RESEARCH ARTICLE

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Effects of Insoluble Cereal Fibre on Body Fat Distribution in the Optimal Fibre Trial

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Scope: The Optimal Fibre Trial (OptiFiT) investigates metabolic effects of insoluble cereal fibre in subjects with impaired glucose tolerance (IGT), showing moderate glycemic and anti-inflammatory benefits, especially in subjects with an obesity-related phenotype. An OptiFiT sub-group is analysed for effects on body fat distribution.

Methods and results: 180 participants with IGT receive a blinded, randomized supplementation with insoluble cereal fibre or placebo for 2 years. Once a year, all subjects undergo fasting blood sampling, oral glucose tolerance test, and anthropometric measurements. A subgroup (n=47) also received magnetic resonance imaging and spectroscopy for quantification of adipose tissue distribution and liver fat content. We compared MR, metabolic and inflammatory outcomes between fibre and placebo group metabolism and inflammation.

Visceral and non-visceral fat, fasting glucose, HbA1c, fasting insulin, insulin resistance, and uric acid decrease only in the fibre group, mirroring effects of the entire cohort. However, after adjustment for weight loss, there are no significant between-group differences. There is a statistical trend for fibre-driven liver fat reduction in subjects with confirmed non-alcoholic fatty liver disease (NAFLD; $n = 19$).

Conclusions: Data and evidence on beneficial effects of insoluble cereal fibre on visceral and hepatic fatstorage is limited, but warrants further research. Targeted trials are required.

1. Introduction

The systemic metabolic disorder of type 2 diabetes mellitus (T2DM) is a systemic burden of modern societies and health care systems. The rising case numbers will soon be followed by an increase in comorbidities, invalidity and premature deaths in most countries of the world. This perspective is not unavoidable, as T2DM onset and progression are strongly influenced by lifestyle factors such as energy balance and specific dietary components. By addressing these factors in a structured prevention setting, T2DM incidence can be reduced by about 50%.[1–4]

More than 60% of T2DM patients are obese, most of them with visceral adiposity. Also up to 75% of T2DM patients are diagnosed with non-alcoholic fatty liver disease (NAFLD).[5] Similar prevalences apply to prediabetes.[6] These fat depots independently increase long-term morbidity for these patients.[7] Thus, simply reducing food intake may lead to diabetes remission, but given discussions about the obesity paradox and limited compliance to dietary restrictions it is still

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unclear how feasible a general approach of fasting techniques or very-low calorie diets might actually be. Despite achieving normal glucose regulation by losing weight, several side effects and the large proportion of primarily non-obese T2DM patients need to be taken into account.

Apart from overnutrition, specific nutritional factors such as saturated fats, alcohol, and insoluble dietary fibre contribute to the dietary risk profile for T2DM.[8] However, these factors, too, are hard to modulate in a long-term perspective for most of the subjects. Also, up to now, these factors are merely described as risk-associated on the basis of cohort studies, while interventional data is limited. The impressive risk reduction by high intake of insoluble cereal fibre has recently been addressed by the first long-term randomized controlled trial (RCT)—the Optimal Fibre trial (OptiFiT). It demonstrated small-to-moderate dose-dependent effects on 2-h glucose and HbA1c levels as well as on an inflammatory outcome.[9,10] In subjects with combined impaired fasting glucose (IFG) and glucose intolerance, a phenotype linked to both obesity and NAFLD, glycemic improvements were stronger than in subjects with isolated impaired glucose tolerance (IGT).[11] Stratification by obesity did not show a relevant effect-modulation for glycemic improvements, but for reductions in leukocyte count, a measure for systemic inflammation.[12] Dose-dependent analysis of the trial corroborated these findings and underlined a potential involvement of liver fat reduction in the overall metabolic amelioration.[10]

Insoluble cereal fibre is typically poorly fermentable; therefore, production of small-chain fatty acids in the gut is unlikely to play an important mechanistic role for this type of dietary fibre.[13,14] Still, high intake of insoluble cereal fibre is associated with a reduced risk for NAFLD, showing stronger effect sizes than fruit and vegetable fibre, both of which are mainly soluble.[15,16] While there is not a single human RCT, specifically investigating the effect of insoluble dietary fibre on liver fat, there is at least some preclinical evidence for such effects in rats.[17] In humans, subjects with higher intake of insoluble fibre have smaller visceral adipose tissue depots.[18,19] Also, whole grain intake seems to actively reduce inflammation and abdominal body fat, irrespective of weight loss.[20] However, this could be related to various whole grain components, including proteins, minerals, vitamins and different types of fibre. Once again, up to now there is also no publication on specific effects of insoluble cereal fibre on visceral fat. Previous rodent studies using cellulose supplements did not show a reduction in visceral fat mass, but anti-inflammatory changes in the gut microbiome.[21,22]

In all previous assessments within OptiFiT, surrogate measures for visceral fat—waist circumference or waist-to-hip ratio—and NAFLD—fatty liver index (FLI) or other scores—were used, considering their limitation especially in longitudinal studies.[23] However, a subgroup of the OptiFiT cohort underwent a detailed study protocol including magnetic resonance imaging and spectroscopy (MRI/MRS), providing precise data on body fat distribution and liver fat content. Based on these data, we want to clarify the involvement of pathological fat depots in the glycemic improvements by supplementation with specifically insoluble cereal fibre as the first clinical study so far.

2. Research Design and Methods

The study protocol was approved by the ethics committee of the University of Potsdam as well as the ethics committee of the Charité, and all individuals gave written informed consent. The trial was registered at clinicaltrials.gov (NCT 01681173). In our previous core paper, we already reported the details for ethics approval, study registration and recruitment, documented the inclusion and exclusion criteria and described the overall study design.[9] 180 subjects with IGT were recruited. This metabolic subtype of prediabetes was chosen, as it bears an elevated risk for diabetes onset and long-term complications.[24] Major metabolic outcomes were assessed once a year, including fasting blood sampling, oral glucose tolerance test, and anthropometric measurements. A subgroup of the cohort ($n = 47$) also received MRI and MRS according to previously defined protocols. Subjects with and without MR examination did not differ from each other with respect to sex, age, BMI, or glycemic state. Selection for MR examination was done in a randomized fashion before allocation to the intervention groups. Subjects with and without MR data received the same intervention. 28 of the subjects with MR data completed the first year of intervention, which consisted of the supplementation and the modified lifestyle intervention program PREDIAS.[25] The 12 consultations focused on increased physical activity (240 min week^{-1}) and on dietary recommendations of the German Society for Nutrition (DGE): Fat intake < 30 kcal%, intake of saturated fat < 10 kcal%, intake of total dietary fibre > 15 g/1000 kcal. Dietary fibre should be gained from whole-grain products, legumes, vegetables, and low-sugar fruits such as berries. Low-fat dairy and meat products, soft margarines, and healthy vegetable oils were recommended to sustain a low-fat profile.

Dietary baseline status and interventional compliance was assessed by 4-day food records. Nutrient intake, including all macro- and several micronutrients, was determined using

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the nutrition software PRODI 5.8 based on Bundeslebensmittelschlüssel 3.0.[26]

2.1. Dietary Supplement

Details on the supplementation procedure, measurements and laboratory parameters have been given in the core paper.[9] Patients' adherence to the supplementation was controlled by weighing the frequently returned supplement tins after each dispension period.

2.2. Calculations

Insulin resistance was assessed by the homeostasis model assessment homeostasis model assessment insulin resistance index[27] and the insulin sensitivity index of blood free fatty acids[28] as well as the dynamic insulin sensitivity index by Belfiore.[29] We also assessed the hepatic insulin clearance according to the established formula.[30]

In order to mirror findings of the entire cohort, we also report the FLI in addition to MR results.[31]

2.3. Statistical Analyses

In order to provide parallel data to the core publication, this analysis was done by intention-to-treat principles, as well. Missing data was filled by the last-observation-carried-forward method, therefore both completers and non-completers are included. We used the Kolmogorov-Smirnov test in order to determine normal distribution of our data. Given the frequent absence of normal distribution, we decided to conduct non-parametric tests throughout the entire trial ensuring a uniform representation of our data. We used Mann–Whitney tests for cross-sectional comparisons and Wilcoxon tests for longitudinal comparisons. All data are presented as means ± standard deviation. The results were considered significantly different if $p < 0.05$. All statistical analyses were performed using SPSS for Windows program version 22.0 (SPSS Inc, Chicago, IL, USA).

3. Results

Baseline data for this sub-cohort is given in **Table 1**. There are no differences between fibre and placebo group.

Baseline and interventional state of dietary intake are shown in **Table 2**. While there were no differences before the intervention, intake of total (and in particular: insoluble) fibre was significant higher in the fibre group.

Interventional changes are presented in **Table 3**. Within the placebo group, body weight was the only variable with a significant decrease, while in the fibre group, anthropometric, glycemic, and other metabolic parameters improved significantly. While there was no significant difference in change of body weight between the groups, there were such differences for total body fat, non-visceral, and visceral fat, as well as, liver fat content. After adjustment for change in body weight, none of these results remained statistically significant.

Table 1. Characteristics of participants at study entry.

	Fibre group ($n = 22$)	Placebo group ($n = 25$)	p-value
Age	60 ± 9	60 ± 9	n.s.
Sex (female)	64%	44%	n.s.
Anthropometry			
Weight [kg]	88.9 ± 14.2	90.2 ± 18.4	n.s.
Waist circumference [cm]	102.8 ± 10.1	103.9 ± 13.0	n.s.
Hip circumference [cm]	109.7 ± 12.5	108.6 ± 10.0	n.s.
WHR	0.94 ± 0.08	0.96 ± 0.09	n.s.
BIA—Body fat [%]	37.6 ± 9.5	35.6 ± 8.0	n.s.
Magnet resonance imaging and spectroscopy/Liver fat indices			
Total body fat [L]	20.8 ± 6.9	20.1 ± 6.0	n.s.
Non-visceral fat [L]	15.7 ± 6.3	14.3 ± 5.0	n.s.
Visceral fat [L]	5.0 ± 1.3	5.8 ± 2.5	n.s.
Ratio of visceral and subcutaneous fat [%]	26.2 ± 8.8	28.9 ± 10.1	n.s.
Liver fat content [%]	10.3 ± 7.1	11.1 ± 11.0	n.s.
Fatty liver index	65 ± 25	68 ± 29	n.s.
Glycemic metabolic outcomes			
Fasting glucose [mg dl^{-1}]	111.8 ± 10.8	109.8 ± 13.6	n.s.
2-h glucose [mg dl^{-1}]	166.6 ± 30.2	175.2 ± 47.0	n.s.
HbA_{1c} [%]	5.6 ± 0.3	5.7 ± 0.4	n.s.
Fasting insulin [mU L^{-1}]	9.7 ± 5.3	10.7 ± 6.3	n.s.
Fasting C-peptide [µg L^{-1}]	1.6 ± 0.6	2.0 ± 0.9	n.s.
HOMA-IR	2.7 ± 1.5	2.8 ± 2.1	n.s.
ISI_{ffa}	0.90 ± 0.34	0.87 ± 0.31	n.s.
Belfiore index	0.64 ± 0.19	0.68 ± 0.34	n.s.
$HIC_{c\text{-}peptide}$ [mU μg^{-1}]	4.2 ± 1.5	4.9 ± 1.9	n.s.
Further metabolic outcomes			
HDL cholesterol [mmol L^{-1}]	1.3 ± 0.2	1.3 ± 0.3	n.s.
LDL cholesterol [mmol L^{-1}]	3.7 ± 0.8	3.6 ± 0.7	n.s.
CRP [mg L^{-1}]	5.0 ± 4.9	2.8 ± 2.7	n.s.
Leukocyte count [Gpt L^{-1}]	5.85 ± 1.35	5.66 ± 1.73	n.s.
Uric acid [µmol L^{-1}]	355 ± 63	360 ± 82	n.s.

Data are means (SD), significant differences between the groups: $*p < 0.05$, $**p < 0.01$, $***p < 0.001$.

When comparing the groups, we found a trendwise stronger reduction in HbA1c in the fibre group (fibre: −0.1 ± 0.4% vs placebo: 0.2 ± 0.5 µmol L^{-1}; delta −0.3 ± 0.1 µmol L^{-1}; $p = 0.048$; $p_{adj} = 0.071$), replicating results from our core paper.[9] We also found a trend towards stronger reduction in uric acid levels (fibre: −33 ± 38 µmol L^{-1} vs placebo: 0 ± 60 µmol L^{-1}; delta −33 ± 15 µmol L^{-1}; $p = 0.041$; $p_{adj} = 0.078$), which was also seen in our earlier publication.[9] However, the differences were not statistically significant after adjustment for weight change.

When selecting patients fulfilling criteria for NAFLD at baseline (liver fat content > 5.56%; $n = 31$), the trendwise effect on liver fat was numerically stronger, but did not reach significance either (fibre: −3.3 ± 6.7%-pts vs placebo: 0.1 ± 4.0%-pts.; delta −3.4 ± 1.9%-pts.; $p = 0.083$).

Analysis by as-treated principles did not lead to relevantly different results for any outcome. However, based on the as-treated data set, a putative effect on liver fat as seen in our study

Table 2. Baseline status and changes in lifestyle habits during intervention.

	Fibre ($n = 22$)	Placebo ($n = 25$)	p-value
Total energy intake [kcal day^{-1}]	2022 ± 460	2161 ± 699	n.s.
Carbohydrate intake [g day^{-1}]	215 ± 58	242 ± 91	n.s.
Carbohydrate intake [kcal%]	44 ± 7	46 ± 8	n.s.
Fat intake [g day^{-1}]	80 ± 22	85 ± 31	n.s.
Fat intake [kcal%]	37 ± 6	36 ± 6	n.s.
Protein intake [g day^{-1}]	79 ± 23	85 ± 25	n.s.
Protein intake [kcal%]	16 ± 4	17 ± 3	n.s.
Dietary fibre intake [g 1000 kcal^{-1}]	10 ± 2	11 ± 3	n.s.
Total dietary fibre intake [g day^{-1}]	21 ± 5	23 ± 8	n.s.
insoluble	14 ± 3	15 ± 5	n.s.
soluble	6 ± 2	7 ± 2	n.s.
Magnesium [mg day^{-1}]	336 ± 73	361 ± 108	n.s.
Calcium [mg day^{-1}]	872 ± 230	951 ± 345	n.s.
Iron [mg day^{-1}]	12 ± 3	12 ± 4	n.s.
Vitamin C [mg day^{-1}]	134 ± 57	166 ± 70	n.s.
Vitamin D [µg day^{-1}]	6 ± 5	6 ± 7	n.s.
Alcohol [g day^{-1}]	15 ± 19	10 ± 16	n.s.
Change during one year			
Total energy intake [kcal day^{-1}]	−134 ± 418	−126 ± 596	n.s.
Carbohydrate intake [g day^{-1}]	−2 ± 39	−13 ± 73	n.s.
Carbohydrate intake [kcal%]	3 ± 7	1 ± 7	n.s.
Fat intake [g day^{-1}]	−4 ± 29	−9 ± 29	n.s.
Fat intake [kcal%]	1 ± 8	−2 ± 5	n.s.
Protein intake [g day^{-1}]	−9 ± 18	4 ± 28	n.s.
Protein intake [kcal%]	−1 ± 3	1 ± 3	n.s.
Dietary fibre intake [g 1000 kcal^{-1}]	10 ± 4***	2 ± 3*	<0.001
Total dietary fibre intake [g day^{-1}]	12 ± 9***	1 ± 7	<0.001
Insoluble	12 ± 7***	2 ± 5	<0.001
Soluble	1 ± 1*	−0 ± 2	0.021
Magnesium [mg day^{-1}]	2 ± 86	−8 ± 86	n.s.
Calcium [mg day^{-1}]	33 ± 223	95 ± 386	n.s.
Iron [mg day^{-1}]	−2 ± 3	−0 ± 4	n.s.
Vitamin C [mg day^{-1}]	12 ± 56	9 ± 54	n.s.
Vitamin D [µg day^{-1}]	−0 ± 9	−2 ± 7	n.s.
Alcohol [g day^{-1}]	−9 ± 22	−2 ± 11	n.s.

Data are means (SD). Nutrient intakes were calculated from four-day food records; *Significant changes within the groups or differences between the groups: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

($n = 19$ subjects with NAFLD at baseline; fibre: −5.4 ± 8.0%-pts vs placebo: 0.0 ± 5.2%-pts; delta −5.4 ± 3.0%-pts.; $p = 0.090$) could be demonstrated in a new trial with 84 subjects (90% power).

4. Discussion

In our current analysis of OptiFiT, we find no conclusive evidence for effects of insoluble cereal fibre on body fat distribution of liver fat content. Mainly accountable to the limited sample size of the small MR subgroup (in comparison to the entire cohort), both metabolic outcomes such as HbA1c, postprandial glucose or uric acid levels as well as MR-based assessed body fat compartments and intrahepatic lipid storage failed to reach a statistically significant difference between the intervention groups.

Table 3. Changes during one year of lifestyle intervention.

	Fibre group ($n = 22$)	Placebo group ($n = 25$)	p-value	p-value$_{adj}$
Anthropometry				
Weight [kg]	−3.7 ± 5.7**	−1.8 ± 4.7**	n.s.	n.s.
Waist circumference [cm]	−2.8 ± 5.6*	−1.3 ± 5.1	n.s.	n.s.
Hip circumference [cm]	−2.3 ± 3.5**	−0.7 ± 3.4	n.s.	n.s.
WHR	−0.01 ± 0.04	−0.01 ± 0.04	n.s.	n.s.
BIA—Body fat [%]	−1.9 ± 4.1	−1.6 ± 3.9	n.s.	n.s.
Magnet resonance imaging and spectroscopy/Liver fat indices				
Total body fat [L]	−1.3 ± 2.8**	−0.1 ± 2.2	0.041	n.s.
Non-visceral fat [L]	−0.8 ± 2.1*	0.0 ± 1.5	0.039	n.s.
Visceral fat [L]	−0.4 ± 0.7**	−0.2 ± 0.9	0.019	n.s.
Ratio of visceral and subcutaneous fat [%]	−0.5 ± 1.0*	0.1 ± 2.1	n.s.	n.s.
Liver fat content [%]	−1.5 ± 6.2	0.1 ± 3.4	0.035	n.s.
Fatty liver index	−8 ± 17*	−4 ± 12	n.s.	n.s.
Glycemic metabolic outcomes				
Fasting glucose [mg dl^{-1}]	−4.7 ± 9.2*	−3.0 ± 7.9	n.s.	n.s.
2-h glucose [mg dl^{-1}]	−10.3 ± 35.6	−11.1 ± 40.7	n.s.	n.s.
HbA_{1c} [%]	−0.1 ± 0.4	0.2 ± 0.5	0.048	n.s.
Fasting insulin [mU L^{-1}]	−2.3 ± 3.5**	0.0 ± 5.8	n.s.	n.s.
Fasting C-peptide [µg L^{-1}]	−0.3 ± 0.5	0.1 ± 1.0	n.s.	n.s.
HOMA-IR	−0.7 ± 1.0**	−0.1 ± 1.6	n.s.	n.s.
ISI_{ffa}	−0.14 ± 0.30	−0.12 ± 0.30	n.s.	n.s.
Belfiore index	0.15 ± 0.18**	0.13 ± 0.26	n.s.	n.s.
$HIC_{c\text{-}peptide}$ [mU µg^{-1}]	1.1 ± 1.4*	1.1 ± 2.5	n.s.	n.s.
Further metabolic outcomes				
HDL cholesterol [mmol L^{-1}	0.0 ± 0.2	−0.1 ± 0.2	n.s.	n.s.
LDL cholesterol [mmol L^{-1}]	−0.2 ± 0.4*	−0.1 ± 0.5	n.s.	n.s.
CRP [mg L^{-1}]	−0.3 ± 4.0	−1.0 ± 2.4	n.s.	n.s.
Leukocyte count [Gpt L^{-1}]	−0.46 ± 1.16	−0.02 ± 0.81	n.s.	n.s.
Uric acid [µmol L^{-1}]	−33 ± 38**	0 ± 60	0.041	n.s.

Data are means (SD). *Significant changes within the groups or differences between the groups: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$; Primary p-value from Mann–Whitney test, adjusted p-value from ANOVA with weight change as co-variable.

Our study is the first human RCT investigating the effect of insoluble cereal fibre on measures of visceral adiposity and NAFLD. While cohort studies consistently imply a role of non-digestible carbohydrates in the prevention of NAFLD and the accumulation of visceral fat,[15,16,18,19] RCTs in humans are still sparse and were mainly using whole grain food products rather than specific fibre supplements.[20] Several rodent trials indicate, that both inflammation and liver fat content could be reduced by interventions with cellulose and other types of insoluble fibre.[17,21,22] Our OptiFiT dataset encourages further interventional research in humans.

Numerically, the reported difference in HbA1c is replicating our earlier results from this trial, indicating that this subgroup is representative for the entire cohort. Beneficial effects of whole-grain products, in particular driven by insoluble fibre, have been published in other studies, too.[32]

In addition to that, we demonstrate a trendwise benefit for uric acid, a common surrogate parameter for the metabolic syndrome and in particular inflammation and NAFLD. This is mirrored by a similar trend for visceral fat amount and liver fat content, which remained completely unchanged in the placebo group and seemed to decrease in the fibre group. This finding is in line with our recent paper, showing that subjects with combined IFG and IGT achieve stronger reductions in postprandial glucose levels. Combined IFG-IGT is more tightly associated to obesity and NAFLD when compared to isolated IGT.[33,34] It has to be assumed, that better improvements of glycemia are related to a phenotype-specific responsiveness, which could be connected to either visceral obesity or hepatic fat storage. Other diabetes prevention trials have demonstrated, that IFG-IGT subjects are more responsive to lifestyle treatment or insulin-sensitizing drugs that those with normal fasting glucose.[35–37] Lifestyle treatments in general and insoluble fibre in particular seem to primarily act via amelioration of insulin resistance rather than beta-cell failure.[38,39] Our supplement—which was also used in the previous ProFiMet study—also appears to affect bile acid metabolism, which might provide another link to liver function.[40] Anti-inflammatory effects of insoluble fibre were also seen in earlier analyses of OptiFiT, corroborating findings from association studies.[9,12,41,42]

We are of course aware of limitations of our study. The combined intervention with lifestyle program and supplementation may lead to combined effects, to differential changes in energy intake, energy expenditure, and nutrient composition. We even need to consider subjects in the placebo group with an undesired high fibre intake, even though they just kept sticking to the dietary recommendations apart from the supplement. However, both groups did not differ in any aspect of lifestyle changes, including energy balance and diet composition. This covers all macronutrients, dietary fibre from food (not the supplement) and a selection of micronutrients, mirroring the intake of vegetables and fruits, animal-based products and alcoholic beverages. Despite lacking a significantly different weight loss between fibre and placebo, we adjusted our results for weight change. Most subjects actually failed to increase their fibre intake by means of regular diet as it is seen in earlier trials.[43] The majority of our patients surpassed the desired level of insoluble fibers by supplementation, only.[9,10] Similarly, the low-fat regime was not followed as thoroughly as scheduled. Reducing fat intake below 30 kcal% is a typical goal in lifestyle intervention studies, but it is rarely achieved for a long time.[1–4] As this flaw is apparent in both of our intervention groups, we do not expect a modulating impact on the fibre effect. With respect to our pedometer data, a confounding effect of physical activity seems unplausible, as we found no significant difference between the groups.

The sample size is very limited and—given the strict inclusion criteria and the undesired skewed sex distribution—does not allow generalizable deductions for all prediabetes patients. Still, the sample size is comparable to other pilot studies investigating the effect of a single nutrient, supplement or food product on liver fat content,[44–47] and mirrors the per-group sample sizes of previous RCTs addressing other metabolic outcomes of supplementation with insoluble cereal fibre.[38,48,49]

As for the previous publications of OpTiFiT, we are convinced that using 4-day food records and drug accounting of supplements was the best way to report dietary compliance, including all sources of dietary fibre. Biomarkers for fibre intake are not available.

In summary, we report no statistically significant effects of a one-year intervention with twice-daily supplements containing insoluble fibre on either glycometabolic or body fat distribution in the MR subgroup of IGT subjects in OptiFiT. The numerical effect size for HbA1c, uric acid, visceral fat volume, and liver fat content warrants further targeted studies on poorly fermentable, insoluble cereal fibre.

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Conflict of Interest

S.K. and C.H. received a travel grant from Rettenmaier & Soehne, Holzmuehle, Germany, including conference fees and accommodation. The authors declare no further conflicts of interest associated with this manuscript. The sponsors were neither involved in study design, data collection nor publication.

Author Contributions

S.K. wrote the paper. C.H., C.G., and U.D. conducted the experiments by dietary consultation, collected and interpreted referring data. S.K., M.K., and A.L.B. performed all medical examinations and the medical supervision for the participants and collected and interpreted referring data. J.M. acquired and analyzed MR data. S.K. and N.M.T.M. performed the statistical analysis. C.G., A.M.A., M.O.W., and A.F.H.P. designed the study. All authors read and revised the manuscript, contributed to discussion, and approved the final version of this paper. S.K. is responsible for the integrity of the work as a whole and serves as guarantor of this work.

Data Availability Statement

Data sets are available by request to the corresponding author.

Keywords

diabetes mellitus type 2, diabetes prevention, impaired glucose tolerance, insoluble dietary fibre, liver fat, non-alcoholic fatty liver disease, prediabetes, visceral adipose tissue

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