

ORIGINAL ARTICLE

Impact of weight and weight change on normalization of prediabetes and on persistence of normal glucose tolerance in an older population: the KORA S4/F4 study

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Background and aims: In a population-based cohort study with older subjects and without specific interventions, we investigated the impact of body mass index (BMI) and BMI change (as well as waist circumference and change of waist circumference) on reversion from prediabetes to normal glucose tolerance (NGT) and on long-term persistence of NGT.

Materials and methods: Oral glucose tolerance tests were conducted at baseline and at follow-up in a cohort study in Southern Germany (KORA S4/F4; 1223 subjects without diabetes aged 55–74 years at baseline in 1999–2001; 887 subjects (73%), of whom 436 had prediabetes at baseline, participated in the follow-up 7 years later).

Results: BMI reduction, but not initial BMI, predicted reversion from prediabetes to NGT. The odds ratio (OR) for returning to NGT was 1.43 (95% CI: 1.18–1.73) for a BMI decrease of 1 kg m^{-2} , after adjustment for age, sex, baseline glucose values and lifestyle factors. Initial BMI had no effect on reversion to NGT (OR = 0.98, 95% CI: 0.91–1.06, per kg m^{-2}). Persistence of NGT was associated with baseline BMI (OR = 0.94, 95% CI: 0.88–0.998) and BMI reduction (OR = 1.16, 95% CI: 1.02–1.33, per decrease by 1 kg m^{-2}). For waist circumference and change of waist circumference similar results were obtained.

Conclusion: In older adults, weight loss strongly increased the chances of returning from prediabetes to NGT irrespective of initial BMI. Long-term persistence of NGT depended both on initial BMI and on BMI change.

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Keywords: prediabetes; normal glucose tolerance; body mass index; waist circumference; weight loss; body weight change

Introduction

Obesity is a strong risk factor for type 2 diabetes,^{1,2} and, moreover, in several studies weight change was shown to have an additional impact on diabetes incidence after adjustment for initial body mass index (BMI).^{3,4} In the Diabetes Prevention Program and the Diabetes Prevention

Study it was shown that lifestyle intervention, including moderate weight loss, substantially reduced the risk of diabetes in high-risk subjects.^{5,6} Although reversion to normal glucose tolerance (NGT) is not a rare event,^{7,8} the effects of weight and weight change on reversion from prediabetes to NGT have been investigated much less.^{9–14} Two of these studies focus on children and adolescents,^{9,10} and the findings in the other four studies are rather inconclusive.^{11–14} In some other studies the influence of initial BMI on the progression from NGT to prediabetes was investigated,^{15,16} but little is known about the association of weight and weight change with persistence of NGT in older people.¹⁷

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Thus, the objective of this study is to assess the role of weight and weight change for the reversion from prediabetes to NGT, and for long-term persistence of NGT in an older population without lifestyle intervention. Moreover, we investigate the effects of waist circumference and change of waist circumference on reversion to NGT and on persistence of NGT.

Materials and methods

Study population

The KORA (Cooperative Health Research in the Region of Augsburg) S4 survey is a population-based study in Southern Germany conducted between 1999 and 2001 (age range of study participants 25–74 years). The primary study sample in the age range between 55 and 74 years consisted of 2656 subjects. Of those, 1653 (62%) subjects participated (1999–2001), who were all Caucasians. After excluding participants with known diabetes and further drop-outs, 1353 subjects had a standard oral glucose tolerance test (OGTT) at baseline.

All study participants who had completed the baseline survey were invited to a follow-up examination 7 years later (2006–2008). The present study includes only participants without known or newly diagnosed diabetes at baseline, who successfully completed a baseline OGTT ($n = 1223$) and who lived within the study region at the time of the follow-up examination. Among those individuals, 98 subjects died before 2006, and 887 (73%) participated in the follow-up (OGTT). Informed consent was obtained from all participants. The surveys were approved by the ethics committee of the Bavarian Medical Association.

In all, 33 subjects with clinically diagnosed type 2 diabetes between baseline and follow-up examination were excluded from all analyses because knowledge of the disease might influence lifestyle and medication and thus might have an impact on weight and waist circumference.

Ascertainment of type 2 diabetes and prediabetes

Self-reported incident diabetes cases and the date of diabetes diagnosis were validated by contacting the general practitioners who treated the participants. In non-diabetic subjects, OGTT was performed during the morning hours (between 0700 and 1100 hours). Participants were asked to fast for at least 10 h overnight, to avoid strenuous physical activity on the day before the examination and to refrain from smoking before and during the test. The exclusion criterion for performing the OGTT was the presence of acute illnesses (such as infection, fever and acute gastrointestinal diseases). Fasting venous blood glucose was sampled and 75 g of anhydrous glucose in aqueous solution (volume 300 ml) was given (Dextro OGT, Boehringer Mannheim, Mannheim, Germany).

Incident diabetes was defined based on (1) validated physician diagnoses or (2) newly diagnosed diabetes (fasting

glucose $\geq 7.0 \text{ mmol l}^{-1}$ or 2-h glucose $\geq 11.1 \text{ mmol l}^{-1}$). Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) were defined according to the 2003 ADA diagnostic criteria¹⁸ (IFG: fasting glucose $5.6\text{--}6.9 \text{ mmol l}^{-1}$, IGT: 2-h glucose $7.8\text{--}11.0 \text{ mmol l}^{-1}$). Prediabetes included isolated IFG, isolated IGT, and combined IFG and IGT (IFG + IGT).

Anthropometric and laboratory measurements were described previously.¹⁹ Information about medical history, smoking, alcohol consumption and physical activity was gathered in a structured interview. Participants who reported less than 1 h of leisure-time physical activity per week in summer or winter were classified as inactive. Moderate alcohol intake was defined as >0 and $<40 \text{ g}$ per day in men, and >0 and $<20 \text{ g}$ per day in women; high alcohol intake as $\geq 40 \text{ g}$ per day in men and $\geq 20 \text{ g}$ per day in women. Low HDL cholesterol was defined as $\leq 40 \text{ mg dl}^{-1}$ in men and $\leq 50 \text{ mg dl}^{-1}$ in women. Hypertriglyceridaemia was defined as triglycerides $\geq 175 \text{ mg dl}^{-1}$. Dietary intake was assessed with a short 27-item qualitative food frequency list. The participants were asked to recall their 'average intake' of each item in the following six frequency categories: almost daily, several times per week, about once a week, several times per month, once a month or less and never. Details on a very similar food frequency list have been described elsewhere.²⁰

Definition of reversion to NGT

To make sure that reversion to NGT corresponded with clinically relevant changes of glucose values, subjects with prediabetes at baseline were defined as reverts to NGT only if

- (1) they had isolated IFG at baseline, had NGT in the follow-up examination, and fasting glucose had decreased by more than 5 mg dl^{-1} between both examinations, or
- (2) they had isolated IGT at baseline, had NGT in the follow-up examination, and their 2-h glucose had decreased by more than 10 mg dl^{-1} between both examinations, or
- (3) they had combined IFG and IGT at baseline, had NGT in the follow-up examination, and either their fasting glucose had decreased by more than 5 mg dl^{-1} or their 2-h glucose had decreased by more than 10 mg dl^{-1} between both the examinations.

Definition of persistence of NGT

NGT was considered as persistent if subjects had NGT at both baseline and follow-up examinations, or if they had NGT at baseline and

- (1) subjects had isolated IFG in the follow-up examination, but fasting glucose had not increased by more than 5 mg dl^{-1} between both examinations, or
- (2) subjects had isolated IGT in the follow-up examination, but their 2-h glucose had not increased by more than 10 mg dl^{-1} between both examinations, or

- (3) subjects had combined IFG and IGT in the follow-up examination, but neither their fasting glucose had increased by more than 5 mg dl^{-1} nor their 2-h glucose had increased by more than 10 mg dl^{-1} between both examinations.

Statistical analyses

Baseline characteristics and changes of these characteristics over time were compared (1) between subjects with prediabetes at baseline reverting to NGT and those who did not revert to NGT, and (2) between subjects with persistent NGT and those without persistent NGT. For these comparisons, F-tests were used in case of normally distributed variables. For log-normal variables, F-tests were performed on a log-scale. Logistic regression was used to compare binomial proportions. All comparisons were adjusted for age and sex.

Multivariate logistic regression models were fitted (1) for subjects with prediabetes at baseline to calculate odds ratio (OR) with 95% CI for the relationship between initial BMI and BMI change, and reversion to NGT (yes/no), and (2) for subjects with NGT at baseline to calculate OR with 95% CI for the relationship between BMI and BMI change, and persistence of NGT (yes/no). Initial BMI was introduced as a continuous variable; BMI change was included as a continuous variable, and separately as a categorical variable. In additional analyses, initial waist circumference and change of waist circumference were included in the models instead of BMI and BMI change. For both return to NGT and persistence of NGT as dependent variables, three different models were fitted: In a basic model, sex and age were included as covariables. In a second model, fasting glucose, 2-h glucose, parental diabetes and lifestyle factors (diet, coffee intake, alcohol intake, smoking and physical activity) were added to the basic model. In a third model, age, sex, fasting glucose, 2-h glucose, parental diabetes, hypertriglyceridaemia, change of triglycerides, HDL cholesterol (dichotomous), change of HDL cholesterol and hypertension were introduced as covariables.

Finally, the effects of initial BMI and BMI change on reversion to NGT were analysed separately for overweight ($25 \text{ kg m}^{-2} \leq \text{BMI} < 30 \text{ kg m}^{-2}$) and for obese ($\text{BMI} \geq 30 \text{ kg m}^{-2}$) subjects. The number of subjects with normal weight ($\text{BMI} < 25 \text{ kg m}^{-2}$) was too small for a meaningful analysis of this aspect.

Results

Among 405 subjects with prediabetes at baseline, 66 (16.3%) returned to NGT in the follow-up examination 7 years later with clinically relevant improvements in either fasting or 2-h glucose. In Table 1, baseline characteristics and changes over time in potential predictors of reversion to NGT were compared between subjects who returned or did not return to NGT. The proportion of subjects with a decline in BMI of at least 1 kg m^{-2} was about twice as large in reverters as in

non-reverters, and, vice versa, the proportion of subjects with an increase in BMI of more than 1 kg m^{-2} was more than twice as large in non-reverters as in reverters. Subjects who returned to NGT showed a 1.4-cm-lower increase in waist circumference.

Among 449 subjects with NGT at baseline, 321 (71.5%) still had NGT in the follow-up examination. Table 2 presents baseline characteristics, as well as changes over time of some of these characteristics for subjects with persistent NGT and for subjects progressing to prediabetes or T2DM. Subjects with persistent NGT had a smaller initial BMI, were less likely to gain more than 1 kg m^{-2} in BMI, had a smaller waist circumference at baseline and gained less waist circumference.

As shown in Table 3, BMI reduction, but not BMI at baseline, predicted reversion to NGT from prediabetes in three models with different sets of covariates. The ORs (95% CI) for returning to NGT were 7.9 (3.0–20.9) and 3.6 (1.6–8.2) for subjects with BMI decline ($\leq -1 \text{ kg m}^{-2}$) and stable BMI (> -1 , but $\leq 1 \text{ kg m}^{-2}$), respectively, compared with subjects with BMI increase $> 1 \text{ kg m}^{-2}$, after adjustment for age, sex, baseline glucose levels and lifestyle factors (model 2). Initial BMI had no significant effect on return to NGT (OR = 0.98, 95% CI: 0.91–1.06, per kg m^{-2}). Similarly, change of waist circumference, but not initial waist circumference, was associated with conversion to NGT in all the three models.

The logistic regression models for the prediction of reversion to NGT were also done separately for overweight and obese subjects (data not shown in Table 3). In both strata, similar effects of BMI at baseline and BMI change on reversion to NGT were found as in the analyses of the whole study group. For BMI decline ($\leq -1 \text{ kg m}^{-2}$), ORs (95% CI) were 7.0 (1.8–27.8) in overweight and 7.1 (1.3–39.3) in obese subjects, compared with subjects with BMI increase $> 1 \text{ kg m}^{-2}$. For stable BMI (> -1 , but $\leq 1 \text{ kg m}^{-2}$), ORs (95% CI) were 3.0 (1.01–8.9) in overweight and 3.5 (0.7–16.3) in obese subjects compared with subjects with BMI increase.

Initial BMI as well as initial waist circumference significantly predicted persistence of NGT in three different models (Table 4). BMI change and change of waist circumference were significantly associated with persistence of NGT in model 1. These associations were attenuated in models 2 and 3, especially when lipids were included as covariables.

Some additional analyses were done (prediction of 10% changes in fasting glucose and in 2-h glucose; multiple linear regression analyses with changes in glucose values as dependent variables). These additional analyses and analyses regarding transitions between glucose tolerance classes led to similar results (see Supplementary appendix, Tables 5–8).

Discussion

This study showed that reversion from prediabetes to NGT in older subjects was predicted by BMI reduction, but not by initial BMI (and similarly, by change of waist circumference, but not by waist circumference at baseline). Moreover, there

Table 1 Baseline characteristics and changes over time of subjects with prediabetes at baseline: the KORA S4/F4 cohort study^{a,b}

	Persistence of prediabetes or transition to diabetes	Return to NGT	P
N	339	66	
Sex (women) (%)	39.2	60.6	0.002 ^{*,c}
Age	63.6 ± 5.2	63.7 ± 6.1	0.97 ^d
BMI (kg m ⁻²)	28.9 ± 3.9	28.5 ± 3.9	0.39 ^d
BMI			0.80 ^c
< 25 kg m ⁻² (%)	14.2	15.2	
≥ 25 kg m ⁻² , < 30 kg m ⁻² (%)	52.8	54.6	
≥ 30 kg m ⁻² (%)	33.0	30.3	
Change in BMI (kg m ⁻²)	0.50 ± 1.60	-0.19 ± 1.6	0.001 ^{*,d}
Change in BMI			
≤ -1 kg m ⁻² (%)	12.4	27.3	< 0.001 ^{*,c}
> -1 kg m ⁻² , ≤ 1 kg m ⁻² (%)	52.8	59.1	
> 1 kg m ⁻² (%)	34.8	13.6	
Waist circumference (cm)	97.5 ± 10.9	93.8 ± 9.2	0.20 ^d
Change in waist circumference (cm)	3.1 ± 5.4	1.7 ± 5.8	0.04 ^{*,d}
Hypertension (%) ^e	61.1	44.6	0.03 ^{*,c}
Systolic blood pressure (mm Hg)	138.1 ± 17.7	132.7 ± 16.4	0.11 ^d
Change in systolic blood pressure (mm Hg)	-5.5 ± 19.1	-4.4 ± 19.6	0.75 ^d
Diastolic blood pressure (mm Hg)	82.3 ± 10.0	80.6 ± 9.6	0.62 ^d
Change in diastolic blood pressure (mm Hg)	-6.3 ± 10.1	-6.6 ± 8.9	0.64 ^d
Fasting glucose (mg dl ⁻¹)	105.9 ± 7.1	102.0 ± 6.4	< 0.001 ^{*,d}
2-h glucose (mg dl ⁻¹)	126.7 ± 32.1	118.3 ± 30.9	0.02 ^{*,d}
HbA1c (%)	5.65 ± 0.33	5.55 ± 0.33	0.01 ^{*,d}
Fasting insulin (mU l ⁻¹)	11.1 (8.55, 15.9)	10.0 (6.9, 13.1)	0.03 ^{*,f}
Hypertriglyceridaemia (%) ^g	23.8	7.8	0.016 ^{*,c}
Triglycerides (mg dl ⁻¹)	121.0 (88.5, 173.0)	113.5 (81.0, 139.5)	0.13 ^f
Change in triglycerides (mg dl ⁻¹)	2.6 ± 62.9	-13.9 ± 46.6	0.04 ^{*,d}
Low HDL cholesterol (%) ^h	19.9	7.6	0.009 ^{*,c}
HDL cholesterol (mg dl ⁻¹)	56.9 ± 16.1	61.7 ± 13.9	0.17 ^d
Change in HDL cholesterol (mg dl ⁻¹)	-3.7 ± 9.8	0.1 ± 13.4	0.003 ^{*,d}
Parental diabetes (%)	26.3	27.3	0.90 ^c
Physically active (%)	46.9	41.5	0.43 ^c
Active or past smokers (%)	47.8	43.9	0.41 ^c
Alcohol consumption			
Abstinent (%)	19.5	23.1	0.97 ^c
Moderate (%)	57.5	55.4	
High (%)	23.0	21.5	

Abbreviations: BMI, body mass index; NGT, normal glucose tolerance. ^aChanges over time are calculated as value at follow-up minus value at baseline. ^bMean value ± standard deviation, median (first quartile, third quartile). ^cLogistic regression. ^dF-test. ^eBlood pressure of 140/90 mm Hg or higher, or antihypertensive medicine. ^flog F-test. ^g≥ 175 mg dl⁻¹ of triglycerides. ^hLow HDL cholesterol was defined as ≤ 40 mg dl⁻¹ in men and ≤ 50 mg dl⁻¹ in women. All analyses adjusted for age and sex. **P* < 0.05; ***P* < 0.01.

was a dose-response relationship between BMI change and normalization of glucose tolerance, and even a relatively small decline of BMI of at least 1 kg m⁻² led to a substantially larger chance of reverting to NGT irrespective of initial BMI. Contrary to the results for reversion to NGT, persistence of NGT was associated with change of BMI and with initial BMI and, similarly, with change of waist circumference and with initial waist circumference.

The role of anthropometric measures and their changes for the reversion from prediabetes to NGT have rarely been investigated. Findings of an Iranian study were in line with our results: in this study with middle-aged subjects, who were first-degree relatives of patients with type 2 diabetes,

change of waist circumference, but not initial waist circumference, predicted return to NGT.¹¹ In a Swedish study, initial BMI and initial waist circumference did also not predict return from prediabetes to NGT.¹² However, contrary to our study, a significant influence of weight loss on normalization of blood glucose was not reported. In a Chinese study, transitions from NGT and IGT, respectively, to the categories of NGT, IGT and T2DM were investigated, and weight gain was lowest in subjects converting from IGT to NGT.¹³ Shimizu *et al.*¹⁴ reported that weight change was only associated with reversion to NGT in subjects who were obese or tending to obesity but not in normal-weight or slim individuals. In the present study, this association was seen

Table 2 Baseline characteristics and changes over time of subjects with normal glucose tolerance at baseline: the KORA S4/F4 cohort study^{a,b}

	Persistence of normal glucose tolerance	Transition to prediabetes or to type 2 diabetes	P
N	321	128	
Sex (females) (%)	56.7	58.6	0.60 ^c
Age	62.2 ± 5.4	63.8 ± 5.5	0.006 ^{***,d}
BMI (kg m ⁻²)	26.8 ± 3.7	28.4 ± 4.1	<0.001 ^{***,d}
BMI			0.008 ^{***,c}
<25 kg m ⁻² (%)	30.7	16.4	
≥25 kg m ⁻² , <30 kg m ⁻² (%)	52.4	56.3	
≥30 kg m ⁻² (%)	16.9	27.3	
Change in BMI (kg m ⁻²)	0.2 ± 1.6	0.6 ± 2.1	0.011 ^{*,d}
Change in BMI			0.004 ^{***,c}
≤-1 kg m ⁻² (%)	17.6	15.0	
>-1 kg m ⁻² , ≤1 kg m ⁻² (%)	57.7	45.7	
>1 kg m ⁻² (%)	24.8	39.4	
Waist circumference (cm)	90.4 ± 10.6	93.7 ± 9.9	0.001 ^{***,d}
Change in waist circumference (cm)	2.6 ± 5.4	3.9 ± 6.2	0.02 ^{*,d}
Hypertension (%) ^e	36.7	44.5	0.25 ^c
Systolic blood pressure (mm Hg)	127.9 ± 18.4	130.9 ± 19.4	0.32 ^d
Change in systolic blood pressure (mm Hg)	-4.1 ± 19.6	-7.4 ± 21.6	0.29 ^d
Diastolic blood pressure (mm Hg)	77.6 ± 9.7	77.7 ± 10.4	0.84 ^d
Change in diastolic blood pressure (mm Hg)	-4.2 ± 19.6	-5.7 ± 11.1	0.38 ^d
Fasting glucose (mg dl ⁻¹)	91.6 ± 5.2	92.8 ± 4.4	0.014 ^{*,d}
2-h glucose (mg dl ⁻¹)	96.0 ± 20.6	107.8 ± 17.6	<0.001 ^{***,d}
HbA1c (%)	5.53 ± 0.35	5.56 ± 0.32	0.74 ^d
Fasting insulin (mU l ⁻¹)	8.1 (6.0, 11.4)	9.0 (6.6, 13.4)	0.13 ^f
Hypertriglyceridaemia (%) ^g	12.7	11.0	0.80 ^c
Triglycerides (mg dl ⁻¹)	101.5 (73.0, 144.0)	105.0 (74.0, 136.0)	0.70 ^f
Change in triglycerides (mg dl ⁻¹)	-1.8 ± 48.1	12.0 ± 64.1	0.009 ^{***,d}
Low HDL cholesterol ^h	11.5	19.5	0.02 ^{*,c}
HDL cholesterol (mg dl ⁻¹)	62.3 ± 16.9	58.7 ± 16.2	0.02 ^{*,d}
Change in HDL cholesterol (mg dl ⁻¹)	-2.4 ± 11.5	-2.1 ± 10.9	0.83 ^d
Parental diabetes (%)	16.5	26.6	0.004 ^{***,c}
Physically active (%)	53.0	39.8	0.02 ^{*,c}
Active or past smokers (%)	49.7	43.8	0.39 ^d
Alcohol consumption			
Abstinent (%)	25.7	32.0	0.20 ^c
Moderate (%)	56.1	47.7	
High (%)	18.2	20.3	

Abbreviation: BMI, body mass index. ^aMean value ± s.d., median (first quartile, third quartile). ^bChanges over time are calculated as value at follow-up minus value at baseline. ^cLogistic regression. ^dF-test. ^eBlood pressure of 140/90 mm Hg or higher, or antihypertensive medicine. ^flog F-test. ^gHypertriglyceridaemia was defined as triglycerides ≥ 175 mg dl⁻¹ of triglycerides. ^hLow HDL cholesterol was defined as ≤ 40 mg dl⁻¹ in men and ≤ 50 mg dl⁻¹ in women. All analyses adjusted for age and sex. **P* < 0.05, ***P* < 0.01.

both for obese and for overweight persons. For normal-weight individuals, a meaningful separate analysis could not be performed in the present study owing to the small number of subjects with normal or low BMI.

The partly different findings in the few other studies on the association of weight change with normalization of prediabetes might have different reasons. It cannot be ruled out that rather small numbers of participants and non-participation bias the results in some studies. In addition, the association between weight change and normalization of prediabetes might also depend on ethnicity. Given similar BMI, Asian Indians were shown to have more abdominal and visceral fat than Caucasians.²¹ Thus, the effects of weight change might be different in these two ethnic groups. Moreover, several

studies found that the strength of association of diabetes with obesity differed in Asians and Caucasians^{22,23}—although the studies discussed here are about normalization of prediabetes, this might be a hint that in different ethnicities change of BMI or waist circumference could have different effects on what happens to subjects with prediabetes.

The findings of the present study fit well in those of the Diabetes Prevention Program and the Diabetes Prevention Study, which demonstrated that lifestyle intervention including weight loss strongly reduced the risk of diabetes in high-risk subjects.^{5,6} Thus, weight loss has positive effects in subjects with prediabetes by reducing the risk of progressing to diabetes and by increasing the chance of reverting to NGT.

Table 3 Predictors^a of return to normal glucose tolerance at 7-year follow-up in subjects with prediabetes at baseline (multiple logistic regression models, odds ratios, 95% confidence intervals): KORA S4/F4 cohort study

	Model 1 ^b	Model 2 ^c	Model 3 ^d
BMI (baseline) (per kg m ⁻²) ^e	0.96 (0.90–1.03)	0.98 (0.91–1.06)	1.02 (0.94–1.10)
BMI change (per kg m ⁻² decline)	1.35 (1.13–1.61)	1.43 (1.18–1.73)	1.39 (1.13–1.72)
BMI (baseline) (per kg m ⁻²) ^f	0.96 (0.89–1.03)	0.98 (0.91–1.06)	1.01 (0.93–1.10)
BMI change			
≤ -1 kg m ⁻²	6.22 (2.53–15.28)	7.94 (3.02–20.91)	9.71 (3.41–27.68)
> -1 kg m ⁻² , ≤ 1 kg m ⁻²	3.04 (1.40–6.59)	3.60 (1.59–8.15)	2.98 (1.26–7.02)
> 1 kg m ⁻² (ref)	1	1	1
Waist circumference (baseline) (per 5 cm)	0.90 (0.78–1.04)	0.94 (0.80–1.10)	1.06 (0.90–1.25)
Change of waist circumference (per 5 cm decline)	1.31 (1.03–1.68)	1.40 (1.08–1.82)	1.34 (1.01–1.78)

Abbreviation: BMI, body mass index. ^aBMI change and change of waist circumference refer to the 7-year follow-up. ^bModel 1: adjusted for age and sex. ^cModel 2: adjusted for age, sex, fasting plasma glucose (baseline), 2-h glucose (baseline), parental diabetes, physical activity, intake of salad and vegetables, intake of meat, intake of sausage, alcohol consumption, coffee consumption and smoking. ^dModel 3: adjusted for age, sex, fasting plasma glucose (baseline), 2-h glucose (baseline), parental diabetes, hypertriglyceridaemia, change of triglycerides, HDL cholesterol (dichotomous), change of HDL cholesterol and hypertension. ^eOdds ratios refer to models including BMI (baseline)+continuous measures of BMI change. ^fOdds ratios refer to models including BMI (baseline)+categorical measures of BMI change. Bold numbers are significant at 0.05 level.

Table 4 Predictors^a of persistence of normal glucose tolerance in 7-year follow-up in subjects with normal glucose tolerance at baseline (multiple logistic regression models, odds ratios, 95% confidence intervals): KORA S4/F4 cohort study

	Model 1 ^b	Model 2 ^c	Model 3 ^d
BMI (baseline) (per kg m ⁻²) ^e	0.90 (0.85–0.95)	0.94 (0.88–0.998)	0.93 (0.88–0.99)
BMI change (per kg m ⁻² decline)	1.20 (1.05–1.36)	1.16 (1.02–1.33)	1.13 (0.98–1.30)
BMI (baseline) (per kg m ⁻²) ^f	0.91 (0.86–0.96)	0.94 (0.89–1.001)	0.93 (0.88–0.99)
BMI change			
≤ -1 kg m ⁻²	2.39 (1.24–4.61)	2.02 (1.01–4.02)	1.95 (0.95–4.00)
> -1 kg m ⁻² , ≤ 1 kg m ⁻²	1.97 (1.22–3.18)	1.58 (0.94–2.66)	1.54 (0.91–2.59)
> 1 kg m ⁻² (ref)	1	1	1
Waist circumference (baseline) (per 5 cm)	0.82 (0.73–0.92)	0.90 (0.80–1.02)	0.87 (0.77–0.99)
Change of waist circumference (per 5 cm decline)	1.28 (1.06–1.54)	1.19 (0.97–1.46)	1.15 (0.94–1.42)

Abbreviation: BMI, body mass index. ^aBMI change and change of waist circumference refer to the 7-year follow-up. ^bModel 1: adjusted for age and sex. ^cModel 2: adjusted for age, sex, fasting plasma glucose (baseline), 2-h glucose (baseline), parental diabetes, physical activity, intake of salad and vegetables, intake of meat, intake of sausage, alcohol consumption, coffee consumption and smoking. ^dModel 3: adjusted for age, sex, fasting plasma glucose (baseline), 2-h glucose (baseline), parental diabetes, hypertriglyceridaemia, change of triglycerides, HDL cholesterol (dichotomous), change of HDL cholesterol and hypertension. ^eOdds ratios refer to models including BMI (baseline)+continuous measures of BMI change. ^fOdds ratios refer to models including BMI (baseline)+categorical measures of BMI change. Bold numbers are significant at 0.05 level.

The finding that persistence of NGT is associated with baseline BMI and with BMI reduction is consistent with findings of several studies reporting that both initial weight and weight gain are associated with the risk of diabetes.^{3,4} However, these studies were not restricted to subjects with initial normoglycaemia and focused only on progression to diabetes. In the Mexico City Diabetes Study, nonconverters who remained in the NGT status had statistically lower baseline values of BMI and weight circumference than subjects with initial NGT who developed diabetes in 7 years of follow-up.¹⁷

Individual subjects might return from prediabetes to NGT due to very small changes in glucose values. In view of the only moderate reproducibility of measurements of fasting plasma glucose and 2-h glucose,²⁴ such individual transitions might also occur owing to chance (that is,

intraindividual biological variation or measurement errors). Nevertheless, the rate of reversion to NGT was probably not grossly overestimated, because (1) clinically relevant changes in glucose levels were required for reversion to NGT (fasting plasma glucose: decrease of more than 5 mg dl⁻¹, 2-h glucose: decrease of more than 10 mg dl⁻¹) and (2) glucose levels increase with age so that misclassification of transition from prediabetes to NGT, after a 7-year follow-up, is unlikely.

Additional analyses (prediction of 10% changes in fasting glucose and 2-h glucose; multiple linear regression analyses with changes in glucose values as dependent variables) showed that the results based on transitions between glucose tolerance classes are robust and can be confirmed using different strategies of analyses (see Supplementary appendix, Tables 5–8).

The present study had several limitations. First, fasting plasma glucose and 2-h glucose were only measured once at baseline and in the follow-up examination, and we did not capture subjects switching more than once between categories of blood glucose. However, as explained above, inaccuracies in glucose measurements should not lead to a large overestimate of normalization of prediabetes. Second, participants were informed about their clinical parameters after the baseline study, and we cannot exclude that subjects with prediabetes at baseline might have seen their general practitioner or started taking anti-diabetic drugs as response to the examination results. However, no such advice to study participants with prediabetes was included in the communication of baseline examination results. The strengths of our study are the prospective design and the well-defined population sample consisting of older subjects in whom reversion to NGT as well as persistence of NGT were rarely investigated before. A comprehensive set of possible predictors was taken into account including changes of most baseline variables.

In conclusion, this study shows that in older people weight loss, but not initial weight, predicted reversion to NGT, whereas both variables had an influence on persistence of NGT. In a public health perspective, it is especially important that weight change has an effect on return to NGT even in obese subjects, and that this effect is even seen for a moderate decline of BMI.

Conflict of interest

The authors declare no conflict of interest.

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