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This is the published version of a paper published in *British Journal of Nutrition*.

Citation for the original published paper (version of record):

Heikkila, H., Krachler, B., Rauramaa, R., Schwab, U. (2014)
Diet, insulin secretion and insulin sensitivity: the Dose-Responses to Exercise Training (DR's EXTRA) Study (ISRCTN45977199).
British Journal of Nutrition, 112(9): 1530-1541
http://dx.doi.org/10.1017/S0007114514002426

Access to the published version may require subscription.

N.B. When citing this work, cite the original published paper.

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http://urn.kb.se/resolve?urn=urn:nbn:se:umu:diva-96926

British Journal of Nutrition (2014), **112**, 1530–1541
doi:10.1017/S0007114514002426
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Diet, insulin secretion and insulin sensitivity – the Dose–Responses to Exercise Training (DR's EXTRA) Study (ISRCTN45977199)

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(Submitted 19 December 2013 – Final revision received 2 July 2014 – Accepted 14 July 2014 – First published online 18 September 2014)

Abstract

Intakes of saturated fat (SF) and dietary fibre, body mass and physical activity are all associated with the incidence of type 2 diabetes mellitus. Their relative importance for the maintenance of normal glucose metabolism is not fully known. In a population-based sample of 1114 individuals, aged 58–78 years, dietary intakes were assessed by 4 d food records and cardiorespiratory fitness as maximal oxygen uptake. Insulin secretion, insulin sensitivity, the early-phase disposition index (DI30) and the total disposition index (DI120) were assessed based on an oral glucose tolerance test. Linear associations were modelled using linear regression. Combined effects were studied by introducing SF and fibre intakes, as well as cardiorespiratory fitness and waist circumference (WC) as dichotomised variables in general linear models. Intakes of dietary fibre and whole-grain bread were positively associated with insulin sensitivity, independent of physical fitness and WC. In women, dietary fibre intake was also positively associated with DI30. The negative association of high WC with DI30 was attenuated by a combination of low SF intake and high cardiorespiratory fitness. In conclusion, dietary fibre and a combination of low SF intake and high cardiorespiratory fitness may contribute to the maintenance of normal glucose metabolism, independent of WC.

Key words: Saturated fat intake: Dietary fibre intake: Cardiorespiratory fitness: Disposition index

Among dietary factors, a high intake of saturated fat (SF) and a low intake of dietary fibre have been most strongly associated with the incidence of type 2 diabetes mellitus (T2DM)[1,2], although there is some controversy whether high SF intake *per se* increases the risk of T2DM[3,4]. Overweight and lack of physical activity are further known risk factors for T2DM[5]. To investigate possible causative mechanisms, their associations with insulin secretion, peripheral and hepatic insulin sensitivity are of interest.

A high intake of SF has been associated with impaired insulin sensitivity[6], predominantly hepatic[7,8] according to some studies. In addition, subjects with a low intake of SF and high fitness have a lower adiposity-related risk of elevated fasting plasma glucose concentrations[9]. In contrast, dietary fibre intake has been associated with both increased insulin sensitivity[10] and increased insulin secretion[11,12]. As assessment of insulin secretion *per se* without taking insulin sensitivity into account has been shown to provide only a limited insight; therefore, the use of the disposition index has been suggested for an assessment of insulin secretion [13]. To our knowledge, only one study has reported an association between overall dietary fibre intake and the disposition index[14], and an association between habitual fat quality and the disposition index has not been reported in any study.

As various dietary factors and physical activity are known to accumulate[15] and interact[16], simultaneous measurements of these lifestyle factors are essential. Yet, most studies of glucose metabolism have been carried out in selected groups of subjects, without objectively measured data on physical activity/cardiorespiratory fitness. The aim of the present study was to investigate the associations of dietary factors and glucose

Abbreviations: 2hP-gluc, 2 h plasma glucose concentration; DI30, early-phase disposition index; E%, percentage of energy; fP-gluc, fasting plasma glucose concentration; HOMA-IR, homeostatic model assessment of insulin resistance; Matsuda-IS, homeostatic model assessment of insulin resistance; OGTT, oral glucose tolerance test; Secr120, index of later-phase insulin secretion; SF, saturated fat; T2DM, type 2 diabetes mellitus; WC, waist circumference.

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British Journal of Nutrition

metabolism in a population-based sample with the objective measurement of cardiorespiratory fitness.

Subjects and methods

Study population

The present study was based on the baseline data from a population-based randomised controlled trial, the DR's EXTRA (Dose–Responses to Exercise Training) Study, described in detail previously[17]. The target population was a representative sample of 3000 men and women who lived in the city of Kuopio in Finland and who were 55–74 years of age in 2002. A total of 1479 individuals participated in the baseline examinations in 2005–6. The initial assessment consisted of four appointments at weekly intervals: (1) anthropometric data including waist circumference (WC); (2) dietary intake; (3) cardiorespiratory fitness; (4) oral glucose tolerance test (OGTT). After excluding the individuals with previously diagnosed T2DM, missing or insufficient data, the present study population consisted of 1114 individuals. The number of subjects with BMI $<25\,kg/m^2$ was 334 (30·0 %), those with BMI 25–30 kg/m^2 was 540 (48·5 %) and those with BMI $>30\,kg/m^2$ was 240 (21·5 %). The number of subjects with normal glucose metabolism (fasting plasma glucose concentration (fP-gluc) <6·1 mmol/l and 2 h plasma glucose concentration (2hP-gluc) <7·8 mmol/l) was 804 (72·2 % of the study population), with isolated impaired fasting plasma glucose concentration (fP-gluc 6·1–6·9 mmol/l and 2hP-gluc <7·8 mmol/l) was 121 (10·9 %), isolated impaired glucose tolerance concentration (fP-gluc <6·1 mmol/l and 2hP-gluc 7·8–11·1 mmol/l) was 94 (8·4 %), concurrent impaired fasting plasma glucose concentration and impaired glucose tolerance (fP-gluc 6·1–6·9 mmol/l and 2hP-gluc 7·8–11·1 mmol/l) was 47 (4·2 %) and newly diagnosed T2DM (fP-gluc ≥7 mmol/l and 2hP-gluc ≥11·2 mmol/l) was 48 (4·3 %). All subjects gave their written informed consent. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the Joint Ethics Committee of the University of Kuopio and Kuopio University Hospital. Written informed consent was obtained from all subjects.

Assessment of dietary intake

Dietary intake was assessed by a 4 d food record, including three consecutive weekdays and one weekend day. A researcher defined the recording dates. The subjects received the food records with verbal and written instructions at the first study visit. The food records were returned at the second visit 1 week later. A nutritionist or a specially trained research nurse checked the food records and completed missing information. The amount of food consumed was estimated by a picture booklet of portion sizes[18], household gauges or weighing. Data from the food records were analysed using the MicroNutrica® nutrient calculation software (version 2.5; Finnish Social Insurance Institution) based on Finnish analyses and international food composition tables[19].

Assessment of cardiorespiratory fitness

Cardiorespiratory fitness (VO_{2max}) was assessed by defining maximal oxygen uptake from respiratory gas analysis during a maximal symptom-limited exercise stress test on a bicycle ergometer (Ergoline) to exhaustion as described previously[20]. The measured VO_{2max} of each participant was transformed into the percentage of expected normal VO_{2max} on the basis of sex, body weight, height and age × body weight using the residual method. In the residual method, VO_{2max} in ml of oxygen per min was set as the dependent variable and sex, body weight, height and age × body weight as independent variables into linear regression analysis. The value of expected normal VO_{2max} was calculated for each participant using the sex-specific formula derived from the linear regression analysis. The linear regression analysis and the calculation of expected normal VO_{2max} for each participant were performed separately for men and women due to the known difference in VO_{2max} between sexes. The percentage of expected normal VO_{2max} (fitness) was then calculated by dividing the value of the participant's measured VO_{2max} by the sex-specific expected normal VO_{2max} of the participant. This measure limits the body-weight bias introduced by dividing VO_{2max} by total body weight[21].

Assessment of insulin sensitivity and insulin secretion

The selected indices for insulin sensitivity and insulin secretion were the best-performed indices in a validation study with a large selection of indices[22]. The participants of that study were of same ethnicity (Finnish) as the subjects in the DR's EXTRA Study. HOMA-IR (homeostatic model assessment of insulin resistance) was the selected index for the assessment of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance[23,24] due to its comparable performance with other surrogate indices of hepatic insulin resistance[25] and its predictive power on the incidence of T2DM[26]. The following indices for insulin sensitivity and insulin secretion were used: Matsuda-IS (Matsuda insulin sensitivity index, i.e. whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; units used in the calculation were in mU/l for insulin and in mg/dl for glucose (a conversion factor of 18·014 was used to convert units of glucose from mmol/l into mg/dl))[23]; HOMA-IR (fasting glucose (mmol/l) × fasting insulin (mU/l)/22·5); Secr120 (InsAUC120/GluAUC120, i.e. an index of total insulin secretion during the OGTT; calculated as a quotient of insulin AUC and glucose AUC between the time points 0 and 120 min of OGTT, where the trapezoidal method was used for the calculation of the entire AUC (not incremental AUC); units used in the calculation were as follows: glucose (mmol/l) and insulin (pmol/l) (a conversion factor of 6·945 was used to provide insulin into pmol/l))[22]; Secr30 (InsAUC30/GluAUC30, i.e. an index of early-phase insulin secretion during the OGTT; calculated for the time interval between 0 and 30 min of OGTT, otherwise calculated in the same way as for Secr120)[22]; total disposition index (DI120, i.e. an index of total insulin secretion during the

OGTT that takes whole-body insulin sensitivity into account; calculated as a product of Secr120 and Matsuda-IS)[22]; early-phase disposition index (DI30, i.e. an index of early-phase insulin secretion that takes whole-body insulin sensitivity into account; calculated as a product of Secr30 and Matsuda-IS)[22].

Statistical analyses

Statistical analyses were performed using the SPSS statistical software for Windows, version 19.0 (IBM Corporation Released 2010) and IBM SPSS Statistics for Windows, version 19.0 (IBM Corporation). A linear regression analysis was used to assess the associations between the selected dietary factors and the indices of glucose and insulin metabolism. The analysis was adjusted for age, sex, fitness and WC with sex-specific standardisation. Combined effects of WC, SF intake, dietary fibre intake and fitness were studied with a general linear model. The analyses with the general linear model were adjusted for age and sex, and Bonferroni correction was used for controlling multiple pairwise testing. For the combined analysis, fitness was dichotomised at above or below 100 % of expected normal VO_{2max}. Cut-offs for WC (97·0 cm in men and 86·5 cm in women), reported SF intake (11·4 % of energy (E%) in men and 11·4 E% in women) and dietary fibre intake (3·0 g/MJ or 12·7 g/1000 kcal in men and 3·3 g/MJ or 13·9 g/1000 kcal in women) were derived from median values by sex, i.e. low and high. Combined effects were studied by comparing the means of each index of glucose and insulin metabolism among eight categories defined either by dichotomised SF intake, fitness and WC or by dichotomised dietary fibre intake, fitness and WC. The subjects with an optimal lifestyle profile, i.e. those with either low SF intake, high fitness and low WC or those with high dietary fibre intake, low fitness and low WC, were used as a reference group for seven pairwise comparisons. In addition, three pairwise comparisons of means were performed in a subpopulation of subjects with high WC where a reference category of subjects was defined by low SF intake and high fitness or by high dietary fibre intake and low fitness. Analyses with SF intake were performed also in a subpopulation with total fat intake below the median intake of 30·5 E% (*n* 557) based on the observation by Vessby *et al.*[6] on the effects of dietary fat quality on whole-body insulin resistance only in subjects with total fat below the median intake. Logarithmic transformations ($\log_{10}$) based on visually interpreted distribution histograms of normality were applied for all outcome variables to provide normally distributed variables. All independent variables followed a normal distribution except for sex and intakes of cheese and butter, of which the latter two were skewed to the right. However, residuals of the linear regression analysis with cheese or butter intakes were normally distributed. A P value of $<0{\cdot}05$ was considered as significant.

Results

Intakes of dietary fibre and whole-grain bread were associated with Matsuda-IS, independent of cardiorespiratory fitness and WC (Table 1, *n* 1114). In women, dietary fibre was also associated with DI30 and inversely with HOMA-IR (Table 2). In men, no other associations independent of WC were found (Table 3).

Indices of insulin secretion that take whole-body insulin sensitivity into account, i.e. DI30 and DI120, were directly associated with dietary fibre intake. Indices for insulin secretion *per se*, i.e. Secr30 and Secr120, were negatively associated with dietary fibre intake. The directions of associations were similarly reversed for a vast majority of dietary factors studied.

In subjects with a total fat intake below 30·5 E%, intake of SF was positively associated with HOMA-IR and inversely with Matsuda-IS and DI30, independent of cardiorespiratory fitness (Table 4). The subjects with low SF intake together with high fitness were protected against the high WC-associated lower DI30 (Table 5). In women, the decrease in DI30 caused by high WC was nearly halved with the optimal lifestyle profile; i.e. a significant difference between 207 and 142 (Δ 65) and a non-significant difference between 207 and 173 (Δ 34) were observed (Table 6). The subjects in the other three categories with high WC and with non-optimal SF intake and fitness profile had a lower DI30 when compared with the reference group with low WC, low SF intake and high fitness. These findings were not present in men (Table 7), but were observed also in the subpopulation with total fat intake below the median intake of 30·5 E% (Table 8). Similarly, the optimal lifestyle profile also protected against the high WC-associated lower DI120 in the subpopulation with low total fat intake.

The combined high dietary fibre intake and high fitness did not protect against high WC-associated lowering of DI30 (Tables 9–11), in contrast to the observation with SF intake together with fitness on DI30. The combined high dietary fibre intake and high fitness also did not differentiate the DI30 among the subjects with low WC. The combined low dietary fibre intake and low fitness was associated with lower Matsuda-IS among the subjects with low WC; however, this lifestyle combination did not modify the Matsuda-IS among the subjects with high WC. Further analyses found that these results were evident only in women.

Discussion

In this population-based study of 1114 middle-aged and elderly men and women, low SF intake together with high cardiorespiratory fitness attenuated the negative association between WC and the DI30. Intake of dietary fibre was positively associated with insulin sensitivity, independent of both physical fitness and WC. In women, intake of dietary fibre was also positively associated with DI30. Overall, the observations were stronger in women.

The observed associations between dietary fibre/whole-grain bread and insulin sensitivity are in line with an earlier finding of increased insulin sensitivity when on a diet rich in cereal fibre[27]. The association between dietary fibre intake and the DI30 in women supports the earlier finding on the association between dietary fibre intake assessed with FFQ and pancreatic functionality assessed with the frequently

Table 1. Associations between dietary factors and indices of glucose metabolism in DR's EXTRA (Dose–Responses to Exercise Training) baseline among the total study-specific population of 1114 subjects

(β-Coefficients and *P* values)

	Whole-body insulin sensitivity				Insulin secretion				Disposition indices				
	HOMA-IR		Matsuda-IS		Secr30		Secr120		DI30		DI120		
	β	*P*	β	*P*	*B*	*P*	β	*P*	β	*P*	β	*P*	
Fibre (g/MJ)*†	−0·094	0·002	0·142	<0·001	−0·072	0·017	−0·092	0·002	0·084	0·005	0·081	0·006	Model 1
	−0·088	0·004	0·133	<0·001	−0·067	0·029	−0·084	0·006	0·079	0·009	0·078	0·009	Model 2
	−0·025	0·351	0·069	0·008	0·034	0·255	−0·049	0·093	0·039	0·173	0·030	0·280	Model 3
Whole-grain bread (g/MJ)*†	−0·046	0·125	0·090	0·003	−0·066	0·028	−0·078	0·009	0·027	0·363	0·022	0·458	Model 1
	−0·044	0·143	0·086	0·004	−0·063	0·034	−0·075	0·012	0·025	0·399	0·020	0·489	Model 2
	−0·031	0·229	0·073	0·004	−0·057	0·049	−0·068	0·018	0·017	0·548	0·011	0·694	Model 3
Vegetables, fruit and berries (g/MJ)*†	−0·041	0·197	0·053	0·100	−0·026	0·412	−0·044	0·176	0·036	0·258	0·024	0·451	Model 1
	−0·036	0·262	0·043	0·179	−0·021	0·524	−0·036	0·269	0·031	0·329	0·020	0·523	Model 2
	−0·016	0·563	0·023	0·405	−0·010	0·745	−0·024	0·428	0·018	0·542	0·005	0·862	Model 3
SF (E%)*	0·044	0·139	−0·040	0·183	0·024	0·416	0·033	0·267	−0·023	0·441	−0·018	0·536	Model 1
	0·042	0·163	−0·035	0·238	0·022	0·472	0·029	0·326	−0·020	0·490	−0·016	0·577	Model 2
	0·004	0·876	0·003	0·900	0·002	0·945	0·009	0·767	0·003	0·901	0·012	0·656	Model 3
Butter (g/MJ)*†	0·038	0·200	−0·025	0·407	0·034	0·257	0·033	0·267	0·002	0·935	−0·001	0·996	Model 1
	0·037	0·218	−0·022	0·459	0·032	0·281	0·031	0·300	0·004	0·897	0·001	0·995	Model 2
	0·021	0·402	−0·006	0·801	0·024	0·399	0·022	0·433	0·014	0·626	0·012	0·654	Model 3
Cheese (g/MJ)*†	−0·043	0·161	0·047	0·117	−0·035	0·243	−0·038	0·216	0·013	0·667	0·015	0·604	Model 1
	−0·042	0·168	0·046	0·126	−0·035	0·254	−0·036	0·229	0·012	0·685	0·015	0·616	Model 2
	−0·027	0·305	0·031	0·231	−0·027	0·360	−0·028	0·334	0·003	0·927	0·004	0·897	Model 3

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; SF, saturated fat intake in percentage of energy intake.

* Log-transformed glucose metabolism indices were analysed as outcome variables using linear regression analysis. Dietary factors assessed by 4 d food records were analysed separately (no mutual adjustment) as explanatory variables, adjusted in model 1 for age and sex, in model 2 for age, sex and fitness (percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake) and in model 3 for age, sex, fitness and sex-specifically standardised waist circumference. The strength of an association is expressed per 1 SD (standardised coefficient) of the selected dietary factor and indicated by a β value. A *P* value of <0·05 was considered as significant.

† Daily food intake (g) divided by daily energy intake (MJ). Due to the interpretation of the strength of associations with standardised coefficients, daily food intakes in g per 4184 kJ (1000 kcal) provided the same β values.

Table 2. Associations between dietary factors and indices of glucose metabolism in DR's EXTRA (Dose–Responses to Exercise Training) baseline among women (β-Coefficients and *P* values, *n* 576)

	Whole-body insulin sensitivity				Insulin secretion				Disposition indices				
	HOMA-IR		Matsuda-IS		Secr30		Secr120		DI30		DI120		
	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	
Fibre (g/MJ)*†	−0·109	0·009	0·156	<0·001	−0·061	0·142	−0·100	0·017	0·116	0·005	0·101	0·014	Model 1
	−0·104	0·013	0·146	<0·001	−0·058	0·164	−0·095	0·023	0·109	0·008	0·094	0·022	Model 2
	−0·074	0·035	0·117	0·001	−0·045	0·270	−0·081	0·046	0·088	0·021	0·069	0·060	Model 3
Whole-grain bread (g/MJ)*†	−0·058	0·165	0·107	0·009	−0·086	0·038	−0·115	0·006	0·037	0·369	0·019	0·643	Model 1
	−0·053	0·202	0·100	0·015	−0·084	0·044	−0·111	0·008	0·031	0·457	0·013	0·754	Model 2
	−0·055	0·118	0·101	0·004	−0·085	0·037	−0·112	0·006	0·032	0·406	0·014	0·700	Model 3
Vegetables, fruit and berries (g/MJ)*†	−0·055	0·193	0·069	0·097	−0·015	0·716	−0·027	0·527	0·065	0·119	0·067	0·107	Model 1
	−0·052	0·212	0·065	0·116	−0·014	0·739	−0·025	0·560	0·062	0·137	0·064	0·122	Model 2
	−0·037	0·293	0·050	0·152	−0·007	0·860	−0·017	0·673	0·051	0·183	0·051	0·164	Model 3
SF (E%)*	0·038	0·364	−0·031	0·450	−0·008	0·847	0·011	0·799	−0·046	0·264	−0·034	0·413	Model 1
	0·038	0·366	−0·031	0·452	−0·008	0·845	0·010	0·802	−0·046	0·266	−0·034	0·415	Model 2
	0·012	0·735	−0·006	0·867	−0·020	0·629	−0·002	0·961	−0·028	0·464	−0·012	0·744	Model 3
Butter (g/MJ)*†	0·036	0·393	−0·024	0·569	0·031	0·453	0·010	0·820	0·005	0·912	−0·022	0·591	Model 1
	0·033	0·426	−0·019	0·641	0·030	0·474	0·007	0·862	0·008	0·846	−0·019	0·646	Model 2
	0·004	0·898	0·009	0·803	0·017	0·671	−0·007	0·871	0·028	0·463	0·005	0·890	Model 3
Cheese (g/MJ)*†	−0·014	0·735	0·033	0·423	−0·060	0·154	−0·065	0·122	−0·025	0·545	−0·032	0·445	Model 1
	−0·010	0·811	0·026	0·527	−0·058	0·170	−0·061	0·144	−0·031	0·456	−0·037	0·369	Model 2
	0·002	0·955	0·014	0·679	−0·052	0·200	−0·056	0·171	−0·039	0·306	−0·047	0·198	Model 3

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; SF, saturated fat intake in percentage of energy intake.

* Log-transformed glucose metabolism indices were analysed as outcome variables using linear regression analysis. Dietary factors assessed by 4 d food records were analysed separately (no mutual adjustment) as explanatory variables, adjusted in model 1 for age, in model 2 for age and fitness (percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake) and in model 3 for age, fitness and sex-specifically standardised waist circumference. The strength of an association is expressed per 1 SD (standardised coefficient) of the selected dietary factor and indicated by a β value. A *P* value of <0·05 was considered as significant.

† Daily food intake (g) divided by daily energy intake (MJ). Due to the interpretation of the strength of associations with standardised coefficients, daily food intakes in g per 4184 kJ (1000 kcal) provided the same β values.

Table 3. Associations between dietary factors and indices of glucose metabolism in DR's EXTRA (Dose–Responses to Exercise Training) baseline among men (β-Coefficients and *P* values, *n* 538)

	Whole-body insulin sensitivity				Insulin secretion				Disposition indices				
	HOMA-IR		Matsuda-IS		Secr30		Secr120		DI30		DI120		
	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	
Fibre (g/MJ)*†	−0·072	0·098	0·118	0·007	−0·079	0·068	−0·081	0·062	0·043	0·323	0·055	0·209	Model 1
	−0·067	0·126	0·108	0·013	−0·071	0·104	−0·070	0·107	0·041	0·351	0·055	0·209	Model 2
	0·026	0·501	0·012	0·755	−0·016	0·702	−0·012	0·768	−0·012	0·788	−0·007	0·861	Model 3
Whole-grain bread (g/MJ)*†	−0·035	0·412	0·075	0·084	−0·049	0·225	−0·050	0·252	0·018	0·684	0·024	0·575	Model 1
	−0·035	0·411	0·075	0·082	−0·049	0·253	−0·050	0·248	0·018	0·684	0·024	0·575	Model 2
	−0·010	0·783	0·048	0·191	−0·034	0·406	−0·034	0·408	0·003	0·934	0·007	0·858	Model 3
Vegetables, fruit and berries (g/MJ)*†	−0·017	0·702	0·019	0·661	−0·032	0·454	−0·052	0·226	−0·010	0·825	−0·035	0·411	Model 1
	−0·008	0·849	0·003	0·937	−0·020	0·652	−0·036	0·407	−0·013	0·757	−0·036	0·405	Model 2
	0·011	0·782	−0·016	0·660	−0·008	0·842	−0·024	0·560	−0·024	0·566	−0·049	0·234	Model 3
SF (E%)*	0·053	0·216	−0·053	0·224	0·055	0·202	0·056	0·198	−0·002	0·963	−0·006	0·890	Model 1
	0·049	0·262	−0·043	0·314	0·047	0·272	0·046	0·290	0·000	0·996	−0·006	0·892	Model 2
	−0·001	0·981	0·009	0·814	0·018	0·664	0·015	0·724	0·028	0·498	0·028	0·500	Model 3
Butter (g/MJ)*†	0·042	0·328	−0·028	0·517	0·037	0·397	0·052	0·227	−0·001	0·978	0·017	0·701	Model 1
	0·042	0·336	−0·027	0·536	0·035	0·411	0·051	0·238	−0·001	0·984	0·017	0·701	Model 2
	0·036	0·344	−0·021	0·578	0·032	0·438	0·047	0·250	0·002	0·954	0·021	0·616	Model 3
Cheese (g/MJ)*†	−0·073	0·090	0·062	0·153	−0·010	0·815	−0·010	0·826	0·057	0·187	0·070	0·108	Model 1
	−0·077	0·078	0·068	0·117	−0·015	0·734	−0·015	0·720	0·059	0·177	0·070	0·108	Model 2
	−0·057	0·133	0·047	0·204	−0·003	0·941	−0·003	0·938	0·048	0·254	0·057	0·167	Model 3

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; SF, saturated fat intake in percentage of energy intake.

* Log-transformed glucose metabolism indices were analysed as outcome variables using linear regression analysis. Dietary factors assessed by 4 d food records were analysed separately (no mutual adjustment) as explanatory variables, adjusted in model 1 for age, in model 2 for age and fitness (percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake) and in model 3 for age, fitness and sex-specifically standardised waist circumference. The strength of an association is expressed per 1 SD (standardised coefficient) of the selected dietary factor and indicated by a β value. A *P* value of $<0{\cdot}05$ was considered as significant.

† Daily food intake (g) divided by daily energy intake (MJ). Due to the interpretation of the strength of associations with standardised coefficients, daily food intakes in g per 4184 kJ (1000 kcal) provided the same β values.

Table 4. Associations between saturated fat intake and indices of glucose metabolism in DR's EXTRA (Dose–Responses to Exercise Training) baseline among subjects with total fat intake below the median of 30·5 % of energy (E%)
(*β*-Coefficients and *P* values, *n* 557)

	Whole-body insulin sensitivity				Insulin secretion				Disposition indices				
	HOMA-IR		Matsuda-IS		Secr30		Secr120		DI30		DI120		
	β	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	
SF (E%)*	0·093	0·028	−0·102	0·015	0·027	0·527	0·051	0·233	−0·091	0·029	−0·080	0·052	Model 1
	0·089	0·034	−0·097	0·020	0·023	0·581	0·047	0·268	−0·088	0·034	−0·078	0·060	Model 2
	0·044	0·238	−0·050	0·171	0·003	0·935	0·022	0·584	−0·056	0·156	−0·043	0·264	Model 3

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; SF, saturated fat intake in percentage of energy intake.
* Log-transformed glucose metabolism indices were analysed as outcome variables using linear regression analysis. Dietary factors assessed by 4 d food records were analysed separately (no mutual adjustment) as explanatory variables, adjusted in model 1 for age and sex, in model 2 for age, sex and fitness (percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake) and in model 3 for age, sex, fitness and sex-specifically standardised waist circumference. The strength of an association is expressed per 1 SD (standardised coefficient) of the selected dietary factor and indicated by a *β* value. A *P* value of $<0·05$ was considered as significant.

sampled intravenous glucose tolerance test[14]. In addition, the present finding suggests that this association is independent of cardiorespiratory fitness and stronger in women than in men. Because increase in physical activity is known to improve insulin sensitivity[28], the present finding emphasises the independent contribution of dietary fibre and whole-grain products on insulin sensitivity. However, dietary fibre intake was inversely associated with the indices of insulin secretion *per se*, i.e. Secr30 and Secr120. The directions of associations for indices of insulin secretion *per se* and for the corresponding disposition indices were similarly reversed for a majority of dietary factors. This reversal of associations can be explained by the hyperbolic law: the product of β-cell function and insulin sensitivity remains unchanged in an individual whose β-cells respond to a decrease in insulin sensitivity by adequately increasing insulin secretion[13]. Therefore, when a dietary factor is associated with insulin sensitivity and maximum β-cell secretion capacity has not been reached, the same dietary factor is consequently associated inversely with insulin secretion. Thus, in the present population-based data, dietary fibre (independent of cardiorespiratory fitness) is associated not only with the maintenance of insulin sensitivity, but also with early-phase insulin secretion.

Women with high WC, but with a suboptimal lifestyle profile, i.e. either high SF intake or low fitness, had a significantly lower DI30 when compared with the reference category. Similarly, the beneficial effects of the lowering of SF intake on the disposition index were observed in women, but not in men[29]. However, that study did not include obese subjects and baseline fitness correlated with the insulin-sensitising effect of a low-SF diet but not with diet-induced changes in disposition index. Obesity-induced inflammation is a possible

Table 5. Means of indices of glucose metabolism defined by dichotomised cardiorespiratory fitness, waist circumference (WC) and saturated fat (SF)‡ intake in DR's EXTRA (Dose–Responses to Exercise Training) baseline among the total study-specific population of 1114 subjects§

			Whole-body insulin sensitivity		Insulin secretion		Disposition indices	
			HOMA-IR	Matsuda-IS	Secr30	Secr120	DI30	DI120
High fitness	Low WC	Low SF	1·33	8·75	23·3	37·9	184	288
		High SF	1·25	9·18	23·1	35·6	191	292
	High WC*	Low SF	2·28†	5·56†	34·1†	52·0†	159	235†
		High SF	2·43†	5·50†	33·0†	52·7†	146†	230†
Low fitness	Low WC	Low SF	1·43	8·37	27·1	42·5	189	292
		High SF	1·39	8·22	25·1	41·3	184	291
	High WC*	Low SF	2·24†	5·43†	33·6†	52·6†	156†	235†
		High SF	2·46†	5·10†	33·4†	52·8†	142†	220†

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; fitness, percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake; low *v.* high, cut-off defined by the median value for WC (97·0 cm (*n* 538, 48 %) in men and 86·5 cm (*n* 576, 52 %) in women) and SF (11·4 % of energy (E%) in men and 11·4 E% in women) and for fitness dichotomised at above or below 100 % of expected normal maximal oxygen uptake.
* Among the four categories with high WC, significantly different from the subjects with high fitness, high WC and low SF intake. No significant differences were found.
† Significantly different from the subjects with high fitness, low WC and low SF intake.
‡ SF intake assessed by 4 d food records.
§ Log-transformed glucose metabolism indices were compared using the general linear model, adjusted for age and sex, and using Bonferroni correction for multiple pairwise testing. Means displayed are non-log-transformed and non-adjusted values. A *P* value of $<0·05$ was considered as significant.

British Journal of Nutrition

Table 6. Means of indices of glucose metabolism defined by dichotomised cardiorespiratory fitness, waist circumference (WC) and saturated fat (SF)‡ intake in 576 women of the DR's EXTRA (Dose–Responses to Exercise Training) baseline§

			Whole-body insulin sensitivity		Insulin secretion		Disposition indices	
			HOMA-IR	Matsuda-IS	Secr30	Secr120	DI30	DI120
High fitness	Low WC	Low SF	1·18	9·46	23·6	37·6	207	316
		High SF	1·08	9·97	22·3	34·8	211	324
	High WC*	Low SF	2·26†	5·65†	35·8†	55·9†	173	255†
		High SF	2·49†	5·32†	35·0†	55·6†	154†	239†
Low fitness	Low WC	Low SF	1·41	8·29	30·0	45·9	216	327
		High SF	1·30	8·33	26·2	41·8	195	305
	High WC*	Low SF	2·01†	5·92†	32·3†	49·8†	169†	248†
		High SF	2·29†	5·38†	31·7	49·8†	142†	222†

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; fitness, percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake; low *v.* high, cut-off defined by the median value for WC (86·5 cm) and SF (11·4 % of energy) and for fitness dichotomised at above or below 100 % of expected normal maximal oxygen uptake.

* Among the four categories with high WC, significantly different from the subjects with high fitness, high WC and low SF intake. No significant differences were found.

† Significantly different from the subjects with high fitness, low WC and low SF intake.

‡ SF intake assessed by 4 d food records.

§ Log-transformed glucose metabolism indices were compared using the general linear model, adjusted for age, and using Bonferroni correction for multiple pairwise testing. Means displayed are non-log-transformed and non-adjusted values. A P value of $<0·05$ was considered as significant.

mediator and may explain the observed sex differences: an increase in body weight has been shown to elevate inflammatory markers[30]. This pro-inflammatory effect of adiposity is more pronounced in women[30]. Inflammatory activity in obese subjects may cause insulin resistance[31], which in turn may cause decreased insulin secretion[32]. Therefore, the pro-inflammatory effects of SF[31]- and physical activity-induced reduction in inflammation[33] may contribute to the more pronounced differences found in DI30 among women. The present study extends our knowledge that high fitness may have an important role together with low habitual SF intake to counteract even the adiposity-associated decrease in DI30 among women. High fitness alone could not counteract the negative association of high SF intake with DI30.

Low SF intake and high fitness did not differentiate adiposity-associated insulin sensitivity/resistance significantly as was found with adiposity-associated DI30. This suggests that the long-term effects of SF intake and fitness on insulin

Table 7. Means of indices of glucose metabolism defined by dichotomised cardiorespiratory fitness, waist circumference (WC) and saturated fat (SF)‡ intake in 538 men of the DR's EXTRA (Dose–Responses to Exercise Training) baseline§

			Whole-body insulin sensitivity		Insulin secretion		Disposition indices	
			HOMA-IR	Matsuda-IS	Secr30	Secr120	DI30	DI120
High fitness	Low WC	Low SF	1·47	8·07	23·1	38·2	162	261
		High SF	1·43	8·33	23·9	36·6	170	258
	High WC*	Low SF	2·30†	5·47†	32·5†	48·1	146	215
		High SF	2·36†	5·70†	30·7	49·6	137	221
Low fitness	Low WC	Low SF	1·44	8·47	23·7	38·5	157	252
		High SF	1·47	8·11	23·9	40·8	173	276
	High WC*	Low SF	2·50†	4·86†	35·0†	55·9†	141	219†
		High SF	2·66†	4·77†	35·4†	56·2†	142	217

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; fitness, percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake; low *v.* high, cut-off defined by the median value for WC (97·0 cm) and SF (11·4 % of energy) and for fitness dichotomised at above or below 100 % of expected normal maximal oxygen uptake.

* Among the four categories with high WC, significantly different from the subjects with high fitness, high WC and low SF intake. No significant differences were found.

† Significantly different from the subjects with high fitness, low WC and low SF intake.

‡ SF intake assessed by 4 d food records.

§ Log-transformed glucose metabolism indices were compared using the general linear model, adjusted for age, and using Bonferroni correction for multiple pairwise testing. Means displayed are non-log-transformed and non-adjusted values. A P value of $<0·05$ was considered as significant.

British Journal of Nutrition

Table 8. Means of indices of glucose metabolism defined by dichotomised cardiorespiratory fitness, waist circumference (WC) and saturated fat (SF)‡ intake in DR's EXTRA (Dose–Responses to Exercise Training) baseline among the subjects with total fat intake below the median of 30·5 % of energy (E%) (*n* 557)§

			Whole-body insulin sensitivity		Insulin secretion		Disposition indices	
			HOMA-IR	Matsuda-IS	Secr30	Secr120	DI30	DI120
High fitness	Low WC	Low SF	1·30	8·64	24·3	38·2	192	290
		High SF	1·30	8·71	21·7	35·6	172	276
	High WC*	Low SF	2·15†	5·81†	33·2	51·6	158‖	241
		High SF	2·44†	5·18†	33·4	52·1	143†	215†
Low fitness	Low WC	Low SF	1·48	8·14	27·5	41·6	184	280
		High SF	1·41	8·37	25·6	42·8	192	300
	High WC*	Low SF	2·21†	5·80†	33·3	51·9	164†‖	242†
		High SF	2·55†	4·53†	35·0†	56·6†	137†	220†

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; fitness, percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake; low *v.* high, cut-off defined by the median value for WC (96·9 cm (*n* 252, 45 %) in men and 86·5 cm (*n* 305, 55 %) in women) and SF (9·4 E% in men and 9·6 E% in women) and for fitness dichotomised at above or below 100 % of expected normal maximal oxygen uptake.

* Among the four categories with high WC, significantly different from the subjects with high fitness, high WC and low SF intake. No significant differences were found.

† Significantly different from the subjects with high fitness, low WC and low SF intake.

‡ SF intake assessed by 4 d food records.

§ Log-transformed glucose metabolism indices were compared using the general linear model, adjusted for age and sex, and using Bonferroni correction for multiple pairwise testing. Means displayed are non-log-transformed and non-adjusted values. A P value of $<0{\cdot}05$ was considered as significant.

‖ Age- and sex-adjusted log-transformed mean for the non-adjusted DI30 value of 158 was 2·146 (95 % CI 2·092, 2·200) and, respectively, the adjusted value for the non-adjusted DI30 value of 164 was 2·131 (95 % CI 2·081, 2·181). This explains why the estimated log-transformed mean for 164 is indicated ($P=0{\cdot}026$) and for 158 ($P=0{\cdot}166$) is not indicated to differ from the estimated log-transformed mean for the reference value of 192.

sensitivity/resistance may be reflected better in DI30 than in insulin sensitivity/resistance *per se*. Also in a previous study, SF intake appeared to be more important for maintaining normal glucose metabolism in overweight and obese subjects[34]. The observed associations between HOMA-IR/Matsuda-IS and SF intake only in subjects with limited total fat intake are supported by earlier findings in an intervention setting[6]. SF intake-dependent changes in HOMA-IR and Matsuda-IS (β values) were similar, whereas fibre intake correlated with smaller changes in HOMA-IR compared with Matsuda-IS. This observation suggests that SF intake may have a greater relative impact on hepatic insulin resistance

Table 9. Means of indices of glucose metabolism defined by dichotomised cardiorespiratory fitness, waist circumference (WC) and dietary fibre intake in DR's EXTRA (Dose–Responses to Exercise Training) baseline among the total study-specific population of 1114 subjects‡

			Whole-body insulin sensitivity		Insulin secretion		Disposition indices	
			HOMA-IR	Matsuda-IS	Secr30	Secr120	DI30	DI120
High fitness	Low WC	High fibre	1·29	9·35	23·4	37·0	196	299
		Low fibre	1·30	8·38	22·9	36·8	175	276
	High WC*	High fibre	2·41†	5·74†	32·9†	51·1†	161†	237†
		Low fibre	2·32†	5·37†	33·9†	53·4†	145†	229†
Low fitness	Low WC	High fibre	1·35	8·50	25·4	41·3	190	297
		Low fibre	1·47	8·06†	26·7	42·6	183	286
	High WC*	High fibre	2·31†	5·52†	31·4†	49·7†	147†	226†
		Low fibre	2·39†	5·05†	35·2†	55·1†	149†	228†

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; fitness, percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake; fibre, dietary fibre intake assessed by 4 d food records; low *v.* high, cut-off defined by the median value for WC (97·0 cm in men and 86·5 cm in women) and fibre (3·0 g/MJ or 12·7 g/1000 kcal in men and 3·3 g/MJ or 13·9 g/1000 kcal in women) and for fitness dichotomised at above or below 100 % of expected normal maximal oxygen uptake.

† Significantly different from the subjects with high fitness, low WC and high fibre intake.

* Among the four categories with high WC, significantly different from the subjects with high fitness, high WC and high fibre intake. No significant differences were found.

‡ Log-transformed glucose metabolism indices were compared using the general linear model, adjusted for age and sex, and using Bonferroni correction for multiple pairwise testing. Means displayed are non-log-transformed and non-adjusted values. A P value of $<0{\cdot}05$ was considered as significant.

British Journal of Nutrition

Table 10. Means of indices of glucose metabolism defined by dichotomised cardiorespiratory fitness, waist circumference (WC) and dietary fibre intake in 576 women of the DR's EXTRA (Dose–Responses to Exercise Training) baseline‡

			Whole-body insulin sensitivity		Insulin secretion		Disposition indices	
			HOMA-IR	Matsuda-IS	Secr30	Secr120	DI30	DI120
High fitness	Low WC	High fibre	1·08	10·43	23·6	36·1	231	341
		Low fibre	1·20	8·82	22·3	36·5	183	295
	High WC*	High fibre	2·27†	5·89†	33·6†	52·9†	168†	248†
		Low fibre	2·50†	5·06†	37·1†	58·5†	156†	244†
Low fitness	Low WC	High fibre	1·31	8·43	27·5	42·3	212	322
		Low fibre	1·40	8·17†	28·9	45·8	199	309
	High WC*	High fibre	2·03†	6·24†	29·4	44·8	159†	237†
		Low fibre	2·25†	5·18†	34·0†	53·7†	152†	233†

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; fitness, percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake; fibre, dietary fibre intake assessed by 4 d food records; low *v.* high, cut-off defined by the median value for WC (86·5 cm) and fibre (3·3 g/MJ or 13·9 g/1000 kcal) and for fitness dichotomised at above or below 100 % of expected normal maximal oxygen uptake.

* Among the four categories with high WC, significantly different from the subjects with high fitness, high WC and high fibre intake. No significant differences were found.

† Significantly different from the subjects with high fitness, low WC and high fibre intake.

‡ Log-transformed glucose metabolism indices were compared using the general linear model, adjusted for age, and using Bonferroni correction for multiple pairwise testing. Means displayed are non-log-transformed and non-adjusted values. A P value of $<0·05$ was considered as significant.

than dietary fibre intake. Similarly, a short-term intervention with a hyperenergetic diet providing 20 E% from SF induced hepatic, but not peripheral, insulin resistance[8]. Possible pathophysiological mechanisms have been described as follows: insulin resistance pronounced in obese[35], together with decreased insulin secretion, leads to hyperglycaemia[13], which, in turn, may decrease insulin secretion via hyperglycaemia-induced incretin resistance[36] and via an overall glucotoxic effect on β-cells[37,38]. Furthermore, elevated levels of SFA in the blood may via the induction of hexokinase impair endocrine pancreas function[39]. Physical activity may augment physiological glucose metabolism via improved insulin sensitivity[28]. The lipotoxic effect of high levels of NEFA on β-cells[38] is also a potential pathophysiological mechanism: high concentration of NEFA is common in overweight adults[40], and a diet high in SF elevates[41], whereas physical activity attenuates plasma NEFA concentration[28]. Our data suggest that the DI30 is the most sensitive of the studied markers regarding lifestyle-mediated homeostasis of glucose metabolism. Our findings expand on our previous short

Table 11. Means of indices of glucose metabolism defined by dichotomised cardiorespiratory fitness, waist circumference (WC) and dietary fibre intake in 538 men of the DR's EXTRA (Dose–Responses to Exercise Training) baseline‡

			Whole-body insulin sensitivity		Insulin secretion		Disposition indices	
			HOMA-IR	Matsuda-IS	Secr30	Secr120	DI30	DI120
High fitness	Low WC	High fibre	1·48	8·38	23·2	37·7	165	262
		Low fibre	1·41	7·87	23·7	37·2	165	255
	High WC*	High fibre	2·61†	5·54†	32·0	48·7	150	221
		Low fibre	2·17†	5·63†	31·3	49·0	136	216
Low fitness	Low WC	High fibre	1·39	8·58	23·2	40·2	165	268
		Low fibre	1·54	7·95	24·4	39·1	165	261
	High WC*	High fibre	2·61†	4·74†	33·6†	55·1†	135	214
		Low fibre	2·56†	4·88†	36·6†	56·9†	147	221

HOMA-IR, index of whole-body insulin resistance with an emphasis on the assessment of hepatic insulin resistance; Matsuda-IS, index of whole-body insulin sensitivity with an emphasis on the assessment of peripheral insulin sensitivity; Secr30, index of early-phase insulin secretion; Secr120, index of later-phase insulin secretion; DI30, index of early-phase insulin secretion that takes insulin sensitivity into account; DI120, index of later-phase insulin secretion that takes insulin sensitivity into account; fitness, percentage of expected normal cardiorespiratory fitness assessed as maximal oxygen uptake; fibre, dietary fibre intake assessed by 4 d food records; low *v.* high, cut-off defined by the median value for WC (97·0 cm) and fibre (3·0 g/MJ or 12·7 g/1000 kcal) and for fitness dichotomised at above or below 100 % of expected normal maximal oxygen uptake.

* Among the four categories with high WC, significantly different from the subjects with high fitness, high WC and high fibre intake. No significant differences were found.

† Significantly different from the subjects with high fitness, low WC and high fibre intake.

‡ Log-transformed glucose metabolism indices were compared using the general linear model, adjusted for age, and using Bonferroni correction for multiple pairwise testing. Means displayed are non-log-transformed and non-adjusted values. A P value of $<0·05$ was considered as significant.

British Journal of Nutrition

report that SF intake and fitness may modulate the adiposity-related risk of elevated fasting plasma glucose[9]. Plasma glucose concentrations remain normal as long as the maximum capacity to secrete insulin is not reached (hyperbolic law)[13]. Hence, the combination of both insulin sensitivity/resistance and insulin secretion is a more sensitive marker of the association between nutrient intake and glucose metabolism. Measures of insulin sensitivity and early-phase insulin secretion derived from the OGTT are less precise than intravenous methods. Conclusive specificity of OGTT-derived indices for either early- or second-phase insulin secretion cannot be postulated[42], nor are HOMA-IR- and Matsuda-IS-specific methods that differentiate hepatic and peripheral insulin sensitivity/resistance, respectively[24]. Yet, the selected indices are less resource-intensive and allow an assessment of insulin sensitivity and insulin secretion also in larger samples, such as those in the present study. Moreover, early-phase insulin secretion calculated from an OGTT may be more physiologic than intravenous methods because the gastrointestinal contribution to insulin secretion is not bypassed[43]. Furthermore, the OGTT-derived DI30 used in the present study is an independent predictor of T2DM incidence[44].

The cross-sectional setting of the study cannot delineate causality. The possibility of the effect of unknown or residual confounding cannot be ruled out, either. Moreover, as illustrated by the Look AHEAD study, favourable changes in risk factors may not always translate into a lower incidence of endpoints[45]. The major strengths of the present study are the use of a 4 d food record to assess dietary intake and maximal exercise tests with a direct measurement of oxygen consumption for cardiorespiratory fitness and the oral glucose tolerance test to assess insulin secretion and insulin sensitivity. The use of a population-based sample of middle-aged and elderly subjects increases the external validity of the present study. Seasonal variation in diet may not have been captured at an individual level; however, as the examination of the present study population was spread out over 1·5 years, introduction of a general bias is unlikely.

In conclusion, intake of dietary fibre and whole-grain bread were positively associated with insulin sensitivity, independent of physical fitness and WC. In women, dietary fibre intake was also positively associated with the markers of early-phase insulin secretion. Moreover, the deleterious effect of abdominal obesity may be attenuated by a combination of low SF intake together with high fitness.

Acknowledgements

The DR's EXTRA Study was supported by grants from the Ministry of Education and Culture of Finland (627; 2004–2011), the Academy of Finland (104943, 123885), the European Commission FP6 Integrated Project (LSHM-CT-2004-005272; EXGENESIS), the Kuopio University Hospital, the Finnish Diabetes Association, the Finnish Foundation for Cardiovascular Research, the Päivikki and Sakari Sohlberg Foundation, the City of Kuopio and the Social Insurance Institution of Finland. The present study, including the analysis of DR's EXTRA baseline data and reporting of the results, was supported by the Juho Vainio Foundation (to H. M. H.) and the Diabetes Research Foundation (to H. M. H.). None of the funders had any role in the design and analysis of the study or in the writing of this article.

The authors' contributions are as follows: R. R. contributed to the study conception and design; H. M. H. contributed to the data collection; H. M. H., B. K., R. R. and U. S. S. contributed to the study-specific research questions; H. M. H. and B. K. analysed the data; H. M. H., B. K., R. R. and U. S. S. contributed to the data interpretation and discussion; H. M. H. drafted the manuscript; H. M. H., B. K., R. R. and U. S. S. revised the manuscript; R. R. was a guarantor of the study.

The authors declare that there are no conflicts of interest.

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