Citation:

van de Vijver LP, van den Bosch LM, van den Brandt PA, Goldbohm RA. Whole-grain consumption, dietary fibre intake and body mass index in the Netherlands cohort study. Eur J Clin Nutr. 2009 Jan;63(1):31-8. Epub 2007 Sep 26.

PubMed ID: 17895913

Study Design:

Cross-sectional

Class:

D - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- To assess the association between consumption of whole-grain foods and (cereal) fiber intake with body mass index (BMI) as well as the association of consumption of those foods with being overweight (BMI ≥ 25-29.9) or obese (BMI≥30) in the population of the Netherlands Cohorts Study (NLCS), both in a cross-sectional setting and in a prospective setting in a smaller sample

Inclusion Criteria:

- For primary cross-sectional study, random subcohort of 5000 Dutch men and women, between ages 55-69 were drawn from the Netherlands Cohort Study (NLCS) at baseline in 1986
- For secondary prospective study, a smaller population of the subcohort participated in a reproducibility study of the self-administered questionnaire over a 5 year period. Each participant re-did the self-administered questionnaire, 1x, and were placed in an independent random sample of about 300 subjects each (repeated questionnaire in either year 1, year 2, year 3, year 4 or year 5)

Exclusion Criteria:

- Subjects were excluded from cross-sectional analysis and secondary prospective analysis who:
  - had prevalent cancer at baseline or cancer diagnosis within 1 year after baseline
  - died within 1 year after baseline
  - had missing weight or height or incomplete or inconsistent dietary questionnaires
- Subjects in prospective analysis were also excluded if they died between 1 year after baseline and 1st year after completing repeated questionnaire.

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Description of Study Protocol:

- Primary cross sectional study is based on the baseline data of the subcohort (1986)
  - subjects answered extensive self-administered questionnaire which included self-reported variables on dietary habits and other risk factors for cancer such as height, weight, weight at age 20, smoking habits, physical activity, medical history etc.
- Secondary prospective study is based on data from 1995 reproducibility study of Golbohm et al. with additional exclusion criteria as noted above
  - Results were used to calculate changes in BMI between the two measurements (range of as little as 1 year difference to up to 5 year between measurements)--calculated as change in BMI per year because of different time intervals between baseline and repeat measure

Dietary Intake/Dietary Assessment Methodology (if applicable):

- At baseline for the cross-sectional study and prospective studies, participants completed a section in the self-administered questionnaire that included a 150- item semi-quantitative food-frequency section (validated against 9-day diet record {Goldbohm *et al*., 1994} with Pearson correlation coefficient for dietary fiber - unadjusted and adjusted for energy and sex- was 0.74) . It concentrated on participants' habitual consumption during the preceding year
- each subject's individual frequencies and serving sizes were recalculated into mean daily intake(g day ^{1})
- "All grain"- calculated as sum score of food items: bran, wheat germs, muesli, oat or whole wheat porridge*, brown rice* and cooked grains* such as millet, buckwheat etc. (* recalculated as dry product to avoid unbalanced weighting to sum score)
- "Whole grain"- does not include bran and wheat germs
- "Total brown bread"- sum score of brown (mixture of wholemeal and white flour), wholemeal and rye bread
- "Fiber"- measured as g/day
- "Fiber Density"- measured as g per MJ
- "Fiber from grain"- measured as g day
- "Fiber density from grain"- measured as g per MJ

Secondary prospective study: self-administered questionnaire was repeated. Results were used to calculate changes in diet between the two measurements (range of as little as 1 year difference to up to 5 year between measurements)

Blinding used (if applicable): N/A

Intervention (if applicable): N/A

Statistical Analysis: Primary Cross-sectional study

- Performed separate analyses for men and women but to enhance comparability, a fixed set of confounding variables (noted as age, energy intake, intake of animal protein, education, smoking status, number of cigarettes, and consumption of fruit and vegetables) was used for all data analyses
- Calculated descriptive data for all variables
- Employed multi-variate regression analysis with 2 continuous outcome variables (BMI and change in BMI between the age of 20 years and baseline), adjusting for potential

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confounders in several steps
- Performed regressions coefficients (ß) and 95% confidence intervals and two-sided 5% significance levels in the baseline cross-sectional data for exposure variables (see above) with BMI as a continuous variable.
- Logistic regression was used to estimate odds rations for analyses with outcome variables "overweight" and "obesity" . Multivariate odds ratios (ORs) and 95% CIs were performed in baseline data for those outcome variables
- Conducted sensitivity analyses excluding the most likely under-and over-reporters in the data set to assess impact of under-and overreporting of energy intake on investigated associations. Details, if needed, are available on p.33, paragraph 2.

Statistical Analysis of smaller prospective study: not described

Recruitment

- Not described; would probably have to go back to article describing original Netherlands Cohort Study from which these populations were derived. Original NLCS sample was derived from more than 120,000 Dutch men and women picked randomly from municipal population registries across the country

Design

- Primary study: cross sectional (variables all from baseline except for continuous variable of BMI which was calculated from change in BMI from self-reported weight at 20 years and baseline study year)
- Secondary study: prospective

Data Collection Summary:

Timing of Measurements:

- For primary cross-sectional study: 1x measure in 1986
- For smaller prospective study: 2 measures: at baseline and range of 1-5 years after, depending upon random sample group

Dependent Variables: Cross-sectional study:

- Continuous:
  - BMI (calculation done from self-report height, weight)
  - Change in BMI between the age of 20 years (gathered from initial self-report) and baseline study year data was used
- Categorical:
  - Overweight (BMI ≥ 25 to 30)
  - Obese (BMI ≥30)

Prospective study:

- Continuous:
  - Change in BMI from baseline to repeat self-report measure (1-5 years later)- measured by change between 2 measures. To account for different time intervals between baseline and repeated measurement, change in BMI was divided by length of interval in years, resulting in final calculation in BMI per year

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- Change in diet from baseline to repeat self-report measure (1-5 years later)

Independent Variables

- All grain = bran, germs, muesli, porridge, brown rice and cooked grains (expressed as dry weight)
- **Whole grain = All grain without bran and germs (* NOTE this definition when looking at study conclusions)**
- Total brown bread =- sum of brown (mixture of wholemeal and white flour), wholemeal and rye bread
- "Total fiber" measured as g day and g per MJ
- "Fiber from grain"- measured as g day and g per MJ

Control Variables:

- age, energy intake, intake of animal protein, education, smoking status, number of cigarettes and consumption of fruit and vegetables

Description of Actual Data Sample:

Initial N: 5000 men and women for cross-sectional study, 1546 men and women for prospective study

Attrition (final N): 4237 subjects (2078 men, 2159 women) after inclusion/exclusion criteria used for cross-sectional study;

1257 subjects (50% women, 50% men) for prospective study after inclusion/exclusion criteria used

Age: 55-69 years

Ethnicity: Not described other than Dutch

Other relevant demographics: (cross-sectional only: no description for prospective sub-study but it was a subgroup of same subcohort)

- Men: Tendency of higher protein and lower CHO intake, highest percentage of smokers in normal weight category and lower over successive BMI categories (overweight and obese), dietary fiber intake only slightly lower in overweight and obese men
- Women: Tendency of lower alcohol intake , more gallstones in higher BMI categories
- Both sexes: In overweight or obese categories, more suffered from CVD, HTN, Type II Diabetes, fewer suffered from intestinal disorders and more reported to have followed a energy-restricted diet in the past 5 years
- Both sexes: Proportion of whole-grain food consumption decreased as BMI categories increased, no consistent trend for amount of brown bread (90% of population consumption)

Anthropometrics: (cross-sectional only: no description for prospective sub-study but it was a subgroup of same subcohort)

- Mean age comparable in different BMI categories (61 to 62 years)
- Similar: 47% of men overweight or obese vs 44% of women
- Different: 4 % of obese men (Note: ONLY 79 men which is a small sample for conclusions on obesity with men) vs 9 % women

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Location: the Netherlands

Summary of Results:

Key Findings: (Related to Table 1 below):

- For men: (See ** and * below for P values)--significant inverse relationship between whole grain variables as well as fiber and BMI in age-adjusted model, age-and energy-adjusted model (results not shown) and in multivariate model
- In both men and women, estimated that a 1 g day higher intake of dry whole grains associated with a 0.03 kg/m² lower BMI (decrease of 1 unit BMI thus corresponds to 33g/day increase in dry whole grain)
- For women, inverse associations for whole grain variables in age and mutivariate-adjusted model but no association for fiber (any category).

Table I: Regression coefficients (ß) and 95% confidence intervals (95% CIs) in the baseline data for BMI (continuous) and exposure variables in Cross-sectional study (For Table 1: Legend definitions: a = Adjusted for age, energy intake, intake of animal protein, education, smoking status, number of cigarettes and consumption of fruit and vegetables. * = P,0.05, ** = P<0.01. NOTE: Definition of variables is in section above)

Increase in BMI per unit increase in intake	Age-Adjusted		Multivariate[a]	
	ß	95% CI	ß	95% CI
Men:				
All grain (g/day)	-0.03**	-0.04, -0.02	-0.03**	-0.04, -0.02
Whole grain (g/day)	-0.04**	-0.05, -0.02	-0.03**	-0.05, -0.02
Total brown bread (10 g/day)	-0.01	-0.02, 0.00	-0.01	-0.02, 0.01
Fiber (g/day)	-0.02*	-0.03, -0.00	-0.04**	-0.06, -0.02
Fiber density (g/ MJ)	-0.07	-0.21, 0.06	-0.29**	-0.45, -0.12
Fiber from grain (g/day)	-0.04**	-0.06, -0.02	-0.04**	-0.06, -0.02
Fiber density from grain (g/ MJ)	-0.29**	-0.48,-0.11	-0.32**	-0.51,-0.13

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Women:				
All grain (g/day)	-0.05**	-0.07, -0.03	-0.03**	-0.05,-0.01
Whole grain (g/day)	-0.05**	-0.07, -0.03	-0.04**	-0.06,-0.01
Total brown bread (10 g/day)	0.01	-0.01, 0.04	0.04*	0.01, 0.06
Fiber (g/day)	-0.01	-0.03, 0.01	0.02	-0.01, 0.06
Fiber density (g/ MJ)	0.27**	0.10, 0.44	0.12	-0.11, 0.35
Fiber from grain (g/day)	-.0.03	-0.07, 0.00	0.01	-0.03,0.05
Fiber density from grain (g/ MJ)	0.14	-0.12, 0.04	0.10	-0.16, 0.36

Key Findings related to Table 2 below:

- For men: high intake of whole grain associated with lower risk of being obese or overweight. Higher fiber also associated with lower risk of overweight but not statistically significant inverse associations were observed between fiber intake and risk of being obese (thought to be due to small number of obese men)
- For women: high intake of whole-grain products associated with a lower risk of being overweight or obese. High intake of brown bread and fiber associated with higher risk of obesity

Table 2: Multivariate odds ratios (ORs) and 95% confidence intervals (95% CIs) in baseline data for the outcome variables overweight and obesity compared to normal weight (BMI <25) (For Table 2: Legend definitions: a = Adjusted for age, energy intake, intake of animal protein, education, smoking status, number of cigarettes and consumption of fruit and vegetables. * = P,0.05, ** = P<0.01. NOTE: Definition of variables is in section above)

Increment per unit increase in intake	Overweight (BMI ≥ 25)		Obesity (BMI ≥ 30)	
	OR 95% CI		OR 95% CI	
Men:				
All grain (g/day)	0.98**	0.97,0.99	0.90**	0.83,0.97
Whole grain (g/day)	0.98**	0.96,0.99	0.90**	0.84,0.98

Other Findings:

While there was an inverse association between whole-grain consumption and BMI and risk of overweight and obesity in both men (M) and

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Total brown bread (10 g/day)	0.99	0.98,1.01	1.00	0.97,1.03
Fiber (g/day)	0.98**	0.96,0.99	0.97	0.92,1.01
Fiber density (g/ MJ)	0.84**	0.73,0.96	0.81	0.55,1.19
Fiber from grain (g/day)	0.98**	0.96,0.99	0.97	0.92,1.02
Fiber density from grain (g/ MJ)	0.82**	0.70,0.95	0.80	0.52,1.25
Women:				
All grain (g/day)	0.98**	0.97,0.99	0.97*	0.94,1.00
Whole grain (g/day)	0.98**	0.96,0.99	0.96*	0.93,0.99
Total brown bread (10 g/day)	1.01	0.99,1.03	1.04**	1.01,1.07
Fiber (g/day)	1.01	0.99,1.03	1.04**	1.00,1.08
Fiber density (g/ MJ)	1.06	0.92,1.22	1.26	1.00,1.60
Fiber from grain (g/day)	1.00	0.97,1.02	1.03	0.98,1.07
Fiber density from grain (g/ MJ)	1.00	0.85,1.17	1.25	0.95,1.64

women (W), although **there was a stronger association in men**.

Men had a 10% (95% CI 2-16%) lower risk of obesity as compared to normal wt. for each additional g of (dry) grain consumption. (Caveat from reviewer: population of obese men was only 79)

Women had a 4% (95% CI 1-7%) lower risk of obesity as compared to normal wt. for each additional g of (dry) grain consumption --

(Using USDA Food Guide Pyramid): 1 serving cooked grain per day, corresponding to 1 oz. dry grain, corresponds to ORs (95% CI) for **overweight** of 0.51 (0.36-0.73) in men and 0.55 (0.36-0.83) in women. ORs (95%CI) for obesity are 0.06 (0.01-0.53)in men and 0.32 (0.12-0.85) in women for same amount of whole grain

Initially fiber and cereal fiber intake were inversely associated with BMI in men only. Associations were similar after exclusion of likely under-and over-reporters of energy. A retrospective analysis of baseline fiber intake and weight gain after the age of 20 years also showed a slight inverse association.

In prospective study, of subjects with repeated measurements(**Data not shown**), a change (S.D.) in body weight between the repeated measurement and baseline of 0.1 (2.3) kg and 0 (1.7) kg per year for men and women respectively was noted. No change associated with BMI change and fiber. No change associated between baseline values of exposure variables (fiber, whole grain etc.,) and changes in BMI between repeated measurement

Author Conclusion:

- The results of this study in a healthy middle-aged population in the Netherlands indicate that men and women with a high intake of whole grains have a lower BMI and a lower risk of overweight and obesity than men or women with a low intake of whole grains.
- Cross-sectional design of the study does not allow conclusions about the causality of the association but the consistency of the association between whole-grain consumption and BMI and its biological plausibility are in line with a causal association
- Intervention studies are needed to find out whether consumption of whole grain decreases the risk of becoming overweight. The results for dietary fiber and wholemeal bread were less clear. This may be due to methodological problems in dietary and BMI assessments, residual confounding, physiological reasons or a combination of these factors

Reviewer Comments:

Authors note following limitations:

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- *Self-reported height and weight resulting in non-differential and probably also differential misclassification according to BMI. Both would result in underestimation of true association (although majority of other studies are similar)*
- *As is typical of all observational studies, there may be residual confounding, particularly those determinants of attitudes or healthy lifestyle factors not captured and measured.*
- *It is possible that women, more often than men, underreport the energy-containing foods and possibly over-report fiber intake. (Reviewer's note: there were also 9% (N =197) obese females versus 4% (N = 79) obese males in this study). That being said, they think results for whole-grain foods were much less susceptible to such biases. (see pl.36 at bottom of page for details).*

Reviewer's comments:

- *Believe there was no attrition in this study (both sets) due to measurement only at baseline (in 1986). Did not get impression that continuous variable of BMI was from 20 years later, which seems a lot different than eating habits now, versus then*
- *Small population of obese men, while noted as an issue by authors, may signify that results are just a starting point for other studies to verify associations are valid*
- *Did not directly control for physical activity.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes

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2.	**Was the selection of study subjects/patients free from bias?**		Yes
	2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
	2.2.	Were criteria applied equally to all study groups?	Yes
	2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
	2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**		Yes
	3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
	3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
	3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
	3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	???
	3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
	3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**		No
	4.1.	Were follow-up methods described and the same for all groups?	No
	4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
	4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	???
	4.4.	Were reasons for withdrawals similar across groups?	???
	4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**		N/A

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5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	No
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

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	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes

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