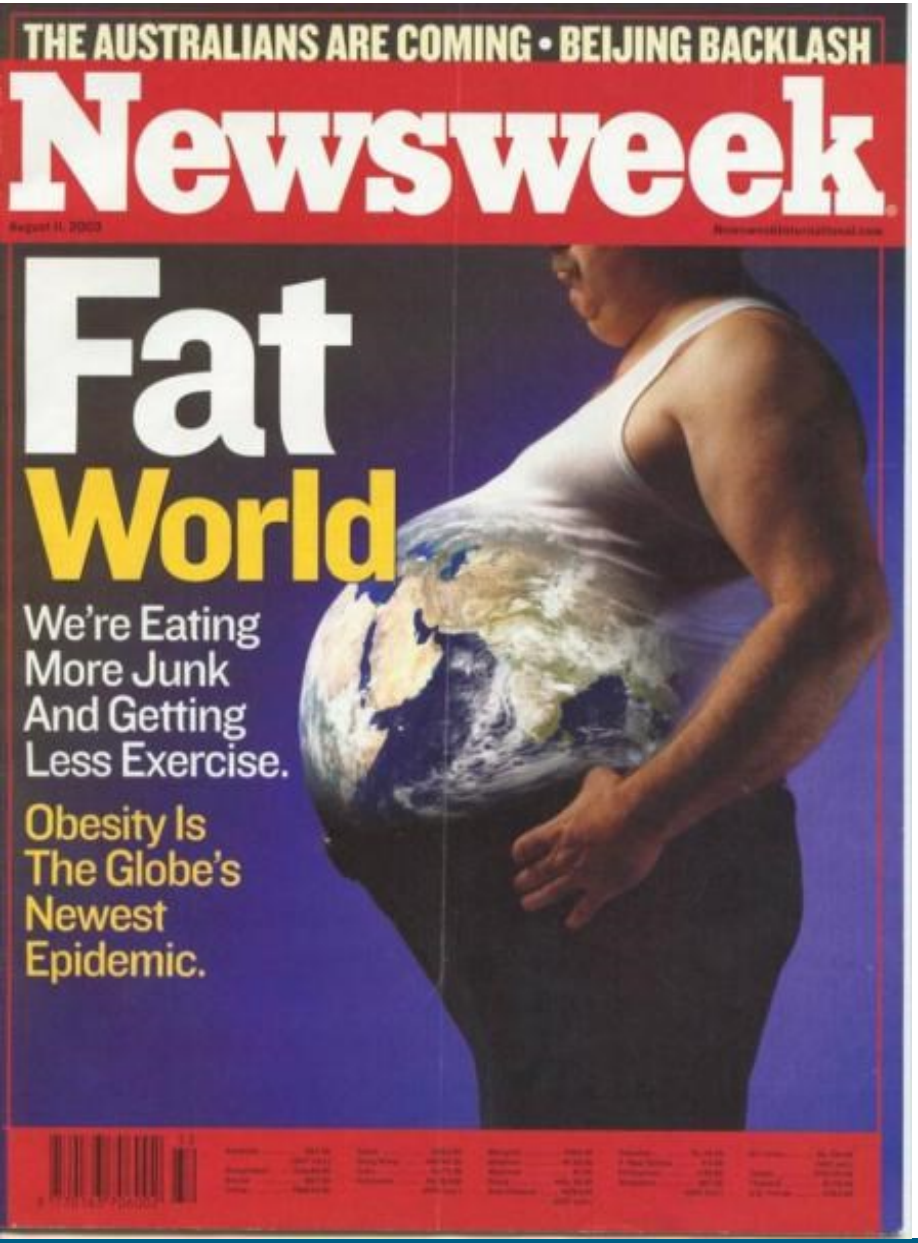
Sjømat og helse konferansen, Bergen, September 14-15, 2016

Kan (mager) sjømat beskytte mot fedme og diabetes?

Bjørn Liaset

Nasjonalt institutt for ernærings- og sjømatforskning(NIFES)

Bergen, Norway



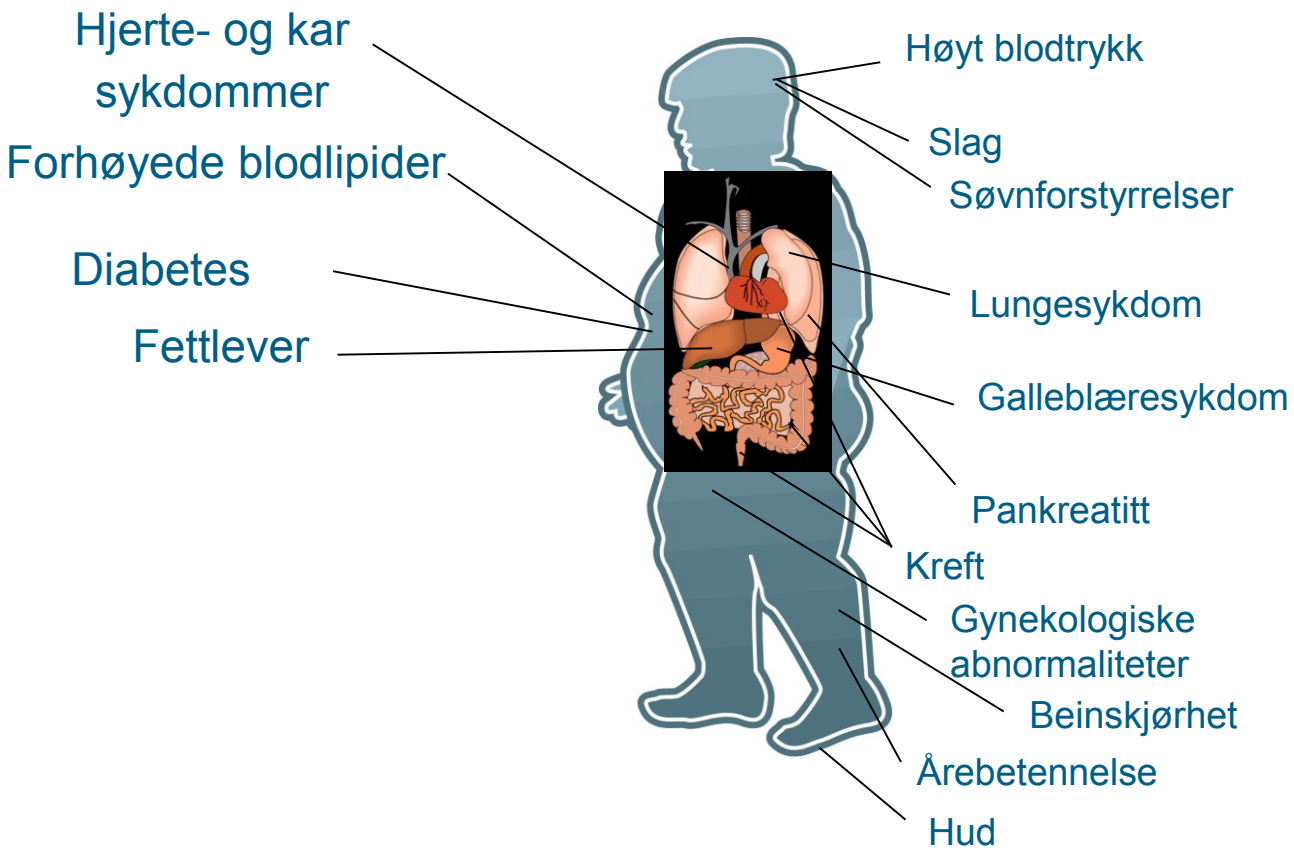
World Health Organization

Undervekt

Overvekt

Overvekt og fedme medfører økt risiko for:

World Health Organization



Overvekt og fedme medfører økt risiko for:

World Health Organization

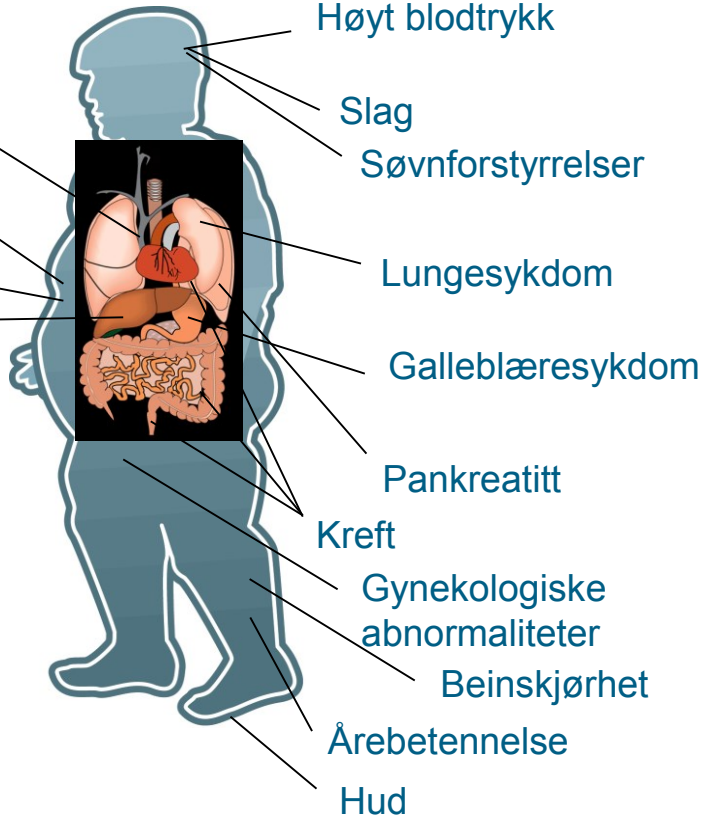
Hjerte- og kar-sjuke (1)

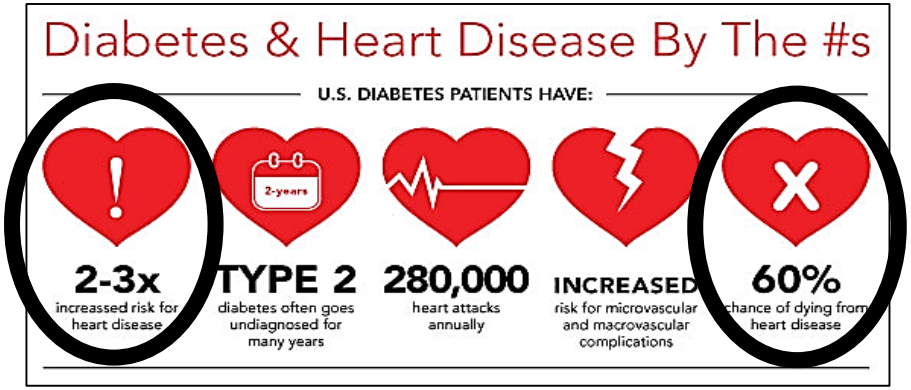
Forhøyede blodlipider

Diabetes (9)

Fettlever

Lozano R, 2012 Lancet

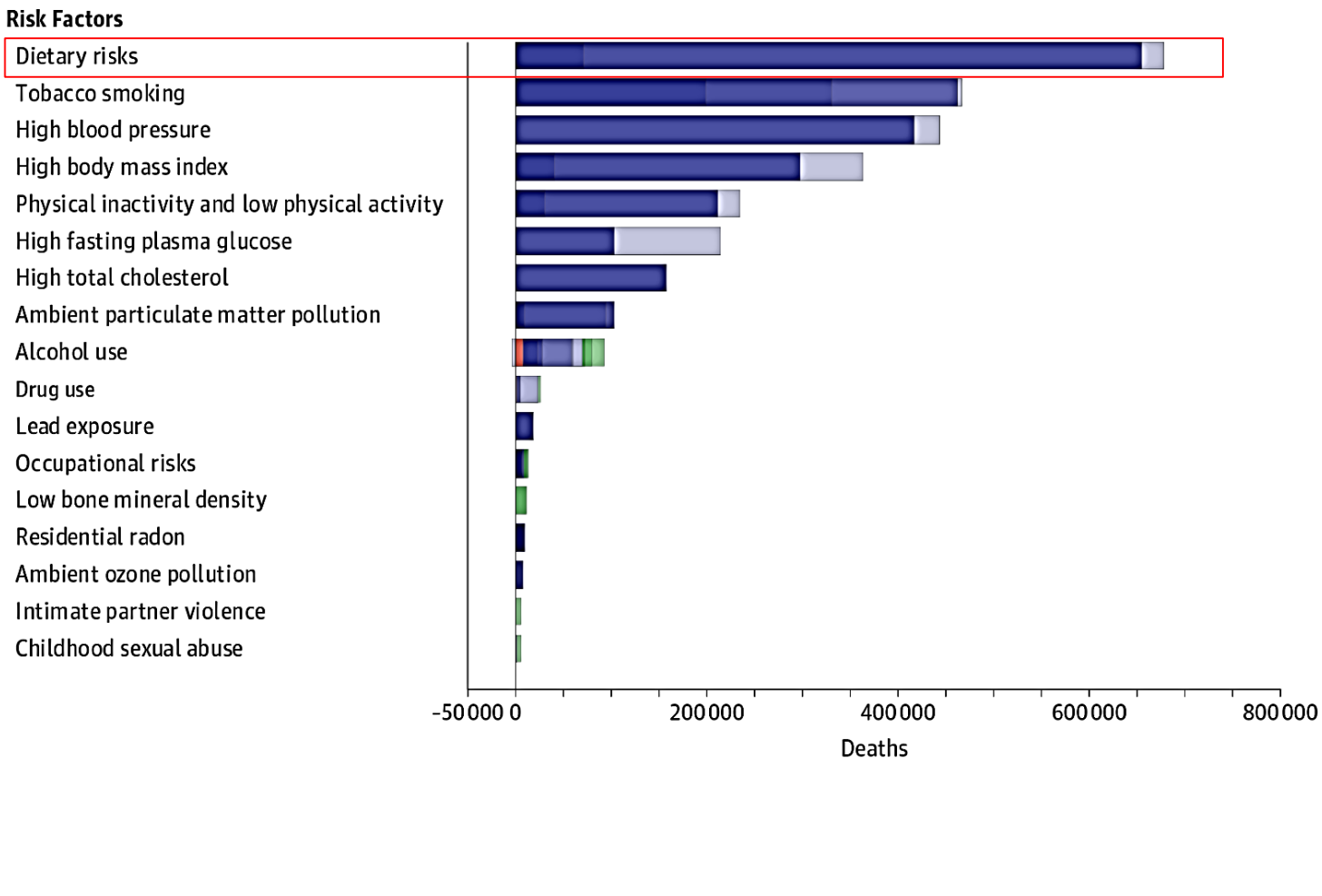




Korleis påverkar ulike typar diett utvikling av fedme og risikofaktorar for diabetes og hjarte- og karsjuke?

The State of U.S health, 2010

NIFES

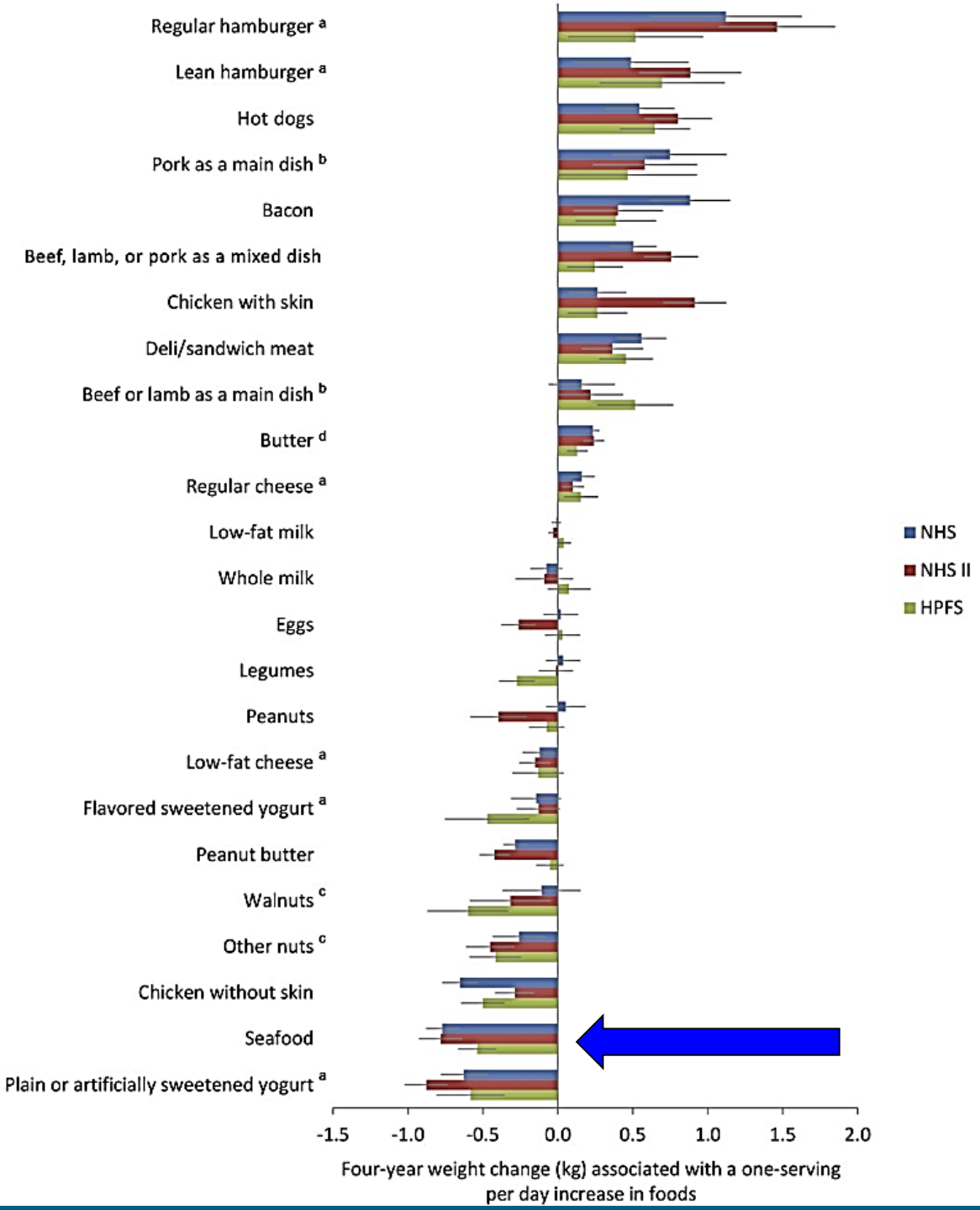


Diett er den leiande enkeltfaktor for dårleg helse i USA – dette gjeld også globalt

US Burden of Disease Collaborators, 2013 JAMA

ng over tid

NIFES



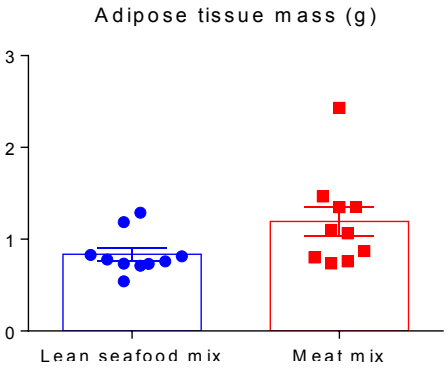
3 separate US prospective cohort studies based on 16 to 24 years of follow-up for:

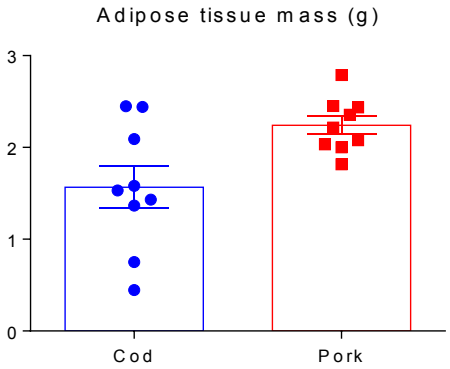
- 46,994 women in the NHS,
- 47,928 women in the NHS II,
- 25,862 men in the HPFS.

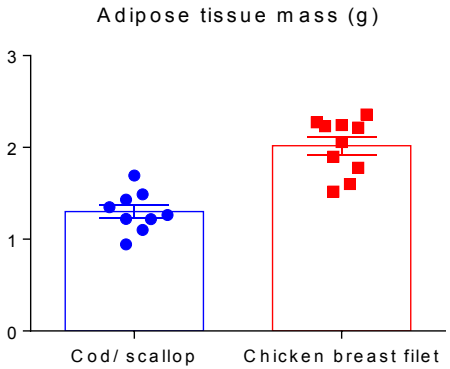
Vil vi sjå same utvikling i fedme i intervensjonsstudier med sjømat vs kjøt ?

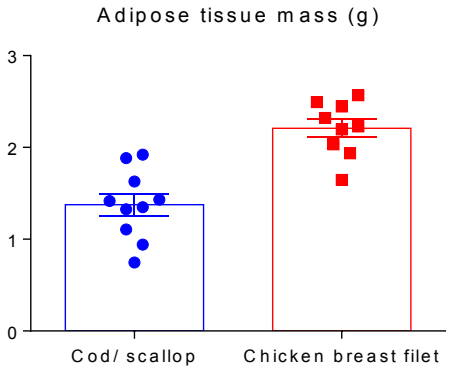
Smith JD, 2015 Am J Clin Nutr
Mozaffarian D, 2016 Circulation

Musestudier med mager sjømat og fedme







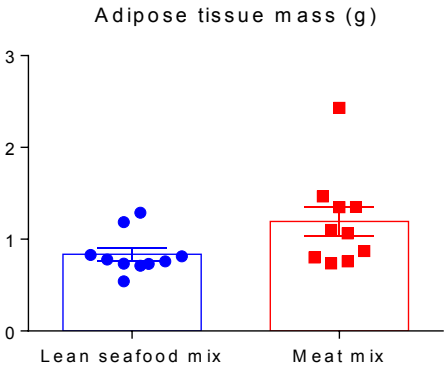


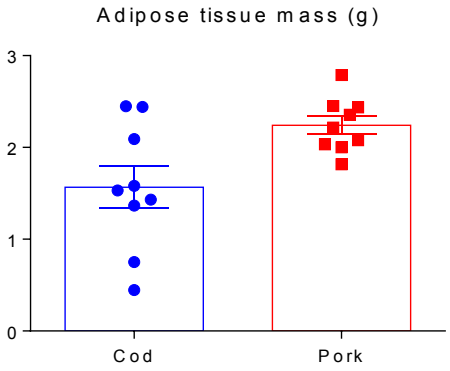
Gjennomsnitt skilnad bukfett = **33 %**

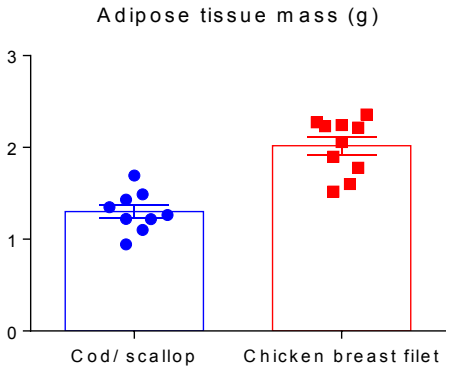
Holm JB, 2016 J Nutr Biochem; Liisberg U, 2016 J Nutr Biochem; Unpublished data

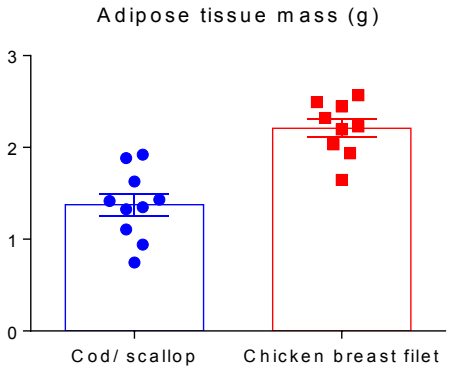
Musestudier med mager sjømat og fedme

NIFES

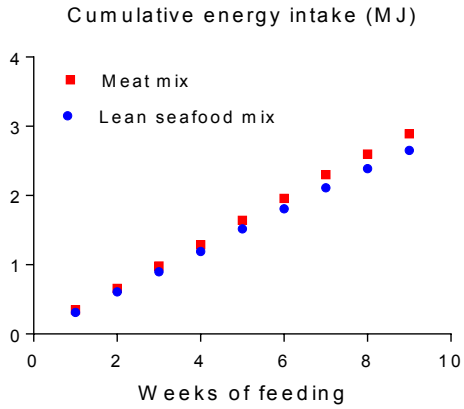


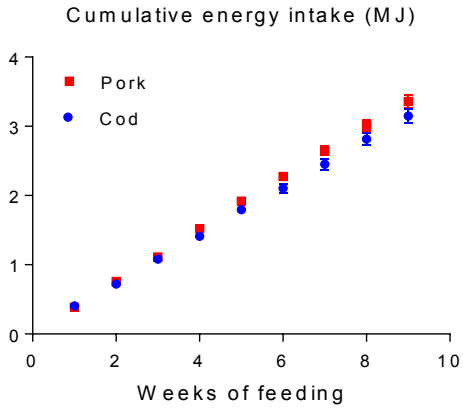


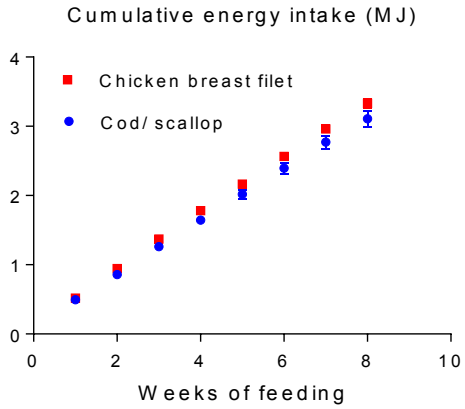


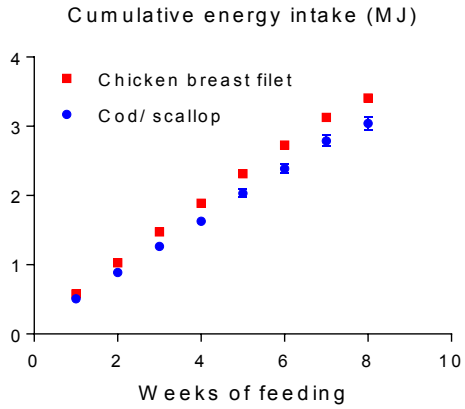


Gjennomsnitt skilnad bukfett = **33 %**







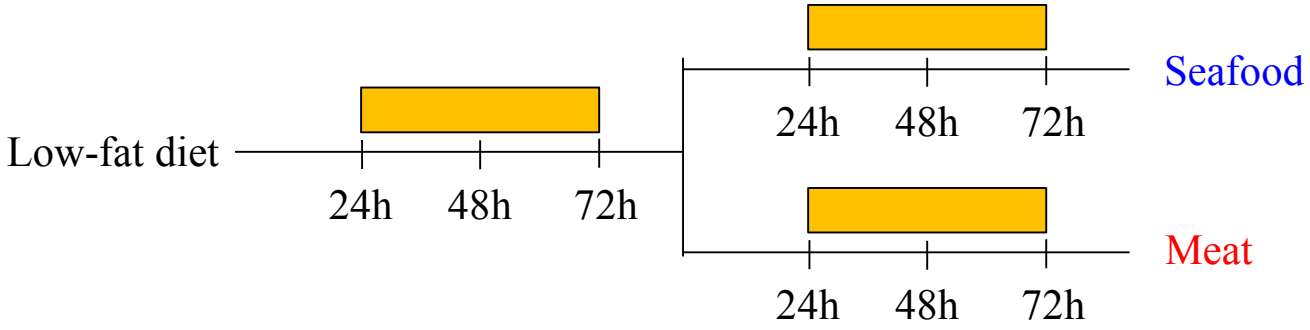


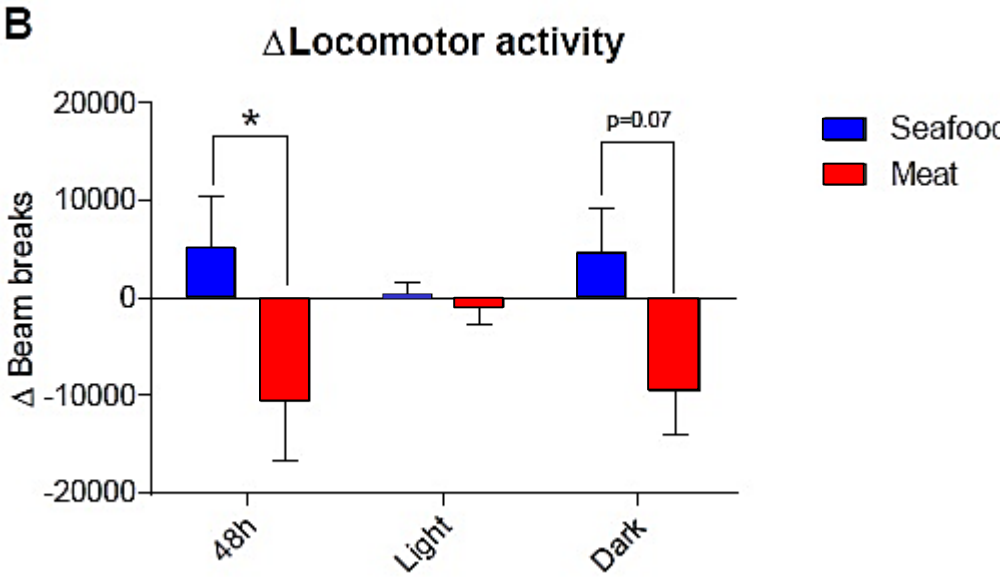
Gjennomsnitt skilnad spist energi = **8 %**

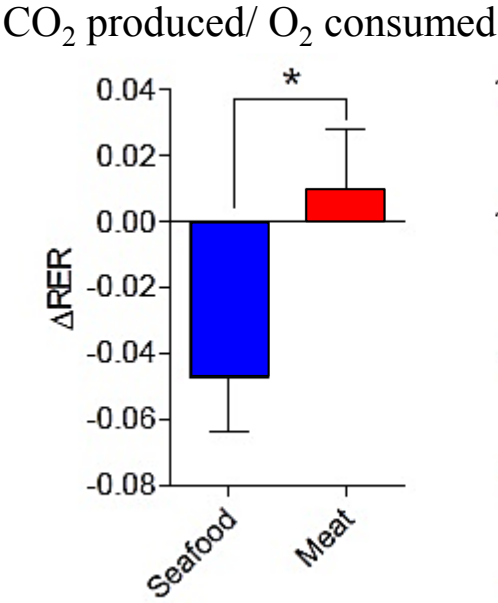
Holm JB, 2016 J Nutr Biochem; Liisberg U, 2016 J Nutr Biochem; Unpublished data

Musestudier med mager sjømat og fedme

NIFES







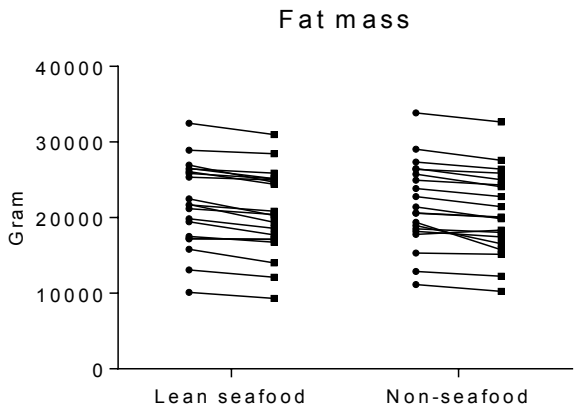
Skilnad i spontan røyrsle og karbohydrat forbrenning

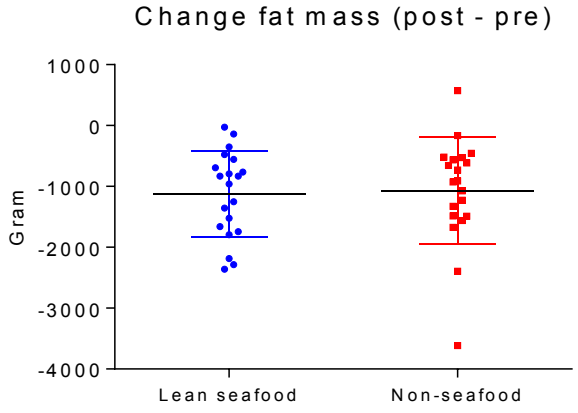
Holm JB, 2016 J Nutr Biochem

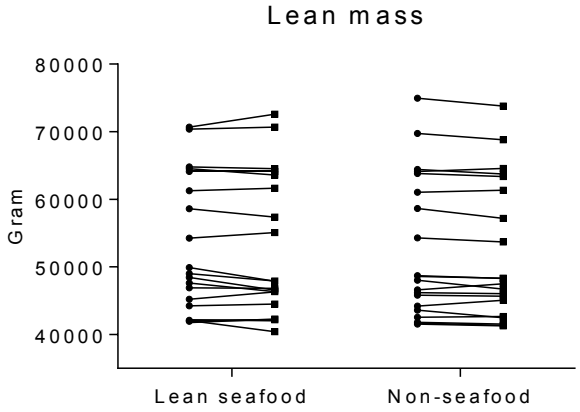
Studie med mager sjømat i friske voksne

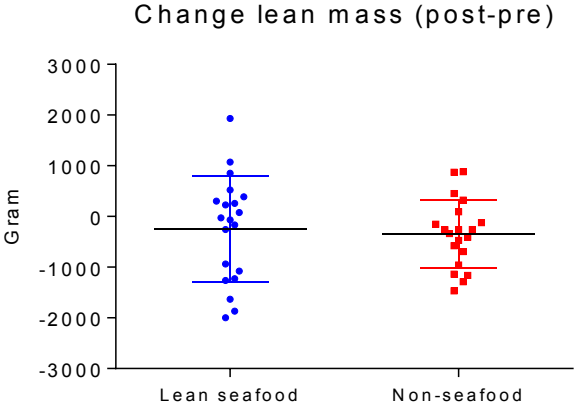
NIFES

- Overkrysningsstudie
- 4-vekers diettperiode
- n = 19 og 20
- DEXA måling









Inntak av mager sjømat og magert kjøt førte til lik nedgang i fettmasse

Aadland EK 2016 J Nutr

Oppsummering fedme

NIFES

Kan inntak av mager sjømat, samanlikna med inntak av magert kjøt beskytte mot fedme?

- Inntak av mager sjømat minkar utvikling av fedme i mus, men **lik påverknad av kroppsamansetnad** i friske, normalvektige vaksne i løpet av 4 veker med balanserte diettar og kontrollerte betingelsar

Påverkar inntak av mager sjømat risikofaktorar for diabetes og hjarte- og karsjuke?

Studie med mager sjømat i friske voksne

NIFES

Torsk
Sei
Lyr
Kamskjell

Primært endepunkt:

- Risikofaktorar hjarte- og karsjuke

Storfe
Svin
Kyllingfilet
Kalkunfilet
Egg
Lav-fett meieri

Sekundært endepunkt:

- Risikofaktorar T2D

Randomisert kontrollert studie

Overkrysningsstudie

NIFES

Lean seafood
n = 9

Non-seafood
n = 11

Lean seafood
n = 11

Non-seafood
n = 8

Run-in
period 1,
(3 wk)

Diet period 1 (4 wk)

Washout
-period,
(5 wk)

Run-in
period 2,
(3 wk)

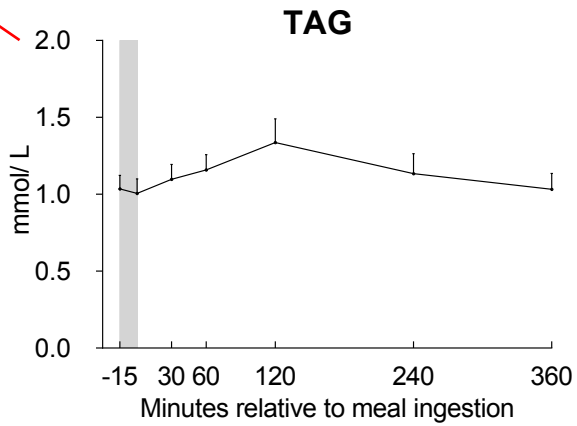
Diet period 2 (4 wk)

Test meal cod
or beef

Test meal cod
or beef

Test meal cod
or beef

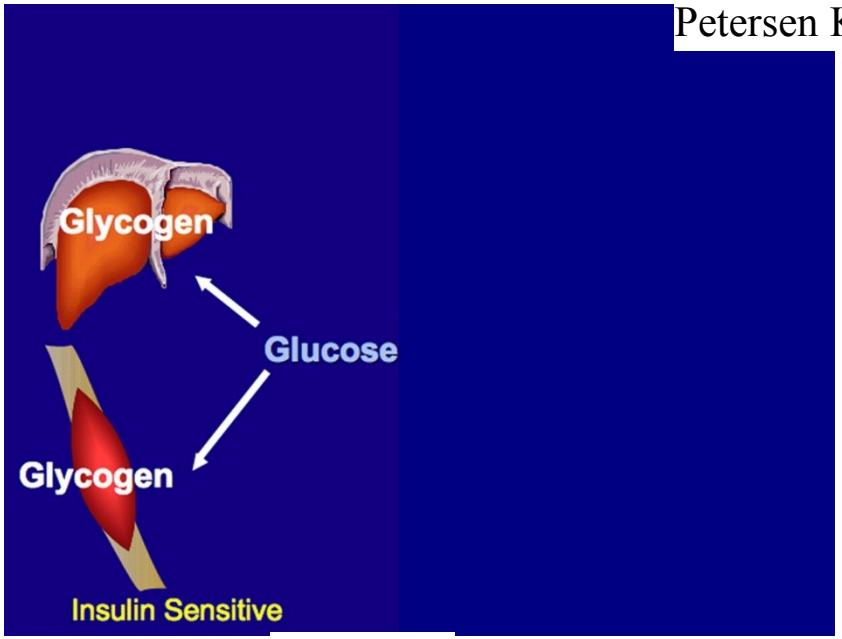
Test meal cod
or beef

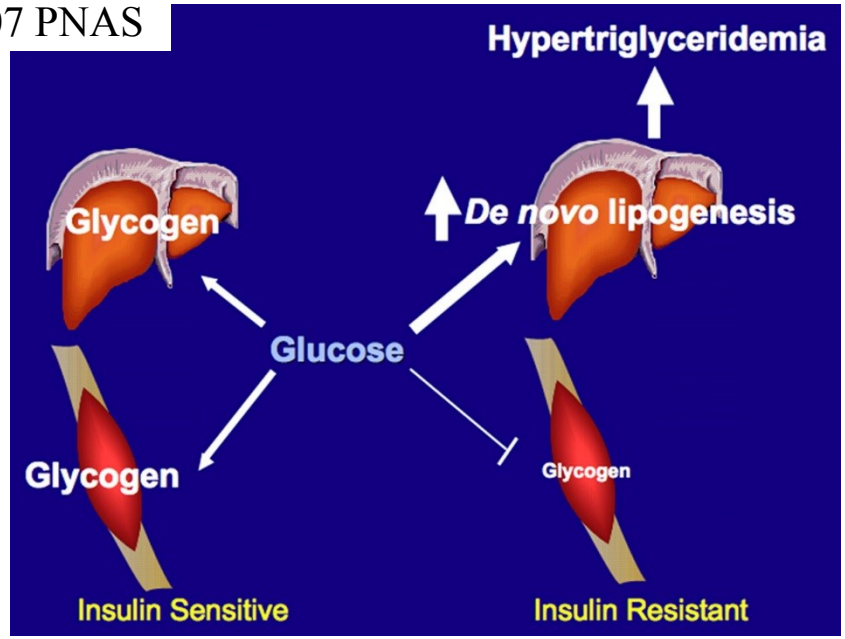


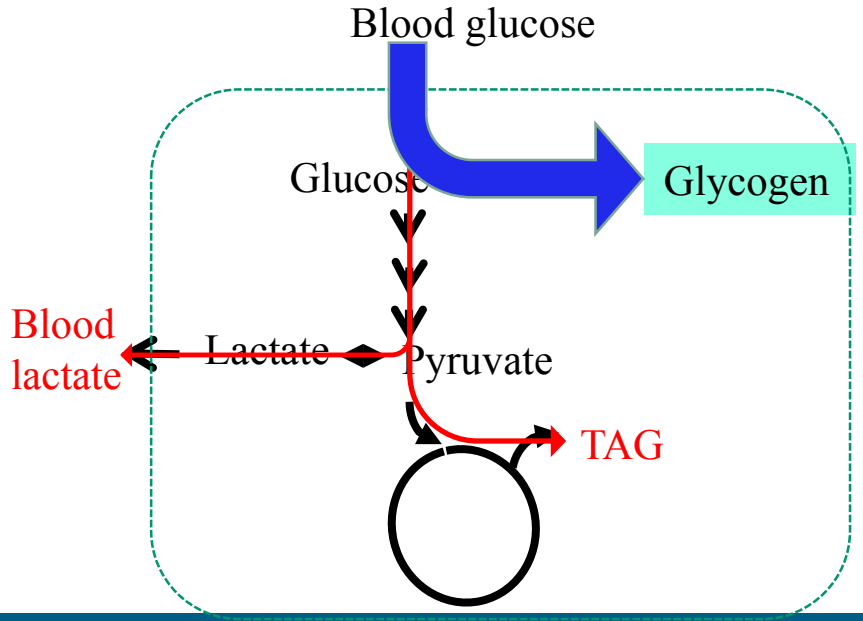
Insulin resistanse og hyperlipidemia

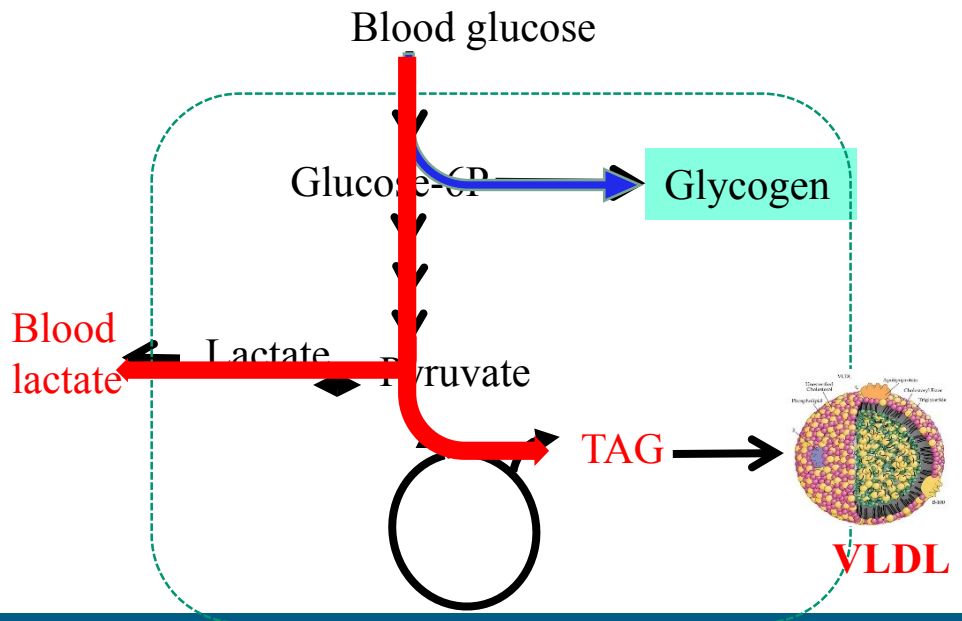
NIFES

Petersen KF 2007 PNAS

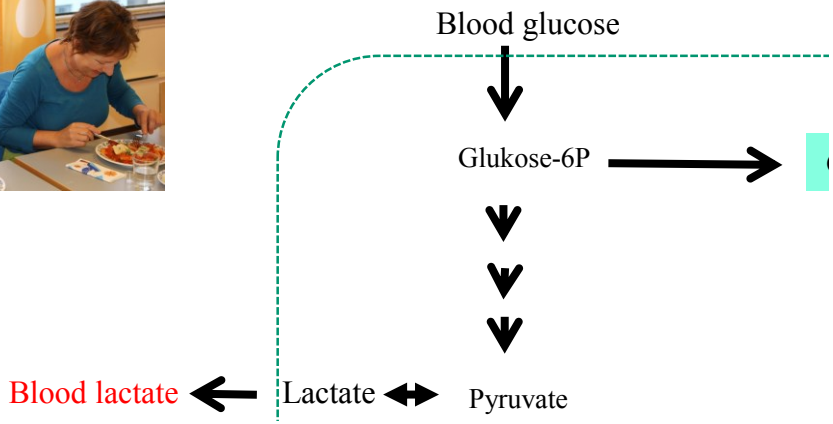


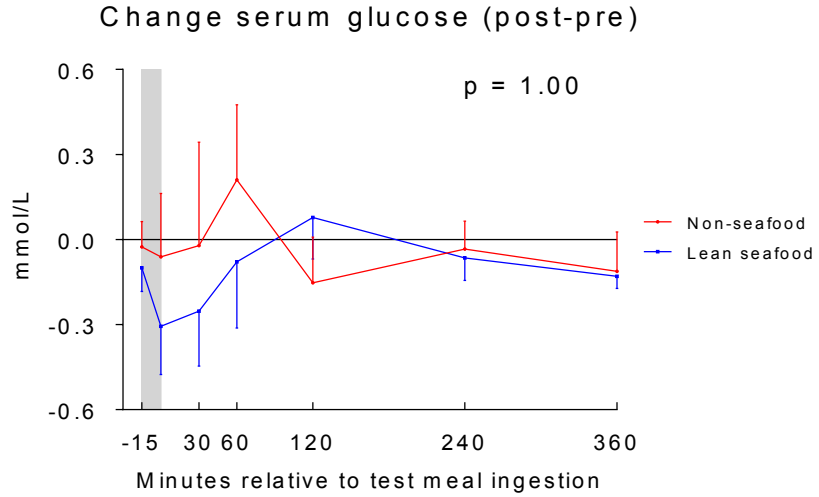




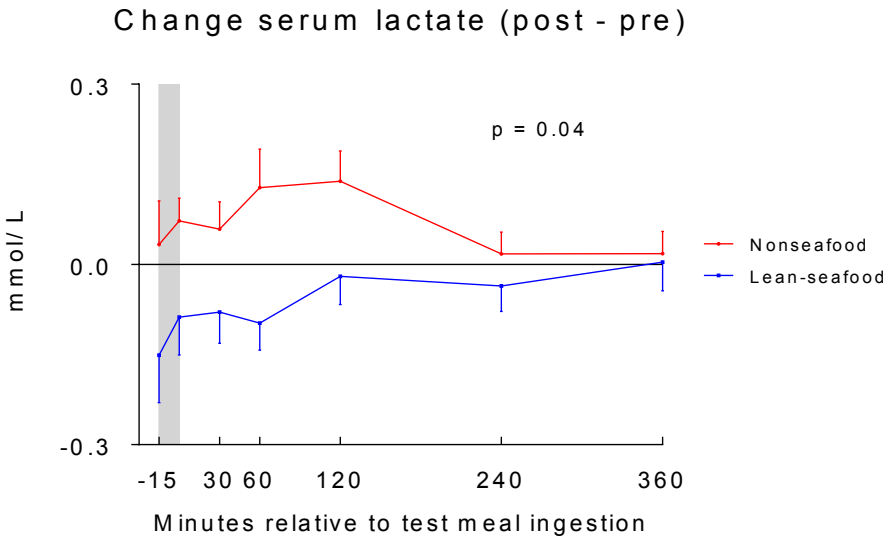


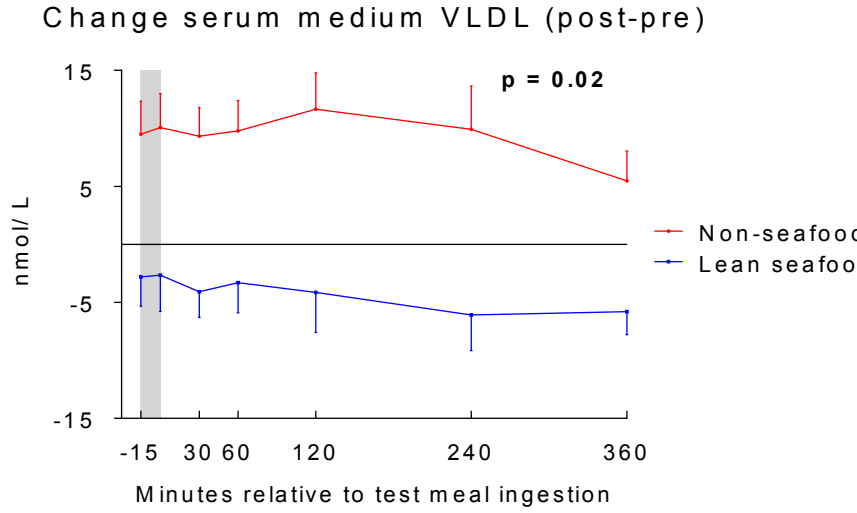
Mager sjømat inntak, glukose- og fettmetabolisme i friske voksne





AG





Aadland EK 2016 J Nutr

Aadland EK 2015 AJCN

Oppsummering

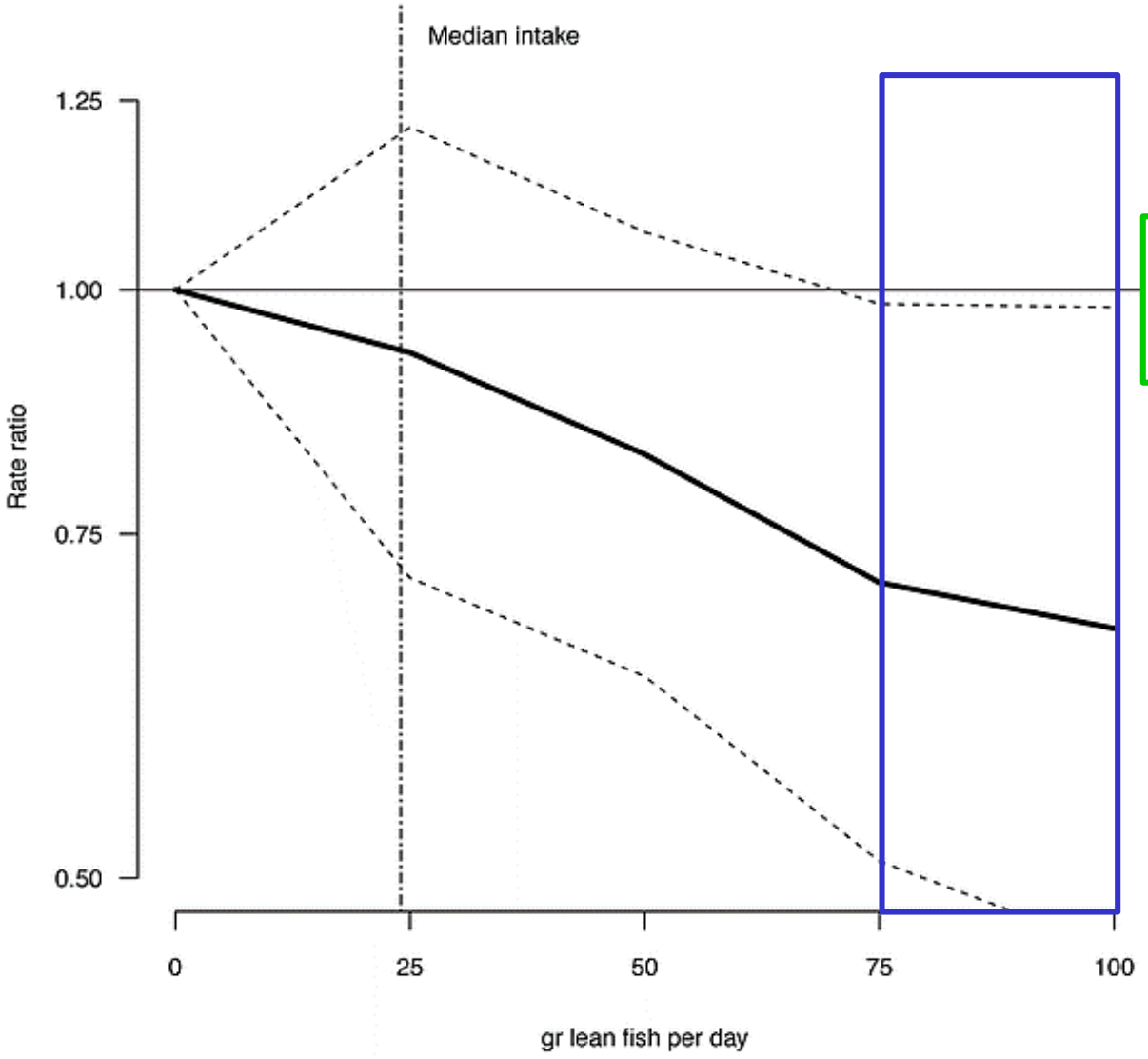
Kan inntak av mager sjømat, samanlikna med inntak av magert kjøt beskytte diabetes?

- Risikomarkørar diabetes og hjarte- og karsjuke:
  - Både i musestudier og i intervensjonsstudiet med friske voksne førte inntak av mager sjømat til ein **reduksjon av risikomarkørar** assosiert med seinare utvikling av **diabetes** og/eller **hjarte- og karsjuke**
- Kan ikkje dra konklusjon ut frå eit intervensjonsstudie med høgt inntak av mager sjømat, men våre data er i samsvar med eit observasjonsstudie frå Tromsø:

Mager sjømat reduserer diabetes risiko

NIFES

Prospective study in Norwegian women, n= 21 954



Redusert risiko for å utvikle T2D ved dagleg inntak av **75 og 100 g** mager fisk

Rylander C, 2014 PLoS ONE

Vegen vidare……

- Underliggande årsaker til observasjonar ikkje kjende
- Fleire uavklarte spørsmål omkring inntak av mager sjømat:

Trimethylamine N-Oxide (TMAO) og CVD

NIFES

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 25, 2013 VOL. 368 NO. 17

Intestinal Microbial Metabolism of Phosphatidylcholine and Cardiovascular Risk

W.H. Wilson Tang, M.D., Zeneng Wang, Ph.D., Bruce S. Levison, Ph.D., Robert A. Koeth, B.S., Earl B. Britt, M.D., Xiaoming Fu, M.S., Yuping Wu, Ph.D., and Stanley L. Hazen, M.D., Ph.D.

ABSTRACT

BACKGROUND

Recent studies in animals have shown a mechanistic link between intestinal microbial metabolism of the choline moiety in dietary phosphatidylcholine (lecithin) and coronary artery disease through the production of a proatherosclerotic metabolite, trimethylamine-*N*-oxide (TMAO). We investigated the relationship among intestinal microbiota-dependent metabolism of dietary phosphatidylcholine, TMAO levels, and adverse cardiovascular events in humans.

METHODS

We quantified plasma and urinary levels of TMAO and plasma choline and betaine levels by means of liquid chromatography and online tandem mass spectrometry after a phosphatidylcholine challenge (ingestion of two hard-boiled eggs and deuterium [d9]-labeled phosphatidylcholine) in healthy participants before and after the suppression of intestinal microbiota with oral broad-spectrum antibiotics. We further examined the relationship between fasting plasma levels of TMAO and incident major adverse cardiovascular events (death, myocardial infarction, or stroke) during 3 years of follow-up in 4007 patients undergoing elective coronary angiography.

RESULTS

Time-dependent increases in levels of both TMAO and its d9 isotopologue, as well as other choline metabolites, were detected after the phosphatidylcholine challenge. Plasma levels of TMAO were markedly suppressed after the administration of antibiotics and then reappeared after withdrawal of antibiotics. Increased plasma levels of TMAO were associated with an increased risk of a major adverse cardiovascular event (hazard ratio for highest vs. lowest TMAO quartile, 2.54; 95% confidence interval, 1.96 to 3.28; P<0.001). An elevated TMAO level predicted an increased risk of major adverse cardiovascular events after adjustment for traditional risk factors (P<0.001), as well as in lower-risk subgroups.

From the Department of Cellular and Molecular Medicine, Lerner Research Institute, Cleveland Clinic, Cleveland. Address reprint requests to Dr. Hazen at the Cleveland Clinic, 9500 Euclid Ave. NC-10, Cleveland, OH 44195, or at hazens@ccf.org.

N Engl J Med 2013;368:1575-84.
DOI: 10.1056/NEJMoa1109400

ARTICLE

doi:10.1038/nature09922

Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease

Zeneng Wang[1,2], Elizabeth Klipfell[1,2], Brian J. Bennett[3], Robert Koeth[1], Bruce S. Levison[1,2], Brandon DuGar[1], Ariel E. Feldstein[1,2], Earl B. Britt[1,2], Xiaoming Fu[1,2], Yoon-Mi Chung[1,2], Yuping Wu[4], Phil Schauer[5], Jonathan D. Smith[1,6], Hooman Allayee[7], W. H. Wilson Tang[1,2,6], Joseph A. DiDonato[1,2], Aldons J. Lusis[3] & Stanley L. Hazen[1,2,6]

Metabolomics studies hold promise for the discovery of pathways linked to disease processes. Cardiovascular disease (CVD) represents the leading cause of death and morbidity worldwide. Here we used a metabolomics approach to generate unbiased small-molecule metabolic profiles in plasma that predict risk for CVD. Three metabolites of the dietary lipid phosphatidylcholine—choline, trimethylamine *N*-oxide (TMAO) and betaine—were identified and then shown to predict risk for CVD in an independent large clinical cohort. Dietary supplementation of mice with choline, TMAO or betaine promoted upregulation of multiple macrophage scavenger receptors linked to atherosclerosis, and supplementation with choline or TMAO promoted atherosclerosis. Studies using germ-free mice confirmed a critical role for dietary choline and gut flora in TMAO production, augmented macrophage cholesterol accumulation and foam cell formation. Suppression of intestinal microflora in atherosclerosis-prone mice inhibited dietary-choline-enhanced atherosclerosis. Genetic variations controlling expression of flavin monooxygenases, an enzymatic source of TMAO,

SCIENTIFIC REPORTS

OPEN

Relationship of Serum Trimethylamine N-Oxide (TMAO) Levels with early Atherosclerosis in Humans

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Accepted: 09 May 2016
Published: 27 May 2016

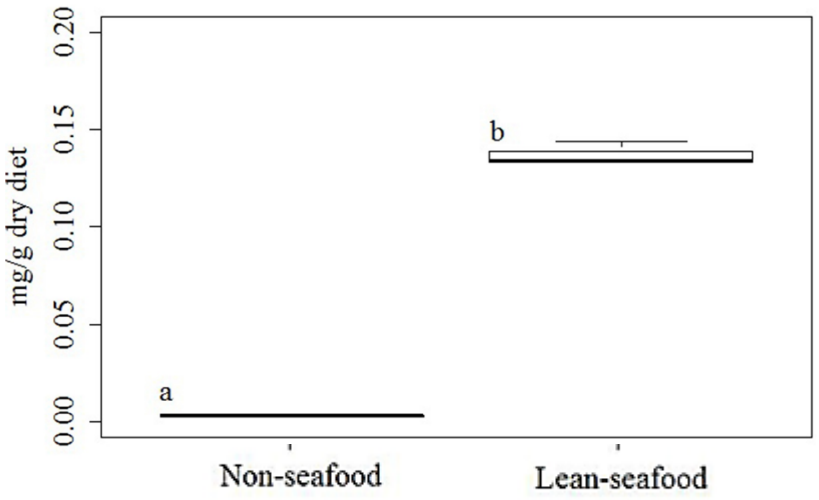
Elko Randrianarisoa[1,2,*], Angela Lehn-Stefan[1,2,3,*], Xiaolin Wang[4], Miriam Hoene[1,2], Andreas Peter[1,2,3], Silke S Heinzmann[3,5], Xinjie Zhao[4], Ingmar Königsrainer[6], Alfred Königsrainer[6], Bernd Balletshofer[1], Jürgen Machann[2,3], Fritz Schick[2,3,7], Andreas Fritsche[1,2,3], Hans-Ulrich Häring[1,2,3], Guowang Xu[4], Rainer Lehmann[1,2,3] & Norbert Stefan[1,2,3]

Circulating trimethylamine N-Oxide (TMAO) levels predict cardiovascular disease (CVD), possibly by impacting on cholesterol metabolism and oxidative stress. Because hepatic TMAO production is regulated by insulin signalling and it is unclear whether and to what extent circulating TMAO levels associate with CVD risk, independently of insulin resistance and its important determinants fatty liver and visceral obesity, we have now addressed this question in 220 subjects who participated in the Tübingen Lifestyle Intervention Program. Visceral fat mass ($r = 0.40$, $p < 0.0001$), liver fat content ($r = 0.23$, $p = 0.0005$) and TMAO levels ($r = 0.26$, $p < 0.0001$) associated positively, and insulin sensitivity associated negatively ($r = -0.18$, $p = 0.009$) with carotid intima-media thickness (cIMT). Higher TMAO levels (std.—Beta 0.11, $p = 0.03$) predicted increased cIMT, independently of age, sex and visceral fat mass. While during the lifestyle intervention most cardiovascular risk parameters improved, mean TMAO levels did not change ($p = 0.18$). However, cIMT decreased significantly ($p = 0.0056$) only in subjects in the tertile with the largest decrease of TMAO levels (>20%). We provide novel information that increased serum TMAO levels associate with increased cIMT, independently of established cardiovascular risk markers, including insulin resistance, visceral obesity and fatty liver. Furthermore, the decrease of cIMT during a lifestyle intervention may be related to the decrease of TMAO levels.

Mager sjømat inntak aukar TMAO

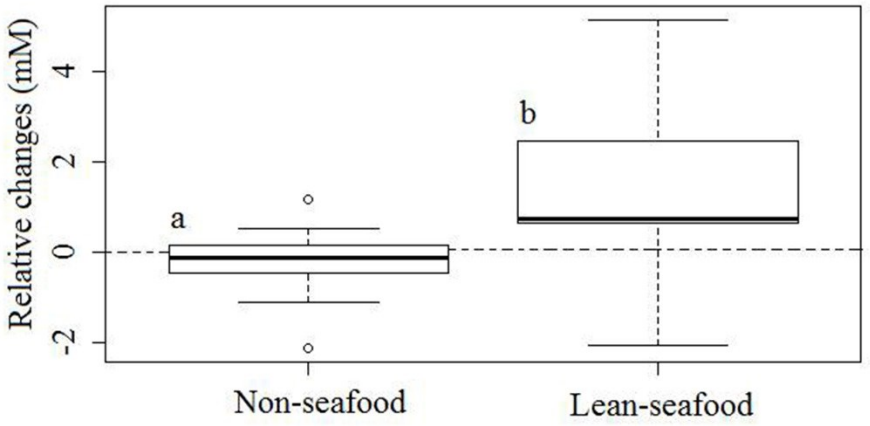
A

TMAO in diets

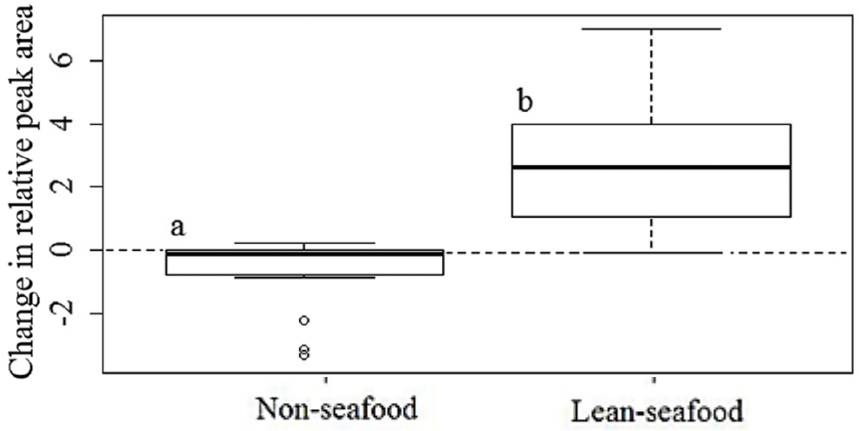


Fysiologisk relevans auka TMAO?

Change in fasting serum TMAO concentration



Change in morning spot urine TMAO concentration



Schmedes M, 2016 Mol Nutr Food Res

Takk til gode kollegaer:

Mice studies

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Human intervention study

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Takk for merksemda!

Forbrukerinspektørene, onsdag 7.sept 2016:

Familien spiste fisk hver dag i én måned

– Hadde aldri trodd på så store forandringer.

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