



Institut des nutraceutiques
et des aliments fonctionnels

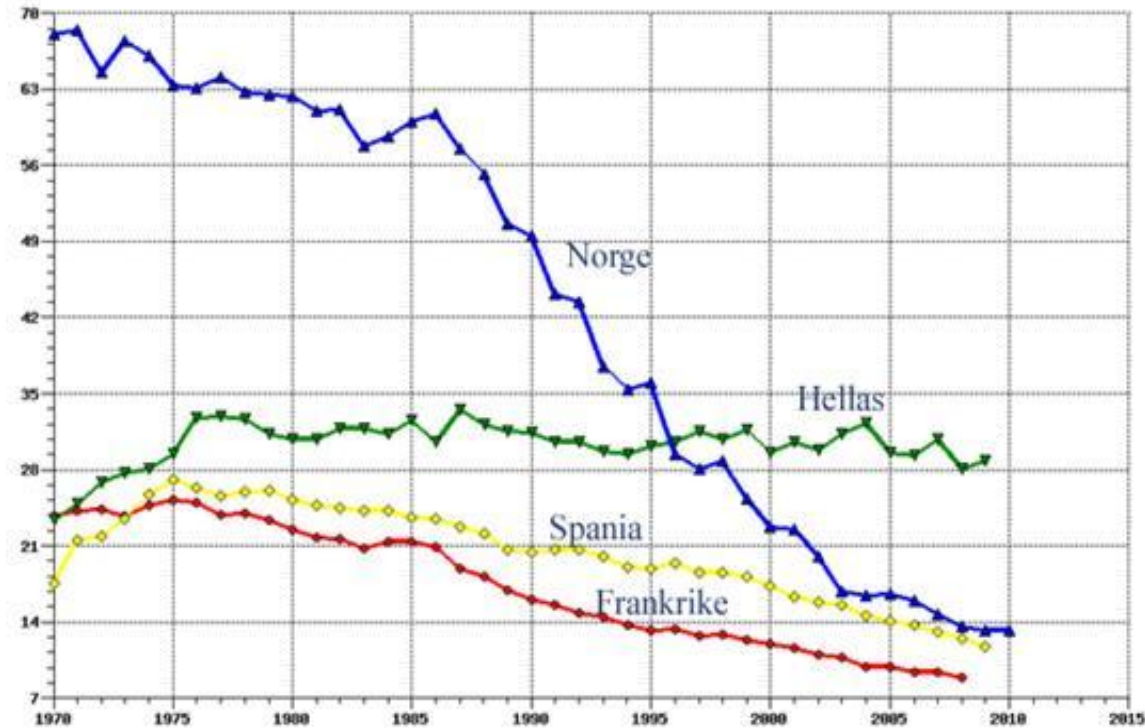
Marine proteins and heart disease

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and
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Marine FagDag
November 29, 2012



Decline in heart disease in Norway



A strong decline in the prevalence of heart disease has been observed in Norway due a reduction in smoking, blood cholesterol and blood pressure.

Reikvam & Hagen. *Journal of the Norwegian Medical Association*, 2011

Increase in the prevalence of type 2 diabetes in the world and in Norway

The prevalence of type 2 diabetes is increasing in the world: it was estimated to 8.3% in 2011 and will be 9.9% in 2030.

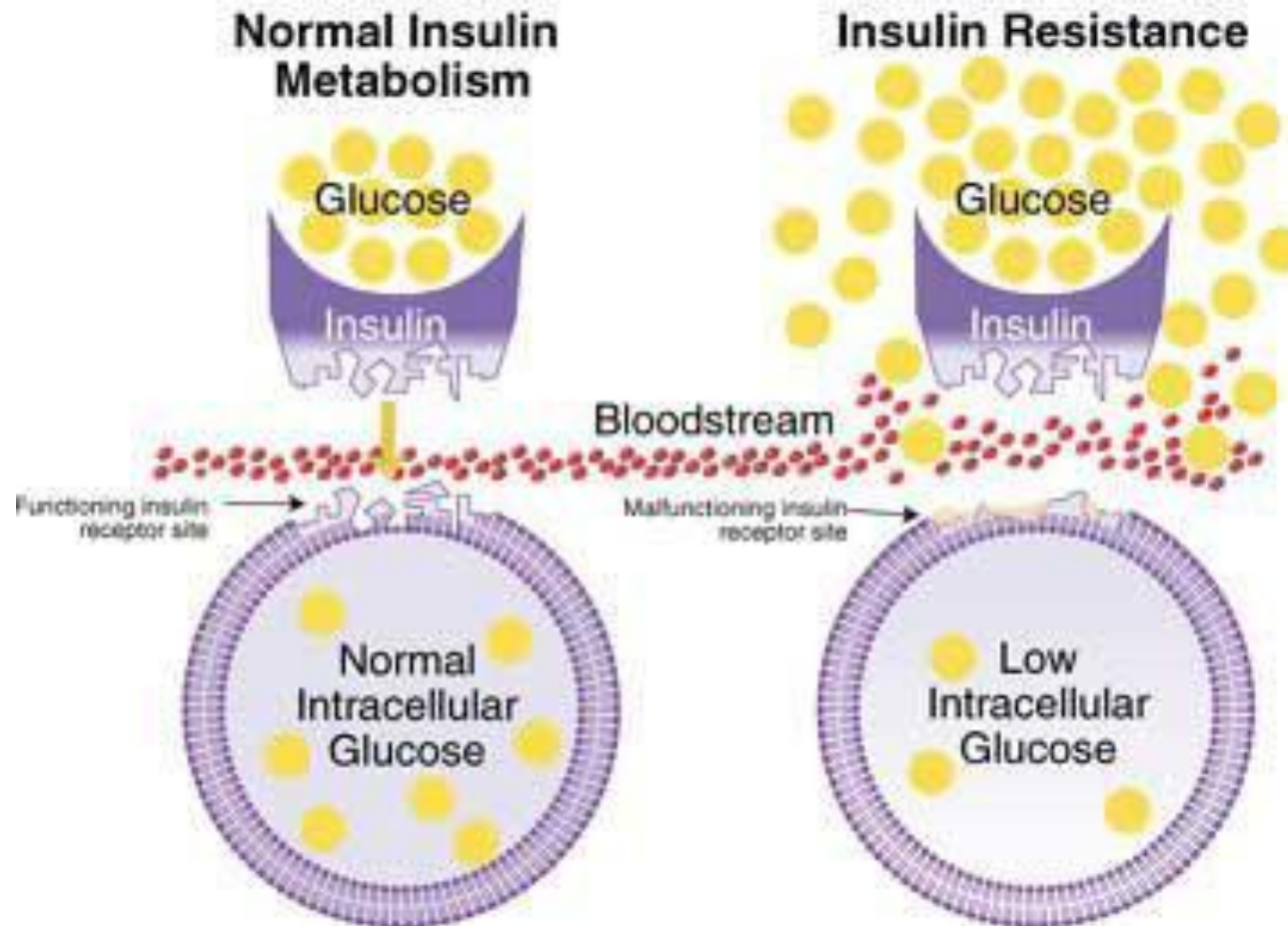
IDF, 2009

In Norway, the estimated prevalence was 4.3% in 2007 and is projected to rise to 5.4% in 2025.

IDF, 2009

Among people who die with diabetes, the main cause of death is cardiovascular disease.

Insulin resistance is preclinical condition to type 2 diabetes





Insulin resistance
(animal studies)

Fish protein
(animal studies)



Fasting insulinemia



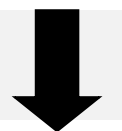
Fasting glycemia



Triglycerides



LDL cholesterol



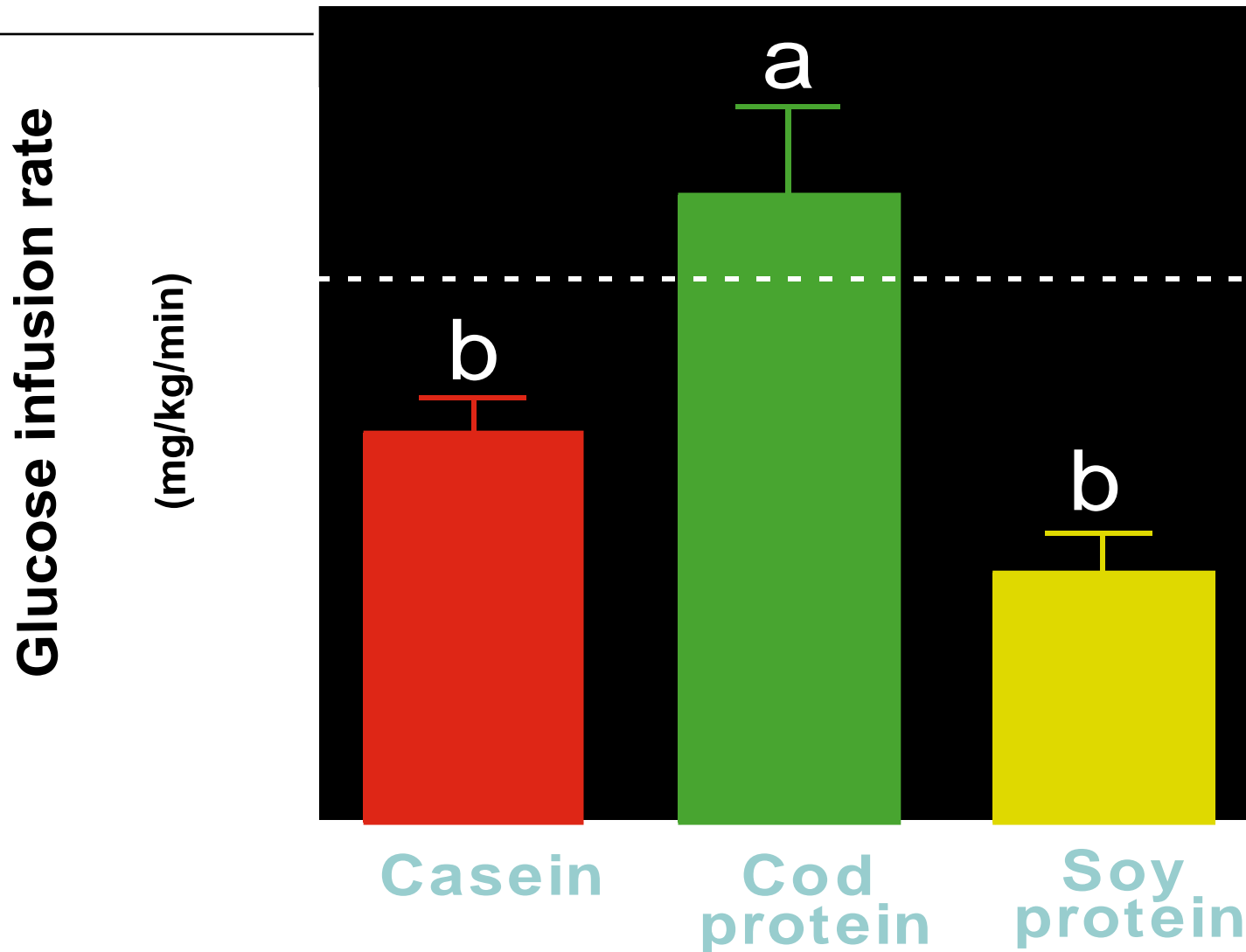
HDL cholesterol



Hypertension

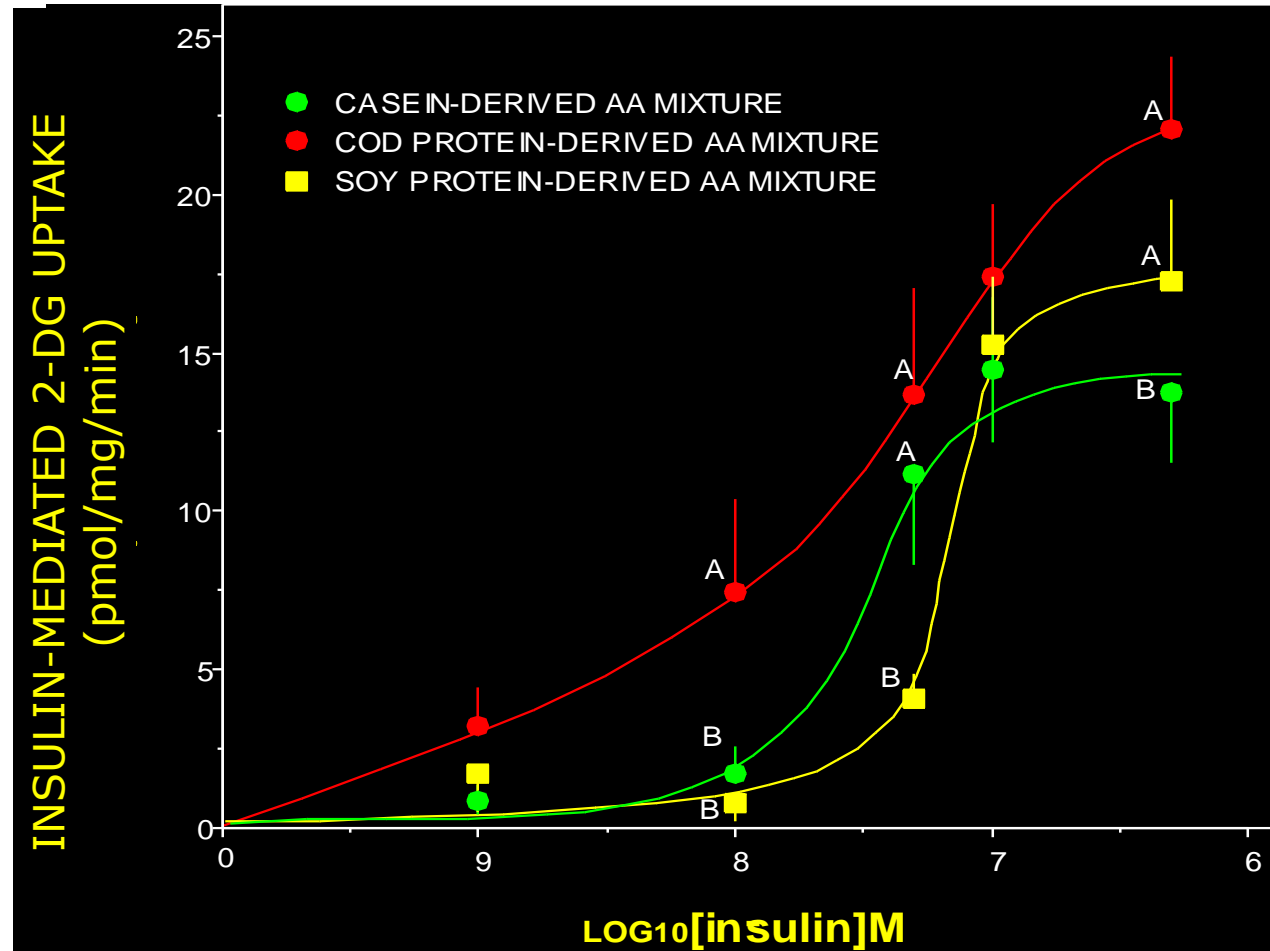


*Cod protein normalized insulin sensitivity
in high-fat fed rats*

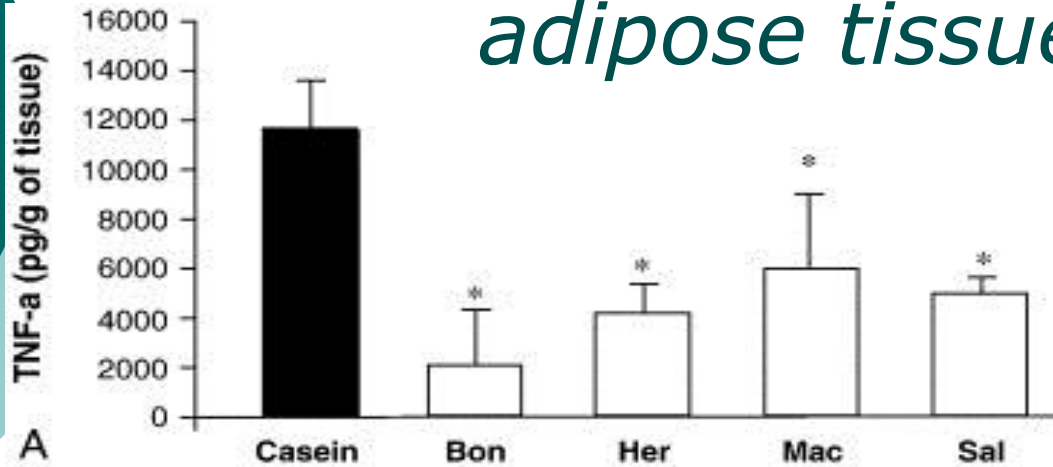


(Lavigne et al. Am J Physiol Endocrinol Metab 2001 ;281 :E62-E71)

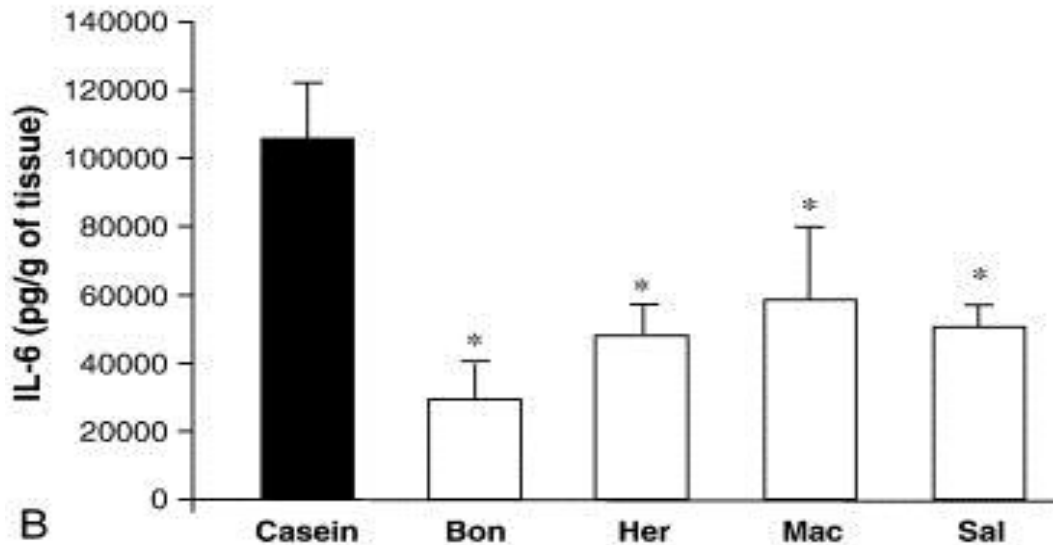
Amino acid mixtures and in vitro insulin sensitivity



Inflammatory cytokines in visceral adipose tissue (retroperitoneal)



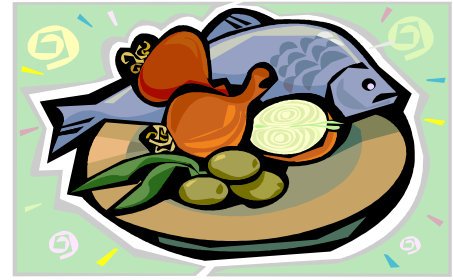
↓TNF- α & IL-6
following the consumption
of fish protein sources



* $p < 0.05$ vs
casein.

Pilon G et al. Metabolism.
2011;60:1122-30.

Human studies



Hypothesis:

Fish (cod) protein improves cardiovascular risk compared with other animal proteins in humans.

Objective:

To compare the effects of fish (cod) protein to those of other animal proteins on plasma lipids, insulin sensitivity and reduces inflammatory markers in insulin-resistant humans.

Experimental diets

	Diets	
	BPVEM	Lean fish
Energy (Kj)	10984	10920
Carbohydrate (% energy)	51	52
Lipids (% energy)	32	32
Protein (% energy)	19	18
PUFA (g)	25	26
MUFA (g)	39	39
SFA (g)	22	23
PUFA:MUFA:SFA	1.1:1.8:1.0	1.1:1.7:1.0
Omega-3 (g)	3.5	3.3
Omega-6 (g)	20.9	21.6
Cholesterol (mg)	228	220
Dietary fibers (g)	28.0	29.7
Calcium (mg)	1595	1487
Vitamin D (μ g)	15.3	12.8

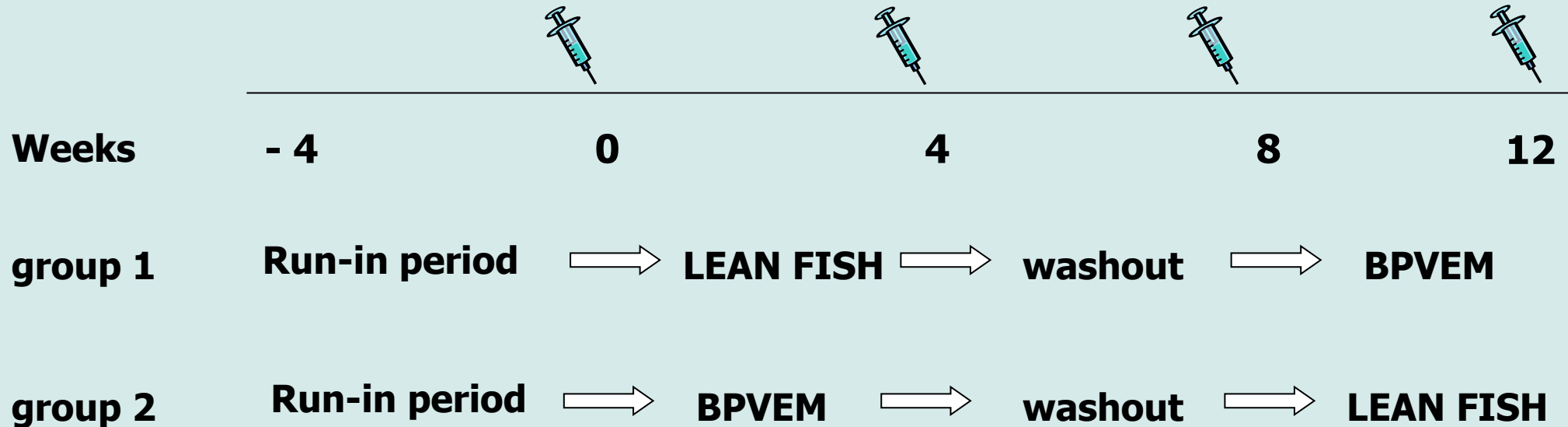
¹x \pm SEM; n = 19. BPVEM, beef, pork, eggs, milk products

Experimental design (crossover)

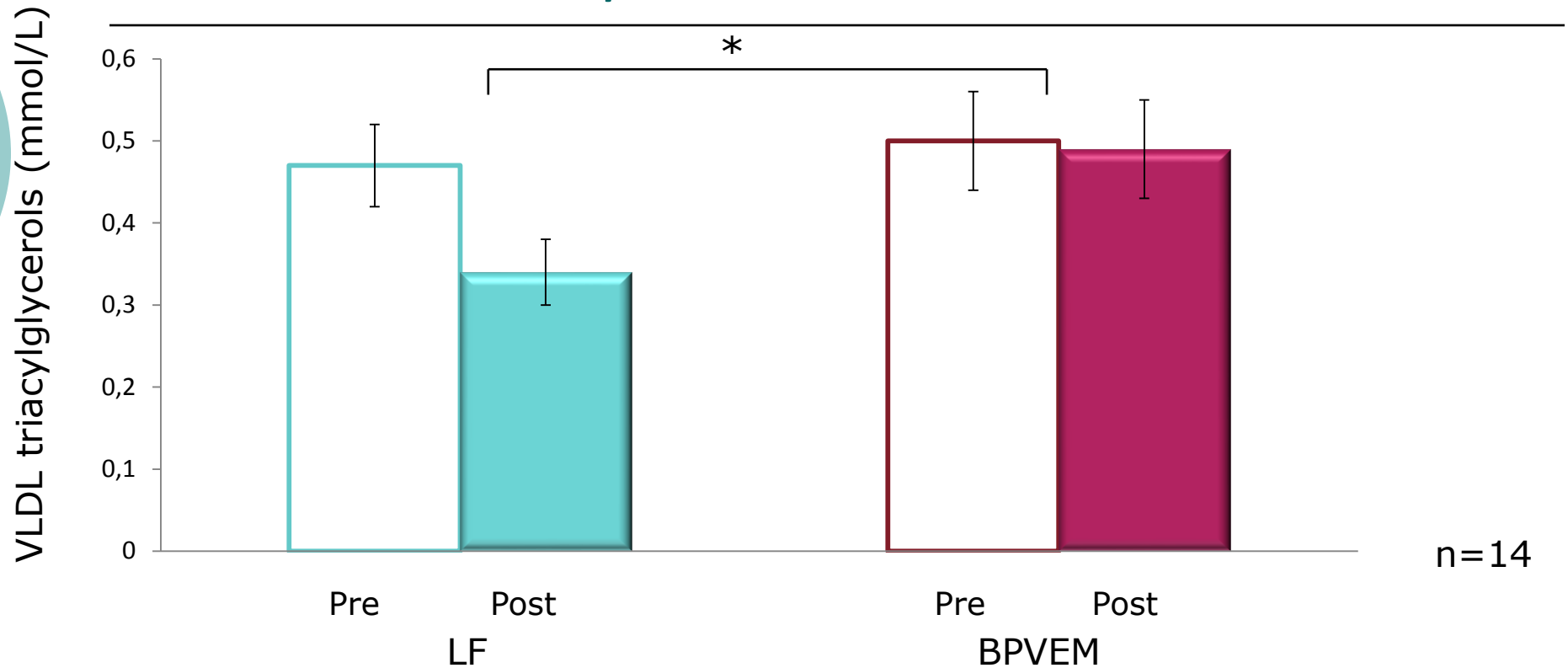
Legend



= Blood sampling



Lean fish diet reduced VLDL triacylglycerols in normolipidemic women



• $p < 0.05$ between changes following lean fish and BPVEM diets
BPVEM: beef, pork, veal, eggs, milk and milk products

Dietary protein sources and risk of coronary disease in women

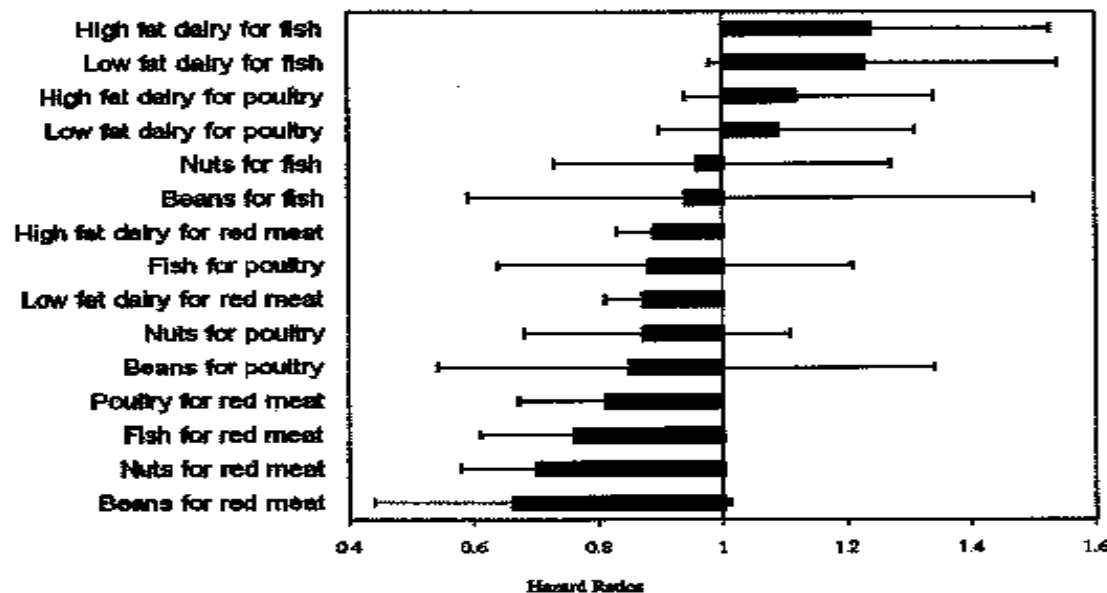
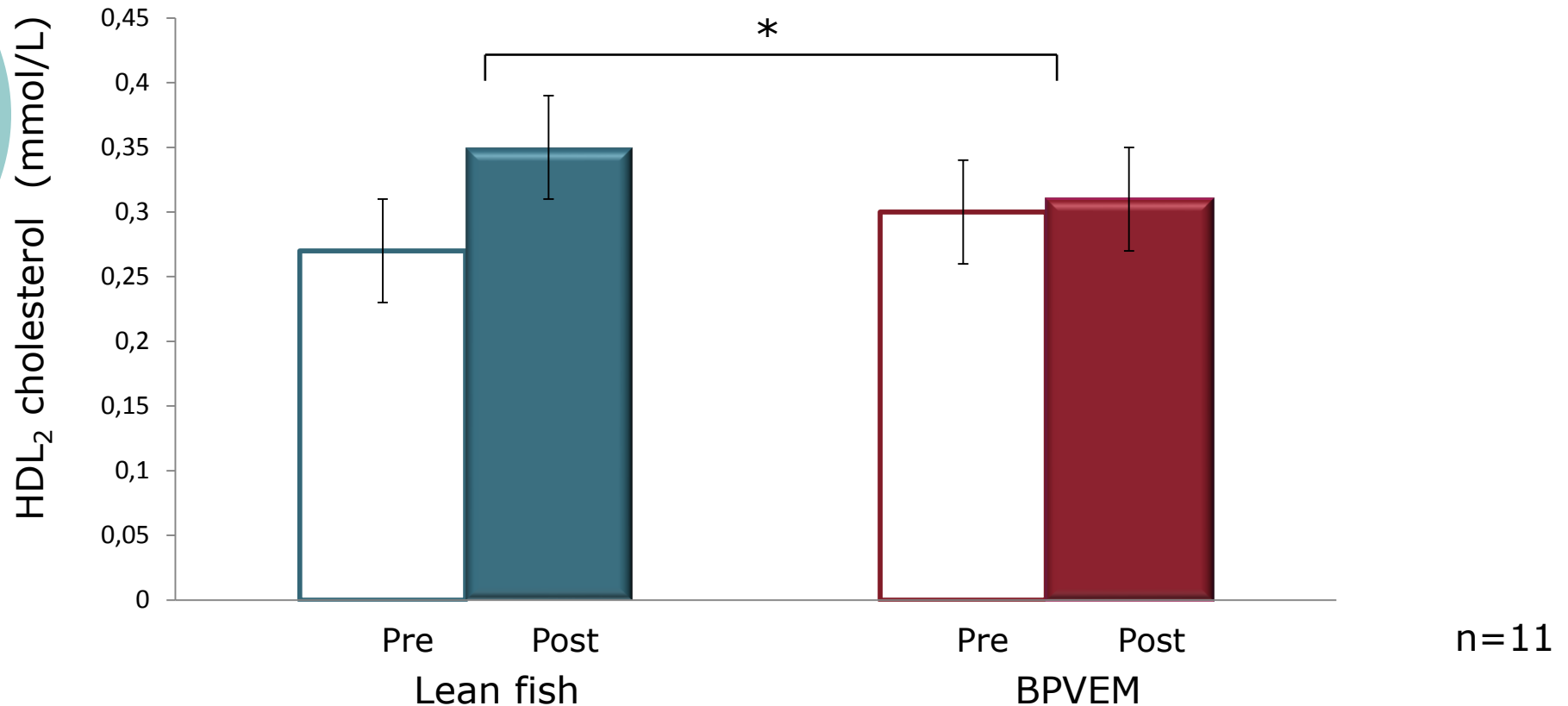


Figure. RRs and 95% CIs for CHD associated with replacement of a major dietary protein source with another.

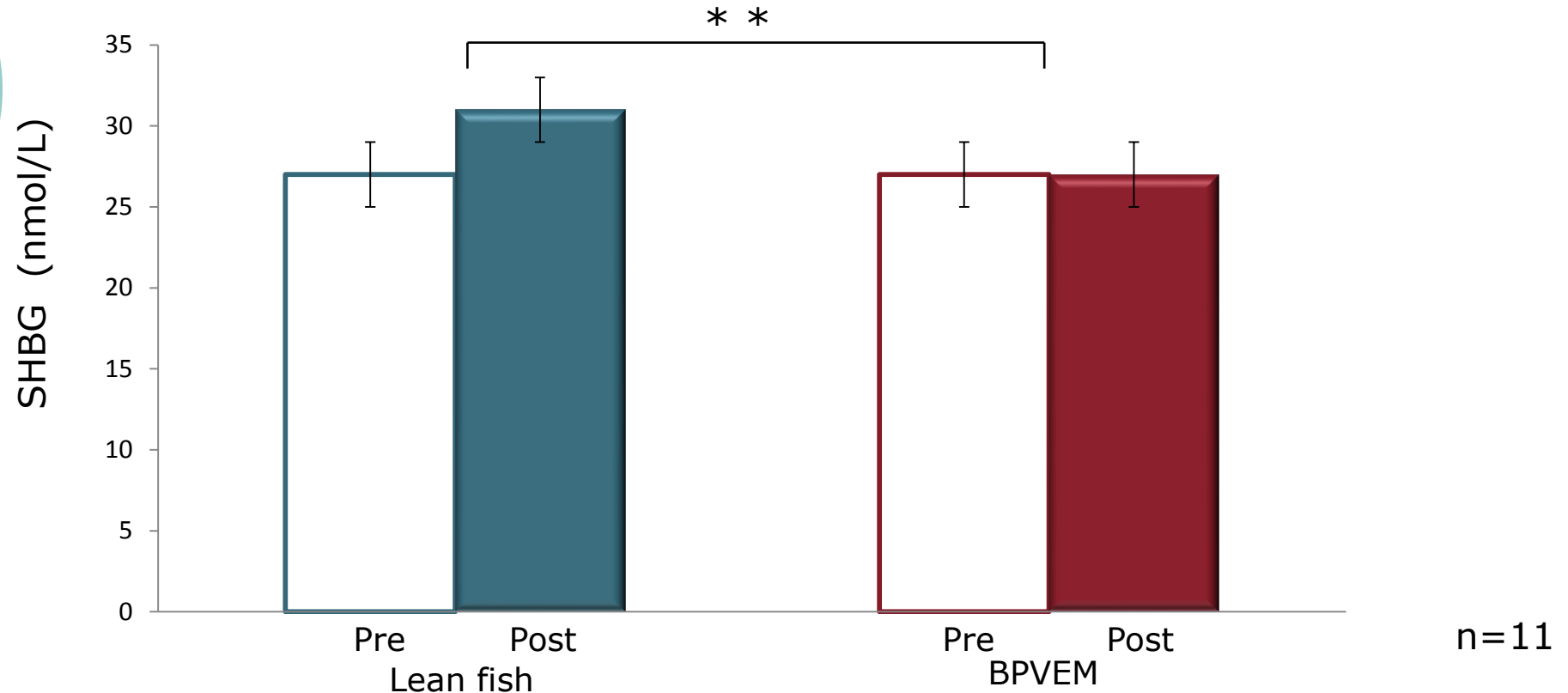
Human prospective study, n= 84 136

Lean fish diet increased HDL₂ cholesterol in normolipidemic men



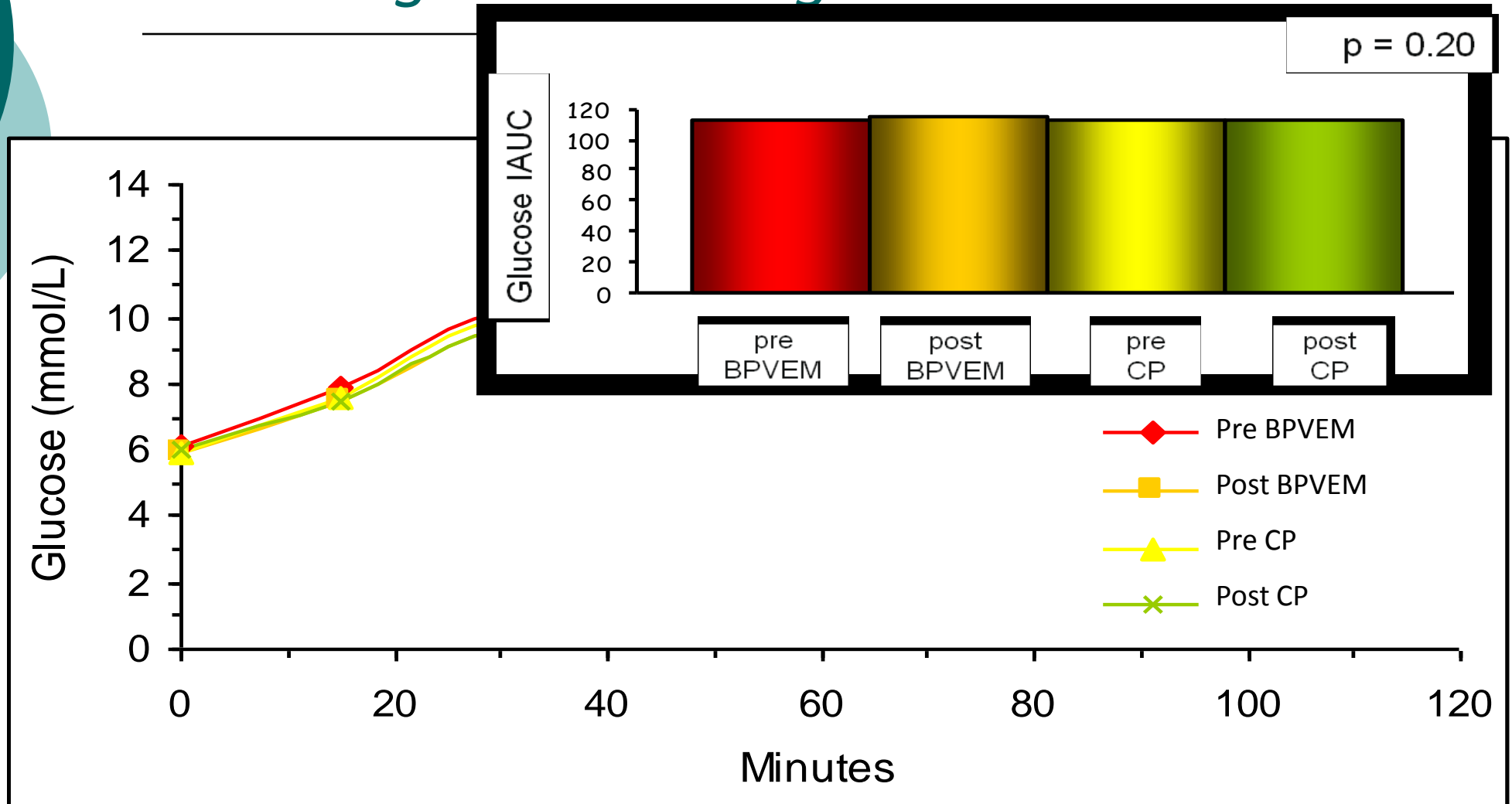
* $p < 0.05$ between changes following lean fish and BPVEM and diets
BPVEM: beef, pork, veal, eggs, milk and milk products

Lean fish diet increased SHBG in normolipidemic men



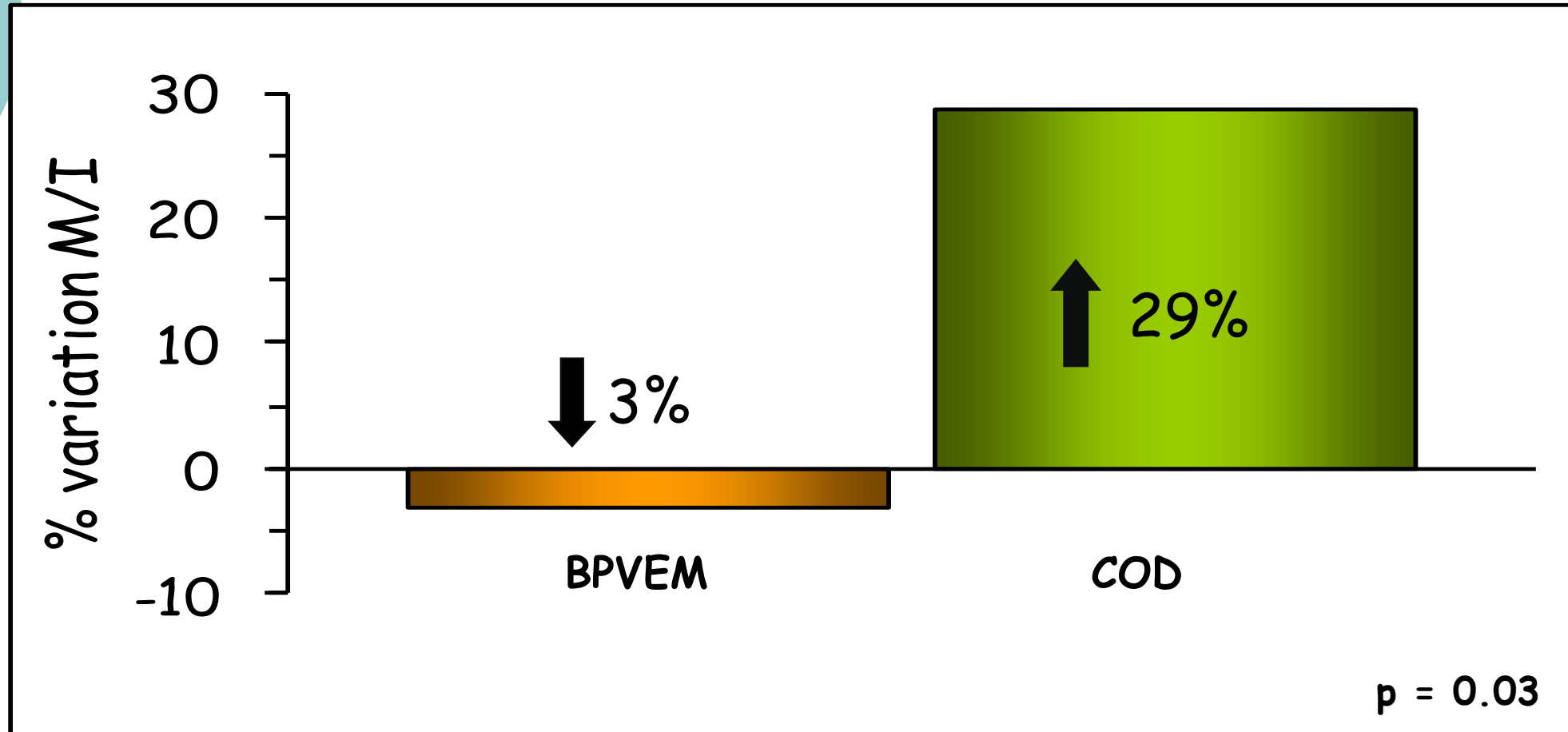
** $p < 0.01$ between changes following BPVEM and lean fish diets
BPVEM: beef, pork, veal, eggs, milk and milk products

Plasma glucose during OGTT

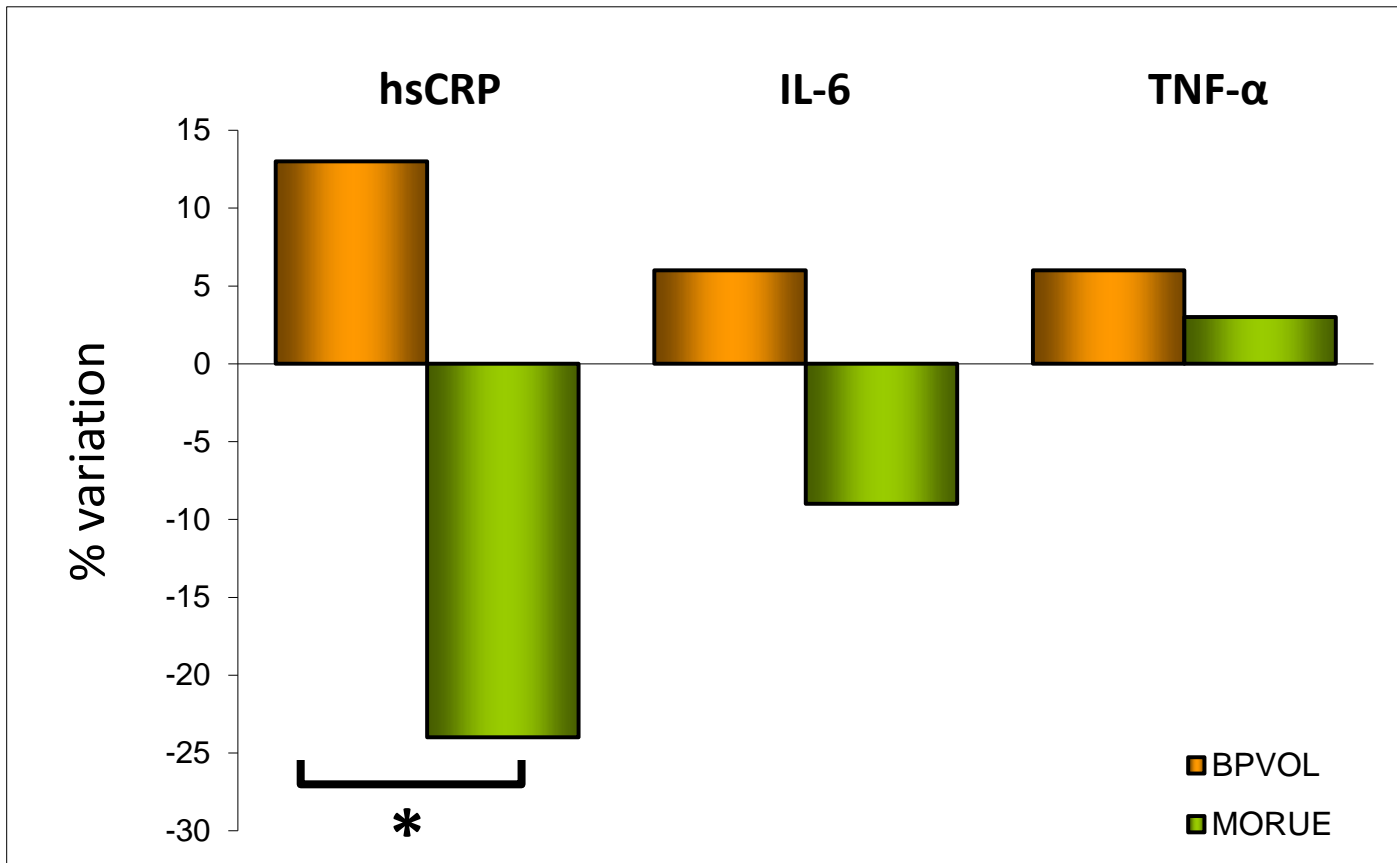


(Ouellet et al. Diabetes Care 2007 ;30 :2816-2821)

Cod protein improved insulin sensitivity in obese insulin-resistant men and women



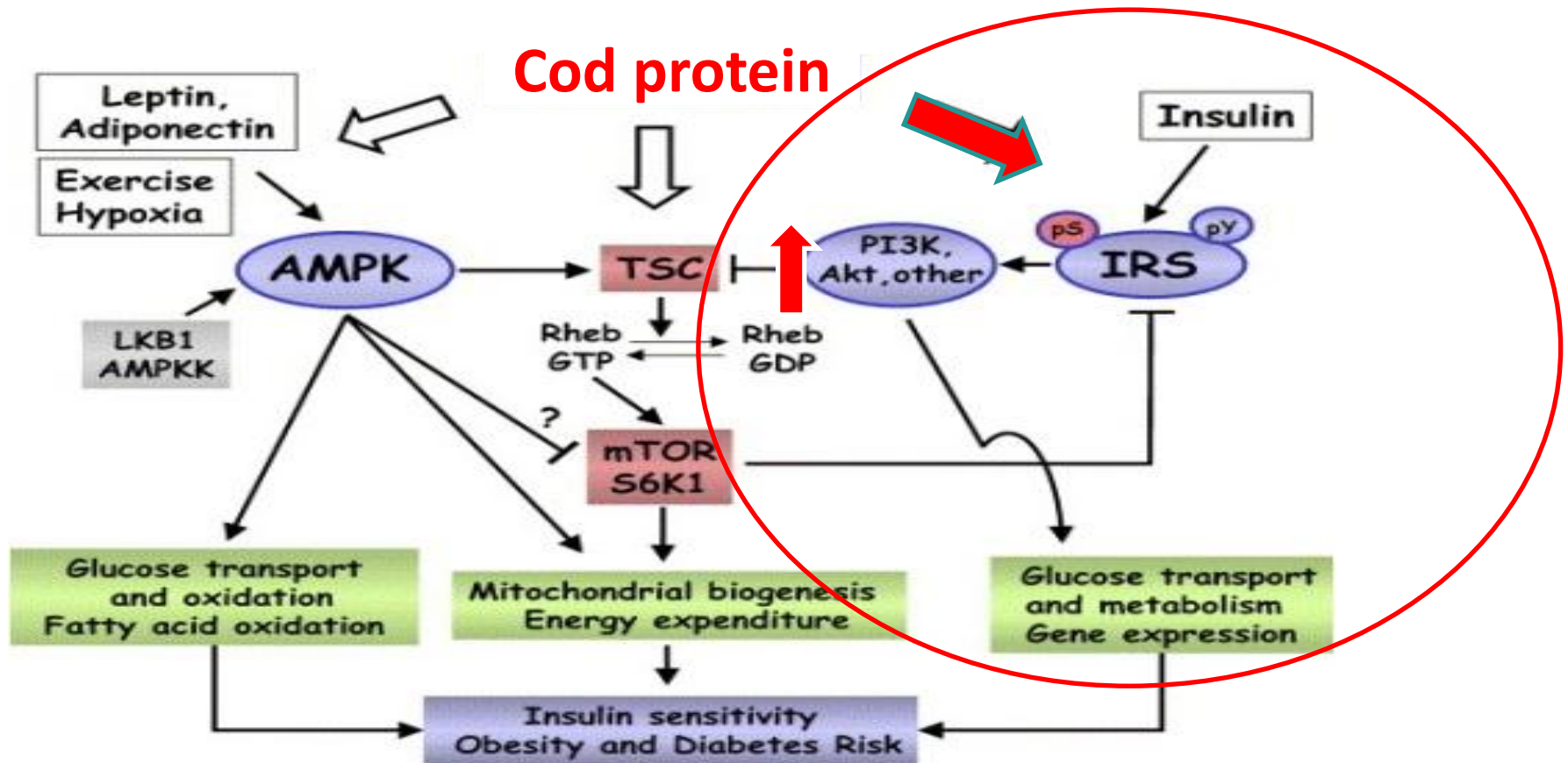
Cod protein reduced hsCRP, an inflammatory marker, in obese insulin-resistant men and women



P = 0.04

(Ouellet et al. J. Nutr 2008;138: 2386–2391)

Cod protein contributes to enhance insulin signalling in insulin resistant humans



Amino acid content of experimental diets

Amino acids	BPVEM	Cod
Alanine	5,5	6,0
Arginine	6,3	7,0
Aspartic acid	10,1	11,6
Glutamic acid	23,4	21,1
Glycine	5,0	5,2
Histidine	3,4	3,1
Isoleucine	5,4	5,0
Leucine	9,3	8,6
Methionine	2,5	2,7
Lysine	7,8	8,2
Phenylalanine	5,1	4,8
Proline	7,9	5,6
Serine	5,3	5,0
Threonine	4,6	4,5
Tyrosine	4,2	3,7
Valine	6,2	5,7

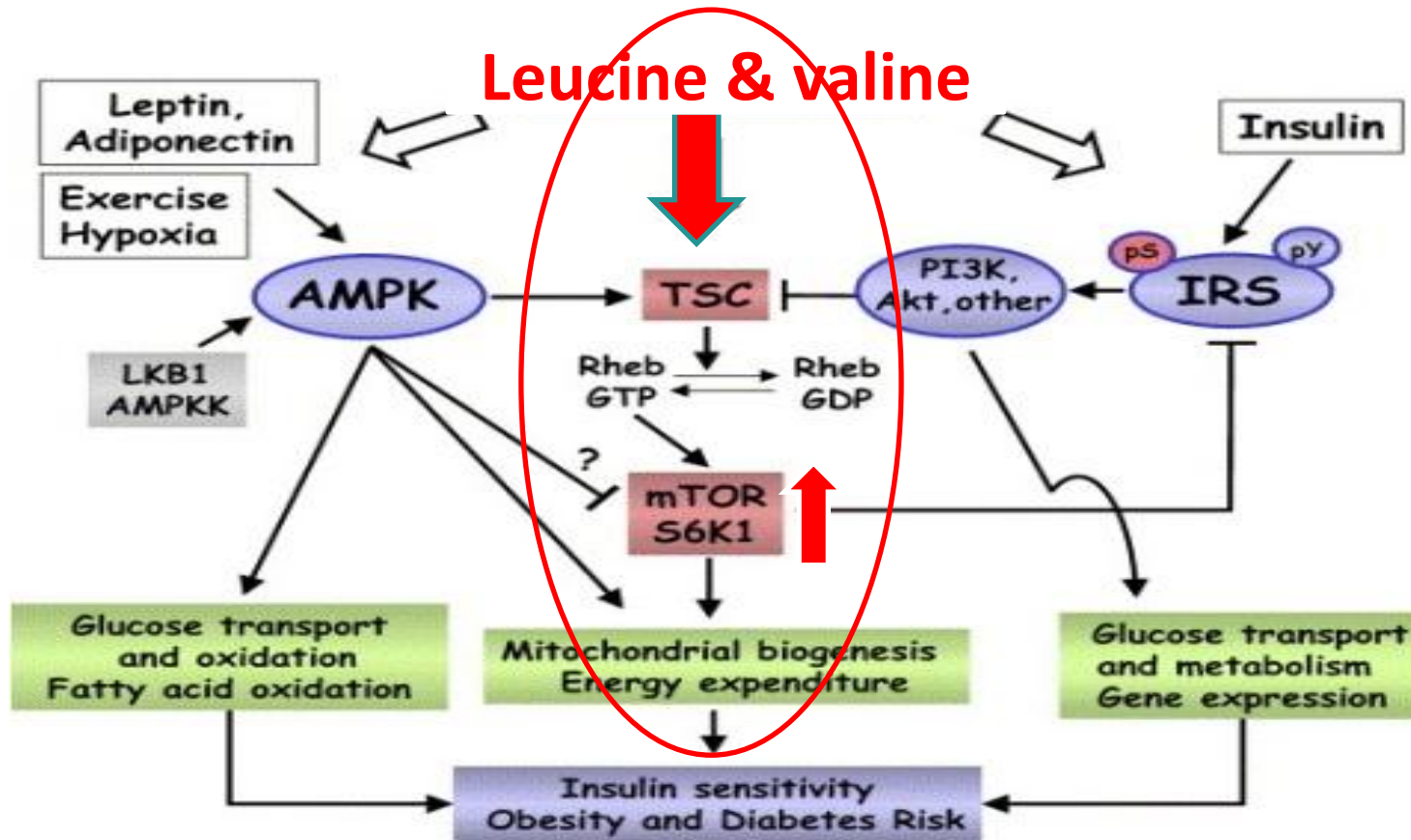
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(Ouellet et al. Diabetes Care 2007 ;30 :2816-2821)

Mode of action of leucine and valine



Conclusion (Controlled studies)

These results indicate that fish (cod) protein may improve blood lipids in healthy subjects, and insulin sensitivity in overweight/obese insulin-resistant men and women.

These beneficial effects may be partly mediated by attenuated low-grade inflammation associated with insulin resistance and type 2 diabetes.

The insulin-sensitizing effect of cod protein may result from an activation of insulin signalling cascade, partly through an increase in IRS-1 associated PI 3-kinase activity.

Free-living Study

Fish gelatin supplementation in insulin-resistant subjects consuming omega-3 PUFA supplement

Hélène Jacques, Julie Bisson, Eliane Picard-Deland, Julie Marois, Charles Lavigne, Bruce Holub, Eugene Chu, Jiri Frohlich, John Hill, André Marette, S. John Weisnagel

Picard-Deland E et al. J Nutr Sci, in press.

Bisson J et al. Manuscript in preparation.

Objective

To test whether fish protein supplement enhances the effects of fish n-3 PUFA, also given as a supplement, on plasma lipid profile and other markers of CVD risk in obese insulin-resistant subjects.

Choice of the ingredients

Marine fish oil: *1.8 g marine omega-3 FA*
(*Capsules, Ocean Nutrition Canada*)



Fish protein source: *Fish Gelatin (Norland Products, Nova Scotia Canada)*
given in a broth



Results-Plasma lipid response

	Omega-3			Omega-3+Fish Gelatin			P value
	Pre	Post	Δ	Pre	Post	Δ	
Blood lipids (mmol/L)							
Total Cholesterol	5.7 ± 0.3	5.5 ± 0.3	-0.2 ± 0.1	5.4 ± 0.3	5.4 ± 0.3	-0.06 ± 0.10	0.30
Triglycerides	1.5 ± 0.1	1.2 ± 0.1	-0.2 ± 0.1	1.5 ± 0.1	1.2 ± 0.1	-0.3 ± 0.10	0.58*
HDL-Cholesterol	1.1 ± 0.04	1.1 ± 0.1	0.04 ± 0.03	1.0 ± 0.1	1.1 ± 0.1	0.09 ± 0.03	0.13
LDL-Cholesterol	4.0 ± 0.3	3.8 ± 0.2	-0.14 ± 0.1	3.7 ± 0.2	3.7 ± 0.2	-0.02 ± 0.08	0.24
Total Chol/HDL-Chol	5.5 ± 0.4	5.1 ± 0.4	-0.4 ± 0.1	5.5 ± 0.4	5.0 ± 0.4	-0.5 ± 0.1	0.46

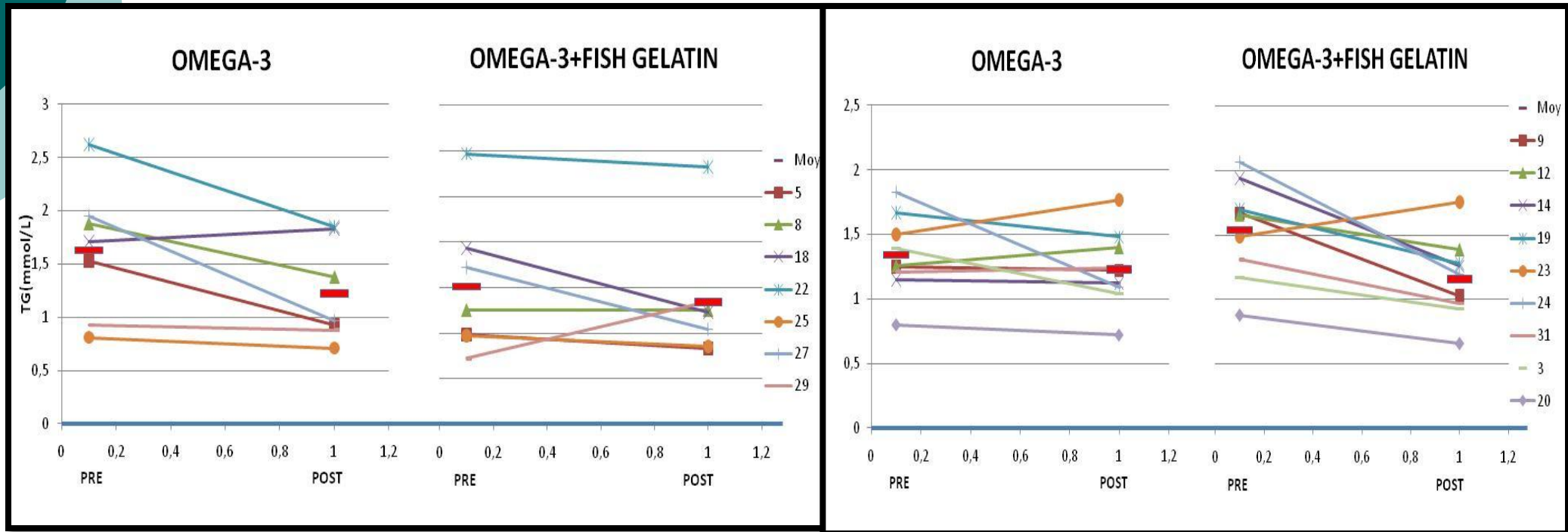
Mean ± SEM

*** Gender effect**

Sex-dependent response on triglycerides

Men

Women



P=0.02

Fish gelatin potentiates the decreasing effects of n-3 PUFA on plasma triglycerides in women

Results-Inflammatory and cardiovascular markers

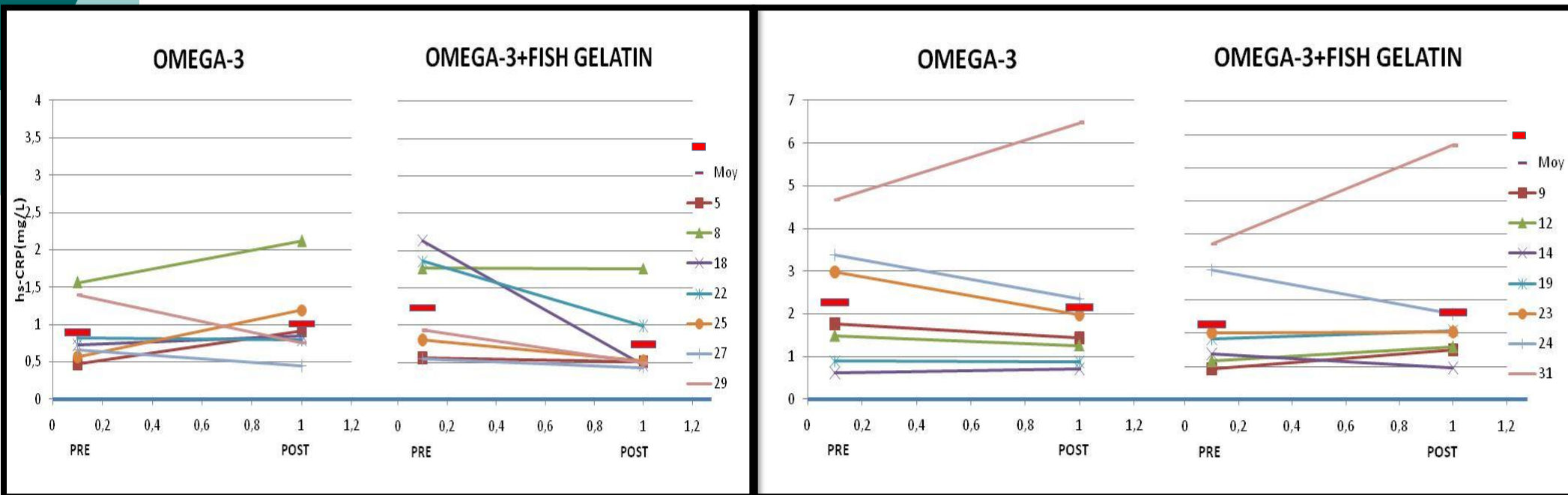
	Omega-3			Omega-3+Fish Gelatin			P value
	Pre	Post	Δ	Pre	Post	Δ	
MCP-1 (pg/ml) ²	650 ± 44	665 ± 47.0	15.3 ± 49.6	579 ± 57	633 ± 44.0	53.0 ± 33.3	0.30
TNF-α (pg/ml) ²	6.73 ± 1.31	5.83 ± 0.66	-0.90 ± 0.82	4.93 ± 0.47	5.33 ± 0.46	0.40 ± 0.42	0.12
hs-CRP (mg/L)	1.57 ± 0.34	1.58 ± 0.41	0.01 ± 0.20	1.75 ± 0.32	1.68 ± 0.50	-0.07 ± 0.29	0.70*
IL-10 (pg/ml) ²	1.06 ± 0.78	0.21 ± 0.07	-0.85 ± 0.77	1.94 ± 1.43	0.49 ± 0.25	-1.45 ± 1.52	0.82
IL-1β (pg/ml) ²	9.29 ± 2.14	6.17 ± 1.86	-3.12 ± 2.80	7.08 ± 2.09	5.42 ± 1.67	-1.66 ± 1.25	0.61
IL-1ra (pg/ml)	115 ± 7.0	111 ± 11.0	-3.20 ± 7.86	119 ± 9.0	111 ± 7.31	-7.0 ± 5.90	0.69
IL-6 (pg/ml)	116 ± 38.0	81.6 ± 27.3	-34.7 ± 36.5	99.7 ± 29.5	59.3 ± 24.1	-40.3 ± 29.2	0.90
PAI-1 (ng/ml)	2.18 ± 0.38	3.45 ± 0.73	1.27 ± 0.58	1.78 ± 0.43	3.14 ± 0.46	1.36 ± 0.26	0.96
Adiponectin (ug/ml)	14.3 ± 1.3	14.8 ± 1.5	0.46 ± 0.69	13.4 ± 1.6	14.7 ± 1.53	1.25 ± 1.40	0.82
Homocysteine (umol/L)	10.1 ± 0.4	9.56 ± 0.45	-0.53 ± 0.36	9.49 ± 0.55	9.76 ± 0.44	0.28 ± 0.44	0.19
Leptin (ng/ml)	16.6 ± 2.5	15.2 ± 2.4	-1.40 ± 0.89	18.0 ± 3.5	16.5 ± 2.60	-1.48 ± 1.91	0.81
Cystatin C (mg/L)	0.76 ± 0.03	0.72 ± 0.03	-0.03 ± 0.01	0.73 ± 0.03	0.71 ± 0.03	-0.02 ± 170	0.73
Résistin (ng/ml)	26.7 ± 2.6	36.6 ± 4.4	9.92 ± 3.33	26.2 ± 2.5	35.7 ± 4.32	9.49 ± 4.02	0.86
Serum amyloid A (ug/ml)	82.4 ± 35.0	51.2 ± 6.1	-31.2 ± 34.7	112 ± 57.0	63.3 ± 10.5	-48.6 ± 17.2	0.47
Myeloperoxidase (pg/ml)	39.1 ± 11.0	75.0 ± 27.8	35.9 ± 18.3	40.7 ± 8.8	62.3 ± 15.2	21.7 ± 14.9	0.99
ADMA (ug/L)	87.0 ± 2.5	112 ± 14	24.9 ± 13.4	83.7 ± 4.2	97.6 ± 10.1	13.9 ± 11.0	0.35

Mean ± SEM; * Gender effect

Sex-dependent response on hsCRP

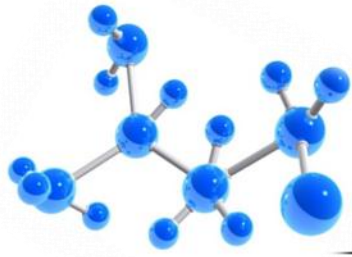
Men

Women



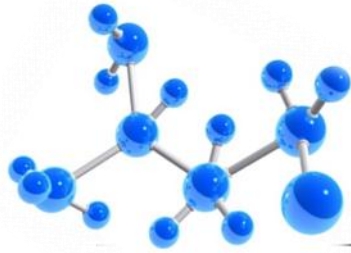
P=0.03

Fish gelatin counteracted the slight increasing effect of n-3 PUFA on plasma hsCRP in men.



Conclusion (Free-living study)

In free living conditions, fish gelatin, given as a supplement, may exert a beneficial effect on CVD risk by lipid-lowering and anti-inflammatory effect in free-living insulin-resistant women and men, respectively.



Key messages

The prevalence of insulin resistance and type 2 diabetes is increasing in the world and in Norway.

Fish protein may help to prevent type 2 diabetes and heart disease by improving blood lipids and insulin sensitivity.

We need further studies to determine all the potential of fish protein in preventing type 2 diabetes and heart disease.

Research Team for Human Trials on Fish protein at Université Laval

Collaborators: S. John Weisnagel, MD, endocrinologist

André Marette, PhD (Univ. Laval)

Réjeanne Gougeon, PhD (McGill Univ.)

Coordinator: Julie Marois MSc, PDt

Graduate students: Annie Gascon MSc, PDt

Brigitte Lacaille MSc, PDt

Eliane Picard-Deland MSc, PDt

Julie Bisson MSc, PDt

Véronique Ouellet, PhD, PDt

Undergraduate students: 4 per year

*On-going collaborative study:
Ability of a seafood protein diet to modulate postprandial
metabolism in human-beings*

Eli Kristin Aadland, PhD candidate, University of Bergen & NIFES

Ingvild Eide Graff, NIFES, Bergen

Gunnar Mellgren, Haukeland University Hospital, Bergen

Oddrun Anita Gudbrandsen, University of Bergen

Charles Lavigne, NIFES, Bergen

Jutta Dierkes, University of Bergen

Hélène Jacques, Laval University, Quebec, Canada

Bjorn Liaset, NIFES, Bergen, SIP project leader

BON APPÉTIT!



BON APPÉTIT!





Takk!

Spørsmål?