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Geachte,
In het achtergronddocument aangaande voedingspatronen zie ik geen referentie naar de zeer recente publicatie in de Lancet:
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2815%2960461-5/abstract

De studieopzet waarin de interventie staat beschreven heb ik bijgevoegd.

vriendelijke groeten,
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Research Article

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER): Study design and progress

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Abstract

Background: Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) is a multi-center, randomized, controlled trial ongoing in Finland.

Materials: Participants (1200 individuals at risk of cognitive decline) are recruited from previous population-based non-intervention studies. Inclusion criteria are CAIDE Dementia Risk Score ≥ 6 and cognitive performance at the mean level or slightly lower than expected for age (but not substantial impairment) assessed with the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological battery. The 2-year multidomain intervention consists of: nutritional guidance; exercise; cognitive training and social activity; and management of metabolic and vascular risk factors. Persons in the control group receive regular health advice. The primary outcome is cognitive performance as measured by the modified Neuropsychological Test Battery, Stroop test, and Trail Making Test. Main secondary outcomes are: dementia (after extended follow-up); disability; depressive symptoms; vascular risk factors and outcomes; quality of life; utilization of health resources; and neuroimaging measures.

Results: Screening began in September 2009 and was completed in December 2011. All 1200 persons are enrolled and the intervention is ongoing as planned. Baseline clinical characteristics indicate that several vascular risk factors and unhealthy lifestyle–related factors are present, creating a window of opportunity for prevention. The intervention will be completed during 2014.

Conclusions: The FINGER is at the forefront of international collaborative efforts to solve the clinical and public health problems of early identification of individuals at increased risk of late-life cognitive impairment, and of developing intervention strategies to prevent or delay the onset of cognitive impairment and dementia.

Keywords: Cognitive impairment; Dementia; Alzheimer's disease; Lifestyle; Intervention; Randomized trial

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1. Introduction

Cognitive impairment is one of the most frequent chronic conditions in the elderly [1], and the worldwide costs of dementia have been estimated to exceed those of other chronic diseases such as diabetes [2]. Alzheimer's disease (AD), the major cause of dementia, has reached epidemic proportions, with a large human, social, and economic burden [3]. However, postponing AD onset by only 5 years may halve the projected AD prevalence in the future [4,5].

The importance of finding methods to delay onset and/or modify progression of cognitive impairment/dementia was recently emphasized in a report of the National Institutes of Health (NIH) in USA [6]. Formulated by an independent panel of health professionals and public representatives from outside the AD research field, the report highlighted the need for high-quality, randomized, controlled trials (RCTs). As cognitive impairment/dementia has a multifactorial etiology, resulting from interactions between both genetic and environmental factors (Figure 1), the report recommended conducting RCTs with multidimensional interventions, combining interventions for multiple risk factors, and controlling for many other factors [6]. Conducting trials initially in individuals at high risk was also recommended as a more efficient approach.

Within the AD/dementia research field, a consensus has emerged that intervention strategies must be initiated as early as possible, even before significant symptoms begin to appear. This goal can be achieved, for example, by incorporating the classical clinical trial approach to disease into a public health model, with long-term longitudinal databases including large populations. Establishing comprehensive databases for studies on aging can create the opportunity to formulate and validate tools for early detection of people who are at increased risk of late-life cognitive impairment, to identify important targets (risk factors) for preventive interventions, and to test such interventions in RCTs.

The first initiatives with an international perspective have already been established, including the Leon Thal Symposia [7], Prevent Alzheimer's Disease by 2020 (PAD2020, http://www.pad2020.org), and the European Dementia Prevention Initiative (EDPI, http://www.edpi.org). It has been suggested that a worldwide database could be built by integrating and expanding already existing cohorts and registries [7]. The multidomain Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) has been at the forefront of these efforts, and the FINGER is actively planning collaborations and integrating efforts with other groups launching similar projects.

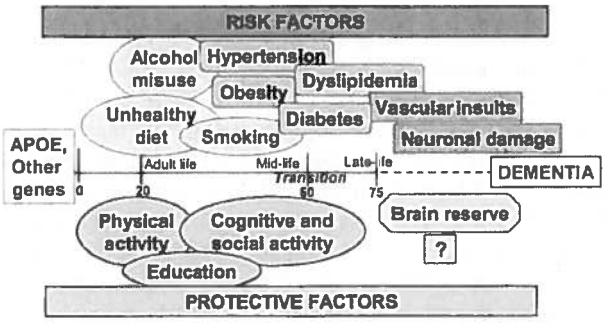

Fig. 1. Risk and protective factors for dementia.

The FINGER also provides a useful example of how a national dementia prevention research platform can be constructed using existing platforms for other chronic diseases. The study was initiated within the Academy of Finland Public Health Challenges Program, and is mainly based on the population of the FINRISK study, the Finnish survey database for monitoring of risk factors for chronic diseases. The FINRISK Study consists of large population-based surveys carried out since 1972 every 5 years using independent, random, and representative population samples from different parts of Finland [8]. The age range for the surveys is 25–74 years, and data are regularly linked to national hospital and drug registers. The first surveys were conducted within international cardiovascular disease prevention projects [9,10], but some cohorts were further investigated in the Cardiovascular Risk Factors, Aging and Incidence of Dementia (CAIDE) study [11]. FINGER participants are previous FINRISK participants screened with the CAIDE Dementia Risk Score (Table 1) [11].

Two earlier intervention trials in Finland were important sources of inspiration for the FINGER. The Diabetes Prevention Study (now completed) is a landmark RCT showing the effectiveness and feasibility of physical exercise and dietary interventions as preventive measures in people with impaired glucose tolerance [12]. It showed that trial participants can be motivated to make major longer term changes in their lifestyle. The ongoing 4-year exercise and the dietary intervention study Dose-Responses to Exercise Training (DRs EXTRA) had a drop-out rate of only 8% after 2 years, and its intervention protocol served as a model for the FINGER [13].

Table 1
CAIDE Dementia Risk Score: Probability of dementia in 20 years according to midlife risk score categories

Risk factor		Points		
Age	<47 years	0		
	47–53 years	3	Total score	Dementia risk
	>53 years	4	0–5	1.0%
Education	>10 years	0	6–7	1.9%
	7–9 years	2	8–9	4.2%
	<9 years	3	10–11	7.4%
Gender	Female	0	12–15	16.4%
	Male	1		
Blood pressure	<140 mm Hg	0		
	>140 mm Hg	2		
Body mass index	<30 kg/m^2	0		
	>30 kg/m^2	2		
Total cholesterol	<6.5 mmol/L	0		
	>6.5 mmol/L	2		
Physical activity	Yes	0		
	No	1		

The main objective of the FINGER is to investigate the extent to which a multidomain intervention can prevent/delay cognitive impairment in elderly at increased risk of cognitive decline. The 2-year intervention consists of nutritional guidance, exercise, cognitive training, and social stimulation, and intensive monitoring and management of metabolic and vascular risk factors. The aim of this article is to present the study design of the FINGER and describe some of the baseline characteristics of its participants.

2. Methods

2.1. Study design

The FINGER is a multicenter RCT (ClinicalTrials.gov identifier: NCT01041989) enrolling at least 1200 independently living persons from six cities (Helsinki, Vantaa, Kuopio, Oulu, Seinäjoki, Turku) in Finland. Each site is led by an experienced subgroup leader and run by a skilled study team. A monitoring committee ensures that the protocol of each intervention domain is followed carefully at each study site. Double blinding will be pursued as completely as possible, but in lifestyle interventions it may not be perfectly achieved. Participants in the FINGER are not actively told which group they belong to. Investigators evaluating outcome measures are blinded for the randomization group, and participants are also advised not to discuss the intervention during evaluation sessions. Cognitive testing and cognitive training sessions are conducted by different psychologists.

2.2. Selection of study participants: Inclusion and exclusion criteria

Participants in the FINGER are 60–77 years of age at the beginning of the study, recruited from previous random, population-based, nonintervention surveys (i.e., FINRISK). They are prescreened with the CAIDE Dementia Risk Score, and those scoring at least 6 points are further screened with the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological test battery [14]. For inclusion, at least one of the following criteria must be fulfilled: (1) Word List Memory Task (10 words × 3) ≤19 words; (2) Word List Recall ≤75%; or (3) Mini-Mental State Examination (MMSE) [15] ≤26/30 points. These criteria select persons with cognitive performance at the mean level or slightly lower than expected for age according to Finnish population norms [16], but without substantial cognitive decline. Exclusion criteria are conditions affecting safe engagement in the intervention (especially the exercise component): malignant diseases; major depression; dementia/substantial cognitive decline; MMSE <20; symptomatic cardiovascular disease; revascularization within 1 year; severe loss of vision, hearing, or communicative ability; conditions preventing cooperation [17] as judged by the study physician; as well as coincident participation in any intervention trial.

2.3. Intervention program

At baseline all participants receive oral and written information and advice on healthy diet and level of physical, cognitive, and social activities beneficial for vascular risk factors management and disability prevention from the study nurse. The study population is then randomized into two groups equal in size, to receive either an intensive multidomain intervention or regular health advice. Randomization was performed in blocks of four persons (two persons randomly allocated to each group) at each site by running a computer program that uses a linear congruential generator coded with a structured query language for random numbers. All participants (both the regular health advice group and the intensive multidomain intervention group) meet the study nurse three times after randomization and the physician at the final visit after 2 years. At each meeting with the study nurse, blood pressure, weight, and hip and waist circumference are measured. Blood samples are taken four times during the study and each time the participants receive their laboratory test results via mail, with general written information about the significance of these values together with advice for seeking medical care if needed.

In addition to what is given to both groups, the participants in the intensive intervention group receive all four components of the intervention: (1) nutritional guidance; (2) physical exercise; (3) cognitive training and social activity; and (4) intensive monitoring and management of metabolic and vascular risk factors (Figure 2). The different components of the multidomain intervention are initiated in a stepwise manner to facilitate adherence to each component.

The *nutritional intervention* includes individual counseling sessions (three meetings with the study nutritionist during the first year) and group sessions (six times during the first year and one to three times during the second year). Individual sessions include tailoring of the participant's daily diet. Group meetings provide more information and support for facilitating lifestyle changes, and include discussions and practical exercises, such as tools to assess one's own dietary behavior (e.g., tests to assess fat or fiber intake). The diet is based mainly on the Finnish Nutrition Recommendations [18]. Participants are advised to consume a diet with 10–20% of daily energy (E%) from proteins, 25–35E% from fat (<10E% from saturated plus transfatty acids, 10–20E% from monounsaturated fatty acids, 5–10E% from polyunsaturated fatty acids [including 2.5–3 g/day n-3 fatty acids]), 45–55E% from carbohydrates (<10E% refined sugar), 25–35 g/day dietary fiber, <5 g/day salt, and <5E% from alcohol.

These goals are achieved by recommending: high consumption of fruit and vegetables; whole grain in all cereal products; low-fat options in milk and meat products; sucrose intake <50 g/day; using vegetable margarine and rapeseed oil instead of butter; and consumption of fish in at least two portions per week. Because there is not sufficient evidence for the benefits of using dietary supplements (e.g., vitamins such as E or the B group related to cognitive

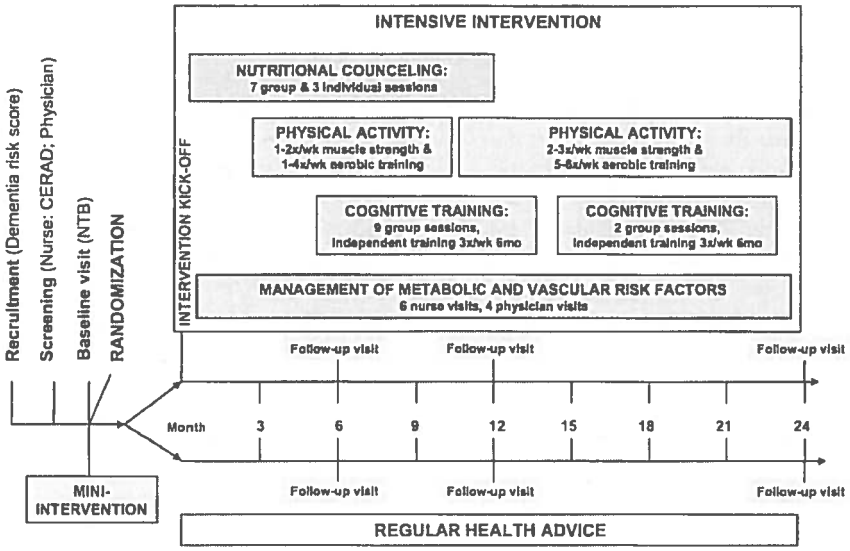

Fig. 2. FINGER protocol.

functioning in some studies) [6], the aim is to achieve an adequate intake with a balanced diet. However, vitamin D supplementation (10–20 μg/day) is advised [19], and fish oil supplements are recommended for participants not consuming fatty fish. Additional dietary measures can be taken according to individual needs related to disease history and medication. The need for weight loss is considered individually and energy intake that facilitates 5–10% of body weight reduction is recommended only if necessary. Food consumption and nutrient intake is assessed by 3-day food records at baseline, 12 months, and 24 months. Additional information on specific foods (i.e., fish) is assessed by a food frequency questionnaire.

The *physical exercise training program* is based on international guidelines [20] and represents a modified version of the Dose-Responses to Exercise Training (DR's EXTRA) study protocol [13]. Training is guided and supervised by study physiotherapists. The intervention comprises individually tailored, progressive muscle strength training and aerobic exercise programs, including exercises to maintain and improve postural balance (Table 2). The muscle strength training is conducted at the gym and guided by study physiotherapists during the first 6 months. The progressive strength training program is based on repetition maximum (RM) measurements at baseline and remeasurements at 1, 3, 6, 10, 15, and 20 months. The strength training program is standardized to include exercises for the eight main muscle groups (knee extension and flexion, abdomen and back muscles, rotation, upper back and arm muscles, and press bench for lower extremity muscles). Postural balance exercises are done during each training session at the gym. Individual aerobic training is planned together with each study participant and comprises activities preferred by the participant. Aerobic group activities, such as Nordic walking, aqua gym, jogging, and gymnastics, are also provided in the study. Muscle strength training and aerobic exercise are recorded in diaries throughout the intervention period.

Cognitive training targets cognitive domains most sensitive to aging and with a central role in everyday situations (episodic memory, executive function, mental speed, and working memory). The selection of the training was guided by a model that highlights three separate but related executive functions [21]. Training is done in group sessions and individually using a computer-based program that was specially adapted for the FINGER from protocols previously shown to be effective in shorter term RCTs [22]. Certain tasks were added to offer variation to this year-long training program. The cognitive training consists of 10 group sessions lead by a psychologist (approximately 60–90 minutes/session), when the computer program is introduced, and group discussions on memory-related themes are conducted. Discussions cover topics such as age-related changes in cognition, memory strategies, and every-day memory training. The computer-based training includes two periods of independent training of 6 months each, when participants train using the cognitive training program three times/week, 10–15 minutes/session, for a total of 72 training sessions per

Table 2
Progression of the resistance and aerobic training program

	0–1 mo	1–3 mo	3–6 mo	6–24 mo
Resistance exercise				
Exercise frequency per week	1–2	1–2	2	2–3
Duration of exercise (min)	30–45	30–60	45–60	60
Number of muscle groups	8–10	8–10	8–10	8–10
Repetitions/set	8–15	10–20	8–20	8–20
Load % 1RM	40–50	60	70	70–80
Number of sets	2	2–3	1–3	2–3
Aerobic exercise				
Exercise frequency per week	2	2–3	3–4	3–5
Duration of exercise (min)	30–45	30–45	30–60	45–60

period. Computer-based exercises enable an individual-adjusted increase in difficulty levels to facilitate a maximal effect of training. The effect of training is evaluated in testing sessions at the beginning, at 3 months and at the end of the independent training period. *Social activities* are stimulated through the numerous group meetings of all intervention components. A visit to the local Alzheimer Society offices is organized for each group. The participants are provided with information of the value of an active lifestyle and social connectedness. The amount of participation in social and cognitive activities, recorded in activity diaries, is evaluated at baseline, 1 year, and 2 years.

The *monitoring and maintenance of metabolic and vascular factors* begins with a risk factor assessment according to the latest national evidence-based guidelines [23–25]. The intensive intervention group members meet the study nurse every 3 months during the first year, and every 6 months during the second year for anthropometric measurements (weight, blood pressure, hip, and waist circumference). They also meet the study physician at 3, 6, 12, and 24 months for evaluation of laboratory test results, anthropometric measures, and cardiovascular and metabolic conditions. Participants in the intervention group are given oral and written information on the importance of reducing these risk factors. Motivating participants to make necessary lifestyle changes is an essential part of the meetings with the physician and nurse. When initiation or adjustment of pharmacologic treatment is necessary, participants are recommended to contact their own physician at the primary health care center.

2.4. Follow-up and outcome measurements

All participants meet the study nurse at screening, baseline, and months 6, 12, and 24, and the study physician at screening and month 24 for a general health evaluation. The cognitive status of each participant is assessed by a psychologist, and information on health status, socioeconomic factors, and lifestyles is gathered at baseline, 12 months, and 24 months.

The *primary outcome* of the FINGER is cognitive performance measured by modified Neuropsychological Test Battery (mNTB) composite z score evaluating several cognitive domains and Stroop test and Trail Making Test (A and B). The mNTB is an extended version of the original NTB and it is a sensitive measure for mild cognitive changes more typical for AD [26]. The additional tasks are used to detect executive dysfunctions more characteristic for vascular cognitive impairment [27].

Secondary outcomes are: (1) Incidence of dementia and AD. Final diagnoses will be made by a cognitive evaluation board according to standard criteria (DSM-IV [28] and NINCDS-ADRDA [29]). An extended follow-up of at least 7 years is needed to investigate the effect of the intervention on this outcome. (2) Cognition evaluated with mNTB domain z scores (memory, executive functioning, and cognitive speed), executive functioning z score (derived from the Stroop test and Trail Making Test), MMSE, CDR-SB, prospective memory [30], subjective memory, and memory problems perceived by a proxy [31]. (3) Vascular risk factors; (4) cardiovascular and cerebrovascular morbidity and mortality. (5) Dietary intake (food records, food frequency questionnaires). (6) Dietary markers (i.e., erythrocyte fatty acid composition, serum folate, S-B_{12}, homocysteine) and other biomarkers (i.e., inflammation, oxidative stress, lipid and glucose metabolism). (7) Disability (ADCS-ADL questionnaire completed by a proxy). Mobility limitations and the level of physical functioning are assessed with the Short Physical Performance Battery (SPPB; standing balance test, timed sit-to-stand test, 4-m comfortable walking time) [32], grip strength, and 10-m maximal walking time. For about 400 participants in the Helsinki and Vantaa cohorts postural balance is evaluated using force platform (Good Balance; Metitur, Ltd., Finland) measurements, and for 250 participants in Turku maximal isometric and dynamic knee extensor strength measurements are done using the leg extension/curl device (HURlabs, Ltd., Finland). (8) Falls (self-reported within the previous 12 months). (9) Cardiorespiratory fitness, measured for 400 participants by a maximal symptom-limited exercise test on a cycle ergometer. (10) Depressive symptoms (Zung scale) [33]. (11) Health-related quality of life (RAND-36/SF-36 and 15D instruments, [34,35]). (12) Utilization of health resources—questionnaire data [36] and register data. (13) Individuals' experience of participation in the study, inquired at 24 months. All scales have been selected according to recent recommendations (i.e., www.ema.europa.eu) and experiences in Finland.

Exploratory outcomes are brain magnetic resonance imaging (MRI) for about 100 participants in the cohorts from Kuopio, Oulu, Seinäjoki, and Turku, and for 60 participants in the Turku cohort also [^{11}C]PIB and [^{18}F]FDG positron emission tomography (PET) imaging and cerebrospinal fluid (CSF) measures, enabling analyses of AD biomarkers and a study of the newly proposed AD criteria [37,38]. Echocardiography, ultrasound examination of the right carotid artery, measurement of pulse wave velocity, and collection of 24-hour urine for measurements of microalbumin are done for about 200 participants in the Turku cohort. The exploratory outcomes subsamples include the first consecutive participants randomized when imaging became available for the FINGER in the aforementioned centers (equal numbers from the control and intervention groups).

2.5. Statistical considerations

Sample size calculations were based on the expected modified NTB score. Considering previous studies in mild AD [26], an NTB decline of approximately −0.21 z score with an SD of 0.5 would be expected in the control group during 2 years (calculated as half of the decline in mild AD, and with larger SD due to the more heterogeneous FINGER participant group). With 5% significance level and

90% power, the sample size required at the end of the trial is approximately 500 persons per group to detect a 50% difference in change in NTB score between the two groups. In addition, this sample size will have >80% power to detect a smaller difference of 40% in change in NTB score between the two groups. Based on earlier Finnish lifestyle interventions, DR's EXTRA [13] and the Diabetes Prevention Study [12], a drop-out rate of 10% during the trial was assumed, and a starting size of 600 persons per group was therefore considered to be sufficient. During the intervention period, dementia incidence will still be low in this relatively young population (10 per 1000). An extended follow-up (7 years since enrollment for each participant) is planned to evaluate the longer term effects of the intervention on cognition (NTB and dementia/AD). Dementia incidence is estimated at 20 per 1000, giving, at 7 years, 95% power to detect differences expecting the intervention to decrease dementia incidence by 50%.

Preliminary *statistical analyses* will involve the univariate examination of the distribution of each covariate of interest to identify outliers and assess skewness. Besides the mNTB total composite z score, domain z scores will be created from mNTB components measuring memory, executive functioning, and cognitive speed. An additional z score for executive functioning will include: the score difference between Trail Making Test conditions B and A (a purer executive function measure of set shifting); and the score difference between various Stroop test conditions (a purer executive function measure of attention and inhibition). Primary and secondary outcomes will be analyzed using a multilevel model for change with level 1 estimating rate of individual change and level 2 estimating rate of between-person differences in change. The model may also be extended to predict nonlinear and discontinuous change of outcome. When the outcome of interest is binary, such as incidence of dementia/AD, a discrete time hazard regression model will be used. The model may be extended to polynomial effect of time on hazard. In these models, intervention group will be included as covariate. Other time-invariant and time-varying covariates may also be included as predictors. The effects of the intervention on primary and secondary outcomes will also be evaluated in subanalyses stratified by age, gender, baseline cognition, level of risk factors (including *APOE* ε4 genotype), and the level of adherence to the different domains of the intervention. The adherence to each domain will be defined based on the level of participation (divided into three groups: no participation; less than half of the proposed activities; and more than half of the proposed activities).

2.6. Ethics and safety aspects

The FINGER has been approved by the coordinating ethics committee of the hospital district for the Helsinki and Uusimaa region. Participants give their written informed consent before enrollment in the study. The principles of good clinical practice are applied in the intervention. The National Institute for Health and Welfare has patient insurance for all participants. Safety issues of the intervention (especially the exercise component) are carefully considered. The safety committee meets regularly for assessment of any occurring adverse events.

2.7. Data management process

A computerized logistics system created at the National Institute for Health and Welfare (THL) is used to schedule appointments and to follow-up the collected data, including forms and blood samples. The data are collected and sent to the THL without personal identifying information, using number-coded stickers that are unique for each visit. The link between the participant, visit, and code is kept in the logistics system at the THL. Data are analyzed (laboratory samples) or recorded (forms) and stored in the analysis database, where all changes can be tracked.

2.8. Study progress

Starting from September 2009, about 5500 individuals were invited to the FINGER screening examination. Of these, approximately 48% participated. The preliminary analyses show that the nonparticipants had lower education and were older than the participants.

The target of identifying and randomizing 1200 participants was achieved in December 2011. All four intervention domains have been initiated according to schedule for each wave of intervention groups, and the 2-year intervention period will end at the beginning of 2014. Electronic data entry and processing is currently ongoing.

Some baseline characteristics of the first 1118 participants are summarized in Table 3. The mean (SD) age was 68.6 (4.6) years, level of education 10.0 (3.4) years, and MMSE score 26.7 (2.1) points. Vascular risk factors were frequent, indicating a window of opportunity for the intervention: 53.3% of participants had systolic blood pressure (SBP) >140 mm Hg, and 16.1% had diastolic blood pressure (DBP) >90 mm Hg. Of the participants, 42.8% were overweight (body mass index [BMI] 25–30 kg/m^2) and 32.7% obese (BMI >30 kg/m^2). Serum total cholesterol level was >5.0 mmol/L in 53.9% of the participants, high-density lipoprotein (HDL) was <1 mmol/L in 10.3%, and low-density lipoprotein (LDL) was >3 mmol/L in 51.5% of the participants. Impaired fasting glucose (>6.1 mmol/L) was seen in 38.6%.

3. Discussion

The FINGER investigates whether a multidomain intervention can prevent or delay cognitive impairment in an older population at increased risk of cognitive decline. Risk and protective factors are chosen based on the best available knowledge, with focus on simultaneously addressing several such factors to obtain an optimal prevention

Table 3
Some initial characteristics based on the first 1118 randomized participants

	Baseline
Age (years)	68.6 (4.6)
Men/women (%)	53.4/46.6
Education (years)	10.0 (3.4)
MMSE	26.7 (2.1)
SBP (mm Hg)	141.2 (16.3)
DBP (mm Hg)	81.0 (9.3)
LDL-C (mmol/L)	3.09 (0.87)
HDL-C (mmol/L)	1.44 (0.38)
BMI (kg/m^2)	28.8 (4.4)
Fasting glucose (mmol/L)	6.1 (0.9)

effect [6]. An integrative, transdisciplinary approach is ensured by the inclusion of factors shared by AD and other major chronic diseases.

Some positive effects on cognition have been reported by single-domain lifestyle interventions [39,40], but large, long-term intervention studies combining different approaches have not been conducted so far for the prevention of cognitive decline and dementia. Disappointing results of previous trials with single agents in older patients or already cognitively impaired persons have pointed out several key issues, which the FINGER takes into account to the extent possible with the available resources [41]. Inclusion criteria select a population at increased risk of cognitive decline, but without substantial cognitive impairment. Given epidemiologic data linking midlife vascular risk factors to dementia and AD in late life [11], it would have been of interest to include even participants <60 years of age, but this would have required a much larger sample size and longer follow-up time. Recruiting participants from the FINRISK database ensures a truly population-based sample, offering the possibility of extrapolating the results to the general population. In addition, the information on earlier lifestyle and vascular factors from FINRISK offers detailed baseline data for the FINGER, which is very rare in RCTs. The clinical characteristics of the first participants indicate that several vascular risk factors and unhealthy lifestyle–related factors are present, creating a window of opportunity for the intervention. Preliminary findings also suggest that the participants in the FINGER are motivated to follow the study protocol. However, it seems that people in the oldest age groups and those with the highest values on dementia risk score are less likely to participate. A similar trend is often seen in RCTs. Further, cardiovascular disease prevention programs have led to a significant decrease in some vascular risk factors and raised awareness of a healthy lifestyle in Finland [9], and significant differences between intervention and regular health advice groups may be more difficult to detect.

Outcome measures in cognition-related RCTs have long been a matter of debate. Instead of focusing mainly on conversion to dementia, the FINGER uses, as primary outcomes, sensitive neuropsychological tests for mild changes in cognitive performance of both the Alzheimer and vascular types. Another major advantage in the FINGER is the possibility of investigating potential mechanisms behind the effects of the intervention, by detailed biomarker measurements (blood, CSF, MRI, PET) and analyses of patterns of change over time.

Because several chronic diseases among older people have overlapping risk and protective factors, conducting prevention RCTs raises major ethical issues. It is no longer possible to have a traditional control group where such factors (i.e., those known to increase the risk for cardiovascular or cerebrovascular conditions) are left untreated. The control group of the FINGER is given the health advice regularly offered by nurses and physicians in primary care settings. In addition, all participants are recommended to contact their regular physician in case initiation or adjustment of medication is considered necessary.

The FINGER design resulted from carefully balancing these key methodological issues with currently available resources. In theory, the study is powered to detect a 40–50% difference in change in cognitive scores between intervention and control groups. However, in everyday life even a smaller impact on cognitive decline may be important. Results from the FINGER can provide both high-quality scientific knowledge on the effects of a multidomain intervention in older people and some of the means to translate this knowledge into practice. The broad range of secondary outcomes enables the estimation of total benefit and cost-effectiveness of the intervention. Preliminary analyses in a Swedish/Finnish setting have already indicated that preventive interventions in dementia can be cost-effective [42], and similar analyses based on the FINGER data can provide useful information for health-policy decision-makers. Using experiences from the application of the diabetes prevention programs in several countries [43], findings from the FINGER could be extended beyond Finland as well. Lessons learned from this multidomain intervention trial will help in the planning and conducting of future larger interventions and in the implementation of preventive strategies in at-risk populations, while simultaneously facilitating international collaborations and future interoperability of data among researchers.

Together with two other large multidomain prevention RCTs (www.edpi.org), the FINGER is at one end of the current spectrum of intervention trials in AD/cognitive impairment. At the other end are treatment RCTs using disease-modifying drugs (i.e., anti-amyloid therapy) in genetically at-risk groups or those with an established biomarker burden [44]. The shift toward presymptomatic and pre-dementia stages of AD has brought prevention and treatment RCTs much closer to each other than before.

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RESEARCH IN CONTEXTTEXT

1. **Systematic review:** We identified larger multidomain randomized, controlled trials (RCTs) by searches of ClinicalTrials.gov and International Standard Randomized Controlled Trial Number Register. Search terms: "prevention of dementia OR prevention of Alzheimer disease." Further selection criteria: primary outcome dementia/cognitive impairment; at least two combined interventions (exercise, cognitive, or social activities; diet; drug/dietary supplement; etc.); age _40 years; duration _1 year; size _500 participants. Criteria were based on National Institutes of Health Q4 (NIH) report recommendations (6). We identified two ongoing studies, the Multidomain Alzheimer Preventive Trial (MAPT, NCT00672685) and Prevention of Dementia by Intensive Vascular Care (Pre-DIVA, ISRCTN29711771). Results are not yet available.
2. **Interpretation:** The population-based FINGER study addresses whether a multidomain intervention (nutritional guidance; exercise, cognitive and social activities; and vascular factors management) can prevent or delay cognitive impairment in the elderly at increased risk of cognitive decline.
3. **Future directions:** FINGER experiences can be used in planning and conducting larger, multinational dementia prevention RCTs.

FINGER study group

The FINGER study group is comprised of the following individuals: main investigator: Miia Kivipelto, MD, PhD; coordination: Satu Ahtiluoto, MD, and Tiia Ngandu, MD, PhD; subcohort leaders: Miia Kivipelto (Helsinki cohort), Tiina Laatikainen, MD, PhD (Vantaa cohort), Hilkka Soininen, MD, PhD (Kuopio cohort), Timo Strandberg, MD, PhD (Oulu cohort), Antti Jula, MD, PhD (Turku cohort), and Jaakko Tuomilehto, MD, PhD (Seinäjoki cohort); statistical analyses: Markku Peltonen, PhD, Risto Sippola, MSc, and Esko Levälahti, MSc; intervention supervision: Jaana Lindström, PhD, Jenni Lehtisalo, MSc (nutrition component), Rainer Rauramaa, MD, PhD, Satu Pajala, PhD (physical exercise component), Tuomo Hänninen, PhD, Tiia Ngandu (cognitive component), Timo Strandberg, Riitta Antikainen, MD, PhD, and Jaakko Tuomilehto (vascular risk factor component). The cognitive component was designed in collaboration with Lars Bäckman (Karolinska Institutet, Sweden) and Anna Stigsdotter-Neely (Umeå University, Sweden). Other study members and collaborators include: Raimo Sulkava, MD, PhD, Alina Solomon, MD, PhD, Teemu Paajanen, PhD, Marko Grönholm, MSc, Francesca Mangialasche, MD, PhD, and Juha Rinne MD, PhD.

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Van: Michel Bien
Verzonden: vrijdag 3 april 2015 9:49
Aan: GR_RGV2015
Onderwerp: RE: Randomized Controlled Trial cognitive decline
Bijlagen: GLiMMER-illustrative-references.pdf

Geachte,

Vanuit de True Health Coalition is een lijst opgesteld met referenties. Deze heb ik bijgevoegd. De eerste 4 studies zijn in ieder geval niet opgenomen in het achtergronddocument voedingspatronen. Daarna ben ik gestopt met de crosscheck; ik vermoed dat het grootste deel van deze studies niet is meegenomen in de review. Op deze lijst staan zeer veel studies naar de effecten van voeding en beweging op ziektes en intermediaire, zachte eindpunten. In een aantal gevallen is ook sterfte onderzocht.

Verder is er tijdens de American College of Cardiology een studie gepresenteerd over de effecten van het mediterrane eetpatroon:
http://www.acc.org/about-acc/press-releases/2015/03/04/16/36/mediterranean-diet-cuts-heart-disease-risk-by-nearly-half

Ook in de US worden de guidelines herschreven en zijn er ook open commentaarrondes en achtergronddocumenten. Het zou kunnen dat in deze documenten ook artikelen staan die in de Nederlandse reviewrondes zijn gemist.
http://www.health.gov/dietaryguidelines/2015-scientific-report/

Ik hoop dat deze studies kunnen bijdragen aan de sterkte van de bewijsvoering, zodat er nog meer duidelijkheid komt over de juiste voedingspatronen.

Als aanvulling op het aangeleverde document: de True Health Coalition is recent opgezet om wereldwijd met een stem de waarheden over lifestyle intervention te verkondigen.
http://glimmerinitiative.org/

Kunt u alstublieft een ontvangstbevestiging sturen?

Bij voorbaat dank en met vriendelijke groeten,

drs. Michel Bien
Volendam

From:
To: rgv2015@gr.nl
Subject: Randomized Controlled Trial cognitive decline
Date: Tue, 31 Mar 2015 22:45:20 +0200

Geachte,
In het achtergronddocument aangaande voedingspatronen zie ik geen referentie naar de zeer recente publicatie in de Lancet:
http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2815%2960461-5/abstract

De studieopzet waarin de interventie staat beschreven heb ik bijgevoegd.

vriendelijke groeten,
drs. Michel Bien
Medisch Bioloog
Sportvoedingsadviseur
Volendam

TRUE HEALTH COALITION

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Commentaar ontvangen per email 1 april 2015

Geachte Gezondheidsraad,

Hierbij het commentaar van ETC t.a.v. de documenten over “voedingspatronen”. Het lijkt ons dat onze eerder aanbevelingen vooral van toepassing zijn op dit onderwerp, vandaar dat ik nogmaals uw aandacht vraag voor onze email van 6 februari hieronder.

Met vriendelijke groet,

Arine Valstar

From: Arine Valstar

Sent: vrijdag 6 februari 2015 14:39

To: 'RGV2015@gr.nl'

Cc: Joanne Harnmeijer; Odile Beckers; Wim Hiemstra; Marga De Jong; Ingrid Flink; 'Erik Gerritsen'

Subject: Commentaar ronde richtlijnen goede voeding 2015

Geachte Gezondheidsraad,

Graag maakt ETC gebruik van de mogelijkheid te reageren in deze commentaar ronde richtlijnen goede voeding 2015. Deze email betreft niet slechts een van de achtergrond documenten maar veeleer het ter harte nemen van recent geformuleerde evidence-based duurzaamheids uitgangspunten in het opstellen van de nieuwe richtlijn in 2015.

De timing biedt een uitgelezen kans voor Nederland om als een van de eerste Europesche landen de aanbeveling van het inspirerende en invloedrijke Live Well for LIFE project van december 2014 uit te voeren. Met EU financiering heeft het Wereldnatuurfonds de afgelopen 4 jaar in verschillende Europese landen samen met stakeholders onderzocht hoe duurzame en gezonde voedingspatronen er uit zien waarbij de vermindering van uitstoot van broeikasgassen in de Europesche food supply chain naast biodiversiteit centraal stonden.

De aanbevelingen roepen de lidstaten ten eerste op om nationale voedingrichtlijnen te herzien en hierin naast gezondheids- ook duurzaamheids doelen op te nemen!

Dit is zelfs key recommendation 1 A.

Voor meer informatie verwijs ik graag naar de final recommendations http://livewellforlife.eu/wp-content/uploads/2014/12/LiveWell-for-LIFE_Rec-Report_English_Final.pdf voor de andere aanbevelingen en naar “A balance of healthy and sustainable food choices for France, Spain and Sweden” http://livewellforlife.eu/wp-content/uploads/2014/03/LiveWell_Report-Sum_2013_DTsmallpdf.com_.pdf/ . Meer en ook zeer informatieve studies van dit project zijn beschikbaar op http://livewellforlife.eu/knowledge-centre .

Met vriendelijke groet,

Arine Valstar
Adviseur voeding en voedsel
ETC
Kastanjelaan 5
3833 AN Leusden
http://www.etc-international.org

Van: Christine Grit
Verzonden: dinsdag 28 april 2015 13:27
Aan: GR_RGV2O15
Onderwerp: Respons op derde serie achtergronddocumenten Gezondheidsraad RGV

Geachte mevrouw/heer,

Bijgaand doe ik u onze opmerkingen en commentaren toekomen op basis van de derde serie achtergronddocumenten bij de nieuwe Richtlijnen goede voeding van de Gezondheidsraad. Tevens is er nog een additioneel artikel bijgevoegd.

Ik hoop dat dit document de Commissie van de GR behulpzaam kan zijn in het uiteindelijk formuleren van de nieuwe RGV.

Met vriendelijke groet,

Christine Grit
Manager Voeding & Gezondheid

FNLI

EGV 15 09 A
Notitie

Consultatierespons op 4 achtergronddocumenten

Onderwerp Achtergronddocumenten Groente en fruit, Natrium, Vis en Voedingspatronen

Datum | 28 april 2015

Inleiding
Als eerste willen we ook bij deze derde reeks achtergrond documenten de Commissie bedanken voor het kunnen inzien van de Werkwijze en de achtergronddocumenten voor de Richtlijnen goede voeding (Rgv) 2015. Ook bij deze set documenten willen we graag de Commissie complimenteren met het vele werk dat hiertoe moet zijn uitgevoerd. Opnieuw is een reeks zeer grondig uitgewerkte documenten beschikbaar gesteld en dat is wat ons betreft zeker een compliment waard.

We maken vervolgens graag van de gelegenheid gebruik om te reageren op de verschillende achtergronddocumenten die bij deze derde ronde zijn verspreid voor consultatie. Alle 4 achtergronddocumenten zijn in onze achterban doorgenomen waarbij uiteraard de door de Commissie gestelde vragen zoveel mogelijk centraal hebben gestaan. De reacties op de verschillende documenten volgen vanaf pagina 2 van deze consultatierespons. De documenten worden in alfabetische volgorde behandeld, te beginnen bij 'groente en fruit' en eindigend bij 'voedingspatronen'.

In onze eerste respons hebben we een algemeen punt naar voren gebracht en hebben we ook enige kanttekeningen bij de gevolgde werkwijze geplaatst. We gaan er vanuit dat deze punten als bekend kunnen worden verondersteld, en willen daarom hier alleen doorgeven dat het algemene punt en de bewuste kanttekeningen van toepassing blijven.

Voedingspatronen

Opmerkingen vooraf
Voorop zij gesteld dat wij inzien dat het erg lastig is om het thema "voedingspatronen" op een wetenschappelijk onderbouwde manier te bespreken. Dat de Commissie hier met dit achtergrond document een poging toe doet, is zeer te prijzen. Het is wel zeer wenselijk omdat de focus op individuele voedingsmiddelen en/of voedingsstoffen veelal geen volledig beeld kan geven voor de gezondheid op de langere termijn. Daar komt nog bij dat de uiteindelijke Richtlijnen goede voeding ook in een voedingspatroon zouden moeten resulteren, en wel een voedingspatroon dat bescherming biedt tegen of de risico's verlaagt op het verkrijgen van bepaalde welvaartsziekten of precursors daarvan. Met andere woorden: een aanbevolen voedingspatroon. In dit document wordt op zeer grondige wijze het beschikbare onderzoek doorgelicht.

De Commissie erkent dat de definities van verschillende voedingspatronen onderling sterk verschillen, en heeft zelf geen criteria opgesteld voor de verschillende opties die er zijn voor deze verschillende voedingspatronen. Ondanks deze ernstige beperking wordt er bij sommige aandoeningen toch voor gekozen om stevige uitspraken te doen inzake de bewijskracht, met name bij de interventie onderzoeken. Hoe is dit überhaupt mogelijk in een situatie waarbij er geen definities zijn, anders dan een globale indicatie van de (wisselende) samenstelling?

Het valt ons op dat er één studie is die een vergelijking maakt met het Nederlandse voedingspatroon (verwijzing nummer 19, op pagina 15, regel 344 met opmerking mede gefinancierd door de voedingsmiddelenindustrie). Wij vragen ons af of de GR geen studie/monitoring heeft laten uitvoeren naar de 10-jaars effecten van de vastgestelde richtlijnen goede voeding uit 2006 en de daarbij behorende voedingsadviezen? We zijn ons ervan bewust dat de GR dit niet zelf kan doen maar een en ander had wellicht geïnstigeerd kunnen worden met ondersteuning van het Ministerie van VWS.

Naar onze mening is het een omissie van de Commissie om geen rekening te houden met andere aandoeningen of problemen die een gevolg zouden kunnen zijn van bepaalde voedingspatronen dan de in de inleiding genoemde. Zo wordt er bijvoorbeeld geen rekening gehouden met bepaalde specifieke vormen van ondervoeding bij een veganistische voeding of met het relatief vaak aanwezig zijn van bloedarmoede bij vrouwen en het feit dat dit specifieke eisen stelt aan een vegetarische, en zeker een veganistische, voeding. Ook wordt er niet gekeken naar typische aandoeningen die voorkomen bij een bepaalde variant van de Aziatische voeding (wordt aldaar nader toegelicht). Hoewel uiteraard bloeddruk, LDL cholesterolgehalte, het gewicht en het risico op chronische ziekten voor de gezondheid op langere termijn van grote betekenis zijn voor de volksgezondheid, kan men niet stellen dat andere, eveneens veelal langdurige, aandoeningen niet van belang zijn. Het zou onzes inziens een dimensie toevoegen aan dit achtergrond document als ook de (mogelijke) aanwezigheid van deze aandoeningen zou zijn meegewogen in het uiteindelijke oordeel over de verschillende voedingspatronen. Nu lijkt het oordeel teveel af te hangen van een beperkt aantal

aandoeningen terwijl de andere voedingsgerelateerde aandoeningen onbesproken blijven. Ook valt op dat dieetbeperkingen bij sommige delen van de bevolking nergens zijn meegenomen in de analyses.

Laag-vet voedingspatronen worden op meerdere plaatsen in het document besproken (al ontbreken deze wel bij de beschrijvingen van de voorbeelden van voedingspatronen op pagina 5 en 6). Hoog-vet voedingspatronen, vergezeld door een beperking van de hoeveelheid koolhydraten echter niet. Laag-koolhydraat voedingspatronen worden in de media vaak genoemd in de positieve zin, als zouden dergelijke voedingen bescherming bieden tegen allerhande aandoeningen die wél in dit rapport aan de orde worden gesteld.

Als laatste zouden we willen opmerken dat er in de literatuur steeds meer aanwijzingen zijn dat een permanente (beperkte) calorische restrictie positieve effecten heeft op de gezondheid op de langere termijn. Tóch wordt hier geen aandacht aan besteed. We begrijpen uiteraard dat het beperken van de calorieën de facto in elk voedingspatroon kan worden opgenomen en de facto onafhankelijk kan zijn van een voedingspatroon als zodanig. Echter, er wordt evenmin een ander achtergronddocument aan deze aanwijzingen gewijd. Wij zouden derhalve willen aanbevelen om aan dit thema op een of andere wijze in één van de achtergrond documenten aandacht te besteden.

Gedetailleerde opmerkingen per pagina en regel.

Pagina 5, regels 87-88
Kruiden en specerijen worden uitgebreid gebruikt. Er ontbreken echter opmerkingen over de hoeveelheid zout in een dergelijke voeding. Tóch zou ook dat meegenomen moeten worden bij het bekijken van de gevolgen voor de gezondheid van dergelijke voedingspatronen.

Pagina 5, regel 90
De opmerking wordt gemaakt dat de inname van suiker gering is. Het is correct dat een Mediterraan voedingspatroon in de eerste helft van de 20e eeuw weinig suikerbevattende producten bevatte. Maar hier wordt geen rekening gehouden met twee belangrijke punten:

1. In een (traditioneel) Mediterraans voedingspatroon werden wellicht weinig suikerbevattende producten geconsumeerd maar dat zegt uiteindelijk weinig over de uiteindelijke suikerinname. Immers, de koffie werd en wordt gedronken met een stevige hoeveelheid suiker, en ook de zoetheid van kant en klare toetjes en gebaksoorten die men in dergelijke landen in de huidige tijd tegenkomt, maakt duidelijk dat er in de huishouding in het verleden relatief veel suiker moet zijn toegevoegd aan dergelijke huisgemaakte producten, wellicht zelfs meer dan men in de "Westerse landen" toevoegde.
2. In het begin van de 20e eeuw werd ook het zogenaamde Westerse voedingspatroon gekenmerkt door weinig suikerbevattende producten. Wél

werd er in de huishouding aan veel producten suiker toegevoegd. Maar het is zeer de vraag of dit meer was dan in een traditioneel Mediterraan huishouden.

De belangrijkste kanttekening die wij bij deze twee punten willen plaatsen, is dat de rol van de hoeveelheid suiker onterecht téveel nadruk krijgt als een belangrijke medeveroorzaker van de verschillende aandoeningen die aan de orde worden gesteld in het achtergronddocument.

Pagina 5, Regels 91-92
Dit is een taalkundig puntje: "Een aantal" is enkelvoud, geen meervoud. Er is een aantal overeenkomsten (en niet "er zijn").

Pagina 5, Regels 96-97
Het feit dat het voedingspatroon in Japan en andere Aziatische eilanden sterk afwijkt voor wat betreft de hoeveelheid vis en schaal- en schelpdieren alsmede de hoeveelheid zout, zou een belangrijke reden kunnen zijn voor verschillen in gezondheidseffecten van die patronen op de langere termijn. Ten eerste omdat zowel zout als vis al vrij lang bekende consumptiefactoren zijn in relatie tot hart- en vaatziekten (inclusief hoge bloeddruk). Ten tweede omdat deze afwijkende factoren ten opzichte van andere Aziatische gebieden ook een belangrijke rol spelen bij de ontwikkeling van andere aandoeningen dan die welke voornamelijk bij de Richtlijnen goede voeding worden besproken en doorgewerkt. Zo is bekend dat in Japan, zeker in het verleden, het aantal maagzweren relatief hoog was in vergelijking met veel andere landen. Tóch worden in dit document (noch in de andere achtergronddocumenten) hier opmerkingen over gemaakt. Zeker in relatie tot dit afwijkende voedingspatroon, lijkt dit een een zwaarwegende omissie te zijn.

Pagina 6, regel 104
Wij vragen ons af of het voor de gezondheid van de mens relevant is dat het vlees afkomstig is van vee uit de wei en kip uit de vrije uitloop. Door het expliciet te benoemen, wordt die indruk echter wel gewekt.

Pagina 6, regels 120-125
Naar onze mening zouden uitsluitend voedingen met een sterke mate van wetenschappelijke onderbouwing als 'gezonde voeding' kunnen worden gecategoriseerd. Diëten om gewicht te verliezen, tenzij het gaat om een gezonde voeding in de bovengenoemde context (er zijn ook mensen die via een gezonde voeding gewicht hopen te verliezen), zouden hier niet toe moeten worden gerekend. Voedingspatronen volgens richtlijnen en Dash voeding echter wel.

Pagina 9, regel 198
Zo zou het gebruik van een vegetarisch voedingspatroon in plaats van een omnivoor voedingspatroon de bloeddruk verlagen en de bewijskracht daarvoor zou groot zijn. Het

lijkt ons dat het niet mogelijk is een dergelijke uitspraak te doen, en wel om de volgende redenen[1].

- De verschillen in voedingspatroon tussen omnivoren onderling zijn bijzonder groot. Sommigen eten bijvoorbeeld veel meer vlees dan anderen terwijl behalve het aanwezige vlees in de voeding de resterende samenstelling van de voeding ook van groot belang is voor de gezondheid op langere termijn, misschien wel groter dan louter de afwezigheid van vlees bij de vegetariërs.
- Onduidelijk wordt of het vleesconsumptiepatroon van de omnivoor als zodanig nog een rol speelt: ligt de nadruk op varkens-, rund-, kippen- of ander vlees in het voedingspatroon, of is er sprake van een evenwichtige combinatie daartussen.
- In hoeverre telt de consumptie van vis mee? Strikt genomen is een persoon die wel vis eet, geen vegetariër maar in hoeverre is dat in de onderzoeken ook het geval? En, in hoeverre zijn er verschillen tussen lacto-ovo vegetariërs en mensen die geen vlees eten maar wel vis?
- Steeds meer mensen kunnen beter beschreven worden als flexitariërs dan als zuivere omnivoren of vegetariërs. Tóch wordt deze groeiende groep mensen bij deze onderzoeken eenvoudig als omnivoor neergezet. Voor de goede orde moet daarbij worden opgemerkt dat de groep flexitariërs veelal ook bewust leeft en qua overige kenmerken van leefstijl zich dichtbij die van de vegetariërs bevindt.
- De Commissie is zich er van bewust dat vegetariërs gemiddeld op andere leefstijl terreinen dan het voedingspatroon veelal 'beter' scoren dan omnivoren. Tóch wordt er grotendeels voorbijgegaan aan de effecten van die andere leefstijlfactoren als men de effecten van de variabele "voedingspatronen" zo sterk bewezen acht.

Hierbij kan nog worden aangetekend dat een dergelijke opsomming van redenen bij elke vergelijking tussen voedingspatronen kan worden gemaakt. Wellicht dat het beter zou zijn om te spreken van "aannemelijkheid" in plaats van een grote bewijskracht. Er zijn namelijk teveel andere factoren die een rol kunnen spelen bij de gevonden effecten (zowel in de voedingspatronen als zodanig, de voedingspatronen onderling als in vergelijking met andere leefstijlfactoren) om aan een voedingspatroon zonder duidelijke definitie van criteria een grote bewijskracht toe te kennen.

Pagina 11, regel 260

Wij vragen ons af wat de redenen zijn om het aanwezig zijn van een calorische restrictie als criterium te hanteren om een onderzoek uit te sluiten van de selectie. Immers, het zal in een dergelijk onderzoek niet gaan om een calorische restrictie in de vorm van een "afval dieet" welke zeer eenzijdig van samenstelling kan zijn. Wij erkennen dat de effecten op bepaalde intermediaire punten (zoals gewicht) bij het mee laten wegen van studies met een restrictie niet meer aan het voedingspatroon kunnen worden gekoppeld.

[1] Wij hebben uiteraard gezien dat een aantal van de hier opgesomde redenen in het hoofdstuk 'Cohortonderzoeken bij vegetariërs' wel aan de orde zijn gesteld

Onzes inziens zou een beter criterium kunnen zijn dat een calorische restrictie gecombineerd met een eenzijdig voedingspatroon geen deel uit zou mogen maken van de selectie. Tevens vragen wij ons af waarom onderzoeken die uiteindelijk zouden kunnen leiden tot een hogere energie-inname dan wél aan de selectiecriteria voldoen. Want hier geldt het omgekeerde: een eventuele verandering in gewicht kan door de additionele kcalorieën evenmin nog aan het voedingspatroon worden gekoppeld. Bij Predimed worden onder twee van de condities additioneel voedingsmiddelen verstrekt met een relatief hoge calorische waarde. Onduidelijk wordt of hier uiteindelijk sprake is geweest van vervanging of dat de proefpersonen eenvoudig meer calorieën zijn gaan consumeren. Bij het onderzoek van Bos et al. (hier niet meegenomen maar wel in de paragraaf over LDL cholesterol) wordt er expliciet melding van wordt gemaakt dat dit een iso-calorische interventie betreft. Indien het van belang is dat er sprake is van iso-calorische interventies of juist dat het aantal kcalorieën er niet toe doet, zou dit vermeld moeten worden en – liefst – ook toegelicht. Temeer daar dit in de andere paragrafen over interventies wel wordt meegenomen.

Pagina 54-55, regel 1359 (tabel, onderaan op pagina 55).
Het zou "Healthy Eating Index" moeten zijn.

Pagina 64, regels 1583-1584
Hier ontbreekt de bij de conclusies behorende bevinding over de bewijskracht. Deze wordt uiteindelijk wel vermeld (pagina 65, regel 1610) maar niet in vetgedrukte vorm bij het begin van de paragraaf.

Pagina 65, regel 1613 (tabel)
Het zou "Alternative Eating Index" moeten zijn.

Pagina 71, regels 1743-1754
Inm de conclusie van hoofdstuk 4 waarin cohortonderzoeken naar voedingspatronen worden besproken, staat vermeld dat een hoge score op indexen voor een aanbevolen voedingspatroon ten opzichte van een lage score, omgekeerd samenhangt met het het risico op een aantal (chronische) ziekten. Opvallend is dat gesteld wordt dat een aanbevolen voedingspatroon weinig (toegevoegde) suiker bevat maar dat in veel van de gehanteerde indexen er überhaupt niet op de hoeveelheid suiker wordt gescoord. Dit geldt bijvoorbeeld voor de Mediterrane indexen terwijl in andere aanbevolen voedingspatronen er bijvoorbeeld slechts voor één of twee bronnen wordt gescoord. Het gaat onzes inziens daarom wat ver om de hoeveelheid suiker mee te nemen in de conclusies aangezien die niet bekend is.

Pagina 73, regel 1793
Niet voedignspatronen maar voedingspatronen.

Literatuursuggestie (artikel is bijgevoegd):

Mikael Fogelholm, Sigmund Anderssen, Ingibjorg Gunnarsdottir and Marjaana Lahti-Koski, Dietary macronutrients and food consumption as determinants of long-term weight change in adult populations: a systematic literature review, Food & Nutrition Research 2012. 56: 19103

Review Article

CoAction Publishing

Dietary macronutrients and food consumption as determinants of long-term weight change in adult populations: a systematic literature review

Mikael Fogelholm[1]*, Sigmund Anderssen[2], Ingibjörg Gunnarsdottir[3] and Marjaana Lahti-Koski[4]

[1]Department of Food and Environmental Sciences, University of Helsinki, Helsinki, Finland; [2]Department of Sports Medicine, Norwegian School of Sport Sciences, Oslo, Norway; [3]Faculty of Food Science and Nutrition, University of Iceland, Reykjavik, Iceland; [4]Finnish Heart Association, Helsinki, Finland

Abstract

This systematic literature review examined the role of dietary macronutrient composition, food consumption and dietary patterns in predicting weight or waist circumference (WC) change, with and without prior weight reduction. The literature search covered year 2000 and onwards. Prospective cohort studies, case–control studies and interventions were included. The studies had adult (18–70 y), mostly Caucasian participants. Out of a total of 1,517 abstracts, 119 full papers were identified as potentially relevant. After a careful scrutiny, 50 papers were quality graded as A (highest), B or C. Forty-three papers with grading A or B were included in evidence grading, which was done separately for all exposure-outcome combinations. The grade of evidence was classified as convincing, probable, suggestive or no conclusion. We found probable evidence for high intake of dietary fibre and nuts predicting less weight gain, and for high intake of meat in predicting more weight gain. Suggestive evidence was found for a protective role against increasing weight from whole grains, cereal fibre, high-fat dairy products and high scores in an index describing a prudent dietary pattern. Likewise, there was suggestive evidence for both fibre and fruit intake in protection against larger increases in WC. Also suggestive evidence was found for high intake of refined grains, and sweets and desserts in predicting more weight gain, and for refined (white) bread and high energy density in predicting larger increases in WC. The results suggested that the proportion of macronutrients in the diet was not important in predicting changes in weight or WC. In contrast, plenty of fibre-rich foods and dairy products, and less refined grains, meat and sugar-rich foods and drinks were associated with less weight gain in prospective cohort studies. The results on the role of dietary macronutrient composition in prevention of weight regain (after prior weight loss) were inconclusive.

Keywords: *obesity*; *weight gain*; *weight maintenance*; *diet*; *fat*; *carbohydrates*; *protein*; *nutrition*

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The prevalence of obesity has increased globally during the past 30 y (1). According to the WHO statistics, 35% of adults aged 20 y and older were overweight (BMI $\geq$25 kg/m^2) in 2008 (2). The worldwide prevalence of obesity has nearly doubled between 1980 and 2008. Moreover, WHO has estimated that worldwide 2.8 million people die each year as a result of being overweight or obese, and an estimated 35.8 million (2.3%) of global disability-adjusted life-years are caused by overweight or obesity. A recent European study concluded that in a worst-case scenario almost every third European adult might be obese by year 2015 (3).

The total food supply has increased during the last decades (4). When compared against the secular trends in obesity, an increase in food supply and a concomitant increase in total energy intake are likely to be one of the

Citation: Food & Nutrition Research 2012. **56:** 19103 - http://dx.doi.org/10.3402/fnr.v56i0.19103

major drivers in the obesity epidemic (1). However, the role of dietary macronutrient composition, intake of specific food items or dietary patterns in development of obesity is not clear.

During the last decade, a few narrative reviews have addressed the role of diet in prevention of weight gain (5–7). Systematic reviews and meta-analyses have focused on specific issues, like the role of sugar-sweetened beverages (8–10). The results have been inconclusive. Moreover, we are not aware of any recent (last 5 y) and broad systematic reviews examining the associations of dietary macronutrients, food intake and dietary patterns vs. change in weight or waist circumference (WC) in adult populations. These data are needed to, e.g. give supporting evidence in formulating new nutrition recommendations. The present work was done in connection to the 2012 Nordic Nutrition Recommendations. The purpose of this systematic literature review was to examine the associations of dietary macronutrient composition, food consumption and dietary patterns in prevention of weight or WC gain, with and without prior weight reduction.

Methods

Research questions and definitions

The research questions were formulated separately for studies on primary prevention of weight gain and for studies addressing weight regain after prior weight reduction.

(1) Primary prevention of obesity (maintenance of body weight and/or WC):

What is the effect of different *dietary macronutrient composition* on long-term ($\geq$1 y) change in weight/WC/body fat in an adult population?

(2) Prevention of weight regain after weight loss (or maintenance of reduced body weight):

What is the effect of different *dietary macronutrient composition* on long-term ($\geq$1 y) change in weight/WC/body fat in individuals who have deliberately reduced their weight by at least 5%?

In the search, dietary macronutrient composition was defined as containing:

(1) carbohydrates, fat and protein as % in energy intake
(2) fat quality in diet: variation in saturated (SFA), monounsaturated (MUFA) or polyunsaturated (PUFA) fatty acids, as % in energy intake or g/day
(3) sugar intake as g/day or % in energy intake
(4) fibre (fiber) intake as g/day

Several of the papers selected for the review contained data on food consumption or dietary patterns. Consequently, the review was expanded to include different food items and food groups, such as cereal products, whole-grain cereals, fruit, vegetables, milk and milk products, meat, etc. Moreover, we also included studies using a whole-diet approach, such as the Mediterranean diet or an index for healthy eating (according to existing dietary recommendations).

The search terms are shown in Appendix 1. The databases used were PubMed and SweMed/SweMed+ (the latter was used to identify Nordic articles not published in PubMed).

Inclusion criteria

The *a priori* defined inclusion criteria were as follows:
Publication year

– year 2000 and later

Study type

– Cross-sectional: *excluded*
– Follow-up (cohort): *included* but minimum follow-up 1 y
– Case–control: *included*
– Weight-maintenance interventions: *included* with the following criteria: (1) intentional mean weight loss at least 5%; (2) at least 6 months follow-up. The follow-up (after weight reduction) could be non-randomised (observational cohort study) or a randomised intervention. In the latter case, the randomisation was done after weight loss, in the beginning of the weight-maintenance intervention. A further premise was that weight reduction was similar in different weight-maintenance groups. Weight loss interventions were also accepted if the total duration was longer than 3 y.

Age

– Inclusion criteria: adult. Age range 18–70 y.
– Exclusion: studies with >70 y participants only and those in which results were not separately analysed by age (i.e. >70 y participants in their own group)

Race/geographical location

– Studies without Caucasians or with Caucasians as minority group were excluded

Selection and evaluation of papers

The abstracts after the initial search were screened by two of the authors (Sigmund Anderssen and Ingibjörg Gunnarsdottir). All articles suggested by at least one of the two were ordered as full papers. The two other authors (Mikael Fogelholm and Marjaana Lahti-Koski)

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then screened the full papers. Again, papers suggested by at least one of them were at least preliminary included in the quality assessment (most careful scrutiny) and evaluation table. Also reviews were ordered as full papers. However, they were not eventually included in the quality grading, because of too much variation in, for example, inclusion criteria, years covered and age groups included.

The quality assessment of the papers was done according to the principles of the Nordic Nutrition Recommendation 2012 working group (11). In short, all papers were evaluated according to a three-scale grading: A = high quality studies with very low level of potential bias; B = some bias, but not enough to invalidate the results; C = significant bias and weaknesses that may invalidate the results. The preliminary quality assessments and construction of summary tables were done individually (Marjaana Lahti-Koski: macronutrients and weight change; SA and IG: food consumption and weight change, dietary patterns and weight change; MF: weight change after weight reduction), but the final product was cross-checked together by all authors.

After the quality grading, four summary tables (macronutrients, food consumption, dietary patterns and weight change after weight reduction) were formed from all studies quality graded A or B. In these tables, the results were arranged according to exposure and outcome variables. However, we did not separate unadjusted and adjusted (to BMI) WC. We always chose the model with most adjustments as the statistical outcome. Moreover, we used analyses with sexes combined, if possible. Otherwise the results of men and women are presented separately. We did not use any other stratification variables, such as prior weight change or smoking.

The grading of evidence was based on the summary tables and a four-class grading: convincing (high), probable (moderate), suggestive (low) and no conclusion (insufficient). The minimum requirement for 'suggestive' was two studies showing an association, and no conflicting results. If some studies showed ns (neither positive nor negative association), it was decided that for 'suggestive evidence', the number of results showing an association was required to be at least two higher than those showing no association.

Results

A total of 1,517 abstracts were initially screened for eligibility (Fig. 1). Out of these, 119 were selected and ordered as full papers. A total of 50 papers were quality graded (12–61). These include 41 papers identified through the original literature search and nine additional papers (17, 30, 31, 32, 36, 45, 47, 51, 55) found from the reference lists of the other publications or 'related citations' in PubMed. The reasons for excluding 78 full papers (5, 8–10, 62–135) are shown in Appendix 2. The number of studies with data on body composition was

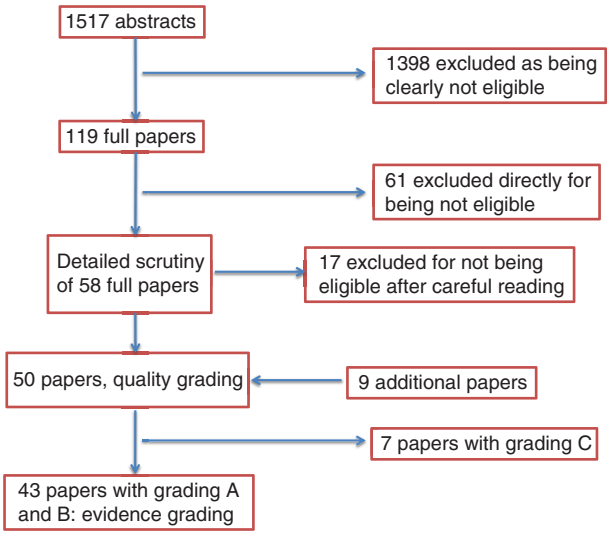

Fig. 1. Flow-chart of the systematic literature review process.

low and therefore our analyses are based only on weight (BMI) and WC.

The evidence tables (Appendix 3–6) present all studies with quality assessment. Studies on the association between macronutrients and weight change are presented in Appendix 3. Studies using energy density as an exposure were also included here. Studies on food contsumption and weight change are presented in Appendix 4. Studies using glycaemic index (GI) or glycaemic load (GL) as the main exposure variable are also shown here. Appendix 5 presents the studies on dietary patterns and weight change, and Appendix 6 shows studies on weight change after prior weight reduction (studies on weight regain). The results are summarised for the grading of evidence in Tables 1–4 (in the text).

Macronutrients and change in weight or WC

Most of the studies used for the grading of evidence for the association between macronutrient intake and weight change were prospective cohort studies (Table 1 and Appendix 3). The spread of exposures against the two optional outcomes (change in weight or WC) was large, and most exposure-outcome combinations were assessed by only one or two studies. This leads inevitably to difficulties in finding any evidence for associations between macronutrient intakes and weight change.

The evidence linking high fibre intake to prevention of weight gain was considered probable. In addition, three suggestive associations were found, for cereal fibre against weight change, and for fibre and energy density against change in WC. Five studies assessed weight gain in relation to fibre intake. The association was negative (high fibre intake indicated smaller weight gain) in three studies (14, 18, 21, 26), while one (19) did not find an association. A similar, albeit slightly weaker conclusion was obtained

Table 1. Summary of studies on the association between dietary macronutrients and weight change (see Appendix 1).

Exposure	Outcome variable	No. of participants	Reported associations			Number of studies rated as A or B[1]	Strength of evidence	References
			+	ns	−			
Carbohydrates	Weight	39,275		2		A: 1, B: 1	No conclusion	17, 19
CHO from foods with simple sugars	WC	44,817	1W	1M	B: 1	B: 1	No conclusion	17
CHO from fruit and vegetables	WC	44,817		1M	1W	B: 1	No conclusion	17
CHO from potatoes	WC	44,817	1W	1M		B: 1	No conclusion	17
CHO from refined grains	WC	44,817	1W	1M		B: 1	No conclusion	17
Fibre	Weight	270,307		1	4	A: 3, B: 2	Probable	14, 18, 19, 21, 26
Fibre	WC	106,019		1M	1	B: 3	Suggestive	14, 20, 23
					1W			
					1M			
Fruit fibre	Weight	27,082			1M	B: 1	No conclusion	35
Cereal fibre	Weight	116,514			1	B: 2	Suggestive	14, 35
					1M			
Protein	Weight	49,277		1		A: 1	No conclusion	19
Protein	WC	44,817			1	B: 1	No conclusion	17
Fat	Weight	257,991	1	3		A: 2, B: 4	No conclusion	16–19, 25, 42
			2W	1M				
Fat	WC	44,817	1			B: 1	No conclusion	17
SFA	Weight	130,950	1W	1		B: 2	No conclusion	15, 16
SFA	WC	89,432		1		B: 1	No conclusion	16
MUFA	Weight	130,950		1	1W	B: 2	No conclusion	15, 16
MUFA	WC	89,432		1		B: 1	No conclusion	16
PUFA	Weight	130,950	1W	1		B: 2	No conclusion	15, 16
PUFA	WC	89,432		1		B: 1	No conclusion	16
TFA	Weight	41,518	1W			B: 1	No conclusion	15
TFA substituted for CHO	WC	16,587	1M			B: 1	No conclusion	20
TFA substituted for PUFA	WC	16,587	1M			B: 1	No conclusion	20
Vegetable fat	WC	44,817	1W			B: 1	No conclusion	17
Energy density	Weight	141,220	1W	2		A: 1, B: 2	No conclusion	12, 13, 19
Energy density	WC	138,063	2			B: 2	Suggestive	13, 23

CHO, carbohydrates; SFA, saturated fatty acids; PUFA, polyunsaturated fatty-acids; TFA, trans fatty acids; W, waist circumference; M, men; W, women; +, associated with increased weight gain; ns, no association with weight change; −, associated with decreased weight gain (prevention of weight gain).

[1]Some studies included several analyses (e.g. separately for men and women). Therefore, the number of results may be greater than the number of studies.

for cereal fibre (14, 35). Also studies analysing the association between fruit fibre against weight change (35), or the association between total fibre and change in WC (14, 23), tended to favour a protective role of fibre intake.

The other suggestive evidence on the role of dietary macronutrients in development of obesity was observed for energy density (total energy intake divided by the weight of food consumed) against change in WC: both identified studies (13, 23) reported that higher energy density was associated with larger increase in WC. The results on energy density against weight change were less consistent. Bes-Rastrollo et al. (12) reported that an increase in energy density was associated with a simultaneous increase in weight, while two other studies (13, 19) did not find an association.

The intake of total carbohydrates, fats and proteins did not show consistent associations with weight gain. Especially in the case of fat intake vs. weight change, the number of studies (four) was in fact relatively high, but the results were quite evenly dispersed between a positive association (higher fat intake would increase weight gain) (25, 42) and no significant association (16, 17). Similarly, the results on intake of SFA or PUFA against development of obesity indicated either a positive (15) or no significant association (16). Field et al. (15) linked MUFA with protection of weight gain, but this finding was not confirmed in the study of Forouhi et al. (16). Koh-Banerhee et al. (20) investigated the role of trans-fatty acids (TFA): their results suggested that TFA, when substituted for carbohydrates or PUFA, are associated with increased WC. Also Field et al. (15) found a positive association between TFA intake and weight gain. Hence, all three analyses showed that high intake of TFA predicts weight gain. The lack of multiple data on specific combinations prevents us from making a stronger conclusion.

Howard et al. reported that higher intake of total carbohydrates protected against weight gain in women (18), but Halkjaer et al. (17) did not find an association between carbohydrate intake and change in weight or WC. The source of carbohydrates may be relevant, however, since Halkjaer et al. (17) reported a positive association between carbohydrates from foods with simple sugars, from potatoes and from refined grains, against change in WC in women. In contrast, they also found that high carbohydrates intake from vegetables (women only) and fruit protected against an increase in WC.

The role of protein in prevention of an increase in weight or WC was inconsistent: the two identified studies reported a neutral (19) or negative (17) association.

Foods and change in weight or WC

Compared with the association between macronutrients and weight change, a few more 'suggestive' associations were found (Table 2 and Appendix 4). According to the data, high intake of whole grains, fruit, nuts and high-fat dairy protect against increasing obesity, whereas refined grains, white bread, meat and sweets and desserts seem to promote gains in weight or WC. Unfortunately, even here the main challenge in making broader conclusions was that the number of studies for a specific combination of exposure and outcome was limited (rarely more than two data points).

The suggestive association linking high intake of whole grains to lower weight gain was based on two cohort studies (35, 36). No other studies in this combination of exposure and outcome were found. However, Halkjaer et al. (32) did not find an association between the intake of wholegrain bread and change in WC. Two studies (33, 39) reported that a high intake of fruit predicted smaller increase in WC, with no conflicting results. On the other hand, studies linking fruit to changes in weight were not equally consistent (36, 45).

Three studies reported a negative association between intake of nuts and change in weight (30, 36, 60), and no conflicting data were found. The evidence was regarded as probable. Unfortunately, these studies are not fully independent, since two of them are partly or totally based on data from the Nurses' Health Study (30, 36).

Several studies have investigated the role of dairy products in prevention of weight gain. Again, the definition of exposure variable was inconsistent (dairy in general, high-fat dairy, low-fat dairy, etc.) and this left only a few relevant combinations for assessment in this review. Both studies examining the relationship between high-fat dairy and weight gain reported a negative association, that is, higher intake of these dairy products was associated with smaller gains in weight (38, 50). Also some other studies found a protective role for dairy products (33, 36, 39, 41), while others did not report any significant associations between dairy intake and change in weight or WC (32, 38). There were no studies with a positive association between any kind of dairy products and change in weight or WC.

The intake of refined bread was associated with an increase in WC in both studies identified for this review (32, 39). A similar supporting evidence was observed for the positive association between refined grain and weight change (21, 36).

Three studies reported a positive association between meat intake and weight change (40, 44, 50) and this evidence was regarded as probable. The studies of Rosell et al. (40) and Vergnaud et al. (44) are not, however, totally independent: the former was based on a subpopulation of the EPIC-cohort, while the latter used the entire cohort for analyses. Some other studies also linked higher intake of meat, poultry or processed meat with an increase in weight or WC (33, 36, 39). No association were reported by a few (28, 32, 33), whereas Halkjaer et al. (33)

Table 2. Summary of studies on the association between food consumption and weight change (see Appendix 2).

Exposure	Outcome variable	No of participants	Reported associations			Number of studies rated as A or B[1]	Strength of evidence	References
			+	ns	−			
Breakfast cereals	Risk of obesity	17,881			1M	B: 1	No conclusion	27
Whole grains	Weight	147,959			1 1M	B: 2	Suggestive	35, 36
Wholegrain bread	WC	2,436		1		B: 1	No conclusion	32
Refined grains	Weight	194,968	2			B: 2	Suggestive	21, 36
Refined (white) bread	WC	51,067	2			B: 2	Suggestive	32, 39
Fruit	Weight	494,680		1	1	B: 2	No conclusion	36, 45
Fruit	WC	91,327			2	B: 1	Suggestive	33, 39
Fruit and vegetables	WC	2,436		1		B: 1	No conclusion	32
Vegetables	Weight	494,680		1	1	B: 2	No conclusion	36, 45
Vegetables	WC	91,327		1M	1 1W	B: 2	No conclusion	33, 39
Potato chips	Weight	120,877	1			B: 1	No conclusion	36
Potatoes	Weight	120,877	1			B: 1	No conclusion	36
Potatoes	WC	93,763	1 1W	1 1M		B: 2	No conclusion	32, 33, 39
Nut consumption	Weight	180,930			2 1W	B: 3	Probable	30, 36, 60
Olive oil	Weight	7,368		1		B: 1	No conclusion	29
Butter	Weight	120,877	1			B: 1	No conclusion	36
Butter and/or margarine	WC	93,763	1	1 1M	1W	B: 3	No conclusion	32, 33, 39
Dairy, general	Weight	42,856		1M	1W	B: 2	No conclusion	38, 41
Dairy, general	WC	48,631			1	B: 1	No conclusion	39
Dairy, high-fat	WC	42,696		1M	1W	B: 1	No conclusion	33
Dairy, high-fat/whole-fat	Weight	29,823			1 1M	B: 2	Suggestive	38, 50
Dairy, low-fat dairy	Weight	23,504		1		B: 1	No conclusion	38
Dairy, milk and cheese	WC	2,436		1		B: 1	No conclusion	32
Dairy, yoghurt	Weight	120,877			1	B: 1	No conclusion	36
Meat, general	Weight	380,122	3			B: 3	Probable	40, 44, 50
Meat, poultry	WC	42,696	1W	1M		B: 1	No conclusion	33
Meat, processed meat	Weight	120,877	1			B: 1	No conclusion	36
Meat, processed meat	WC	91,327	1 1W	1M		B: 2	No conclusion	33, 39
Meat, red (unprocessed) meat	Weight	128,071	1	1		B: 2	No conclusion	28, 36
Meat, red meat	WC	45,132		1	1	B: 2	No conclusion	32, 33
Hamburgers, pizza and sausages	Weight	7,194	1				No conclusion	28
Fish	WC	2,436		1		B: 1	No conclusion	32
SSSD	Weight	58,797	1W	1		B: 2	No conclusion	28, 43
SSSD	WC	48,631	1			B: 1	No conclusion	39
Sweetened fruit juice	Weight	7,194		1		B: 1	No conclusion	28
Sweets and desserts	Weight	138,246	2			B: 2	Suggestive	36, 42
Sugar and confectionary	WC	48,632	1			B: 1	No conclusion	39
Cakes and chocolate	WC	2,436		1		B: 1	No conclusion	32
Sauce	Weight	17,369	1W	1M		B: 1	No conclusion	42
Snack foods	WC	42,696	1			B: 1	No conclusion	33
GI	Weight	89,808	1W	1		B: 2	No conclusion	31, 34

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Table 2 (*Continued*)

Exposure	Outcome variable	No of participants	Reported associations +	ns	−	Number of studies rated as A or B[1]	Strength of evidence	References
				1M				
GI	WC	49,007	1, 1W	1M		B: 2	No conclusion	23, 34
GL	Weight	89,808	1	1		B: 2	No conclusion	31, 34
GL	WC	49,383	1W	1		B: 2	No conclusion	23, 34
				1M				

WC, waist circumference; M, men; W, women; GI, glycaemic index; GL, glycaemic load; SSSD, sugar-sweetened soft drink; +, associated with increased weight gain; ns, no association with weight change; –, associated with decreased weight gain (prevention of weight gain).
[1]Some studies included several analyses (e.g. separately for men and women). Therefore, the number of results may be greater than the number of studies.

found that higher intake of red meat protected against an increase in WC, adjusted for BMI.

Two studies reported that a high intake of sweets and desserts, was associated with larger weight increases (36, 42). This association could be classified as suggestive. Two studies found a positive association between intake of sugar-sweetened soft drinks (SSSD) and weight or WC gain (39, 43), while such as association was not confirmed in a third study (28). However, there were no studies suggesting an inverse association of sugar-rich foods and change in weight or WC.

The few results linking GI or GL to changes in weight or WC were dispersed between a positive (23, 31, 34) and no association (23, 34). It may be worth noting that a positive association between GI/GL vs. change in weight or WC was more often observed in women than in men (23, 34).

Dietary patterns and weight change

We identified five studies with results on the relationship between dietary patterns and weight change (Table 3 and Appendix 5). Three of these used an index of the Mediterranean diet (47, 49, 50) and two others the American Diet Quality Index (48, 51). The index for Mediterranean diet is based on the consumption of 'positive' (e.g. fruit, vegetables, legumes, whole grains, fish, olive oil) and 'negative' (e.g. meat and dairy) food items. The Diet Quality Index is based on US dietary recommendations: it is a measure of how well an individual meets the recommendations for SFA, cholesterol, sodium, total fat and total carbohydrate.

Both studies using the Diet Quality Index reported that meeting the recommendations was associated with less weight gain during the follow-up (48, 51). The evidence is suggestive. Two studies with the Mediterranean index supported this conclusion (47, 49), while the third study did not find an association between Mediterranean dietary patterns and weight change after all statistical adjustments (50).

Macronutrients and prevention of weight regain after weight loss

Only nine studies were identified with data on the association between dietary macronutrient composition and weight gain after prior weight reduction (Table 4 and Appendix 6). All six studies classified as A or B were randomised weight-maintenance interventions. Delbridge et al. (59) prescribed a weight-maintenance diet with energy intake corresponding to 1.3 × estimated resting energy expenditure, but all other studies used *ad lib* energy intake throughout the weight-maintenance phase. Overall, the results were inconclusive and it was not possible to make any conclusions.

A high-protein, low-carbohydrate diet protected against weight regain in on study (55), but no effects were observed in three other studies (52, 53, 59). Due et al. (54) found that both a high-fat, low-carbohydrate, and a low-fat, high-carbohydrate diet reduced weight regain,

Table 3. Summary of studies on the association between dietary patterns and weight change (see Appendix 3).

Exposure	Outcome variable	No of participants	Reported associations +	ns	−	Number of studies rated as A or B	Strength of evidence	References
Mediterranean diet index	Weight	390,498		1	2	B: 3	No conclusion	47, 49, 50
Healthy/prudent diet index	Weight	7,158			2	A: 1, B: 1	Suggestive	48, 51

+, Associated with increased weight gain; ns, no association with weight change; –, associated with decreased weight gain (prevention of weight gain).

Table 4. Summary of studies on the association between weight-maintenance interventions (prevention of weight regain) and weight change (see Appendix 4).

Exposure	Outcome variable	No of participants	Reported associations			Number of studies rated as A or B	Strength of evidence	References
			+	ns	–			
HP/LC (vs. LP/HC)	Weight	120		2		B: 2	No conclusion	52, 59
HP/LC (vs. CON)	Weight	973		1W	1	A: 1, B: 1	No conclusion	53, 55
HF/LC (vs. CON)	Weight	77			1	A: 1	No conclusion	54
HF/LC (vs. LF/HC)	Weight	99			1	A: 1	No conclusion	54
LF/HC (vs. CON)	Weight	175	1	1		A: 1, B: 1	No conclusion	54, 57
Low GI vs. high GI	Weight	773			1	A: 1	No conclusion	55

H, high; L, low; P, protein; F, fat; C, carbohydrate; CON, control – according to nutrition recommendations; GI, glycaemic index; M, men; W, women; +, associated with increased weight gain; ns, no association with weight change; –, associated with decreased weight gain (prevention of weight gain).

when compared against a control diet with 'normal' macronutrient composition. Also in the study of Swinburn et al. (57), a low-fat, high-carbohydrate protected against weight regain at 2-y follow-up, but this effect was lost 2 y later.

Finally, Larsen et al. (55) found that a diet with low GI prevented weight regain, when compared against a high GI diet. This effect was observed regardless of the macronutrient composition. However, the most effective combination in terms of prevention of weight regain after weight reduction was high-protein, low-carbohydrate diet with low GI.

Discussion

Interpretation of results

The main findings of this systematic review on nutrients and foods in relation to weight change were the following: we found probable evidence for high intake of dietary fibre and nuts predicting less weight gain, and for high intake of meat in predicting more weight gain. Suggestive evidence was found for a protective role against increasing weight from whole grains, cereal fibre, high-fat dairy products and high scores in an index describing a prudent dietary pattern. Likewise, there was suggestive evidence for both fibre and fruit intake in protection against larger increases in WC. Also suggestive evidence was found for high intake of refined grains, and sweets and desserts in predicting more weight gain, and for refined (white) bread and high energy density in predicting larger increases in WC.

A major problem in assessing the grade of evidence was that similar combinations of exposure and outcome variables were eventually quite rare. Therefore, we decided to do a *post hoc* evidence analysis by first combining the outcome variables. Although WC, compared with BMI, may be a slightly stronger risk factor for cardiovascular diseases, Type 2 diabetes and breast and colorectal cancers, they both can be used as a measure of obesity in population studies almost interchangeably (136, 137). Moreover, to get more studies into one evidence grading, we grouped foods by their closeness of nutrient composition. The results of these *post hoc* analyses are shown in Table 5. Since we may violate the strict rules of evidence grading by subjectively combining different exposure variables, this analysis is 'unofficial' and the grading of evidence is not shown in the table.

We combined studies with fibre, vegetables, fruit, fruit fibre, carbohydrates from fruit & vegetables, whole grains, whole grain bread or nuts as an exposure variable into one group called 'fibre-rich foods'. Some studies included several analyses, either separately for men and women, or for different exposure and/or outcome variables. Hence, the identified 14 studies included a total of 28 analyses. Out of these, 21 results (13 with both sexes, 4 with only women and 4 with only men) indicated that a higher intake of at least one of these 'fibre-rich foods' is associated with prevention of obesity. Eight analyses did not find a significant association. In this light, the evidence for a protective role of fibre-rich foods in general might be considered moderately strong.

The use of fibre-rich products reduce dietary energy density by increasing the volume of food without bringing additional absorbable energy (12). Fruit and vegetables have a low GI, whereas fibre-rich bread may induce a lowered insulin response and delayed glucose decline (138). Both properties could increase satiety and reduce energy consumption (139). In addition, other biologically active compounds in fruit, vegetables and whole grain (e.g. phenolic compounds and phytoestrogens) may be related to weight control (35).

Nuts may be regarded as a 'special case' among fibre-rich products, not least because of their high fat content. Nevertheless, even earlier epidemiological evidence suggests an inverse association between nut consumption and body weight (140). The proposed mechanisms include increased energy expenditure due to high protein and

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Table 5. Post hoc analyses: evidence for association between grouped exposure variables (taken from summary Tables 1 and 2) against grouped outcome variables (BMI and waist circumference not separated).

Group name	Exposure variables	Effect			No of studies[1]	References
		+	ns	–		
Fibre-rich foods	Fibre, vegetables, fruit, fruit fibre, carbohydrates from fruit and vegetables, whole grains, whole grain bread, nuts		5 3M	13 4W 4M	14	14, 17–21, 23, 26, 30, 35, 36, 39, 45, 60
Refined grains	Refined grains, carbohydrates from refined grains, refined bread	5			4	17, 21, 36, 39
Potatoes	Potatoes, carbohydrates from potatoes	1 1W	1 1M		3	17, 32, 36
Dairy	Dairy general, high-fat dairy, low-fat dairy, milk and cheese, yoghurt		2 2M	3 2W 1M	5	36, 38, 39, 41, 50
Meat	Meat general, poultry, processed meat unprocessed or red meat	6 2W	2 2M	1	8	28, 32, 33, 36, 39, 40, 44, 50
Healthy diet	Index of Mediterranean diet, index of healthy/prudent diet		1	4	5	47–51

M, men; W, women; +, associated with increased weight gain; ns, no association with weight change; –, associated with decreased weight gain (prevention of weight gain).

[1]Some studies included several analyses, either separately for men and women, or for different exposure and/or outcome variables. Therefore, the number of results may be greater than the number of studies.

unsaturated fatty-acid content, enhanced satiety and ineffective absorption of fat (140). Short-term interventions have not shown any effects of nuts on body weight, whereas nut consumption seems to improve blood lipid levels in a dose-related manner (141).

Refined grains, carbohydrates from refined grains and refined bread formed a group called 'refined grain foods'. Four studies included five analyses, and all of them showed an association between high intake of refined grains and increasing obesity. The level of evidence could be regarded as probable, but slightly weaker than the evidence seen for fibre-rich foods. Refined grain products have often high GI, high insulin response and a fast glucose decline even below baseline in an oral test (138). These properties could increase hunger and enhance lipogenesis, thereby promoting obesity (142). The different effects of whole-grain and refined cereals speak for separating different types of cereals in the food pyramid.

Also potatoes have high GI, and therefore it could be plausible to think that they – like refined grains – could induce obesity. The results of our review were not very convincing: two analyses supported the above hypothesis, while two other did not find an association between potato consumption and weight or WC change. It is possible that the way potatoes are prepared is important: Mozaffarian et al. (36) reported a positive association between potato consumption and weight gain, but in this study a majority of the potatoes was French fries.

All dairy products were combined to form a new group called 'dairy foods'. In our 'official' analyses, we found suggestive evidence for a protecting role of high-fat dairy foods. The combined data did not strengthen this result. A total of four analyses showed a positive association between dairy food consumption and increasing obesity, whereas five analyses did not report any associations. If there indeed is an association between dairy products and prevention of weight gain, the proposed mechanisms might be related to calcium, protein or biopeptides (143). More research is needed to find out whether the mechanism could be related to milk fat. Earlier studies have, in contrast, indicated that unsaturated, rather than saturated, fatty acids may promote postprandial fat oxidation and stimulate diet-induced thermogenesis (144). The two studies showing an association between high-fat dairy and less weight gain (38, 50) did not very clearly specify their definition of dairy products, e.g. if only milk products were included. However, butter was apparently not included in either study.

A majority of the studies support the hypothesis that a high consumption of meat and meat products predict more weight gain. This finding might be considered confusing, because of the proposed satiating effects of protein (145). However, meat is energy dense and might thereby increase energy intake (44). It is also possible that meat intake only reflects some undetected dietary or lifestyle patterns that contribute to weight gain (44).

Yet another possibility is that meat increases fat-free mass and that BMI in this case would be misleading. Interestingly, the two studies showing a preventive role for protein or meat used WC as the outcome (17, 33). On the other hand, two studies identified poultry or processed meat as a predictor of larger gains in WC (33, 39).

We found suggestive evidence for an obesity-promoting role of sweets and desserts. Since the contribution of sweets to total energy intake is small (146), a likely explanation for this finding is residual confounding, that is, consumption of sweets probably mirror some other unhealthy dietary and/or physical activity patterns that lead to positive energy balance. In fact, we were rather expecting to find an association between the use of SSSD and weight gain. Out of the identified three studies, two suggested that SSSD predict weight or WC gain (39, 43), but the third (28) found an association only in a subgroup with prior weight gain. Hence, according to our strict rules we had to classify these data as inconclusive. Recent systematic reviews have also produced conflicting results on the association between SSSD and weight gain (8–10). A majority of the results suggesting a positive association between SSSD and weight gain have studied children and adolescents (8, 9). The compilation of different sugar-containing foods into one analysis did not bring any additional insights.

It is perhaps not a surprise that adherence to a presumed healthy diet predicts less weight gain. It is interesting that the Healthy Diet Index is in fact composed of items without any clear association with weight (total fat, saturated fat, dietary cholesterol, salt, carbohydrates) – and yet a diet fulfilling these requirements is at the same time suitable for weight control. The Mediterranean Diet Index is built from foods and many of the 'positive' foods are high in dietary fibre and these foods have in this review been identified as predictors of better weight control. Moreover, meat is considered a 'negative' item in the Mediterranean Diet Index and we found suggestive evidence for meat as a predictor for weight gain. The only discrepancy is related to dairy products which are 'negative' in the Mediterranean Diet Index, but, if anything, protective against weight gain in our review.

Methodological considerations

The criteria for A-grading were very strict. Because of the understandable crudeness of epidemiological methods, all really large studies (e.g. EPIC, Nurses' Health Study, etc.) were classified as B, while some clearly smaller studies sometimes received an A-rating. In the end, this did not have an impact on the analyses, since all studies classified as A or B were included in the summary tables.

Most of the studies identified for this review were prospective cohort designs. Although interventions would be much stronger in identifying causal effects, the possibility to study long-term (5–20 y) weight changes by using an intervention design would be extremely challenging and expensive. All prospective cohort studies need careful control for potential confounders. Although practically all A- and B-graded cohorts in our review were able to control for a multiple of potential confounding variables, residual confounding cannot be ruled out (147). Therefore, it is unclear whether the identified positive or negative associations really are effects of nutrients or foods vs. weight or WC.

One interesting point is whether energy intake should be included in the model. While adjusting for total energy intake may control for over- and under-reporting, energy intake is also a potential mechanism explaining the association between a nutrient/food and weight gain. Therefore, adjusting for energy intake might be regarded as overadjustment, which may dilute the real association between food/nutrient and weight change. For future studies, it would be recommendable to present models with energy intake as the only differing variable (to see if the inclusion of energy intake in the model has an effect on the results). We did not look for a potential association between total energy intake and weight change, since a positive energy balance is too much dependent on the level of total physical activity and energy expenditure. A scrutiny on the interaction between physical activity and diet, against weight change, was also outside the focus of this review.

Measurements of dietary intake and food consumption at baseline are usually inaccurate. Most of the population studies covered in this review used a food frequency questionnaire (FFQ). Although many of the FFQ's have been validated (see Appendix 3–5), the validation was often restricted to certain nutrients. For instance, we are not aware of a FFQ planned to assess GI or dietary density. In addition to inaccurate baseline estimation, an individual's dietary pattern may change during the follow-up. These lead to misclassifications of exposure and to at least some attenuation of association towards unity (type II error). In this light it is interesting to note that there were very few totally conflicting findings (same exposure showing both negative and positive association with the outcome). If some of the non-significant findings were indeed type II errors, there may be in reality more associations between diet and weight change than found in the present review.

Another point – which is in a way opposite to the previous – is that the large number of participants in several studies allows identification of even very small differences between groups (e.g. lowest vs. highest 25%). The practical significance of these differences is uncertain. Most studies have assessed the association between single nutrients and food items against weight change, but aggregating single foods into composite scores yields more robust estimations (36, 39). By combining exposure

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variables (foods) into larger groups, as shown in Table 5, we wanted to improve the robustness of our analysis. To be meaningful, however, even these results should probably be translated into diet-level recommendations.

Many cohorts were initiated more than 10 y ago. This is perhaps not very meaningful for analyses using foods, food groups or dietary patterns. However, since a certain macronutrient composition can be achieved by different food choices, the interpretation of the oldest studies should be done with care: for instance, a certain proportion of carbohydrates and fat in a diet in 1980s might be related to different food choices than a similar macronutrient distribution in 2012. This may also have a relevance to the association between macronutrients and weight gain. Finally, it may relevant to repeat that the review covered publication years 2000–2012, and this may have excluded important older studies. Moreover, although PubMed is a very comprehensive database and it covers all major international medical journals, it is possible that some additional studies could have been identified by using, e.g. EMBASE or Scopus. The potential bias caused by using only PubMed and SweMed+is, however, considered negligible.

Conclusion

In this systematic review covering publications from year 2000 onwards, we found probable evidence for high intake of dietary fibre and nuts predicting less weight gain, and for high intake of meat in predicting more weight gain. Suggestive evidence was found for a protective role against increasing weight from whole grains, cereal fibre, high-fat dairy products and high scores in an index describing a prudent dietary pattern. Likewise, there was suggestive evidence for both fibre and fruit intake in protection against larger increases in WC. Also suggestive evidence was found for high intake of refined grains, and sweets and desserts in predicting more weight gain, and for refined (white) bread and high energy density in predicting larger increases in WC. When foods with similar nutrient composition were combined for an unofficial analysis, fibre-rich foods in general predicted less weight gain and this association could be regarded as moderately strong (probably). The associations between foods and dietary patterns vs. weight gain were stronger compared to those between macronutrients vs. weight gain. In general, the results suggest that the proportion of macronutrients in the diet is not important in prevention of obesity. In contrast, plenty of fibre-rich foods and dairy products, and less refined grains, meat and sugar-rich foods and drinks were associated with less weight gain in prospective cohort studies.

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Appendix 1

Search terms:

Set I

(1) Dietary carbohydrates.mesh. OR
(2) Dietary fats.mesh. OR (as free text) 'saturated fats' OR 'monounsaturated fats' OR 'polyunsaturated fats' [TI, AB] OR
(3) Fatty acids, unsaturated.mesh. OR
(4) Proteins.mesh. OR
(5) Dietary fiber.mesh. OR
(6) Energy intake.mesh. OR
(7) Diet, Carbohydrate-Restricted.mesh. OR
(8) Diet, fat-restricted.mesh. OR
(9) Diet, Mediterranean.mesh. OR
(10) Diet, Protein-restricted.mesh. OR
(11) Diet, vegetarian.mesh. OR
(12) Ketogenic diet.mesh.

AND

Set II

(1) Body weight.mesh. (narrower terms: overweight.mesh., including obesity.mesh.) OR
(2) Waist-Hip Ratio.mesh. OR 'waist girth' OR
(3) Waist Circumference.mesh. OR
(4) Body composition.mesh. (incl. narrower term: body fat distribution.mesh. and adiposity.mesh.) OR
(5) Adipose tissue.mesh. (incl. narrower term: abdominal fat.mesh.) OR 'body fat' OR
(6) body mass index.mesh. OR 'fat mass'

AND

Set III

maintenance* OR gain* OR regain* (cannot use too common words, like: change OR changes OR changing)

Set I and Set II and Set III = Group I

Set IV

weight gain.mesh.
OR
'weight gain' OR 'Gain, Weight' OR 'Gains, Weight' OR 'Weight Gains' [TI, AB]

Set I AND Set IV = Group II

Group I
OR
Group II

AND

RCT. PT OR mesh
OR
cohort studies.mesh. (incl. term: longitudinal studies.mesh. OR prospective studies.mesh.)
OR
intervention studies.mesh.
OR

Citation: Food & Nutrition Research 2012, **56**: 19103 - http://dx.doi.org/10.3402/fnr.v56i0.19103

meta-analysis, mesh OR pt
OR
'systematic review' OR 'systematic reviews' OR 'Cochrane database syst rev'
OR 'randomised controlled' OR 'randomised controlled' OR meta-analysis
human, 2000

Appendix 2

Reasons for excluding full papers ($n = 78$) from the quality grading

References	Reason for exclusion
Anderson et al. (62)	Macronutrient data not shown
Astrup (5)	Review, but concentrates on weight reduction only (not on weight management)
Astrup et al. (63)	Concentrates on weight reduction only
Ayyad et al. (64)	No macronutrient data, review on weight loss mainly
Azadbakht et al. (65)	Weight reduction only
Bes-Rastrollo et al. (66)	Cross-sectional study
Borg et al. (67)	Originally included in the evaluation but excluded from quality grading: no data on food vs. weight change in a prospective design
Brown et al. (68)	Originally included in the evaluation but excluded from quality grading: the review concentrated on weight reduction interventions with special diets
Burke et al. (70)	No macronutrient data
Burke et al. (69)	Weight reduction only
Burke et al. (71)	Physical activity and nutrition combined, not clear maintenance phase
Cardillo et al. (72)	Originally included in the evaluation but excluded from quality grading: weight loss was different between the groups initially
Carels et al. (73)	Weight reduction only
Carnethon et al. (74)	No results on weight change, MBO as an outcome
Carty et al. (75)	Originally included in the evaluation but excluded from quality grading: same data as Howard et al. (18), but this is a subset with a smaller number of cases
Chen et al. (76)	Weight reduction only
Cheskin et al. (77)	Meal replacements, weight reduction only, no dietary data
Clifton et al. (78)	Weight reduction only
Davis et al. (79)	Meal replacements, weight reduction only, follow-up less than 6 months
Ditschuneit et al. (80)	Meal replacements, weight reduction only
Djuric et al. (81)	Originally included in the evaluation but excluded from quality grading: effects on body weight varied by groups during the first 3 months of the intervention; weight reduction study
Due et al. (82)	Weight reduction only
Duffey et al. (83)	Only eating patterns, no macronutrient data
Eckel et al. (84)	No dietary data
Farshchi et al. (85)	Experimental study, focused on meal pattern and thermic effect of food
Flechtner-Mors et al. (86)	Meal replacements, weight reduction only
Forshee et al. (10)	Originally included in the evaluation but excluded from quality grading: review
French et al. (87)	Originally included in the evaluation but excluded from quality grading: study on visits to fast food restaurants and dietary, behavioural and demographic correlates
Gibson (8)	Originally included in the evaluation but excluded from quality grading: review
Greene et al. (88)	Originally was included in the evaluation but excluded from SLR: weight loss was different between the groups initially
Hensrud (89)	Not a systematic review
Hoy et al. (90)	Study on cancer patients
Jehn et al. (91)	Physical activity and nutrition combined
Karnehed et al. (92)	Originally included in the evaluation but excluded from quality grading: dietary data were collected only at follow-up, not at baseline

Appendix 2 (*Contiuned*)

References	Reason for exclusion
Kaukua et al. (93)	No dietary data
Keogh et al. (94)	Weight reduction only
Kristal et al. (95)	No results on weight change
Kuller et al. (96)	Physical activity and nutrition combined
Lantz et al. (97)	Weight reduction only, comparisons between VLCDs
Layman et al. (98)	Weight reduction only
Lejeune et al. (99)	Originally included in the evaluation but excluded from quality grading: dietary intake not assessed, except for protein intake by urine analysis. Protein supplement used to increase protein intake
Leser et al. (100)	Originally included in the evaluation but excluded from quality grading: very small sample size, dietary intake assessed only in the end of the study, only fat-intake reported, PA assessed, but not used to adjust the results
Lindstrom et al. (101)	Physical activity and nutrition combined
Macdonald et al. (102)	Macronutrient data not shown
Malik et al. (9)	Originally included in the evaluation but excluded from quality grading: review
Marinilli Pinto et al. (103)	Study on counseling, only weight loss results
McAuley et al. (104)	Weight reduction only
Moore et al. (105)	Description of a study, no results included
Moran et al. (106)	Meal replacements, weight reduction only
Mozaffarian et al. (107)	No results on weight change
Ochner et al. (108)	Macronutrient data not shown, mixed race
Packianathan et al. (109)	No macronutrient data, meal replacements, weight reduction only
Palmer et al. (110)	Race: African-American, weight not an outcome
Poppitt et al. (111)	Weight reduction only, short follow-up (6 months)
Raynor et al. (112)	Exercise intervention, study on weight loss, no clear data on macronutrients
Razquin et al. (113)	Originally included in the evaluation but excluded from quality grading: the participants were mostly overweight and obese and had high-risk for cardiovascular diseases; e.g. Type 2 diabetes was an inclusion criteria
Redman et al. (114)	Weight reduction only
Riebe et al. (115)	Physical activity and nutrition combined
Sacks et al. (116)	Weight reduction only
Saris (117)	No dietary intake data
Saris et al. (118)	Weight reduction only
Sasaki et al. (119)	No results on weight change
Schoeller et al. (120)	Study on CLA treatment, no diet, weight reduction only
Sichieri et al. (121)	Originally included in the evaluation but excluded from quality grading: this is a weight reduction study
Simkin-Silverman et al. (122)	Physical activity and nutrition combined
Sloth et al. (123)	Originally included in the evaluation but excluded from quality grading: same database as in Due et al. (82) but fewer cases
Steptoe et al. (124)	No results on weight change, multiple interventions
Stookey et al. (125)	Race: only Asian (Chinese)
Stote et al. (126)	No macronutrient data, study on meal frequency
Svetkey et al. (127)	No macronutrient data, mixed race
Thorpe et al. (128)	Weight reduction only
Turk et al. (129)	Originally included in the evaluation but excluded from quality grading: review
Turner-McGrievy et al. (130)	Weight reduction only
van de Vijver et al. (131)	Cross-sectional design
Vang et al. (132)	No results on weight change, no macronutrient data
Wang et al. (133)	Data on alcohol consumption only
Whigham et al. (134)	Study on CLA treatment, no diet, weight reduction only
Woo et al. (135)	Race: only Asian (Chinese)

Appendix 3
Evidence tables

Table 1. Macronutrients and prevention of weight gain

Reference details, First author, Year, Country	Study design (RCT, CT, cohort, case control etc.)	Population, subject characteristics, Inclusion/exclusion criteria, setting, no. at baseline, male/female, age, ethnicity of the subjects, anthropometry, location	Outcome measures Disease, biological measures	Intervention/exposure	Time between baseline exposure and outcome assessment	Dietary assessment method FFQ, food record Internal validation (y/n)	No of subjects analysed	Intervention (I) (dose interval, duration), Control (C) (active, placebo, usual care etc), compliance, achieved dietary change, adherence to dietary targets, actual dietary change	Follow-up period, drop-out rate (from baseline to follow-up, or from end of intervention to follow-up) Drop out (%)	Results (I, C) (Absolute difference, RR, OR, *p*-value, confidence interval, sensitivity, specificity, observer reliability? etc.)	Confounders adjusted for	Study quality and relevance, Comments (A–C)
Bes-Rastrollo, 2008, US (12)	Cohort	Nurses' health study, 116,671 women, age 36.5 (4.6) y Excluded at baseline (1991) if did not complete FFQ, if they reported EI (<500 or >3,500 kcal/day), history of diabetes or CVD, cancer before 1999 (post test), pregnancy at any time from baseline to post test, no PA data assessed in 1991 and 1997, only baseline data, missing Wt data. Final $n=51,188$.	Wt gain (self-report).	Change in dietary ED (defined as the amount of energy in a given weight of food).	8 y	133-item FFQ	$n=50,026$		8 y. Dropout 57%.	W who increased dietary ED during follow-up the most had a significantly greater weight gain than those who decreased ED the most: 6.42 vs. 4.57 kg (p for trend <0.001).	Age, baseline alcohol intake, PA, smoking, postmenopausal hormone use, oral contraceptives, cereal fibre intake, TFA intake, baseline BMI, change in intake of SSSDs and changes in confounders between time periods.	B Weight self-reported. Details of dietary assessments were lacking in this report, although they have been reported earlier. The comparability of this population (nurses from the US) and Nordic population is not clear.

Du, 2009; Italy, UK, The Netherlands, Germany, Denmark (13)	Cohort	Eight cities/counties in Italy, UK, The Netherlands, Germany and Denmark (EPIC), age 20–78 y, $n=146,543$ at baseline (1992–1998), $n=102,346$ at follow up (1998–2005), excl. pregnancy, missing information on diet, anthropometry or follow-up time, EI/BMR in the top or bottom 1% of EPIC population, unrealistic anthropometric measures, history of cancer, diabetes or CVD at baseline.	Changes in wt and WC. Measured at baseline and two centres also at follow-up. Otherwise self report.	Dietary ED	6.5 (1.9–12.5) y	Country-specific FFQ, self-administered at baseline. Intake calculated using country-specific food composition tables. ED calculated as EI from food divided by the weights of these foods. Drinks (water, alcohol, milk) not included.	$n=89,432$ (42% M)	6.5 (1.9–12.5) y	ED was not associated with weight change, but significantly with WC. For 1 kcal/g ED annual WC change was 0.09 cm/y (95% CI: 001–018)	Age, sex baseline wt, ht and WC, smoking, PA, education, follow-up time, alcohol, EI from beverages for women: also menopausal status and hormone use.	B Large multi-centre study with large variation in results between centres which are difficult to adjust for even though advanced statistical techniques are used. Variation between measured and self-reported body wt.
Du, 2010, the Netherlands (five countries) (14)	Cohort	Eight cities/counties in Italy, UK, The Netherlands, Germany and Denmark (DiOGenes), age 20–78 y, $n=146,543$ at baseline (1992–1998), $n=102,346$ at follow up (1998–2005), excl. pregnancy, missing information on diet, anthrop, or follow-up duration, EI/BMR in the top or bottom 1% of EPIC population, unrealistic anthrop measures, presence of chronic diseases; baseline BMI 25.5–26.7 kg/m^2 for M and 24.4–25.8 kg/m^2 for W, WC 90–95 cm for men and 77–86 cm for women.	Change in wt and WC; measured wt, ht and WC at baseline and in 2 (out of 8) centres at follow-up, self-reported in six centres	Fibre intake: total, cereal fibre, and fruit and vegetable fibre	6.5 y (1.9–12.5 y)	Country-specific FFQs at baseline. For validation reference, see the original article. Enzymatic-gravimetric method (AOAC) to define dietary fibre, except in UK where defined as non-starch polysaccharides using Englyst method	$n=89,432$ (42% M)	6.5.y on average Drop-out 31.2%	10 g fibre intake associated with −39 g (95% CI: −71 to −7 g) wt change/year and −0.08 cm (−0.11, −0.05 cm) change in WC/y, 10 g cereal fibre assoc with −77 g (−127, −26 g) wt change per year, −0.10 cm (−0.18, 0.02 cm) change in WC/y.	Age, sex, baseline wt, ht and WC, smoking, PA, education, alcohol, GI, intake of protein, fat and CHD, total EI, in W menopausal status and hormone use.	B

Field 2007, US (15)	Cohort	Registered nurses, W aged 41–68 y at baseline (1988), $n=41{,}518$, incl.free of CVD, cancer and diabetes at baseline, postal follow-up questionnaires every 2 y, race not reported, baseline BMI 25.0 kg/m^2.	Wt change, BMI in 1994; self-reported wt.	Baseline fat intake (E%), average intake and 8 y change in intake + animal fat/ vegetable fat + PUFA, SFA, trans fats.	8 y	136-item FFQ For validation reference, see the original article.	$n=41{,}518$	8 y. Drop out rates, or number of subjects that were excluded not reported.	beta for 1% difference (substituting 1% of calories from fat for 1% of calories from CHD) baseline fat intake B = 0.11 ($p<0.0001$), PUFA 0.42, SFA 0.40 and TFA 0.54.	Baseline BMI, age, PA, time spent sitting, smoking, menopausal status and protein%.	B Number of subjects 1/3 of the original sample (1976), no data on representa-tiveness of the data, dietary assessment methods poorly described.
Forouhi, 2009, UK (total five countries) (16)	Cohort	EPIC (see Du 2010), $n=146{,}543$, eligible participants 89,432 (58% W), exclusion criteria see Du 2010, mean age 42.5–58.1 y in six cohorts, baseline BMI 26.3 kg/m^2 for M and 25.3 kg/m^2 for W, WC 94.4 cm for M and 80.3 cm for W	Annual change in wt (and WC); measured wt and ht at baseline and in 2 (out of 8) centres at follow-up, self-reported in six centres	Amount and type of diet-ary fat	3.7–10.0 y	Country specific FFQ, habitual intake of medium-sized serving of foods over the past year, in a subsample, also a standardised 24 h recall by using EPIC SOFT. For validation reference, see the original article.	$n=89{,}432$ (58% W)	3.7–10.0 y. No follow-up data available	Weight change 0.90 g/y (95% CI: −0.54 to 2.34) for men and −1.30 g/y (−3.70 to 1.11) for women per 1 g/day energy-adjusted fat intake, a null association for PUFA; MUFA; WC and fat: no significant associations between any fat type and wt change	baseline wt and ht, EI follow-up period, PA, smoking, education, alcohol, protein	B
Halkjaer 2006 (17)	Cohort	50- to 64-y-old M and W living in greater Copenhagen or Aarhus area, random sample. Exclusion: cancer. Baseline $n=54{,}379$, WC 80.0 cm for W and 95.0 cm for M, BMI 24.7 kg/m^2 for W and 26.1 kg/m^2 for M.	Change in WC	Total EI, EI from macronutri-ents, EI from macronutri-ent subgroups based on different food sources.	5 y	192-item FFQ	$n=44{,}817$ (55% W)	5 y. Drop out rate 17.4%.	Neither total EI nor EI from each of the macronutrients was associated with changes in WC, except for an inverse association with protein, especially animal protein. In women, positive associations with changes in WC were seen for CHD from refined grains and po-tatoes and from foods with simple sugars, whereas	Baseline WC, BMI, age, smoking, alcohol, sporting activity, other macronutrients than the one analyzed, energy intake.	B Follow-up wt and WC were self-reported. Power not reported, but apparently adequate.

										carbohydrate from fruit and vegetables was inversely associated and significantly different from any other CHD subgroup. Vegetable fat was positively associated with changes in WC for both M and W.		
Howard, 2006, US (18)	RCT (interven-tion, trial)	$n=56,139$ that provided consent and met >32 E% of fat criterion, of that 7,304 were excluded (e.g. nutritionist judgement, medical condition, eating out), $n=48,835$ that were randomised to intervention ($n=19,541$) and con-trol ($n=29,294$), aged 50–79 y. Mixed race reflecting the characteristics of the general population in US, (non-Hispanic white analysed separately).Baseline BMI 29.1 kg/m^2 and WC 89.0 cm in both groups (I and C).	Mean wt change across follow-up; measured wt, ht, waist and hip.	Reduction of total fat to 20 E% and increase of vegetable and fruit intake to five or more servings and grains six or more servings daily.	Mean follow-up 7.5 y, randomisation between 1993–1998, anthropometric and nutrition data until August 2004.	Women's Health Initiative FFQ at baseline and I y+every 3 y.	$n=14,246$ for Ion and $n=22,083$ for C	See Carty 2010 for intervention; baseline 38.8 E% from fat in I and C, 29.8/38.1 E% at follow-up, SFA: 13.6 E% at baseline, 10.1/13.2 E% at follow-up, CHO: 44.5 E% at base-line, 52.7/44.7 E% at follow-up, fibre: 14.4 g at baseline, 16.9/14.4 g at follow-up.	Mean follow-up 7.5 y; 2,092 (4.3% of C group, 4.3% of I group) were deceased, 1,309 (2.5% C, 2.9% I) stopped follow-up, 670 (1.2% C, 1.6% I) were lost to follow-up.	Decrease in wt 2.2 kg in the I group at year 1 and mean wt 2.2. kg less than in C. A significant difference between I and C (0.5 kg, $p=0.01$) maintained through year 9; W with the greatest reduction in fat intake had the argest wt loss (p for trend <0.001 both for I and C)	Age, race, BMI at baseline, change in dietary intake and PA patterns; secondary ana-lyses adjusted for EI.	A
Iqbal 2006, Denmark (19)	Cohort	Danish citizens living in the western part of Copenhagen County, recruited and examined in 1976 (the 1936 cohort) and 1982 (MONICA), follow-up in 1981 and 1987, respectively, $n=20$, 25 M and W aged 30, 40, 50 and 60 y at baseline, exclusion because of missing	Wt change; ht and wt measured at baseline and follow-up.	Dietary components, ED in particular.	5 y	Weighed 7-day food record at baseline. No data on database, ED calculated including the water content as follows: energy from CHO+prot+fat+alcohol (MJ) divided by	$n=862$ M and $n=900$ W.		Only participation rate reported: ≥79%; in that case assuming that drop- out rate must be less than 21%.	ED not associated with wt change for either sex; in W, protein intake (E%) positively (B=3.87, SE 1.91, $p=0.04$) and fibre intake (g) inversely (B=−22.8, SE 10.6, $p=0.03$) associated with wt change in crude but not in adjusted ($p=0.06$/0.10) analyses.	Age, BMI, PA, educational level, smoking, EI (baseline variables)	A

		information or extreme values, baseline BMI 25.1 kg/m^2 for M and 23.4 kg/m^2 for W.				weight of CHO + prot + fat + alcohol + fibre + ash + water (g)					
Koh-Banerjee, 2003, US (20)	Cohort	The Health Professionals' Follow-up Study with 51,529 male health professionals aged 40–75 y. At baseline in 1986, 17,584 excluded because of death or medical condition, 17,358 because of missing information, final sample 16,587, baseline BMI 24.9–25.2 kg/m^2 (varied across age groups).	Change in WC, self-reported wt and ht (biannual question-naires), self-reported WC with a sent tape measure in 1987 and 1996.	Changes in diet and macronutri-ents	9 y	131-item, semi-quantitative FFQ to assess typical food intake over the previous year, collected in 1986, 1990 and 1994. US Dept of Agriculture, Composition of foods – raw, processed and prepared 1963–1988. Validated among a subset of the study participants. See the original article for the literature reference.	$n = 16{,}587$ M	Reported follow-up rate 65%.	A 2% increment in EI from TFA substituted for PUFA of CHO associated with a 0.77 WC gain, an increase in fibre (12 g/day) predicted WC reduction of 0.63 cm.	Age, baseline WC and BMI, baseline and changes in total EI, alcohol consumption and PA, and changes in smoking; also changes in BMI for investigating associations independent of wt gain	B
Liu, 2003, US (21)	Cohort	Nurses' health study, female nurses ($n = 81{,}757$) aged 38–63 y were followed from 1984 to 1996, exclusion because of diabetes, CVDs or cancers, final baseline population 74,091, baseline BMI 24.5–24.9 kg/m^2 (reported according to quintiles of intake of whole-grains at baseline).	Changes in body wt, self-reported wt every 2 y.	Fibre intake, consumption of whole-grain and refined-grain foods.	12 y	126-item semi-quantitative FFQ 1984, 1986, 1990 and 1994 (average consumption during the previous year). No information on database. See original article for the validation literature reference.	$n = 74{,}091$	Drop-out rates not reported.	Increase in whole grain intake (average wt gain in 2–4 y 1.23 ± 0.02 kg in the highest and 1.52 ± 0.02 kg in the lowest quintiles) and fibre intake (0.97 ± 0.02 kg and 1.73 ± 0.02 kg respectively) associated with less wt gain (p for trend < 0.0001), increase in refined grain intake associated with great-er weight gain (1.57 ± 0.03 kg and 1.14 ± 0.03 kg, $p < 0.0001$); 12 y follow-up: greatest increase (the highest quintile of change)	Age, y of follow-up, change in PA, smoking status, hormone replacement therapy, intakes of alcohol, caffeine and total EI.	B The number of participants at follow-up not reported, physical activity level information from year 1982 but no information on the measurement

									in fibre 1.52 kg (5.16 ± 0.09 kg vs. 3.64 ± 0.09 kg less wt gain than those with the smallest increase (the lowest quintile)		
Mosca, 2004, US (22)	Cohort	A geographically based (San Luis Valley, Colorado) sample (n = 1,351) aged 20–74 y, no history of diabetes, only subjects with normal glucose tolerance included (n = 1,027), exclusions during follow-up because of type 2 diabetes/IGT/IFG, pregnancy, change in smoking status, total n = 782 at baseline: non-Hispanic white M(n = 213) and W (n = 267), Hispanic M (n = 136) and W (n = 166), baseline BMI 25.7 kg/m^2 for M and 24.3 kg/m^2 for W.	Wt change, measured wt and ht	Energy from fat (E%)	11.2 y	24-h recall Nutrition Coordinating Center's nutrient database at University of Minnesota, version 14 (1987)	n = 782 at baseline		The second visit after 4.9 y and the third visit after 11.2 y, visit 1: n = 782, visit 2: n = 536 (68.5%), visit 3: n = 375 (48%), i.e. drop-out 52%	Association between %FAT and estimated wt change was illustrated in a figure showing that wt gain was larger if E% fat 45 vs. 25 (interaction time* %fat from linear mixed model B = 0.013, p = 0.0103), the relationship stronger in W (interaction p = 0.0002) than in M (p = 0.76).	Gsex, ethnicity, baseline PA, baseline BMI, age, smoking, total energy intake	C Small sample size with a high drop-out rate, includes Hispanic subjects, dietary assessment based on 24 h recalls
Romaguera, 2010, Europe (23)	Cohort	EPIC participants who were involved in DiOGenes –project, eight centres from five countries (Italy, Netherlands, Germany, Denmark, UK). Exclusion: pregnancy, chronic diseases, age >60 at baseline, smoking status changed during follow-up. Participants: 19,694 M and 28,937 W. These were selected from 102,346 participants with	WC, adjusted to BMI by residuals.	Dietary ED without drinks, GI and GL.	Median follow-up 5.5 y	Country-specific FFQ. National food composition tables. ED was calculated from solid, semi-solid and liquid foods, but not from drinks. GI database was specially developed using mainly published information. FFQ validation has been	n = 19,694 M and n = 28,937 W.		Median follow-up 5.5 y. Drop-out 30.2% from baseline.	1 kcal/g greater ED predicted a increase in WC of 0.09 cm (95% CI: 0.05–0.13) in M and 0.15 cm (0.09, 0.21) in W; 10 units greater GI predicted an increase in WC of 0.07 cm (0.03, 0.12) in M and 0.06 cm (0.03, 0.10) in W. Among W, lower fibre intake, higher GL, and higher alcohol consumption also predicted a higher WC.	All models: age, baseline wt, ht, and WC, smoking, alcohol, PA, education, menopausal status, etc. Further: Energy from drinks (in the model with ED as the independent variable), total EI (macronutrients), fibre and macronutrients	B Slight variations in the anthropometric techniques between the centres and time-points. Statistical power was not calculated, but appears to be clearly adequate.

		results on both baseline and follow-up.				reported earlier (see the original article for the literature reference)					(GI), fibre, fat, protein and E (GL), GI and macronutrients (fibre).	
Savage, 2008, US (24)	Cohort	White non-Hispanic W ($n=192$) living in Pennsylvania recruited as part of a longitudinal study designed to examine parental influences, eligibility criteria focused on daughters' characteristics, none for mothers (=participants), exclusions because of missing data on wt, final sample ($n=186$), age range 24.1–48.8 y at baseline, baseline BMI 26.9 kg/m^2.	Wt and BMI change, wt and ht measured at each occasion (4 ×, 2 y intervals).	Dietary ED, kcal/g; excluding beverages.	6 y	3 ×24 h recall interviews by telephone within a 2- to 3-week period at each occasion. Nutrition data system for research, University of Minnesota (version 4.01_30); ED (kcal/g) =total energy intake from the food (beverages excluded) divided by the total weight of food.	$n=186$ W		Data collected on four occasions across a 6 y period, at study entry 192 W of whom 183, 177 and 168 reassessed at y 2, 4 and 6. Drop out rate 12%.	ED* time interaction ($p<0.01$): W consuming higher ED diets (ED >1.85 kcal/g) gained more wt (on average 6.4±6.5 kg over 6 y) than W with lower ED diets (ED <1.5 kcal/g) 2.5±6.8 kg.	Initial BMI, dietary fibre intake, caloric beverage intake	C PA not assessed at all, analyses not adjusted for age, total EI, fat E% and CHO E% varied across ED groups.
Sherwood, 2000, US (25)	Randomised trial, but data analysed as a cohort.	Participants for the Pound of Prevention study recruited by direct mailing, newspaper and radio ads etc, free of major chronic diseases, aged 20–45 y, predominantly white. Data derived from 826 W and 218 M (93% of total sample enrolled at baseline) who completed the baseline and at least one of the 3 annual follow-up assessments, baseline BMI 28.0 kg/m^2 for M and 26.8 kg/m^2 for W.	Wt change, body wt and ht measured at baseline and annually.	Macronutrient intake (and PA); total EI, E% from fat and from alcoholic beverages presented in this paper.	3 y	60-item version of Block FFQ to estimate usual dietary intake during the past y. Validation has been reported earlier (see the original article for the literature reference)	$n=826$ W, $n=218$ M	Participants randomised to one of two mail-based educational programs or to a no-contact control group; however, in this paper data analyses as one cohort, in analyses subjects were divided in weight gainers (>5 lb wt gain), wt maintainers	826 W, 218 M at baseline, 759 W and 198 M at y 3.	Increases in E% from fat associated with increases in body wt (coefficient 0.068, SE 0.034, $p=0.045$ in M and coeff. 0.028, SE 0.014, $p=0.042$ in W); no sign differences in mean changes in dietary intake across wt change status (loser, gainer, maintainer).	Age, smoking status, treatment group, baseline wt (and baseline value on respective dependent variables).	B Unable to assess the quality of dietary assessment method without original references for the method.

								(lost/gain ≤5 lb) and wt losers (lost >5 lb).				
Tucker, 2009, US (26)	Cohort	Participants recruited via newspaper adds, flyers and company mass e-mail in two metropolitan areas in the Mountain West, US, eligibility tested by telephone interviews (free from serious diseases, non-smokers, premenopausal, not pregnant), at baseline $n=275$ W, mean age 40.1 y, baseline BMI 24.0 kg/m^2.	Wt and body fat; measured wt at baseline and follow-up, body fat% measured by using air displacement plethysmography the Body Pod.	Fibre intake.	20 months	7-day weighted food records at baseline and follow-up. USDA database and other food databases using ESHA Research software (version 7.6). Women were weighed before and after the week of diet recording to make sure that there was no significant weight change during the week of recording	$n=252$		Complete follow-up data available from 252 W. Drop out 8%.	For each 1 g increase in fibre intake wt decreased by 0.25 kg ($p=0.0061$) and fat decreased by 0.25%-point ($p=0.0052$). Baseline fibre intake was not associated with wt change.	Age, season of assessment, baseline body fat and fibre intake, baseline and changes in fat intake, EI and PA.	A

W, Women; M, Men; Wt, Weight; Ht, Height; WC, Waist circumference; PA, Physical activity; BMI, Body mass index; EI, Energy intake; ED, Energy density; TFA, Trans fatty acids; CHO, Carbohydrates; MUFA, Monounsaturated fatty acids; PUFA, Poly-unsaturated fatty acids; GI, Glycemic index; GL, Glycemic load; Y, Years.

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Appendix 4
Evidence tables

Table 2. Foods and prevention of weight gain

Reference details, First author, Year, Country	Study design (RCT, CT, cohort, case control etc.)	Population, subject characteristics, Inclusion/exclusion criteria, Setting, No at baseline, Male/Female, Age, Ethnicity of the subjects, Anthropometry, Location	Outcome measures Disease, biological measures	Intervention/exposure	Time between baseline exposure and outcome assessment	Dietary assessment method FFQ, food record Internal validation (y/n)	No of subjects analysed	Intervention (I) (dose interval, duration) Control (C) (active, placebo, usual care etc), compliance, achieved dietary change, adherence to dietary targets, actual dietary change	Follow-up period, drop-out rate (from baseline to follow-up, or from end of intervention to follow-up) Drop out (%)	Results (I, C) (Absolute difference, RR, OR, *p*-value, confidence interval, sensitivity, specificity, observer reliability? etc)	Confounders adjusted for	Study quality and relevance, Comments (A–C)
Bazzano, 2005, US (27)	Cohort	Male physicians, 40–84 y in 1982 $n=22{,}066$. Free of CVD, DM and cancer at baseline.	Risk of overweight and wt gain.	Whole and refined grain breakfast cereal intakes.	8 and 13 y	Semiquantitative FFQ.	$n=17{,}881$		8 and 13 y. Dropout $n=635$ (illness), in addition 16.6% lack of breakfast cereal intake information.	RR: 0.78 (8 y) and 0.88 (13 y) M who never or rarely consumed breakfast cereals versus those who consumed $>=1$ serving per day. Consumers of breakfast cereal consistently weighed less than those who consumed cereals less often (p for trend $=0.01$).	Age, smoking, baseline BMI, alcohol, PA, history of hypertension, high cholesterol and use of multivitamins. Also adjustment to fruit, vegetables and dairy: no change in results.	B Semi qualitative FFQ assessed a limited number of foods. Unable to compare breakfast cereal intake to other types of breakfast foods or to skipping breakfast.
Bes-Rastrollo, 2006, Spain (28)	Cohort	University graduates, 7,194 M and W 37 ($\pm$12) y Excl. those who reported total EI ($<$800 or $>$4,200 kcal/day for men and $<$600 or 3,500 kcal/day for women).	Wt change (self-reported). Validated self-report 1.5% mean relative error compared to objective measurement.	Sugar-sweetened soft drinks (SSSD) or consumption of hamburger, pizza, and sausages (HPS). Analyses were also made for red	Median 28.5 months.	Semiquantitative FFQ (136 food items) Validated, see the original article for the reference.	$n=7{,}194$		28.5 month follow-up with $>$90% follow-up rate.	SSSD was associated with wt gain only in subgroup assessment: those who had reported a previous wt gain ($>=$ 3 kg; during the 5 y before this study baseline). Consumption	Sex, total EI from non-SSD sources, fibre, alcohol, milk, PA, smoking, snacking, TV, and baseline wt	B Weigh self-reported. Details of dietary assessments were lacking in this report, although they have been reported earlier. The

				meat and sweetened fruit juice.					of HPS was associated with higher wt gain, independent of consumption of SSSD and of previous wt gain. Fifth compared with the first quintile: OR 1.2 (1.0–1.4; *p* for trend =0.05) Red meat and sweetened fruit juice consumption were not significantly associated with wt gain.		comparability of this population (students from Spain) and Nordic population is not clear.
Bes-Rastrollo, 2006, Spain (29)	Cohort	University graduates, 9,000 M and W37 (±12) y Excl. those who reported total EI (<800 or >4,200 kcal/day for men and <600 or 3,500 kcal/day for women).	Wt gain or likelihood of becoming overweight/obese.	Olive oil consumption.	Median 28.5 months.	Semiquantitative FFQ (136 food items). Validated, see original article for the reference.	*n* =7,368	28.5 month follow-up with >90% follow-up rate.	No significant association between baseline consumption of olive oil and subsequent wt change, nor to the risk of developing overweight and obesity.	Age, sex, total EI, vegetable consumption, PA, smoking, snacking between meals, TV viewing, and baseline BMI.	B Wt self-reported. Details of dietary assessments were lacking in this report, although they have been reported earlier. The comparability of this population (students from Spain) and Nordic population is not clear.
Bes-Rastrollo 2007, Spain (60)	Cohort	University graduates, 9,000 M and W37 (±12) y Excl. those who reported total EI (<800 or >4,200 kcal/day for men and <600 or 3,500	An increase in body wt of at least 5 kg during follow-up. Change in body wt during follow-up. Incident	Nut consumption =walnuts, almonds, hazelnuts, and peanuts.	Median 28 months.	Semiquantitative FFQ (136 food items) Validated, see original article for the reference.	*n* =8,865	Median 28 months., Drop-out 24.3%.	Participants who ate nuts two or more times per week had a significantly lower risk of wt gain (OR: 0.69; 95% CI: 0.53–0.90, *p* for	Sex, baseline BMI, PA, smoking, snacking, television watching.	B Wt self-reported. Details of dietary assessments were lacking in this report,

		kcal/day for women). Baseline $n=11{,}714$.	overweight/ obesity						trend $=0.006$) than those who never or almost never ate nuts. Participants with little nut consumption (never/almost never) gained an average of 424 grams (102,746) more than frequent nut eaters.		although they have been reported earlier. The comparability of this population (students from Spain) and Nordic population is not clear.
Bes-Rastrollo 2009, US (30)	Cohort	Nurse's health study, 116,671 W, age 36.5 ($\pm$4.6) y Excl. at baseline (1991) if did not complete FFQ, if they reported EI ($<$500 or $>$3,500 kcal/day), history of diabetes or CVD, cancer before 1999 (post test), pregnancy at any time from baseline to post test, no PA data assessed in 1991 and 1997, only baseline data, missing wt data.	Weight gain (self-report)	Total nut consumption $=$sum of intakes for peanuts, including peanut butter, and other nuts.	8 y	133-item FFQ Validated, see original article for the literature reference	$n=51{,}188$	8 y. Drop out 56%.	Greater nut consumption ($>$ or $=$2 times/ week compared with never/almost never) was associated with a slightly lower risk of obesity (hazard ratio: 0.77; 95% CI: 0.57–1.02; p for trend $=0.003$).	Age, alcohol, PA, smoking, postmenopausal hormone use, oral contraceptives, baseline BMI, GL, intakes of several dietary components at baseline.	B Wt self-reported. Details of dietary assessments were lacking in this report, although they have been reported earlier. The comparability of this population (nurses from the US) and Nordic population is not clear
Du 2009 (31)	Cohort	Five European countries (Denmark, Germany, Italy, The Netherlands and the UK; DioGenes). A total of 89,432 participants, aged 20–78 y (mean $=$53 y) at baseline.	Wt and WC.	Dietary GI and GL	1.9–12.5 y (mean $=$6.5 y)	Country-specific FFQs at baseline. Enzymatic-gravimetric method (AOAC) to define dietary fibre, except in UK where defined as non-starch polysaccharides using Englyst method	$n=89{,}432$	Median follow-up 6.5 y (range: 1.9 to 12.5 yrs). Drop out 30.2%.	With every 10-unit higher in GI, wt increased by 34 g/y (95% CI: -47 to 115) and WC increased by 0.19 cm/y (0.11, 0.27). With every 50-unit higher in GL, wt increased by 10 g/y (-65, 85) and WC increased by 0.06 cm/y (-0.01, 0.13).	Baseline anthropometrics, demographic and lifestyle factors, follow-up duration and other dietary factors.	B Variation in methods to measure wt and WC (partly self-assessed or reported, variation between the centres), drop-out exceeding 20%.

						Validated earlier for total energy, carbohydrates, dietary fibre and main carbohydrate-containing foods, reported in several earlier papers. See original article for the literature reference					
Halkjær 2004, Denmark (32)	Cohort	Danish M and W, aged 30, 40, 50 or 60 y, randomly selected and representative of Copenhagen County. Attendance at baseline 3,875 (1,845 W, 1,940 M) and at follow-up 2,436 (1,200 W, 1,236 M). Median BMI at baseline 25.2 kg/m^2 in M and 23.5 kg/m^2 in W.	WC	Different food and beverage groups (11 groups).	6 y	26-item FFQ Validated against diet history. The results showed positive correlations.	$n=2{,}436$ (1,200 W, 1,236 M).	6 y. Drop out 36%	Intake of refined bread was positively associated with change in WC, with ($\beta=0.29$ (95% CI: 0.07–0.51) or without ($\beta=0.42$, 95% CI: 0.11–0.73) further adjustment for BMI. Spread on bread, milk and cheese, meat, fish, potatoes, rice, pasta, wholegrain bread, fruits and vegetables, cakes and chocolate were not related to WC.	Age, other food groups than, education, PA, smoking, alcohol.	B Food consumption was assessed with a very short questionnaire. Validity was only briefly described. The statistical power was not reported.
Halkjær, 2009, Denmark (33)	Cohort	All M and W (in Copenhagen and Aarhus) aged 50–64 y invited with no previous history of cancer. 35% ($n=$ 57,053) of the invited participated. In addition 547 were excl. because of newly	Changes in WC.	Different food and beverage groups (21 groups)	5 y	192 semi-quantitative FFQ. Validated against two 7-day weight diet records.	$n=42{,}696$ (22,570 W)	Drop out from baseline 24.5%.	The β-coefficients (95% CI) were assessed against 60 kcal of each food item. Both M and W: Red meat (inverse: W: −0.13, 95% CI: −0.24 to −0.03; M: −0.06, 95% CI: −0.11 to	Baseline WC, BMI, age, smoking, PA, alcohol, EI per day from the 21 food and beverage groups.	B Follow-up weight was self-reported. Drop-out exceeded 20%.

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		diagnosed cancer. Between follow-up and baseline 1,692 died, 435 emigrated, giving 54,379 participants for invitation to follow-up.							−0.003), fruit (inverse: W: −0.07, 95% CI: −0.13 to 0.004; M: −0.10, 95% CI: −0.15 to −0.04) and snack food (positive: W: 0.06, 95% CI: 0.003–0.11; M: 0.09, 95% CI: 0.05–0.13) significantly associated with WC. W only: Inverse; vegetables (−0.36, 95% CI: −0.51 to −0.21), high-fat dairy (−0.09, 95% CI: −0.15 to −0.03), butter (−0.12, 95% CI: –0.20 to −0.04). Positive; processed meat (0.20, 95% CI: 0.04 −0.36), potatoes (0.10, 95% CI: 0.0006–0.19), poultry (0.19, 95% CI: 0.01–0.37).		
Hare-Bruun, 2006, Denmark (34)	Cohort	Random sample of adults drawn in 1982. *N* = 3,608 (79% of sample) participated at original baseline. Follow-up 1987/1988 with a dietary survey in a subset of 552 subjects aged 49 y (baseline in this study). A follow up in 1993/1994. Excl. those with missing data on wt, ht, WC, HC, body fat mass or lean body mass or lean body mass or age,	Changes in body wt, body fat distribution and body composition	Baseline GI and GL (calculated with white bread as the reference food).	6 y	Diet history interview. Average daily intake based on intakes during the previous month. A weighed GI and overall GL were assigned to the diet with the use of values from the 2002 international table of GI and GI values and	*n* = 376 (185 men)	6 y. Drop out 32%.	Positive associations between GI and changes in body wt (β-coefficient for log (body weight): 0.002, 95% CI: 0.0001–0.004), percent body fat and WC in W only. No associations between GI for M and no for GL either sex.	Baseline body wt, age, smoking, years of education, PA, EI, E% from protein, fat and fibre intake.	B Power not reported.

		education, smoking, PA, and diabetes.				by using mean values of different studies measuring the GI of similar foods. GI was expressed with white bread as reference.					
Koh-Banerjee, 2004, US (35)	Cohort	51,529 male health professionals 40–75 y at baseline in 1986. Excluded were those who died, developed CVD, cancer or diabetes before 1994, had missing data on weight measures, dietary intake, PA	Wt gain	Whole-grain, and fibre.	8 y	Semi-quantitative FFQ. Validated among a subset of participants.	$n = 27{,}082$	8 y. Drop-out 47.4%.	Whole-grain intake inversely associated with wt gain, with an observed dose-response relation. For every 40 g/day increment in whole-grain intake – wt gain was reduced by 0.49 kg. Changes in cereal and fruit fibre were inversely related to wt gain.	Age, respective baseline exposure, smoking, baseline wt, and baseline values and changes in refined grains, EI, PA, alcohol, protein, TFA, SFA, MUFA and PUFA.	B Changes against changes. Wt was self-reported.
Mozaffarian, 2011, USA (36)	Cohort study	Participants from Nurses' Health Study, Nurses' Health Study II and Health Professionals Follow-up Study, total $n = 120{,}877$. Initial BMI for NHS and NHS II was 23.7 and 23.0 kg/m^2, and for HPFS 24.7.	Wt change (mean of 4 y periods)	Change in food consumption at baseline of each 4 y period.	NHS: 20 y; NHS II: 12 y; HPFS: 20 y. Analyses were done within 4 y periods covering the above time-period.	FFQ	$n = 120{,}877$	NHS: 20 y; NHS II: 12 y; HPFS: 20 y. Analyses were done within 4 y periods covering the above time-period.	The average 4 y wt gains in kg, against changes in servings, were positively associated with potato chips (0.55, 95% CI: 0.59–0.95), potatoes (0.58, 95% CI: 0.39–0.77), processed meats (0.42, 95% CI: 0.36–0.49), unprocessed meat (0.43, 95% CI: 0.25–0.61), butter (0.14, 95% CI: 0.07–0.20), sweets and desserts (0.19, 95% CI: 0.07–0.30), and refined grains (0.18, 95% CI:	Age, baseline BMI, sleep duration, changes in smoking, PA, television watching and alcohol use.	B Self-reported body wt, reporting of dietary assessment tool and database inadequate.

										0.10–0.26). Negative associations were found with vegetables (−0.10, 95% CI: −0.15 to −0.05), nuts −0.26, 95% CI: −0.44 to –0.08), whole grains −0.17, 95% CI: –0.22 to −0.12), fruits −0.22, 95% CI: −0.29 to −0.16) and yoghurt −0.37, 95% CI: –0.45 to −0.30). Sugar-sweetened beverages were also positively associated with weight change (0.45, 95% CI: 0.38–0.53).		
Poddar, 2009, US (37)	Cohort	Freshmen-level in nutrition 2004. 362 eligible (sex NA). *N* = 76 completed data collection in 2004 and 2005. Age 19.2 (SE 0.1) y.	Body wt and composition changes	Total and low-fat dairy intake.	6 months	7-day food record.	*n* = 76 (65 W)		6 months (drop-out information not given) Drop out 79% (conservative calculation)	Total dairy intake was not associated with wt. Subjects with higher amount of low-fat dairy products gained less body wt.	Race, sex and percent intake of estimated energy requirement	C Details about the recruitment procedure is missing. The students were on average 'normal wt' (BMI 23) and had already a healthy eating habits. Adjustment for PA is not done even though they have the information. Drop-out reason not given

Rajpathak SN, 2006, USA (38)	Cohort study	The Health professionals Follow-up Study ($n=51,529$). M subjects, 40–75 y. Subjects excl. if: <20 y ($n=52$), unreasonable EI ($n=1,596$), cancer, CVD or diabetes at baseline ($n=3,571$) or endpoint ($n=11,027$), no wt data in either 1986 or 1998 ($n=11,779$), no calcium intake data in 1998 ($n=3,889$). BMI at baseline 25.1–25.3 kg/m^2 (across quintiles).	12 y wt change (self reported).	Dairy intakes	12 y	Semiquantitative FFQ, validated against 1 week diet records ($n=127$) (coefficients reported, r $=0.53$ for calcium). US Department of Agriculture, supplemented with information from manufacturers. Pearson correlation between calcium intake from the FFQ and the average intake of two 1-week diet records was 0.53.	Baseline dairy and wt change ($n=23,504$)		12 y. Drop out 17% from baseline measurements.	Small difference in mean wt gain between extreme quintiles of high-fat dairy intake (3.24 ± 0.11 for the lowest quintile compared with 2.86 ± 0.11 for the highest quintile, p for trend $=0.03$).	Age, baseline wt, smoking, alcohol intake, PA, GL, EI, and variety of food and nutrients.	B Self reported weight.
Romaguera 2011, Europe (39)	Cohort	EPIC participants who were involved in DiOGenes –project, eight centres from five countries (Italy, Netherlands, Germany, Denmark, UK). Exclusion: pregnancy, chronic diseases, age >60 at baseline, smoking status changed during follow-up. Participants: 19,694 M and 28,937 W. These were selected from 102,346 participants with results on both baseline and follow-up.	WC, adjusted to BMI by residuals.	Different food groups.	Median follow-up 5.5 y.	Country-specific FFQ.	$n=19,694$ M and $n=28,937$ W, total $n=48,631$.		Median 5.5%. Drop-out 30.2%.	The results were shown as β-coefficients and 95% CI. Negative associations with annual change in WC, adjusted for BMI, were seen for vegetables (–0.08, 95% CI: (–0.11 to –0.03), fruit (–0.04, 95% CI: –0.05 to –0.03), dairy (–0.01, 95% CI: –0.02 to –0.01). Positive associations were reported for potatoes (0.04, 95% CI: 0.01–0.06), white bread	total EI, age, baseline wt, baseline ht, baseline WC(BMI), smoking, alcohol intake, PA, education, follow-up duration, menopausal status (W only), and hormone replacement therapy use (W only),	B Slight variations in the anthropometric techniques between the centres and time-points. Statistical power was not calculated, but appears to be clearly adequate.

										(0.01, 95% CI: 0.01–0.02), processed meat (0.04, 95% CI: 0.02–0.06), margarine (0.03, 95% CI: 0.01–0.05), sugar and confectionary (0.01, 95% CI: 0.00–0.01) and soft-drinks (0.04, 95% CI: 0.02–0.07).		
Rosell, 2006, Sweden (41)	Cohort study	Subjects from the Swedish Mammography Chort, Västmanland and Uppsala. W born 1914–1948, recruited in 1987–1990. Original sample of 90,069. 74% had dietary info ($n=66{,}651$). Follow up in 1997, excl. those who moved away, resulting in $n=56{,}030$. Of those 38,984 completed a FFQ. For the current study subjects were excl. if data on body wt or ht were missing at baseline or follow up ($n=1{,}783$), had a disease ($n=8{,}643$) and extreme changes in BMI ($n=12$). Cohort was restricted to W aged 40–55 at baseline. BMI 23.7 kg/m^2 at baseline.	Annual wt change during follow up.	Dairy food consumption.	9 y.	67-item FFQ in 1987. A 96-item FFQ was used in 1997, and the frequency of dairy products during the previous years was assessed by open ended questions requesting participants to report the number of servings per day or week. Validation against 1 week diet records ($n=129$), coefficients for dairy ranged from 0.33–0.64.	$n=19{,}352$		Dropout 32% from baseline measurements (based on the assumption that the eligible sample was 28,546 incl. only women 40–55 at baseline – not clear in the text).	Women consuming ≥ 1 serving/day whole milk and sour milk or cheese at baseline and did not change their consumption during follow up had decreased risk of mean wt gain of ≥ 1 kg/y compared with those consuming <1 serving/day with no change in follow up (OR 0.85; 95% CI: 0.73–0.99 and OR 0.7; 95% CI: 0.59–0.84, respectively).	Age, ht and wt at baseline, education, parity, intakes at baseline: EI, fat, CHO, protein, fibre and alcohol and the absolute change in intakes of these nutrients during follow-up, and the studied categories of change in intake of the other dairy products.	B EI rather low. Self reported wt at baseline and endpoint.
Rosell M, 2006, UK (40)	Cohort study	Subjects from the EPIC-Oxford ($n=65{,}500$). Age ≥ 20 y M and W. The aim was to recruit participants with a wide range of diets by targeting vegetarians and vegans	Annual wt gain during follow up (self reported).	Meat-eating, fish-eating, vegetarian and vegan.	Median follow-up 5.3 y (range 3.2–9.1 y).	A 130-item FFQ was also used to assess intake in the previous 12 months (validation not reported).	$n=21{,}966$ ($n=5{,}373$ M and $n=16{,}593$ W)		The number of subjects eligible at baseline (after excl.) not available	Mean annual wt gain (g/y) was lower in vegans (284 g, 95% CI: 178, 390 and 303 g, 95% CI: 211, 396, in M and W, respectively)	PA, smoking, marital status, current paid job, age at leaving school, age at menarche, and	B Might not be representative to the Nordic population due to high proportion of

		as well as the general UK population. The current study is based on subjects who completed follow-up questionnaire and had no prevalent malignant neoplasm at baseline ($n=36{,}956$). Excl. if wt was not self reported ($n=1{,}389$), missing data or reporting error ($n=2{,}267$), $\geq$70 y or had suffered from heart attack, stroke, angina or diabetes at baseline ($n=4{,}625$), unclear diet group at baseline ($n=529$) or missing values ($n=6{,}180$). BMI at baseline: M 24.1 kg/m^2, W 23.4 kg/m^2.				Classification of diet groups was based on four questions: Do you eat any meat? Do you eat any fish? Do you eat any eggs? and Do you eat any dairy products? In addition to the questions used to classify the participants dietary intake was assess by a 130-item FFQ. No information on the internal validity of the four questions reported.			compared with meat eaters (406, 95% CI: 373, 439 and 423, 95% CI: 403, 443, in M and W, respectively). Fish eaters (W only) had also lower annual wt gain (338 g, 95% CI: 300–376) than meat eaters.	age, ht, wt at baseline.	vegetarians and vegans in the study. Wt self-reported.
Schulz 2002, Germany (42)	Cohort study	Subjects for the analysis were selected from the EPIC cohort in Potsdam, Germany ($n=27{,}548$). M 24–69 y and W 19–70 with complete data on body wt and disease status at baseline and the first follow-up examination were eligible ($n=24{,}950$). Smokers excl. (and those who had quit $<$2 y prior to baseline), subjects using appetite-suppressing drugs and with diseases were excl., as were pregnant or lactating women. BMI at baseline: W 25.8 kg/m^2, M 27.1 kg/m^2.	Annual wt change (baseline weight measured, follow-up wt self reported). Large wt gain defined as $\geq$2 kg/y.	Food groups (intake of food from different food groups).	Mean follow-up time 2.2 y (range 0.6–5.4 y)	148-item self-administered, validated (validation not reported here) questionnaire for assessment of habitual intake at baseline. At follow up subjects were asked whether they changed their dietary habits (profoundly, partly or not) after baseline.	$n=17{,}369$ ($n=11{,}005$ W and $n=6{,}364$ M)	Drop out 30%.	Large wt gain ($\geq$2 kg/y) was predicted by consumption of sweets. For each 100 g/day increment in sweets intake, the likely hood of observing a large weight gain increased by 48% (OR 1.48; 95% CI: 1.03, 2.13). In W large wt gain was predicted by reported higher fat, sauce and meat (OR 1.75, 95% CI: 1.01–3.06; OR 2.12, 95% CI: 1.17–3.82 and OR 1.36, 95% CI: 1.04–1.79, respectively).	Age, initial body wt and ht, education, weight history (cycling, previous wt loss or gain), medication, menopausal status, life and health contentment, dietary change, PA, prevalent diabetes and thyroid disease.	B Follow up questionnaire limited to changes. Self reported wt at endpoint but measured at baseline.

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Schulze 2004, USA (43)	Cohort study	Subjects from the Nurses' Health Study II ($n=116{,}671$), female US Nurses aged 24–44 y at study initiation 1989. Excl. if they did not complete relevant dietary questions in 1991, had history of diabetes or CVD before 1995 or reported diagnosis of cancer, no report on body wt or had no data on PA. Baseline BMI 24.2–24.80 kg/m^2 across SSSD consumption groups.	Mean wt changes from 1991 to 1995 and from 1995 to 1999 (self reported)	SSSD	4 and 8 y	133-item validated semi quantitative FFQ. Correlation coefficients between the FFQ and multiple dietary records ranged from 0.36 to 0.89. See original article for the literature reference.	$n=51{,}603$ W	Drop out during follow up 66% from the original sample; drop out during follow up 44% of those eligible after excl.	W who increased their consumption of SSSD from low to high ($\leq$1/week to $\geq$1/day) had significantly larger increases in wt (4.69 kg (SE 0.20 kg) during 1991–1995 and 4.2 kg (SE 0.22 kg) during 1995–1999, than W who maintained a low (3.21 kg SE 0.03 kg and 2.04 kg, SE 0.03 kg) or a high (3.12 kg, SE 0.13 kg and 2.21 kg, SE 0.13 kg) intake or substantially reduced their intake (1.34 kg, SE 0.07 kg and 0.15 kg, SE 0.18 kg), during the two time periods, respectively. $p < 0.00$.	Baseline age, alcohol intake, PA, smoking, postmenopausal hormone use, oral contraceptive use, total fat intake and BMI.	B Drop-out rate exceeded 20%
Vergnaud 2010, Europé (44)	Cohort study	EPIC (PANACEA), 521,448 apparently healthy volunteers, 25–70 y from 23 European centres. Individuals with missing information excl., along with subjects with extreme values on anthropometry, pregnant women and extreme EI/ER. $N=497{,}735$ available for the baseline analysis. BMI at baseline: W 25.1 kg/m^2, M 26.6 kg/m^2.	5 y wt change (follow-up range 2–11 y). Measured or self reported at baseline, self reported at endpoint.	Meat consumption (red meat, processed meat and poultry).	Ranged from 2 to 11 y, adjusted to 5 y.	Country specific validated dietary questionnaires (validation not reported here). EPIC Nutrient Database. Dietary calibration study completing an additional 24-h recall (EPIC-SOFT). See original article for the literature reference.	$n=373{,}803$ ($n=103{,}455$ M and $n=270{,}348$ W)	Drop out 25%.	A 100 kcal/day increase in meat consumption was associated with 30 g (95% CI: 24–36) annual increase in wt. Significant for all types of meat, strongest association found for poultry.	Sex, age, indicator of meat consumption, educational level, PA, smoking status, initial BMI, follow-up time, total EI, E from alcohol, and plausible total EI reporting.	B Sample not intended to be representative of each region. Mixed methods of assessing wt as well as dietary intake. Follow-up period different between centres.

Vergnaud 2012, Europe (45)	cohort study	EPIC (PANACEA), 521,448 apparently healthy volunteers, 25–70 y from 23 European centres. Individuals with missing information excl., along with subjects with extreme values on anthropometry, pregnant W and extreme EI/ER. $N = 497{,}735$ available for the baseline analysis. After the follow-up, 373,803 participants (103,455 M and 270,348 W) were included in the analyses.	5 y wt change estimated from the available data (follow-up range 2–11 y). Measured or self reported at baseline, self reported at endpoint.	Fruit and vegetable consumption	Ranged from 2 to 11 y	Country specific validated dietary questionnaire. See original article for the literature reference. EPIC Nutrient Database Biomarkers: Spearman's correlation coefficient between total plasma carotenoids and total fruit and vegetable intakes	$n = 373{,}803$ ($n = 103{,}455$ M and $n = 270{,}348$ W)	Dropout 25%.	Baseline fruit and vegetable intakes were not associated with wt change overall.	Age, vegetable (or fruit) consumption, education, PA, change in smoking, BMI at baseline, follow-up time, EI, alcohol, plausibility of total EI.	B Sample not intended to be representative of each region. Mixed methods of assessing weight as well as dietary intake. Follow-up period different between centres.
Vioque, 2008, Spain (46)	Cohort study	Random sample of 1,799 M and W $\geq$15 y from Valencia. For the follow up 407 subjects were contacted. Average BMI at baseline was 25.8 kg/m^2 in both the original sample and the analysed subjects ($n = 206$).	Changes in body wt (measured). Main outcome defined as wt gain $\geq$3.41 kg over the 10 y follow-up period.	Fruit and vegetable intake	10 y	Semiquantitative FFQ, 10 fruit items and 12 vegetable items. Average correlation coefficients with 1-week dietary records, for 1-y validity and reproducibility of nutrient intakes were 0.47 and 0.40 respectively. See original article for the literature reference	$n = 206$	Drop out from the original sample 89%, but 51% if based on the eligible sample.	OR (95% CI) of $\geq$3.41 kg wt gain in 10 y was 0.21 (0.06, 0.79) in quartile 4 of fruit and vegetable intake compared with the lowest quartile (p for trend 0.024).	Sex, age, educational level, BMI, time spend watching TV, presence of disease, baseline ht, total EI, and energy-adjusted intakes of protein, SFA, MUFA, PUFA, fibre, caffeine and alcohol consumption.	C Low participation rate, inclusion criteria were not clearly reported.

W, Women; M, Men; Wt, Weight; Ht, Height; WC, Waist circumference; PA, Physical activity; BMI, Body mass index; EI, Energy intake; ED, Energy density; TFA, Trans fatty acids; CHO, Carbohydrates; MUFA, Monounsaturated fatty acids; PUFA, Poly-unsaturated fatty acids; GI, Glycemic index; GL, Glycemic load; Y, Years; SSSD, sugar-sweetened soft drink.

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Appendix 5
Evidence tables

Table 3. Diets and prevention of weight gain

Reference details, First author, Year, Country	Study design (RCT, CT, cohort, case control etc.)	Population, subject characteristics, Inclusion/exclusion criteria, setting, no at baseline, male/female, age, ethnicity of the subjects, anthropometry, location	Outcome measures Disease, biological measures	Intervention/ exposure	Time between baseline exposure and outcome assessment	Dietary assessment method FFQ, food record Internal validation (y/*n*)	No of subjects analysed	Intervention (I) (dose interval, duration) Control (C) (active, placebo, usual care etc), compliance, achieved dietary change, adherence to dietary targets, actual dietary change	Follow-up period, drop-out rate (from baseline to follow-up, or from end of intervention to follow-up) Drop out (%)	Results (I, C) (Absolute difference, RR, OR, *p*-value, confidence interval, sensitivity, specificity, observer reliability? etc)	Confounders adjusted for	Study quality and relevance, Comments (A–C)
Beunza 2010, Spain (47)	Cohort	University graduates Excl. those who reported total EI (<800 or >4,200 kcal/day for M and <600 or 3,500 kcal/day for W), pregnancy, CVD at baseline, no wt data. Baseline $n=15,339$, age 38 y, BMI 24.0 kg/m^2	An increase in body wt of at least 5 kg during follow-up. Change in body wt during follow-up, Incident overweight/ obesity	Mediterranean dietary Score (MDS), range 0–9: positive items: vegetables, fruit and nuts, legumes, MUFA: SFA, moderate alcohol consumption, fish; negative: meat and poultry, dairy. See original article for reference.	Mean 5.7 y (median 6.2 y)	Semiquantitative 136-item FFQ. Validated, see original article for the literature reference	$n=10,376$		Mean 5.7 y. Drop out (did not participate in follow-up) was 8%, but a further 24% were excl. due to missing information etc.	Participants with the lowest adherence (≤3 points) to MDS had the highest average yearly wt gain, whereas participants with the highest (≥6 points) adherence exhibited the lowest wt gain (adjusted difference: −0.059 kg/y; 95% CI: 0.008 kg/y; *p* for trend =0.02).	Sex, age, baseline BMI, PA, sedentary behaviour, smoking, snacking, total EI.	B Wt self-reported. The comparability of this population (students from Spain) and Nordic population is not clear.

Quatromoni, 2006, US (48)	Cohort	The Framingham Offspring cohort, baseline at examination 3 (1984–1988) $n=3{,}873$ of whom 2/3 contributed dietary data, incl. those who contributed one or two 8-y follow-up periods ($n=2{,}245$), excl. cancer; average age, 49–56 y) ethnicity not reported. Baseline mean BMI varied from 26.9 to 27.4 in men, and from 25.1 to 25.8 in women, according to different groups of DQI.	8 y wt change, body wt measured	A five-point dietary quality index (DQI): Fat intake <30 E%, SAFA <10 E%, chol <300 mg/day, sodium <2,400 mg/day, CHO >50 E%	8 y (from examination 3 to examination 7, which took place in 1998–2001)	3-day dietary records at exam 3 (1984–1988) and exam 5 (1991–1996). Minnesota Nutrition Data System software (NDS 2.6)	$n=990$ M and $n=1{,}255$ W (1,847 female and 1,433 male observations, since most participant were assessed twice)	Not clearly reported, observation s include same individuals twice, yet reported as numbers	Higher DQI was associated with lower wt gain over 8 y (p for trend <0.01 for M and W), higher DQI associated with less wt gain: beta for 1-unit diff in DQI −0.48 for M and 0.60 for W (Note: wt expressed as pounds).	Age, BMI, smoking cessation, alcohol, PA, intentional changes in eating behaviour, menopausal status (W).	B Drop out rates not reported, ethnicity not known
Romaguera, 2010, Europé (49)	Cohort study	EPIC (PANACEA), $n=521{,}448$ apparently healthy volunteers, 25–70 y from 23 European centres. Individuals with missing information excl., along with subjects with extreme values on anthropometry, pregnant women and extreme EI/ER. Thus $n=497{,}735$ available for the baseline analysis. Baseline BMI not reported.	5 y wt change estimated from the available data (follow-up range 2–11 y). Measured or self reported at baseline, self reported at endpoint.	Adherence to the Mediterranean diet (MED). Scores created from 0 to 18.	Ranged from 2 to 11 y.	Country specific validated dietary questionnaires (validation not reported here)	$n=373{,}803$ ($n=103{,}455$ M and $n=270{,}348$ W)	Dropout 25%.	Two point increase in MED predicted −0.05 kg (95% CI: −0.07 to −0.02 kg) less wt gain in 5 y. High adherence (11–18 points) −0.16 kg (−0.24, −0.07 kg) less wt gain in 5 y than people with low adherence (0–6 points). Protective effects stronger in younger and non-obese.	Sex, age, baseline BMI, follow-up time, educational level, PA, smoking, menopausal status, total EI, and misreporting of EI.	B Sample not intended to be representative of each region. Mixed methods of assessing wt as well as dietary intake. Follow-up period different between centres.

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Sanchez-Villegas 2006, Spain (50)	Cohort	Participants in the SUN cohort study, the recruitment started in December 1999 (ongoing as a dynamic cohort study), for this study participants followed >2 y (n =7,908) included, both M and W, extremely low/ high values for total EI and subjects with missing values excl.	Change in wt and BMI. Wt self-reported.	Adherence to a Mediterranean dietary pattern (MDP).	28 months	A validated semi quantitative 136-item FFQ. Food composition tables for Spain; MDP defined by scores according to the tertile distribution of several components of Mediterranean diet. For validation, see original article for the literature reference.	n =6,319	Drop out 20%	Lowest baseline MDP-scores showed a higher wt gain, but the inverse association did not remain significant after adjusting for confounders, higher meat consumption at baseline associated with greater wt gain (0.41 kg vs. 0.85 kg in lowest vs. highest third), higher consumption of whole-fat dairy products assoc. with lower wt gain (0.64 vs. 0.28 kg in lowest vs. highest third).	Age, sex, baseline BMI, PA during leisure time, smoking, alcohol, EI, change in dietary habits and change in PA.	B Based on self-reported weight
Zamora, 2010, USA (51)	Cohort study	Subjects from the CARDIA study (n =5,115), Birmingham AL; Chicago IL; Minneapolis MN; and Oakland CA. Black (n =2,786) and white (n =2,427) M (47%) and W, 18–30 y at baseline. Baseline BMI 23.7 kg/m^2 (whites). Eligibility criteria, freedom from chronic disease or disability.	Wt gain, 10 kg wt gain (measured)	Diet Quality Index (DQI) as an estimate of adherence to the Dietary Guidelines for Americans. Three categories created, low, medium and high diet quality.	7 and 20 y	Interview-administered questionnaire regarding usual dietary practices and a validated quantitative diet-history questionnaire that assessed consumption of foods over the past month.	n =4,913 (n =2,427 white) at baseline and n =3,739 (n =2,014 white) at 7 y	Drop out 19% at 7 y and 28% at 20 y.	High diet quality associated with significantly less wt gain than low diet quality (11.2 vs. 13.9). Overall (black and white) HR for risk of 10 kg wt gain was 0.75 (95% CI: 0.65–0.87) for high DQI compared with low DQI.	PA, EI, smoking, sociodemographic characteristics.	The number of white subjects included in the 20 y follow up is missing.

W, Women; M, Men; Wt, Weight; Ht, Height; WC, Waist circumference; PA, Physical activity; BMI, Body mass index; EI, Energy intake; ED, Energy density; TFA, Trans fatty acids; CHO, Carbohydrates; MUFA, Monounsaturated fatty acids; PUFA, Poly-unsaturated fatty acids; GI, Glycemic index; GL, Glycemic load; Y, Years.

Appendix 6
Evidence tables

Table 4. Prevention of weight regain after prior weight reduction

Reference details, First author, Year, Country	Study design (RCT, CT, cohort, case control etc.)	Population, subject characteristics, Inclusion/exclusion criteria, Setting, No at baseline, Male/ Female, Age, Ethnicity of the subjects, Anthropometry, Location	Outcome measures Disease, biological measures	Intervention/ exposure	Time between baseline exposure and outcome assessment	Dietary assessment method FFQ, food record Internal validation (y/n)	No of subjects analysed	Intervention (I) (dose interval, duration) Control (C) (active, placebo, usual care etc), compliance, achieved dietary change, adherence to dietary targets, actual dietary change	Follow-up period, drop-out rate (from baseline to follow-up, or from end of intervention to follow-up) Drop out (%)	Results (I, C) (Absolute difference, RR, OR, *p*-value, confidence interval, sensitivity, specificity, observer reliability? Etc.)	Confounders adjusted for	Study quality and relevance, Comments (A–C)
Brinkworth, 2004, Australia (52)	RCT	Incl: BMI 27–40 kg/ m^2, Type 2 diabetes. Excl: proteinuria, liver disease, CVD, gastrointestinal disease of a malignancy. Setting: outpatients. Baseline: low-protein (LP): $n=31$, high-protein (HP): $n=33$ Age 62 y (SD 2 y). Caucasian. Body composition by DXA.	Wt, fat-free mass, fat mass (DXA)	HP vs. LP diet for 12 weeks +52 weeks follow-up. *Ad lib* energy intake.	12+52 weeks follow-up. Only the changes during follow-up are assessed here.	Not reported. Biomarker assay: 24 h urinary urea/ creatinine	LP: $n=19$ $n=7$ M, $n=12$ W); HP $n=19$ ($n=8$ M, $n=11$ W).	LP-diet: 15% protein, 55% CHO, 30% fat. HP-diet: 30% protein, 40% CHO, 30% fat. The diets were supervised for 12 weeks. No measurement of dietary intake.	Follow-up: 52 weeks. Drop out 39% in LP 42% in HP.	Initial wt loss in both groups was 5.3 kg. Wt gain during follow-up: LP: 3.3 kg; HP: 1.5 kg. Difference ns ($p>0.05$). Same result for FFM and FM.	No adjustment. ANOVA used for statistical comparison.	B Small sample size, change of outcomes were not presented, although statistically analysed, no markers of dietary exposure. Note that LP-diet was close to normal dietary recommendations. HP-diet was also a moderately low-CHO-diet.
Dale, 2009, New Zealand (53)	RCT	Incl: W who had lost >5% body wt in the previous 6 months. Excl: chronic physical or psychiatric illness (e.g. diabetes, CVD, etc.), medications which affect wt, pregnancy. $n=200$ at baseline, age 45 y (SD 10 y) .91% white	Wt, fat-free mass, fat mass (by BIA)	2 × 2 factorial design: supporting program: intensive or nurse; diet: high-MUFA or high-CHO. *Ad lib* energy intake.	104 months (2 y).	3-day diet record.	200 (in Intension-to-treat analysis).	High-MUFA: CHO 42%, protein 21%, fat 32%; High-CHO: CHO 47%, protein 19%, fat 30%.	$n=174$ (87%) were followed for 2 y.	Difference between the diet-groups in change from baseline to 2 y: Wt 0.7 kg (95% CI: −1.1 to 2.4), fat mass 0.4 kg (95% CI: −0.3 to 1.1).	Mixed analytical models accounting, e.g. baseline values. The models included terms, e.g. support program etc.	B Statistical power calculation not reported, however the size seemed adequate; dietary assessment database not reported.

Delbridge 2009; Australia (59)	RCT	Incl.: Age 18–75 y, BMI >30 or >27 kg/m^2+ co-morbidities. Excl.: Several diseases, alcohol and drug abuse, lactation, pregnancy. $n=179$ at baseline, $n=141$ randomised, mean age 44 y, (SD 3 y).	Wt, waist WC, body composition (BIA)	Wt-loss diet for 3 months, followed by 12 months RCT (high-protein, HP, or high-carbohydrate, HC, diets). Aim for energy intake during weight maintenance: 1.3 × estimated resting energy expenditure	3+12 months wt-maintenance intervention. Only the changes during intervention are assessed here.	3 days food records, internal validation by 24 h urine urea excretion. Foodworks Professional Edition version 3.02.581	HP $n=71$, HC $n=70$	HP: Protein 30 E%, fat <30 E%, CHO >40%. HC: Protein 15%, fat < 30%, CHO >55%.	$n=82$ completed the RCT. Drop out 40%.	Wt loss during phase 1 (3 months) was 16.5 kg (ns between HP vs. HC). Change during RCT: HP: wt +3.0 kg, FM + 4.2 kg; HC: wt + 4.3 kg, FM: +3.2 kg; ns for all measured variables; results not different for completers only or by ITT analysis).	No adjustments.	A Only concern: statistical power calculation not reported, however the size seemed adequate.
Due, 2008; Denmark (54)	RCT	Incl.: 18–35 y, BMI 28–36 kg/m^2, lost wt >8% during phase 1 (more details in another paper). $n=131$ randomised, age 28 y(SD 5 y).	Wt and body composition by DXA.	Wt-loss diet for 8 weeks, followed by 6 months RCT:MUFA-diet, low-fat diet (LF), or control –diet (C):. *Ad lib* energy intake.	2+6 months wt-maintenance intervention. Only the changes during intervention are assessed here.	Supermarket model: all foods were collected at a 'supermarket' established at the department. The nutrient contents were analysed from a database. Compliance assessed by fatty acid analyses, biopsy from subcutaneous adipose tissue at screening and 6 months. Biomarkers: fat biopsy (fatty acid composition)	MUFA: $n=52$; LF: $n=47$; C: $n=25$	Actual E% in each diet: MUFA-diet: Fat 38%, SFA 7%, MUFA 20%, PUFA 8%, CHO 43%, protein 15%. LF-diet: Fat 24%, SFA 8%, MUFA 8%, PUFA 5%, CHO 56%, protein 16%. C-diet: Fat 32%, SFA 15%, MUFA 10%, PUFA 4%, CHO 50%, protein 16%.	$n=106$ completed the RCT. Drop out 15%.	Wt regains: MUFA 2.5 kg, LF 2.2 kg, CON 3.8 kg (ns). Regain in FM: MUFA 2.2 kg, LF 1.3 kg, C 3.5 kg. Differences (95% CI): MUFA vs. C: 1.9 (0.1–3.7) kg, LF vs. C: 2.5 (0.7–4.4 kg), MUFA vs. LF: 0.7 (−0.9 to −2.2.) kg.	No adjustments.	A
Field, 2001, USA (61)	Cohort study	Incl.: W, participant in nurses' health study; excl.: numerous criteria related to pregnancy, health status, PA etc. $n=$ 47,515 at baseline (1989), age 25–43 y. Wt maintenance analyses were	Self-reported wt (validated against measured weight at baseline, r =0.97).		Wt change 1989–1991, weight-loss maintenance 1991–1995	116-item FFQ, validated previously, see original article for reference.	$n=3{,}916$ W who had lost wt at least 5% between 1989 and 1991.		No data	Fat E% was not associated with wt change. There was a modest positive association between protein E% and weight gain.	Age, smoking, PA, wt cycling history, EI, BMI at age 18, wt change between age 18 and y 1989, wt change between 1989 and 1991	C Dietary data were not reported in details, e.g. no indication whether the data were Edjusted, only small number of the original cohort included in the analysis, dietary intake assessed only once, self-reported wt.

		done with 3,916 women who had lost wt at least 5% between 1989 and 1991.										
Larsen, 2010, eight European countries (55)	RCT	Incl.: Families with one healthy child between 5–17 y, parent 18–65 y, BMI 27–45 kg/m^2, wt-loss >8% during phase 1.n=773, age 42 y (SD 6 y), sex-distribution was not given.	Wt	Wt-reduction for 8 weeks (800 kcal/day), followed by randomisation in one of five groups: low-protein, low-GI (LP-LGI), low-protein, high GI (LP-HGI), high-protein, low-GI (HP-LGI), high-protein, high-GI (HP-HGI) and control (C).	8 weeks+26 weeks wt-maintenance intervention (RCT)	3 days food record at screening, 4 weeks after randomisation and at the end of the intervention. Local food databases, detailed report not in this paper GI was calculated by using glucose as reference, separately from other nutrient analyses. Adherence to diet was verified by urinary nitrogen analyses.	n=773	E%, GI and fibre content of the diets at week 26: LP-LGI: CHO 51%, fat: 30%, protein: 18%, GI 56, fibre 21 g/day. LP-HGI: CHO 51%, fat 31%, protein 17%, GI 62, fibre 20 g/day. HP-LGI: CHO 45%, fat 32%, protein 22%, GI 56, fibre 21 g/day. HP-HGI: CHO 45%, fat 31%, protein 23%, GI 61, fibre 19 g/day. C: CHO 46%, fat 34%, protein 19%, GI 59, fibre 20 g/day.	26 weeks, drop-out 29%	Intention-to-treat: Wt-regain was 0.93 kg less (05% CI: 0.31, 1.55) in groups assigned to HP (regardless of GI), and 0.95 kg less (0.33, 1.57) in groups assigned to LGI (regardless of protein). No interaction between HP and LGI.	Centre, type of centre (shop or intervention), sex, age at screening, BMI at time of randomisation, body wt lost during wt reduction, family type.	A
Phelan, 2006, USA (56)	Cohort study	Individuals registered at National Weight Control Registry (NWCR) between 1995 and 2003, they had lost >13.4 kg wt, W 78.4%, total n= 2,708. Mean age 46.9 y(SD 12.6 y).	Wt (self-reported)	1-y follow-up (no specification for prior wt loss, other than amount >13.4 kg).	1 y	Block Food-frequency questionnaire.	n=2,266		1 y. Drop-out 16.3%.	Baseline energy intake (β=0.10, p=0.002), fast food consumption (β=0.1, p=0.0001) and exercise (β= −0.10, p=0.02) and 1-y increase in energy intake (β=0.05, p=0.04), fat E% (β=0.10, p=0.0001) and fast food	EI, fat, CHO, protein, exercise, breakfast consumption, fast food consumption.	C Power size not calculated, although probably adequate, main part of the study concentrated on differences between different recruitment years, self-reported body wt, initially unclear inclusion criteria (who could register?), selected group (prior wt loss substantial and this was even maintained for at least 1 y)

										($\beta = 0.10$, $p = 0.01$) or 1-y decrease in chol E% ($\beta = -0.12$, $p = 0.0001$) or exercise ($\beta = -0.12$, $p = 0.0001$) were associated with weight regain.		
Swinburn, 2001, New Zealand (57)	RCT	Incl.: Adults with impaired glucose tolerance or otherwise abnormal B-glucose, but not type 2 diabetes. At baseline $n = 176$ (sex-distribution not reported) and at 1 y $n = 136$ ($n = 101$ M, $n = 35$ W; European race 97 (76%), Maori, pacific Islanders and other 24%. Mean age 52.5 y (RF) and 52.0 y (control)	Wt, BMI	1-y RCT: reduced-fat *ad libitum* (RF) versus usual diet, follow-up for 4-y.	1-y intervention +4 y follow-up (total study duration 5 y)	3-day food diary before randomisation and after 1 y. New Zealand data base (Nutritionist III software)	$n = 99$ at 2-y follow-up, $n = 103$ at 4-y follow-up.	RF diet at 1 y: fat 26 E%, CHO 55 E%, protein 19 E%. Usual diet at 1 y: fat 34 E%, CHO 45 E%, protein 17 E%.	Drop-out at 1 y (end of intervention), 23%, at 2-y follow-up 44% and at 4-y follow-up 42% .	2-y follow-up: RF: −1.6 (SD 0.8) kg, usual diet: +2.1 (SD 0.7) kg, $p < 0.01$. At 4-y follow: RF +1.6 (SD 0.6) kg, usual diet: +1.3 (SD 0.7) kg, ns.	Age, sex, ethnicity	B Note: European race only 70% and results were not presented separately for these participants.
White, 2010, UK (58)	RCT	Incl.: BMI between 25 and 35 kg/m^2, free from illness, not on a specific diet or medication affecting wt, no wt-reduction for past 3 months, intention to lose wt. $n = 169$, W, age 37, SD 1.3 y, Scottish (Caucasian).	Wt, WC, body composition (BIA)	3-month intervention: G1: reduced EI, fat and sugar; G2: reduced EI and fat only; G3: control (no reduction in EI), followed by 6 months wt-maintenance follow-up.	3-month intervention and 6-month follow-up (all together 9 months)	7-day unweighed dietary record at baseline, 3 months and 9 months.	$n = 126$ (drop-out 25%)	Composition for intervention diets at 3 months: G1: protein 19 E%, CHO 51 E%, fat 25 E%, sucrose 5 E% G2: Protein 18 E%,CHO 50 E%, fat 27 E%, sucrose 7 E%	6 months	Change in body wt during the 6-month follow-up: G1: –0.1 kg (SD not reported); G2: 0.0 (SD not reported). Similarly: body fat-% was unchanged during follow-up in all groups.	Not indicated	C Rather short follow-up, no power calculations, randomisation not explained, no indications of comparability of the groups, results not adjusted for EI, very low sucrose intakes, lack of clear statistics for wt change.

Aan de Gezondheidsraad, Den Haag, 27 april 2015

Ter attentie van de voorzitter Prof. Dr. W A van Gool
Postbus 16052
2500 BB Den Haag

Geachte heer Van Gool,

De Nederlandse Zuivel Organisatie maakt graag gebruik van de door u geboden mogelijkheid te reageren op de door de Gezondheidsraad in haar derde consultatieronde op haar website gepubliceerde stukken van 31 maart 2015.

Allereerst willen wij onze waardering uitspreken voor de kwaliteit van de enorme hoeveelheid werk die verricht is en die systematisch weergegeven is in de achtergronddocumenten.

Niettemin maken wij u attent op een aantal zaken in het achtergronddocument "voedingspatronen".

1. Tot onze verbazing is er nauwelijks sprake van het gebruik van het begrip nutriëntendichtheid. De enige verwijzing naar dit begrip vinden wij terug in de regels 1218-1221, waar referentie 63 wordt aangehaald. In deze publicatie van Streppel en collega's wordt verslag gedaan van de associatie tussen een score voor nutriëntendichtheid en mortaliteit en risico op hart- en vaatziekten. In de publicatie wordt ook geanalyseerd hoeveel bepaalde voedselgroepen bijdragen aan de score. Deze prospectieve analyse bepaalt dus niet vooraf wat gezien wordt als gezond of minder gezond, zoals bij veel gezondheidsindexen, maar relateert adequate inname van voedingsstoffen in relatie tot energie-inname uit voedingsmiddelen. De NZO begrijpt dan ook niet goed waarom in de regels 1220-1221 gesteld wordt dat deze manier van analyseren buiten beschouwing blijft "o*mdat Streppel en collega's een nutriëntenscore hebben onderzocht en geen score op voedingsmiddelen*.
2. In lijn met voorgaande constateren wij dat het achtergronddocument niet consistent omgaat met scores in relatie tot de effecten van voedingspatronen op gezondheid. Wij willen u er vriendelijk op attenderen dat in de scores die wel voor de aanbevolen voedingspatronen meegenomen zijn, ook nutriënten gescoord zijn / worden (Annex B, pagina's 87 en 88).
3. De NZO investeert al geruime tijd in onderzoek dat associaties probeert vast te stellen tussen nutriëntrijke voeding en gezondheidsuitkomsten. De publicatie van Streppel en collega's is daar een voorbeeld van; tevens verwijzen wij naar een recente publicatie

van Sluik en collega`s (Journal of Nutritional Science (2015), vol. 4, e14, page 1 of 9) waarin onderzocht wordt hoe scores voor nutriëntrijke voeding zich verhouden tot de *Dutch Healthy Eating Index*, ontwikkeld op basis van de Richtlijnen Goede Voeding zoals aanbevolen door de Gezondheids-raad in 2006.

4. Sinds de publicatie van Adam Drewnowski in 2005 (*AJCN 82 (4):721-32*) zijn vele publicaties over het belang van nutriëntrijke voeding verschenen. In deze publicaties is ook terug te vinden welke associaties er bestaan tussen nutriëntendichtheid scores en de Amerikaanse Healthy Eating Index (Drewnowski & Fulgoni, AJCN, 99(5 Suppl):1223S-8S,2014). De NZO is van mening dat het voor de hand ligt om via basisvoedingsmiddelen met een goede nutriëntendichtheid de basis te leggen voor een gezond voedingspatroon.
5. In het achtergronddocument wordt consistent de term “magere zuivelproducten” gebruikt in de besproken voedingspatronen, als vertaling van “low fat dairy products “ en “reduced fat dairy products” in de diverse onderliggende publicaties; volgens de NZO worden echter “magere en halfvolle zuivelproducten “ en “zuivelproducten met een gereduceerd vetgehalte “ (bijvoorbeeld 30+ kaas) bedoeld. Ten einde verwarring te voorkomen pleiten wij ervoor de juiste terminologie te gebruiken.
6. Ook worden gezondheidsvoordelen gerapporteerd voor voedingspatronen waarin magere zuivel meestal een plaats heeft. De plaats van zuivel in de voedingspatronen wordt echter niet duidelijk en consequent benoemd, wat tot verwarring kan leiden. Onder 7. en 8. worden concrete voorbeelden genoemd met suggesties voor verbetering.
7. Op pagina 5 geeft de Commissie een definitie van een Mediterraan voedingspatroon, waarin vermeld wordt dat gebruik van eieren, kaas en melk daarin beperkt is (regel 89). Op pagina 11, in de voetnoot, wordt in de criteria voor het Mediterraan dieet gesproken over “een matig gebruik van zuivel en zuivelproducten”. Ten einde verwarring te voorkomen pleiten wij voor een eenduidige beschrijving, bijv. conform de voetnoot op pagina 11.
8. Een vergelijkbare situatie doet zich voor bij de bespreking van het “New Nordic Diet”. Op pagina 6 staat zuivel niet genoemd in de opsomming van belangrijke voedingsmiddelen. Verderop is de omschrijving: ‘*Dit nieuwe Scandinavische voedingspatroon is een variant op het Mediterrane patroon en bevat voedingsmiddelen die juist in Scandinavische landen veel gebruikt worden, zoals groente, fruit, volkoren graanproducten, magere zuivel, olie, vis en/of noten.*’ (pagina 22, regels 504-508). Ten einde verwarring te voorkomen pleit de NZO ook hier voor een eenduidige definitie op pagina 5, inclusief zuivel, conform de beschrijving op pagina 22. Voor de term “magere zuivel” geldt hier volgens ons dat bedoeld worden “magere en halfvolle zuivelproducten en zuivelproducten met een gereduceerd vetgehalte”.
9. Het achtergronddocument beschrijft dat een vegetarisch voedingspatroon veganistisch of lacto-ovo vegetarisch kan zijn (regels 110-114). In paragraaf 2.2 (regel 175) worden

de effecten van een vegetarisch voedingspatroon op de bloeddruk beschreven. Tabel 1 (regel 200) geeft het resultaat van de meta-analyse weer op basis van 2 veganistische en 5 vegetarische studies. De NZO is van mening dat de conclusie beter het effect van lacto-ovo vegetarische voedingspatronen zou moeten weergeven.

10. Paragraaf 2.5 (regel 604) beschrijft de effecten van Dietary Approaches to Stop Hypertension (DASH)-voedingen op de bloeddruk. De conclusie (regel 635-638), gebaseerd op de meta-analyse van Saneei (2014), luidt: “Het gebruik van een DASH-voedingspatroon met veel groente en fruit *al dan niet in combinatie met* magere zuivelproducten en minder zout verlaagt de systolische bloeddruk met 6 mm Hg en de diastolische met 3 mm Hg ten opzichte van een Amerikaans voedingspatroon”. De NZO wijst er op dat deze conclusie voorbij gaat aan de welbekende en breed gecommuniceerde interventiestudie van Appel LJ et al (N Engl J Med. 336,1117-1124, 1997), waaruit duidelijk blijkt dat een DASH-voeding met zowel groente, fruit en magere en halfvolle zuivel een *groter effect* heeft op zowel de systolische (SBP) als de diastolische bloeddruk (DBP), in vergelijking met de DASH- voeding met alleen groente en fruit. Bovendien leidt een voeding die rijk is aan groenten, fruit en zuivelproducten met een verminderd vetgehalte, bij verschillende niveau’s van zoutinname tot een lagere bloeddruk dan een typisch westerse voeding (Sacks et al, N Engl J Med. 344(1):3-10, 2001).
11. In paragraaf 4.13 (regel 1742) worden de conclusies gepresenteerd over de effecten van het volgen van een aanbevolen voedingspatroon op diverse gezondheidsuitkomsten, in functie van het voldoen aan een vooraf vastgestelde index voor gezondheid. Een hoge score volgens de index heeft gezondheidsvoordelen ten opzichte van een lage index score. De bewijskracht voor deze verbanden wordt als *groot* gepresenteerd. De NZO merkt op dat hier toch enige voorzichtigheid geboden is. Ten eerste is niet eenduidig wat onder hoog of laag moet worden verstaan. Het ontbreken van dosis-respons analyses is ook een duidelijk gemis. Bovendien kunnen de gerapporteerde procentuele risicoverlagingen ook vergeleken worden met studies waarin specifieke voedingsmiddelencategorieën zijn geanalyseerd. Vanuit de zuivelcategorie wijzen wij op 3 voorbeelden die deze opmerkingen onderstrepen en worden weergegeven onder de punten 12-14.
12. De consumptie van melk is geassocieerd met een lager risico op darmkanker, ongeveer 9% per 200 gram per dag (Aune et al, Ann Oncol. 23(1):37-45, 2012). Dit impliceert dat het drinken van 2 glazen melk per dag een vergelijkbare kwantitatieve respons heeft als weergegeven in het achtergronddocument in regel 1753.
13. In regel 1750 wordt een 20% risicoverlaging gerapporteerd voor coronaire hartziekten. In de literatuur is gerapporteerd dat het drinken van 1 glas (halfvolle) melk per dag (~200 ml) geassocieerd is met een 6% lager risico op hart- en vaatziekten (Soedamah-Muthu et al, AJCN 93(1):158-71, 2011). Het inverse verband werd vastgesteld bij melkconsumptie tot 600 ml.

14. De SENECA studie heeft onder meer laten zien dat een aanpassing van een Mediterranean Diet Score voor melkconsumptie leidde tot een andere voorspelling voor overleving. Bij gebruik van de mediaan als afkapwaarde in de index bleek de overleving minder gunstig dan wanneer de P25-P75 percentielen werden gebruikt voor de indexering (van Staveren et al, Public Health Nutr. 5(6A):901-5, 2002).

Wij danken u voor de geboden gelegenheid deze punten onder uw aandacht te brengen.

Met vriendelijke groeten,

Prof dr Gerrit J Hiddink
Manager Research Nutrition & Health
P.O. Box 93044, 2509 AA The Hague, The Netherlands
Benoordenhoutseweg 46, 2596 BC The Hague, The Netherlands

Van: Andries Olie
Verzonden: vrijdag 24 april 2015 17:20
Aan: GR_RGV2015
Onderwerp: Commentaar achtergronddocument voedingspatronen
Bijlagen: Commentaar achtergronddocument Richtlijnen goede voeding 2015 - Voedingspatronen.docx

Geachte heer/mevrouw,

Namens onze directeur, dr.ir. Janine Verheesen, stuur ik u hierbij ons commentaar over het concept van het achtergronddocument Voedingspatronen.

Mocht u nog verdere vragen of opmerkingen hebben dan horen wij dit graag.

Vriendelijke groet en een fijn weekend,

Andries Olie

Manager voeding en gezondheid

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Commentaar achtergronddocument Richtlijnen goede voeding 2015.

Voedingspatronen

Kenniscentrum suiker & voeding (KSV) is verheugd dat de Commissie de gelegenheid biedt commentaar te leveren op de achtergronddocumenten voor de Richtlijnen goede voeding 2015. De achtergronddocumenten zien er gedegen uit met een solide wetenschappelijke onderbouwing en uitleg. Consultatie kan de onderbouwing verder versterken en verbeteren. Graag maken wij daarom van de gelegenheid gebruik om te reageren op het achtergronddocument 'Voedingspatronen'.

Laag-koolhydraat voedingspatronen ontbreken

In het conceptrapport zijn laag-vet voedingspatronen opgenomen en besproken. Hoog-vet voedingspatronen echter niet. Laag koolhydraat voedingspatronen zijn veel in de media geweest de afgelopen jaren, onder andere vanwege het paleolitisch voedingspatroon. KSV zou graag zien dat de Gezondheidsraad ook conclusies maakt ten aanzien van het laag-koolhydraat voedingspatroon in haar rapport. Abstracts van enkele relevante onderzoeken die hiervoor gebruikt kunnen worden staan in de referentielijst[1–4].

Redactioneel commentaar

4.10 Pagina 65, tabel 34: "Alternative Healthy Eating Index" i.p.v. "Alternate Healthy Eating Index"

4.4 Pagina 55, tabel 28 (onderaan): "Healthy Eating Index" i.p.v. "Health Eating Index"

Inhoudelijk commentaar

4.13, pagina 71, regels 1743-1754.

"Een hoge ten opzichte van lage score op indexen voor een aanbevolen voedingspatroon dat hoog scoort op het gebruik van groente, fruit, volkorenproducten, noten, peulvruchten, oliën rijk aan cis-onverzadigde vetzuren, magere zuivel, gevogelte en vis; dat weinig rood en bewerkt vlees, volle zuivel, harde vetten <u>en toegevoegd suiker</u> bevat; en dat matig is in alcohol hangt samen met een:

- *ongeveer 20% lager risico op totale sterfte*
- *ongeveer 20% lager risico op hart- en vaatziekten*
- *ongeveer 20% lager risico op coronaire hartziekten*
- *ongeveer 20% lager risico op beroerte*
- *ongeveer 15% lager risico op diabetes mellitus type 2*
- *ongeveer 15% lager risico op darmkanker."*

In de conclusie van hoofdstuk 4 'Cohortonderzoek naar voedingspatronen' staat vermeld dat een hoge score op indexen voor een aanbevolen voedingspatroon ten opzichte van een lage score, samenhangt met een aantal (chronische) ziekten (zie hierboven). Er wordt gesteld dat een aanbevolen voedingspatroon onder andere weinig toegevoegde suiker bevat. Echter, veel van de indexen die gebruikt zijn in de onderzochte studies onder hoofdstuk 4, scoren niet op toegevoegde suiker. Zo scoren de Mediterrane score (tabel 26, Sofi 2013 en Martinez-Gonzalez 2014), de Modified Mediterranean Diet Score, de Mediterrane Voedingspatroon-index (tabel 27, Women's Health Initiative 2014) en de Relative Mediterranean Diet Score niet op toegevoegde suiker. Andere indexen, zoals de Alternate Healthy Eating Index en de Fung's DASH Index scoren bijvoorbeeld wel op suikerhoudende dranken (de Alternate Healthy Eating Index scoort ook op vruchtensappen), maar

niet op toegevoegde suiker per se. Er zijn naar verhouding weinig studies onder hoofdstuk 4 waar 'toegevoegde suiker' an sich wordt meegenomen in de indexen van voedingspatronen. Het zou daarom redelijk zijn om de conclusie onder 4.13 wat betreft 'toegevoegde suiker' genuanceerder en specifieker te formuleren.

Tot slot willen wij de Commissie bedanken voor het bestuderen van ons commentaar.

Dr.ir. Janine Verheesen
Kenniscentrum suiker & voeding

Referenties

1. Noto, H., Goto, A., Tsujimoto, T. & Noda, M. Low-carbohydrate diets and all-cause mortality: a systematic review and meta-analysis of observational studies. *PLoS One* **8,** (2013).

2. Naude, C. *et al.* Low carbohydrate versus isoenergetic balanced diets for reducing weight and cardiovascular risk: a systematic review and meta-analysis. *PLoS One* **9,** (2014).

3. Lagiou, P. *et al.* Low carbohydrate-high protein diet and mortality in a cohort of Swedish women. *J Intern Med.* **261,** 366–74 (2007).

4. Hu, T. *et al.* Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol* **176,** 44–54 (2012).

Van: Caroline van Rossum
Verzonden: dinsdag 28 april 2015 17:12
Aan: GR_RGV2015
Onderwerp: derde ronde achtergronddocumenten

Beste GR,

Hierbij onze reactie op de achtergronddocumenten van de 3e ronde.

Groet,
Caroline

Caroline van Rossum, PhD
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See http://www.voedselconsumptiepeiling.nl for information on the Dutch food consumption surveys
See http://www.rivm.nl/nevo for information on the Dutch food composition database

Reactie RIVM op concept-achtergrondrapporten RGV ronde 3

dd 28-april 2015

Voedingspatroon.

- In de conclusie wordt een kwantitatief effect gekoppeld aan hoog en laag op een index. Kan dit wel? Wat is dat dan?
- In de conclusie worden alle voedingspatronen op 1 hoop gegooid? Klopt dat?
- Klopt de bewoording dat de Nordic index nieuw is? Is het niet het traditionele patroon? Maar dat het beschreven is is nieuw?
- is het volgende artikel nog relevant? Am J Clin Nutr. 2006 May;83(5):1170-6.

Reactie van de commissie Richtlijnen goede voeding 2015 op het achtergronddocument over voedingspatronen

De commissie heeft op het achtergronddocument over voedingspatronen reacties ontvangen van drs. M. Bien, de Federatie Nederlandse Levensmiddelen Industrie (FNLI), ETC, het Kenniscentrum Suiker & Voeding (KSV), de Nederlandse Zuivel Organisatie (NZO), het Rijksinstituut voor Volksgezondheid en Milieu (RIVM) en Unilever. De commissie heeft de inhoudelijke reacties betrokken bij het opstellen van het definitieve achtergronddocument en over het algemeen de tekstuele suggesties overgenomen.

Geen van de commentaren heeft geresulteerd in wijzigingen van conclusies. Wel wordt nu bij de beschrijving van aanbevolen voedingspatronen consistent gesproken over halfvolle en magere zuivelproducten i.p.v. over magere producten. Dit naar aanleiding van commentaar dat *low-fat* producten zowel halfvolle als magere producten omvatten. Ook is de term ‘toegevoegd suiker’ gepreciseerd tot ‘dranken (en andere producten) met toegevoegd suiker’. Dit omdat veel voedingsindexen niet op toegevoegd suiker scoren, terwijl de indexen die wel op toegevoegd suiker scoren zich overwegend richten op suikerhoudende dranken. Tenslotte is ook een laag zoutgehalte opgenomen in de beschrijving van een aanbevolen voedingspatroon, omdat op dit aspect ook een aantal voedingsindexen scoren.

De nieuwe beschrijving is dus als volgt: “Een aanbevolen voedingspatroon levert veel groente, fruit, volkoren producten, noten, peulvruchten, oliën rijk aan cis-onverzadigde vetzuren, halfvolle en magere zuivel, gevogelte en vis; bevat weinig rood en bewerkt vlees, volle zuivel, harde vetten, keukenzout en dranken (en andere producten) met toegevoegd suiker; en is matig in alcohol.”

Op de volgende pagina’s beschrijft de commissie in een tabel alle inhoudelijke commentaren en wat zij daarmee heeft gedaan.

Tabel Overzicht ontvangen **inhoudelijke** commentaren op achtergronddocument over voedingspatronen en de reactie van de commissie.

Commentatoren	Commentaar	Reactie commissie
Bien	Recente publicatie van Ngandu en collega's in Lancet ontbreekt.[1]	Niet verwerkt. Het interventieonderzoek van Ngandu[1] betreft een interventie die niet alleen gericht is op veranderingen in de voeding, maar ook in lichamelijke activiteit en sociale activiteit en omvat cognitieve training en de behandeling van metabole en vasculaire risicofactoren. Hierdoor is het niet mogelijk een afzonderlijk effect van voeding te bepalen.
Bien	Een studie over Mediterrane voeding en het risico op coronaire hartziekten die tijdens de American College of Cardiology 64th Annual Scientific Session is gepresenteerd ontbreekt.	Niet verwerkt. De commissie baseert zich op peer-reviewed artikelen en niet op abstracts gepresenteerd op congressen.
Bien	Studies die zijn genoemd door True Health Coalition ontbreken.	Niet verwekt. Al deze artikelen betreffen leefstijlinterventies, waarvan voeding een onderdeel vormt. Hierdoor is het niet mogelijk een afzonderlijk effect van voeding te bepalen.
Bien	Het is mogelijk dat in de Amerikaanse richtlijnen artikelen staan die in de Nederlandse achtergronddocumenten gemist zijn.	Niet verwerkt. Het systematische literatuuronderzoek naar voedingspatronen dat in het kader van de Amerikaanse richtlijnen is uitgevoerd[2], is betrokken bij het opstellen van het achtergronddocument hierover.
FNLI	Hoe kan een stevige uitspraak worden gedaan over bewijskracht met name bij interventieonderzoeken, terwijl voedingspatronen niet nauwkeurig gedefinieerd zijn en onderling sterk verschillen.	Niet verwerkt. De commissie kijkt bij haar beoordeling van de bewijsvoering naar het aantal en de kwaliteit van de studies en de consistentie van studies. De beschikbaarheid van voldoende kwalitatief goede RCT's waarvan de resultaten eenduidig zijn biedt de mogelijkheid voor een conclusie met een grote bewijskracht.
FNLI	Wat is het 10-jaarse effect van de Richtlijnen goede voeding (studie/monitoring).	Niet verwerkt. Een dergelijk onderzoek is niet uitgevoerd.

Commentatoren	Commentaar	Reactie commissie
FNLI	Bij voedingspatronen dient rekening te worden gehouden met andere langdurige aandoeningen als ondervoeding (veganistisch voeding), bloedarmoede (stelt eisen aan vegetarische voeding) en maagzweren (Aziatische voeding).	Niet verwerkt. Deze aandoeningen vallen buiten de werkwijze van de commissie, zoals beschreven in het werkwijze document.
FNLI	Dieetbeperkingen bij sommige delen van de bevolking komen niet terug in de analyse.	Niet verwerkt. De Richtlijnen goede voeding zijn gericht op de preventie van chronische ziekten in de algemene bevolking. Specifieke diëten en dieetbeperkingen vallen buiten de werkwijze van de commissie vallen.
FNLI	Laag-vet voedingen worden wel besproken, maar hoog-vet, laag koolhydraten voedingen niet.	Niet verwerkt. Het effect van hoog-vet, laag-koolhydraatvoedingen komt aan de orde in een afzonderlijk achtergronddocument over de uitwisseling van eiwit, vet en koolhydraten. Het onderzoek naar een laag-vet voedingen in het achtergronddocument betrof niet alleen een laag-vet voeding, maar ook het gebruik van extra groente, fruit en volkoren graanproducten.[3]
FNLI	Aanwijzingen dat langdurige, beperkte calorische restrictie positieve effecten heeft op de lange termijn ontbreken in het achtergronddocument.	Niet verwerkt. Onderzoeken naar calorische restrictie vallen buiten de werkwijze van de commissie, zoals beschreven in het werkwijze document.
FNLI	Naast kruiden en specerijen zou zout ook moeten worden meegenomen in de beschrijving van het Mediterrane voedingspatroon.	Niet verwerkt. Zout is geen criterium bij veel Mediterrane voedingsscores.[2]
FNLI	Is het voor de gezondheid van de mens relevant dat het vlees afkomstig is uit van vee uit de wei en de kip uit de vrije uitloop?	Niet verwerkt. De tekst met voorbeelden van voedingspatronen dient als illustratie van in de literatuur beschreven voedingspatronen.
FNLI	Categoriseer uitsluitend voedingen met een sterke mate van wetenschappelijke onderbouwing als ‘ gezonde voeding’. Diëten om gewicht te verliezen horen hier niet per definitie bij.	Verwerkt. De tekst geeft nu aan dat de commissie in het advies onder gezonde voedingspatronen ondermeer patronen volgens richtlijnen, het traditionele Mediterrane voedingspatroon en DASH-voedingen verstaat.

Commentatoren	Commentaar	Reactie commissie
FNLI	Het lijkt niet mogelijk een uitspraak te doen over het effect van een vegetarisch ten opzichte van omnivoor voedingspatroon op de bloeddruk: 1. Verschillen in voedingspatronen tussen omnivoren zijn zeer groot en de resterende samenstelling van de voeding kan van groot belang zijn op de lange termijn. 2. Onduidelijk is of het soort vlees een rol speelt. In hoeverre telt consumptie van vis mee? 3. Steeds meer mensen zijn flexitariër, terwijl deze groep als omnivoor wordt weggezet. Flexitariërs leven vaak bewuster en lijken wat betreft leefstijl meer op vegetariërs. 4. Vegetariërs hebben vaak een betere leefstijl dan omnivoren.	Niet verwerkt. 1. De commissie erkent dat verschillen in andere elementen van de voedingspatronen bij kunnen dragen aan de gezondheid op de lange termijn, maar dat is niet geanalyseerd in deze meta-analyse. 2. Ook is in de meta-analyse geen subgroepanalyse uitgevoerd naar studies met verschillende soorten vlees. In geen van de RCT's is vis onderdeel van de vegetarische interventie. De meta-analyse geeft niet aan of vis onderdeel is van de vleesinterventie. Er waren echter in de meta-analyse geen aanwijzingen voor heterogeniteit, wat erop duidt dat bovenstaande factoren in deze analyse geen grote bron van variatie vormden tussen onderzoeken. 3. Er zijn geen RCT's waarin een flexitarisch voedingspatroon is vergeleken met een omnivoor of vegetarisch voedingspatroon. Er is slechts een cohortonderzoek gevonden waarin flexitariërs aan bod komen.[4] Dat is te weinig om een uitspraak over te doen. 4. De commissie heeft bij haar conclusies rekening gehouden met verschillen in leefstijl tussen vegetariërs en omnivoren. In een groot deel van het cohortonderzoek hiernaar is zo goed mogelijk geadjusteerd voor potentiële confounders. Bij oudere cohortonderzoeken is soms minder uitgebreid geadjusteerd. Als de commissie meent dat (rest)confounding een probleem vormt bij bepaalde cohortonderzoeken, heeft ze in de toelichting aangegeven dat dit een rol kan spelen bij de afwegingen ten aanzien van de bewijskracht.
FNLI	Er zijn te veel factoren die een rol kunnen spelen bij de gevonden effecten van voedingspatronen om aan een voedingspatroon zonder duidelijke definitie van criteria een grote bewijskracht toe te kennen.	Niet verwerkt. De commissie is van mening dat de beschreven voedingspatronen voldoende homogeen zijn (ondermeer door aanwijzingen voor weinig tot geen heterogeniteit) om een conclusie met grote bewijskracht toe te kennen.

Commentatoren	Commentaar	Reactie commissie
FNLI	Waarom vallen onderzoeken naar calorische restrictie buiten de werkwijze, terwijl onderzoeken die kunnen leiden tot een hogere energie-inname wel aan de selectiecriteria voldoen. Bij Predimed krijgen deelnemers extra producten verstrekt en is onduidelijk of hier sprake is van vervanging of dat de deelnemers extra calorieën zijn gaan consumeren. Bij Bos[5] gaat het om een isocalorische interventie. Er ontbreekt een toelichting of bij Predimed mensen in gewicht zijn toegenomen en of dat er toe doet bij de beschreven uitkomstmaten.	Deels verwerkt. De commissie heeft er voor gekozen om onderzoeken naar calorische restrictie niet mee te nemen omdat advies over afvallen buiten de werkwijze valt. Onderzoeken waarin deelnemers het advies krijgen extra van een product te gebruiken onder ad libitum omstandigheden zijn wel meegenomen. Onder ad libitum omstandigheden is er namelijk ruimte om een eventuele verandering in energie-inname te compenseren. In het Predimed onderzoek waren er na drie en twaalf maanden geen significante veranderingen in gewicht binnen en tussen de drie interventiegroepen.[6,7] Bij de Predimed-rapportages over het risico op chronische ziekten na 5 jaar follow-up is voor gewicht gecorrigeerd.[8] Dit is nu toegevoegd aan de tekst.
FNLI, KSG	In de aanbevolen voedingspatronen staat gesteld dat het gaat om weinig (toegevoegde) suiker, terwijl in veel gehanteerde indexen niet op de hoeveelheid suiker wordt gescoord. In sommige indexen wordt op suikerhoudende dranken gescoord. Formuleer daarom de conclusies ten aanzien van toegevoegd suiker genuanceerder en specifieker	Verwerkt. In de beschrijving van de voedingspatronen is (toegevoegde) suiker nu gepreciseerd naar dranken (en andere producten) met toegevoegd suiker.
FNLI	Fogelholm ontbreekt.[9]	Niet verwerkt. Fogelholm[9] beschrijft in haar systematische review enkele RCT's naar voedingspatronen en gewichtsverandering. Een daarvan, de Women's Health Initiative Dietary Modification Trial[10] is beschreven in het achtergronddocument over voedingspatronen. De andere RCT's richten zich op de uitwisseling van macronutriënten, waarover de commissie een afzonderlijk achtergronddocument heeft opgesteld. Cohortonderzoeken naar gewichtsverandering vallen buiten de werkwijze van de commissie.

Commentatoren	Commentaar	Reactie commissie
KSG	Alleen laag-vet voedingen worden besproken. Bespreek ook de effecten van hoog-koolhydraten voedingen, zoals beschreven in.[11-14]	Niet verwerkt. De commissie richt zich bij de beschrijving van cohortonderzoek op voedingspatronen die scoren op voedingsmiddelen en richt zich niet op nutriëntenscores. Daarom blijven de publicaties van Noto[11] en Lagiou[13] buiten beschouwing. Naude[12] vat RCT's samen die gericht zijn op gewichtsverlies. Deze vallen eveneens buiten de werkwijze van de commissie. De meta-analyse van Hu[14] betreft de uitwisseling van koolhydraat en vet en wordt door de commissie meegenomen bij het achtergronddocument over de uitwisseling van eiwit, vet en koolhydraten.
NZO	Het is onduidelijk waarom scores op nutriëntendichtheid van voedingsmiddelen niet wordt meegenomen.	Verwerkt. In de inleiding staat nu duidelijker aangegeven dat de commissie zich richt op voedingspatroonindexen op basis van voedingsmiddelen en dat indexen op basis van nutriënten of nutriëntendichtheid niet zijn meegenomen. De commissie heeft zich tot doel gesteld om zo veel mogelijk op het niveau van voedingsmiddelen richtlijnen af te lijden. Daarom richt de commissie zich in het document op voedingspatronenindexen op het niveau van voedingsmiddelen.
NZO	Bij sommige scores voor aanbevolen voedingspatronen wordt ook op nutriënten gescoord.	Niet verwerkt. Alle beschreven indexen hebben ook op voedingsmiddelen gescoord.
NZO	Sluik heeft in 2015 scores voor nutriëntrijke voeding vergeleken met de Dutch Healthy Eating Index.[15]	Niet verwerkt. Deze publicatie valt buiten de uiterste datum van het literatuuronderzoek, 1 juli 2014.
NZO	In de onderzoeken zijn niet alleen magere, maar ook halfvolle zuivelproducten en producten met een gereduceerd zuivelgehalte gescoord.	Verwerkt. Bij de voedingspatronen wordt nu consistent gesproken van halfvolle en magere zuivel.
NZO	Maak de beschrijving van het Mediterrane patroon eenduidig tussen de inleiding en de voetnoot op pagina 6.	Niet verwerkt. De voetnoot op pagina 6 betreft de definitie die in een specifieke meta-analyse is gehanteerd.

Commentatoren	Commentaar	Reactie commissie
NZO	Maak de beschrijving van het New Nordic Diet eenduidig tussen de inleiding en de beschrijving op pagina 5.	Deels verwerkt. In de inleiding worden de achtergrond en kenmerken van het New Nordic Diet uitgebreider toegelicht dan op pagina 5. Wel is de beschrijving consistent gemaakt.
NZO	De meta-analyse naar een vegetarische voeding en bloeddruk gaat in wezen om een lacto-ovo vegetarische voeding en niet een veganistische voeding.	Niet verwerkt. De conclusie is gebaseerd op zowel onderzoeken naar lacto-ovo vegetarische voedingen (5 studies) als veganistische voedingen (2 studies).
NZO	De conclusie (regel 635-638) dat het gebruik van een DASH-voedingspatroon met veel groente en fruit al dan niet in combinatie met magere zuivelproducten en minder zout verlaagt de systolische bloeddruk met 6 mm Hg en de diastolische met 3 mm Hg ten opzichte van een Amerikaans voedingspatroon gaat voorbij aan het feit dat een DASH-voeding met zowel groente, fruit en magere en halfvolle zuivel een groter effect heeft op zowel de systolische (SBP) als de diastolische bloeddruk (DBP), in vergelijking met de DASH- voeding met alleen groente en fruit.[16] Bovendien leidt een voeding die rijk is aan groenten, fruit en zuivelproducten met een verminderd vetgehalte, bij verschillende niveaus van zoutinname tot een lagere bloeddruk dan een typisch westerse voeding.[17]	Niet verwerkt. Deze conclusie betreft meerdere RCT's naar uiteenlopende DASH-voedingspatronen. De specifieke effecten van zuivel en zout op de bloeddruk komen in achtergronddocumenten over zuivel en natrium aan de orde.

Commentatoren	Commentaar	Reactie commissie
NZO	Er is de nodige voorzichtigheid geboden bij conclusies over de bewijskracht ten aanzien van de effecten van een score op een voedingspatroon en het risico op ziekte. 1. Ten eerste is niet duidelijk wat onder hoog of laag moet worden verstaan. Ook ontbreekt een dosisrespons analyse. 2. Wanneer de gerapporteerde procentuele risicoverlagingen vergeleken worden met studies waarin specifieke voedingsmiddelencategorieën zijn geanalyseerd is de risicodaling vergelijkbaar.[18,19] 3. Tenslotte lijkt de voorspellende waarde van de score afhankelijk van de gehanteerde afkappunten.[20]	Niet verwerkt. 1. De score geeft inderdaad alleen aan in welke mate iemand voldoet aan een gezond voedingspatroon, maar niet welke producten het betreft. Bij de integratie in het advies zal de commissie dan ook de conclusies over voedingspatronen beoordelen in samenhang met die over voedingsmiddelen. 2. De commissie bevestigt dat de risicoverlagingen van voedingspatroonscores niet veel groter of even groot zijn dan van individuele voedingsmiddelen. Een mogelijke verklaring hiervoor is dat er maar weinig mensen hoog scoren op alle aspecten van een gezond voedingspatroon. 3. De commissie beschrijft in het hoofdstuk over de operationalisatie van voedingspatronen dat scores voor een goede voeding kunnen variëren door uiteenlopende afkapwaardes voor specifieke voedingsmiddelen. Dit kan leiden tot heterogeniteit in de bevindingen. De commissie probeert dit te ondervangen door gebruik te maken van systematische reviews en meta-analyses waarin de heterogeniteit tussen de onderzoeken is geanalyseerd.
RIVM	Kan een kwantitatief effect worden gekoppeld aan een hoge en lage score op een index? Wat is die index dan?	Niet verwerkt. De score geeft alleen aan in welke mate iemand voldoet aan een gezond voedingspatroon, maar niet welke producten het betreft. Bij de integratie in het advies zal de commissie dan ook de conclusies over voedingspatronen beoordelen in samenhang met die over voedingsmiddelen.
RIVM	Kun je alle voedingspatronen op een hoop gooien?	Niet verwerkt. Het gaat de commissie bij de conclusie om gemeenschappelijke kenmerken van de verschillende voedingspatronen.
RIVM	Is de Nordic index nieuw?	Niet verwerkt. Het Nordic diet is een Scandinavische variant van het traditionele Mediterrane voedingspatroon en wordt door onderzoekers als New Nordic Diet beschreven.
RIVM	Is het volgende artikel van Waijers nog relevant[21]?	Niet verwerkt. Waijers[21] heeft een posterior analyse uitgevoerd, terwijl de commissie alleen cohortonderzoek naar a priori scores beschrijft.

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