

# Menopause, obesity and sarcopenia

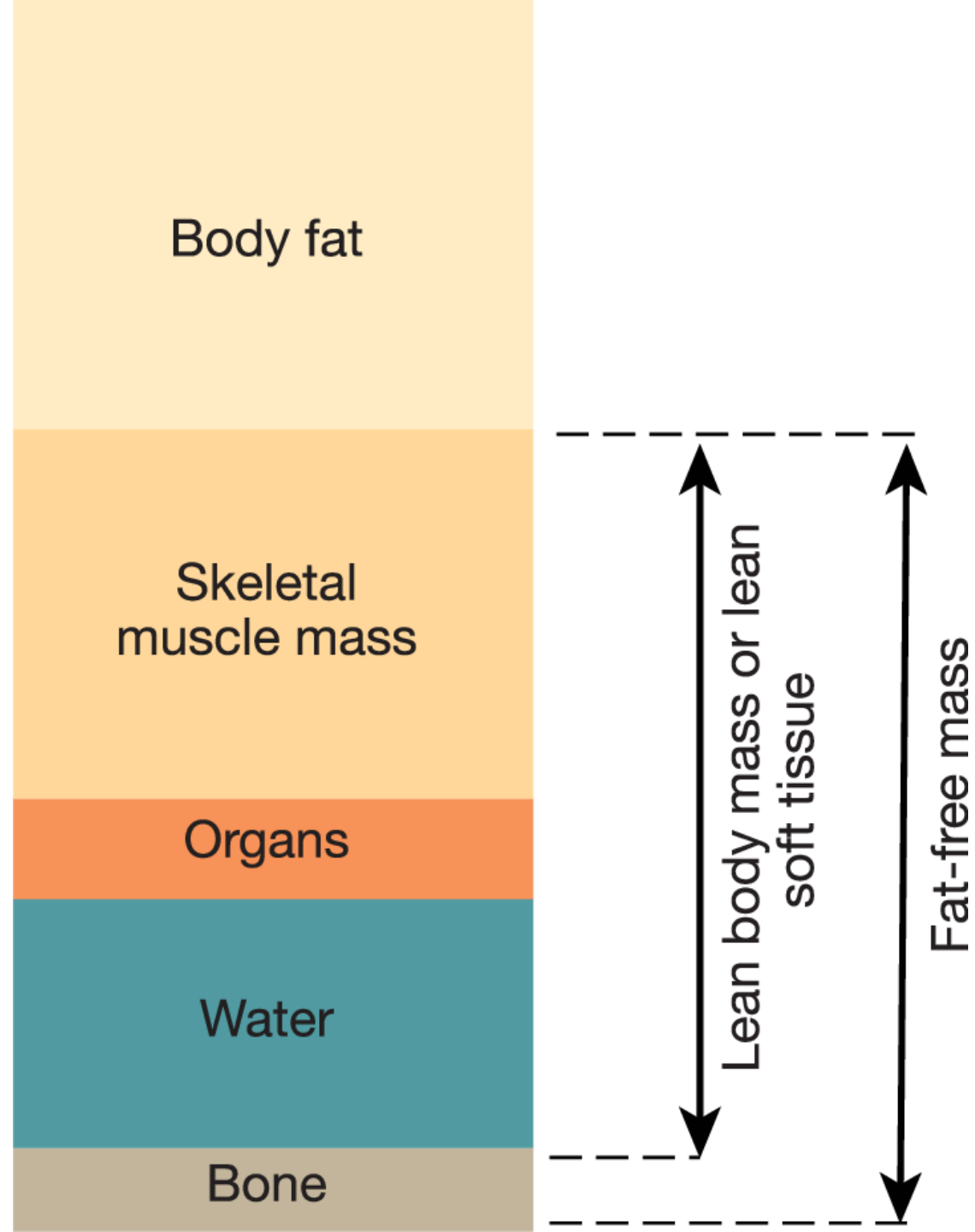
*Prof. dr. Patrick Calders*

*Department of Rehabilitation Sciences*

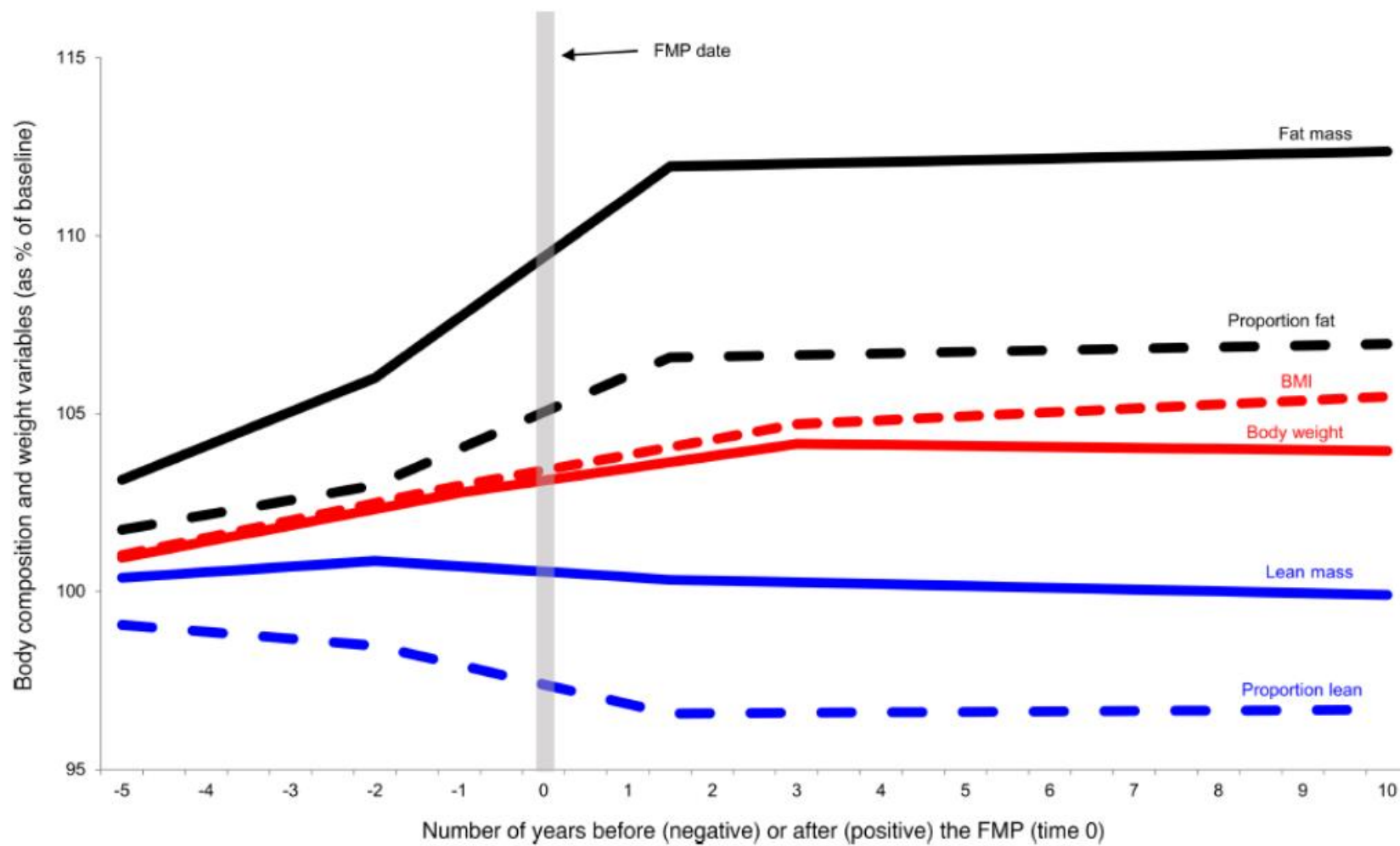
*Faculty of Medicine and Health Sciences*

*Ghent University*

# *Body composition*

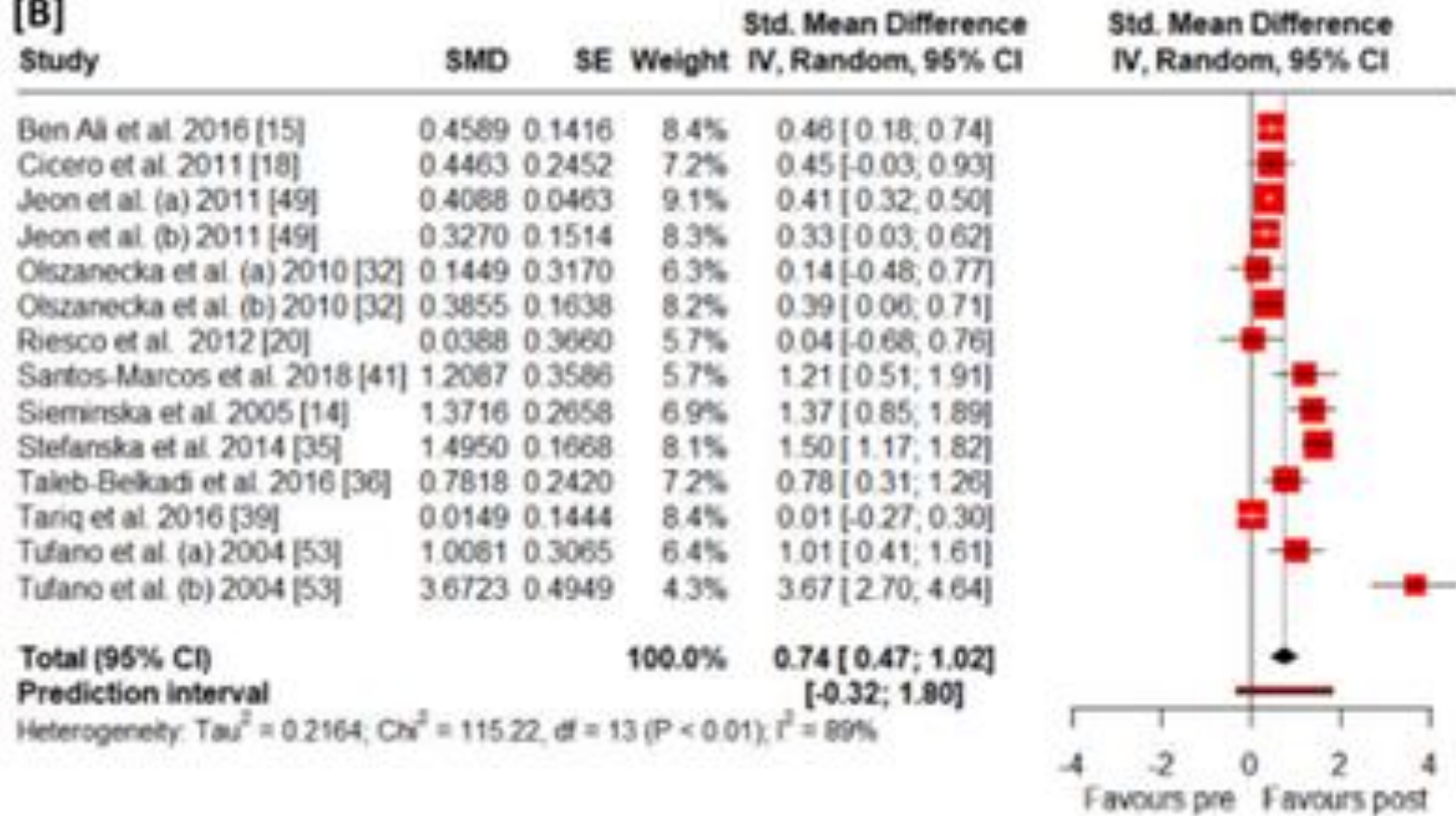


# Body composition

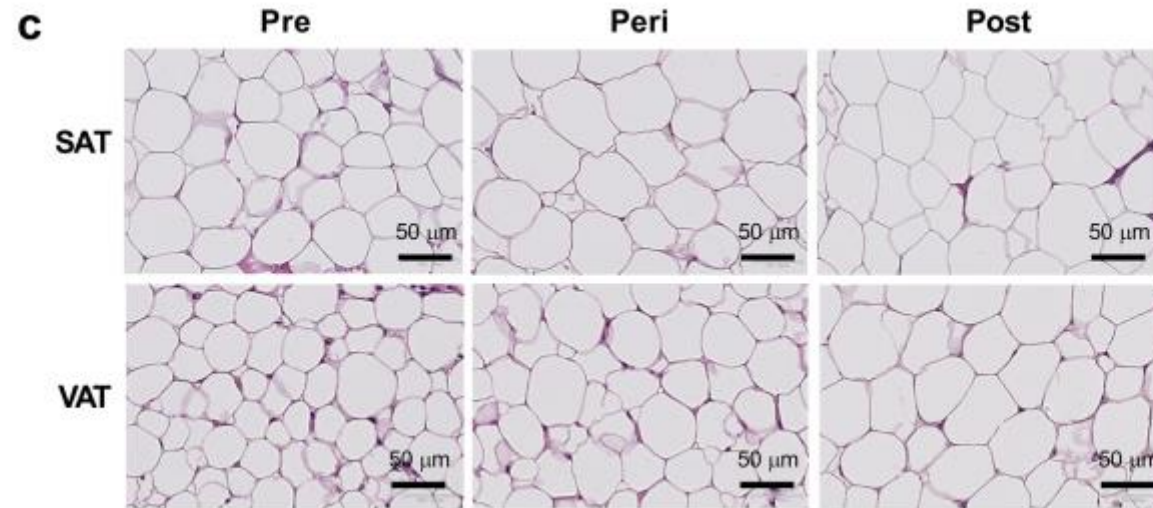
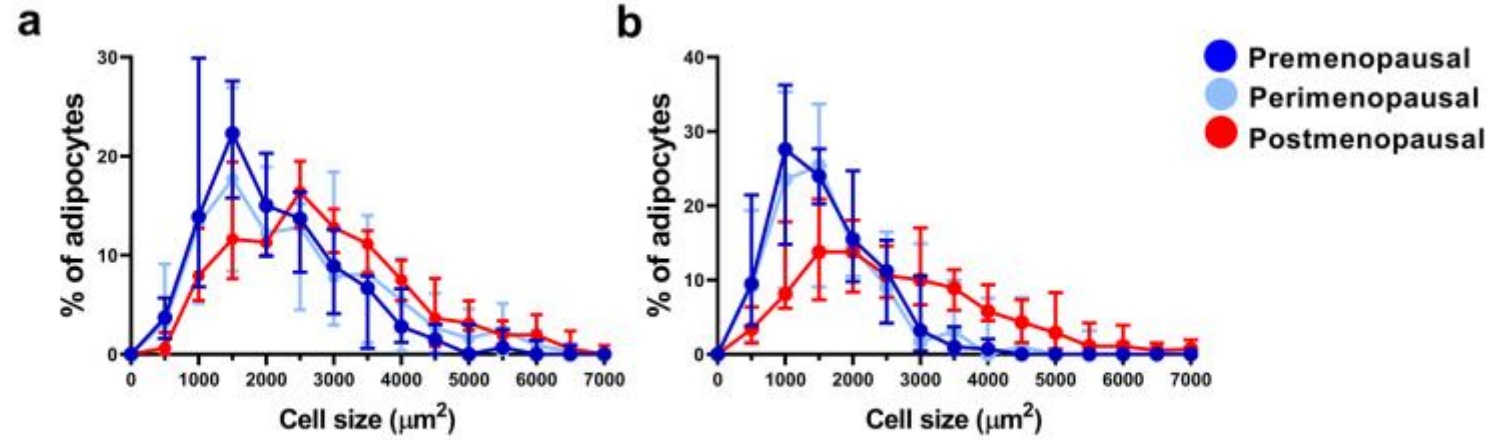


**Figure 2. Model-predicted trajectories of body composition and body weight outcomes relative to the time prior to or after the FMP, SWAN.** Values shown are for an average study participant (i.e., with each model covariate set at its analysis sample mean). Covariates were age at FMP, race, SWAN study site, and HT use.

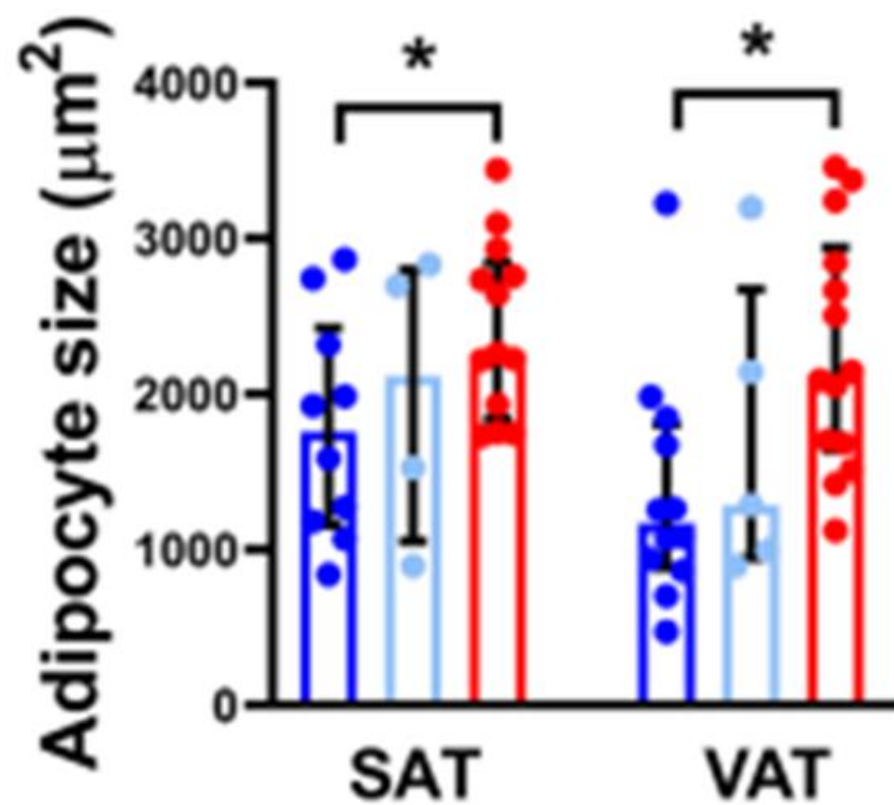
[B]



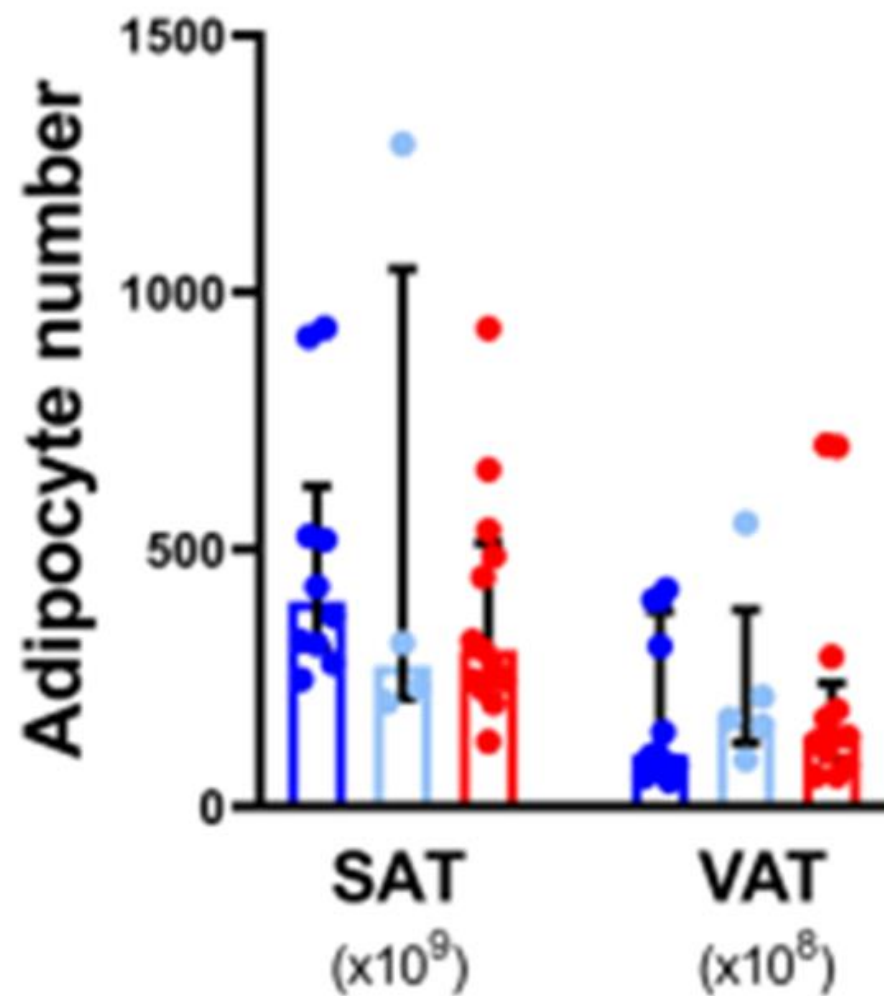
Waist



**d**

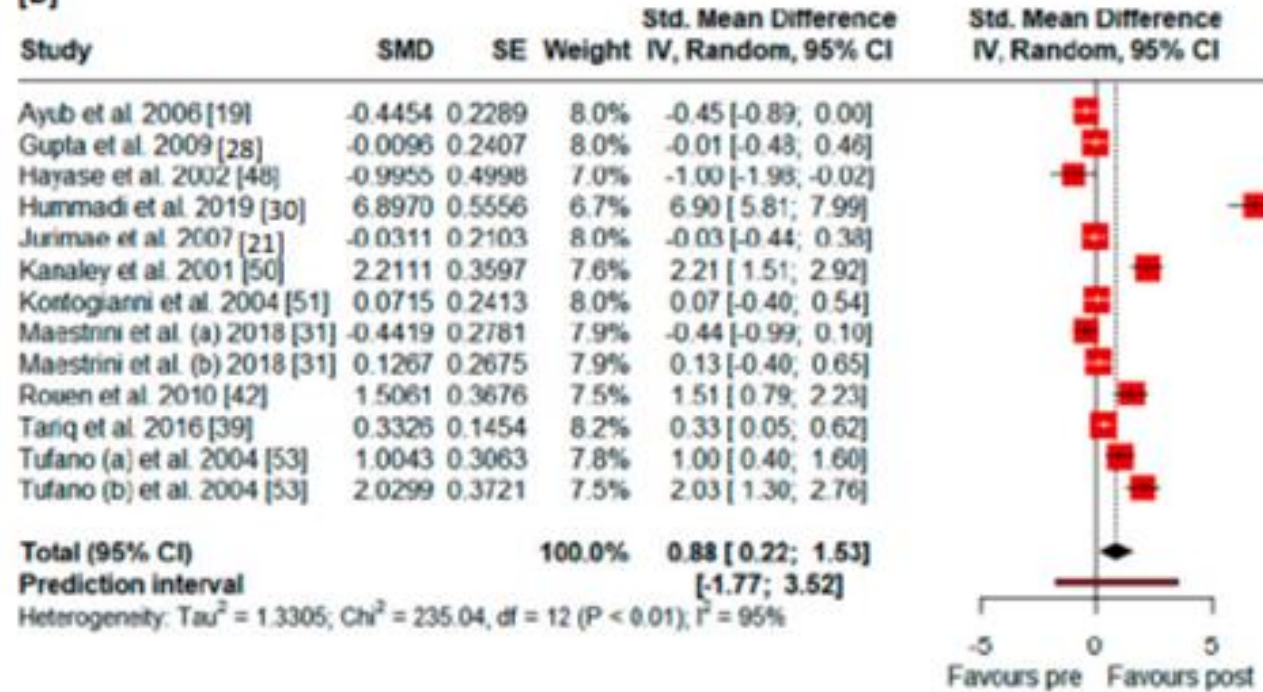


**e**



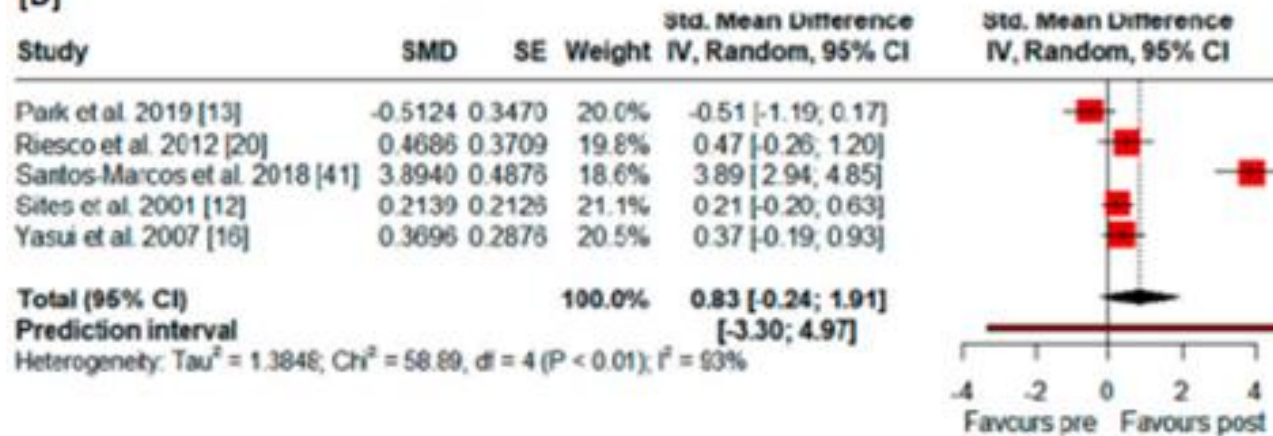


[B]



Leptin

[D]



IL-6

Table 1. *Subject characteristics*

Variable	Pre <i>n</i> = 30	EPeri <i>n</i> = 31	LPeri <i>n</i> = 30	EPost <i>n</i> = 26	LPost <i>n</i> = 27	<i>P</i> Value
Age, yr	38 ± 6	50 ± 3	50 ± 4	55 ± 3	62 ± 4	<b>&lt;0.001</b>
Weight, kg	65.9 ± 9.8	71.3 ± 10.9	67.3 ± 11.9	71.8 ± 12.9	66.6 ± 14.0	0.19
Height, cm	165 ± 6	165 ± 6	166 ± 7	165 ± 6	161 ± 7	0.053
BMI, kg/m <sup>2</sup>	24.3 ± 3.8	26.1 ± 3.9	24.5 ± 3.9	26.6 ± 5.1	25.7 ± 5.1	0.21
WC, cm	80.6 ± 8.0	84.4 ± 10.4	82.1 ± 11.9	87.9 ± 13.9	83.5 ± 10.7	0.23
Total lean mass, kg	42.2 ± 3.6	44.3 ± 5.7	40.5 ± 5.1	42.3 ± 6.3	39.0 ± 5.5	<b>&lt;0.01</b>
ALM, kg	17.8 ± 1.7	18.7 ± 2.7	16.8 ± 2.7	17.6 ± 3.1	16.0 ± 2.6	<b>&lt;0.01</b>
Total fat mass, kg	21.6 ± 7.7	24.7 ± 6.9	24.8 ± 8.1	27.4 ± 8.0	25.7 ± 9.6	0.10
Trunk fat mass, kg	9.5 ± 4.0	12.1 ± 4.2	12.0 ± 4.6	13.2 ± 4.8	12.4 ± 4.9	<b>&lt;0.05</b>
Estradiol, pg/mL <sup>a,b</sup>	79 [64, 110]	70 [37, 141]	34 [10, 94]	11 [10, 15]	10 [10, 14]	<b>&lt;0.001</b>
Estrone, ng/dL <sup>a,b</sup>	61 [41, 70]	60 [34, 88]	43 [30, 69]	26 [24, 33]	26 [23, 37]	<b>&lt;0.001</b>
FSH, $\mu$ IU/mL <sup>b</sup>	6.5 ± 3.4	22.0 ± 30.0	64.1 ± 35.5	72.1 ± 26.1	84.1 ± 33.3	<b>&lt;0.001</b>
Progesterone, ng/dL <sup>a,b</sup>	0.4 [0.2, 0.6]	0.5 [0.2, 0.8]	0.3 [0.2, 0.5]	0.3 [0.1, 0.4]	0.2 [0.1, 0.4]	<b>&lt;0.01</b>
Testosterone, ng/dL <sup>a,b</sup>	24 [22, 33]	22 [17, 35]	20 [17, 25]	18 [17, 23]	17 [17, 35]	0.32
$\dot{V}O_{2peak}$ , mL·kg <sup>-1</sup> ·min <sup>-1c</sup>	31.2 ± 6.4	28.3 ± 4.8	27.5 ± 5.9	26.3 ± 3.6	24.7 ± 7.2	<b>&lt;0.001</b>

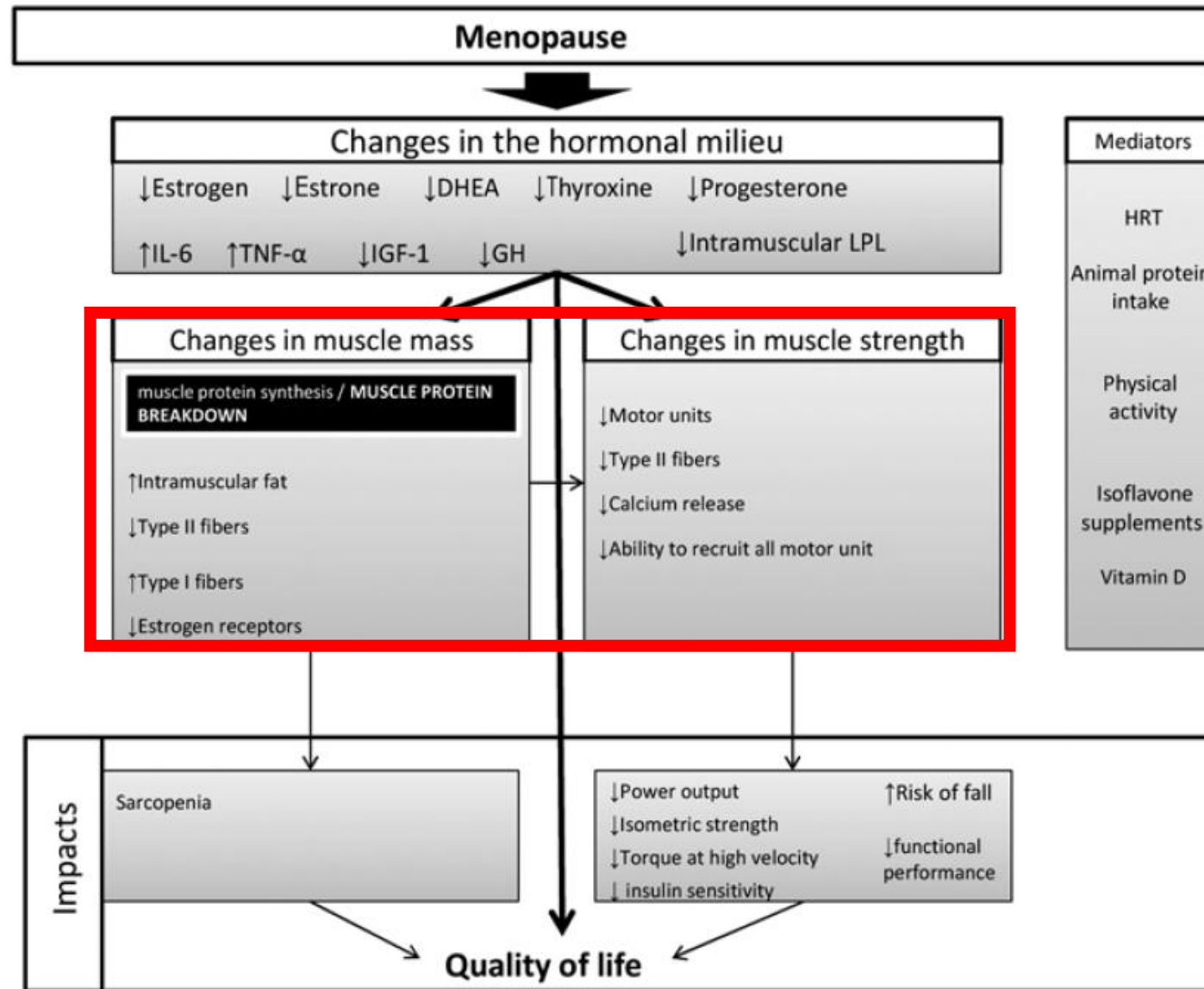
Data are means ± standard deviation or <sup>a</sup>median [interquartile range] for *n* subjects. <sup>b</sup>*n* = 118, <sup>c</sup>*n* = 139. ALM, appendicular lean mass; BMI, body mass index; EPeri, early perimenopausal; EPost, early postmenopausal; FSH, follicle stimulating hormone; LPeri, late perimenopausal; LPost, late postmenopausal; Pre, premenopausal;  $\dot{V}O_{2peak}$ , peak aerobic capacity; WC, waist circumference. Significant *P* values are in bold.



Table 2. *Prevalence of sarcopenia*

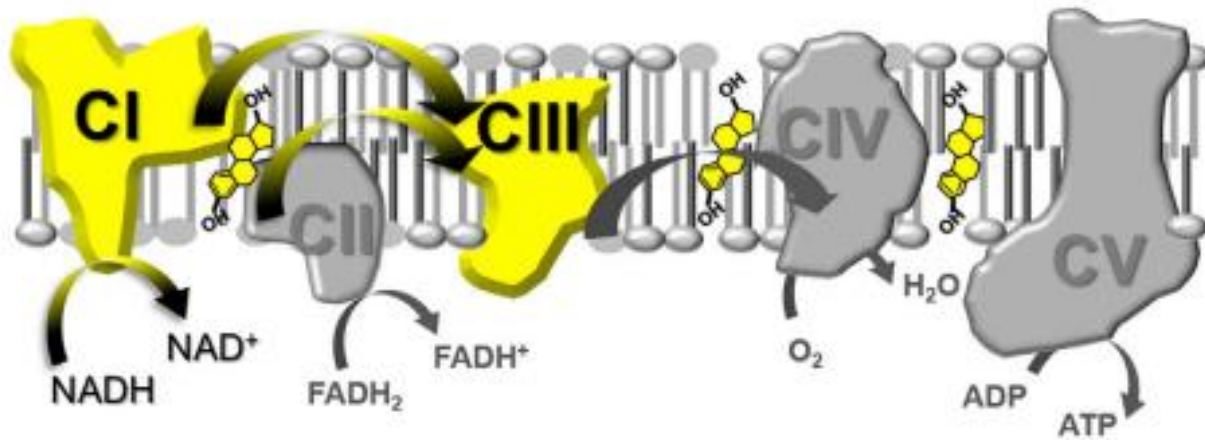
Variable	Pre <i>n</i> = 30	EPeri <i>n</i> = 31	LPeri <i>n</i> = 30	EPost <i>n</i> = 26	LPost <i>n</i> = 27
Below 5.31 kg/m <sup>2</sup> of ALMi <sup>a</sup>					
Sarcopenic, <i>n</i> (%)	0 (0)	0 (0)	3 (10.0)	5 (11.5)	5 (18.5)
Below 5.67 kg/m <sup>2</sup> of ALMi <sup>b</sup>					
Sarcopenic, <i>n</i> (%)	2 (6.7)	1 (3.2)	9 (30.0)	7 (26.9)	9 (33.3)

*n* = no. of subjects. ALMi, appendicular lean mass adjusted by square of height (m<sup>2</sup>); EPeri, early perimenopausal; EPost, early postmenopausal; LPeri, late perimenopausal; LPost, late postmenopausal; Pre, premenopausal. <sup>a</sup>A cut point from Fielding et al. (3) and Newman et al. (27); <sup>b</sup>≥2 SD below the premenopausal group of the present study.



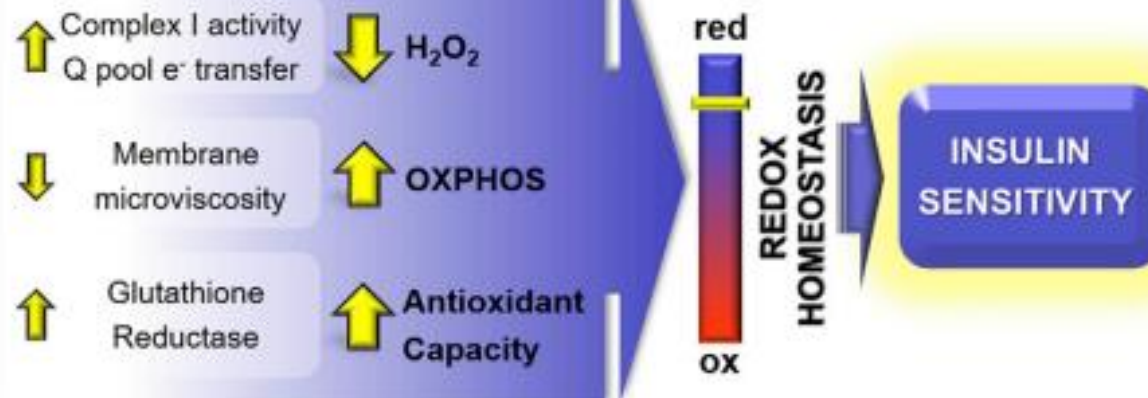
**Figure 1.** Menopause-related changes on muscle mass and its impacts on different characteristics that contribute to quality of life.

## Graphical Abstract



↑  $JO_2$     ↑  $JATP$

### 17 $\beta$ -Estradiol



Cell Metabolism  
27, 167–179, January 9, 2018

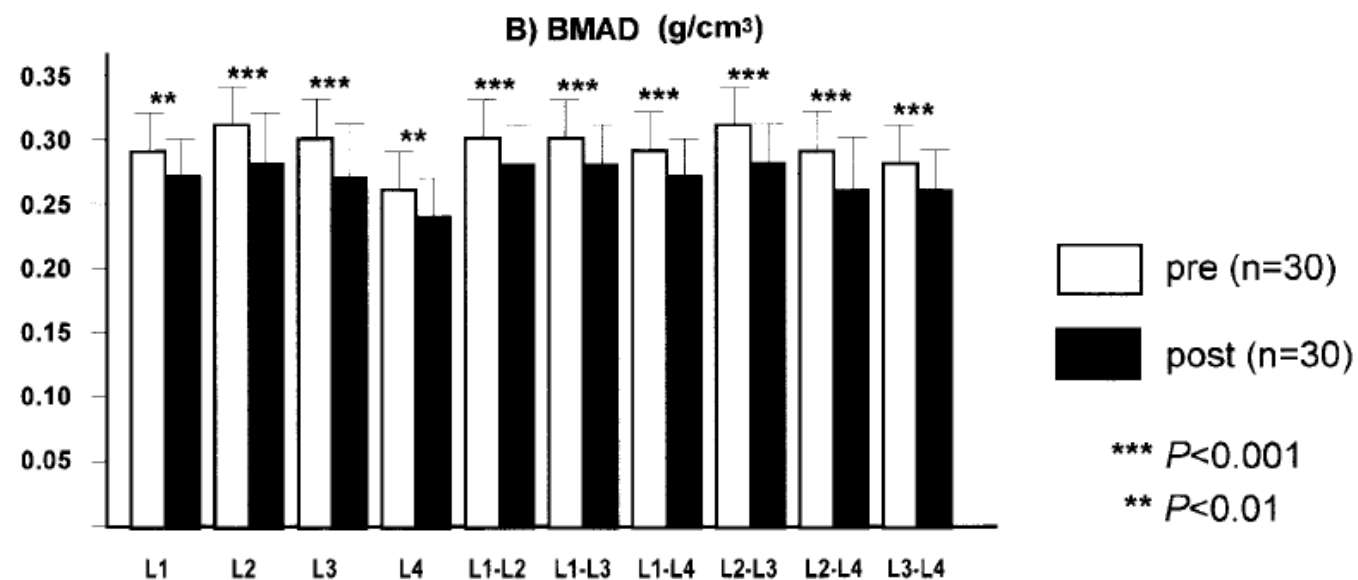
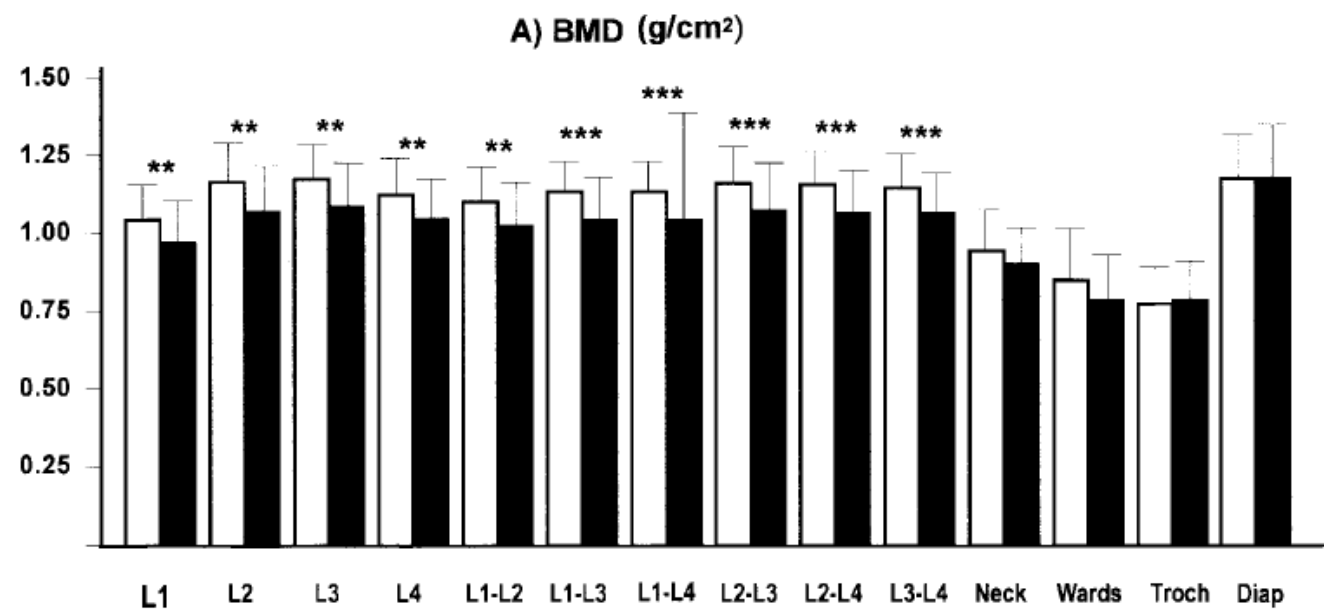
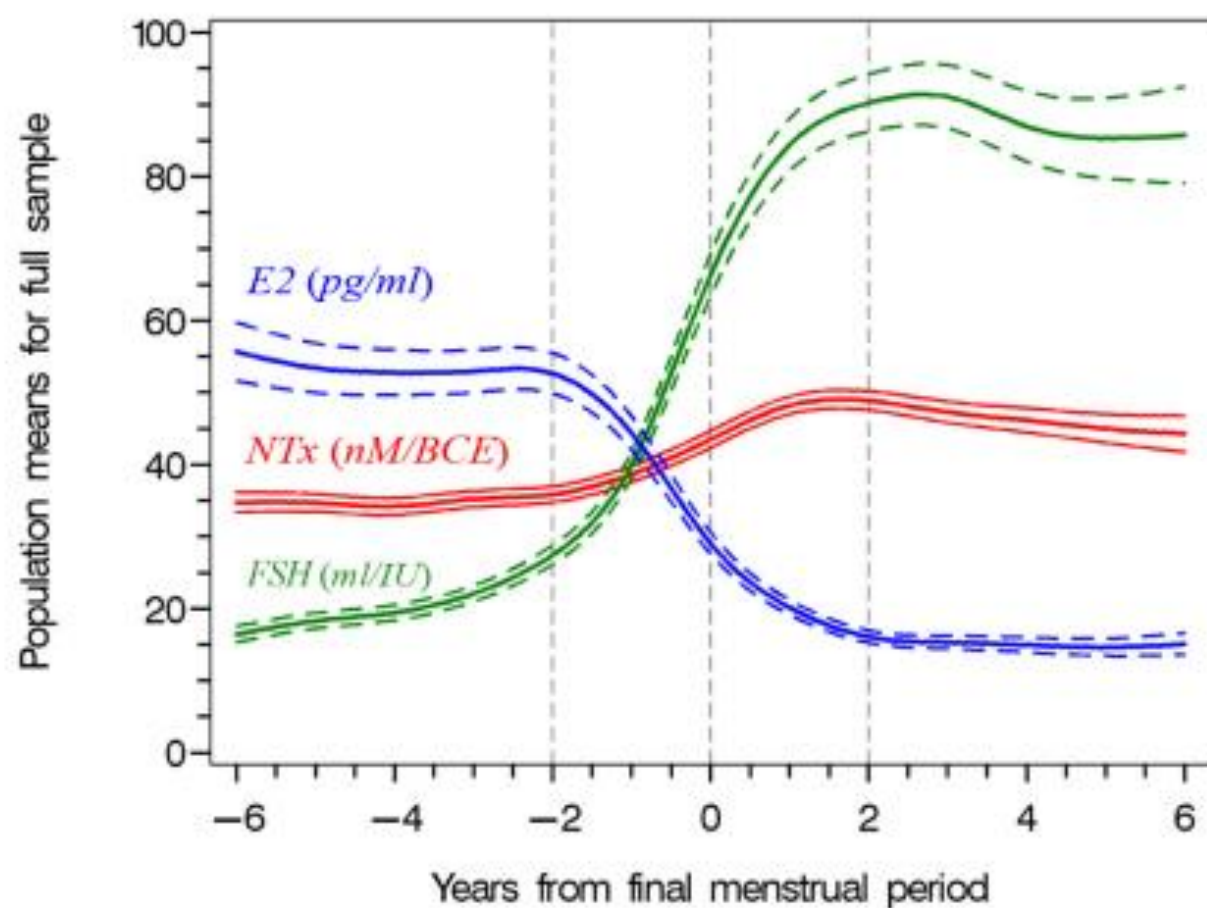


Fig. 1. A) BMD at the spine [lumbar (L) vertebrae] and hip (femur neck, Ward's triangle, trochanter, Troch, and cortical diaphysis, Diap), B), BM(A)D at the spine of pre- (n = 30) and postmenopausal women (n = 30). Mean  $\pm$  SD \*\*\* $p < 0.001$  \*\* $p < 0.01$ .



**Figure 2.** Population mean urine NTX, serum estradiol, and serum FSH levels in relation to years from FMP in the women who experienced a natural FMP ( $n = 918$ ). The dashed lines denote the 95% confidence intervals.



**SUPPLEMENTARY FIGURE 1:** Age-adjusted values of visceral adipose tissue stratified by menopausal hormone therapy status.

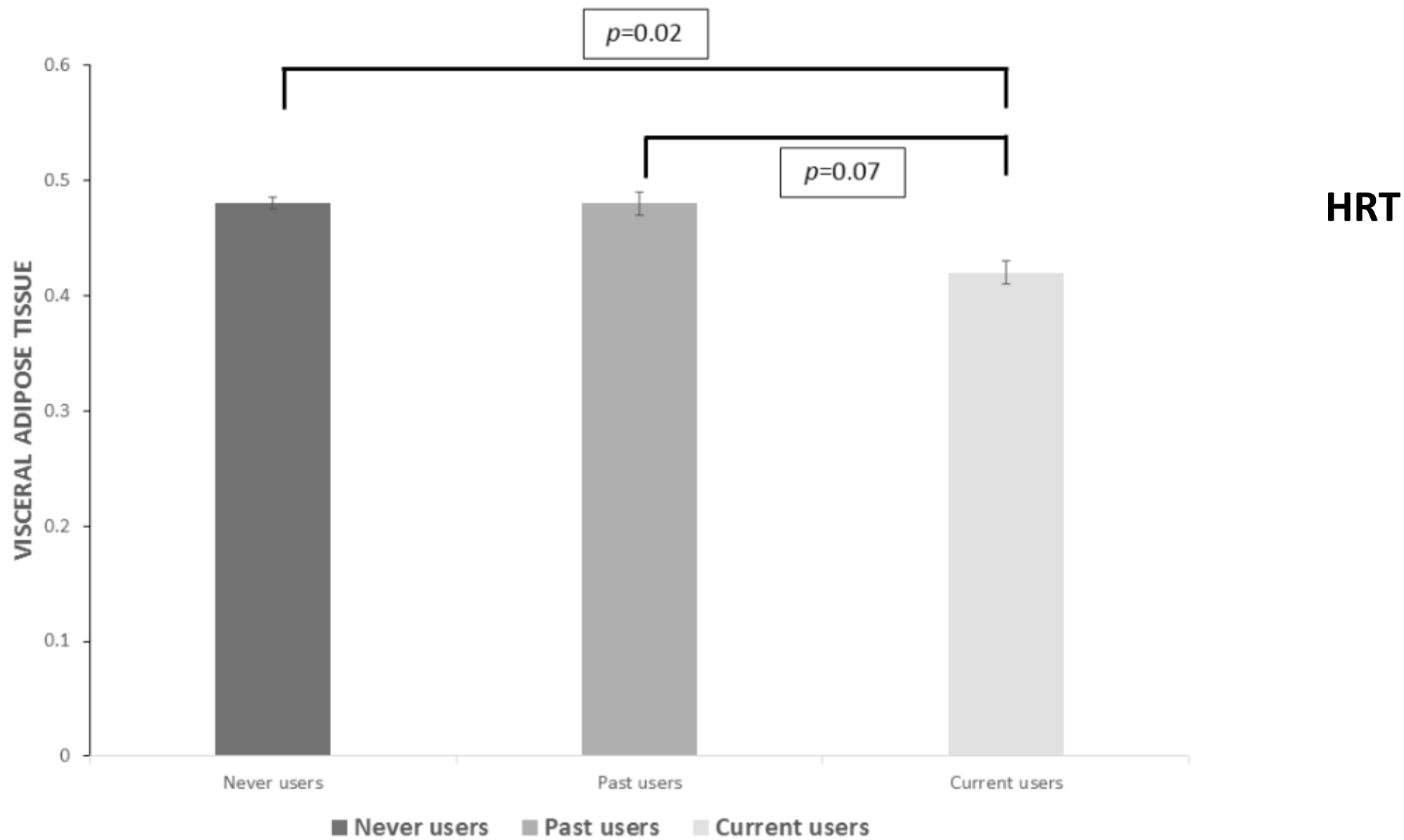
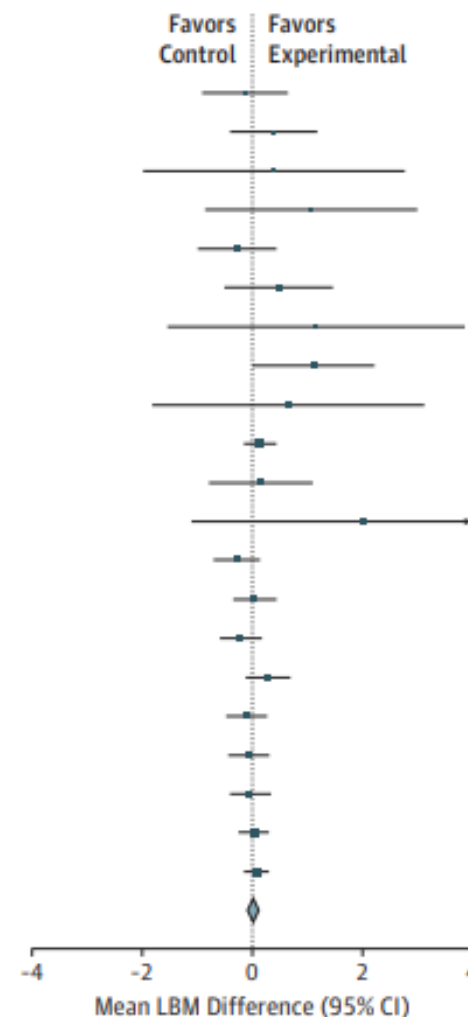
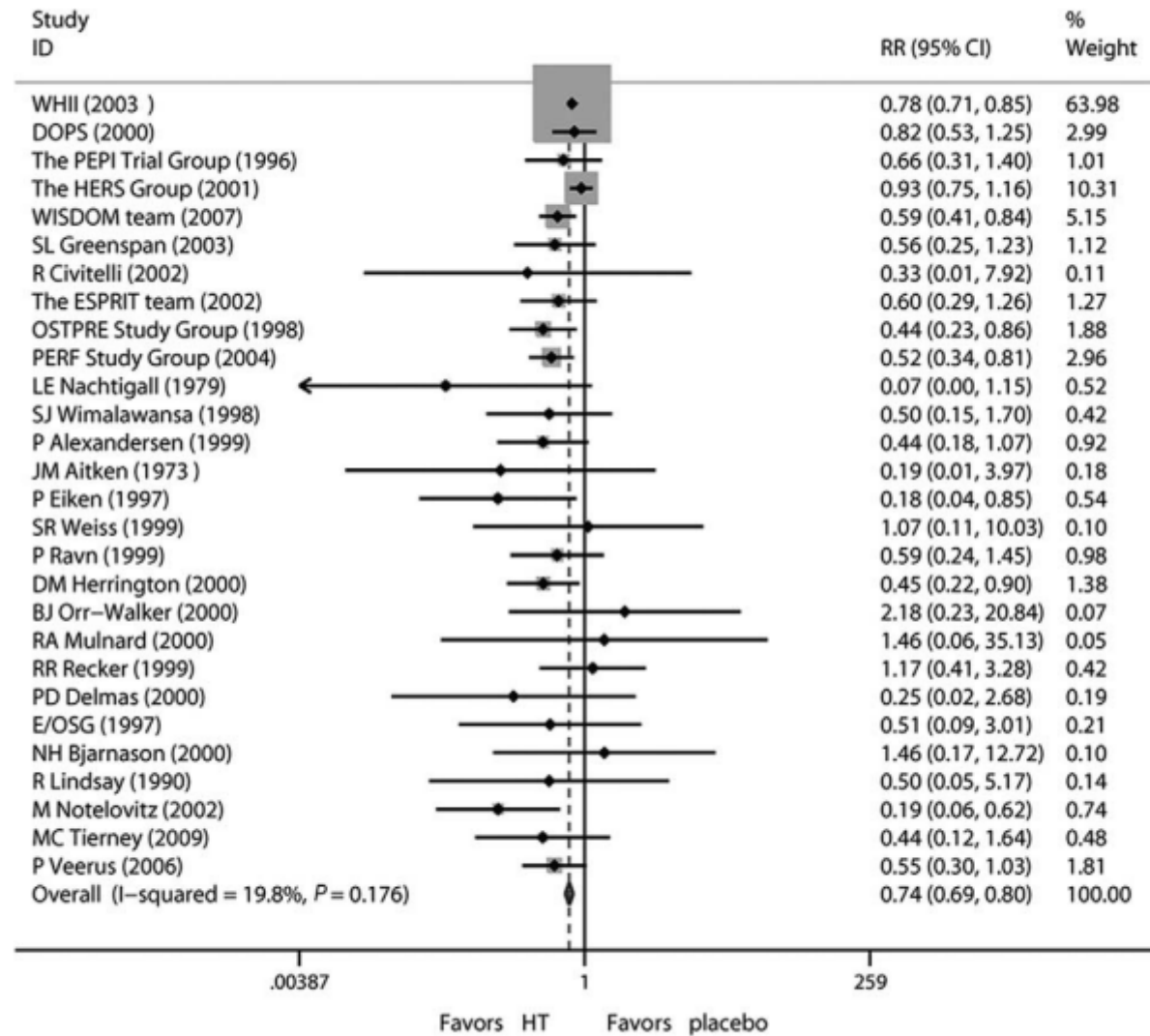


Figure 2. Summary Meta-analysis of the Association Between Hormone Therapy (HT) Intervention and Muscle Mass Outcomes

Study	Receiving HT		No HT		Mean LBM Difference (95% CI)
	Mean (SD) LBM Difference, kg	Total	Mean (SD) LBM Difference, kg	Total	
Hassager and Christiansen, <sup>58</sup> 1989	(1) 0.19 (2.15)	32	0.33 (2.13)	58	-0.14 (-1.06 to 0.78)
Hassager and Christiansen, <sup>58</sup> 1989	(2) 0.81 (1.65)	20	0.33 (2.13)	58	0.48 (-0.43 to 1.39)
Haarbo et al, <sup>48</sup> 1991	(1) -0.20 (5.20)	19	-0.70 (3.85)	24	0.50 (-2.30 to 3.30)
Haarbo et al, <sup>48</sup> 1991	(2) 0.60 (3.70)	19	-0.70 (3.85)	24	1.30 (-1.00 to 3.60)
Aloia et al, <sup>60</sup> 1995	-1.06 (1.64)	30	-0.75 (1.59)	28	-0.31 (-1.14 to 0.52)
Evans et al, <sup>61</sup> 2001	1.10 (1.90)	15	0.50 (1.40)	19	0.60 (-0.55 to 1.75)
Sipilä et al, <sup>52</sup> 2001	1.10 (4.25)	15	-0.30 (4.65)	15	1.40 (-1.79 to 4.59)
Sørensen et al, <sup>59</sup> 2001	0.35 (0.86)	7	-1.00 (1.58)	7	1.34 (0.01 to 2.67)
Blackman et al, <sup>47</sup> 2002	1.20 (4.58)	19	0.40 (3.93)	14	0.80 (-2.11 to 3.71)
Jensen et al, <sup>49</sup> 2003	0.18 (1.77)	268	-0.02 (2.33)	353	0.20 (-0.12 to 0.52)
Kenny et al, <sup>50</sup> 2005	-0.30 (3.37)	71	-0.50 (3.30)	68	0.20 (-0.91 to 1.31)
Pöllänen et al, <sup>51</sup> 2007	1.00 (4.00)	10	-1.40 (3.10)	5	2.40 (-1.28 to 6.08)
Thornycroft et al, <sup>53</sup> 2007	(1A) -0.12 (1.87)	97	0.19 (1.55)	94	-0.31 (-0.80 to 0.18)
Thornycroft et al, <sup>53</sup> 2007	(1B) 0.26 (1.56)	95	0.19 (1.55)	94	0.07 (-0.37 to 0.51)
Thornycroft et al, <sup>53</sup> 2007	(1C) -0.04 (1.51)	89	0.19 (1.55)	94	-0.23 (-0.67 to 0.21)
Thornycroft et al, <sup>53</sup> 2007	(2A) 0.55 (1.48)	86	0.19 (1.55)	94	0.36 (-0.08 to 0.80)
Thornycroft et al, <sup>53</sup> 2007	(2B) 0.10 (1.47)	96	0.19 (1.55)	94	-0.09 (-0.52 to 0.34)
Thornycroft et al, <sup>53</sup> 2007	(2C) 0.13 (1.45)	94	0.19 (1.55)	94	-0.06 (-0.49 to 0.37)
Thornycroft et al, <sup>53</sup> 2007	(2D) 0.16 (1.39)	98	0.19 (1.55)	94	-0.03 (-0.45 to 0.39)
Bea et al, <sup>46</sup> 2011	(1) -0.44 (2.28)	453	-0.50 (2.45)	474	0.06 (-0.24 to 0.36)
Bea et al, <sup>46</sup> 2011	(2) -0.29 (1.99)	543	-0.40 (2.15)	471	0.11 (-0.15 to 0.37)
Total		2176		2276	0.06 (-0.05 to 0.18)

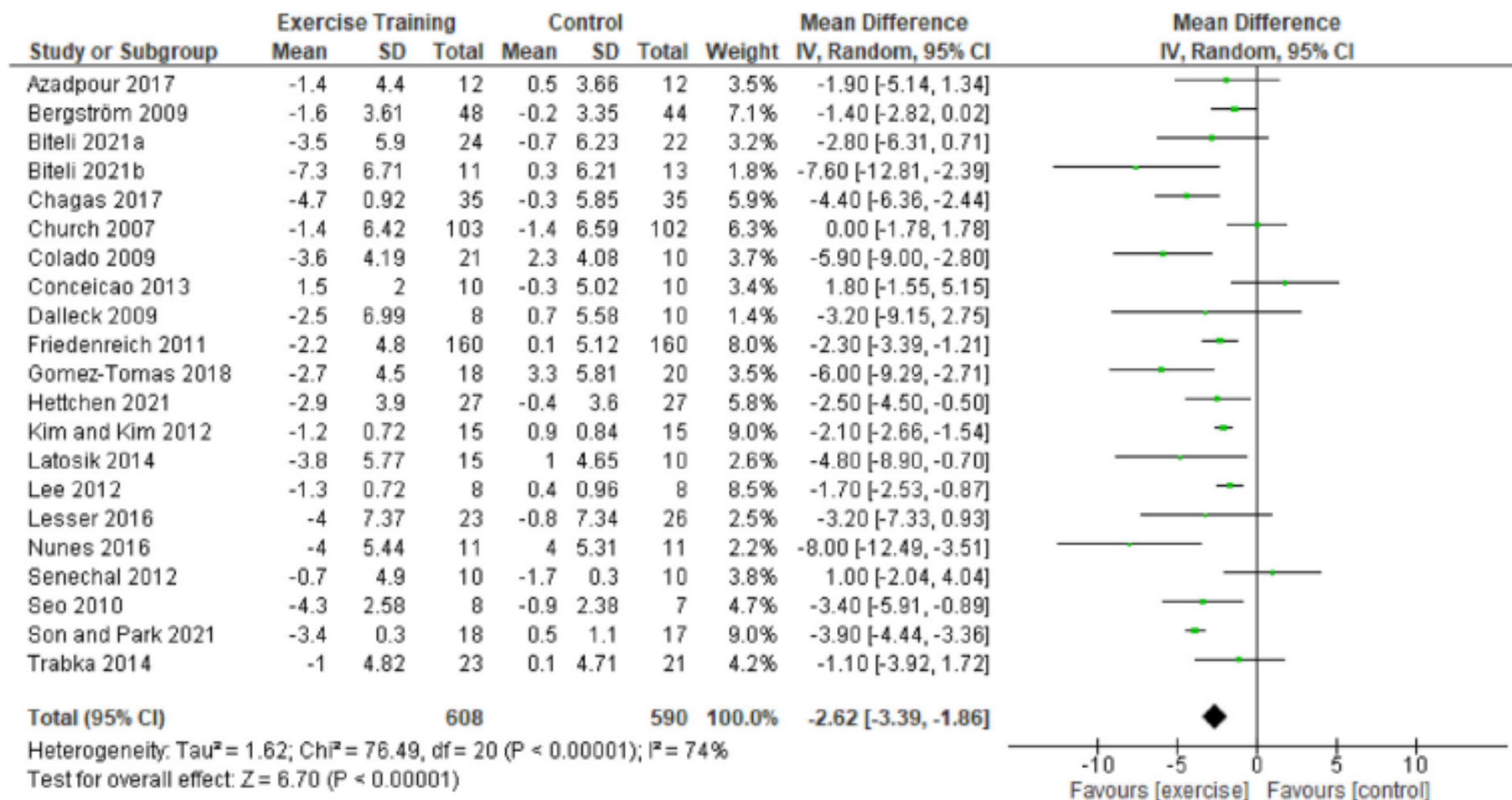
Heterogeneity  $\chi^2 = 17.37$ ;  $df = 20$  ( $P = .63$ );  $I^2 = 0\%$ Test for overall effect  $Z = 1.12$  ( $P = .26$ )

## HORMONE THERAPY ON BONE FRACTURES



**HRT**

3. 2. Forest plot of the association between HT and total fractures. ID, study ID; HT, hormone therapy; RR, relative risk.



## Exercise

**Fig. 2.** Forest plot of randomised controls trials investigating the effect of exercise training vs control on waist circumference using the random effects model. There are a total of 21 studies reporting changes in waist circumference (cm). Negative values favour exercise intervention on the left side. 95% CI: 95% confidence interval; MD: mean difference; SD: standard deviation.

### Meta-analyses

Effects of exercise training on metabolic syndrome risk factors in post-menopausal women – A systematic review and meta-analysis of randomised controlled trials

Abbigail Tan <sup>a,\*</sup>, Rebecca L. Thomas <sup>b</sup>, Matthew D. Campbell <sup>c,d</sup>, Sarah L. Prior <sup>b</sup>, Richard M. Bracken <sup>a</sup>, Rachel Churm <sup>a</sup>

<sup>a</sup> Applied Sports Technology, Exercise and Medicine (A-STEM) Research Centre, Faculty of Science and Engineering, Swansea University, Swansea, UK

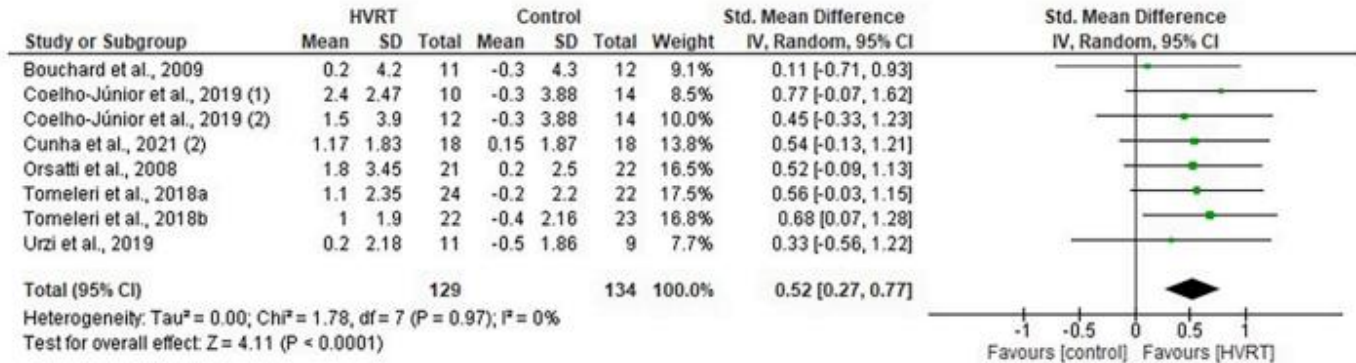
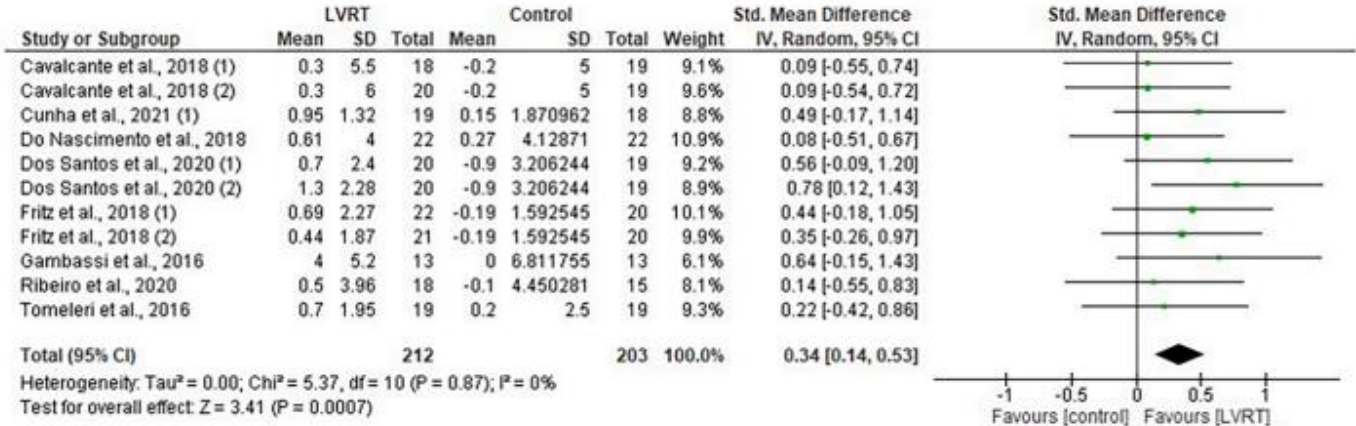
<sup>b</sup> Diabetes Research Group, Grove Building, Swansea University, Swansea, UK

<sup>c</sup> School of Nursing and Health Sciences, Sciences Complex, University of Sunderland, Sunderland, UK

<sup>d</sup> Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds, UK

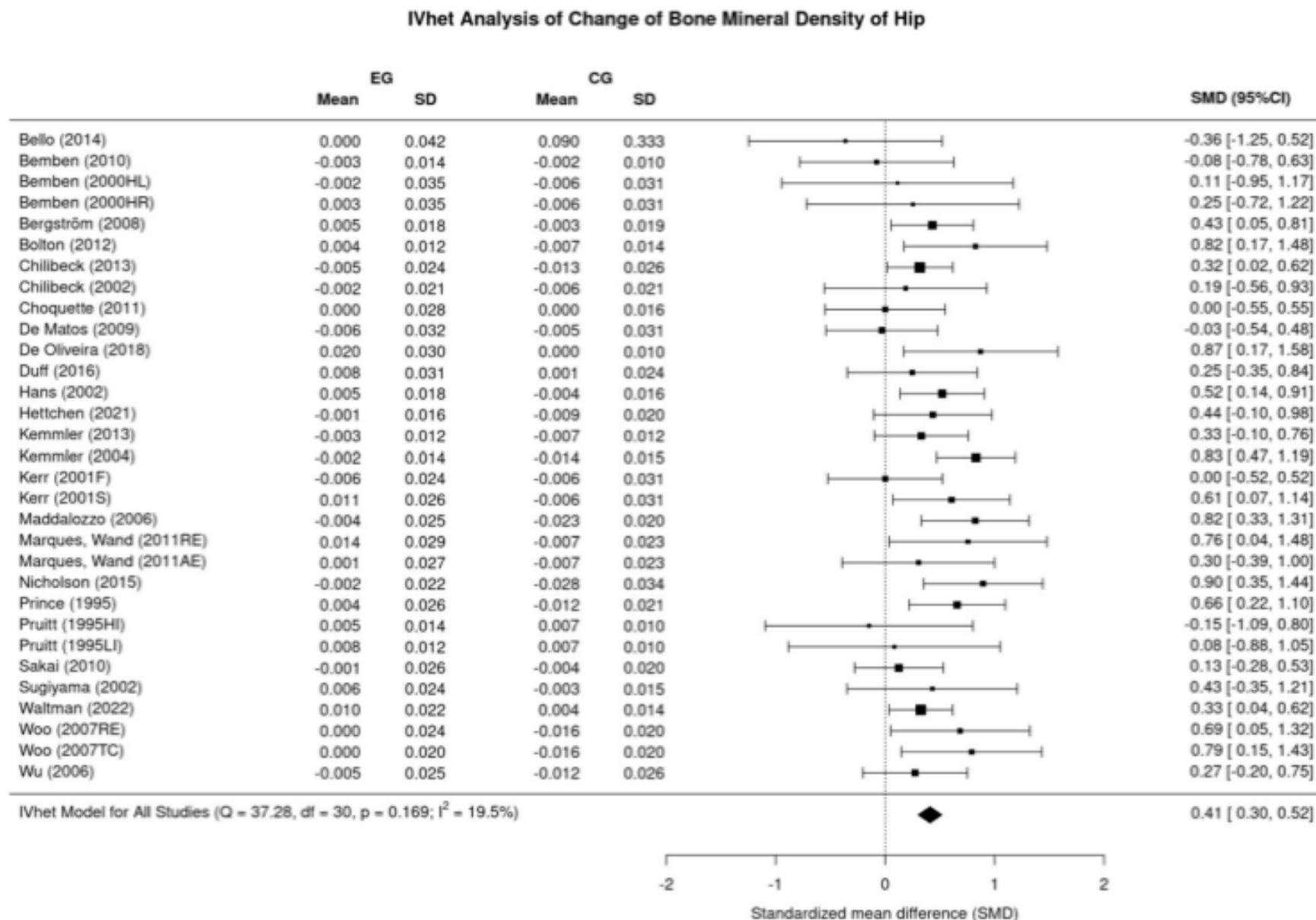


Exercise



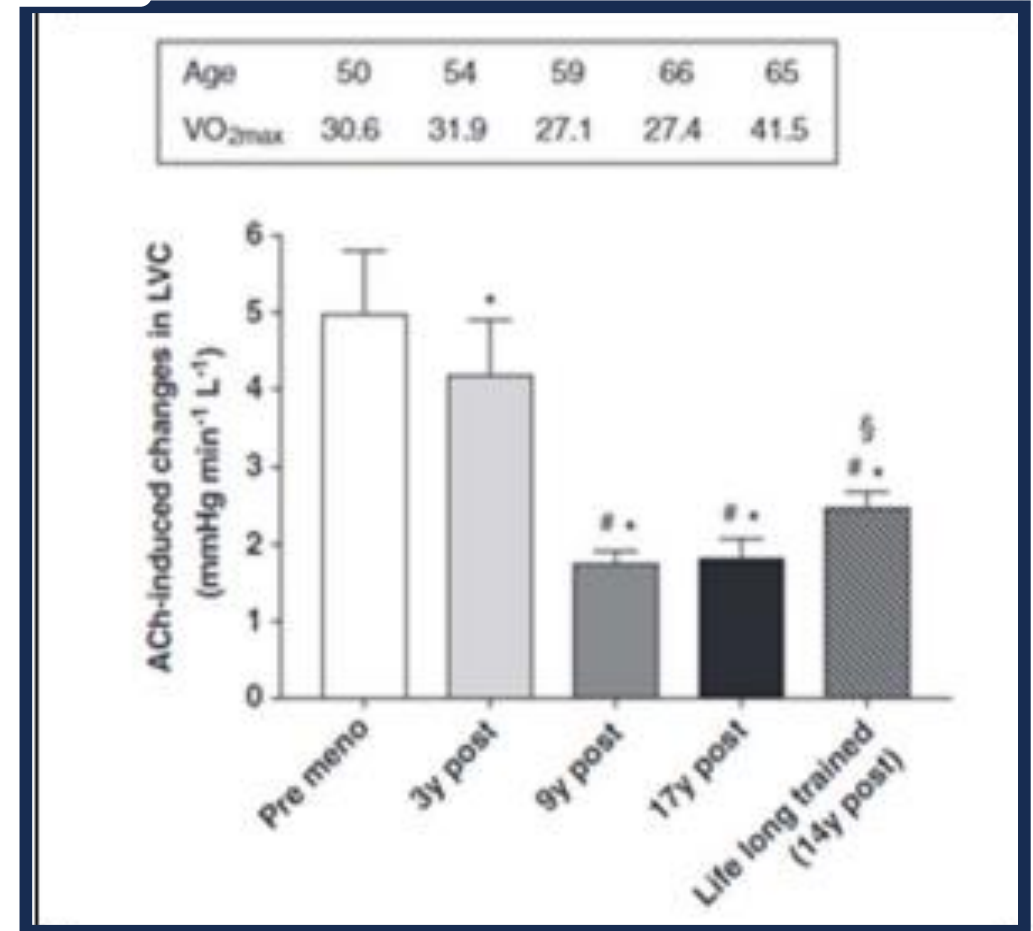
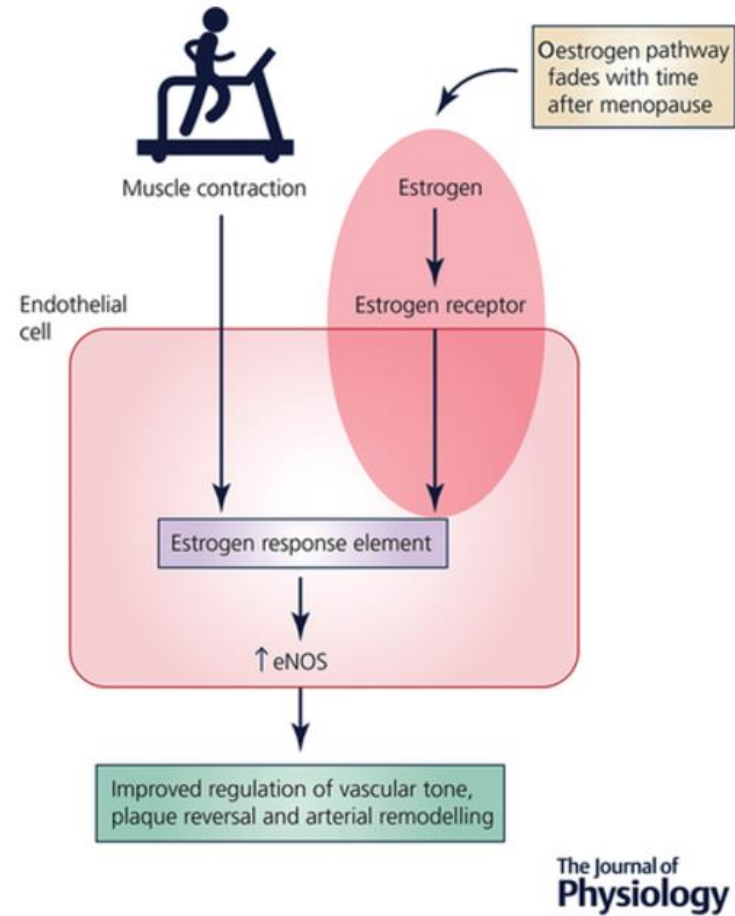
**Fig. 3.** Forest plot of the effects of resistance training volume on muscle hypertrophy. A - Low volume resistance training (LVRT) vs Control and B - High volume resistance training (HVRT) vs Control.



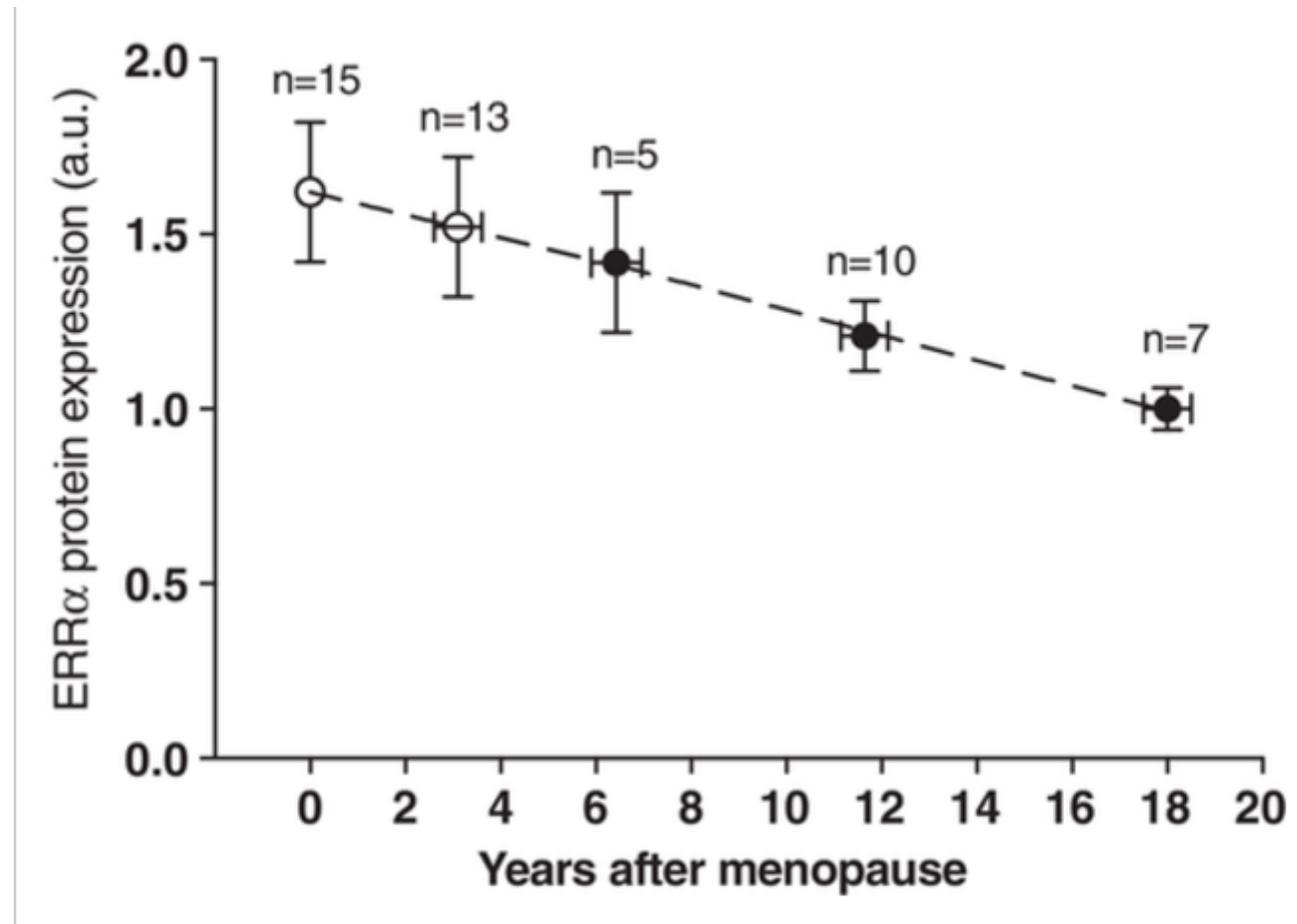


**Fig. 6** Forest plot of meta-analysis results at the total hip (IVhet model). The data are shown as pooled standard mean difference (SMD) with 95% CI for changes in the exercise (EG) versus control groups (CG). Imputation with mean correlation

## Timing hypothesis



Glieman  
&  
Hellsten (2017)



**Figure 3. Protein expression of oestrogen-related receptor  $\alpha$  (ERR $\alpha$ ) as a function of time after menopause in skeletal muscle homogenates from sedentary pre- and postmenopausal women**

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Table 4. Body Composition Changes in  
Exercisers and Nonexercisers

Variable	EX/HRT ( <i>n</i> = 16)	NEX/HRT ( <i>n</i> = 22)	EX/NHRT ( <i>n</i> = 20)	NEX/NHRT ( <i>n</i> = 26)
LST mass				
Total body (kg)	0.6 ± 0.3	0.2 ± 0.4	0.7 ± 0.2*	-0.4 ± 0.2
Arm (kg)	0.2 ± 0.1**	0.1 ± 0.1	0.2 ± 0.1*	0.0 ± 0.0
Leg (kg)	0.1 ± 0.1***	-0.2 ± 0.1	0.1 ± 0.1*	-0.2 ± 0.1
Fat mass				
Total body (kg)	-0.9 ± 0.7	0.1 ± 0.8	-0.6 ± 0.5	1.0 ± 0.7
Arm (kg)	-0.1 ± 0.1	0.1 ± 0.1	0.1 ± 0.7	0.2 ± 0.1
Leg (kg)	-0.7 ± 0.2***	-0.0 ± 0.2	-0.3 ± 0.2	0.2 ± 0.2
Trunk (kg)	-0.2 ± 0.2	-0.0 ± 0.3	-0.4 ± 0.3**	0.6 ± 0.4
Body fat (%)	-1.4 ± 0.8	0.0 ± 0.7	-0.9 ± 0.5*	1.0 ± 0.4

*Notes:* Body composition changes are from baseline to 12 months, within hormone replacement therapy (HRT) and no hormone replacement therapy (NHRT) groups. EX = exercise; NEX = no exercise; LST= lean soft tissue. Values are mean ± SEM. Multiple linear regression with a priori contrasts (HRT vs NHRT, EX/HRT vs NEX/HRT, and EX/NHRT vs NEX/NHRT) was used to determine differences between groups.

\**p* < .05; \*\**p* = .08; \*\*\**p* = .09.

	Estrogen ( <i>n</i> = 15)					Placebo ( <i>n</i> = 16)					Training	Interaction
	Pre		Post		<i>P</i> -value	Pre		Post		<i>P</i> -value		
MVIC Ext (NM)	143	± 23.2	161.6	± 30.2	<b>&lt;0.01</b>	135.2	± 38.8	158.4	± 39.0	<b>&lt;0.01</b>	<b>&lt;0.01</b>	0.43
MVIC Flx (NM)	70.0	± 13.8	76.9	± 16.5	<b>0.03</b>	66.6	± 20.5	78.8	± 23.2	<b>&lt;0.01</b>	<b>0.03</b>	0.19
5 RM leg press (kg)	83.8	± 13.6	132.2	± 19.8	<b>&lt;0.01</b>	89.1	± 25.4	131.8	± 29.5	<b>&lt;0.01</b>	<b>&lt;0.01</b>	0.23
5 RM knee Ext (kg)	40.3	± 10.0	57.8	± 11.0	<b>&lt;0.01</b>	44.1	± 8.7	59.4	± 11.2	<b>&lt;0.01</b>	<b>&lt;0.01</b>	0.31
5 RM knee Flx (kg)	18.6	± 3.8	26.9	± 4.8	<b>&lt;0.01</b>	20.6	± 4.0	28.4	± 6.4	<b>&lt;0.01</b>	<b>&lt;0.01</b>	0.26

Values are presented at mean ± SD. MVIC Ext, maximal voluntary isometric contraction in knee extension; MVIC Flx, maximal voluntary isometric contraction in knee flexion; 5 RM, five-repetition maximum. *P*-values relates to pre vs. post changes within each group and results from Linear mixed model analysis on training effect and training x treatment interaction effects. *P*-values at 0.05 or below are reported in bold.



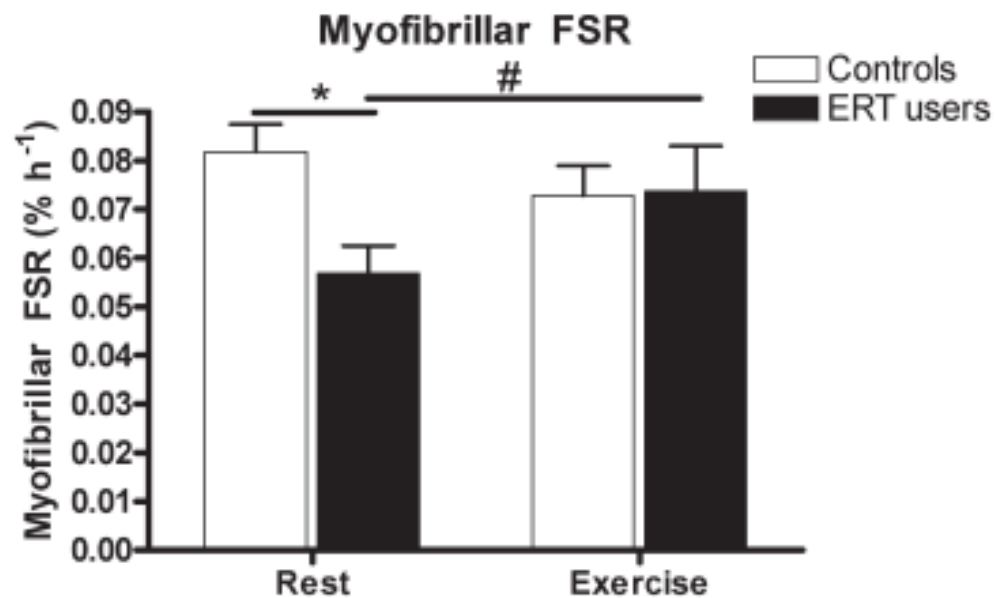


Figure 2. Myofibrillar protein fractional synthesis rate at rest and 24 hours after exercise in women, who use estrogen replacement therapy (ERT), and in women, who do not use ERT (Controls). Values are means  $\pm$  standard error of the mean. Two-way analysis of variance with repeated measures in one factor: ERT users versus Controls,  $p = .18$ ; rest versus exercise,  $p = .34$ ; and interaction between rest or exercise and Controls or ERT,  $p = .005$ . \* $p = .015$  ERT versus Controls. # $p = .010$  ERT<sub>rest</sub> versus ERT<sub>exercise</sub>.



Zijn er nog vragen??