Institut des nutraceutiques et des aliments fonctionnels

Marine proteins and heart disease

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Marine FagDag
November 29, 2012

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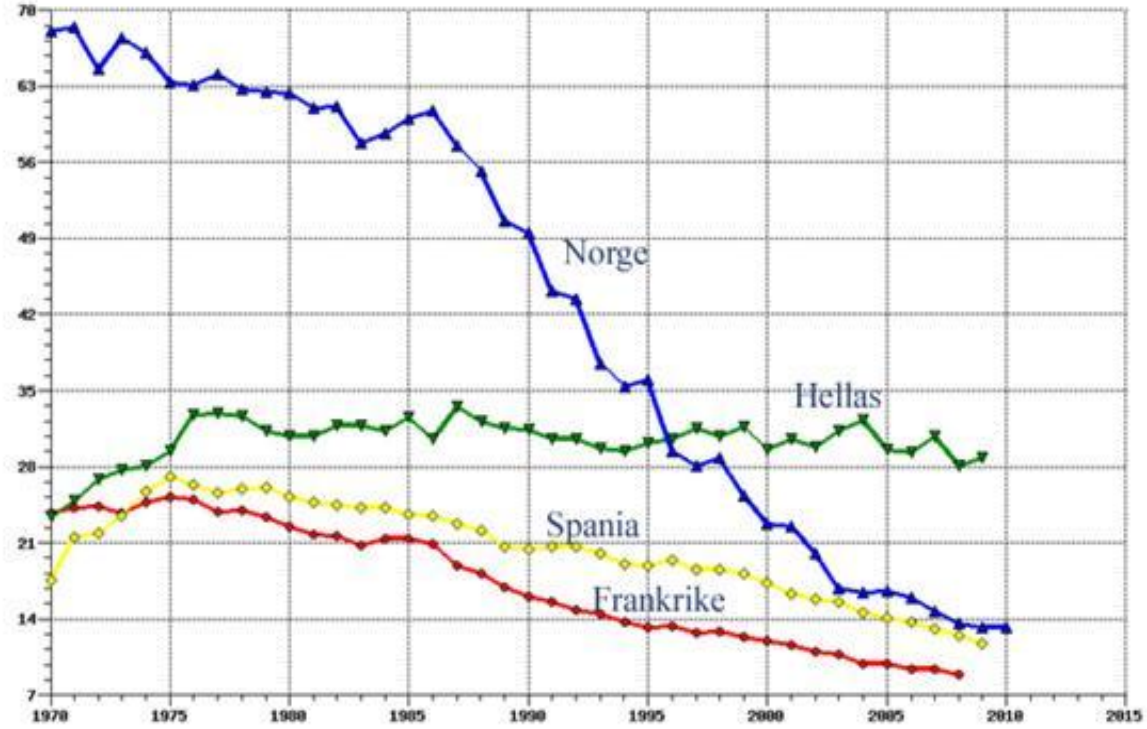
Decline in heart disease in Norway



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.

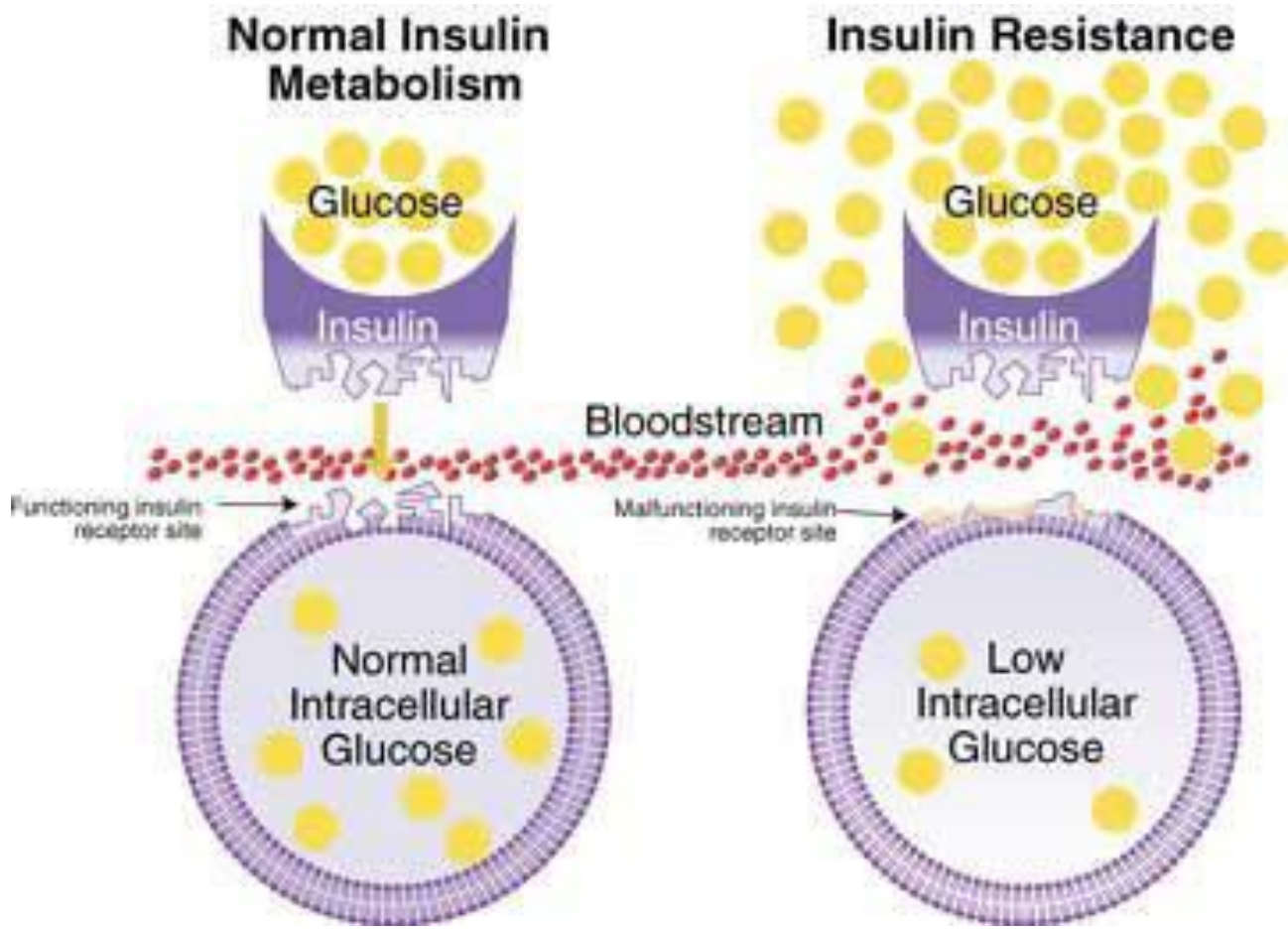
IDF, 2009

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

IDF, 2009

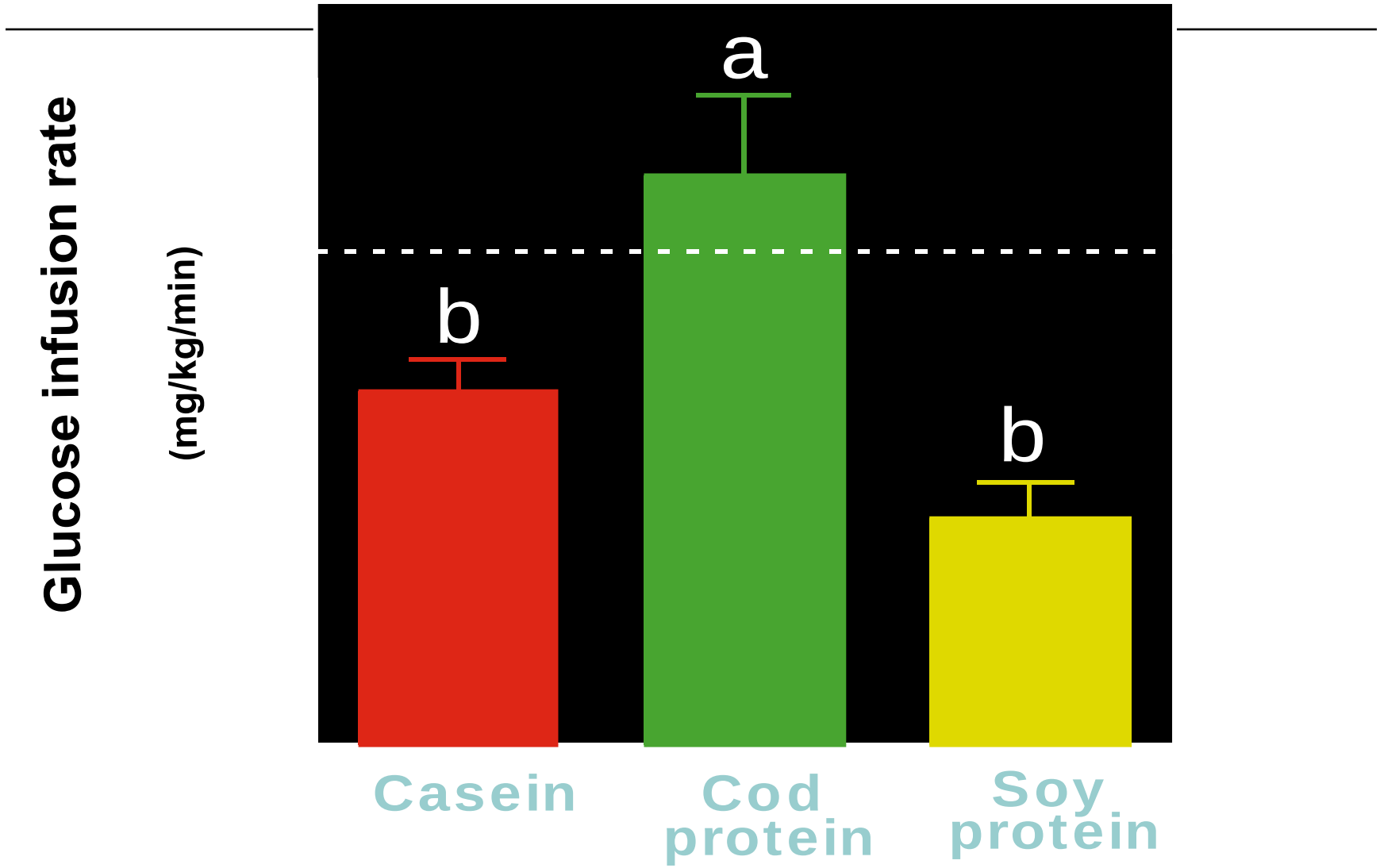
Among people who die with diabetes,
the main cause of death is cardiovascular disease.

Insulin resistance is preclinical condition to type 2 diabetes



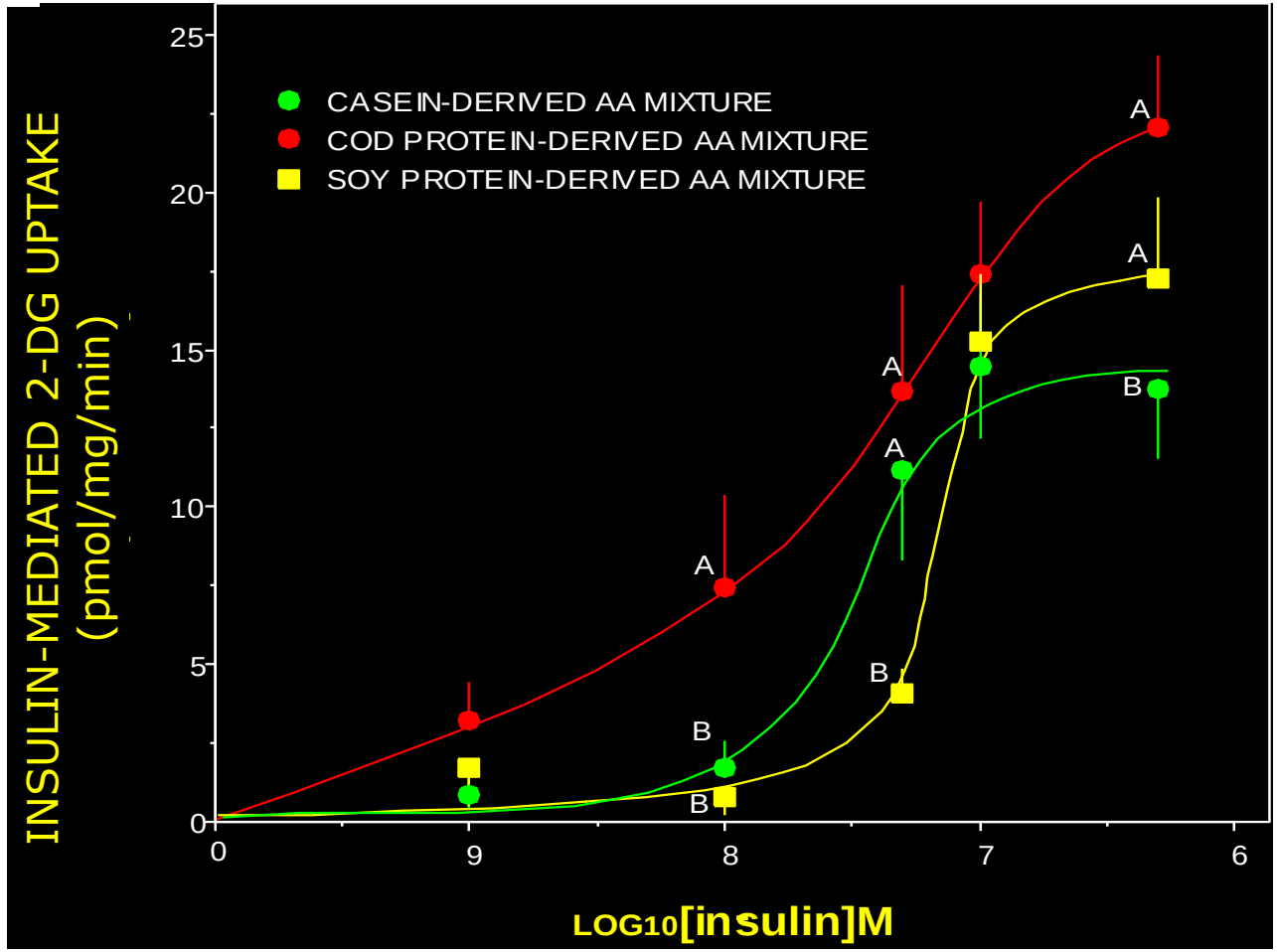
Insulin resistance *(animal studies)*		Fish protein *(animal studies)*
↑	Fasting insulinemia	↓
↑	Fasting glycemia	↓
↑	Triglycerides	↓
↑	LDL cholesterol	—
↓	HDL cholesterol	↑
↑	Hypertension	↓

Cod protein normalized insulin sensitivity in high-fat fed rats



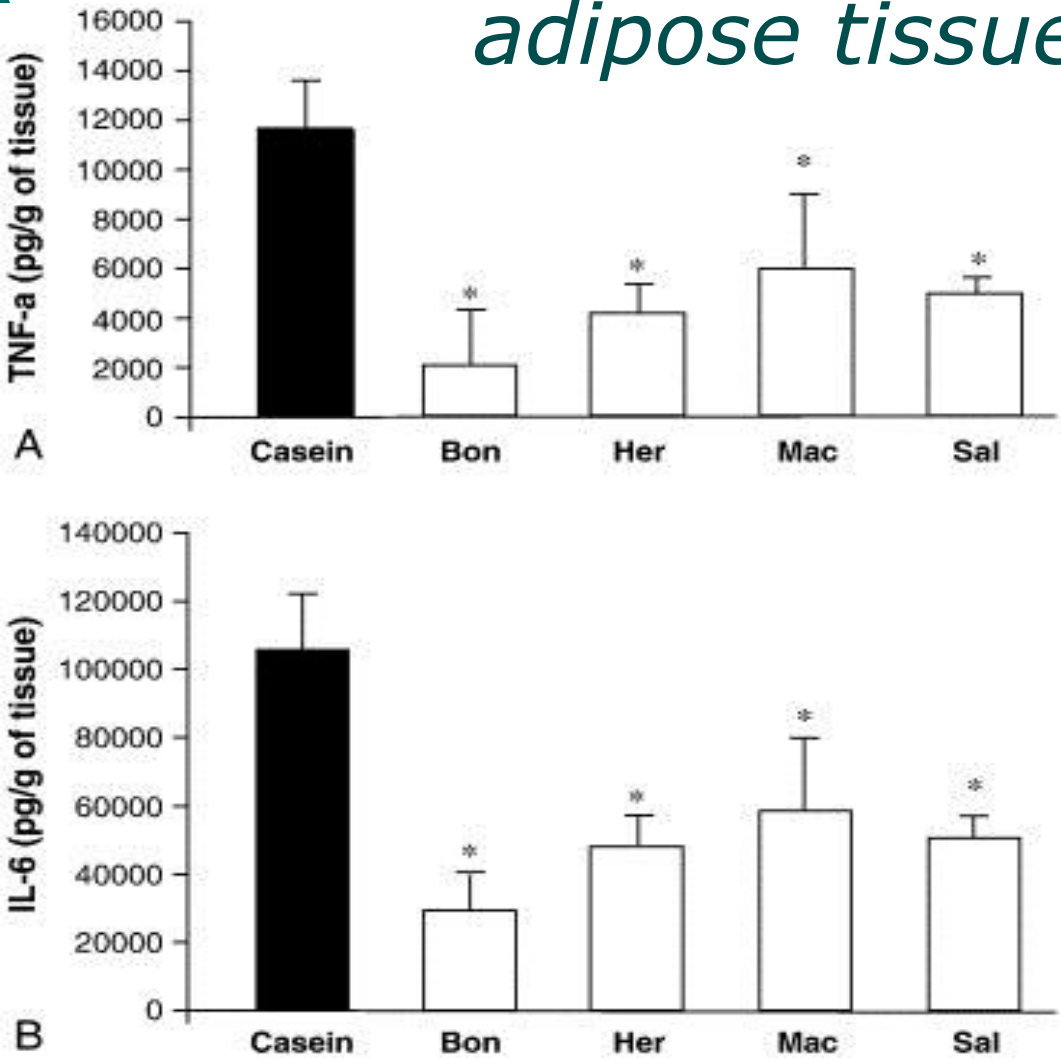
(Lavigne et al. Am J Physiol Endocrinol Metab 2001 ;281 :E62-E71)

Amino acid mixtures and in vitro insulin sensitivity



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

Inflammatory cytokines in visceral adipose tissue (retroperitoneal)

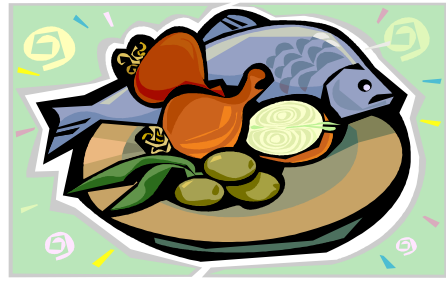


↓TNF- α & IL-6 following the consumption of fish protein sources

*$p < 0.05$ 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:

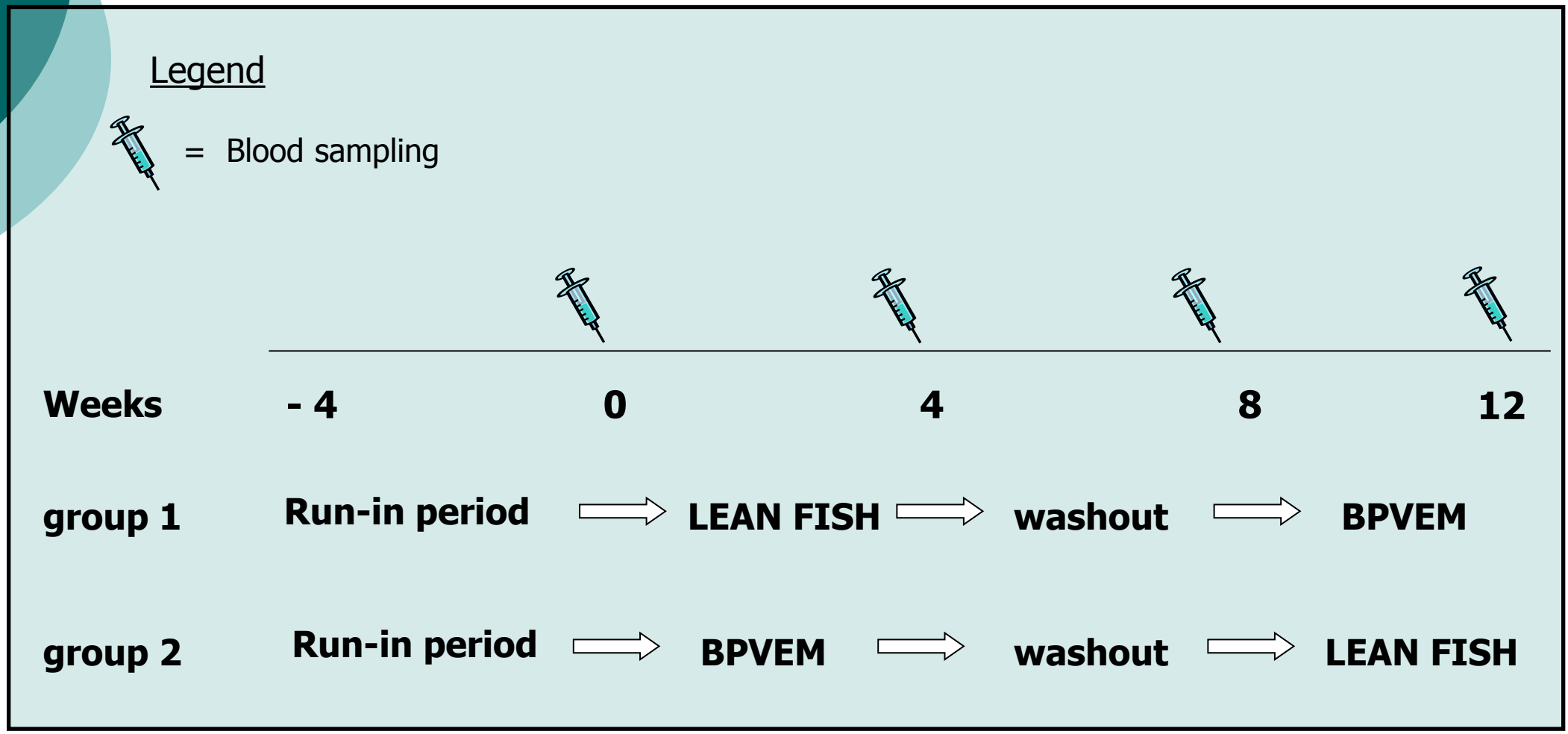
To compare the effects of fish (cod) protein to those of other animal proteins on plasma lipids, insulin sensitivity and reduces inflammatory markers in insulin-resistant humans.

Experimental diets

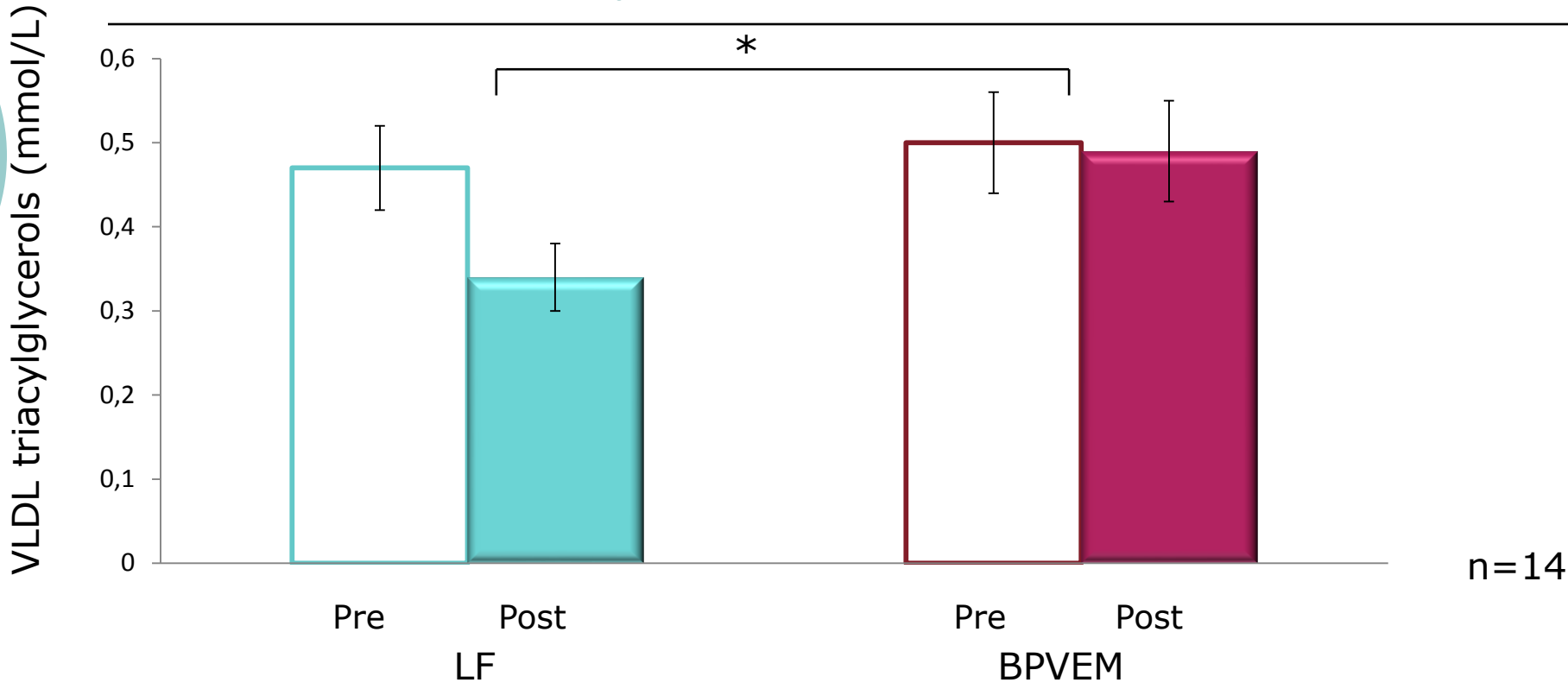
	Diets	
	BPVEM	Lean fish
Energy (Kj)	10984	10920
Carbohydrate (% energy)	51	52
Lipids (% energy)	32	32
Protein (% energy)	19	18
PUFA (g)	25	26
MUFA (g)	39	39
SFA (g)	22	23
PUFA:MUFA:SFA	1.1:1.8:1.0	1.1:1.7:1.0
Omega-3 (g)	3.5	3.3
Omega-6 (g)	20.9	21.6
Cholesterol (mg)	228	220
Dietary fibers (g)	28.0	29.7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

[1] x ± SEM; n = 19. BPVEM, beef, pork, eggs, milk products

Experimental design (crossover)



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

Gascon et al AJCN 1996;63:315-321.

Dietary protein sources and risk of coronary disease in women

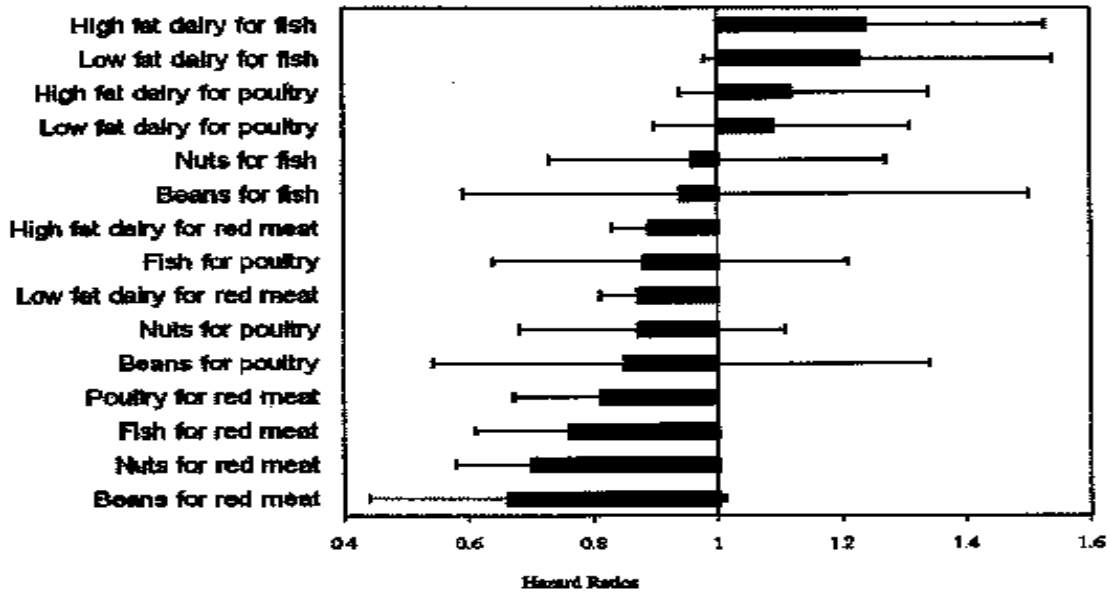
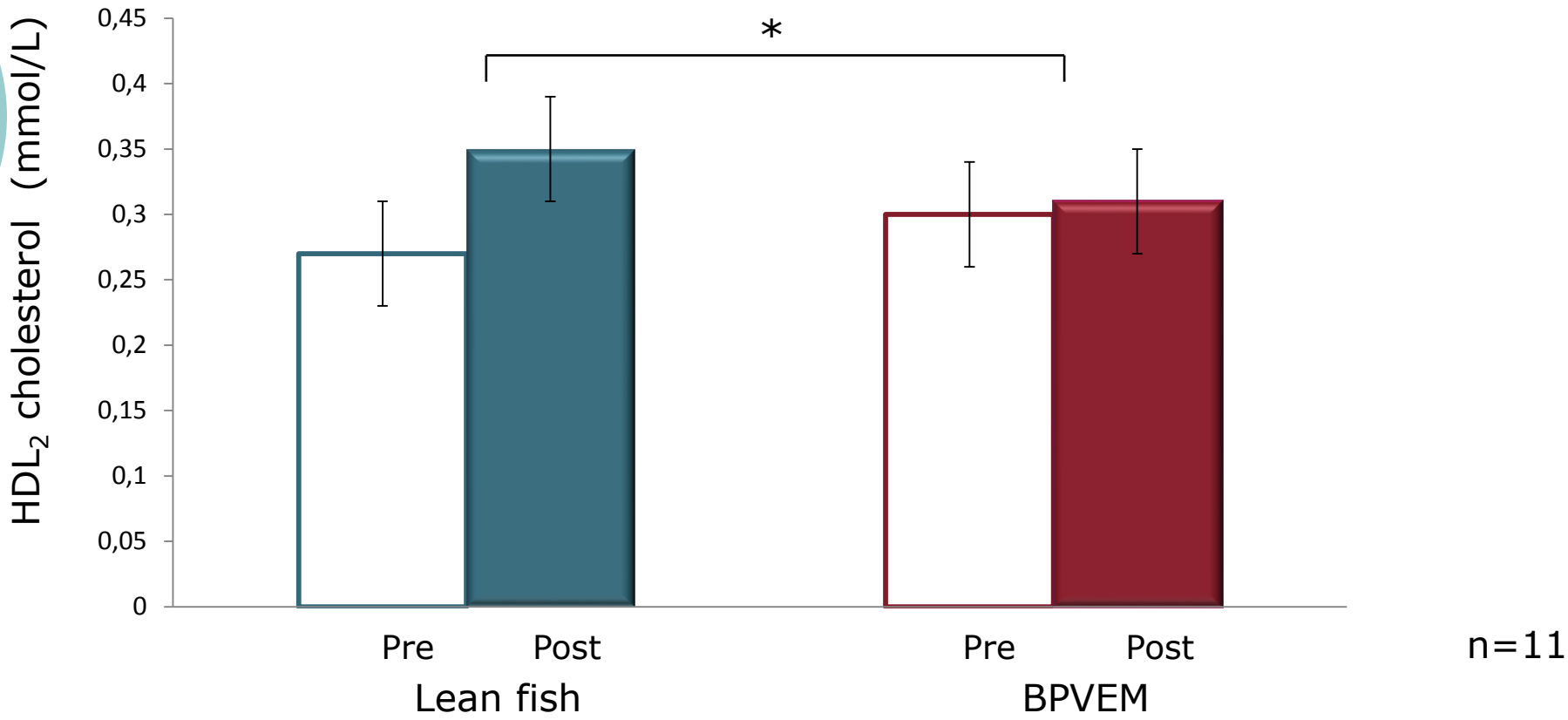


Figure. RRs and 95% CIs for CHD associated with replacement of a major dietary protein source with another.

Human prospective study, n= 84 136

Bernstein et al 2010 Circulation 122: 876 - 883

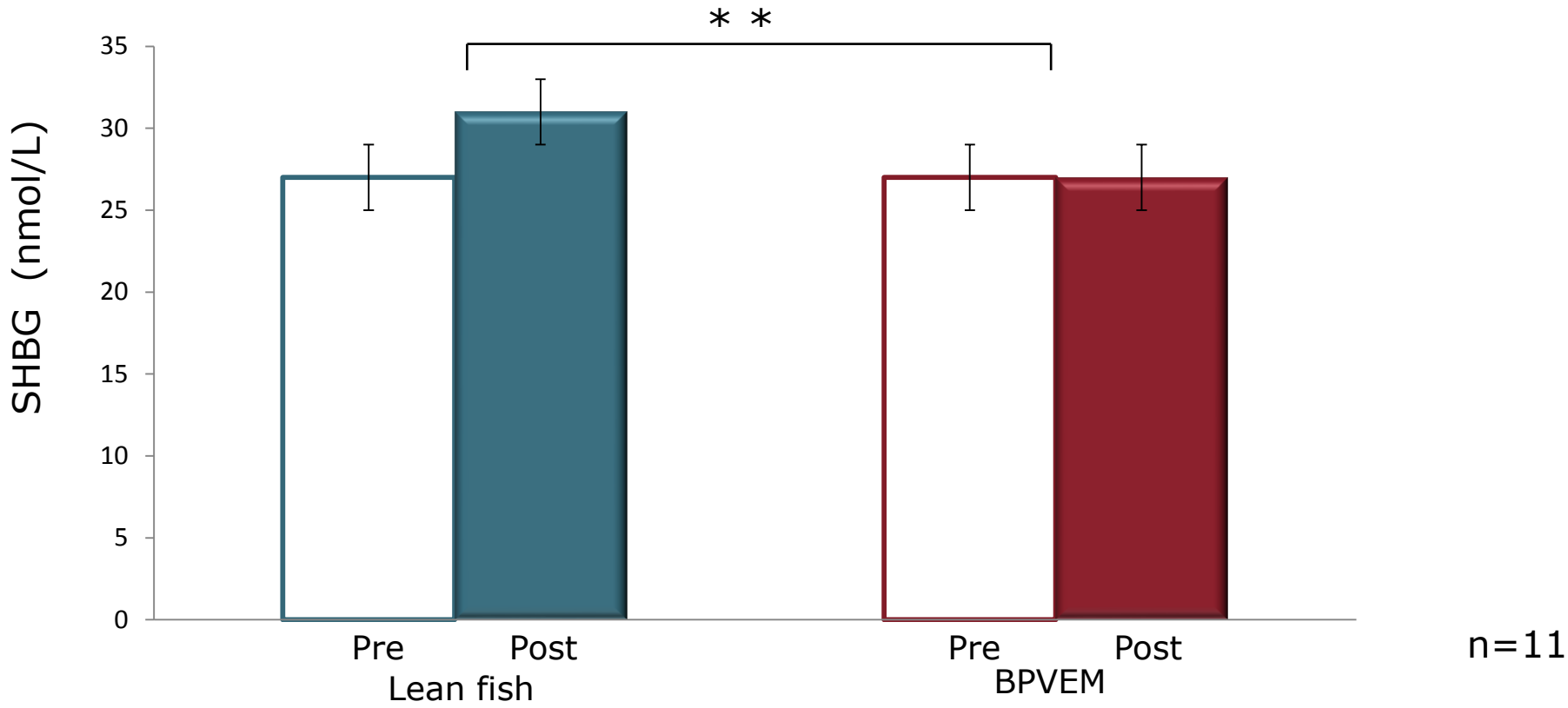
Lean fish diet increased HDL_2 cholesterol in normolipidemic men



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

Lacaille et al JACN 2000;19:745–753.

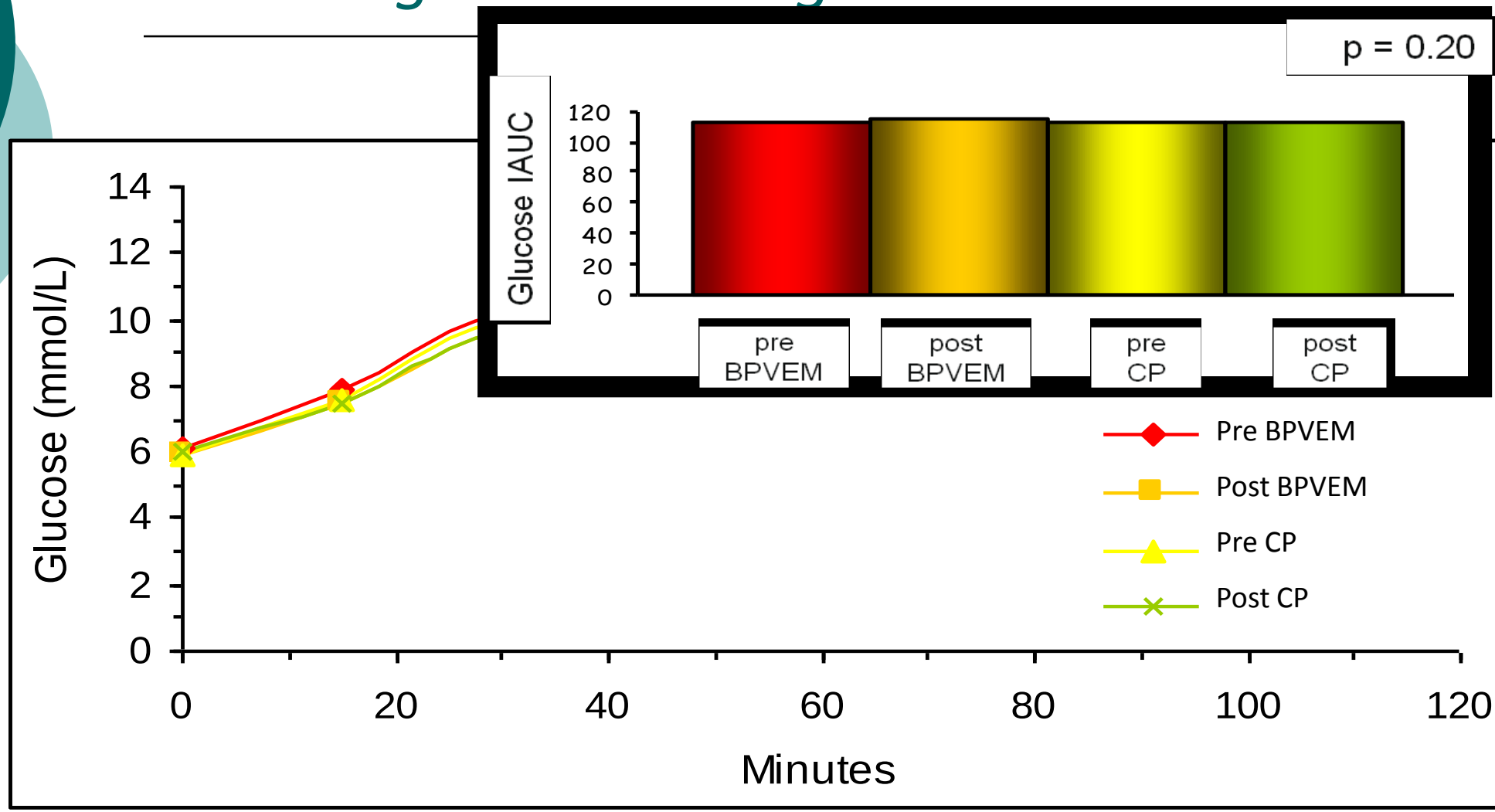
Lean fish diet increased SHBG in normolipidemic men



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

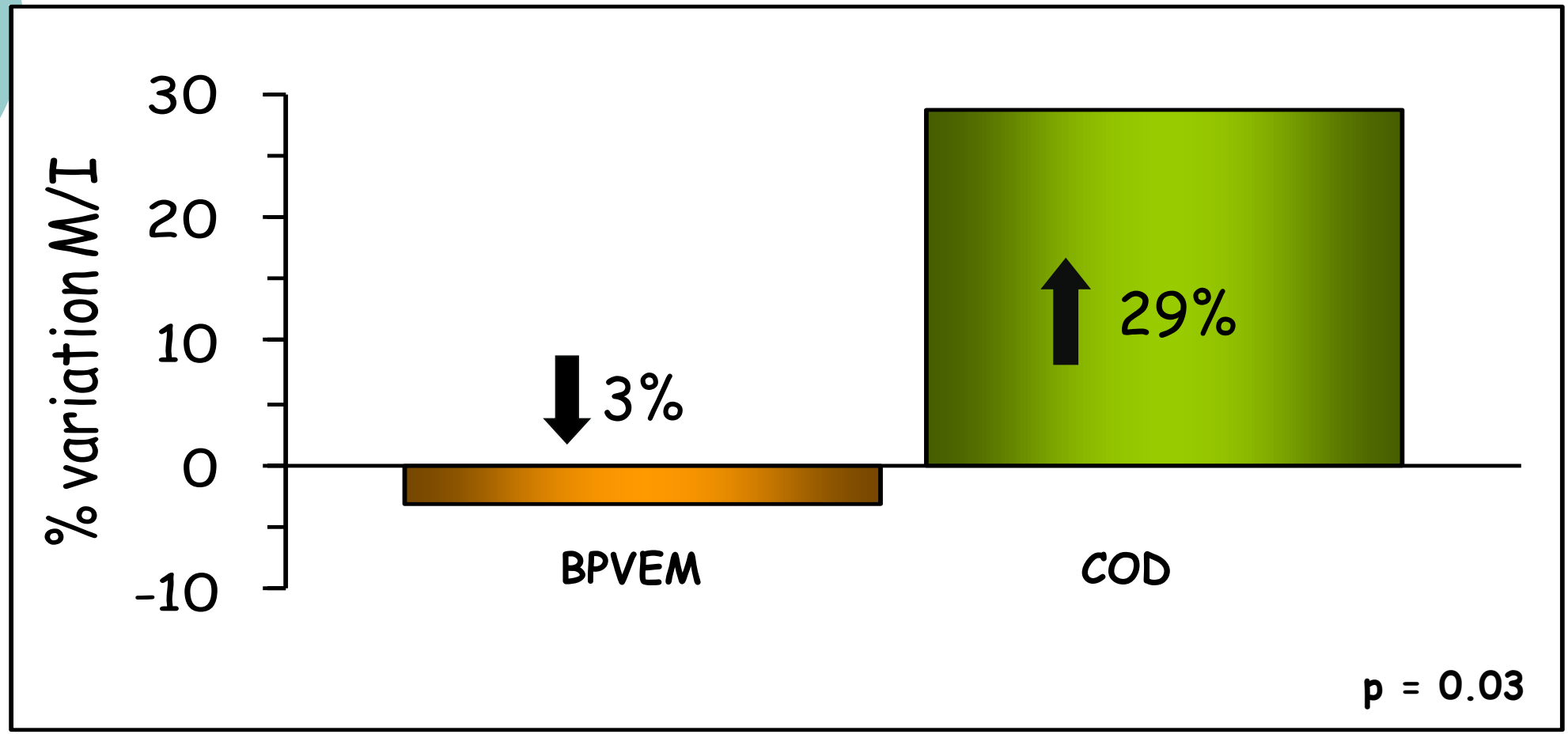
Lacaille et al JACN 2000;19:745–753.

Plasma glucose during OGTT



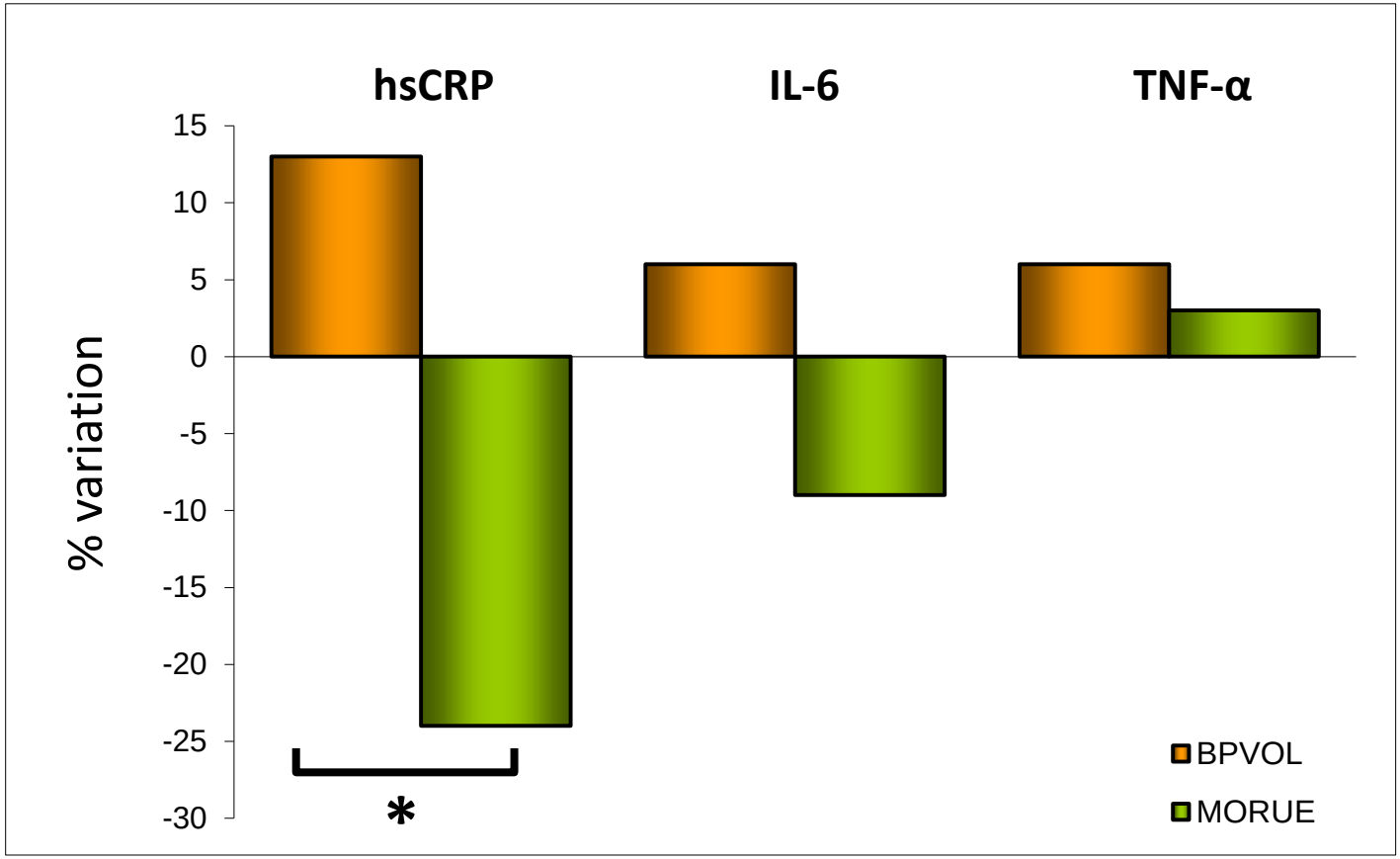
(Ouellet et al. Diabetes Care 2007 ;30 :2816-2821)

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



Ouellet et al. 2007. *Diabetes Care* 30:2816-2821

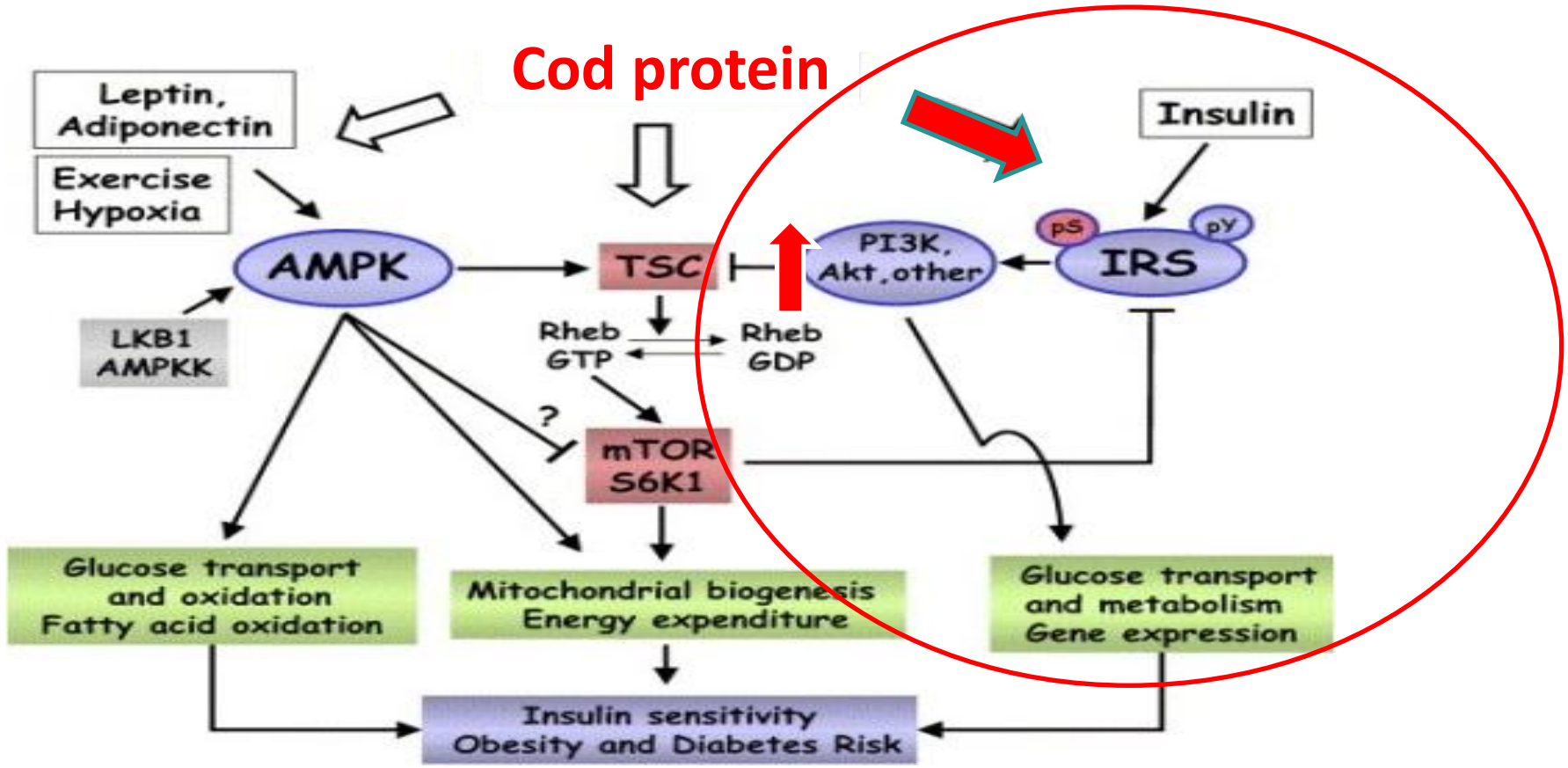
Cod protein reduced hsCRP, an inflammatory marker, in obese insulin-resistant men and women



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

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

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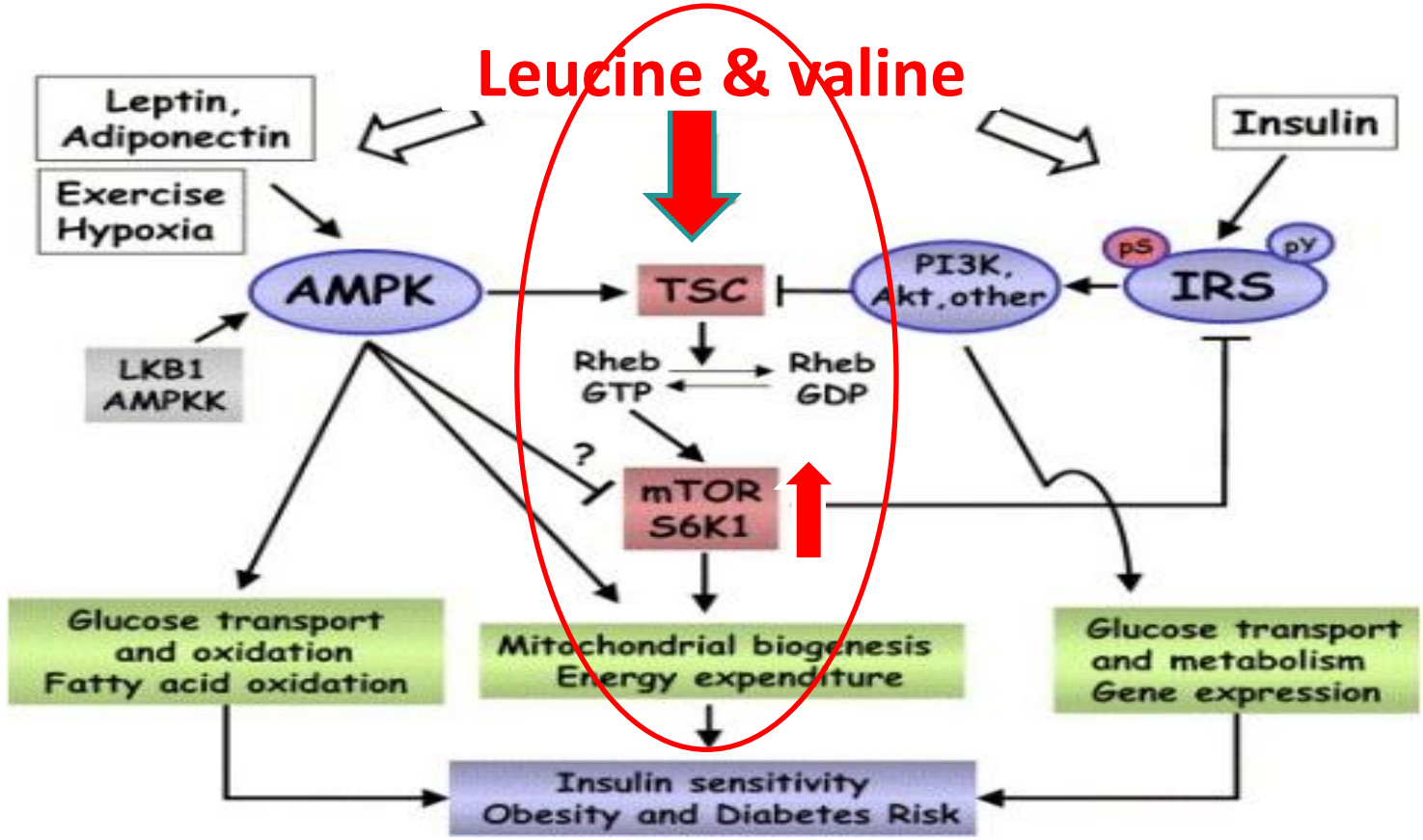
Serine	5,3	5,0
Threonine	4,6	4,5
Tyrosine	4,2	3,7
Valine	6,2	5,7

(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			
	Pre	Post	Δ	Pre	Post	Δ	P value
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**

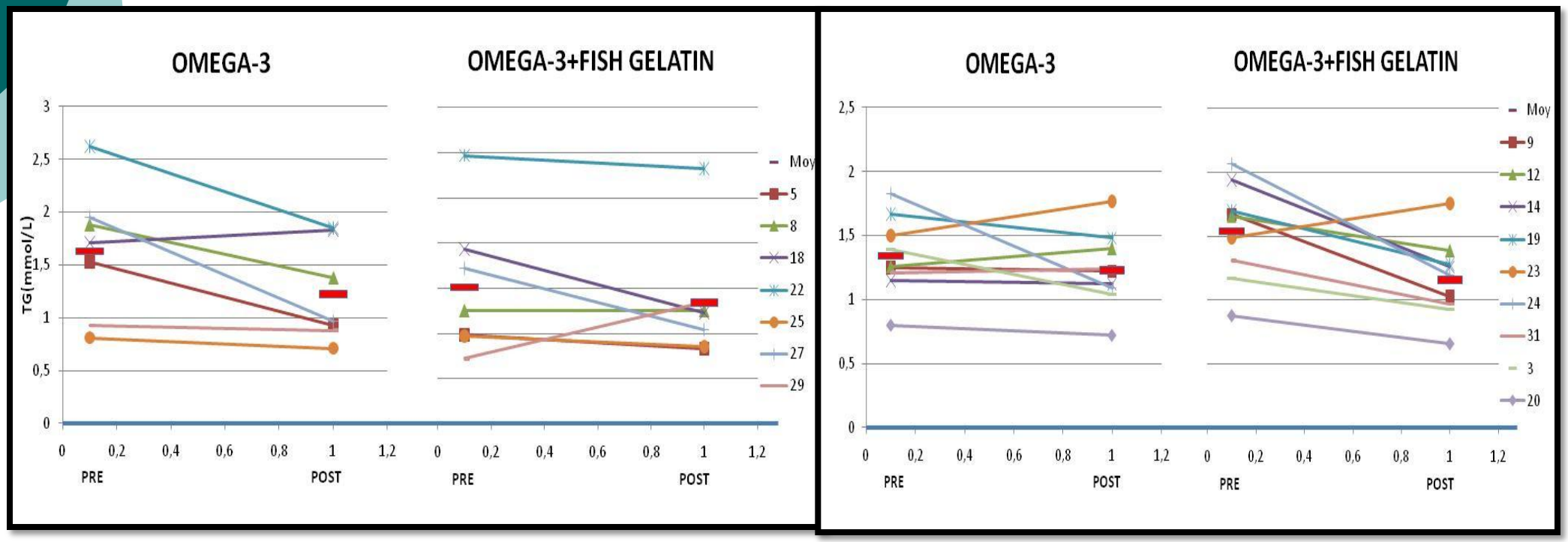
Mean± SEM

*** 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

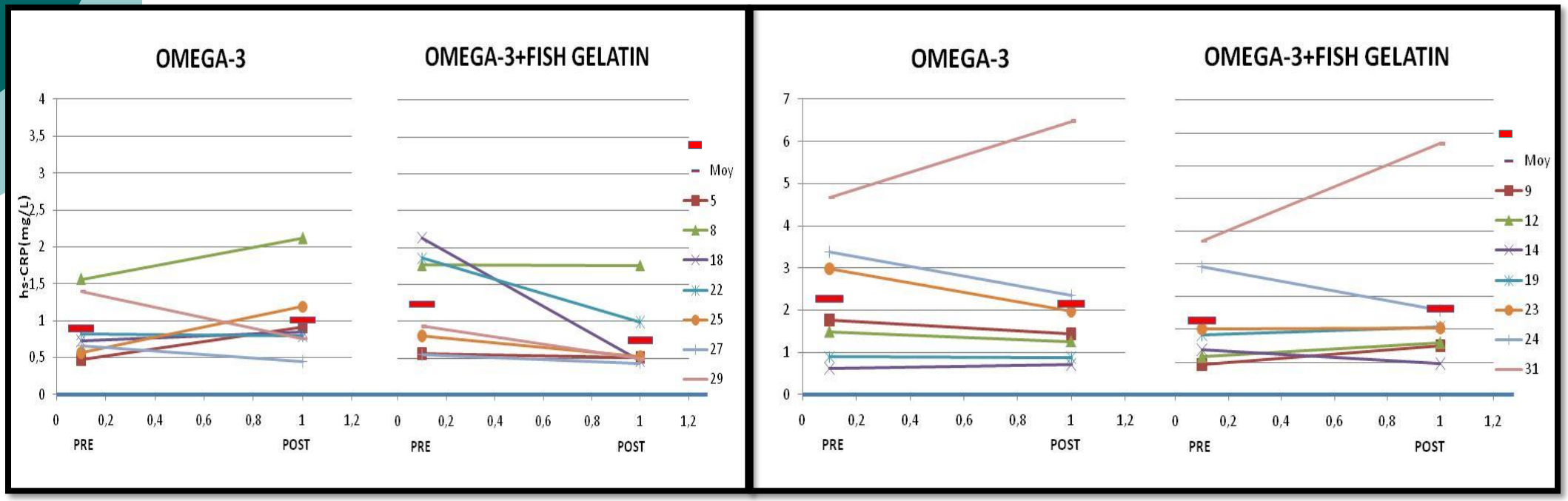
	Omega-3			Omega-3+Fish Gelatin			
	Pre	Post	Δ	Pre	Post	Δ	P value
MCP-1 (pg/ml) [2]	650 ± 44	665 ± 47.0	15.3 ± 49.6	579 ± 57	633 ± 44.0	53.0 ± 33.3	0.30
TNF-α (pg/ml) [2]	6.73 ± 1.31	5.83 ± 0.66	-0.90 ± 0.82	4.93 ± 0.47	5.33 ± 0.46	0.40 ± 0.42	0.12
hs-CRP (mg/L)	1.57 ± 0.34	1.58 ± 0.41	0.01 ± 0.20	1.75 ± 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

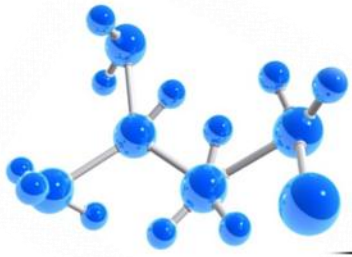
Men

Women



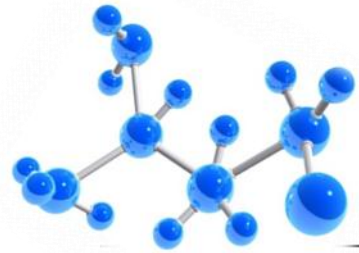
P=0.03

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

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BON APPÉTIT!

BON APPÉTIT!

Takk!

Spørsmål?