#### Short-term Resveratrol supplementation stimulates serum levels of Bone-Specific Alkaline Phosphatase in obese non-diabetic men MM Poulsen<sup>1</sup>, MJ Ornstrup<sup>1</sup>, T Harsløf<sup>1</sup>, N Jessen<sup>1,2</sup>, BL Langdahl<sup>1</sup>, B Richelsen<sup>1</sup>, JO Jørgensen<sup>1</sup>, SB Pedersen<sup>1</sup>

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## BACKGROUND

- Resveratrol (RSV) is a dietary supplement found in redwine
- RSV reduces OVX- and immobilization-induced bone loss in rodens



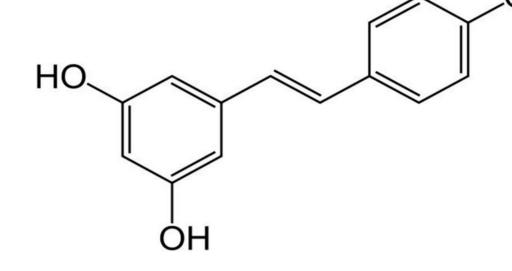
# METHODS

- Randomized, placebo-controlled, double-blind study
- 24 obese (BMI: 34.2±0.7) non-diabetic men were randomly assigned to either 500mg RSV or placebo three times daily for 4 weeks

#### BASELINE



 RSV has anti-inflammatory effects and inhibits RANKL-induced osteoclastogenesis



- RSV stimulates proliferation and differentiation dose-dependently in hMSC-TERT cells, ST2 cells from murine bone marrow, and Human Bone Marrow-derived Mesenchymal Stem Cells (HBMSCs) from one sample of fetal bone marrow
- No human data published

	Resveratrol treatment	
Randomization		
	Placebo treatment	

- Biomarkers of bone metabolism
- Inflammatory parametres
- Circulating hormones
- Whole body DXA scan

Before

After

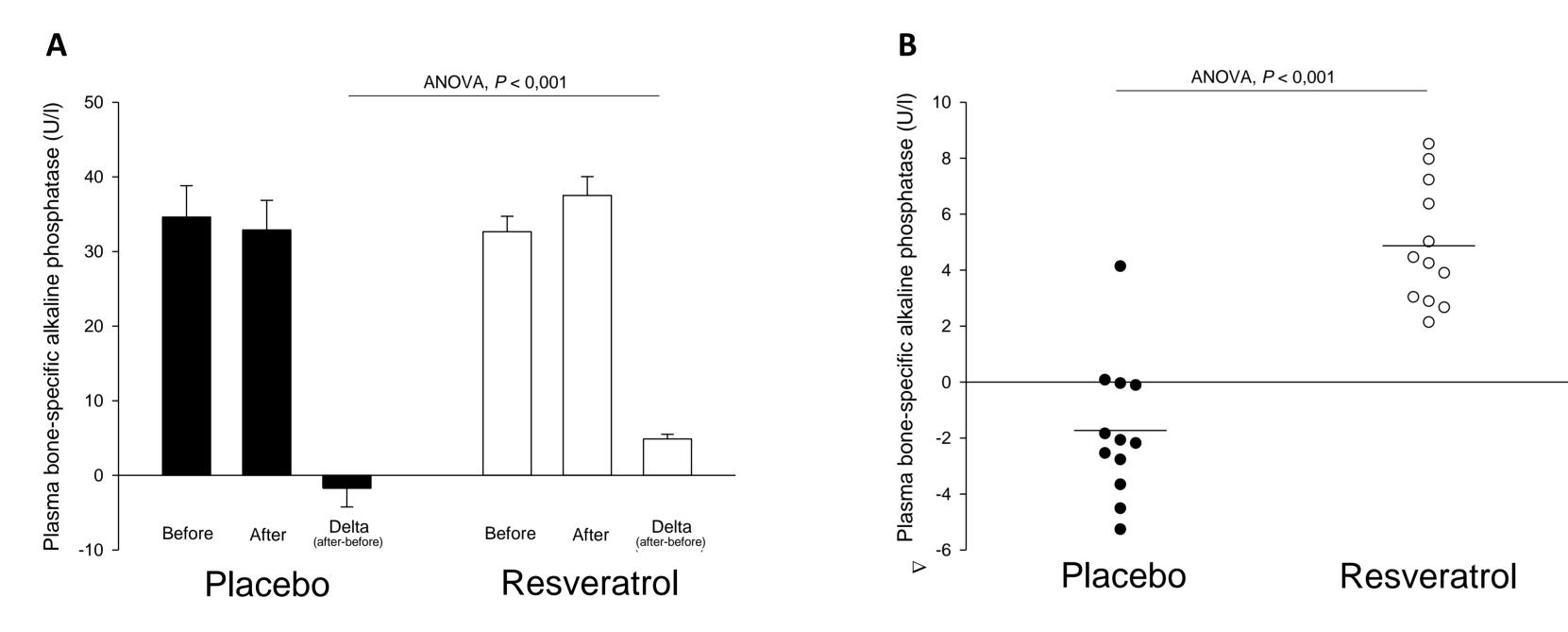
Placebo

- Biomarkers of bone metabolism
- Inflammatory parametres
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### AIM

• The aim of this study was to investigate if RSV impacts bone metabolism in obese non-diabetic men, who participated in a RCT originally designed to study RSVs effects on sugar- and fat- metabolism

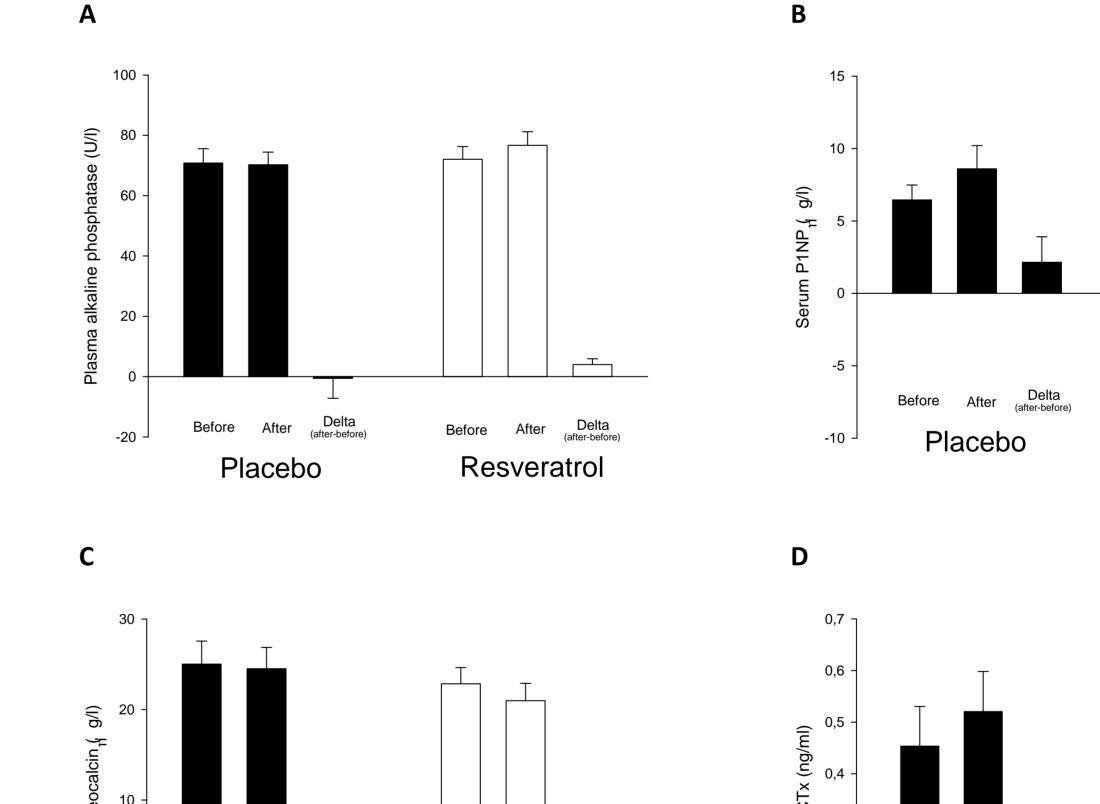
#### RESULTS



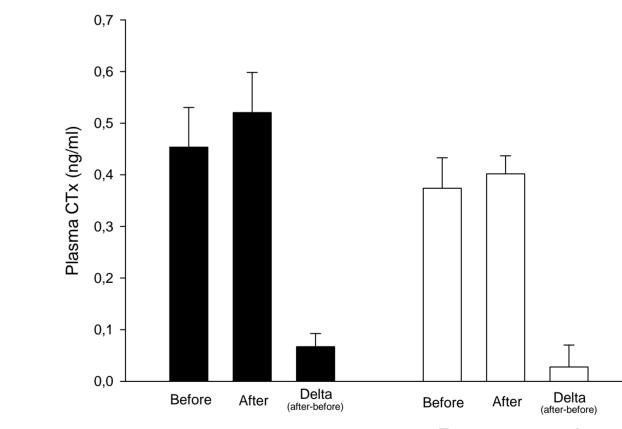
**Figure 1 | Bone-specific alkaline phosphatase.** Plasma levels of bone specific alkaline phosphatase before and after 4 weeks of resveratrol or placebo supplementation. *A*: Absolute changes. Results are presented as group means ± SEM. *B*: Individual delta changes (after-before). *P*-values reflect between-group differences (two way repeated measures ANOVA)

#### Table 1 | Circulating inflammatory markers, hormones and plasma biochemisty

	PLACEBO		RESVERATROL		ANOVA	
	Before	After	Before	After	P-value	
hsCRP (ng/ml)	$\textbf{2.86} \pm \textbf{0.39}$	$\textbf{4.04} \pm \textbf{1.01}$	$4.04\pm0.73$	$\textbf{4.58} \pm \textbf{0.91}$	0.63	
IL6 (pg/ml)	$\textbf{3.21}\pm\textbf{0.96}$	$\textbf{3.59} \pm \textbf{0.72}$	$\textbf{4.84} \pm \textbf{1.07}$	$\textbf{4.50} \pm \textbf{0.77}$	0.60	
TNFα (pg/ml)	$\textbf{4.69} \pm \textbf{0.79}$	$\textbf{5.00} \pm \textbf{1.70}$	$4.24\pm\!\!0.84$	$\textbf{4.14} \pm \textbf{1.00}$	0.82	
MCP1 (pg/ml)	$140.1\pm7.5$	$134.2\pm8.4$	$159.5\pm10.7$	$178.4 \pm 15.9$	0.13	
Leucocytes (10 <sup>9</sup> /l)	$\textbf{5.98} \pm \textbf{0.45}$	$\textbf{6.71} \pm \textbf{0.58}$	$\textbf{6.23} \pm \textbf{0.48}$	$\textbf{5.87} \pm \textbf{0.35}$	0.94	
Leptin (ng/ml)	$19.47\pm3.95$	$18.00 \pm 1.98$	$18.80\pm3.54$	$\textbf{22.97} \pm \textbf{6.65}$	0.32	
Adiponectin (mg/l)	$\textbf{6.09} \pm \textbf{0.65}$	$\textbf{6.65} \pm \textbf{0.71}$	$\textbf{6.71} \pm \textbf{0.74}$	$\textbf{6.93} \pm \textbf{0.74}$	0.17	
ALT (U/I)	$48.5 \pm 5.4$	$54.6 \pm 6.7$	$47.7 \pm 10.2$	$\textbf{46.9} \pm \textbf{8.7}$	0.10	



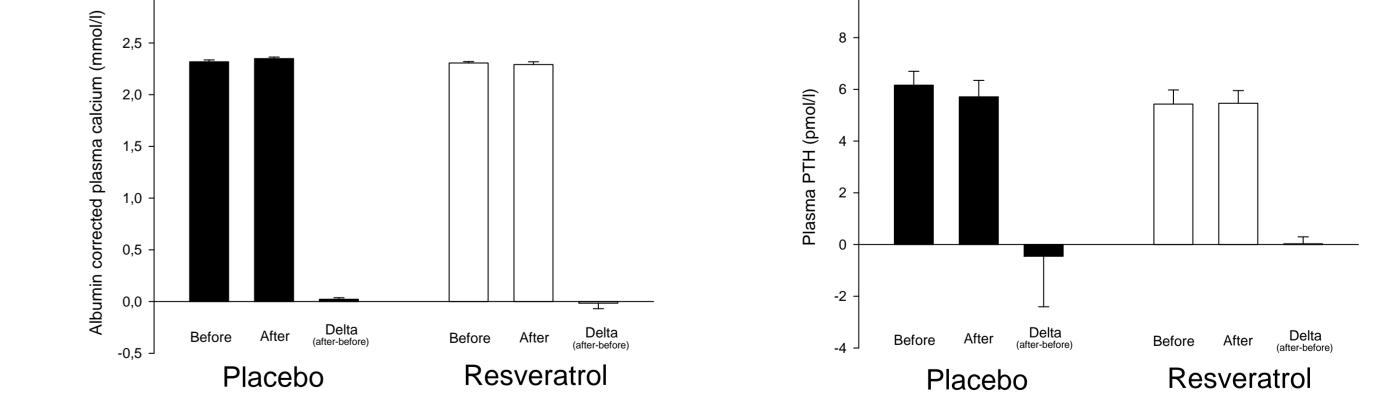
Resveratrol



Placebo Resveratrol

Resveratrol





# CONCLUSION

- RSV increased bone-specific alkaline phosphatase (BAP) significantly after 4 weeks of treatment as compared with placebo (*p* < 0.001)
- No difference was found in other formation markers (P1NP and osteocalcin) or the resorption marker CTx
- Calcium homeostasis was not affected by RSV treatment, and therefore do not explain the isolated increase in BAP
- Circulating BAP is mainly cleared by the liver so the increase could potentially be caused by hepatic impairment, but since alanine transaminase (ALT) was normal and unchanged it seems unlikely
- RSV may influence bone metabolism, but wheather this represents a beneficial effect or rather impair the mineralization process remains unsolved
- A study designed especially to examine the effect of RSV on human bone metabolism is needed and is currently being conducted (www.LIRMOI.com)

#### No authors have conflicts of interest