



OPEN The association of a lifestyle risk index with glycemic status in the German National Cohort (NAKO)

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This cross-sectional analysis examined the association of a Lifestyle Risk Factor Index (LSRI) with the presence of self-reported diabetes or HbA1c levels among participants of the German National Cohort (NAKO), while considering the role of body mass index (BMI) and visceral adipose tissue (VAT). Modified LSRI (mLSRI) scores were calculated from baseline questionnaires assigning points for adherence to alcohol intake, physical activity, smoking, and healthy diet recommendations. Of > 205,000 participants, 18,101 had VAT quantified by magnetic resonance imaging plus complete information on covariates. Diabetes status was self-reported and HbA1c levels ≥ 39 mmol/mol Hb (5.7%) were considered elevated. Polytomous logistic regression estimated prevalence odds ratios (POR) and linear regression computed mean HbA1c levels adjusting for age and sex in model 1 and adding BMI and VAT for model 2. The respective proportions for 0/1, 2, 3, and 4 mLSRI points were 6%, 25%, 51%, and 18%. Among the 17,457 (96.4%) participants without self-reported diabetes, 17.3% had elevated HbA1c levels. Compared to normoglycemia, the highest vs. lowest mLSRI was inversely related to abnormal HbA1c (POR 0.81; 95%CI 0.68–0.97) but the associations were attenuated after adding BMI and VAT. No significant association was seen for diabetes (POR 0.91; 95%CI 0.62–1.32) after full adjustment. In this large sample of predominantly healthy adults, a combination of lifestyles, foremost driven by not smoking, was weakly associated with lower HbA1c levels but not self-reported diabetes. Nevertheless, lifestyle factors may be relevant for glycemic control, possibly due to an influence on adiposity, but this relation cannot be confirmed due to the cross-sectional design.

Keywords Healthy lifestyle, Diabetes mellitus, Glycated hemoglobin, Cohort studies

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Multiple lifestyle factors, in addition to the well-known effect of excess body weight, which may also act as mediator, affect the likelihood to develop type 2 diabetes (T2D)^{1,2}. We hypothesized that the combination of a healthy diet, physical activity, not smoking, and moderate alcohol intake results in joint beneficial health effects as these behaviors are known to be protective against T2D development^{3–5}. To capture this overall benefit, a Lifestyle Risk Factor Index (LSRI) based on four behaviors has been previously developed⁶. As emerging evidence suggests that body fat distribution, in particular the accumulation of visceral adipose tissue (VAT), poses an independent risk beyond body mass index (BMI) to negatively affect glucose metabolism, it is of importance to consider VAT in etiologic investigations⁷. Due to its higher metabolic activity compared to subcutaneous adipose tissue (SAT), VAT appears to be an important predictor of T2D morbidity and mortality beyond BMI⁸. This was shown in a systematic review of 20 cross-sectional studies⁹ and in the European Prospective Investigation into

Cancer and Nutrition (EPIC) where waist circumference, a proxy for VAT, was a predictor of T2D incidence in addition to BMI¹⁰.

Based on the hypothesis that lifestyle factors are associated with glucose metabolism, the current analysis aims to understand the association of the LSRI with abnormal glycemic status while also considering the possible influence of anthropometric characteristics¹¹, i.e., BMI and VAT volume, on glycemic status¹². Hence, this cross-sectional analysis within the German National Cohort (NAKO) estimated the relation of a LSRI with self-reported diabetes and with HbA1c levels as indicator of glycemic status in participants who did not self-report a diabetes diagnosis. An additional aim was to understand the possible role of anthropometric measures in mediating the influence of lifestyle factors on diabetes as well as glycemic status.

Methods

Study sample

The NAKO is a prospective cohort study comprising more than 205,000 participants aged 19–74 years at the baseline examination¹³. Recruitment was performed at 18 study centers throughout Germany based on random sampling through population registries. Of these, 30,920 participants who had no contraindication underwent imaging of the trunk at five MRI centers (Supplementary Fig. 1) were eligible for the current analysis¹⁴. The study protocol, participant information documents, and declaration of consent forms for the baseline examinations including the MRI examinations were approved by relevant ethics committees¹³. All methods in the NAKO were carried out in accordance with relevant guidelines and regulations. The study protocol was approved by the Ethik-Kommission der Bayerischen Landesärztekammer, Germany (Nr. 13023 und 13031). All participants gave written informed consent for all aspects of the data collection and analysis.

Data collection

As part of the baseline study visit during 2014–2019, participants completed touchscreen questionnaires and face-to-face interviews asking about sociodemographic information, lifestyle risk factors (including alcohol intake and smoking), medical history, and other health-related information. A Food Frequency Questionnaire (FFQ) based on the German version of the multilingual European Food Propensity Questionnaire (web application and print version) allowed the estimation of frequency but not the amount using the question “How often have you eaten the following foods during the last 12 months?”¹⁵. Four authors (KN, GM, UN, SS) manually identified items that were relevant to the seven food groups included in the LSRI, i.e., fruits including juice, vegetables including potatoes, fish, processed meats, unprocessed red meats, whole grains, and refined grains, and computed total dietary intake frequency per food group. The Global Physical Activity Questionnaire (GPAQ) assessed physical activity as total time in minutes per week without considering intensity¹⁶.

As exposure, a score of lifestyle risk factors, which was adopted from a publication based on the UK Biobank⁶, was computed from data collected at the NAKO baseline exam. For each component, one point was given if the participant met the definition, which resulted in a range of 0 to 4 points. The points were assigned as follows (Supplementary Table 1): one point each for consuming ≤ 1 (women)/ ≤ 2 (men) alcoholic drinks/day (1 drink equals 14 g alcohol), no current smoking, performing ≥ 150 min/week physical activity, and adhering to $\geq 3/7$ dietary recommendations. The criterion for diet was reduced from scoring 4/7 food groups to adjust for the low adherence to the diet guidelines, thus resulting in a modified LSRI (mLSRI) as compared to Lourida et al.⁶. Given the small number of individuals ($N = 107$) with 0 points, they were combined with those who had 1 point, leading to range from 0/1 to 4 points, with higher values reflecting a healthier lifestyle.

Glycemic status

In all participants, HbA1c values were assessed in baseline EDTA blood samples by high-performance liquid chromatography, capillary electrophoresis, immunoturbidimetry, or immunoassay using the Tosoh G8 and G11 HPLC Analyzer (Tosoh Bioscience Inc., San Francisco, USA), Hemoglobin Testing Systems (D-100, VariantTM II, VariantTM II Turbo; Bio-Rad Laboratories, Hercules, USA), DxC 800 (Beckman Coulter, Brea, USA), Cobas c502 (Roche Diagnostics, Rotkreuz, Switzerland), Capillarys (Sebia, Lisses, France), and Dimension Vista 1500 (Siemens Healthineers, Erlangen, Germany)¹⁷.

The study sample was divided into 3 categories based on glycemic status: (1) Normoglycemic: no self-reported diabetes and normal HbA1c levels below the reference limit of < 39 mmol/mol Hb (5.7%); (2) Diagnosed diabetes: self-reported diabetes at baseline exam (the term T2D is not used as the type of diabetes was not reported) with or without elevated HbA1c; (3) Elevated HbA1c: no self-reported diabetes and above the reference limit of ≥ 39 mmol/mol Hb according to current guidelines^{18,19}. The last group, thus, includes participants with prediabetes (HbA1c ≥ 39 –48 mmol/mol Hb [5.7–6.5%]) and the small number of participants ($N = 114$) with undiagnosed diabetes (HbA1c ≥ 48 mmol/mol Hb, [6.5%]).

Anthropometric measures

Height and weight were assessed by trained personnel at the study centers. BMI categories (< 25 , 25 – < 30 , ≥ 30 kg/m²) were assigned using weight and height¹³. As part of the baseline exam, whole-body magnetic resonance imaging (MRI) was performed at 3 tesla imaging (Magnetom Skyra, Siemens Healthineers, Erlangen, Germany) among a subset of NAKO participants at five imaging sites with referral from six additional study centers following the same standard operating procedure and protocol¹⁴. VAT and SAT volumes (L) were obtained from the T₁-weighted 3D two-point DIXON MRI in axial orientation (3 mm slice thickness, 1.4×1.4 mm in-plane voxel size); their volumes were obtained by deep learning-based image segmentation comprising the whole abdomen from the middle of the femoral heads to the cardiac apex²⁰.

Statistical analysis

After excluding cohort members with missing values for glycemic status ($N = 407$), VAT ($N = 819$), BMI ($N = 407$), smoking ($N = 647$), physical activity ($N = 2,018$), diet ($N = 8,668$), and/or alcohol consumption ($N = 3,062$), 18,101 participants with complete information were included in the analysis. All statistical analyses were conducted using the software package SAS Enterprise Guide 8.4 Update 2 (SAS Institute Inc., Cary, NC, USA). Descriptive statistics were generated for demographic, anthropometric, and lifestyle variables. Due to their non-normal distribution, geometric means and 95% confidence intervals (95% CI) were computed for VAT. To determine the association between the mLSRI and diabetes/glycemic status, polytomous logistic regression to obtain prevalence odds ratios (POR) was applied. The mLSRI was modeled as categorical (0/1, 2, 3 and 4 points) to evaluate differences across categories and as four-level continuous variable to perform trend tests. The basic models were adjusted for age and sex only to evaluate the direct association of mLSRI with diabetes. Further models included BMI or VAT or both variables in addition to age and sex despite their relatively strong correlation ($r = 0.76$; $p < 0.0001$) as continuous variables to evaluate their influence on the mLSRI-diabetes/glycemic status relation. Given our interest in estimating the total effect of the mLSRI on glycemic status and its indirect effect, i.e., the proportion mediated through BMI/VAT, adjustment for BMI or VAT provides an indication if anthropometric variables play a role in this pathway, an acceptable method in a cross-sectional design where it is inappropriate to perform a formal mediation analysis.

Stratified analyses by sex and BMI explored the associations to examine possible effect modification by these well-known determinants of glycemic status. To evaluate the importance of individual lifestyle, the same statistical approach was used with the four mLSRI components as separate variables in one model. For individuals without self-reported diabetes, we applied linear regression to estimate least-squared mean HbA1c levels by mLSRI score and its four individual components as separate variables adjusted for the same covariates as above. In a sensitivity analysis, the main models were repeated using the dietary criterium of 4/7 as proposed by Lourida⁶.

Results

Of 18,101 participants with complete information (56% men and 44% women), 14,318 (79.1%) participants had HbA1 levels within the reference range, 644 (3.6%) reported a diabetes diagnosis, 3,139 (17.3%) had elevated HbA1c levels without a self-reported diabetes diagnosis (Table 1). Of these, 3,025 (16.7%) were in the prediabetes and 114 (0.6%) in the undiagnosed diabetes category. Among participants with self-reported diabetes, only 16% had HbA1c levels within the reference range, while 34% had levels of 39–<48 mmol/mol Hb, and 50% had levels of ≥ 48 mmol/mol Hb. As to BMI, 43.8% were classified as healthy weight (< 25 kg/m²), 38.4% as overweight (25–<30 kg/m²), and 17.8% as obese (≥ 30 kg/m²). The respective proportions for 0/1, 2, 3, and 4 mLSRI points were 6%, 25%, 51%, and 18%. A higher proportion of women than men achieved 4 mLSRI points. Regarding individual mLSRI components, 86% of study participants adhered to recommended physical activity levels, 83% were non-smokers, 86% reported moderate alcohol intake, and 25% adhered to at least 3 out of 7 dietary recommendations. Therefore, an increase from 3 to 4 mLSRI points was mostly due to adherence

Characteristic	Category	mLSRI scores				All
		0/1	2	3	4	
Number (%)		1184 (6)	4429 (25)	9255 (51)	3233 (18)	18,101 (100)
Age, yrs	Mean	48.3	48.5	47.9	48.6	48.2
Sex, %	Male	59.4	59.3	59.2	40.3	55.9
	Female	40.6	40.7	40.8	59.7	44.1
Adherence to lifestyle factors ^b , %	No current smoking	19.9	61.7	95.5	100.0	83.1
	Regular physical activity	33.4	65.3	70.1	100.0	85.7
	Moderate alcohol intake	35.7	68.8	95.0	100.0	85.6
	Healthy diet	1.2	4.4	12.4	100.0	25.3
Diabetes status, %	No self-reported diabetes and HbA1c < 39 mmol/mol Hb	20.5	18.8	16.3	17.0	17.3
	No self-reported diabetes and HbA1c ≥ 39 mmol/mol Hb	75.7	77.6	80.0	79.9	79.1
	Self-reported diabetes	3.8	3.6	3.7	3.1	3.6
BMI (kg/m ²), %	≤ 25	38.7	39.4	43.6	52.0	43.8
	25–<30	41.1	40.6	38.6	33.9	38.4
	≥ 30	20.3	20.0	17.8	14.1	17.8
BMI, kg/m ²	Mean	26.7	26.6	26.2	25.9	26.2
MRI VAT, liter	Geometric mean	3.20	3.01	2.72	2.13	2.70

Table 1. Characteristics of the NAKO study sample in the current analysis. NAKO=German National Cohort; mLSRI=modified Lifestyle Risk Index; BMI=Body Mass Index; MRI=Magnetic Resonance Imaging; VAT=Visceral Adipose Tissue. ^aDefinition of adherence: current not smoking, performing ≥ 150 min/week physical activity, consuming ≤ 1 (women)/ ≤ 2 (men) alcoholic drinks/day (1 drink equals 14 g alcohol), adhering to $\geq 3/7$ dietary recommendations, reduced from scoring 4/7 food groups as proposed by Lourida et al.⁶.

to dietary recommendations, which was highest for fruit plus juice (39%), refined grains (38%), and vegetables (incl. potatoes) (33%), unprocessed red meat (32%), while it was low for fish (17%), processed meat (10%), and whole grains (2%).

In the age-sex adjusted model (Table 2), the respective PORs for diabetes and elevated HbA1c in persons without a reported diabetes diagnosis were 0.69 (95%CI 0.58, 0.83) and 0.68 (95%CI 0.47, 0.98) comparing the highest vs. lowest mLSRI category. Adding BMI, VAT, or both as covariates attenuated the association for elevated HbA1c and eliminated the association with diabetes for the categorical and the continuous mLSRI model. Among persons without self-reported diabetes, high versus low mLSRI score was robustly inversely associated with elevated HbA1c, with PORs of 0.75 (95%CI 0.62, 0.89), 0.83 (95%CI 0.70, 1.00), and 0.81 (95%CI 0.80, 0.97) after adjustment for BMI, VAT, or both, respectively. The models with the continuous mLSRI indicated a 12% lower prevalence of elevated HbA1c per 1 mLSRI score point (POR = 0.88; 95%CI 0.84, 0.93), which was reduced when BMI, VAT, or both (POR = 0.93; 95%CI 0.88, 0.98) were included as covariates. The sensitivity analysis using the published diet criteria showed very similar findings to those using the mLSRI (Supplementary Table 2). With a requirement of adhering to at least 4 food groups, the distribution of LSRI scores from 0/1 to 4 was 7.3%, 28.1%, 58.3%, and 6.3%. Although the PORs varied by a few percentage points, statistical significance

Exposure	Covariates	No self-reported diabetes and HbA1c $\geq$ 39 mmol/mol Hb ^a (N = 3,139)				Self-reported diabetes (N = 644)			
		POR ^b	95% CI		p-trend	POR ^b	95% CI		p-trend
mLSRI cont. ^c	Age, sex	0.88	0.84	0.93	< 0.0001	0.91	0.82	0.99	0.05
mLSRI 2 vs. 0/1		0.85	0.72	1.01		0.86	0.61	1.21	
mLSRI 3 vs. 0/1		0.72	0.61	0.84		0.86	0.62	1.19	
mLSRI 4 vs. 0/1		0.69	0.58	0.83		0.68	0.47	0.98	
mLSRI cont. ^c	Age, sex, BMI	0.91	0.86	0.95	0.0002	0.95	0.86	1.05	0.30
mLSRI 2 vs. 0/1		0.85	0.72	1.01		0.86	0.61	1.22	
mLSRI 3 vs. 0/1		0.73	0.62	0.86		0.88	0.64	1.22	
mLSRI 4 vs. 0/1		0.75	0.62	0.89		0.78	0.54	1.13	
mLSRI cont. ^c	Age, sex, VAT	0.94	0.81	0.99	0.01	1.01	0.91	1.12	0.86
mLSRI 2 vs. 0/1		0.89	0.75	1.05		0.92	0.65	1.31	
mLSRI 3 vs. 0/1		0.79	0.67	0.93		1.01	0.73	1.40	
mLSRI 4 vs. 0/1		0.83	0.70	1.00		0.95	0.65	1.37	
mLSRI cont. ^c	Age, sex, BMI, VAT	0.93	0.88	0.98	0.006	0.99	0.90	1.10	0.92
mLSRI 2 vs. 0/1		0.88	0.74	1.04		0.90	0.64	1.28	
mLSRI 3 vs. 0/1		0.77	0.66	0.91		0.97	0.70	1.34	
mLSRI 4 vs. 0/1		0.81	0.68	0.97		0.91	0.62	1.32	
Individual mLSRI components									
Adherence	Covariates	POR ^d	95% CI		p-values	POR ^d	95% CI		p-values
No current smoking	Age, sex	0.60	0.54	0.66	< 0.0001	0.81	0.65	1.02	0.07
	Age, sex, BMI	0.58	0.52	0.64	< 0.0001	0.75	0.60	0.94	0.01
	Age, sex, VAT	0.58	0.52	0.65	< 0.0001	0.76	0.61	0.95	0.02
	Age, sex, BMI, VAT	0.58	0.52	0.64	< 0.0001	0.75	0.60	0.94	0.01
Healthy diet	Age, sex	0.90	0.81	0.99	0.02	0.76	0.62	0.93	0.007
	Age, sex, BMI	0.95	0.86	1.05	0.33	0.86	0.70	1.05	0.13
	Age, sex, VAT	0.99	0.90	1.09	0.81	0.91	0.74	1.11	0.36
	Age, sex, BMI, VAT	0.99	0.89	1.09	0.77	0.91	0.74	1.11	0.35
Moderate alcohol intake	Age, sex	1.32	1.17	1.48	< 0.0001	1.44	1.14	1.81	0.002
	Age, sex, BMI	1.31	1.16	1.47	< 0.0001	1.42	1.12	1.80	0.003
	Age, sex, VAT	1.36	1.22	1.53	< 0.0001	1.54	1.22	1.95	0.003
	Age, sex, BMI, VAT	1.34	1.20	1.51	< 0.0001	1.50	1.18	1.89	0.0008
Regular physical activity	Age, sex	0.93	0.83	1.05	0.23	0.85	0.68	1.06	0.15
	Age, sex, BMI	1.00	0.89	1.13	0.97	0.98	0.78	1.30	0.83
	Age, sex, VAT	1.06	0.94	1.19	0.33	1.07	0.85	1.35	0.56
	Age, sex, BMI, VAT	1.05	0.94	1.19	0.40	1.06	0.84	1.34	0.62

Table 2. The association of the mLSRI with elevated HbA1c and self-reported diabetes in the NAKO.

^aReference: persons without self-reported diabetes and with HbA1c-levels < 39 mmol/mol Hb. ^bPrevalence odds ratio (POR) and 95% confidence interval (95%CI) from logistic regression with covariates as listed.

^cModel for mLSRI as continuous variable. ^dObtained from logistic regression with covariates as listed and adjusted for all 4 lifestyle risk factors.

did not change for any of the models. The PORs for elevated HbA1c levels remained significant, whereas those self-reported diabetes were not.

In models stratified by sex and BMI (Fig. 1), only the associations for elevated HbA1c levels among men with overweight/obesity, but not in women, were significant. The respective PORs of 0.87 (95%CI 0.78, 0.96) and 0.77 (95%CI 0.68, 0.89) in the simple model were slightly reduced to 0.90 (95%CI 0.81, 1.00) and 0.79 (95%CI 0.69, 0.91) after adjustment for VAT.

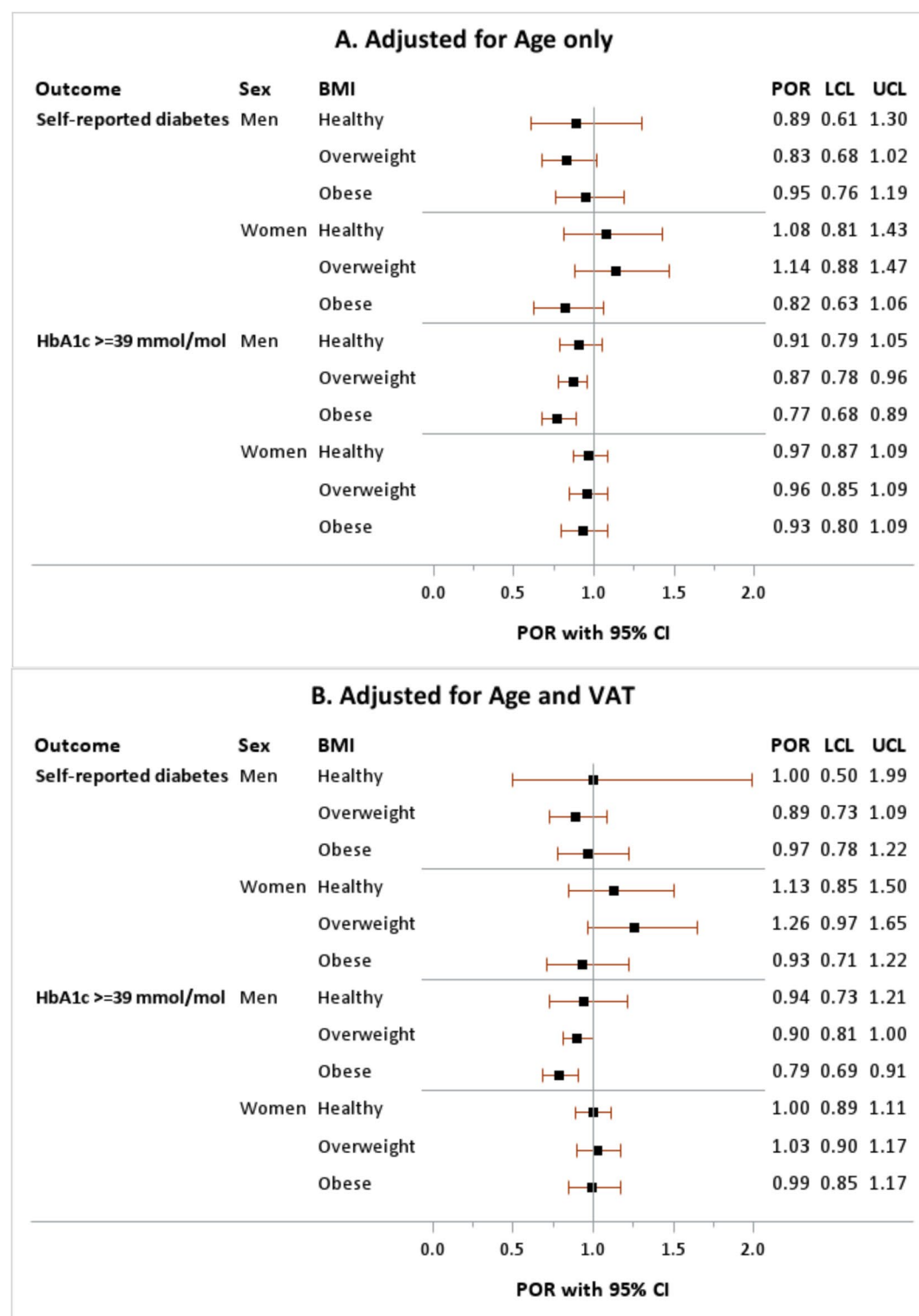


Fig. 1. mLSRI and glycemic status stratified by sex and BMI in the NAKO. Prevalence odds ratios (POR) obtained by polytomous logistic regression with the continuous mLSRI score as exposure.

mLSRI	Number (%)	Covariates	HbA1c (mmol/mol Hb)			
			LSmeans ^a	95% CI		p-value ^b
0/1	1139 (6.5)	Age, sex	35.4	35.1	35.6	Ref
2	4271 (24.5)		35.3	35.2	35.4	0.56
3	8914 (51.1)		35.0	34.9	35.1	0.004
4	3133 (17.9)		34.8	34.7	35.0	0.0002
0/1	1139 (6.5)	Age, sex, BMI	35.3	35.1	35.6	Ref
2	4271 (24.5)		35.3	35.1	35.4	0.62
3	8914 (51.1)		35.0	34.9	35.1	0.015
4	3133 (17.9)		34.9	34.8	35.1	0.006
0/1	1139 (6.5)	Age, sex, VAT	35.2	35.0	35.5	Ref
2	4271 (24.5)		35.2	35.1	35.4	1.00
3	8914 (51.1)		35.0	35.0	35.1	0.13
4	3133 (17.9)		35.0	34.9	35.2	0.15
0/1	1139 (6.5)	Age, sex, BMI, VAT	35.3	35.0	35.5	Ref
2	4271 (24.5)		35.2	35.1	35.4	0.81
3	8914 (51.1)		35.0	34.9	35.1	0.05
4	3133 (17.9)		35.0	34.8	35.1	0.05
Individual LSRI components						
Adherence	Covariates	Yes	95% CI	No	95% CI	p-value ^d
No current smoking	Age, sex	35.2	35.0, 35.3	36.1	35.8, 36.3	< 0.0001
	Age, sex, BMI	35.2	35.0, 35.3	36.1	35.8, 36.3	< 0.0001
	Age, sex, VAT	35.2	35.0, 35.3	36.0	35.8, 36.3	< 0.0001
	Age, sex, BMI, VAT	35.2	35.0, 35.3	36.1	35.8, 36.3	< 0.0001
Healthy diet	Age, sex	35.4	35.2, 35.6	35.8	35.7, 36.0	< 0.0001
	Age, sex, BMI	35.5	35.3, 35.7	35.8	35.6, 35.9	0.003
	Age, sex, VAT	35.5	35.3, 35.7	35.7	35.5, 35.9	0.04
	Age, sex, BMI, VAT	35.5	35.3, 35.7	35.7	35.6, 35.9	0.02
Moderate alcohol intake	Age, sex	35.9	35.8, 36.1	35.3	35.0, 35.5	< 0.0001
	Age, sex, BMI	35.9	35.8, 36.1	35.3	35.1, 35.5	< 0.0001
	Age, sex, VAT	36.0	35.8, 36.1	35.2	35.0, 35.5	< 0.0001
	Age, sex, BMI, VAT	35.9	35.8, 36.1	35.3	35.1, 35.5	< 0.0001
Regular physical activity	Age, sex	35.5	35.4, 35.7	35.7	35.5, 35.9	0.11
	Age, sex, BMI	35.6	35.5, 35.8	35.6	35.4, 35.9	0.93
	Age, sex, VAT	35.7	35.5, 35.8	35.5	35.3, 35.8	0.31
	Age, sex, BMI, VAT	35.6	35.5, 35.8	35.6	35.3, 35.8	0.68

Table 3. Mean HbA1c levels among participants without self-reported diabetes in the NAKO. ^aLeast-square means obtained by general linear regression adjusted for age and sex, plus BMI and log-transformed VAT. ^bAs compared to participants with a mLSRI score of 0/1. ^cLeast-square means for adherence vs. non-adherence obtained by general linear regression plus BMI and log-transformed VAT and all four components. ^dDifference between adherent and non-adherent participants.

The four individual mLSRI components were significantly associated with each other ($r = 0.01$ – 0.10 ; $p < 0.0001$) except for alcohol intake with physical activity ($p = 0.23$). When individual mLSRI components were analyzed as separate variables while adjusting for each other (Table 2), not smoking was associated with an approximately 40% lower likelihood to be classified with elevated HbA1c and no self-reported diabetes and a 19% lower likelihood to be classified with diabetes in the age- and sex-adjusted model. On the other hand, adhering to the moderate alcohol intake recommendation was associated with a 34% and 50% higher likelihood to be classified as elevated HbA1c or self-reported diabetes, respectively. The PORs for adherence to smoking and alcohol recommendations were minimally affected by the inclusion of BMI or VAT. For diet, the weak association in the simple model lost statistical significance after inclusion of BMI or VAT indicating that the relation between the diet and glycemic status may be due to by the anthropometric variables. No statistically significant associations of physical activity with diabetes or elevated HbA1c levels were detected.

Considering HbA1c as a continuous variable (Table 3) again indicated significant inverse associations with the mLSRI in the simple model that were attenuated to the null when VAT was added to the model. While the adjusted means of HbA1c for mLSRI 0/1 vs. 4 in the simple model were 35.4 and 34.8 mmol/mol, the difference was attenuated to 0.3 mmol/mol in the full model. As to individual risk factors, adherence to the smoking and alcohol recommendation was statistically significant although in opposite directions. The significant difference

for adhering to a healthy diet seen in the age/sex-adjusted model was greatly attenuated after the inclusion of BMI and/or VAT, whereas HbA1c was not associated with adherence to physical activity.

Discussion

This analysis detected a relatively weak association of a LSRI, both as published by Lourida⁶ and as modified for our study population, with the presence of self-reported diabetes and with lower HbA1c levels among persons without self-reported diabetes. A possible reason is the low-risk profile of this relatively health conscious population makes it difficult to detect the true impact of dietary or exercise improvements as the reference category of individuals with poor health behaviors is small. Adjustment for anthropometrics attenuated the significant associations given the well-established influence of adiposity and body composition on T2D risk^{7,21} and their relation with LSRI components²², whereas the age- and sex-adjusted models estimate the overall association of the LSRI with glycemic status representing the indirect effect through BMI or VAT as well as the direct effect on glycemia. Not all specific LSRI components showed independent relations with HbA1c. The inverse association of not smoking with abnormal glycemic status was strongest, while the diet component lost statistical significance in the BMI- or VAT-adjusted model. Adherence to the alcohol recommendation was related to higher HbA1c levels, while physical activity showed no association.

Our study broadly agrees with a substantial body of literature describing associations between lifestyle indices and diabetes. As expected, the associations in this cross-sectional study were weaker than those reported by prospective studies, but the novelty of our analysis lies in its detailed analysis of HbA1c values. Two systematic reviews and meta-analyses of prospective studies investigating lifestyle factors included 14 studies, of which 11 overlapped^{21,23}. Adherence to a healthy lifestyle, mostly favorable diet, physical activity, not smoking, moderate alcohol intake, and healthy weight, was associated with 78% and 75% lower risks for T2D than low adherence^{21,23}. Studies that included BMI^{21,23} or other metabolic markers¹¹ showed a stronger association with T2D than simple lifestyle indices supporting BMI's stronger influence on glycemic status than lifestyle alone. More recently, similar lifestyle scores were associated with diabetes in a prospective cohort from Japan²⁴, the UK Biobank²⁵, and also with prediabetes^{26–28}.

Although smokers who quit initially elevate their BMI and T2D risk, smoking may increase T2D risk by inflammation through nicotine and other toxins, damage to pancreatic tissue, or a less healthy lifestyle²⁹. The question why moderate alcohol intake in combination with other healthy behaviors appears to be associated with a lower diabetes risk has been reported in the past as part of meta-analyses and discussed widely^{30,31}, but it is possible that results are affected by the fact that former drinkers with poor health are included in the reference category³². Possible biologic mechanisms for a beneficial influence of alcohol include anti-inflammatory effects and stimulation of high-density cholesterol synthesis if the observed positive association for moderate alcohol intake are not due to the inclusion of former drinkers and people who are non-drinkers due to health problems in the higher LSRI group resulting in a greater likelihood of increased HbA1c in those adhering to no-to-moderate alcohol intake. Estimates of population attributable fractions for indices in relation to diabetes varied widely, but in studies that included BMI, the proportion of preventable cases tended to be higher²¹, e.g., 9 of 10 new cases of diabetes were attributable to BMI, waist circumference, smoking, physical activity, diet in the Cardiovascular Health Study³³ and 80% could have been prevented with everyone in the low-risk category for weight, physical activity, smoking, meat and alcohol intake in the Multiethnic Cohort³⁴.

Possible reasons for the lack of a statistically significant association between the LSRI and diabetes prevalence are the small number of cases as compared to those with elevated HbA1c and, foremost, the low risk profile of the study population and the adoption of healthier lifestyles in participants after a diabetes diagnosis. The fact that 84% of the participants with self-reported diabetes had elevated HbA1c levels indicated that glycemic control has multiple influencing factors. Our results for participants with undiagnosed diabetes support the idea that the LSRI may represent a predictor for abnormal glycemic status.

Variations in findings across studies originate in the definition of index, the amount of detail in the assessment of the behaviors, incorporation of individual foods vs. overall diet quality, self-reports of behavior at one point in time only, incidence rates for diabetes, and differences in screening efforts for diabetes. In the current study, the estimation of physical activity involves substantial measurement error and may be responsible for the lack of association with glycemic status despite the well-known benefits of exercise on diabetes development³⁵. Lastly, our cross-sectional results are not directly comparable to findings of prospective analyses as individuals with known diabetes or abnormal glycemic status may have changed their behavior on the recommendation of health care professionals.

The current analysis has several strengths, foremost the large study sample and the detailed information on numerous risk factors, including MRI-based VAT volume. On the other hand, the cross-sectional design is the most important limitation as reverse causation cannot be excluded. As participants with impaired glycemic status may have modified any or all of the four lifestyle behaviors after becoming aware of their condition, the directionality of the association cannot be determined. Selection bias may be present due to the highly selective participation of relatively health conscious in the NAKO overall (< 20% of those invited) and the fact that not all of the 205,000 participants were offered to undergo an MRI or refused participation. However, in a comparison of our sample with the full NAKO cohort, age, BMI, and smoking did not differ substantially³⁶. The mean age was slightly lower (48.2 vs. 49.9 years) in this report than the NAKO, the respective mean BMI values were slightly higher for women (25.6 vs. 24.9 kg/m²) and similar for men (26.7 vs. 26.6 kg/m²), and current smoking rates were somewhat lower in the subset than in the NAKO (17.3% vs. 22.1% for men and 16.5% vs. 18.9%). Dietary assessment may have been affected by measurement error due to self-reports, recall bias, and the fact that only frequency of intake without information on portion sizes was available¹⁵, it is important to note that the dietary recommendation of the LSRI is defined as servings per day or week not as grams of food⁶. Residual confounding also remains a major concern given the absence of important indicators of socioeconomic status

in the model as they are also associated with lifestyle factors. Finally, residual confounding by socioeconomic factors that were not assessed may have been present.

Compared to survey data in Germany reported as 5.6–7.2% between 1997 and 2011²⁶, the 3.6% self-reported diabetes rate was quite low, possibly due to the young age of the NAKO participants, selection bias, and their low-risk profile although the rate agreed with a previous NAKO report¹⁷. Intake may be overestimated for fruits and vegetables due to the large number of items offered on the questionnaire, whereas whole grains were probably underestimated as the questionnaire included few applicable items. Finally, the current and many published analyses did not consider additional lifestyle risk factors that appear to be important for diabetes, e.g., sleep duration, coffee intake, and socioeconomic status³⁷.

Conclusions

Our findings are compatible with the hypothesis that a combination of healthy lifestyle factors, as captured by a LSRI, may be responsible for a lower probability to experience disturbed glucose metabolism, both self-reported diabetes and HbA1c levels among persons without diabetes. However, the weak associations were primarily driven by smoking behavior not the other three components, the health-conscious behaviors of the study population may have limited our ability to detect associations, and reverse causality cannot be excluded due to the cross-sectional design. The attenuation after inclusion of BMI or VAT due to their association with LSRI²² and their known association with glycemic status is in line with the importance of anthropometric characteristics in diabetes development and their hypothesized role as mediators between lifestyle behaviors and glycemic status.

Data availability

Access to and use of NAKO (German National Cohort) data and biospecimens can be obtained via an electronic application portal (<https://transfer.nako.de/transfer/index>). The codes that support the findings of this study are available from the corresponding author upon request.

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Author contributions

GM, UN, KN, and TP were involved in the conception, design, and conduct of the study and the analysis and interpretation of the results. The statistical analysis was conducted by RK and GM. A writing group (GM, UN, SS, RK, MBS, FB, JM, ML, KN, and TP) prepared the first draft of the manuscript. The remaining authors represented NAKO study centers, contributed to cohort development, and data collection. All authors edited, reviewed, and approved the final version of the manuscript. TP and GM are the guarantors of this work and had full access to all study data and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

The study protocol, participant information documents, and declaration of consent forms for the baseline examinations including the MRI examinations were approved by relevant ethics committees. All participants gave written informed consent.

Additional information

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1038/s41598-026-64631-4>.

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