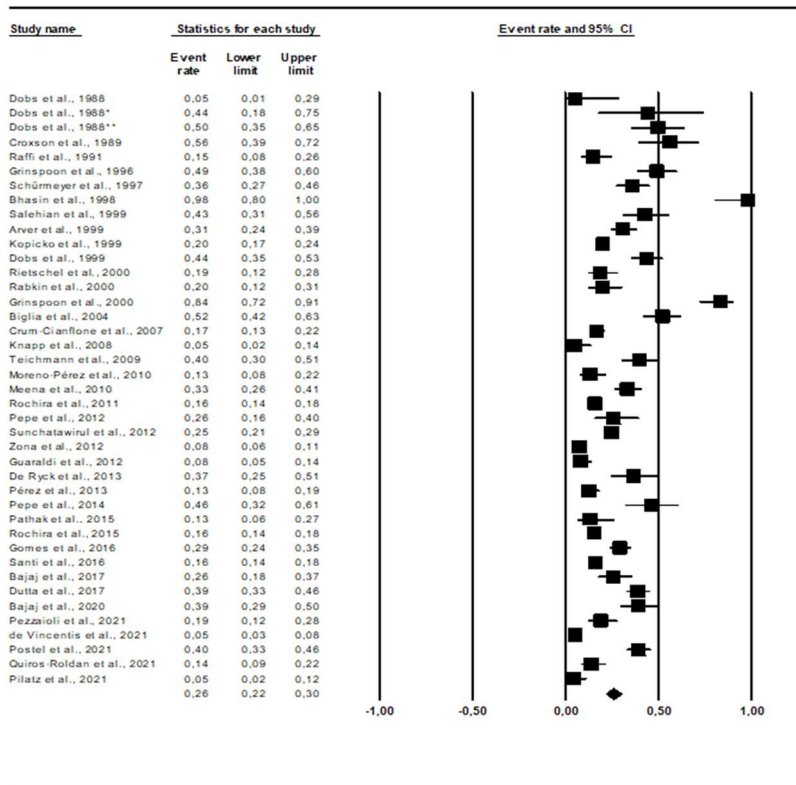


Study	Selection bias	Study design	Data collection	Global rating
Dobs et al, 1988	Weak	Observational Longitudinal	Moderate	Moderate
Croxson et al, 1989	Strong	Observational Case-control	Moderate	Low
Raffi et al, 1991	Weak	Observational Cross-sectional	Moderate	Moderate
Laudat et al, 1995	Strong	Observational Cross-sectional	Moderate	Moderate
Dobs et al, 1996	Weak	Observational Case-control	Moderate	Moderate
Grinspoon et al, 1996	Strong	Observational Cross-sectional	Strong	Moderate
Schürmeyer et al, 1997	Weak	Observational Longitudinal	Moderate	Moderate
Bhasin et al, 1998	Weak	RCT	Strong	High
Arver et al, 1999	Moderate	Observational Case-control	Strong	Moderate
Dobs et al, 1999	Weak	RCT	Strong	High
Kopicko et al, 1999	Weak	Observational Cross-sectional	Moderate	Moderate
Salehian et al, 1999	Strong	Observational Longitudinal	Moderate	Low
Rietschel et al, 2000	Strong	Observational Cross-sectional	Moderate	Low
Rabkin et al, 2000	Weak	RCT	Moderate	Moderate
Grinspoon et al, 2000	Weak	RCT	Moderate	Moderate
Hadigan et al, 2000	Weak	RCT	Strong	High
Biglia et al, 2004	Strong	Observational Case-control	Moderate	Low
Andersen et al, 2007	Strong	Observational Cross-sectional	Moderate	Low
Crum-Cianflone et al, 2007	Weak	Observational Cross-sectional	Moderate	Moderate
Mulligan et al, 2007	Weak	RCT	Strong	High
Knapp et al, 2008	Weak	RCT	Moderate	Moderate
Teichmann et al, 2008	Moderate	Observational Cross-sectional	Moderate	Moderate
Moreno-Pérez et al, 2010	Weak	Observational Cross-sectional	Moderate	Moderate
Meena et al, 2010	Weak	Observational Cross-sectional	Moderate	Moderate
Rochira et al, 2011	Weak	Observational Cross-sectional	Strong	Moderate
Pepe et al, 2012	Weak	Observational Cross-sectional	Strong	Moderate

Sunchatawirul et al, 2012	Weak	Observational Cross-sectional	Moderate	Moderate
Zona et al, 2012	Weak	Observational Case-control	Moderate	Moderate
Guaraldi et al, 2012	Weak	Observational Cross-sectional	Strong	Moderate
De Ryck et al, 2013	Weak	Observational Cross-sectional	Moderate	Moderate
Pérez et al, 2013	Weak	Observational Cross-sectional	Moderate	Moderate
Pepe et al, 2014	Weak	Observational Cross-sectional	Moderate	Moderate
Bhatia et al, 2015	Weak	Observational Cross-sectional	Weak	Low
Pathak et al, 2015	Weak	Observational Longitudinal	Moderate	Moderate
Rochira et al, 2015	Weak	Observational Cross-sectional	Strong	Moderate
Gomes et al, 2016	Weak	Observational Cross-sectional	Weak	Low
Santi et al, 2016	Weak	Observational Cross-sectional	Strong	Moderate
Bajaj et al, 2017	Weak	Observational Case-control	Weak	Low
Dutta et al, 2017	Weak	Observational Cross-sectional	Moderate	Moderate
Price et al, 2019	Weak	Observational Cross-sectional	Strong	Moderate
Bajaj et al, 2020	Weak	Observational Case-control	Moderate	Moderate
Pezzaoli et al, 2020	Weak	Observational Cross-sectional	Moderate	Moderate
de Vincentis et al, 2021	Weak	Observational Cross-sectional	Strong	Moderate
Postel et al, 2021	Moderate	Observational Cross-sectional	Weak	Low
Quiros-Roldan et al, 2021	Weak	Observational Cross-sectional	Moderate	Moderate
Pilatz et al, 2021	Weak	Observational Longitudinal	Moderate	Moderate

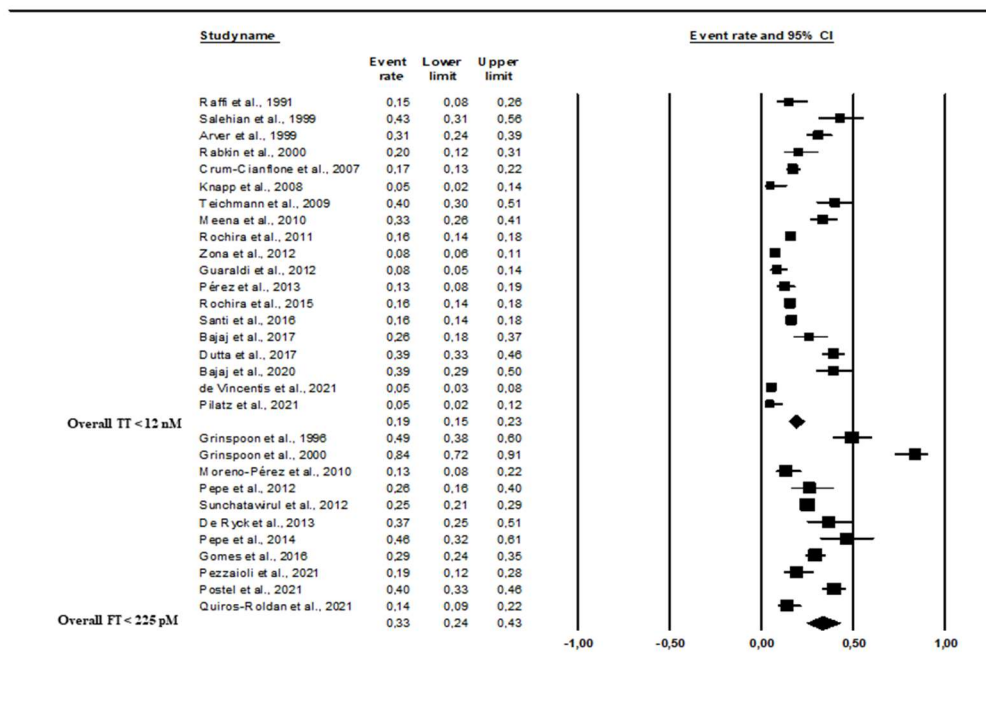
Supplementary Table S1. Quality assessment of the clinical studies included in the meta-analysis

A



Panel A

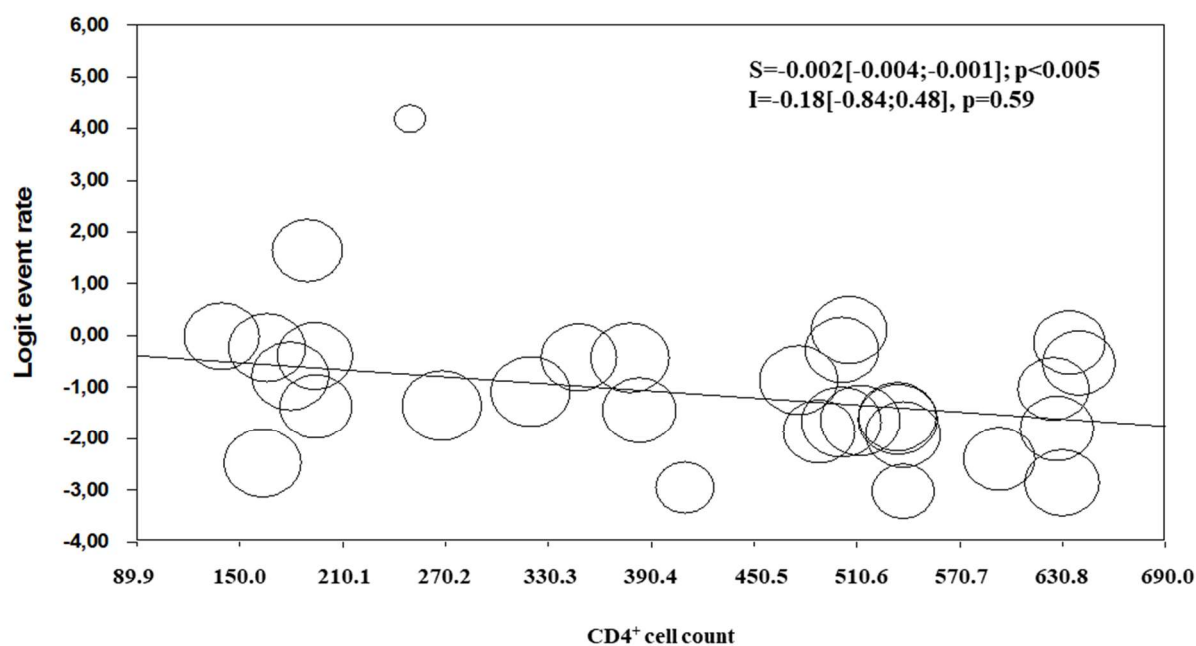
B



Panel B

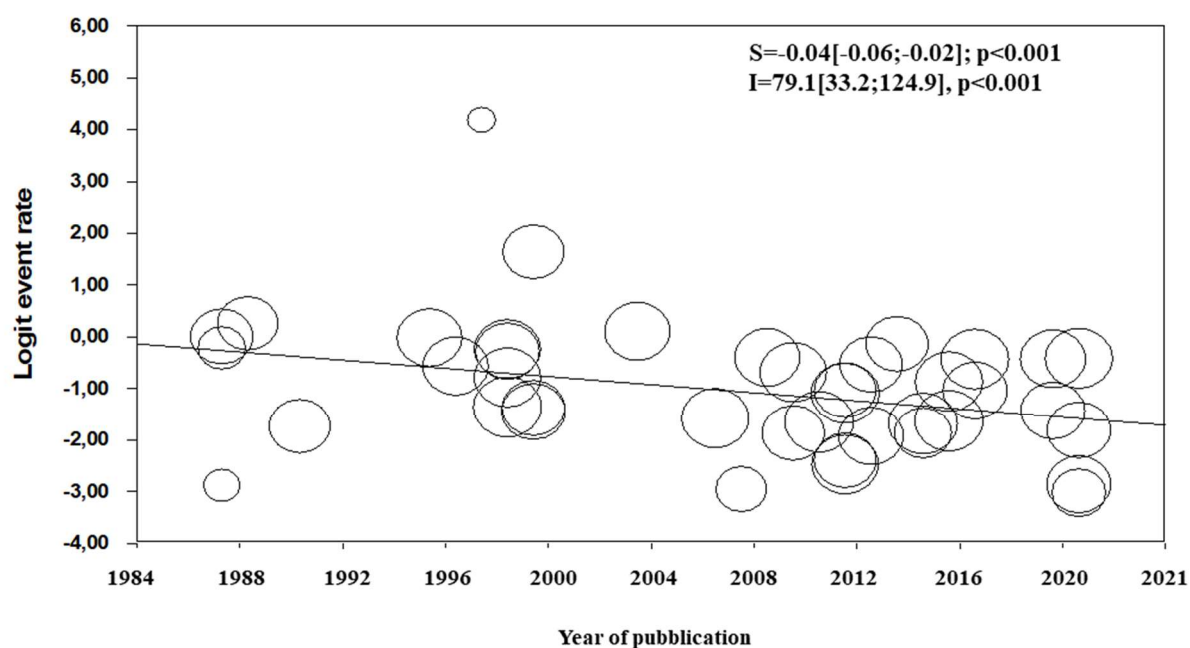
Supplementary Figure S1.(Panel A Panel B)

A



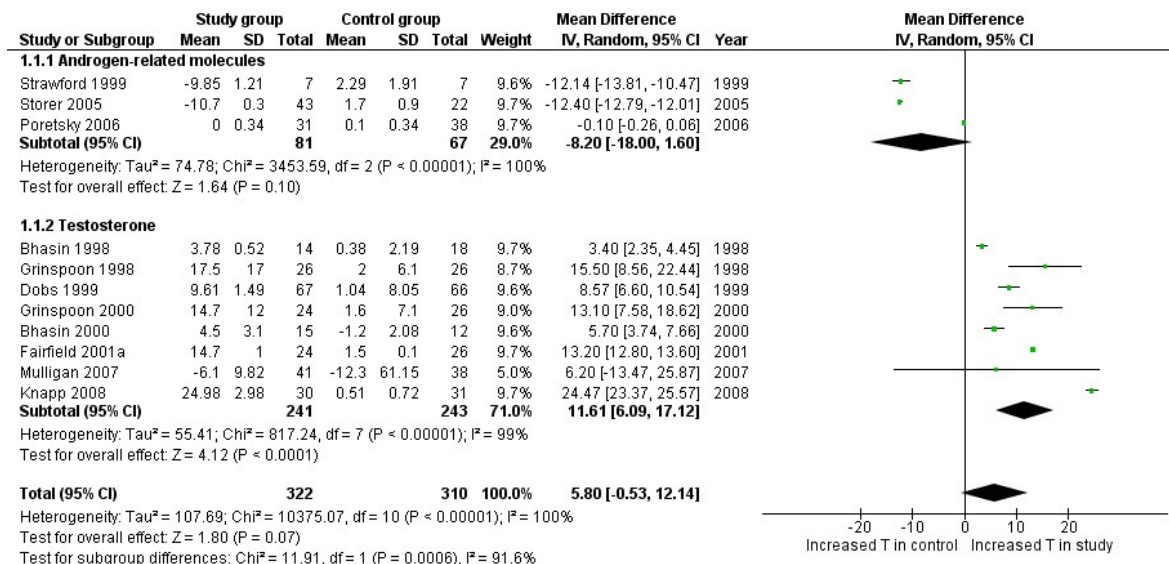
Panel A

B

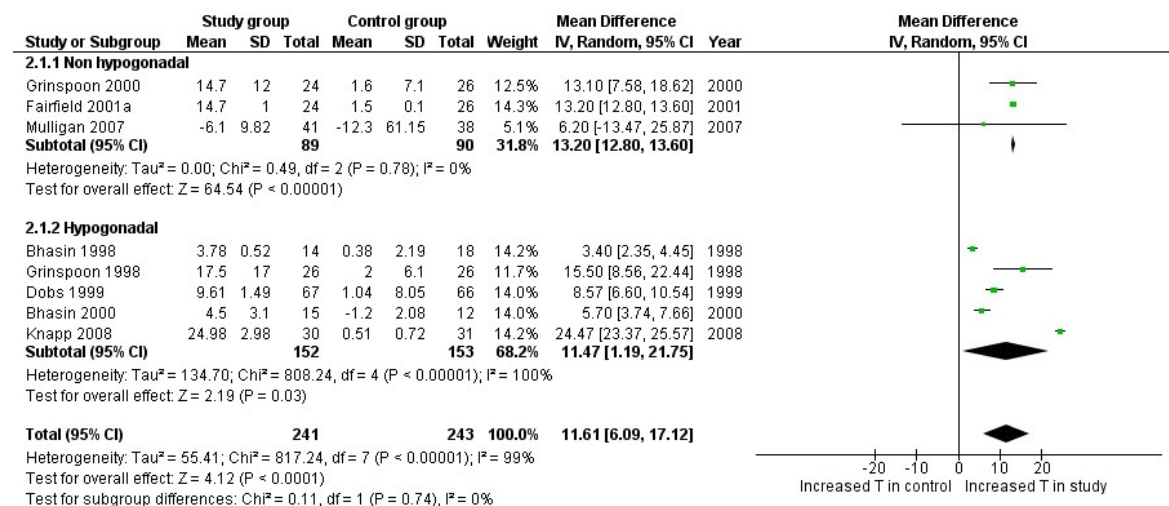


Panel B

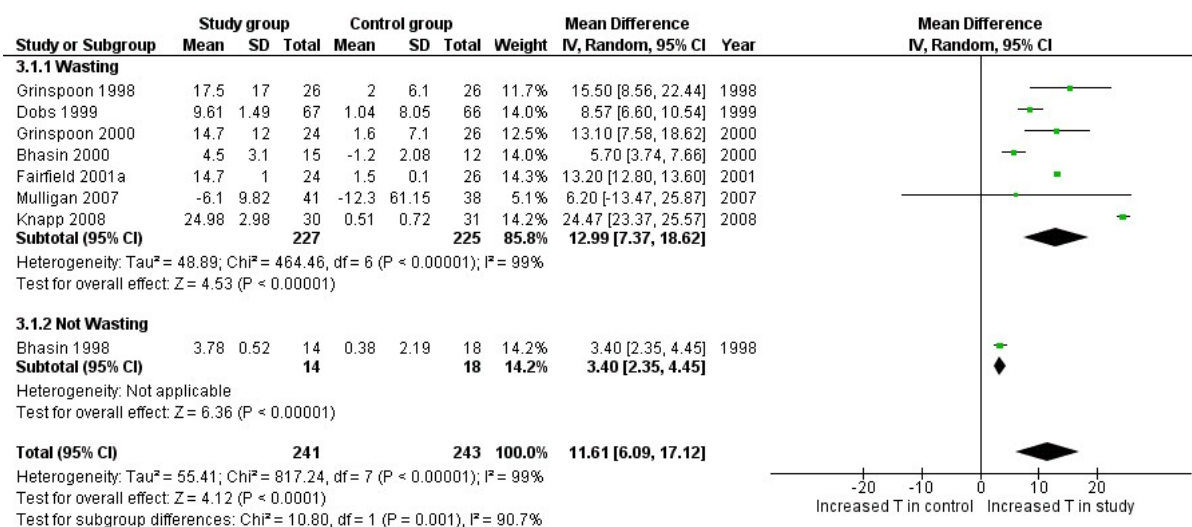
Supplementary Figure S2.(Panel A Panel B)



Panel A

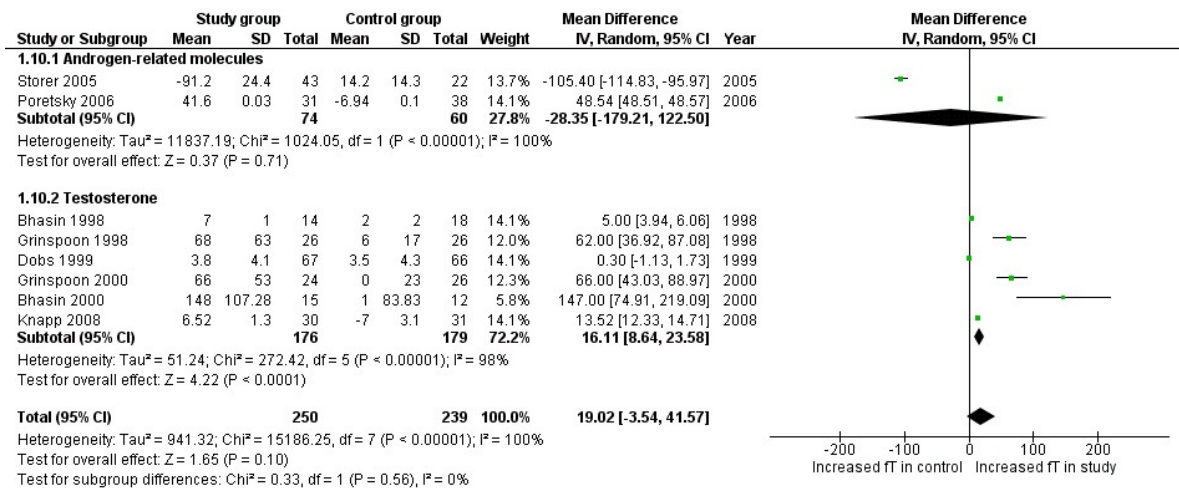


Panel B

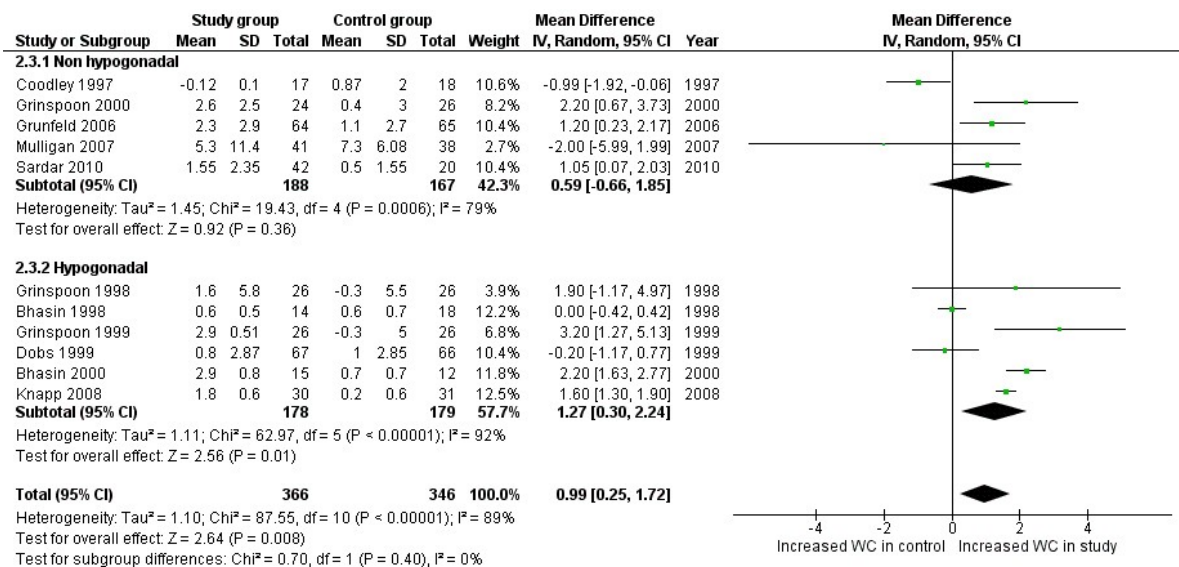


Panel C

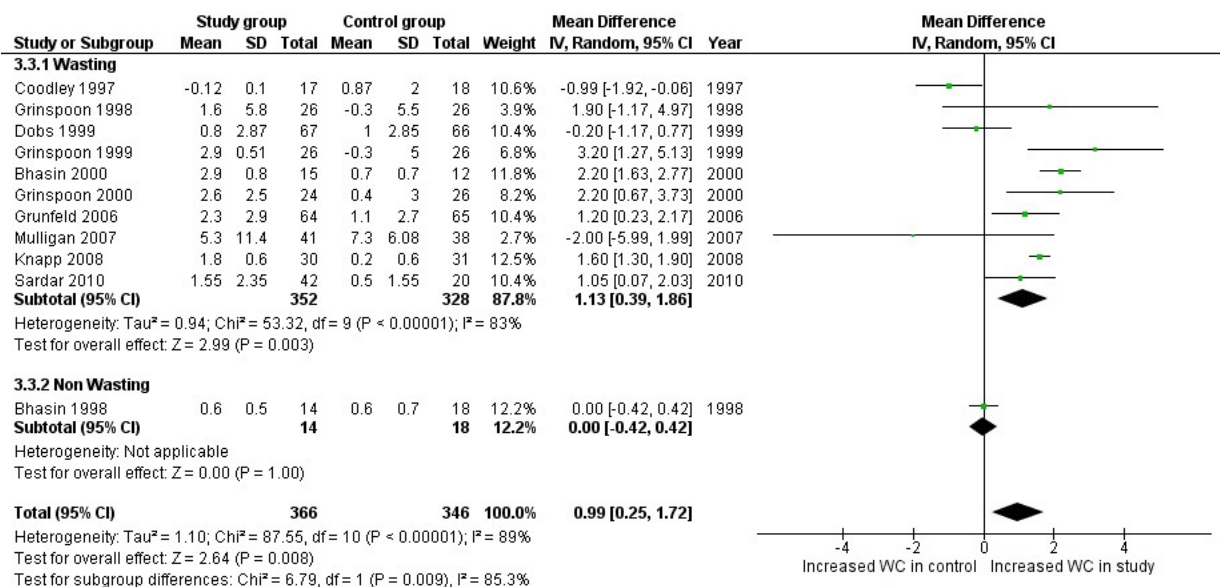
Supplementary Figure S3.(Panel A Panel B Panel C)



Supplementary Figure 4

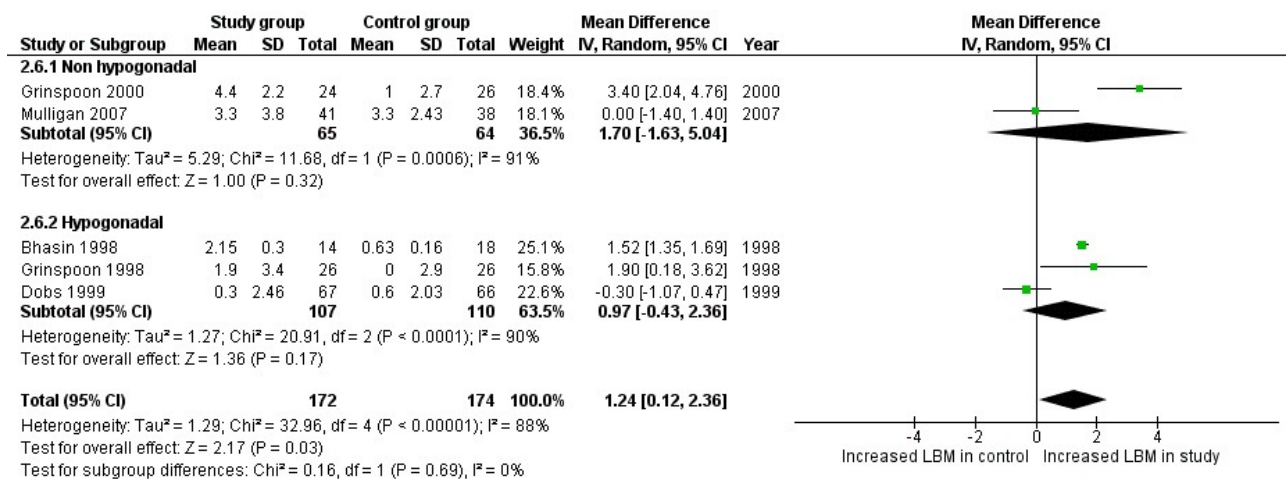


Panel A

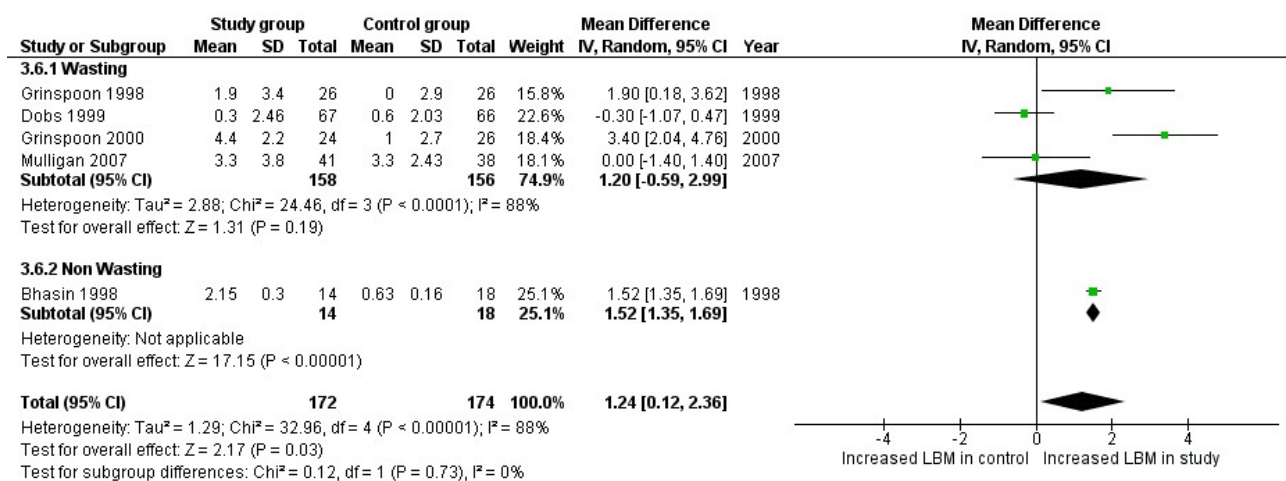


Panel B

Supplementary Figure S5.(Panel A Panel B)

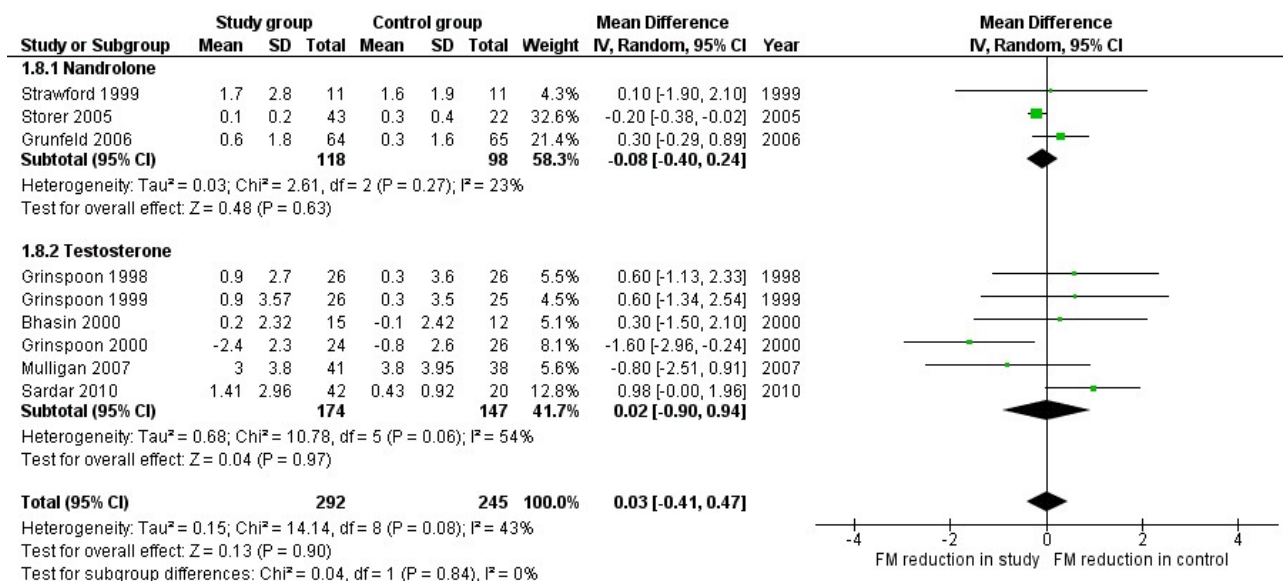


Panel A

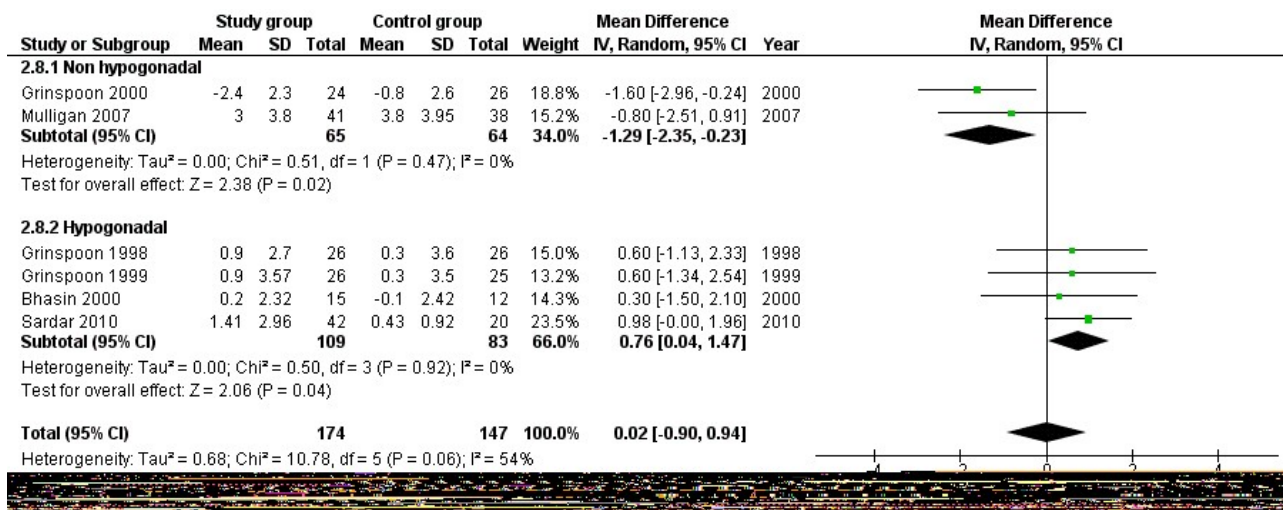


Panel B

Supplementary Figure S6.(Panel A Panel B)



Panel A



Panel B

Supplementary Figure S7.(Panel A Panel B)