BMJ Open Diabetes Research & Care

Association of a lifestyle score with cardiometabolic markers among individuals with diabetes: a cross-sectional study

Christina Baechle,[1,2] Alexander Lang,[1,2] Klaus Strassburger,[1,2] Oliver Kuss ,[1,2,3] Volker Burkart,[2,4] Julia Szendroedi,[2,4,5,6] Karsten Müssig,[2,4,6,7] Katharina Susanne Weber,[2,4,8] Vera Schrauwen-Hinderling,[2,4] Christian Herder ,[2,4,6] Michael Roden ,[2,4,6] Sabrina Schlesinger ,[1,2] for the GDS group

To cite: Baechle C, Lang A, Strassburger K, *et al*. Association of a lifestyle score with cardiometabolic markers among individuals with diabetes: a cross-sectional study. *BMJ Open Diab Res Care* 2023;**11**:e003469. doi:10.1136/bmjdrc-2023-003469

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjdrc-2023-003469).

Received 19 April 2023
Accepted 13 June 2023

For numbered affiliations see end of article.

Correspondence to
Dr Sabrina Schlesinger; schlesin@uni-duesseldorf.de

ABSTRACT

Introduction To investigate the associations of a lifestyle score with various cardiovascular risk markers, indicators for fatty liver disease as well as MRI-determined total, subcutaneous and visceral adipose tissue mass in adults with new-onset diabetes.

Research design and methods This cross-sectional analysis included 196 individuals with type 1 (median age: 35 years; median body mass index (BMI): 24 kg/m²) and 272 with type 2 diabetes (median age: 53 years; median BMI: 31 kg/m²) from the German Diabetes Study. A healthy lifestyle score was generated based on healthy diet, moderate alcohol consumption, recreational activity, non-smoking and non-obese BMI. These factors were summed to form a score ranging from 0 to 5. Multivariable linear and non-linear regression models were used.

Results In total, 8.1% of the individuals adhered to none or one, 17.7% to two, 29.7% to three, 26.7% to four, and 17.7% to all five favorable lifestyle factors. High compared with low adherence to the lifestyle score was associated with more favorable outcome measures, including triglycerides (β (95% CI) −49.1 mg/dL (−76.7; −21.4)), low-density lipoprotein (−16.7 mg/dL (−31.3; −2.0)), and high-density lipoprotein cholesterol (13.5 mg/dL (7.6; 19.4)), glycated hemoglobin (−0.5% (−0.8%; −0.1%)), high-sensitivity C reactive protein (−0.4 mg/dL (−0.6; −0.2)), as well as lower hepatic fat content (−8.3% (−11.9%; −4.7%)), and visceral adipose tissue mass (−1.8 dm³ (−2.9; −0.7)). The dose–response analyses showed that adherence to every additional healthy lifestyle factor was associated with more beneficial risk profiles.

Conclusions Adherence to each additional healthy lifestyle factor was beneficially associated with cardiovascular risk markers, indicators of fatty liver disease and adipose tissue mass. Strongest associations were observed for adherence to all healthy lifestyle factors in combination.

Trial registration number NCT01055093.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ A healthy lifestyle that includes a healthy diet, moderate alcohol consumption, exercise, not smoking and non-obese body mass index has great potential to prevent diabetes and potentially diabetes-related complications in persons with diabetes.

⇒ Little is known about the adherence to a healthy lifestyle score and cardiovascular risk markers, indicators of fatty liver disease, and adipose tissue mass in persons with newly diagnosed type 1 and type 2 diabetes.

WHAT THIS STUDY ADDS

⇒ Adherence to a healthy lifestyle was quite high among persons with newly diagnosed diabetes (8.1% of the individuals adhered to none or one, 17.7% to two, 29.7% to three, 26.7% to four, and 17.7% to all five favorable lifestyle factors).

⇒ A healthy lifestyle score was inversely related to blood lipids, glycated hemoglobin, high-sensitivity C reactive protein, lower hepatic fat content and visceral adipose tissue mass.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Adherence to an overall healthy lifestyle is associated with favorable cardiometabolic risk markers in persons with type 1 and type 2 diabetes and thus should be promoted.

⇒ Prospective studies are needed that investigate these associations as well as clinically relevant outcomes such as the onset of cardiovascular diseases in persons with diabetes over the long term.

INTRODUCTION

In 2021, 537 million people worldwide currently have diabetes, and a further increase is expected.[1] Diabetes is associated with increased risk of several comorbidities and complications, such as cardiovascular diseases, nephropathy, retinopathy, neuropathy, as well as liver diseases.[1–4] Thus, strategies

for early prevention of the progression of diabetes and its comorbidities are of high importance.

Lifestyle behaviors, consisting of a healthful eating pattern (eg, a high intake of whole grains, fruits, vegetables and a low intake of red and processed meat), moderate consumption of alcoholic beverages, regular physical activity, and non-smoking are modifiable factors that play an important role not only for the prevention, but also for the management of diabetes.[5] For example, intensive lifestyle intervention, aiming at weight loss through dietary modification and exercise training, was effective for the reduction of body weight, liver fat, glycated hemoglobin (HbA1c), blood lipids and blood pressure in obese people with diabetes,[6] and can be even effective for type 2 diabetes remission.[7 8] However, it needs to be clarified whether these beneficial effects are exclusively driven by the induced weight loss or whether lifestyle factors, specifically in combination, play a preventive role in diabetes management. In this context, evidence from observational studies indicates that adherence to a healthy lifestyle, based on the combination of nutrition, moderate alcohol consumption, physical activity, non-smoking and being in the normal body weight range, was not only related to the prevention of diabetes, but had also the potential to reduce premature death in individuals with diabetes.[9 10] Each additional healthy lifestyle factor was associated with improved survival in individuals with diabetes, and strongest associations were observed when all lifestyle factors were considered in combination.[9]

Whether an overall healthy lifestyle is already associated with cardiovascular health in persons with newly diagnosed diabetes is not yet clear. Therefore, the aim of this cross-sectional study was to analyze the association between a lifestyle score combining dietary factors, alcohol intake, physical activity, smoking, and obesity, regarding cardiovascular risk markers, indicators for fatty liver disease, and adipose tissue mass in individuals with recently diagnosed diabetes.

METHODS

Data sources

The German Diabetes Study (GDS) is an ongoing prospective cohort study, with the goal to examine the course of diabetes, to identify prognostic factors and the underlying mechanisms of diabetes-related comorbidities and complications. Participants were recruited via advertisements in local newspapers and on the institution's website, as well as via general practitioners, internists, diabetologists and endocrinologists, who received information and flyers in advance. After receiving the contact information, the potential participants were contacted and screened for eligibility for the study in a telephone interview. Further information on recruitment, including the inclusion and exclusion criteria, has already been presented in detail in a previous report.[11] Briefly, the primary inclusion criterion is a diagnosis of type 1 diabetes or type 2 diabetes within the past 12 months in participants aged between 18 and 69 years. The study was registered at ClinicalTrials.gov (NCT01055093).

Study population and design

This cross-sectional analysis was performed in participants with newly diagnosed type 1 diabetes or type 2 diabetes with available baseline information on lifestyle factors (recruitment period: August 2012–August 2020). Thus, only those with completed food frequency questionnaire (FFQ) and completed questionnaire on physical activity were eligible (n=510). Out of these, 15 men and 6 women were excluded due to an implausibly high energy intake exceeding 4000 kcal/day for men or 3500 kcal/day for women, respectively.[12] In addition, one participant was excluded because of a triglyceride (TG) level of more than 2500 mg/dL.[13] Furthermore, 20 individuals were excluded due to missing information on certain lifestyle factors. Thus, the present cross-sectional analysis was based on 468 individuals, 196 with type 1 diabetes and 272 with type 2 diabetes (online supplemental figure 1).

Outcome assessment

The outcome of interest was cardiometabolic risk. We therefore selected a priori known cardiovascular risk markers, including blood pressure, blood lipids, HbA1c, C reactive protein (CRP), liver enzymes, hepatic fat content, a fibrosis index, as well as total adipose tissue, subcutaneous and visceral adipose tissue.

Clinical and laboratory parameters

Systolic and diastolic blood pressure were measured after 5 min rest in sitting position, and the results of three measurements were averaged. Serum TGs, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, high-sensitivity CRP (hsCRP), alanine transaminase (ALT), aspartate transaminase (AST), and gamma-glutamyltransferase (GGT) were quantified on a Hitachi 912 analyzer or a Cobas c311 analyzer (Roche Diagnostics, Mannheim, Germany). Parameters for differentiation of blood cells including platelet concentrations were determined on a Sysmex XP300 (Siemens Healthcare Diagnostics, Erlangen, Germany). HbA1c was measured in EDTA plasma using a Variant-II (Bio-rad, Munich, Germany). ALT, AST, and GGT were used as surrogates of non-alcoholic fatty liver disease, which have recently been shown to better predict non-alcoholic steatohepatitis than other non-invasive scores.[14] In addition, the Fibrosis-4 (FIB-4) Index[15] was calculated to assess the risk of liver fibrosis using the formula:

$$\text{FIB}-4=\frac{\text{age}\times\text{AST}}{\left(\text{platelet count}\times\sqrt{\text{ALT}}\right)}$$

Measures of adipose tissue mass and hepatic fat content

In a subcohort, participants were studied in a whole-body 3 T magnetic resonance (MR) scanner (Philips Achieva, X-series, Eindhoven, the Netherlands) as described previously.[16] Briefly, total subcutaneous and visceral adipose tissue were quantified by whole-body MRI using

transverse multislice turbo-spin echo sequences (n=165 participants). The adipose tissue depots were determined by a single trained operator using SliceOmatic (Tomovision, Magog, Canada) using a built-in semiautomatic segmentation tool. The size of the adipose tissue depots is calculated from the number of pixels grouped within a certain depot and given as volume. Hepatic fat content was assessed using proton MR spectroscopy with a stimulated echo acquisition mode sequence (n=258 participants).

Exposure assessment

Assessment of diet

Habitual dietary intake, including alcohol consumption and total energy intake, was assessed using a validated semiquantitative FFQ with 148 items referring to the past 12 months.[17 18] For the current analyses, a diet score was generated, by using information on usual daily intake of fruits, vegetables, whole grain bread, and red meat.[19] Whole grain bread was considered as an indicator of whole grain intake, since the FFQ does not contain any other information on the consumption of whole grain products.

Assessment of physical activity

The Baecke questionnaire was used to evaluate physical activity within the past 12 months.[20 21] We used the subdimensions 'physical exercise in leisure' and 'leisure and locomotion activities', containing four questions each. The derived sports index and leisure index have a range of 0–5 points each with 5 indicating the highest level of activity. The total activity index can range from 0 to 10 points. All individuals were asked about their past and current smoking habits by a questionnaire.

Assessment of anthropometric measures

Anthropometric measures included body height, weight and waist circumference. Body weight was measured by a trained staff member using a calibrated weighing scale (SECA 285; SECA, Hamburg, Germany) or a stadiometer. The body mass index (BMI) (kg/m^2) was calculated as the quotient of body weight and the square of height.

Calculation of the lifestyle index

For the lifestyle score, the individual five lifestyle variables were categorized as favorable (1 point) or unfavorable (0 points) as previously described[19 22–26]: (1) a diet score was formed comprising the sums of the z-scores of the consumption of fruits, vegetables, and whole grain bread, minus the z-score of the intake of red meat (processed and unprocessed). A favorable dietary behavior was then defined as having a diet index equal or above the median diet score. (2) Alcohol intake: following the recommendations of the German-speaking nutrition societies, sex-specific thresholds for favorable alcohol consumption (men <20 g/day, women <10 g/day) were defined.[27] (3) Physical activity: tertiles of the total activity score were calculated and a score equal or above the second tertile considered an indicator of favorable physical activity. (4) Smoking: not currently smoking was considered as favorable. (5) A BMI <30 kg/m^2 represented a favorable BMI.[19 28] The points of the individual lifestyle factors were added up to an overall lifestyle score, ranging from 0 points (most unfavorable lifestyle) to 5 points (most favorable lifestyle).

Covariates

Age, sex, and socioeconomic status (SES) were collected during a face-to-face interview.[11] For the evaluation of SES, a composite social status index established in German health monitoring was used. The SES index aggregates information on educational level, professional status, and household income (range 3–21; higher scores indicate increasing SES).[29] Furthermore, family history of diabetes (parents or siblings), diabetes treatment (untreated/dietary/pharmacological), and the use of any antihypertensive, lipid-lowering, or anti-inflammatory drugs were assessed in an interview.

Statistical analyses

Categorical variables are described as numbers and percentages, while continuous variables are given as means and SDs or medians (IQR) depending on distribution of the data.

The associations between the lifestyle score and cardiovascular risk markers, markers of liver disease as well as adipose tissue mass were investigated using multivariable linear regression models. The confounders were selected a priori according to knowledge from the scientific literature supplemented by own considerations.[19 26 30 31] Model 1 included age (continuous) and sex. The full model 2 was further adjusted for SES index (continuous), diabetes type, diabetes treatment (untreated/dietary/pharmacological), family history of diabetes (yes/no), and energy intake (continuous). Individuals who reported taking antihypertensive, lipid-lowering or anti-inflammatory medications were excluded from the respective analyses on blood pressure, blood lipids/cholesterol or hsCRP. We calculated β coefficients with 95% CIs by using the lifestyle score as continuous measure. In addition, the associations between the lifestyle score and the continuous dependent variables were modeled with restricted cubic splines placed at three knots (5th, 50th, and 95th percentiles). The results of the fully adjusted regression models are presented graphically along with 95% CIs and p values for the overall association, linearity and non-linearity (Wald X^2 test).

Moreover, we investigated each level of the lifestyle score (adherence to 5, 4, 3 or 2 lifestyle factors) compared with the lowest level (≤1). Since only two individuals had a lifestyle index of 0, the lower two lifestyle index categories were combined (≤1).

To determine the contribution of each single lifestyle component, further linear regression analyses were performed with each lifestyle factor separately as the independent variable using model 2 with mutual adjustment for the remaining lifestyle factors. In sensitivity analyses,

we stratified our linear regression analyses with the lifestyle score as the independent variable by diabetes type and sex. In addition, we recalculated the lifestyle index by focusing on central obesity (defined by waist-to-hip ratio (WHR)) rather than general obesity (defined by BMI). For men, a WHR <0.95 and for women <0.80 were considered favorable.[28] Finally, to account for the aspect that obesity (general and central) is not a classic lifestyle factor but could be a consequence of other lifestyle factors, we examined whether our findings were robust after excluding BMI/WHR from the lifestyle score. For all statistical analyses, SAS V.9.4 (SAS Institute) was used.

RESULTS

Description of the study population

Table 1 shows the characteristics of the total study population and stratified by diabetes type. The study population had a median age of 48.3 years, consisted of more men than women, more individuals with type 2 than type 1 diabetes, and most individuals were of middle or higher SES. Regarding diabetes treatment, diabetes was treated pharmacologically in 79.2% of the individuals, while 16.4% exclusively received lifestyle modification, and 4.4% reported having no diabetes treatment to date.

Distribution of the lifestyle factors

In table 2, the distribution of lifestyle factors in the total study population and stratified by diabetes type is provided. In total, 8.1% of all individuals exhibited one or zero favorable factors, 17.7% two, 29.7% three, 26.7% four, and 17.7% all five factors resulting in a median lifestyle score of 3.0. Individuals with type 1 diabetes adhered to a higher number of favorable lifestyle factors compared with individuals with type 2 diabetes (table 2).

Regarding the single lifestyle factors, individuals with type 1 diabetes reported a more favorable diet score compared with those with type 2 diabetes (favorable diet score: 57.7% vs 44.5%). Alcohol intake was low in this cohort with minimal differences between types of diabetes. Individuals with type 1 diabetes were more often classified in the favorable group of recreational activity compared with individuals with type 2 diabetes (71.4% vs 58.5%). A total of 75.4% of the participants were non-smokers, and the difference between both diabetes groups was negligible. Altogether, 60.9% of the individuals had a BMI <30 kg/m^2, whereas differences between type 1 and type 2 diabetes were observed (type 1 diabetes: 89.3% vs type 2 diabetes: 40.4%).

Association of the lifestyle score with cardiovascular risk markers

In multivariable-adjusted models, the lifestyle score was not associated with systolic or diastolic blood pressure (table 3, figure 1 and online supplemental table 1). However, the lifestyle score was associated with lower levels of TG (β (95% CI) −11.29 mg/dL (−16.80; −5.78 mg/dL)), LDL cholesterol (β (95% CI) −3.84 mg/dL (−6.78; −0.90 mg/dL)), and higher levels of HDL cholesterol (β (95% CI) 2.98 mg/dL (1.79; 4.17 mg/dL)) with adherence to each additional lifestyle factor (table 3); and there was indication for a dose–response association between the lifestyle score and these outcomes (figure 1 and online supplemental table 1). The lifestyle score was also associated with lower HbA1c values (−0.13% (95% CI: −0.21%; −0.06%)) for adherence to each additional lifestyle factor (table 3), and strongest associations were observed for the adherence to all lifestyle factors compared with ≤1 (β (95% CI) for 5 vs ≤1: −0.46% (−0.84%; −0.08%)) (figure 1 and online supplemental table 1). Individuals with stronger adherence to the lifestyle score had lower levels of hsCRP (figure 1), with a difference of −0.09 mg/dL (95% CI: −0.12; −0.05 mg/dL) per additional favorable lifestyle factor (table 3). Strongest associations were observed for adhering to the most favorable lifestyle score compared with the lowest (β for hsCRP (95% CI): −0.41 mg/dL lower (−0.60; −0.23 mg/dL)) (online supplemental table 1).

Association of the lifestyle score with indicators for fatty liver disease

A non-linear association was observed for the lifestyle score and AST: values were lower in individuals adhering to two and three favorable lifestyle factors and above this, the findings were imprecisely estimated (online supplemental table 1 and figure 2). The lifestyle score was also inversely associated with ALT and GGT, per additional lifestyle factor: β (95% CI): −1.63 U/L (−2.92; −0.34 U/L) and −2.49 U/L (−5.12; 0.14 U/L) (table 3), indicating stronger associations already after adhering to two or three favorable lifestyle factors with only minimal benefit beyond this (figure 2). In addition, a dose–response association between the lifestyle score and hepatic fat content was observed (online supplemental table 1 and figure 2). With adherence to each additional lifestyle factor, hepatic fat content was lower by −1.64% (95% CI: −2.39%; −0.89%), and individuals adhering to all favorable factors showed the lowest values of hepatic fat content (5 vs ≤1: β (95% CI): −8.32% (−11.92%; −4.73%)) (online supplemental table 1). No association was observed for the FIB-4 Index after full adjustment (table 3, figure 2 and online supplemental table 1).

Association of the lifestyle score with adipose tissue mass

Regarding adipose tissue distribution, individuals with stronger adherence to the lifestyle score had lower total (β (95% CI): −3.42 dm^3 (−4.67; −2.16 dm^3)), subcutaneous (β (95% CI): −2.89 dm^3 (−4.04; −1.73 dm^3)), and visceral adipose tissue (β (95% CI): −0.47 dm^3 (−0.68; −0.26 dm^3)) per additional favorable lifestyle factor (table 3). There was a dose–response relation between the lifestyle score and these variables (figure 3 and online supplemental table 1).

Subgroup and sensitivity analyses

We did not observe differences for these associations between individuals with type 1 and type 2 diabetes or

Table 1 Characteristics of the study population in total and stratified by diabetes type

	N	Total study population (n=468, 100%)	Type 1 diabetes (n=196, 41.9%)	Type 2 diabetes (n=272, 58.1%)
Age (years)	468	48.3 (36.4–56.0)	34.9 (27.4–45.8)	53.4 (47.5–59.5)
Sex	468			
Men		275 (58.8%)	107 (54.6%)	168 (61.8%)
Women		193 (41.2%)	89 (45.4%)	104 (38.2%)
Socioeconomic status	456	14.3 (12.3–16.1)	14.1 (12.5–16.0)	14.3 (12.2–16.1)
Low		24 (5.3%)	11 (5.9%)	13 (4.8%)
Middle		248 (54.4%)	100 (53.8%)	148 (54.8%)
High		184 (40.4%)	75 (40.3%)	109 (40.4%)
Family history of diabetes (parents, siblings)	429			
Yes		214 (49.9%)	49 (26.5%)	165 (67.6%)
No		215 (50.1%)	136 (73.5%)	79 (32.4%)
Diabetes treatment	456			
Untreated		20 (4.4%)	1 (0.5%)	19 (7.2%)
Dietary		75 (16.4%)	8 (4.2%)	67 (25.4%)
Pharmacological		361 (79.2%)	183 (95.3%)	178 (67.4%)
Energy intake (kcal/day)	468	2227 (1817–2730)	2329 (1932–2838)	2094 (1711–2634)
Antihypertensive medication	468			
Yes		139 (29.7%)	13 (6.6%)	126 (46.3%)
No		329 (70.3%)	183 (93.4%)	146 (53.7%)
Lipid-lowering medication	468			
Yes		48 (10.3%)	6 (3.1%)	42 (15.4%)
No		420 (89.7%)	190 (96.9%)	230 (84.6%)
Non-steroidal anti-inflammatory drugs	468			
Yes		63 (13.5%)	10 (5.1%)	53 (19.5%)
No		405 (86.5%)	186 (94.9%)	219 (80.5%)
Body mass index (BMI)	468	27.9 (24.0–32.7)	24.1 (22.2–27.2)	31.2 (27.4–35.7)
Underweight or normal weight (BMI <25 kg/m^2)		138 (29.5%)	108 (55.1%)	30 (11.0%)
Overweight (BMI 25–<30 kg/m^2)		147 (31.4%)	67 (34.2%)	80 (29.4%)
Obese (BMI ≥30 kg/m^2)		183 (39.1%)	21 (10.7%)	162 (59.6%)
Total adipose tissue (dm^3)	165	22.2 (15.5–31.7)	18.3 (13.0–25.6)	27.7 (19.7–35.2)
Subcutaneous adipose tissue (dm^3)	165	18.4 (13.9–27.6)	17.3 (12.0–22.9)	23.2 (16.1–31.8)
Visceral adipose tissue (dm^3)	165	2.5 (1.1–3.9)	1.1 (0.5–1.8)	3.6 (2.7–4.7)
Hepatic fat content (%)	258	2.0 (0.1–8.1)	0.2 (0.0–1.0)	6.2 (2.2–13.4)
Fibrosis-4 (FIB-4) Index	467	0.9 (0.6–1.2)	0.7 (0.5–1.0)	1.0 (0.8–1.3)
Systolic blood pressure* (mm Hg)	328	131.5 (121.3–142.5)	127.3 (116.5–134.5)	137.5 (127.0–146.5)
Diastolic blood pressure* (mm Hg)	328	81.9 (10.3)	78.0 (8.8)	86.7 (10.0)
Triglycerides† (mg/dL)	420	104.0 (73.0–154.0)	78.5 (59.0–105.0)	124.5 (97.0–187.0)
LDL cholesterol† (mg/dL)	420	123.2 (34.5)	110.1 (29.9)	134.0 (34.4)
HDL cholesterol† (mg/dL)	420	51.0 (42.0–63.0)	61.0 (50.0–72.0)	45.0 (38.0–53.0)
HbA1c (%)	467	6.3 (5.9–6.9)	6.4 (5.8–7.0)	6.3 (5.9–6.8)
HbA1c (mmol/mol)	467	45 (41–52)	46 (40–53)	45 (41–51)
hsCRP‡ (mg/dL)	405	0.16 (0.06–0.37)	0.08 (0.05–0.19)	0.22 (0.10–0.54)
AST (U/L)	468	21.0 (17.0–27.0)	19.0 (16.0–23.0)	23.0 (19.0–29.0)

Continued

Table 1 Continued

	N	Total study population (n=468, 100%)	Type 1 diabetes (n=196, 41.9%)	Type 2 diabetes (n=272, 58.1%)
ALT (U/L)	468	24.0 (17.5–35.5)	19.0 (14.5–24.0)	29.0 (21.0–42.0)
GGT (U/L)	468	23.0 (14.0–38.0)	14.0 (11.0–21.0)	31.0 (21.5–46.5)

Data are presented as means (SD) or medians (first quartile–third quartile) (depending on the (normal) distribution of the respective continuous variable in the total study population) or numbers (percentages).
*Reported only for people who were not taking antihypertensive medication.
†Reported only for people who were not taking lipid-lowering medication.
‡Reported only for people who were not taking non-steroidal anti-inflammatory drugs.
ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyltransferase; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; hsCRP, high-sensitivity C reactive protein; LDL, low-density lipoprotein.

Table 2 Description of the lifestyle variables of the 468 GDS participants

	Total study population (n=468, 100%)	Type 1 diabetes (n=196, 41.9%)	Type 2 diabetes (n=272, 58.1%)
Lifestyle score	3.0 (2.0–4.0)	4.0 (3.0–5.0)	3.0 (2.0–4.0)
≤1	38 (8.1%)	6 (3.1%)	32 (11.8%)
2	83 (17.7%)	23 (11.7%)	60 (22.1%)
3	139 (29.7%)	50 (25.5%)	89 (32.7%)
4	125 (26.7%)	65 (33.2%)	60 (22.1%)
5	83 (17.7%)	52 (26.5%)	31 (11.4%)
Food intake (g/day)			
Fruits	168.3 (102.8–249.9)	167.3 (96.0–250.8)	168.9 (108.2–249.4)
Vegetables	223.3 (170.0–286.6)	230.2 (178.9–304.6)	218.7 (162.8–275.2)
Whole grain bread	33.3 (19.9–58.3)	34.6 (19.0–64.1)	32.8 (19.9–58.3)
Red meat and processed meat	102.8 (59.1–160.2)	108.2 (56.6–164.2)	99.0 (62.5–157.7)
Diet score			
Z-score total diet	−0.30 (−1.50; 1.17)	0.03 (−1.28; 1.36)	−0.50 (−1.59; 1.14)
Favorable (upper half)	234 (50%)	113 (57.7%)	121 (44.5%)
Unfavorable (lower half)	234 (50%)	83 (42.3%)	151 (55.5%)
Alcohol consumption (g/day)	4.6 (1.2–14.5)	6.2 (1.9–15.8)	3.9 (0.9–12.1)
Favorable (men: <20 g/day, women: <10 g/day)	363 (77.6%)	144 (73.5%)	219 (80.5%)
Unfavorable (men: ≥20 g/day, women: ≥10 g/day)	105 (22.4%)	52 (26.5%)	53 (19.5%)
Recreational activity			
Leisure index	3.0 (2.5–3.5)	3.3 (2.8–3.8)	3.0 (2.5–3.5)
Sports index	2.8 (2.3–3.5)	3.0 (2.5–3.8)	2.8 (2.0–3.3)
Favorable (second or third tertile)	299 (63.9%)	140 (71.4%)	159 (58.5%)
Unfavorable (first tertile)	169 (36.1%)	56 (28.6%)	113 (41.5%)
Smoking			
Non-smoker or former smoker	353 (75.4%)	150 (76.5%)	203 (74.6%)
Current smoker	115 (24.6%)	46 (23.5%)	69 (25.4%)
Body mass index (BMI)	27.9 (24.0–32.7)	24.1 (22.2–27.2)	31.2 (27.4–35.7)
BMI <30 kg/m^2	285 (60.9%)	175 (89.3%)	110 (40.4%)
BMI ≥30 kg/m^2	183 (39.1%)	21 (10.7%)	162 (59.6%)

Data are presented as means (SDs) or medians (first quartile–third quartile) (depending on the (normal) distribution of the respective continuous variable in the total study population) or numbers (percentages).
GDS, German Diabetes Study.

Table 3 Association of the lifestyle score per one unit increase with cardiovascular markers, indicators for fatty liver disease and adipose tissue mass: results of linear regression analyses

	Model 1*		Model 2†	
Independent variable	**β (95% CI)**	**P value**	**β (95% CI)**	**P value**
Systolic blood pressure‡ (mm Hg)	−1.65 (−2.93; −0.37)	0.012	−0.59 (−2.00; 0.82)	0.411
Diastolic blood pressure‡ (mm Hg)	−1.37 (−2.27; −0.48)	0.003	−0.77 (−1.75; 0.21)	0.125
Triglycerides§ (mg/dL)	−16.96 (−22.41; −11.50)	<0.0001	−11.29 (−16.80; −5.78)	<0.0001
LDL cholesterol§ (mg/dL)	−4.60 (−7.20; −2.01)	<0.001	−3.84 (−6.78; −0.90)	0.011
HDL cholesterol§ (mg/dL)	4.30 (3.12; 5.48)	<0.0001	2.98 (1.79; 4.17)	<0.0001
HbA1c (%)	−0.12 (−0.19; −0.05)	<0.001	−0.13 (−0.21; −0.06)	<0.001
HbA1c (mmol/mol)	−1.35 (−2.11; −0.60)	<0.001	−1.45 (−2.28; −0.62)	<0.001
hsCRP¶ (mg/dL)	−0.11 (−0.15; −0.08)	<0.0001	−0.09 (−0.12; −0.05)	<0.0001
AST (U/L)	−0.32 (−1.02; 0.37)	0.362	−0.09 (−0.87; 0.69)	0.822
ALT (U/L)	−2.36 (−3.53; −1.20)	<0.0001	−1.63 (−2.92; −0.34)	0.014
GGT (U/L)	−4.09 (−6.37; −1.81)	<0.001	−2.49 (−5.12; 0.14)	0.063
Hepatic fat content (%)	−2.15 (−2.86; −1.45)	<0.0001	−1.64 (−2.39; −0.89)	<0.0001
Fibrosis-4 (FIB-4) Index	0.04 (0.00; 0.07)	0.065	0.01 (−0.03; 0.05)	0.561
Total adipose tissue (dm^3)	−4.08 (−5.34; −2.82)	<0.0001	−3.42 (−4.67; −2.16)	<0.0001
Subcutaneous adipose tissue (dm^3)	−3.50 (−4.64; −2.36)	<0.0001	−2.89 (−4.04; −1.73)	<0.0001
Visceral adipose tissue (dm^3)	−0.53 (−0.74; −0.32)	<0.0001	−0.47 (−0.68; −0.26)	<0.0001

Results are presented as regression coefficient (β) for adherence to each additional lifestyle factor with 95% CI and corresponding p value. Numbers of observations used (model 1/model 2): systolic and diastolic blood pressure: 328/289; triglycerides, LDL cholesterol, HDL cholesterol: 420/363; HbA1c: 467/405; hsCRP: 405/355; AST, ALT, GGT, FIB-4 Index: 467/404; total adipose tissue, visceral adipose tissue, subcutaneous adipose tissue: 165/146.
*Model 1: adjusted for age (years) and sex.
†Model 2: model 1, further adjusted for socioeconomic status score (continuous), diabetes type (type 1 diabetes/type 2 diabetes), diabetes treatment (untreated/dietary/pharmacological), family history of diabetes (yes/no), and energy intake (kcal/day).
‡Reported only for people who were not taking antihypertensive medication.
§Reported only for people who were not taking lipid-lowering medication.
¶Reported only for people who were not taking non-steroidal anti-inflammatory drugs.
ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyltransferase; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; hsCRP, high-sensitivity C reactive protein; LDL, low-density lipoprotein.

between men and women (online supplemental tables 2 and 3). The associations pointed to the same directions in each subgroup and the 95% CIs between the groups overlapped.

When investigating the associations of the single lifestyle factors separately, a BMI <30 kg/m² mostly contributed to the overall associations for the majority of outcome variables. However, the other lifestyle factors further contributed to the observed relations, but to a lesser extent. In general, strongest associations were observed when adhering to all lifestyle factors combined compared with the lifestyle factor separately (online supplemental table 4).

Neither replacing BMI with WHR nor eliminating obesity from the lifestyle index substantially changed our results (online supplemental table 5).

DISCUSSION

Our cross-sectional findings indicate that adherence to a favorable lifestyle was associated with beneficial cardiovascular risk markers, including TGs, LDL and HDL cholesterol, HbA1c, hsCRP, ALT, as well as hepatic fat content, and total, subcutaneous and visceral adipose tissue. We observed dose–response relations for these associations, indicating that adherence to each additional favorable lifestyle factor was associated with more beneficial risk profiles.

Compared with the results of other studies, the GDS participants met more criteria of a favorable lifestyle.[26 30–32] Almost one-third of the GDS participants adhered to three and 44% to four or five favorable lifestyle factors. In comparison, 28% of the EPIC-Potsdam cohort adhered to three and 9% to all four analyzed lifestyle factors, respectively.[26] In people with prevalent diabetes, similar patterns were observed: 34% of the full EPIC cohort with prevalent diabetes adhered to three or more favorable lifestyle factors (GDS: 74%),[19] while 29% of the exclusively male participants with type 2 diabetes from another study met three and 12% four and more favorable lifestyle factors.[24] However, the comparison between the populations is limited by the application of different definition of the lifestyle score, differences

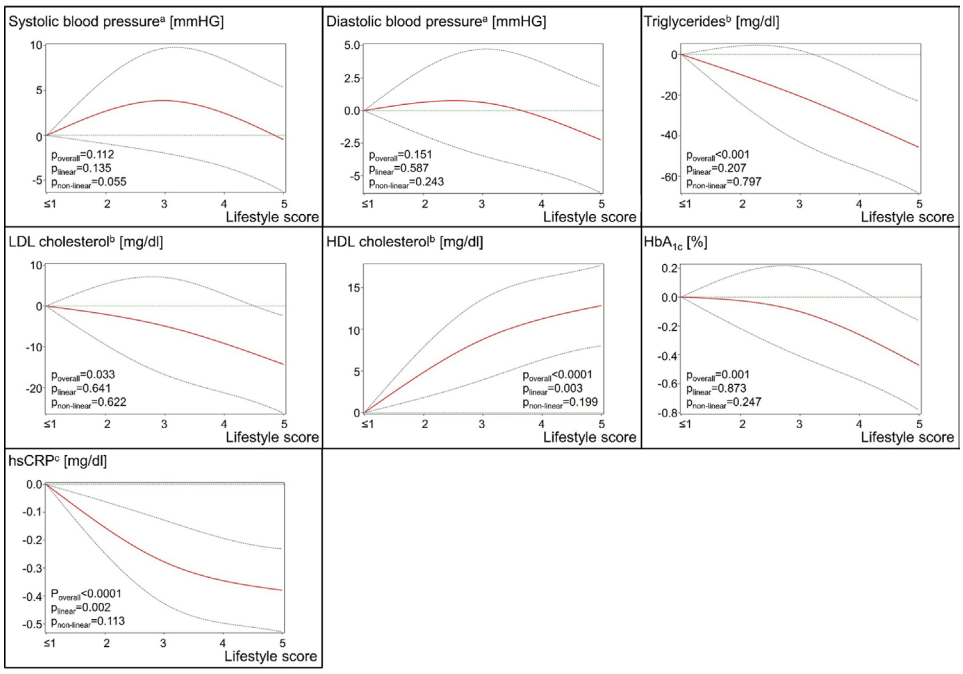

Figure 1 Dose–response associations of the lifestyle score with cardiovascular markers. The figures show the best possible cubic spline (red solid line) with 95% CI (black dashed line). The reference is the value for a lifestyle score ≤1 (green dashed line). All analyses were adjusted for age (years), sex, socioeconomic status score (continuous), diabetes type (type 1 diabetes/type 2 diabetes), diabetes treatment (untreated/dietary/pharmacological), family history of diabetes (yes/no), and energy intake (kcal/day). Numbers of observations used: systolic and diastolic blood pressure: 289; triglycerides, LDL cholesterol, HDL cholesterol: 363; HbA1c: 405; hsCRP: 355. [a]Reported only for people who were not taking antihypertensive medication. [b]Reported only for people who were not taking lipid-lowering medication. [c]Reported only for people who were not taking non-steroidal anti-inflammatory drugs. HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; hsCRP, high-sensitivity C reactive protein; LDL, low-density lipoprotein.

in SES, duration of diabetes of the individuals and age distribution of the cohorts.

Non-pharmacological interventions such as lifestyle modification are a fundamental aspect of diabetes care for treating recent-onset type 2 diabetes,[33] and thus, it is likely that individuals with recent-onset diabetes might at least temporarily change their lifestyle in the direction to a more favorable lifestyle. Changes in adverse metabolic factors by lifestyle modification may contribute to a reduced risk of coronary heart disease or stroke.[34 35] A lower BMI was identified as main contributor, which is consistent with previous studies, showing that a reduction

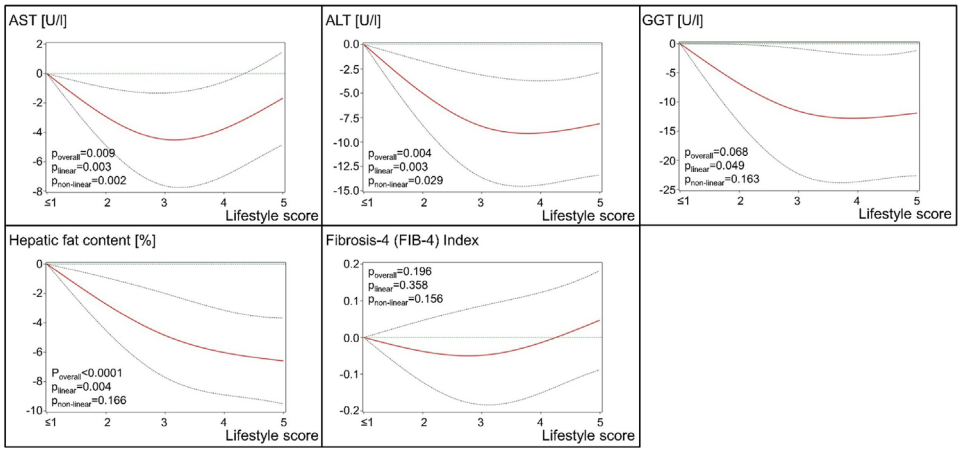

Figure 2 Dose–response associations of the lifestyle score with indicators for fatty liver disease. The figures show the best possible cubic spline (red solid line) with 95% CI (black dashed line). The reference is the value for a lifestyle score ≤1 (green dashed line). All analyses were adjusted for age (years), sex, socioeconomic status score (continuous), diabetes type (type 1 diabetes/type 2 diabetes), diabetes treatment (untreated/dietary/pharmacological), family history of diabetes (yes/no), and energy intake (kcal/day). Numbers of observations used: AST, ALT, GGT: 405; hepatic fat content: 228; FIB-4: 404. ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyltransferase.

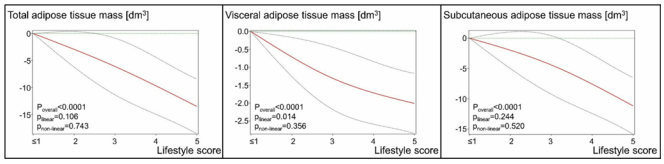

Figure 3 Dose–response associations of the lifestyle score with adipose tissue mass. The figures show the best possible cubic spline (red solid line) with 95% CI (black dashed line). The reference is the value for a lifestyle score ≤1 (green dashed line). All analyses were adjusted for age (years), sex, socioeconomic status score (continuous), diabetes type (type 1 diabetes/type 2 diabetes), diabetes treatment (untreated/dietary/pharmacological), family history of diabetes (yes/no), and energy intake (kcal/day). Numbers of observations used: 146.

of body weight yielded to more beneficial levels of cardiovascular and hepatic risk markers and weight loss.[36–39] However, our findings showed strongest associations for the combination of all favorable lifestyle factors: the more favorable lifestyle factors were followed, the more beneficial the results were for cardiovascular and liver health as well as adipose tissue mass. In addition, the findings were robust when we excluded obesity as a factor from our lifestyle score.

The present study only examined associations between lifestyle factors and various cardiovascular risk markers. Beyond this, findings from the Nurses' Health Study and the Health Professionals Follow-Up Study applying a lifestyle score based on diet, physical activity, smoking and alcohol intake point to the same direction, even regarding 'hard' cardiovascular endpoints. The HRs for the adherence to each additional lifestyle factor were 0.86 (95% CI: 0.80; 0.92) for cardiovascular disease, 0.88 (95% CI: 0.82; 0.95) for coronary heart disease, 0.79 (95% CI: 0.68; 0.91) for stroke, and 0.73 (95% CI: 0.66; 0.82) for cardiovascular disease-related mortality.[23]

The lifestyle score is a simplification to reflect a general healthy or unhealthy lifestyle behavior. However, the single aspects were not considered in their whole spectrum. For example: for diet, a simple score, including the intake of fruits, vegetables, whole grain bread and red and processed meat, was generated. It is likely that this score was not specific enough to reflect the whole spectrum of a favorable dietary pattern. In this context, there is indication that the Mediterranean diet, the Dietary Approaches to Stop Hypertension diet, or a low-fat diet is associated with blood pressure, lipid levels, HbA1c, and hsCRP independent of BMI or body weight change.[40–44] Thus, in future analyses in individuals with new-onset diabetes, dietary factors and physical activity especially need further investigation by considering comprehensive exposures. These may also complement our findings by analyzing longitudinal associations between lifestyle factors in combination and various outcomes, taking into account changes in lifestyle over the observation period.

Our study has strengths and limitations that need to be discussed. Strengths of this study include the well-characterized study population examined shortly after diagnosis of diabetes, the comprehensive assessment of lifestyle factors, and the detailed assessment of hepatic fat content and adipose tissue distribution. However, the following limitations should be considered. First, the cross-sectional study design does not allow any conclusions about cause–effect relationships. Second, the recent diagnosis of diabetes and other disorders such as hypertension or hyperlipidemia may have prompted lifestyle changes, but these may not yet have affected the outcomes studied, resulting in an underestimation of the association between lifestyle and the respective outcomes. Third, information on the lifestyle factors diet, alcohol consumption, physical activity, and smoking status was self-reported and therefore may have been subject to measurement error and misclassification. However, validated instruments were applied[17 18 20 21] and individuals with implausible energy intake were excluded from the analyses. Fourth, the lifestyle score is based on single lifestyle factors, which were included as binary variables. This categorization caused loss of information and the whole spectrum of, for example, the dietary behavior or physical activity, was not covered and could not be investigated. However, this concept is a well-known tool in health research[19 22–26] and its application provides insights into the synergetic associations of the combination of lifestyle factors. Finally, we cannot rule out selection bias because of the comprehensive study protocol of the GDS and its exclusion criteria. In addition, the SES of GDS participants[11] and adherence to healthy lifestyle factors are higher compared with other cohorts. Therefore, these results may not be generalizable to all people with diabetes.

In conclusion, the findings showed that in individuals with type 1 and type 2 diabetes, the adherence to each additional lifestyle factor was associated with more favorable cardiovascular risk markers and lower liver fat content as well as adipose tissue mass. The more favorable lifestyle factors were met, the more favorable were the cardiometabolic risk profile. Studies are needed that prospectively investigate these associations.

Author affiliations
[1]Institute for Biometrics and Epidemiology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University, Duesseldorf, Germany
[2]German Center for Diabetes Research (DZD), Partner Duesseldorf, Muenchen-Neuherberg, Germany
[3]Center for Health and Society, Medical Faculty and University Hospital Duesseldorf, Heinrich Heine University, Duesseldorf, Germany
[4]Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University, Duesseldorf, Germany
[5]Internal Medicine I and Clinical Chemistry, University Hospital Heidelberg, Heidelberg, Germany
[6]Department of Endocrinology and Diabetology, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine Uinversity, Duesseldorf, Germany
[7]Department of Internal Medicine and Gastroenterology, Niels Stensen Hospitals, Franziskus Hospital Harderberg, Georgsmarienhutte, Germany
[8]Institute for Epidemiology, Kiel University, Kiel, Germany

Acknowledgements We appreciate the voluntary participation of all German Diabetes Study (GDS) participants. Furthermore, we thank the staff of the Clinical Research Center at the Institute for Clinical Diabetology, German Diabetes Center (DDZ), for their excellent contribution to the GDS.

Collaborators The GDS Group consists of H Al-Hasani, A E Buyken, G Geerling, A Icks, K Jandeleit-Dahm, J Kotzka, E Lammert, W Rathmann, S Trenkamp, D Ziegler.

Contributors VB, JS, KM, KSW, CH and MR collected the data. CB, AL and SS performed the statistical analyses. KS and OK advised on statistical analyses. CB and SS wrote a draft of the manuscript. CB, AL, MR and SS interpreted the data and contributed to the discussion. All authors critically reviewed the manuscript. All authors read and approved the final manuscript. MR is the guarantor of this work and had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Funding The German Diabetes Study (GDS) was initiated and financed by the German Diabetes Center (DDZ), which is funded by the German Federal Ministry of Health (Berlin, Germany), the Ministry of Innovation, Science, Research and Technology of the state North Rhine-Westphalia (Düsseldorf, Germany), and grants from the German Federal Ministry of Education and Research (Berlin, Germany) to the DZD.

Disclaimer The funders had no role in the study design, data collection, data analysis, data interpretation or preparation of this manuscript.

Competing interests MR has been on scientific advisory boards of Allergan, AstraZeneca, Bristol Myers Squibb, Eli Lilly, Gilead Sciences, Inventiva, Intercept Pharma, Novartis, Novo Nordisk, Servier Laboratories, Target NRW and Terra Firma; and received support for investigator-initiated studies from Boehringer Ingelheim, Nutricia/Danone and Sanofi-Aventis. CH received a research grant from Sanofi-Aventis outside the submitted work. SS received a research grant from ALPRO outside the submitted work. The other authors declare that they have no conflicts of interest to disclose.

Patient consent for publication Not required.

Ethics approval This study involves human participants. The study complies with the Declaration of Helsinki and was approved by the ethics committee of the University of Düsseldorf (ref. 4508). All participants provided their written informed consent.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement The data that support the findings of this study are available from the GDS but restrictions apply to the availability of these data, which were used under license for the current study and therefore are not publicly available. Data are however available from the authors upon reasonable request and with permission of the GDS.

ORCID iDs

Oliver Kuss http://orcid.org/0000-0003-3301-5869
Christian Herder http://orcid.org/0000-0002-2050-093X
Michael Roden http://orcid.org/0000-0001-8200-6382
Sabrina Schlesinger http://orcid.org/0000-0003-4244-0832

REFERENCES

1 International Diabetes Federation (IDF). *IDF diabetes atlas*. Brussels, 2021. Available: https://diabetesatlas.org/idfawp/resource-files/2021/07/IDF_Atlas_10th_Edition_2021.pdf
2 Harding JL, Pavkov ME, Magliano DJ, *et al*. Global trends in diabetes complications: a review of current evidence. *Diabetologia* 2019;62:3–16.
3 Bönhof GJ, Herder C, Strom A, *et al*. Emerging biomarkers, tools, and treatments for diabetic polyneuropathy. *Endocr Rev* 2019;40:153–92.
4 Herder C, Roden M, Ziegler D. Novel insights into sensorimotor and cardiovascular autonomic neuropathy from recent-onset diabetes and population-based cohorts. *Trends Endocrinol Metab* 2019;30:286–98.
5 American Diabetes Association. 5. LIFESTYLE management: standards of medical care in diabetes-2019. *Diabetes Care* 2019;42:S46–60.
6 Pi-Sunyer X. The look AHEAD trial: a review and discussion of its outcomes. *Curr Nutr Rep* 2014;3:387–91.
7 Taheri S, Zaghloul H, Chagoury O, *et al*. Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-I): an open-label, parallel-group, randomised controlled trial. *Lancet Diabetes Endocrinol* 2020;8:477–89.
8 Lean ME, Leslie WS, Barnes AC, *et al*. Primary care-led weight management for remission of type 2 diabetes (direct): an open-label, cluster-randomised trial. *Lancet* 2018;391:541–51.
9 Schlesinger S, Neuenschwander M, Ballon A, *et al*. Adherence to healthy lifestyles and incidence of diabetes and mortality among individuals with diabetes: a systematic review and meta-analysis of prospective studies. *J Epidemiol Community Health* 2020;74:481–7.
10 Han H, Cao Y, Feng C, *et al*. Association of a healthy lifestyle with all-cause and cause-specific mortality among individuals with type 2 diabetes: a prospective study in UK Biobank. *Diabetes Care* 2022;45:319–29.
11 Szendroedi J, Saxena A, Weber KS, *et al*. Cohort profile: the German diabetes study (GDS). *Cardiovasc Diabetol* 2016;15:59.
12 Willett WC. *Nutritional epidemiology*. 3rd ed. Oxford: Oxford Univ. Press, 2013.
13 Estiri H, Klann JG, Murphy SN. A clustering approach for detecting implausible observation values in electronic health records data. *BMC Med Inform Decis Mak* 2019;19:142.
14 Bril F, McPhaul MJ, Caulfield MP, *et al*. Performance of plasma biomarkers and diagnostic panels for nonalcoholic steatohepatitis and advanced fibrosis in patients with type 2 diabetes. *Diabetes Care* 2020;43:290–7.
15 McPherson S, Hardy T, Dufour J-F, *et al*. Age as a confounding factor for the accurate non-invasive diagnosis of advanced NAFLD fibrosis. *Am J Gastroenterol* 2017;112:740–51.
16 Kahl S, Straßburger K, Nowotny B, *et al*. Comparison of liver fat indices for the diagnosis of hepatic steatosis and insulin resistance. *PLoS One* 2014;9:e94059.
17 Nöthlings U, Hoffmann K, Bergmann MM, *et al*. Fitting portion sizes in a self-administered food frequency questionnaire. *J Nutr* 2007;137:2781–6.
18 Noethlings U, Hoffmann K, Bergmann MM, *et al*. Portion size adds limited information on variance in food intake of participants in the EPIC-Potsdam study. *J Nutr* 2003;133:510–5.
19 Nöthlings U, Ford ES, Kröger J, *et al*. Lifestyle factors and mortality among adults with diabetes: findings from the European prospective investigation into cancer and nutrition-potsdam study*. *J Diabetes* 2010;2:112–7.
20 Florindo AA, Latorre M do RD de O. Validation and reliability of the Baecke questionnaire for the evaluation of habitual physical activity in adult men. *Rev Bras Med Esporte* 2003;9:129–35.
21 Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *Am J Clin Nutr* 1982;36:936–42.
22 Rajaobelina K, Dow C, Romana Mancini F, *et al*. Population attributable fractions of the main type 2 diabetes mellitus risk factors in women: findings from the French E3N cohort. *J Diabetes* 2019;11:242–53.
23 Liu G, Li Y, Hu Y, *et al*. Influence of lifestyle on incident cardiovascular disease and mortality in patients with diabetes mellitus. *J Am Coll Cardiol* 2018;71:2867–76.
24 Patel YR, Gadiraju TV, Gaziano JM, *et al*. Adherence to healthy lifestyle factors and risk of death in men with diabetes mellitus: the physicians' health study. *Clin Nutr* 2018;37:139–43.
25 Li Y, Ley SH, Tobias DK, *et al*. Birth weight and later life adherence to unhealthy lifestyles in predicting type 2 diabetes: prospective cohort study. *BMJ* 2015;351:h3672.
26 Ford ES, Bergmann MM, Kröger J, *et al*. Healthy living is the best revenge: findings from the European prospective investigation into cancer and nutrition-Potsdam study. *Arch Intern Med* 2009;169:1355–62.

27 Deutsche Gesellschaft für Ernährung, Österreichische Gesellschaft für Ernährung, Schweizerische Gesellschaft für Ernährung. *D-A-CH: Referenzwerte für die Nährstoffzufuhr*. 2nd ed. Bonn: Neuer Umschau Buchverlag, 2015.
28 World Health Organization (WHO). *Obesity - Preventing and Managing the Global Epidemic: Report on a WHO Consultation*. Geneva: World Health Organization, 2000.
29 Lampert T, Kroll L, Müters S, *et al*. Measurement of socioeconomic status in the German health interview and examination survey for adults (Degs1). *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2013;56:631–6.
30 Lv J, Yu C, Guo Y, *et al*. Adherence to a healthy lifestyle and the risk of type 2 diabetes in Chinese adults. *Int J Epidemiol* 2017;46:1410–20.
31 Pronk NP, Lowry M, Kottke TE, *et al*. The association between optimal lifestyle adherence and short-term incidence of chronic conditions among employees. *Popul Health Manag* 2010;13:289–95.
32 Elwood P, Galante J, Pickering J, *et al*. Healthy lifestyles reduce the incidence of chronic diseases and dementia: evidence from the Caerphilly cohort study. *PLoS One* 2013;8:e81877.
33 Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF). *Nationale Versorgungsleitlinie Typ-2-diabetes: Teilpublikation der Langfassung*. Berlin, 2021.
34 Yun J-S, Ko S-H. Current trends in epidemiology of cardiovascular disease and cardiovascular risk management in type 2 diabetes. *Metabolism* 2021;123:154838.
35 Arnett DK, Blumenthal RS, Albert MA, *et al*. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *Circulation* 2019;140:e596–646.
36 Marin-Alejandre BA, Cantero I, Perez-Diaz-Del-Campo N, *et al*. Effects of two personalized dietary strategies during a 2-year intervention in subjects with nonalcoholic fatty liver disease: a randomized trial. *Liver Int* 2021;41:1532–44.
37 Lim SL, Johal J, Ong KW, *et al*. Lifestyle intervention enabled by mobile technology on weight loss in patients with nonalcoholic fatty liver disease: randomized controlled trial. *JMIR Mhealth Uhealth* 2020;8:e14802.
38 Macek P, Terek-Derszniak M, Biskup M, *et al*. A two-year follow-up cohort study-improved clinical control over CVD risk factors through weight loss in middle-aged and older adults. *J Clin Med* 2020;9:2904.
39 Pinho CPS, Diniz A da S, Arruda I de, *et al*. Effects of weight loss on adipose visceral and subcutaneous tissue in overweight adults. *Clin Nutr* 2018;37:1252–8.
40 Evangelista LS, Jose MM, Sallam H, *et al*. High-protein vs. standard-protein diets in overweight and obese patients with heart failure and diabetes mellitus: findings of the pro-HEART trial. *ESC Heart Fail* 2021;8:1342–8.
41 Perry CA, Van Guilder GP, Hossain M, *et al*. Cardiometabolic changes in response to a calorie-restricted DASH diet in obese older adults. *Front Nutr* 2021;8:647847.
42 Meslier V, Laiola M, Roager HM, *et al*. Mediterranean diet intervention in overweight and obese subjects LOWERS plasma cholesterol and causes changes in the gut Microbiome and metabolome independently of energy intake. *Gut* 2020;69:1258–68.
43 Kirwan JP, Malin SK, Scelsi AR, *et al*. A whole-grain diet reduces cardiovascular risk factors in overweight and obese adults: a randomized controlled trial. *J Nutr* 2016;146:2244–51.
44 Gaesser GA, Angadi SS, Sawyer BJ. Exercise and diet, independent of weight loss, improve cardiometabolic risk profile in overweight and obese individuals. *Phys Sportsmed* 2011;39:87–97.