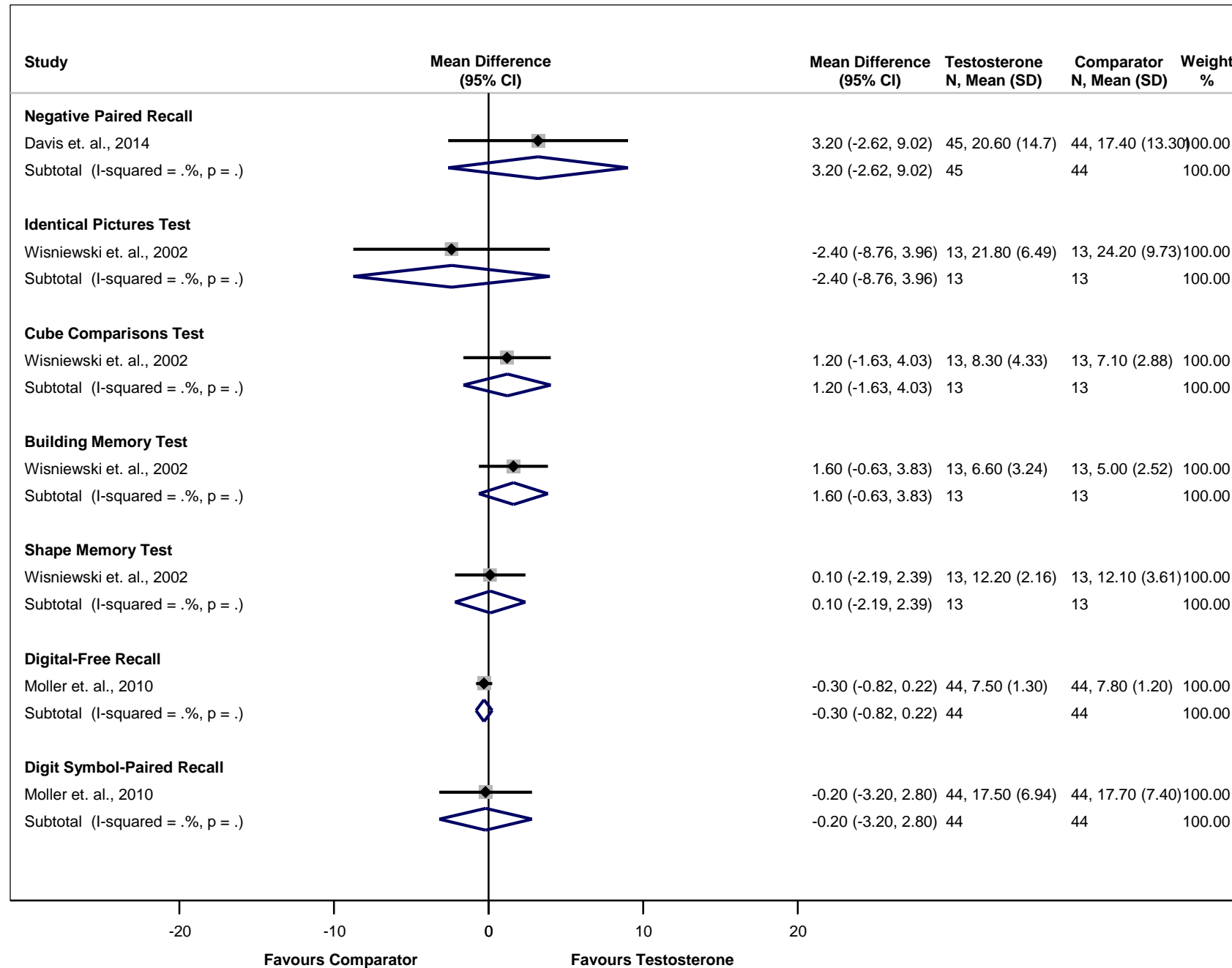
sFigure 22D: Forest plot of comparison: Testosterone versus Comparator: Cardio-metabolic Risk Markers



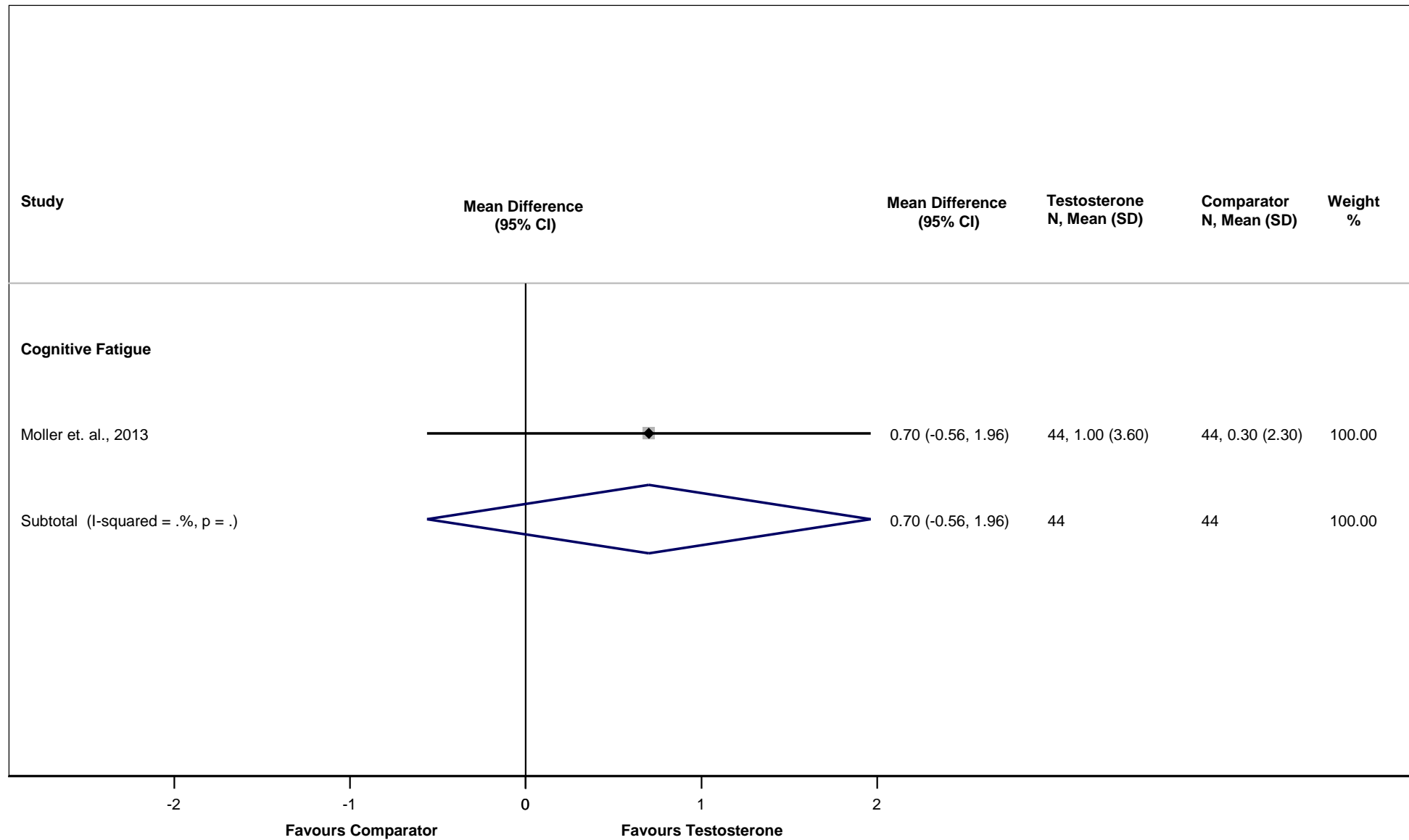
sFigure 23: Forest plot of comparison: Testosterone versus Comparator: Cognitive Health: Memory Function



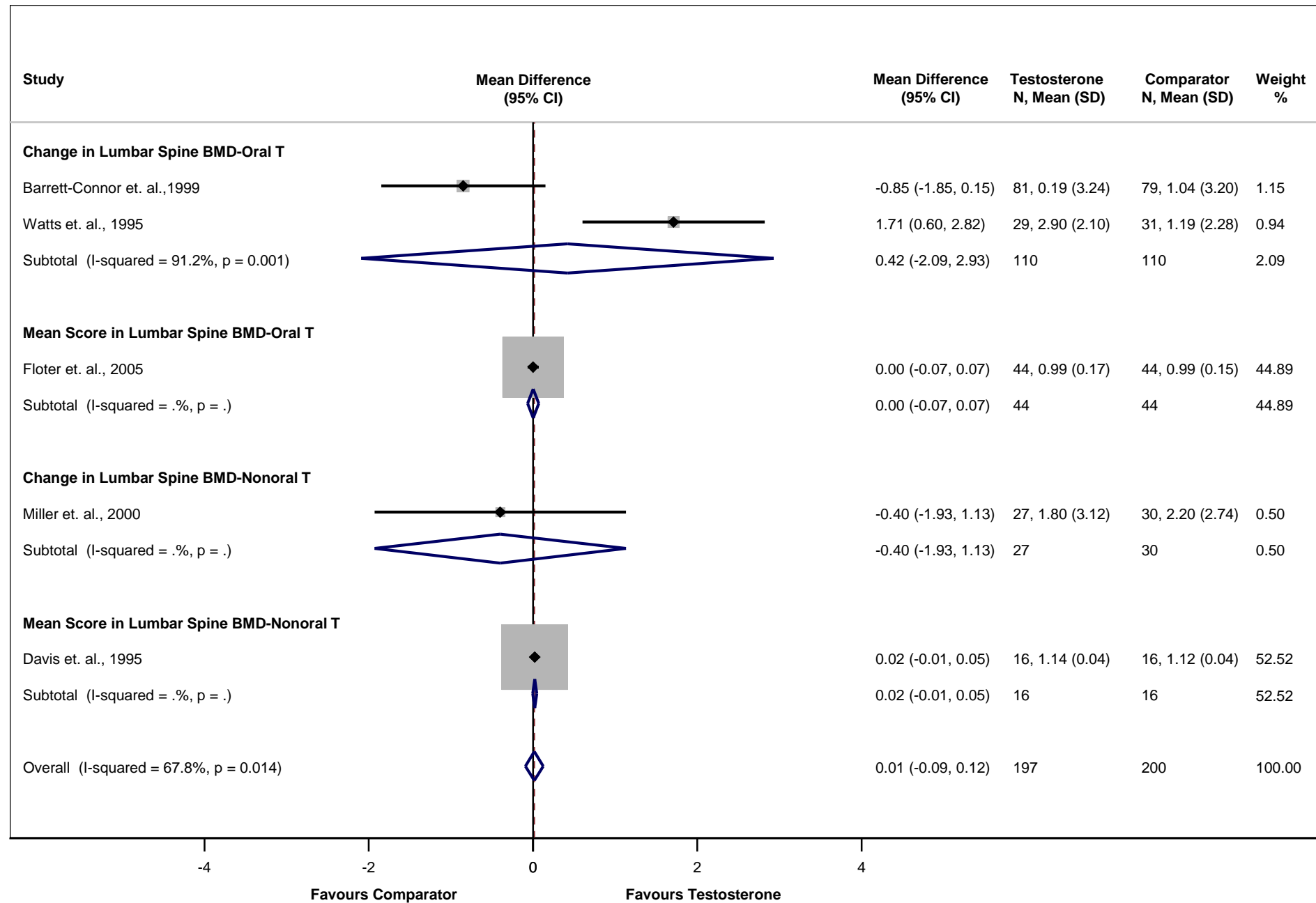
sFigure 24: Forest plot of comparison: Testosterone versus Comparator: Cognitive Health: Cognitive Performance



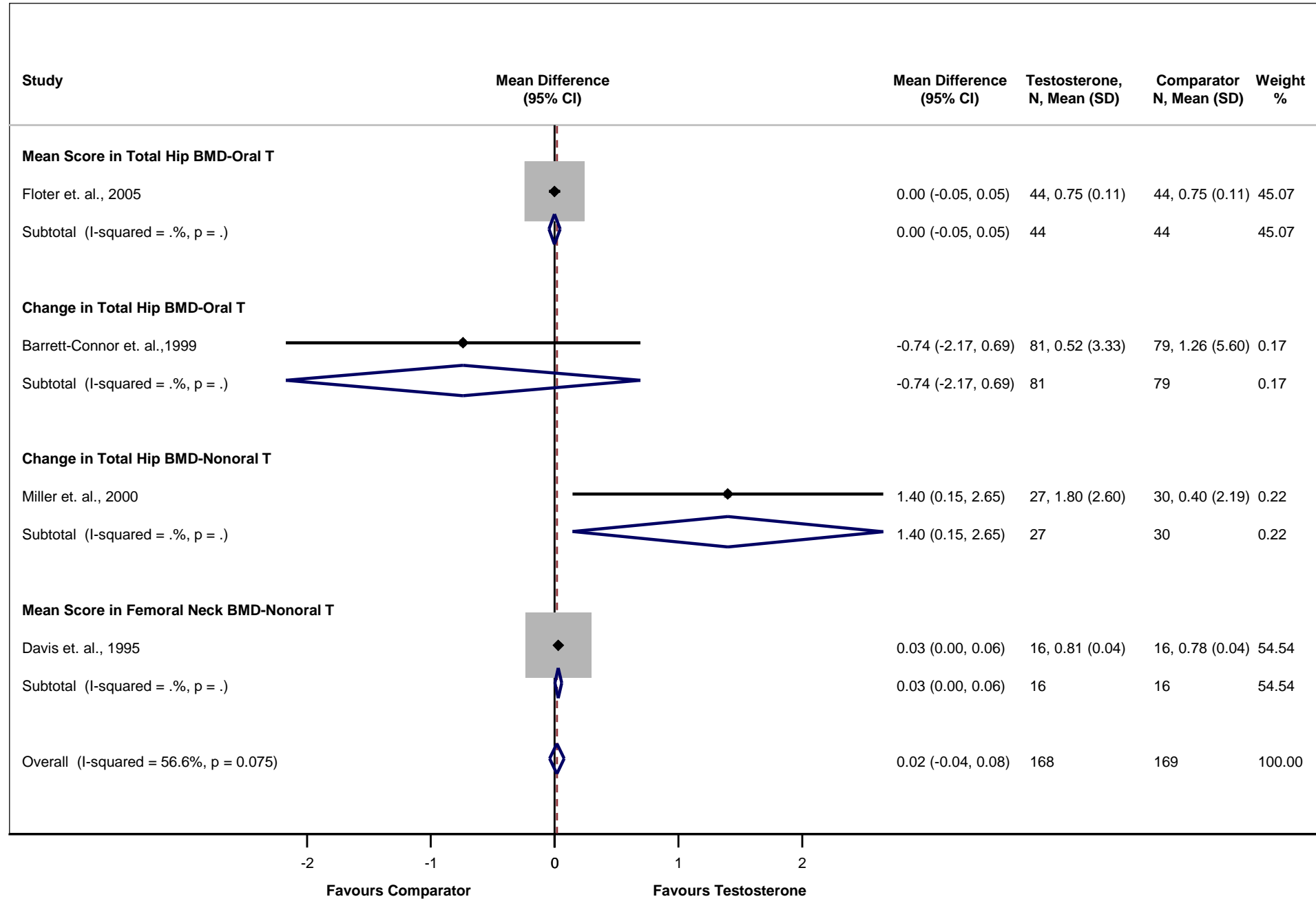
sFigure 25: Forest plot of comparison: Testosterone versus Comparator: Cognitive Health: Cognitive Fatigue



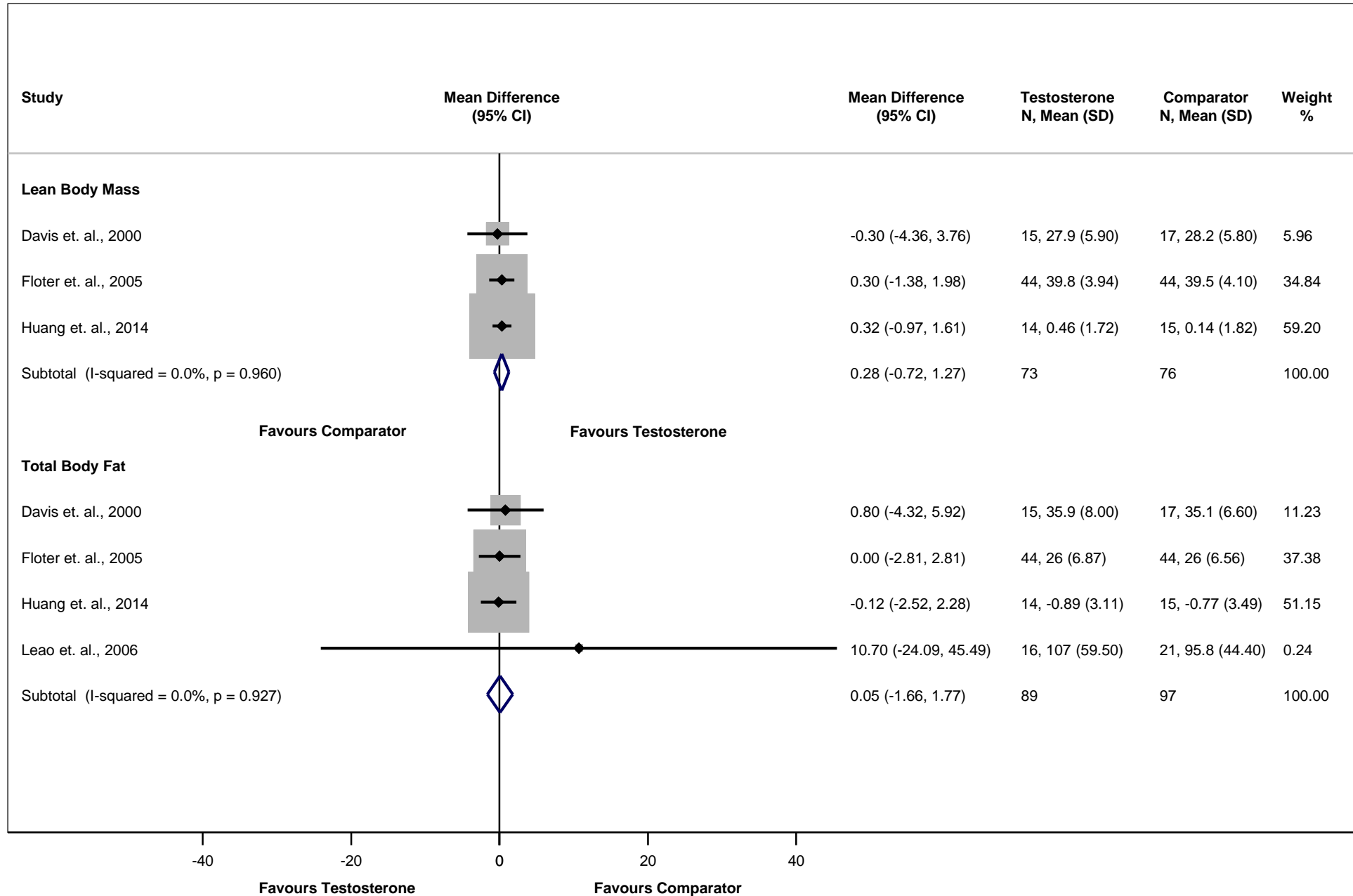
sFigure 26: Forest plot of comparison: Testosterone versus Comparator: Musculoskeletal Health: Lumbar Spine Bone Mineral Density at 12 Months



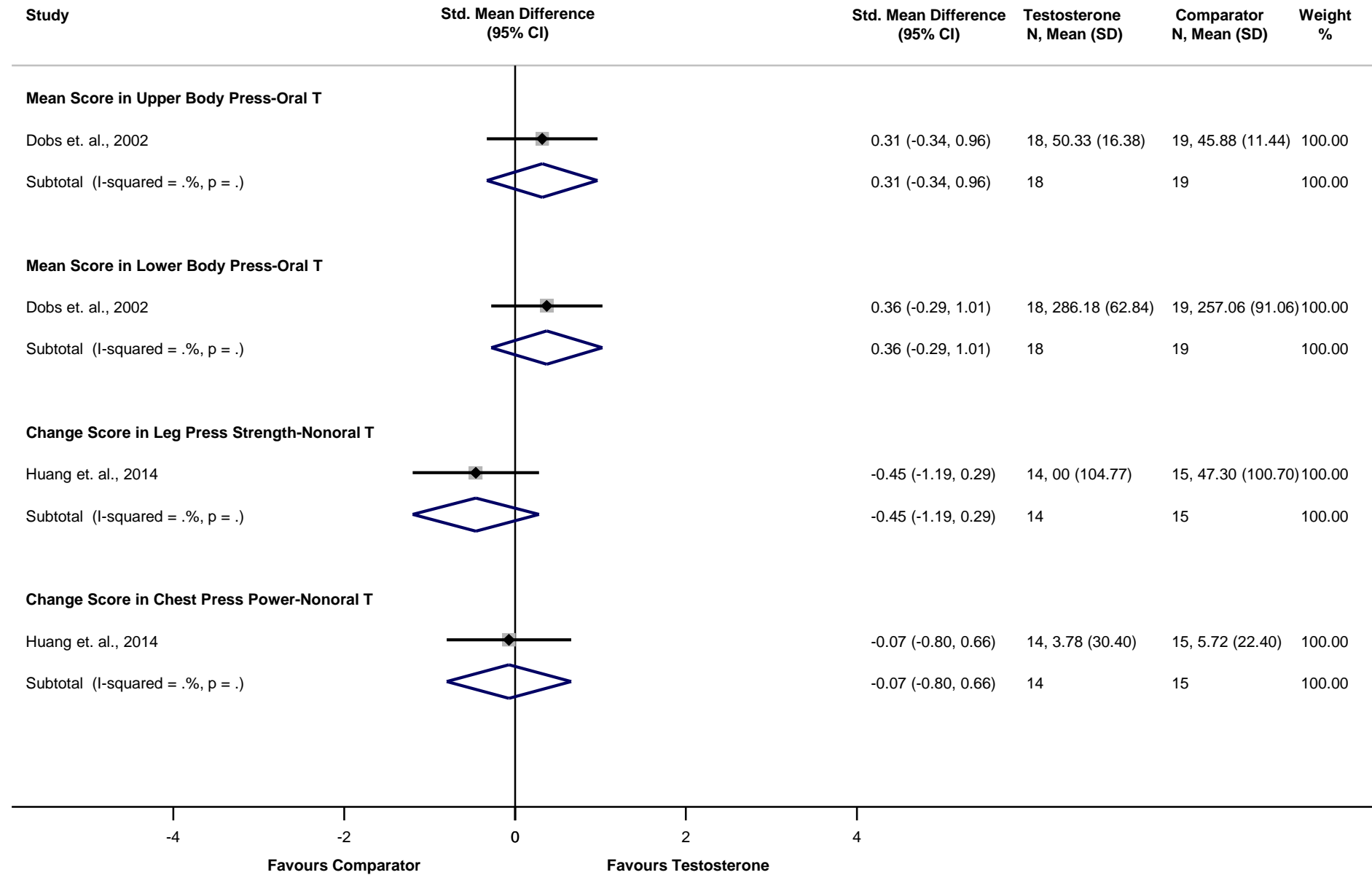
sFigure 27: Forest plot of comparison: Testosterone versus Comparator: Musculoskeletal Health: Hip/Femoral Neck Bone Mineral Density at 12 Months



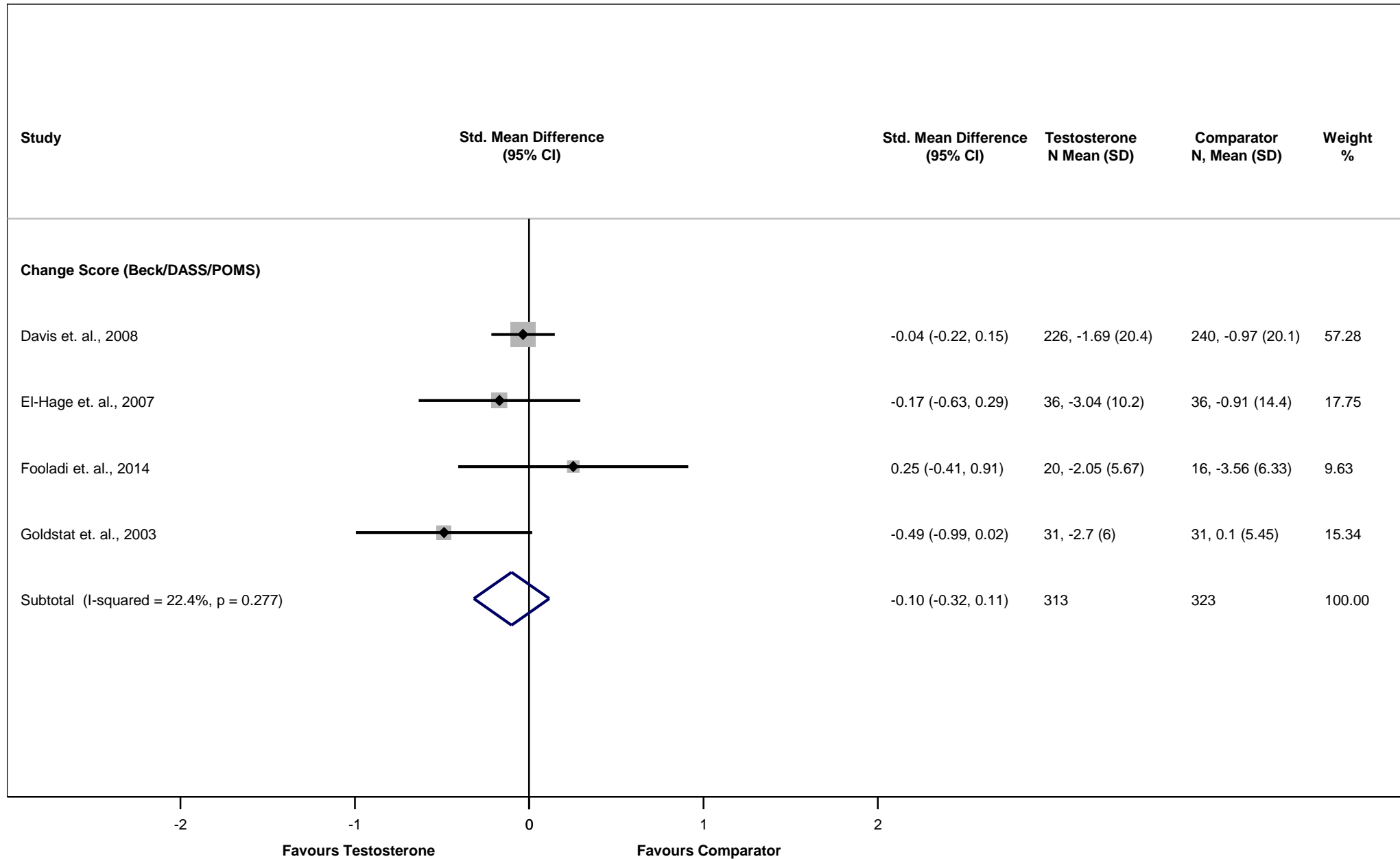
sFigure 28: Forest plot of comparison: Testosterone versus Comparator: Musculoskeletal Health: Body Composition: Lean Body Mass and Total Body Fat



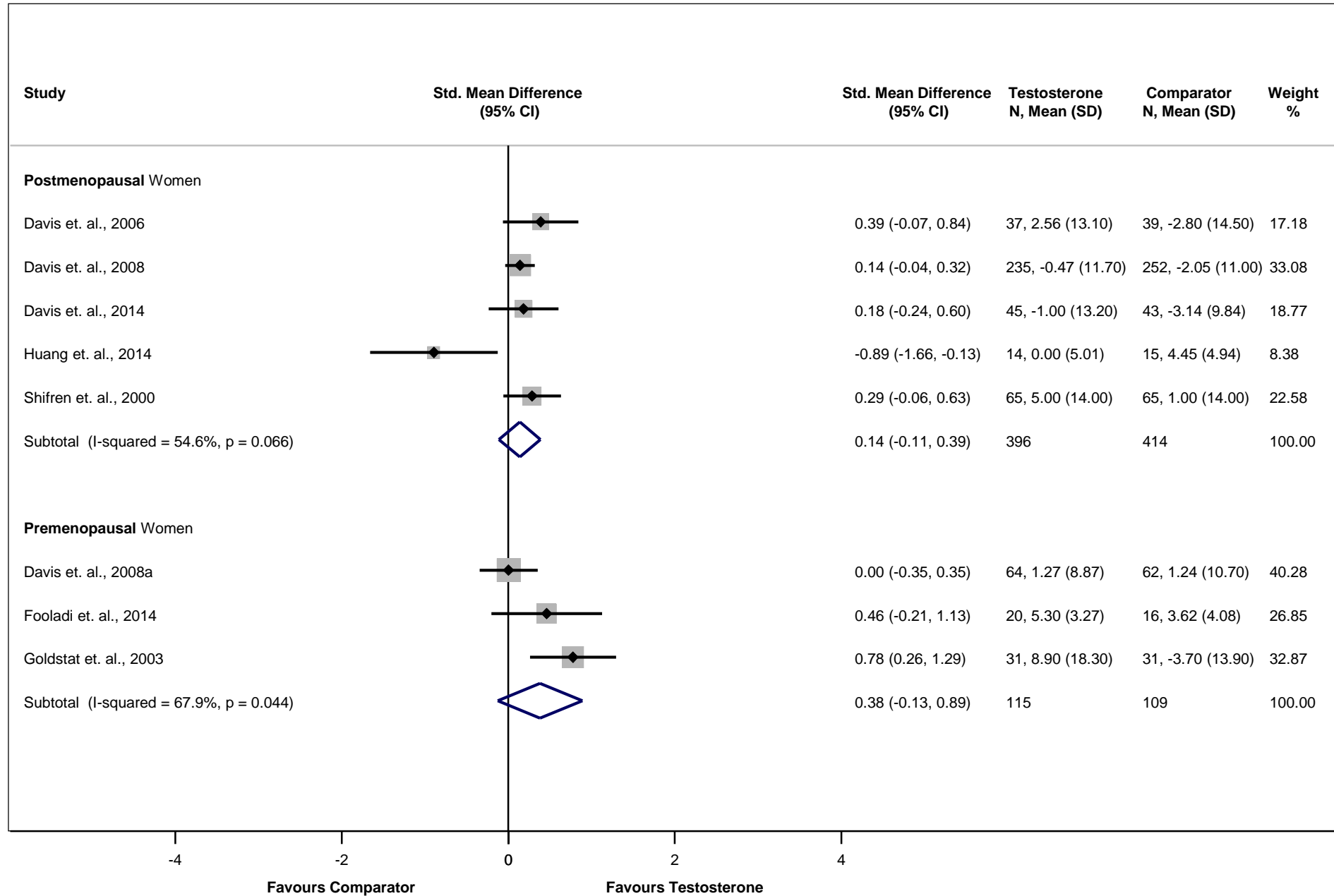
sFigure 29: Forest plot of comparison: Testosterone versus Comparator: Musculoskeletal Health: Muscle Strength



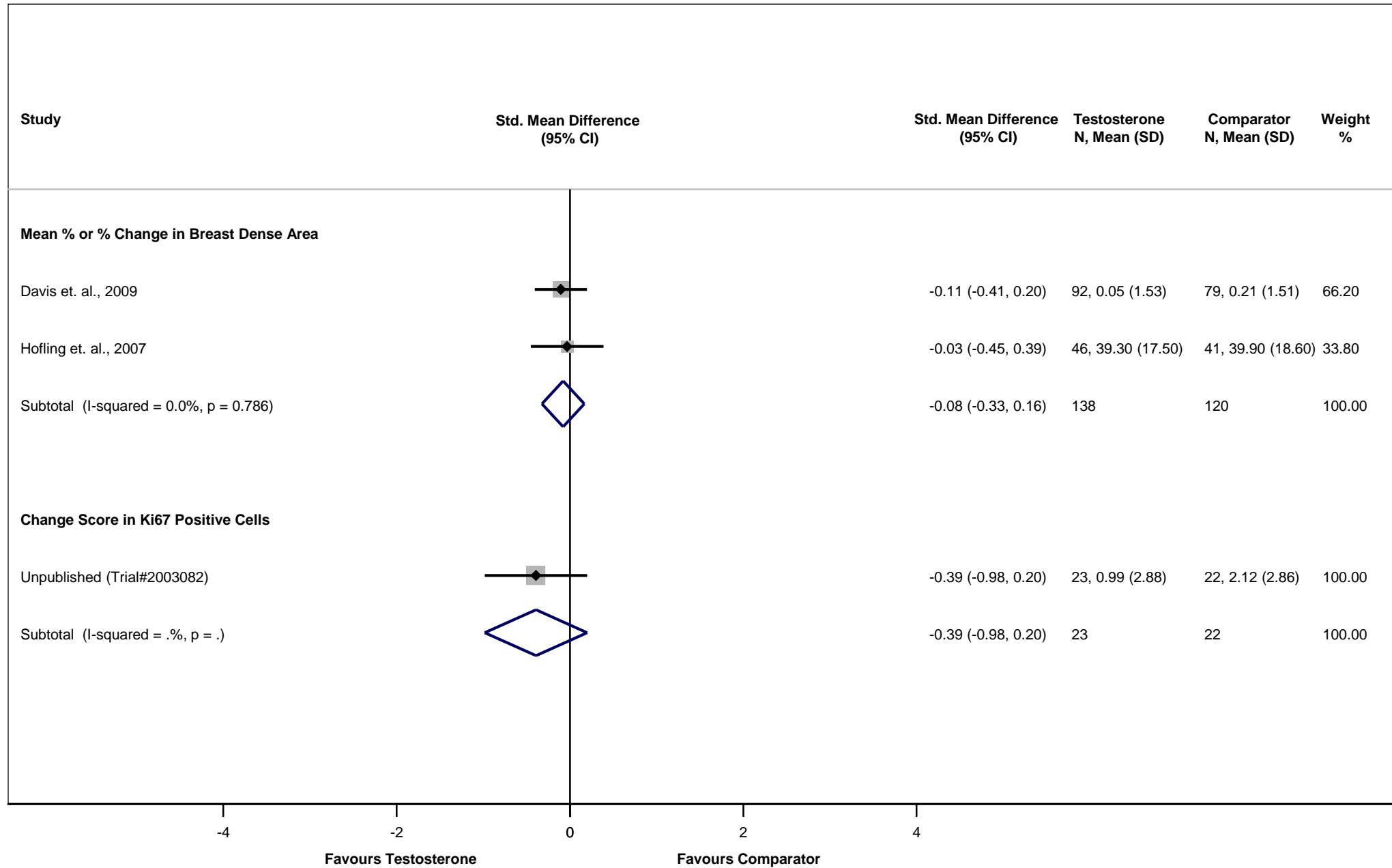
sFigure 30: Forest plot of comparison: Testosterone versus Comparator: Depressive Mood



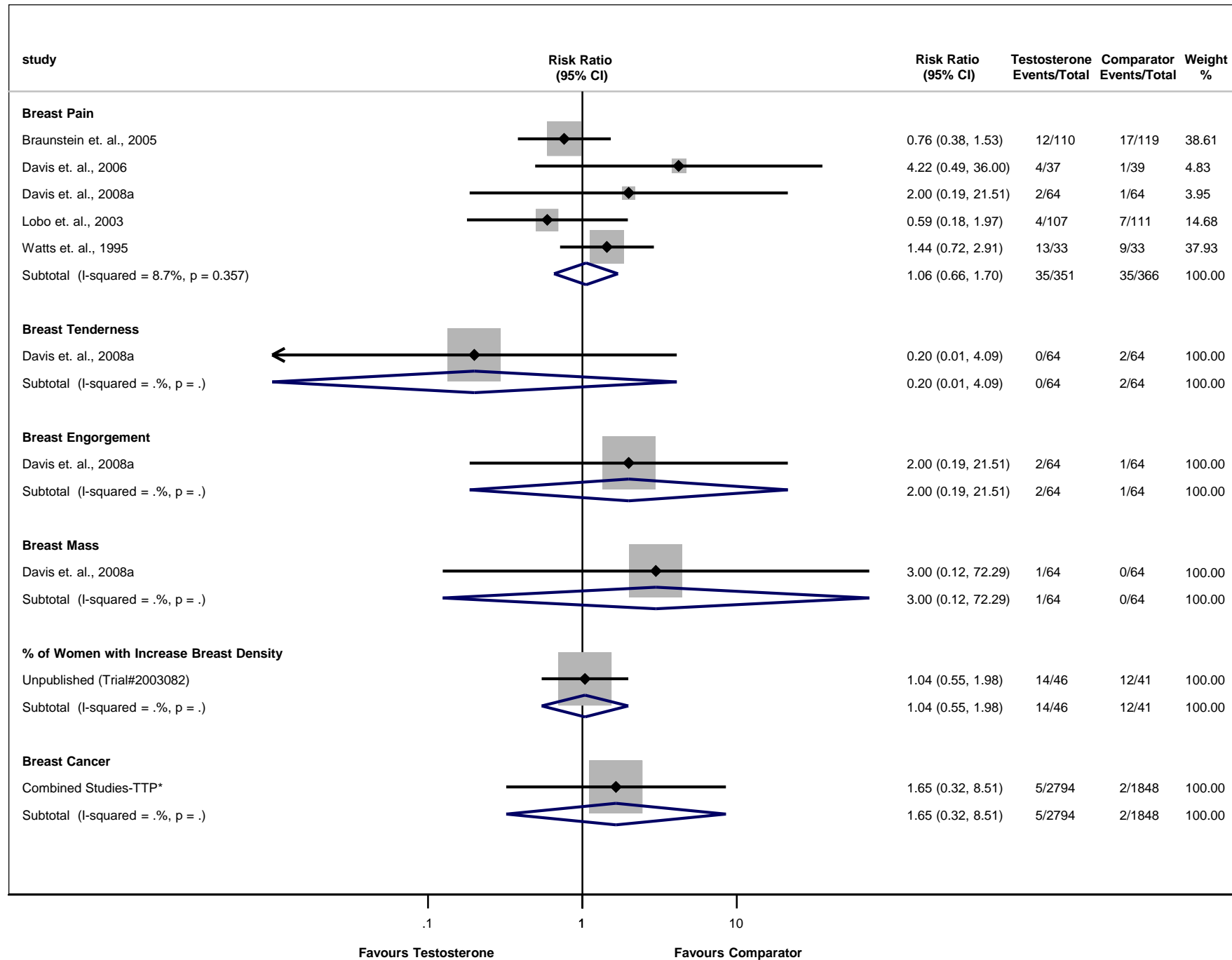
sFigure 31: Forest plot of comparison: Testosterone versus Comparator: Psychological General Well-being by Menopausal Status



sFigure 32: Forest plot of comparison: Testosterone versus Comparator: Breast Health

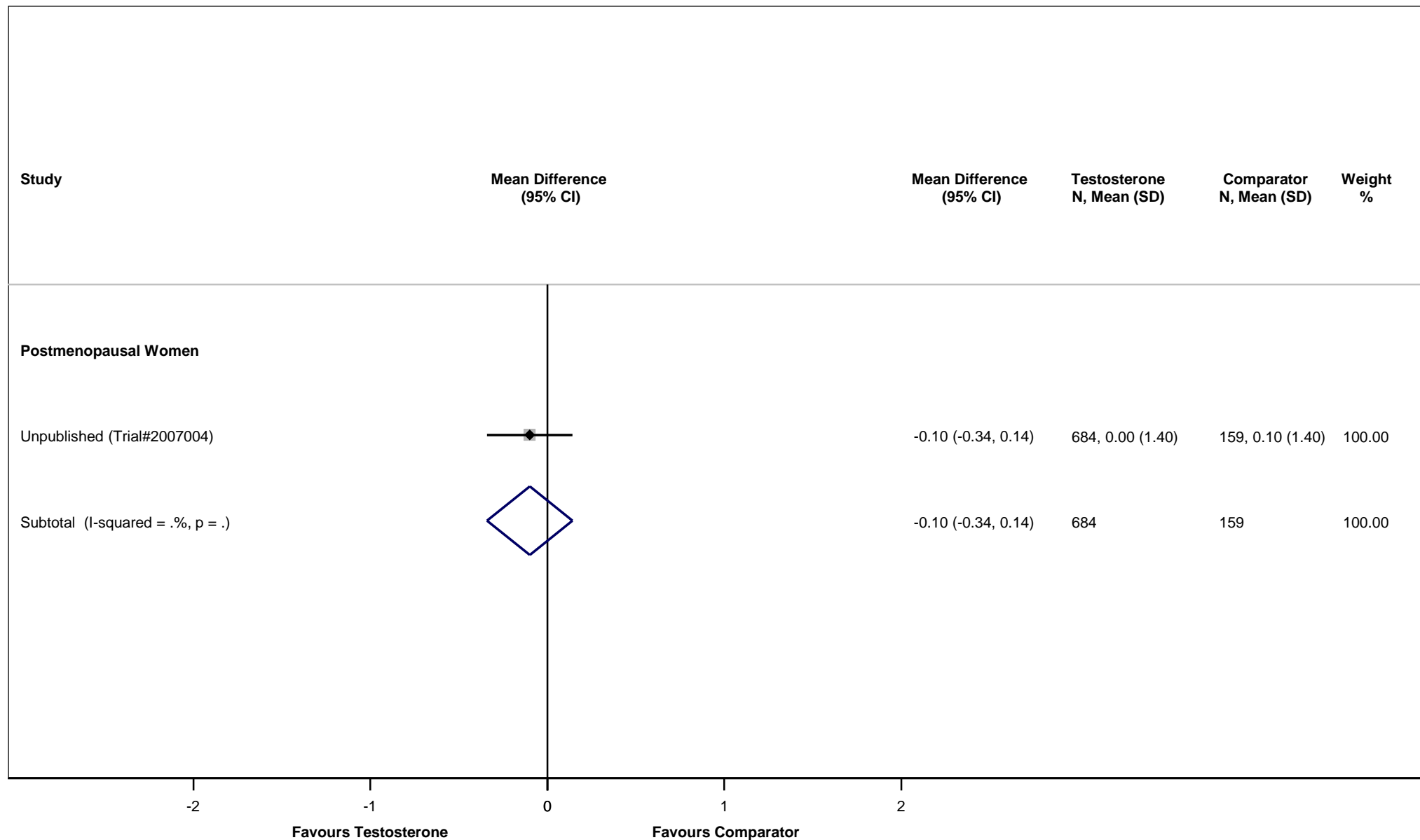


sFigure 33: Forest plot of comparison: Testosterone versus Comparator: Breast Outcomes/Events

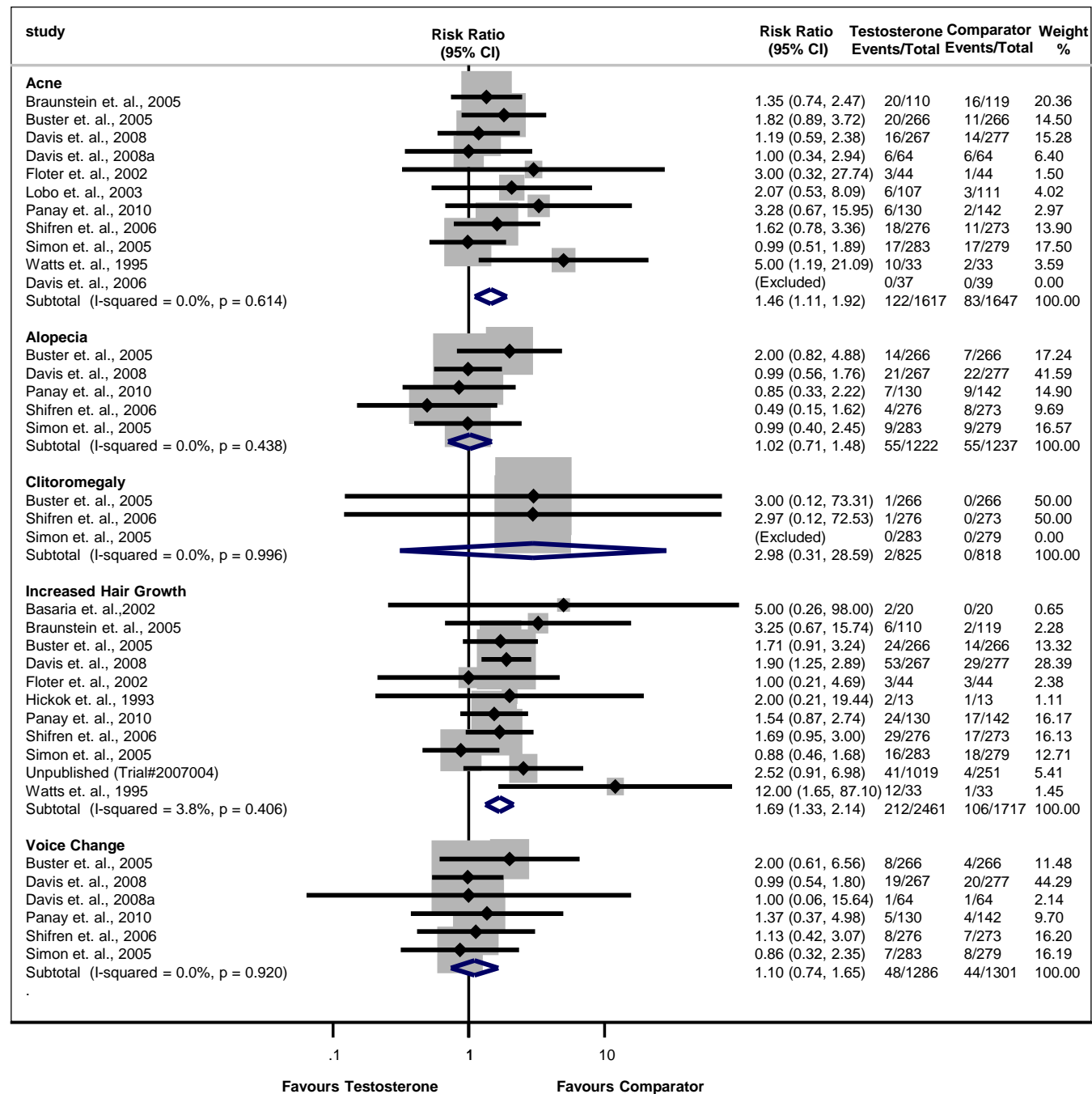


*Combined Studies-TTP includes 9 RCTs that used transdermal T patch: Braunstein et al. 2005, Buster et al. 2005, Davis et al. 2006, Davis et al. 2008, Panay et al. 2010, Simon et al. 2005, Shifren et al. 2006, Unpublished (Trial#2002005), 2009, and Unpublished (Trial#2007004), 2011.

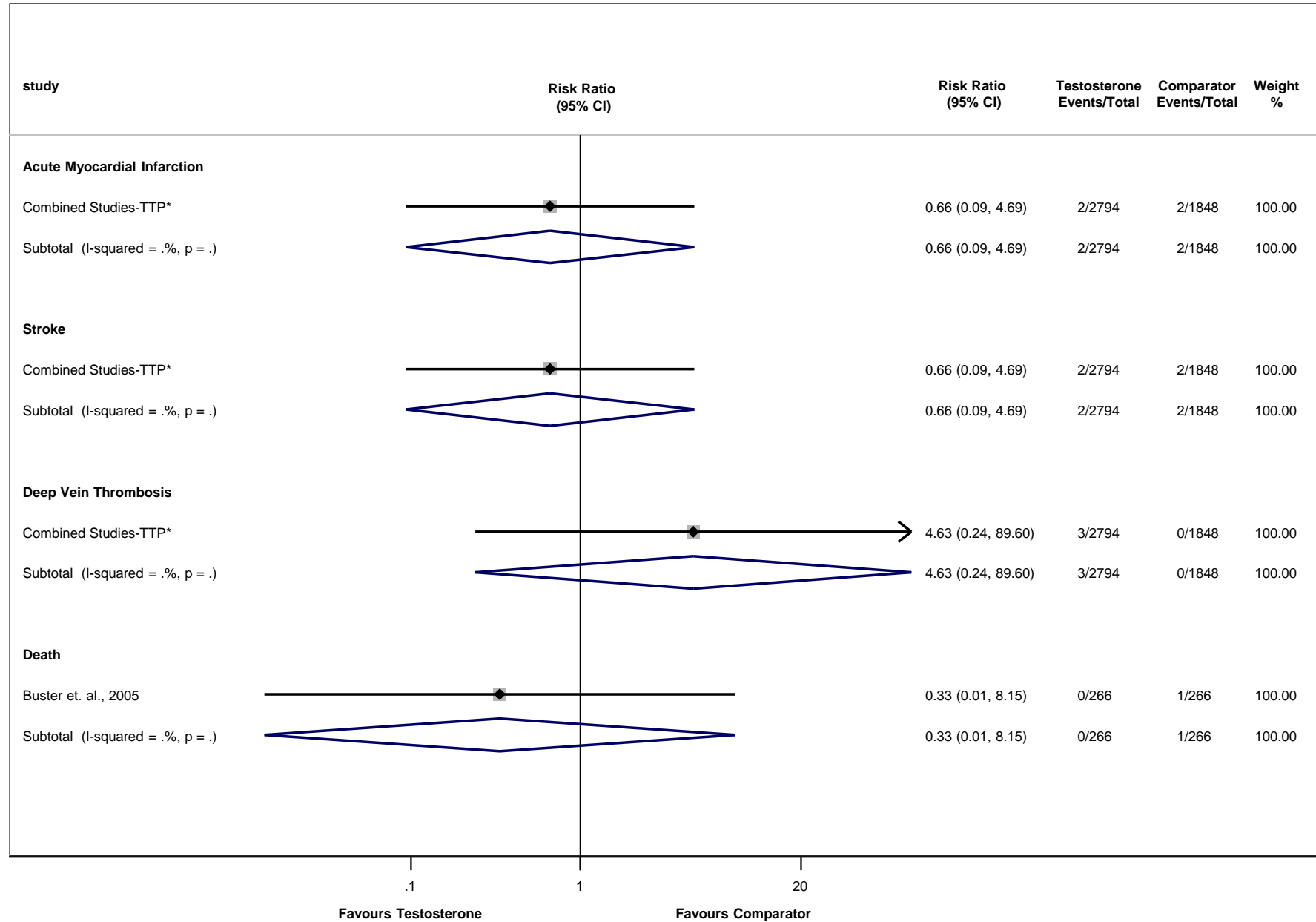
Figure 34: Forest plot of comparison: Testosterone versus Comparator: Endometrial Thickness (Mean Change)



sFigure 35: Forest plot of comparison: Testosterone versus Comparator: Androgenic Events



sFigure 36: Forest plot of comparison: Testosterone versus Comparator: Cardiovascular Events



*Combined Studies-TTP includes 9 RCTs that used transdermal T patch: Braunstein et al. 2005, Buster et al. 2005, Davis et al. 2006, Davis et al. 2008, Panay et al. 2010, Simon et al. 2005, Shifren et al. 2006, Unpublished (Trial#2002005), 2009, and Unpublished (Trial#2007004), 2011.

Figure 38: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Barrett-Connor et. al.,1999	+	+	+	+	-	+	+
Basaria et. al.,2002	+	+	+	+	?	+	+
Braunstein et. al., 2005	+	+	+	+	-	+	+
Buster et. al., 2005	+	+	+	+	-	+	+
Davis et. al., 1995	+	+	-	+	+	+	+
Davis et. al., 2006	+	+	+	+	-	+	+
Davis et. al., 2008	+	+	+	+	-	+	+
Davis et. al., 2008a	+	+	+	+	-	+	+
Davis et. al., 2014	+	+	+	+	+	+	+
de Paula et. al., 2007	+	?	+	+	?	+	-
Dias et. al., 2006	?	?	+	+	-	+	-
Dobs et. al., 2002	?	?	+	+	?	+	+
El-Hage et. al., 2007	+	+	+	+	+	+	+
Floter et. al., 2002	?	?	+	+	-	+	+
Fooladi et. al., 2014	+	+	+	+	+	+	+
Goldstat et. al., 2003	+	+	+	+	-	+	+
Gruber et. al., 1998	?	?	?	?	?	?	+
Hickok et. al., 1993	+	+	+	+	+	+	-
Hoffing et. al., 2007	+	+	+	+	+	+	+
Huang et. al., 2014	+	+	+	+	+	+	+
Leao et. al., 2006	?	+	+	+	+	+	-
Liu et. al., 2011	?	?	+	+	-	?	+
Lobo et. al., 2003	?	?	+	+	+	+	+
Miller et. al., 2000	?	?	+	+	-	+	+
Moller et. al., 2010	?	+	+	+	+	+	+
Nathorst-Boos et. al., 2006	+	+	+	+	+	+	+
Panay et. al., 2010	+	+	+	+	-	+	+
Penteado et. al., 2008	?	?	+	+	+	+	+
Shifren et. al., 2000	?	?	+	+	+	+	+
Shifren et. al., 2006	+	+	+	+	-	+	+
Simon et. al., 1999	?	?	+	+	+	+	+
Simon et. al., 2005	+	+	+	+	+	+	+
Unpublished (Trial#2002005)	+	+	+	+	-	-	+
Unpublished (Trial#2007004)	?	?	+	+	-	+	?
Watts et. al., 1995	+	?	+	+	?	+	+
Wisniewski et. al., 2002	?	+	+	+	?	+	+

Figure 39: Contour enhanced funnel plot for random effects meta-analysis of mean difference in sexual Desire

