Fuldkorn og sundhed

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Frej 14. november 2016

STØTTET AF
promilleafgiftsfonden
for landbrug

Miljø- og
Fødevareministeriet
gudp

Sundhedseffekter af fuldkorn
- *mulige mekanismer*

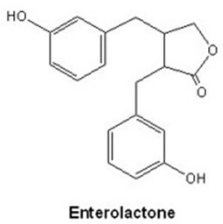
"Mekaniske" effekter:

- Hurtigere transittid
- Indpakning af carcinogener
- Langsommere mavetøming
- Øget mæthed

Indirekte effekter:

- Produktion af SCFA – butyrat
- Glucose/insulin balance
- Lavere kolesterol (β-glucan)
- Lavere blodtryk?
- Nedsat inflammation?

- Mikrobiomet??



Enterolactone

Forskning i fuldkorn

Kost, kræft og helbred
– en befolkningsundersøgelse

Hovedundersøgelse 1993–1997

57.054 RASKE personer i alderen 50–64 år

- 27.179 mænd
- 29.875 kvinder

Fulgt over tid for opstået sygdom – ca. 18 år

- 10.000 døde
- 1.200 diagnosticeret med tarmkræft
- 1.700 diagnosticeret med prostatakræft
- 1.800 diagnosticeret med brystkræft
- 2.300 diagnosticeret med hjertesygdom

Kost, kræft og helbred
– en befolkningsundersøgelse

Kostspørgeskema

Livsstilsspørgeskema

Biologiske målinger

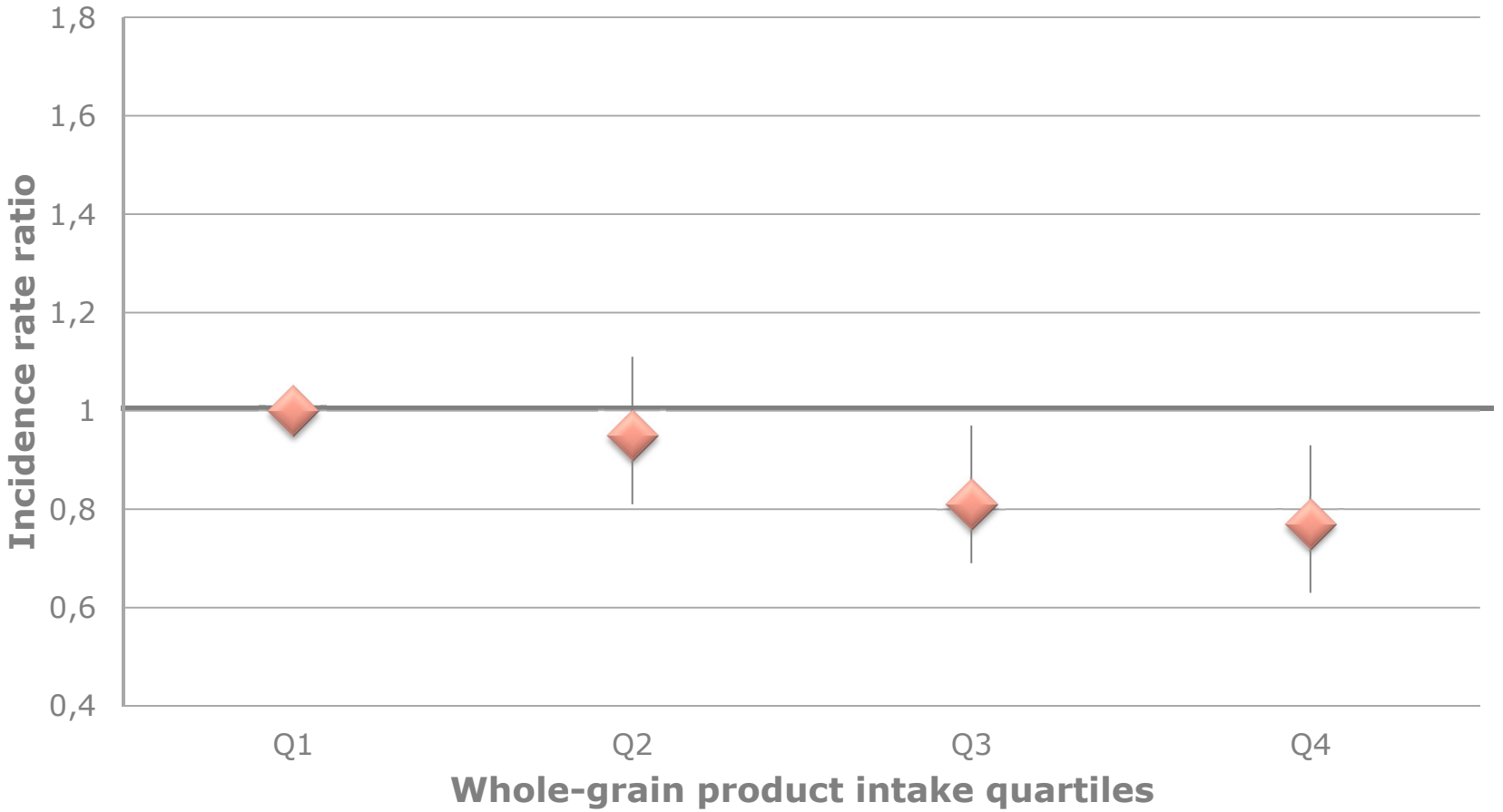
- Blodprøve
- Urinprøve
- Fedtbiopsi
- Tånegleklip

Desuden

- Vægt, højde, BMI, ståhøjde, siddehøjde
- Blodtryk, taljemål, hoftemål

Tarmkræft

Fuldkornsproduktsindtag (g produkt/dag) og tarmkræftincidens



Kyrø et al., Cancer Causes & Control, 2013

Forebyggelse af tarmkræft

- Tredje hyppigste kræftform
- >40% tilfælde
  → kan tilskrives overvægt/fedme, usund kost/ernæring samt fysisk inaktivitet
- Kostfibre→ beskytter!!!
  - Klassificeret som "convincing" i 2011
- Måske især kostfibre fra cerealier samt fuldkorn

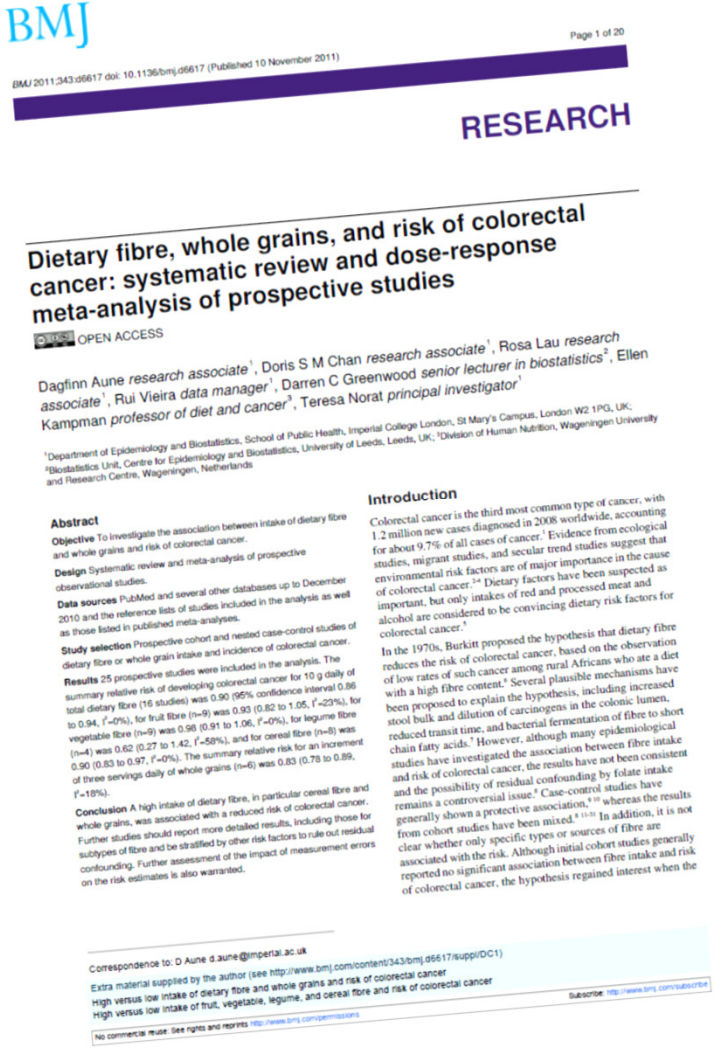
FOOD, NUTRITION, PHYSICAL ACTIVITY AND CANCERS OF THE COLON AND THE RECTUM 2011

	DECREASES RISK	INCREASES RISK
Convincing	Physical activity[1,2] Foods containing dietary fibre[3]	Red meat[4,5] Processed meat[4,6] Alcoholic drinks (men)[7] Body fatness Abdominal fatness Adult attained height[8]
Probable	Garlic Milk[9] Calcium[10]	Alcoholic drinks (women)[7]

World Cancer Research Fund / American Institute for Cancer (WCRF/AICR) Research, Continuous Update Project, 2011 & WCRF/AICR Policy and Action for Cancer Prevention, 2009

Metaanalyse

– baggrund for WCRF/AICR klassificering som ”convincing”



BMJ

BMJ 2011;343:d6617 doi: 10.1136/bmj.d6617 (Published 10 November 2011) Page 1 of 20

RESEARCH

Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies

OPEN ACCESS

Dagfinn Aune *research associate*[1], Doris S M Chan *research associate*[1], Rosa Lau *research associate*[1], Rui Vieira *data manager*[1], Darren C Greenwood *senior lecturer in biostatistics*[2], Ellen Kampman *professor of diet and cancer*[3], Teresa Norat *principal investigator*[1]

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Abstract

Objective To investigate the association between intake of dietary fibre and whole grains and risk of colorectal cancer.

Design Systematic review and meta-analysis of prospective observational studies.

Data sources PubMed and several other databases up to December 2010 and the reference lists of studies included in the analysis as well as those listed in published meta-analyses.

Study selection Prospective cohort and nested case-control studies of dietary fibre or whole grain intake and incidence of colorectal cancer.

Results 25 prospective studies were included in the analysis. The summary relative risk of developing colorectal cancer for 10 g daily of total dietary fibre (16 studies) was 0.90 (95% confidence interval 0.86 to 0.94, I^2=0%), for fruit fibre (n=9) was 0.93 (0.82 to 1.05, I^2=23%), for vegetable fibre (n=9) was 0.98 (0.91 to 1.06, I^2=0%), for legume fibre (n=4) was 0.62 (0.27 to 1.42, I^2=58%), and for cereal fibre (n=8) was 0.90 (0.83 to 0.97, I^2=0%). The summary relative risk for an increment of three servings daily of whole grains (n=6) was 0.83 (0.78 to 0.89, I^2=18%).

Conclusion A high intake of dietary fibre, in particular cereal fibre and whole grains, was associated with a reduced risk of colorectal cancer. Further studies should report more detailed results, including those for subtypes of fibre and be stratified by other risk factors to rule out residual confounding. Further assessment of the impact of measurement errors on the risk estimates is also warranted.

Introduction

Colorectal cancer is the third most common type of cancer, with 1.2 million new cases diagnosed in 2008 worldwide, accounting for about 9.7% of all cases of cancer.[1] Evidence from ecological studies, migrant studies, and secular trend studies suggest that environmental risk factors are of major importance in the cause of colorectal cancer.[2-4] Dietary factors have been suspected as important, but only intakes of red and processed meat and alcohol are considered to be convincing dietary risk factors for colorectal cancer.[5]

In the 1970s, Burkitt proposed the hypothesis that dietary fibre reduces the risk of colorectal cancer, based on the observation of low rates of such cancer among rural Africans who ate a diet with a high fibre content.[6] Several plausible mechanisms have been proposed to explain the hypothesis, including increased stool bulk and dilution of carcinogens in the colonic lumen, reduced transit time, and bacterial fermentation of fibre to short chain fatty acids.[7] However, although many epidemiological studies have investigated the association between fibre intake and risk of colorectal cancer, the results have not been consistent and the possibility of residual confounding by folate intake remains a controversial issue.[8] Case-control studies have generally shown a protective association,[9 10] whereas the results from cohort studies have been mixed.[8 11-31] In addition, it is not clear whether only specific types or sources of fibre are associated with the risk. Although initial cohort studies generally reported no significant association between fibre intake and risk of colorectal cancer, the hypothesis regained interest when the

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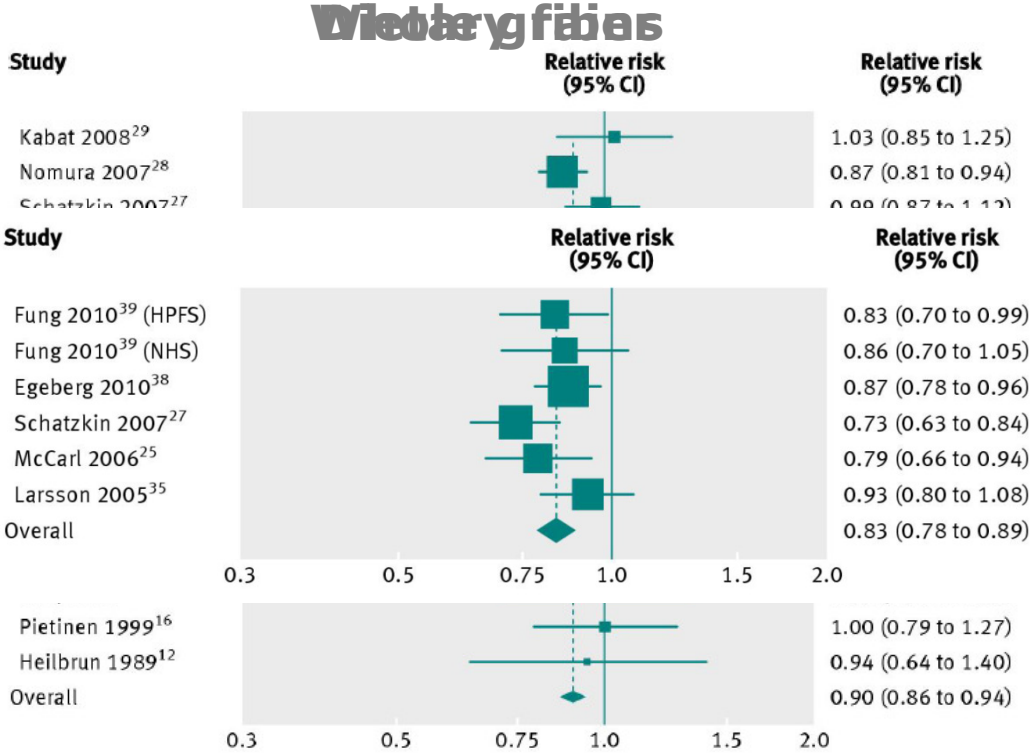
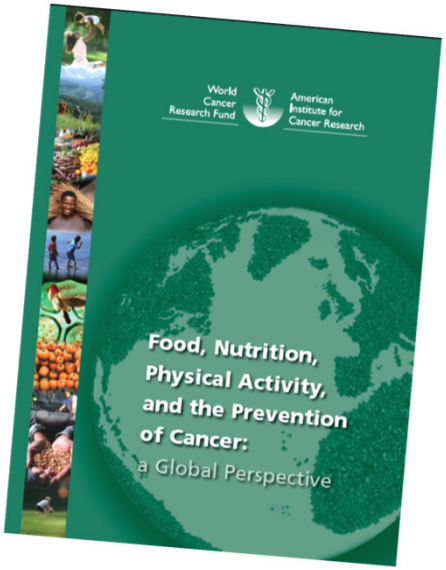
Extra material supplied by the author (see http://www.bmj.com/content/343/bmj.d6617/suppl/DC1)
High versus low intake of dietary fibre and whole grains and risk of colorectal cancer
High versus low intake of fruit, vegetable, legume, and cereal fibre and risk of colorectal cancer

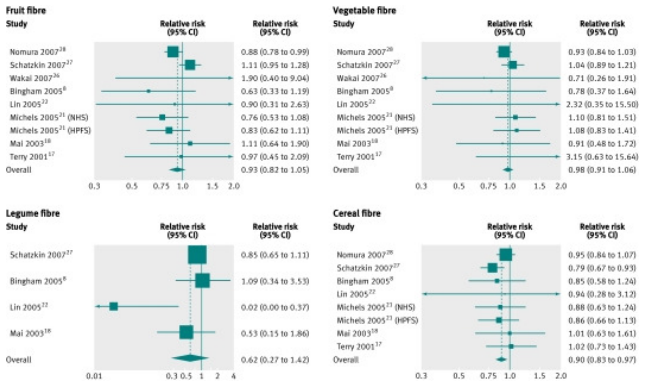


Aune et al., BMJ, 2011

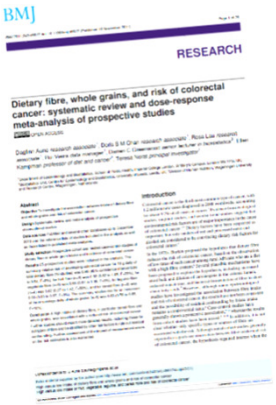
Opsummering - evidens

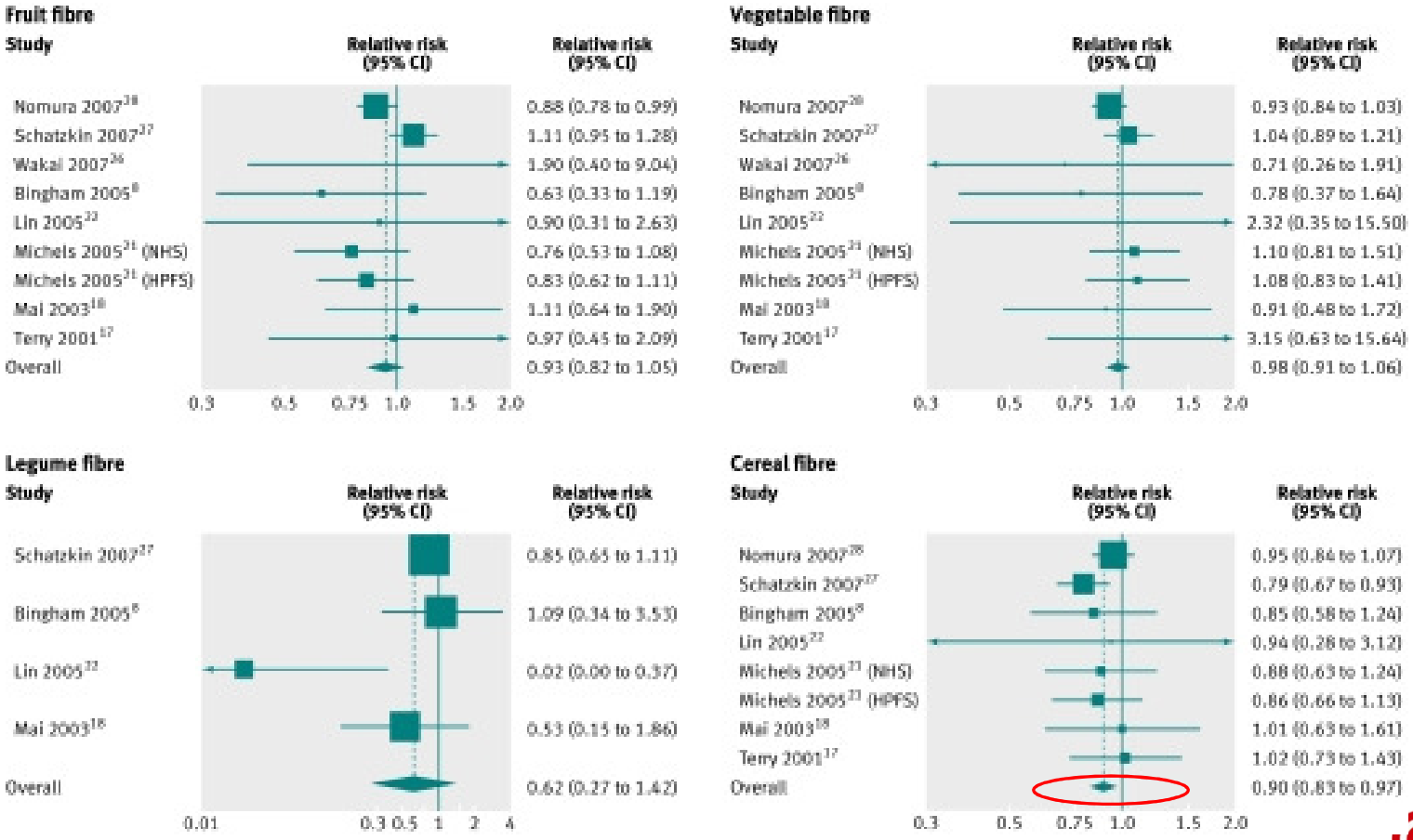
- På nuværende tidspunkt ikke tilstrækkelig evidens til at klassificere fuldkorn som ”convincing” – evidens kun for kostfibre overordnet





World Cancer Research Fund / American Institute for Cancer Research (WCRF/AICR)





Aune et al., BMJ, 2011

Hjertesygdom

Whole grain consumption and risk of cardiovascular disease, cancer, and all cause and cause specific mortality: systematic review and dose-response meta-analysis of prospective studies

Dagfinn Aune,[1, 2] NaNa Keum,[3] Edward Giovannucci,[3, 4, 5] Lars T Fadnes,[6] Paolo Boffetta,[7] Darren C Greenwood,[8] Serena Tonstad,[9] Lars J Vatten,[1] Elio Riboli,[2] Teresa Norat[2]

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Additional material is published online only. To view please visit the journal online.

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ABSTRACT

OBJECTIVE

To quantify the dose-response relation between consumption of whole grain and specific types of grains and the risk of cardiovascular disease, total cancer, and all cause and cause specific mortality.

DATA SOURCES

PubMed and Embase searched up to 3 April 2016.

STUDY SELECTION

Prospective studies reporting adjusted relative risk estimates for the association between intake of whole grains or specific types of grains and cardiovascular disease, total cancer, all cause or cause specific mortality.

DATA SYNTHESIS

Summary relative risks and 95% confidence intervals calculated with a random effects model.

RESULTS

45 studies (64 publications) were included. The summary relative risks per 90 g/day increase in whole grain intake (90 g is equivalent to three servings—for example, two slices of bread and one bowl of cereal or one and a half pieces of pita bread made from whole grains) was 0.81 (95% confidence interval 0.75 to 0.87; I^2=9%, n=7 studies) for coronary heart disease, 0.88 (0.75 to 1.03; I^2=56%, n=6) for stroke, and 0.78 (0.73 to 0.85; I^2=40%, n=10) for cardiovascular disease, with similar results when studies were stratified by whether the outcome was incidence or mortality. The relative risks for morality were 0.85 (0.80 to 0.91; I^2=37%, n=6) for total cancer, 0.83 (0.77 to 0.90; I^2=83%, n=11) for all causes, 0.78 (0.70 to 0.87; I^2=0%, n=4) for respiratory disease, 0.49 (0.23 to 1.05; I^2=85%, n=4) for diabetes, 0.74 (0.56 to 0.96; I^2=0%, n=3) for infectious diseases, 1.15 (0.66 to 2.02; I^2=79%, n=2) for diseases of the nervous system disease, and 0.78 (0.75 to 0.82; I^2=0%, n=5) for all non-cardiovascular, non-cancer causes. Reductions in risk were observed up to an intake of 210-225 g/day (seven to seven and a half servings per day) for most of the outcomes. Intakes of specific types of whole grains including whole grain bread, whole grain breakfast cereals, and added bran, as well as total bread and total breakfast cereals were also associated with reduced risks of cardiovascular disease and/or all cause mortality, but there was little evidence of an association with refined grains, white rice, total rice, or total grains.

CONCLUSIONS

This meta-analysis provides further evidence that whole grain intake is associated with a reduced risk of coronary heart disease, cardiovascular disease, and total cancer, and mortality from all causes, respiratory diseases, infectious diseases, diabetes, and all non-cardiovascular, non-cancer causes. These findings support dietary guidelines that recommend increased intake of whole grain to reduce the risk of chronic diseases and premature mortality.

WHAT IS ALREADY KNOWN ON THIS TOPIC

A high intake of whole grains has been associated with a lower risk of type 2 diabetes, cardiovascular disease, and weight gain

Recommendations for whole grain intake have often been unclear or inconsistent with regard to the amount and types of whole grain foods that should be consumed to reduce chronic disease and risk of mortality

WHAT THIS STUDY ADDS

A high intake of whole grains was associated with reduced risk of coronary heart disease, cardiovascular disease, total cancer, and all cause mortality, as well as mortality from respiratory disease, infectious disease, diabetes, and all non-cardiovascular, non-cancer causes

Reductions in risk were observed up to an intake of 210-225 g/day (seven to seven and a half servings/day) and for whole grain bread, whole grain breakfast cereals, and added bran

The results strongly support dietary recommendations to increase intake of whole grain foods in the general population to reduce risk of chronic diseases and premature mortality

Introduction

Cardiovascular disease and cancer remain the two most common causes of death and in 2013 accounted for 25.5 million deaths worldwide.[1] Grains are one of the major staple foods consumed around the world and provide 56% of the energy and 50% of the protein intake. They constitute the largest component of recommended daily intake in all dietary guidelines.[2] Because of their important role in most diets around the world, interest in the health effects of grain consumption, and in particular whole grains, is increasing.[3 4] A high intake of whole grains has been associated with a reduced risk of type 2 diabetes,[5] coronary heart disease,[6] and obesity.[6]

Whole grains contain endosperm, germ, and bran, in contrast with refined grains, which have the germ and bran removed during the milling process. Whole grains are good sources of fibre, B vitamins, and some trace minerals such as iron, magnesium, and zinc.[7] These nutrients are found in the outer layer of the grains or the bran that function as a protective shell for the germ and endosperm inside. The germ is nourishment for the seed and contains antioxidants, vitamin E, and some B vitamins, while the endosperm provides carbohydrates,

Fuldkorn og hjertesygdom

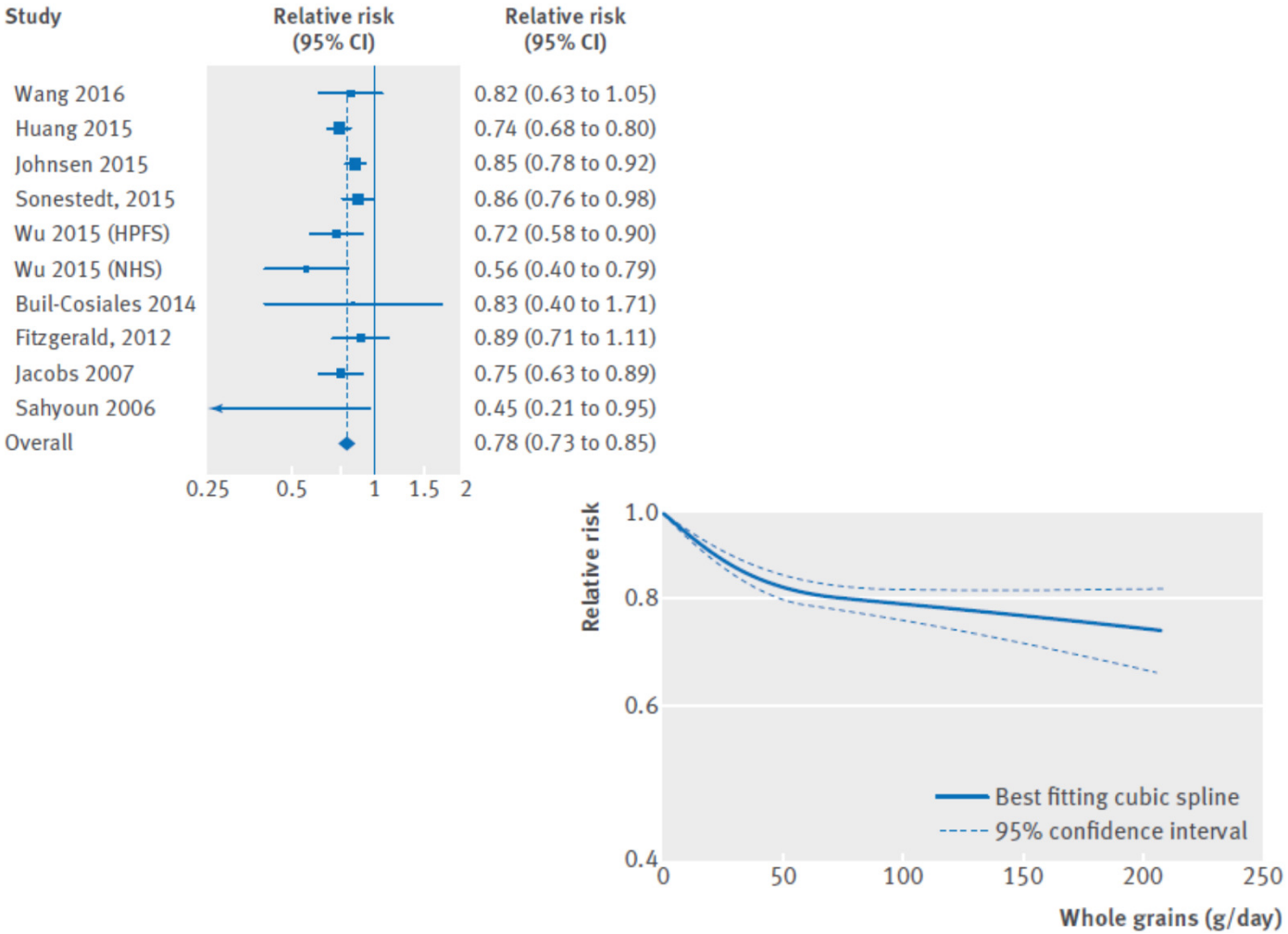
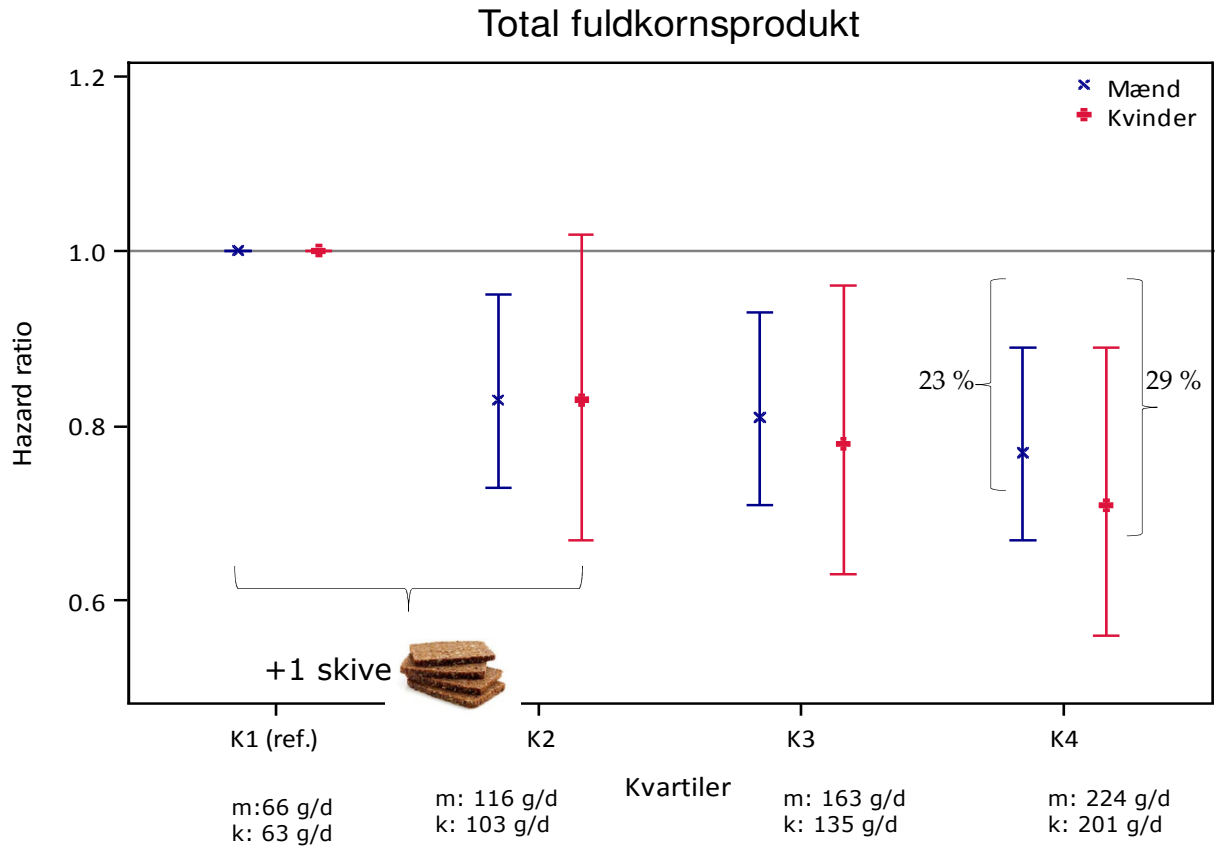


Fig 4 | Forest plot for consumption of whole grains (per 90 g/day) and risk of cardiovascular disease, with graph illustrating non-linear response

Fuldkorn og hjertesygdom



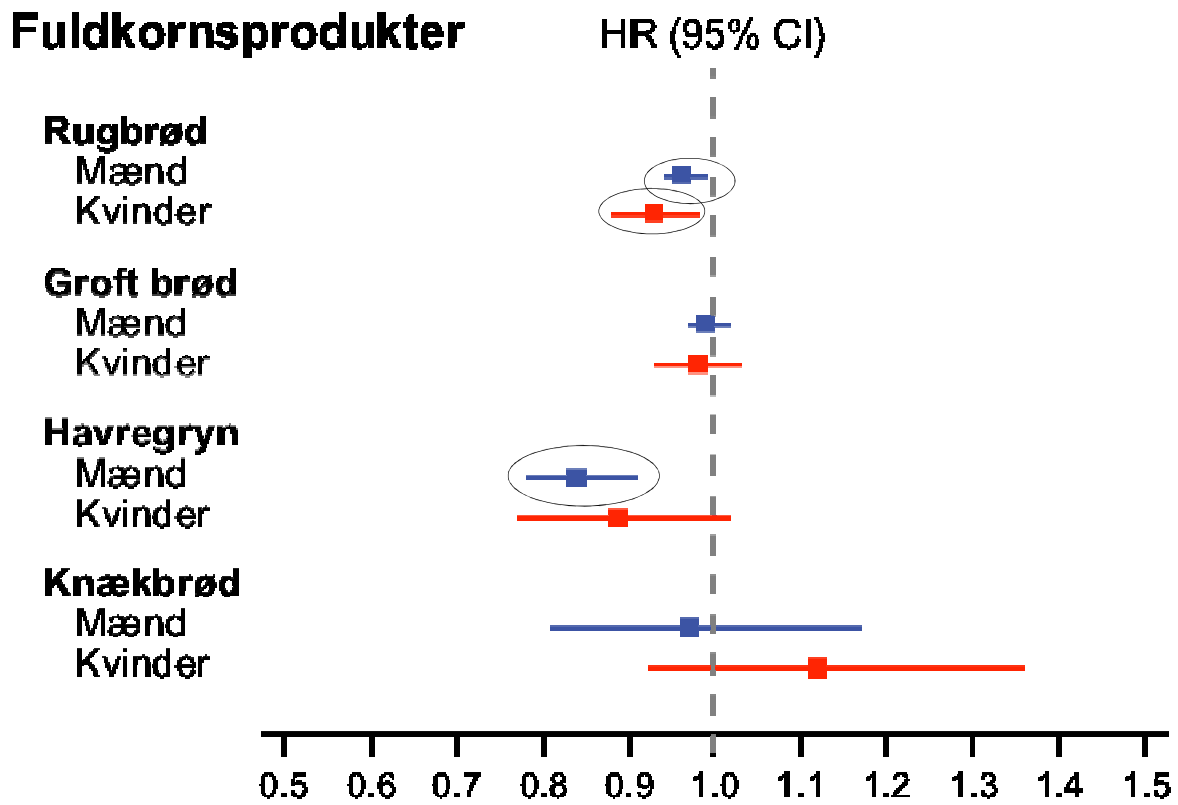
p for trend=<0,001

*Justeret for: alder, tid under studiet, års uddannelse, rygning (status, pakke-år), alkohol fra øl/spiritus (afholdende, g/d), alkohol fra vin (afholdende, g/d), fysisk aktivitet, menopausal status (kvinder), hormonterapi (kvinder), frugt, grønt, fisk, rødt kød, forarbejdet kød.

Helnæs *et al*. Am J Clin Nutr 2016

Fuldkorn og hjertesygdom

25 grams stigning i indtaget af fuldkornsprodukter



*Gensidigt justeret for fuldkornsprodukter samt alder, tid under studiet, års uddannelse, rygning (status, pakke-år), alkohol fra øl/spiritus (afholdende, g/d), alkohol fra vin (afholdende, g/d), fysisk aktivitet, menopausal status (kvinder), hormonterapi (kvinder), frugt, grønt, fisk, rødt kød, forarbejdet kød.

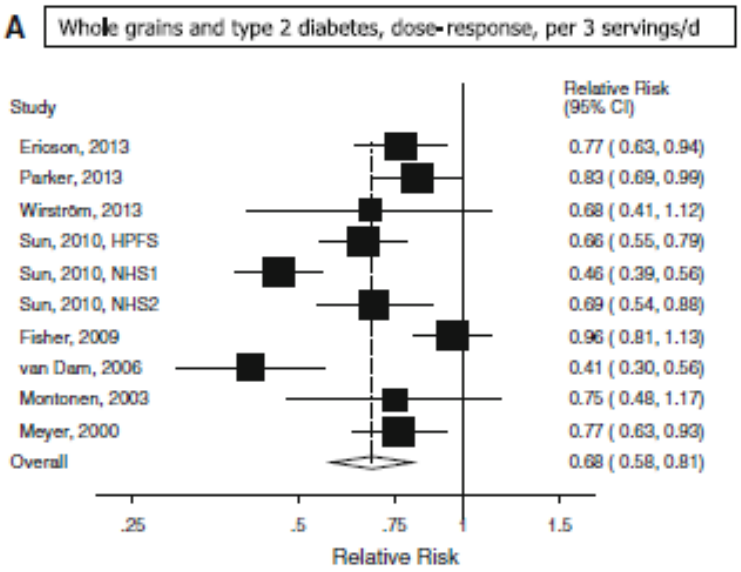
Helnæs *et al*. Am J Clin Nutr 2016

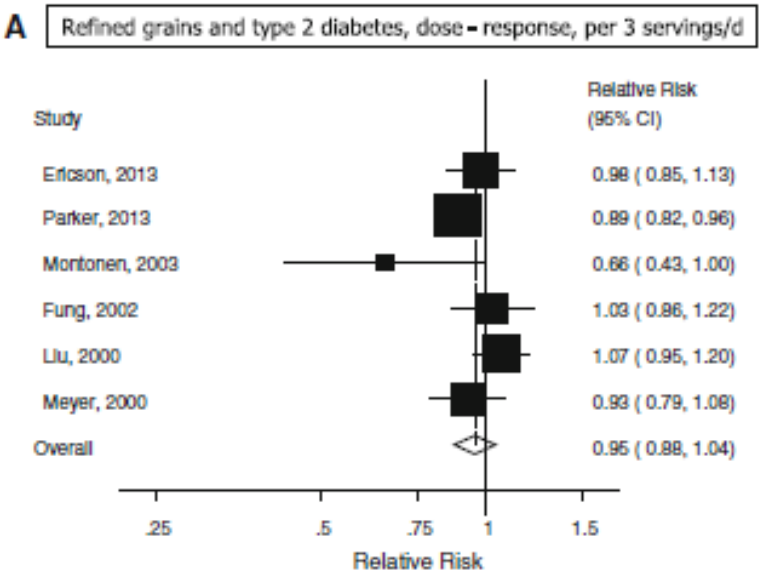
Opsummering - evidens

- Stigende evidens for en sammenhæng
- Er havren særlig vigtig?

Diabetes

Fuldkorn – type 2 diabetes





1 serving WG= 16 gram/dag

Eur J Epidemiol (2013) 28:845–858

Opsummering - evidens

- Fuldkorn ser ud til at være klart relateret til nedsat forekomst af diabetes!

Fuldkorn og dødelighed

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Fuldkorn og dødelighed

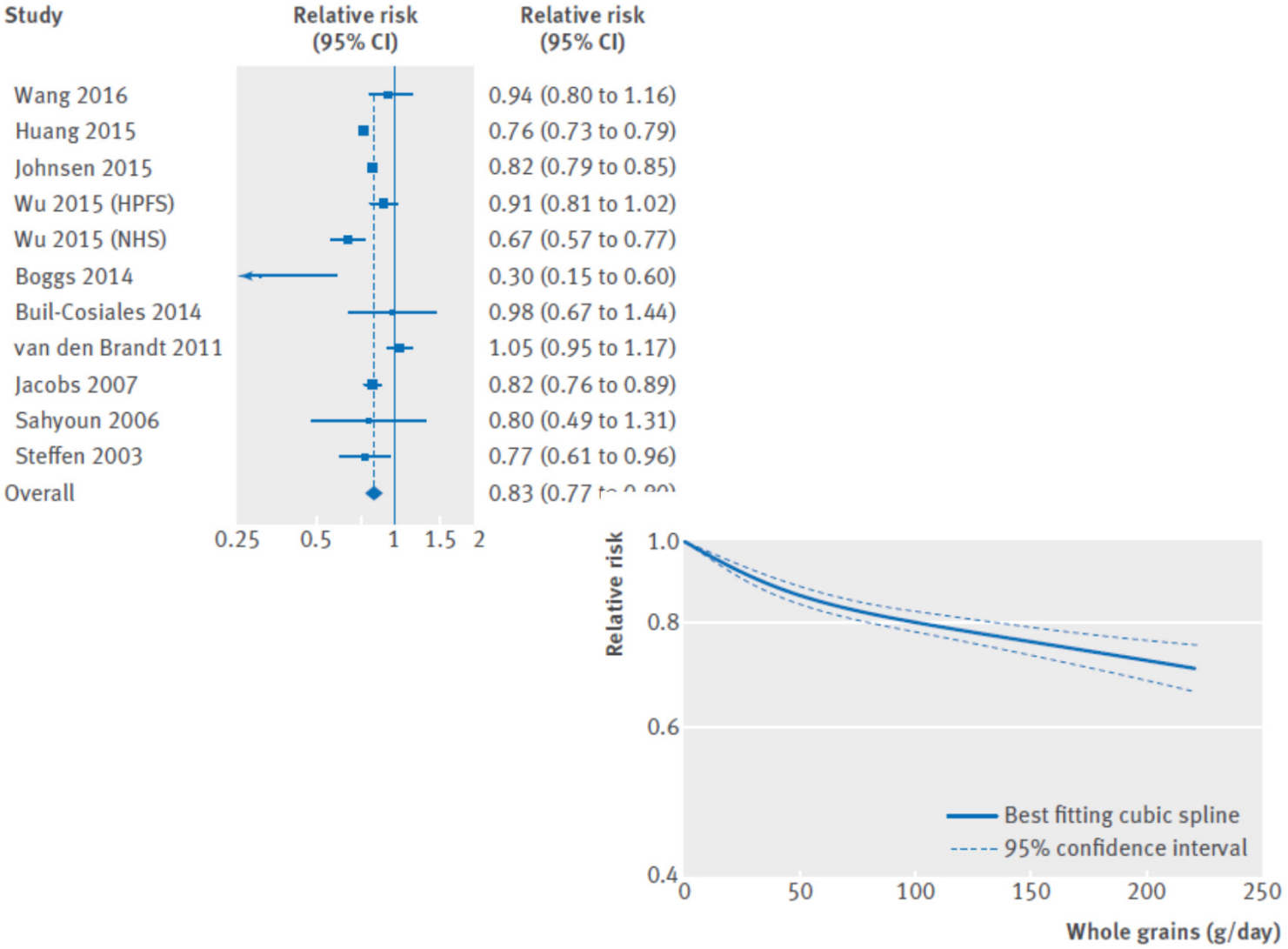


Fig 6 | Forest plot for consumption of whole grains (per 90 g/day) and risk of all cause mortality, with graph illustrating non-linear response

Fuldkornsindtag hos folk diagnosticeret med

- Kræft
- Hjertesygdom
- Diabetes

Planteøstrogener



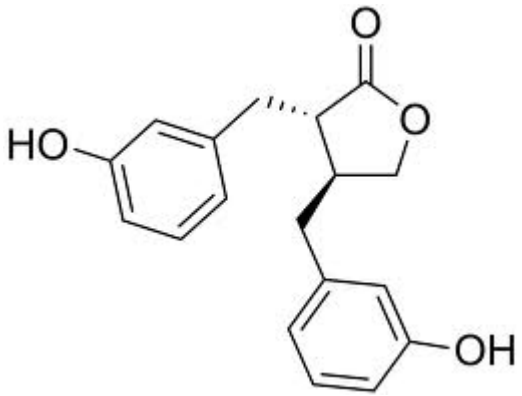
Planteøstrogener

- Stoffer der ligner det kvindelige kønshormon østrogen
- Soja: Isoflavoner
- Fiberrige fødevarer: Lignaner/enterolacton

Enterolakton

- Ligner det kvindelige kønshormon østrogen og kaldes derfor et planteøstrogen
- Virker antioxidativt og er vist at hæmme væksten af cancerceller

Enterolacton har derfor en potentiel cancerforebyggende rolle!



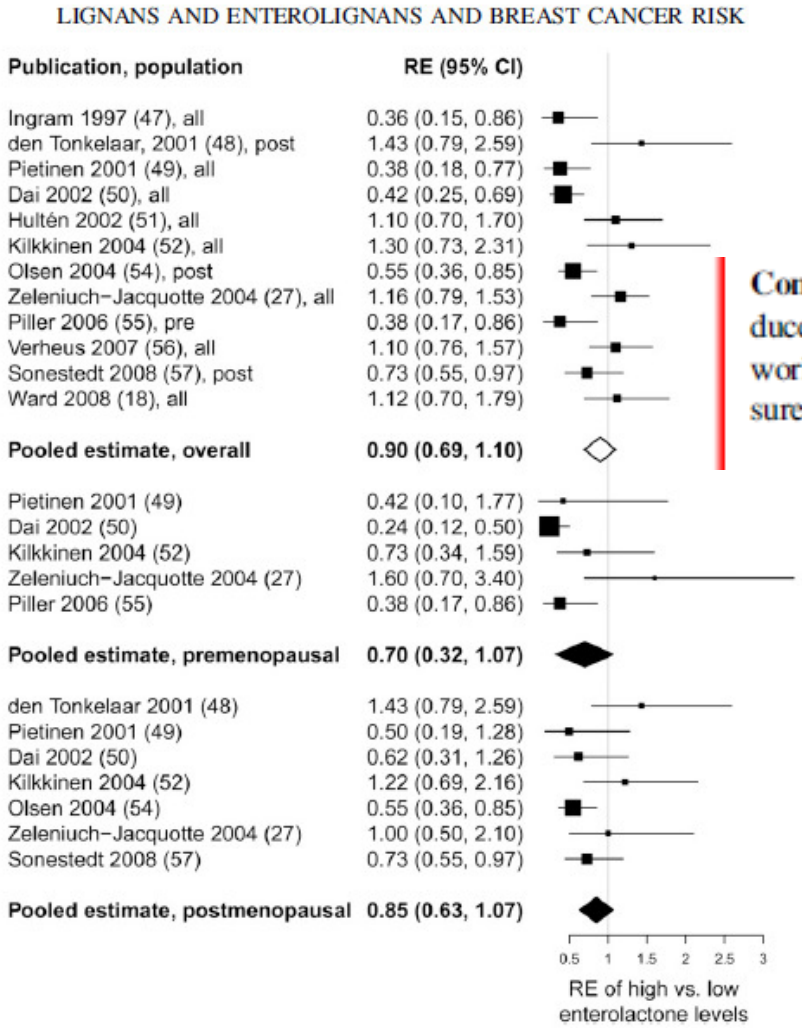
Enterolakton

Quartiles of serum enterolactone concentration

	0.1-14.4 nmol/l	**14.5-28.1 nmol/l**	**28.2-47.9 nmol/l**	**48.0-454.6 nmol/l**
	IRR (95% CI)	**IRR (95% CI)**	**IRR (95% CI)**	**IRR (95% CI)**
All	0.77 (0.51-1.15)	1	0.80 (0.53-1.21)	0.55 (0.36-0.85)
ER+	0.77 (0.48-1.24)	1	0.95 (0.59-1.53)	0.67 (0.41-1.08)
ER-	0.61 (0.25-1.53)	1	0.43 (0.16-1.15)	0.26 (0.09-0.77)

Olsen et al., Journal of Nutrition, 2004

Meta-analyses of lignans and enterolignans in relation to breast cancer risk[1–3]



Conclusions: High lignan exposure may be associated with a reduced breast cancer risk in postmenopausal women. Additional work is warranted to clarify the association between lignan exposure and breast cancer risk. *Am J Clin Nutr* 2010;92:141–53.

Buck, 2010
Am J Clin Nutr

Buck et al., American Journal of Clinical Nutrition, 2010

Lignaner – prognose efter brystkræft

Published in final edited form as:
Breast Cancer Res Treat. 2010 July ; 122(1): 229–235. doi:10.1007/s10549-009-0681-x.

Dietary lignan intakes in relation to survival among women with breast cancer: the Western New York Exposures and Breast Cancer (WEB) Study

Susan E. McCann[1], **Lilian U. Thompson**[2], **Jing Nie**[3], **Joan Dorn**[3], **Maurizio Trevisan**[4], **Peter G. Shields**[5], **Christine B. Ambrosone**[1], **Stephen B. Edge**[6], **Hsin-Fang Li**[1], **Christina Kasprzak**[1], and **Jo L. Freudenheim**[3]

Susan E. McCann: susan.mccann@roswellpark.org

Postmenopausal (n = 807)		
All cause mortality		
<155	33	1.00
155–227	33	0.91 (0.55–1.52)
227–318	29	0.78 (0.46–1.33)
>318	21	0.49 (0.26–0.91)
P for trend		0.02
Breast cancer mortality		
<155	18	1.00
155–227	20	0.94 (0.48–1.87)
227–318	11	0.51 (0.23–1.15)
>318	7	0.29 (0.11–0.76)
P for trend		0.01

Cox proportional hazards adjusting for age, race, total energy, stage at diagnosis, body mass index, and education

Enterolakton – prognose efter brystkræft

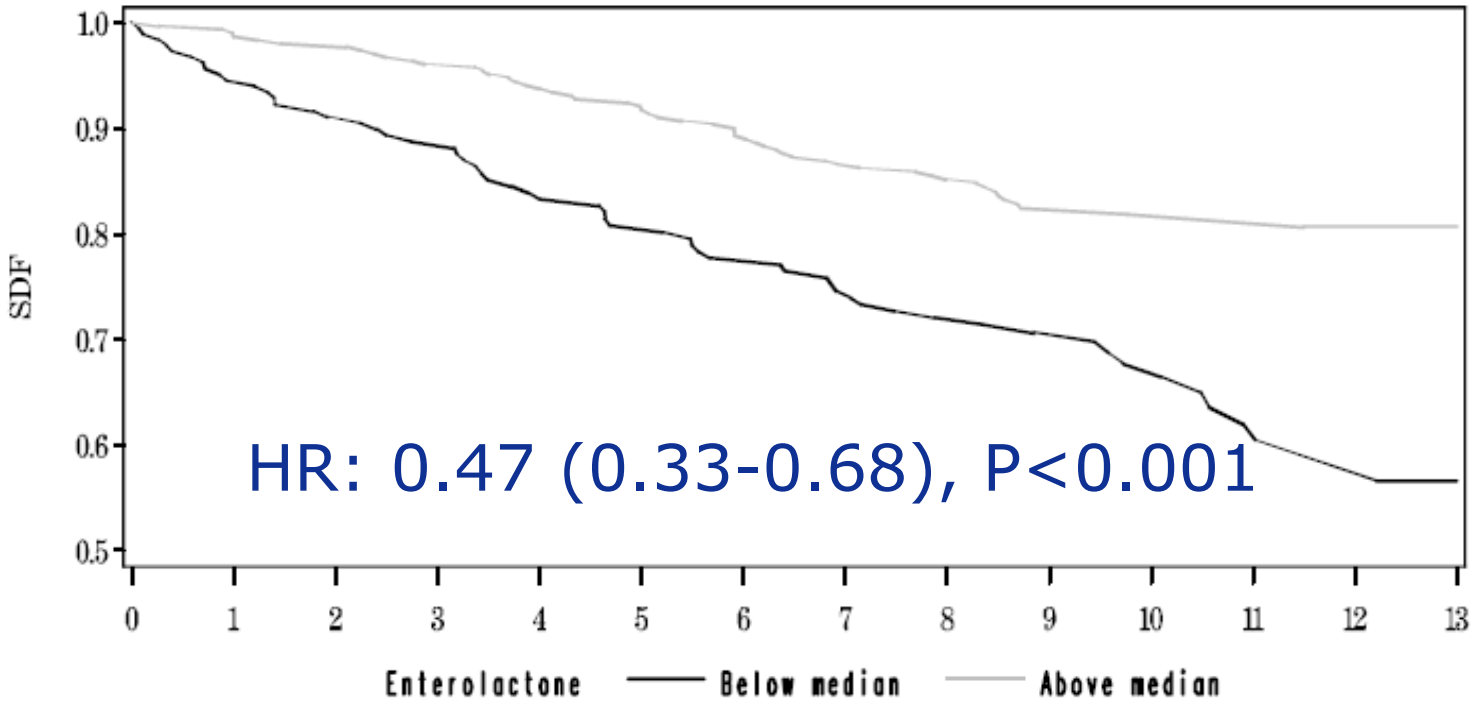
Breast Cancer Res Treat (2011) 128:883–889
DOI 10.1007/s10549-011-1397-2

EPIDEMIOLOGY

Prediagnostic plasma enterolactone levels and mortality among women with breast cancer

Anja Olsen · Jane Christensen · Knud Erik Bach Knudsen · Nina Føns Johnsen · Kim Overvad · Anne Tjønneland

Dødelighed



Olsen et al., Breast Cancer Research & Treatment, 2011

Enterolacton og brystkræft - metaanalyse

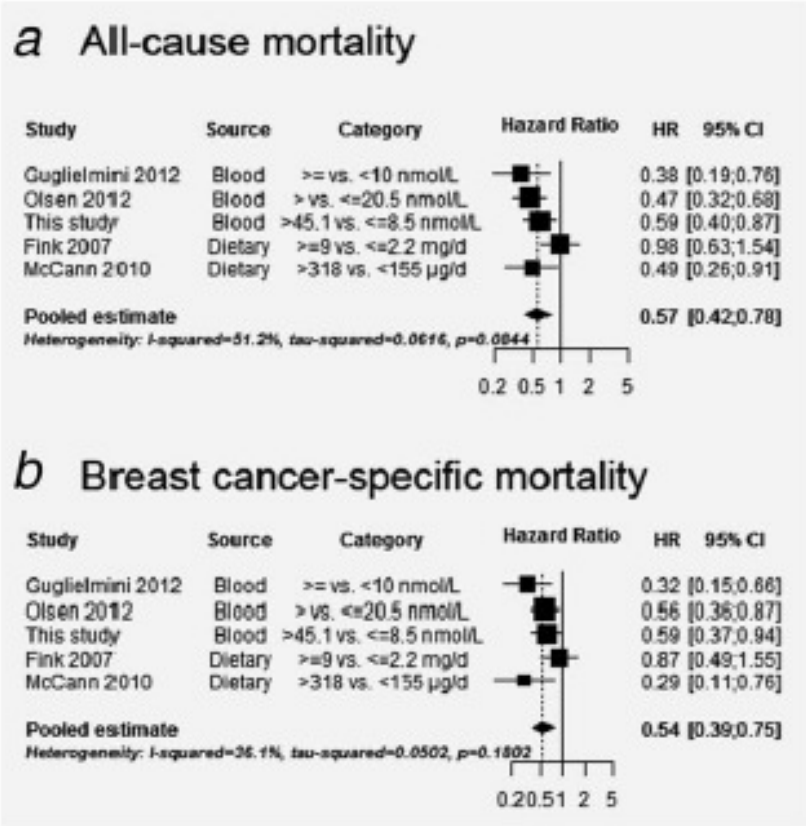


Figure 1. Meta-analysis: Association between lignan exposure and breast cancer prognosis in postmenopausal women. Results for all-cause mortality (*a*) and breast cancer-specific mortality (*b*) are pre-

Int. J. Cancer: **135**, 923–933 (2014)

367,903 women

11,784 women

Death
All causes: 1,483
Breast cancer: 753

Baseline
1992–2000

Diagnosed with breast cancer
2004–2009

End of follow-up
2006–2010

Median 6 years

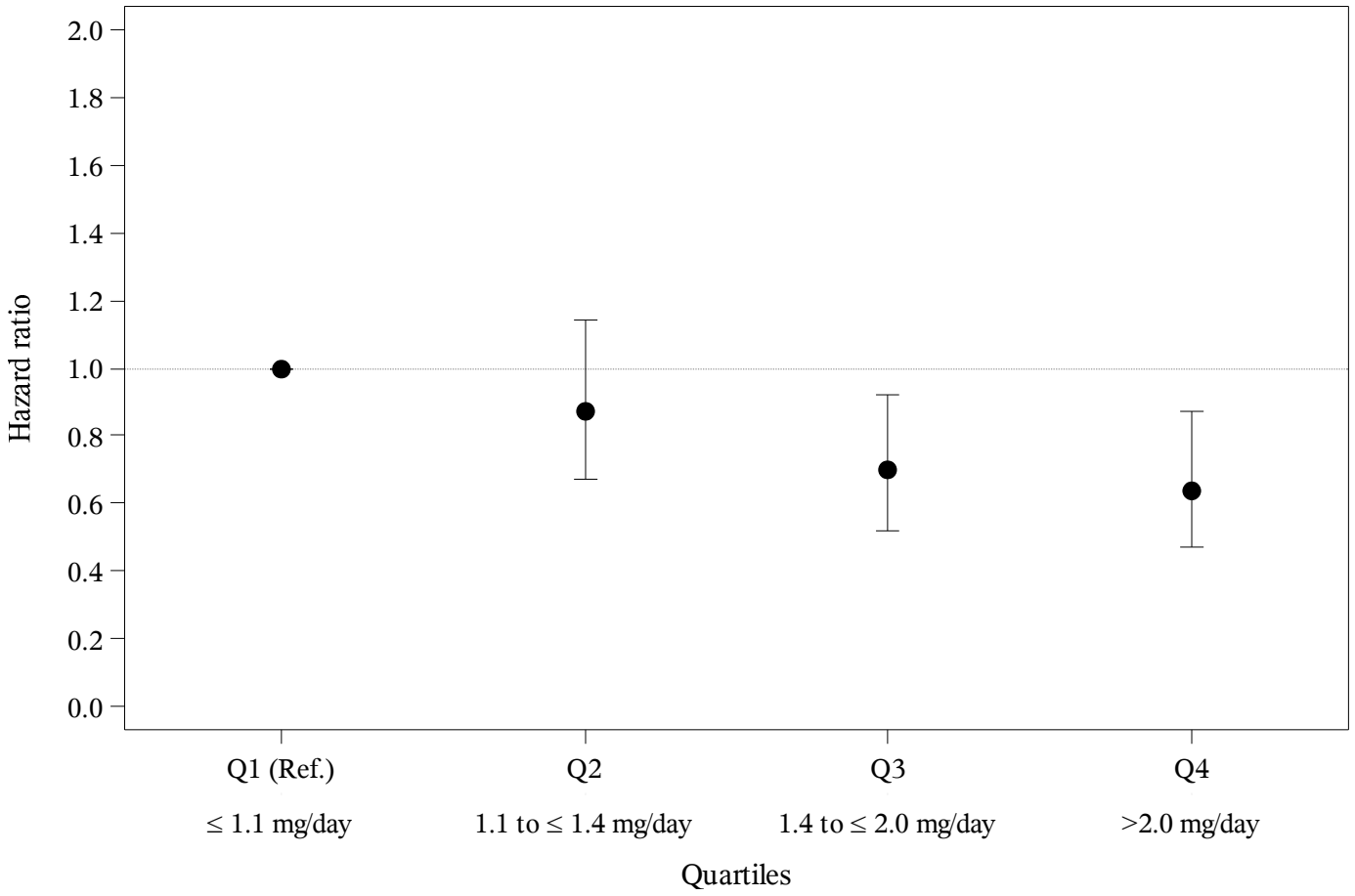
Phenol-Explorer

Followed from diagnosis until:

- Endpoints (death, BC death)
- Or censoring (last day of contact or end of follow-up)

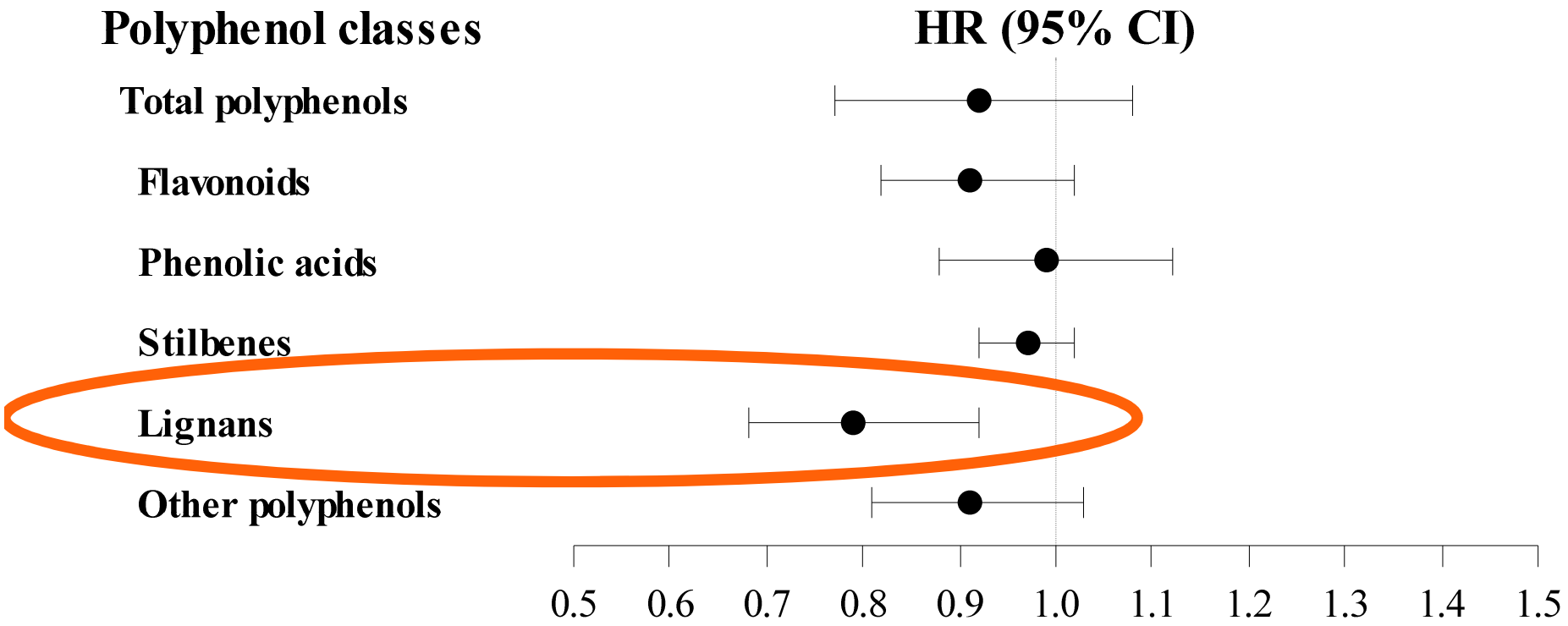
Kyrø et al., Breast Cancer Research & Treatment, 2015

Lignan-indtag, brystkræft dødelighed



Kyrø et al., Breast Cancer Research & Treatment, 2015

Polyphenol classes and breast-cancer mortality – postmenopausal women



Kyrø et al., Breast Cancer Research & Treatment, 2015

Sygdomskontrol blandt diabetikere

NUTRITION REVIEWS

Special Article

Fiber intake and glycemic control in patients with type 2 diabetes mellitus: a systematic review with meta-analysis of randomized controlled trials

Flávia M Silva, Caroline K Kramer, Jussara C de Almeida, Thais Steemburgo, Jorge Luiz Gross, and Mirela J Azevedo

−1.78). In conclusion, increased fiber intake improved glycemic control, indicating it should be considered as an adjunctive tool in the treatment of patients with type 2 diabetes.

Opsummering - evidens

- Alt tyder på, at kostfibre og fuldkorn er gavnlige i forhold til prognose blandt patienter med kronisk sygdom
- Endnu mangler meget forskning!

Fuldkorn og sundhed

- Det mest lovende indenfor ernæringsområdet!
- God evidens for: tarmkræft, hjertesygdom og type 2 diabetes
- Lovende perspektiver i forhold til ”generel sundhed” – også for patienter med kronisk sygdom
- Mange uudforskede mekanismer
- Andre fiberrige fødevarer er også relevante, men måske er fuldkorn bedst!

BMJ 2016;353:i3046 doi: 10.1136/bmj.i3046 (Published 14 June 2016)

EDITORIALS

Whole grains and public health

OPEN ACCESS

Small increases in population intake could bring substantial benefits

Cecilie Kyrø *postdoctoral researcher* , Anne Tjønneland *head of research*

Danish Cancer Society Research Center, Strandboulevarden 49, 2100 Copenhagen, Denmark

Whole grains consist of the entire grain, and, unlike refined grains, they still contain bran, and germ, which are rich in dietary fibre and micronutrients. Whole grains were once neglected by researchers in favour of studies on dietary fibre, which found that cereal fibres were particularly healthy.[1] As cereal fibres are found in whole grains together with micronutrients and phytochemicals, the focus of research shifted towards observational studies of whole grain intake. A large body of evidence on whole grains in relation to health outcomes has accumulated over the past 10 or 15 years.

In a linked article, Aune and colleagues (doi:10.1136/bmj.i2716) report on their meta-analysis of 45 cohort studies, showing that a higher intake of whole grains is associated with a lower risk of cardiovascular disease and total cancer and all cause and disease specific mortality.[2] Several mechanisms could explain the association between intake and a lower risk of major diseases and death. Whole grains have beneficial effects on glucose-insulin homeostasis, blood lipids, and gastrointestinal health.[3] The new meta-analysis, however, has several weaknesses, including poor information on the assessment of whole grain intake in many of the included studies and few studies for some endpoints such as mortality from diabetes and infectious diseases.

Future studies should improve the assessment of whole grain intake by reporting intakes in a similar way,[4] using biomarkers to track compliance in randomised trials, and using validated assessment methods in observational studies.[5] We still need more and better research on the biological mechanisms of health effects and the contribution to health of different grain types. For instance, studies suggest that whole grain oats and rye might be more beneficial than whole grain wheat in relation to cardiovascular disease.[6] In most countries, cereals are a major energy source, and surprisingly little attention has been paid to the quality of cereals in dietary recommendations—that is, whether they are refined or "whole." National guidance in Scandinavian countries recommends a whole grain intake of 75 g/day per 10 MJ.[7] UK guidance is much less specific, with advice to choose "whole grain, brown or high fibre varieties whenever you can."[8] Currently, the whole grain intake in the UK is far below the intake recommended in Scandinavian countries (fig 1).

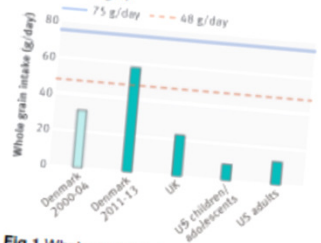


Fig 1 Whole grain intake in Denmark in people aged 4-75 in 2000-04 and 2011-13,[9] in UK in people aged >1.5 in 2008-11[8], and in US in children/adolescents and adults in 2009-10.[10] Graph shows recommended intake by Scandinavian food and health authorities (75 g/day), and intake representing three servings (about 48 g/day or 90 g product/day). Intakes are measured as mean intake in g/day in Denmark, as median g/day/10 MJ in UK, and mean intakes calculated from ounce equivalents (about one serving)/day to g/day in US. One ounce equivalent/serving is equal to 16 g/day[4 11]

Lessons can be learnt from Denmark, where the intake of whole grains has almost doubled over the past 10 years (fig 1). This improvement is thanks to the combined efforts of the food and health authorities, non-governmental organisations (NGOs), and industry. The Danish Whole Grain Partnership set product standards to ensure that foods granted a whole grain logo satisfied strict content criteria for at least a minimum amount of whole grain and less than the maximum allowable amounts of added sugar and salt.[12]

If and when other countries follow Scandinavia's lead and set specific recommendations for whole grain intake, the authorities should take great care not to promote whole grain foods with high sugar and salt content. These food items could attenuate

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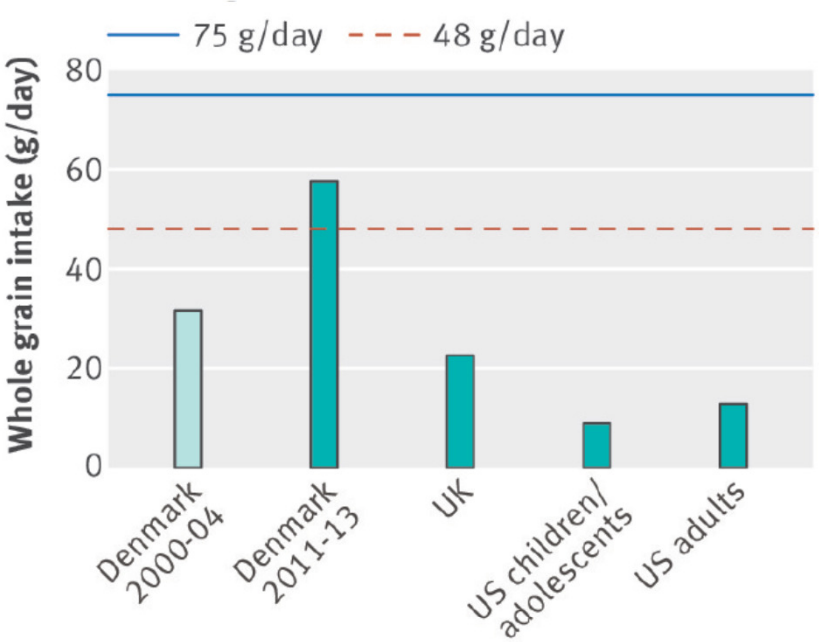

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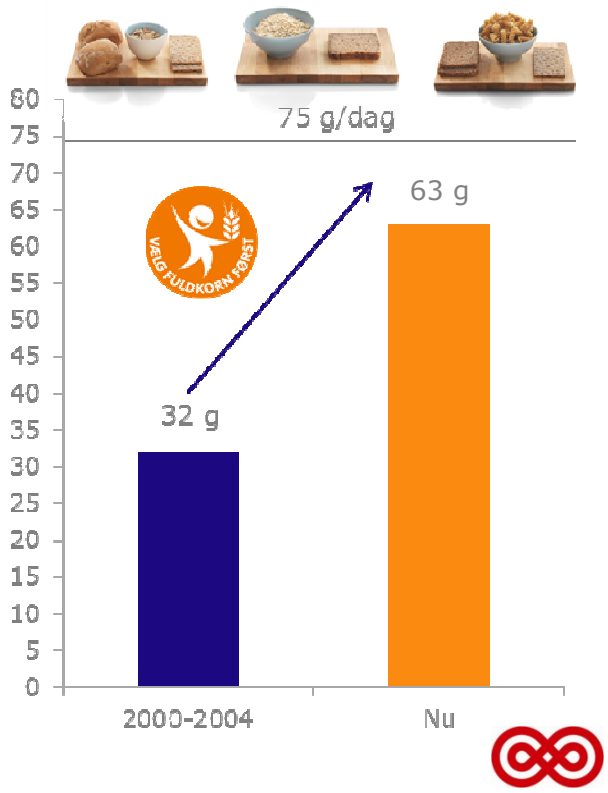
Kyrø & Tjønneland, BMJ, 2016

Perspektiver

- Mikrobiomet
- Tidlig diagnostik – anbefalinger rettet mod ”patienter” eller og andre særlige grupper
- Internationale muligheder



Tak for opmærksomheden!!!