DOI: 10.1111/j.1464-5491.2009.02863.x

Original Article: Epidemiology

Incidence of Type 2 diabetes in the elderly German population and the effect of clinical and lifestyle risk factors: KORA S4/F4 cohort study

W. Rathmann*, K. Strassburger*, M. Heier*†, R. Holle‡, B. Thorand†, G. Giani* and C. Meisinger†

*Institute of Biometrics and Epidemiology, German Diabetes Centre, Leibniz Centre for Diabetes Research at Heinrich Heine University, Düsseldorf, †Helmholtz Zentrum München, German Research Centre of Environmental Health, Institute of Epidemiology, Neuherberg and ‡Helmholtz Zentrum München, German Research Center of Environmental Health, Institute of Health Economics and Health Care Management, Neuherberg, Germany

Accepted 23 September 2009

Abstract

Aims To determine the incidence of Type 2 diabetes in an elderly population in Germany and its association with clinical and lifestyle factors.

Methods Oral glucose tolerance tests (OGTT, World Health Organization criteria) were carried out in a random sample of 1353 subjects (age group 55–74 years; 62% response) in Augsburg (Southern Germany) (1999–2001). The cohort was re-investigated in 2006–2008. Of those individuals without diabetes (baseline), 887 (74%) participated in the follow-up.

Results Ninety-three (10.5%) developed diabetes during the 7-year follow-up period {standardized incidence rates [95% confidence interval (CI)] per 1000 person-years: total 15.5; 12.6, 19.1; men 20.2; 15.6, 26.1; women 11.3; 7.9, 16.1}. In both sexes, those who developed diabetes were slightly older, were more obese, had a more adverse metabolic profile (higher glucose values, HbA_{1c}, fasting insulin, uric acid, and triglycerides) and were more likely to have hypertension at baseline than were participants remaining free of diabetes ($P < 0.05$). On stepwise logistic regression, age, parental diabetes, body mass index, uric acid, current smoking, HbA_{1c} and fasting and 2-h glucose (OGTT) were strong predictors of diabetes incidence. The risk of diabetes was higher in subjects with isolated impaired glucose tolerance (odds ratio 8.8; 95% CI 5.0, 15.6) than in isolated impaired fasting glucose (4.7; 2.2, 10.0), although the difference did not reach statistical significance.

Conclusions For the first time, we have estimated the incidence of Type 2 diabetes in an elderly German cohort and demonstrated that it is among the highest in Europe. The OGTT appears to be useful in identifying individuals with high Type 2 diabetes risk. Our results support a role of smoking in the progression to diabetes.

Diabet. Med. 26, 1212–1219 (2009)

Keywords impaired fasting glucose, impaired glucose tolerance, incidence, smoking, Type 2 diabetes

Abbreviations BIF, bootstrap inclusion frequency; BMI, body mass index; CI, confidence interval; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment–insulin resistance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; I-IFG, isolated impaired fasting glucose; I-IGT, isolated impaired glucose tolerance; KORA, Cooperative Health Research in the Region of Augsburg; OGTT, oral glucose tolerance test; OR, odds ratio; PY, person-years

Introduction

In Europe, a diabetes prevalence of 7.8% in the adult population (age 20–79 years) or 48.4 million persons has been estimated in 2003 [1]. The prevalence is higher in Europe than in other regions of the world, partly a consequence of the increase in the proportion of elderly individuals. Currently, about one-third of the European population is > 50 years old, and this proportion will rise to > 40% by 2025 [1,2]. Without effective prevention, diabetes prevalence in Europe is expected to increase to 9.1% or 58.6 million in 2025 [1]. This will place an enormous social and financial burden on the declining working population in Europe.

Correspondence to: Dr Wolfgang Rathmann, MSPH, Institute of Biometrics and Epidemiology, German Diabetes Centre, Auf'm Hennekamp 65, D-40225 Düsseldorf, Germany. E-mail: rathmann@ddz.uni-duesseldorf.de

Despite the increasing prevalence and great human and economic burden, population-based epidemiological data on Type 2 diabetes are scarce in the European Union [3,4]. In Germany, the country with the largest population in Europe, there are only data on self-reported diabetes, e.g. from the National Health Survey [5].

We have carried out oral glucose tolerance tests (OGTT) in participants aged 55–74 years as part of the population-based Cooperative Health Research in the Region of Augsburg (KORA) Survey S4 (1999–2001) [6]. In 2006–2008 we performed a follow-up to determine for the first time the incidence of Type 2 diabetes in Germany based on OGTT.

Most epidemiological studies on modifiable risk factors of Type 2 diabetes (e.g. obesity, low physical activity, smoking) have been carried out in middle-aged populations [7]. Due to the ageing of the European population it is important to determine whether these risk factors have the same importance in the elderly. The KORA S4/F4 cohort study provides an opportunity to study these risk factors for Type 2 diabetes in an elderly population.

Patients and methods

Study population

The study sample involved 2656 subjects aged 55–74 years living in the city of Augsburg and 16 towns and villages from the surrounding counties in 1999 (about 600 000 inhabitants) [6]. Informed consent was obtained from the participants. Overall, 1653 (62%) subjects participated. After excluding those with known diabetes and further drop-outs, 1353 subjects had an OGTT at baseline [6].

This cohort was re-investigated in 2006–2008. The present study includes only participants without known or newly diagnosed diabetes at baseline, who successfully completed a baseline OGTT, and who lived within the study region at the time of the follow-up examination (n = 1202). Of those individuals, 887 (74%) participated in the follow-up (OGTT), 18% refused to participate and 8% had died before 2006.

Ascertainment of diabetes and prediabetes

Those participants with incident diabetes (self-reports) and the date of diagnosis were validated by contacting the subjects' general practitioners. It can be assumed that the great majority of cases of incident diabetes in this age group had Type 2 diabetes. Among all other subjects, OGTTs were performed during the morning after overnight fasting. Fasting venous blood glucose was sampled and 75 g of anhydrous glucose were given (Dextro OGT; Boehringer Mannheim, Mannheim, Germany). Incident diabetes was defined based on (i) validated physician diagnosis, or (ii) newly diagnosed diabetes (≥ 7.0 mmol/l fasting or ≥ 11.1 mmol/l 2-h glucose).

Baseline glucose tolerance categories were defined as normoglycaemia, impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) according to the 1999 World Health Organization diagnostic criteria [8]. We used the original IFG criteria (6.1–6.9 mmol/l) for the present analysis, as recommended by the European Diabetes Epidemiology Group [9]. Prediabetes was divided into isolated IFG (I-IFG), isolated IGT (I-IGT), and combined IFG and IGT (IFG+IGT).

Anthropometric measurements and interviews

Height, weight, waist circumference, systolic and diastolic blood pressure were measured based on standard protocols as described elsewhere [6]. Hypertension was defined by blood pressure of ≥ 140/90 mmHg, or use of antihypertensive medication in people reporting a previous diagnosis of hypertension.

Medical interviewers gathered baseline information on sociodemographic variables, medical history, medication use, physical activity level, alcohol consumption, and parental history of diabetes. Participants with < 1 h of physical activity per week during leisure time in either summer or winter were classified as inactive. Participants were asked whether they were current smokers (regular, occasional). Low socioeconomic status was defined based on education, occupation, and income as previously described [10].

Laboratory measurements (baseline and follow-up)

Blood was collected without stasis. After blood withdrawal the blood samples were centrifuged and kept cool (4°C) until analysis of blood glucose in the central laboratory, which took place within a maximum of 6 h after withdrawal. Blood glucose, HbA_{1c}, total and high-density lipoprotein (HDL)-cholesterol, triglycerides and serum uric acid were determined as described elsewhere [6]. Serum adiponectin concentration was measured using the radioimmunoassay from Linco Research (St Charles, MO, USA) [11,12]. Fasting insulin was determined using a microparticle enzyme immunoassay (Abbott Laboratories, Ludwigshafen, Germany). The homeostasis model assessment–insulin resistance (HOMA-IR) score was calculated [fasting plasma glucose (mmol/l) × fasting serum insulin (mU/l)/22.5].

Statistical analysis

The duration of follow-up was estimated as the interval between the date of baseline and follow-up examination or the date of diabetes diagnosis. Incidence rates and corresponding 95% confidence intervals (CI) were calculated per 1000 person-years (PY), assuming a constant diabetes risk during the follow-up period. Age- and sex-standardized incidence was calculated by direct standardization using the German population in 2007 as the standard population. The 7-year cumulative diabetes incidence (%) was also estimated. Baseline characteristics (attendees vs. non-attendees in the follow-up; diabetes cases vs. control subjects) were compared using t-tests, Mann–Whitney

U-tests, or Fisher's exact tests. Adiponectin, insulin, HOMA-IR, triglycerides and creatinine were log-transformed.

In age- and sex-adjusted logistic regression models, all risk factors (see Table 1) were individually tested for their associations with Type 2 diabetes. First, all variables with *P*-values > 0.25 were excluded (diastolic blood pressure, alcohol intake, physical activity, socioeconomic status). To avoid collinearity, we additionally excluded waist circumference [correlation with body mass index (BMI): $r = 0.76$] and HOMA-IR (correlation with insulin: $r = 0.99$). Then, stepwise multivariable regression was used to build the final model. For each continuous variable in the model, odds ratios (OR) were calculated for an increase of 1 SD of the value, in order to compare their importance. Bootstrap sampling (2000 random samples with replacement) was used for studying model stability. Generally, important variables should be included in most of the bootstrap replications. The bootstrap inclusion frequency (BIF) has been used as a criterion for the importance of variables (e.g. BIF < 50%: less important variable) [13]. Finally, sex-specific models were fitted using the variables included in the final model. The level of statistical significance was 5%. The analyses were carried out using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

The mean baseline age of the participants ($n = 887$) was 63 years, and about half were female (Table 1). Mean baseline BMI and waist circumference were 28.1 kg/m^2 and 94.5 cm, respectively. Participants in the follow-up examination were slightly younger, had a higher socio-economic status, a smaller waist circumference, and were less likely to be current smokers at baseline than the non-participants ($n = 315$) (Table 1). Furthermore, they were more likely to be physically active, and less likely to have hypertension than those who refused to participate. Finally, study participants had slightly lower mean fasting and 2-h glucose values than non-participants.

Ninety-three (10.5%) individuals developed Type 2 diabetes during the 7-year follow-up, corresponding to an incidence rate of 15.1 (95% CI 12.1, 18.5) per 1000 PY (Table 2). A comparable total rate was observed after standardization according to the German population (2007). Men had an almost twofold higher standardized Type 2 diabetes incidence rate than women.

The incidence rate increased sharply from those with normoglycaemia at baseline to those with combined elevations of fasting and postprandial glucose (Table 2). Both I-IFG and

Table 1 Baseline characteristics of those who participated and those who did not participate in the follow-up (age group 55–74 years): KORA S4/F4 study (Augsburg, Southern Germany)

	Participants	Non-participants	*P*-value
N	887	315	—
Age (years)	63.2 ± 5.4	65.7 ± 5.3	< 0.0001
Female (%)	49.4	48.9	0.8960
Place of residence: urban (%)	46.4	45.7	0.8950
Low socioeconomic status (%)	25.4	37.7	< 0.0001
Known maternal or paternal diabetes (%)	22.9	19.6	0.2342
BMI (kg/m^2)	28.1 ± 4.0	28.5 ± 4.6	0.1443
Waist circumference (cm)	94.5 ± 11.1	96.4 ± 11.6	0.0089
Inactive during leisure time (%)	52.9	63.3	0.0018
Current smokers (%)	12.4	17.8	Global *P*:
Ex-smokers (%)	36.1	38.4	0.0200
Alcohol intake (women ≥ 20 g/day; men ≥ 40 g/day) (%)	20.6	19.5	0.7437
Adiponectin (μg/ml)*	9.0 [6.2, 12.3]	9.8 [7.3, 13.3]	0.0152
Fasting glucose (mmol/l)	5.5 ± 0.5	5.6 ± 0.6	0.0295
2-h glucose (mmol/l)	6.3 ± 1.7	6.6 ± 1.9	0.0041
Fasting insulin (mU/l)*	9.7 [6.9, 14.2]	10.1 [6.9, 14.4]	0.7131
HOMA-IR*	2.4 [1.6, 3.5]	2.5 [1.7,3.7]	0.4786
HbA_{1c} (%)	5.6 ± 0.4	5.6 ± 0.4	0.1418
Cholesterol (mmol/l)	6.3 ± 1.1	6.3 ± 1.1	0.4271
HDL-cholesterol (mmol/l)	1.5 ± 0.4	1.5 ± 0.4	0.5003
Triglycerides (mmol/l)*	1.3 [0.9, 1.8]	1.3 [1.0, 1.8]	0.8896
Serum uric acid (mmol/l)	0.33 ± 0.08	0.34 ± 0.09	0.4021
Serum creatinine (μmol/l)*	75 [66.3, 84.9]	74 [65.4, 84.9]	0.2442
Systolic blood pressure (mmHg)	133 ± 19	137 ± 21	0.0017
Diastolic blood pressure (mmHg)	80 ± 10	80 ± 10	0.8894
Actual hypertension (%)	49.0	58.9	0.0025
Intake of lipid-lowering agents (%)	10.5	12.4	0.3464

Data are means ± SD.
*Median and 25th and 75th percentiles, or proportions. *P*-values: *t*-tests, Mann–Whitney *U*-tests, or Fisher's exact tests.
BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment–insulin resistance.

Table 2 Seven-year diabetes incidence according to baseline glucose tolerance status in the elderly population (55–74 years): KORA S4/F4 (Augsburg, Southern Germany)

	Persons at risk (*n*)	Incident diabetes (*n*)	Odds ratio (95% CI)	Incidence rate per 1000 person-years (95% CI)
Normal glucose tolerance	649	25	1.0	5.5 (3.5, 8.0)
Isolated IFG	71	12	4.7 (2.2, 10.0)	24.2 (12.5, 42.3)
Isolated IGT	120	34	8.8 (5.0,15.6)	42.0 (29.0, 58.7)
Combined IFG and IGT	47	22	21.2 (10.4, 43.3)	77.9 (48.8, 117.9)
Total	887	93	—	15.1 (12.2, 18.5)
Standardized incidence rates*				
Total*				15.5 (12.6, 19.1)
Men*				20.2 (15.6, 26.1)
Women*				11.3 (7.9, 16.1)

Odds ratios are age- and sex-adjusted.
*Direct standardization (age, sex) using the German population (31 December 2007) as standard population.
IFG, impaired fasting glucose; IGT, impaired glucose tolerance.

I-IGT were associated with a significantly increased risk of developing Type 2 diabetes. The risk of incident diabetes was higher in I-IGT than in I-IFG, but the difference did not reach statistical significance. Individuals with combined IFG+IGT had an extremely increased likelihood to develop diabetes compared with those with normoglycaemia. About half of the study participants with combined IFG+IGT at baseline converted to Type 2 diabetes during the follow-up, whereas the cumulative incidence among individuals with I-IFG (16.9%) and I-IGT (28.3%) was considerably lower. A large proportion of subjects with I-IFG or I-IGT remained in the prediabetic state (I-IFG 56.4%; I-IGT 42.4%).

Table 3 shows the sex-specific baseline characteristics of incident Type 2 diabetes cases compared with those participants without diabetes during the follow-up. In both sexes, cases were slightly older, were more obese, and had a more adverse metabolic profile at baseline (higher glucose values, HbA_{1c}, fasting insulin, uric acid and triglycerides) than participants without diabetes ($P < 0.05$). Furthermore, adiponectin concentrations were significantly lower in Type 2 diabetes cases than control subjects in both sexes ($P < 0.05$). Finally, in both men and women, hypertension was more prevalent among those who developed diabetes. In men only, parental diabetes was more often reported by cases than by control subjects. Furthermore, in men only, there was an indication that physical inactivity was more prevalent in cases ($P = 0.06$). The proportion of individuals with a high alcohol intake was similar in cases and controls in men. In women, a high alcohol intake was observed in only one participant who developed diabetes, whereas 16.1% of control subjects had a high intake. Finally, HDL-cholesterol concentrations were significantly lower in Type 2 diabetes cases than in control subjects in women only ($P < 0.05$).

Table 4 shows the sex- and age-adjusted ORs for having incident Type 2 diabetes for various known risk factor categories. Obesity, in particular central obesity (waist circumference: men ≥ 102 cm, women ≥ 88 cm) was strongly related to the risk of developing diabetes in both men and women. Furthermore, Type 2 diabetes risk was about twofold higher among subjects with hypertension in both sexes. In sex-specific analyses, age, parental diabetes and physical inactivity were significantly related to the development of Type 2 diabetes in men only. Current smoking was a risk factor for diabetes in men, although not statistically significant ($P = 0.07$).

In multivariable logistic regression models (stepwise selection), baseline fasting and 2-h glucose, and HbA_{1c} were strong predictors of Type 2 diabetes incidence (Table 5). The OR for an increase by 1 SD in 2-h glucose was somewhat larger than for fasting glucose and HbA_{1c}. BMI, parental diabetes, uric acid and age were also significantly associated with progression to Type 2 diabetes. Finally, current smoking was independently associated with diabetes in the total sample, whereas ex-smokers had no significantly increased diabetes risk. In sex-specific regression models, only 2-h glucose, HbA_{1c} and serum uric acid were predictors of incident Type 2 diabetes in both men and women (Table 5). Age, BMI, fasting glucose, parental diabetes and current smoking were significantly related to the development of diabetes in men only.

All selected variables showed a BIF > 50% (except BMI: 0.46), indicating sufficient model stability. In particular, fasting and 2-h glucose were included in 88% and 100% of the replications, respectively. A bootstrap validation of the final model showed that the OR estimates, CIs and *P*-values were in good accordance with their bootstrapped counterparts.

Discussion

For the first time, we have estimated the incidence rate of Type 2 diabetes in a population-based cohort study in Germany using OGTT (age group 55–74 years: standardized rate 15.5 per 1000 PY). If we assume that this incidence is valid for the overall population in Germany, this estimate corresponds to about 270 000 new cases of Type 2 diabetes each year in the elderly population (55–74 years). In a previous analysis from the

Table 3 Sex-specific baseline characteristics according to diabetes status at follow-up (incident diabetes vs. non-diabetic control subjects)

	Men		Women	
	Incident cases	Control subjects	Incident cases	Control subjects
N	60	389	33	405
Age (years)	65.4 ± 5.2*	63.1 ± 5.5*	65.3 ± 5.4*	62.8 ± 5.3*
Urban residency (%)	51.7	46.3	57.6	44.7
Low SES (%)	18.3	16.8	33.3	34.2
Parental diabetes (%)	35.0*	18.6*	36.4	24.2
BMI (kg/m^2)	30.3 ± 3.7*	27.7 ± 3.2*	30.2 ± 3.4*	28.0 ± 4.6*
Waist circumference (cm)	105.0 ± 9.0*	98.9 ± 8.7*	95.3 ± 8.1*	88.6 ± 10.6*
Physically inactive (%)	33.3	46.4	54.6	49.1
Current smokers (%)	16.7	15.0	9.1	9.6
Ex-smokers (%)	61.7	49.5	21.2	20.7
High alcohol intake (%)†	28.3	25.4	3.0*	16.3*
Adiponectin (μg/ml)	5.5 [4.5, 8.3]*	7.4 [5.3, 9.6]*	10.1 [7.1, 12.2]*	11.4 [8.8, 14.8]*
Fasting glucose (mmol/l)	6.0 ± 0.6*	5.5 ± 0.5*	5.7 ± 0.5*	5.3 ± 0.5*
2-h glucose (mmol/l)	8.2 ± 1.9*	6.0 ± 1.6*	8.0 ± 1.6*	6.1 ± 1.5*
Fasting insulin (mU/l)	15.5 [10.5, 21.5]*	9.3 [6.6, 13.1]*	10.5 [9.0, 15.9]*	9.2 [6.9, 13.5]*
HOMA-IR	4.1 [2.6, 5.9]*	2.3 [1.6, 3.3]*	2.9 [2.3, 4.6]*	2.2 [1.6, 3.3]*
HbA_{1c} (%)	5.8 ± 0.3*	5.5 ± 0.3*	5.9 ± 0.5*	5.6 ± 0.3*
Cholesterol (mmol/l)	6.1 ± 1.1	6.2 ± 1.0	6.6 ± 1.2	6.5 ± 1.1
HDL-cholesterol (mmol/l)	1.3 ± 0.3	1.4 ± 0.4	1.4 ± 0.3*	1.7 ± 0.4*
Triglycerides (mmol/l)	1.4 [1.2, 2.0]*	1.4 [0.9, 1.9]*	1.7 [1.3, 1.9]*	1.2 [0.9, 1.6]*
Serum uric acid (mmol/l)	0.41 ± 0.08*	0.37 ± 0.08*	0.34 ± 0.06*	0.29 ± 0.06*
Creatinine (μmol/l)	84 [75.2, 93.7]	84 [76.0, 91.1]	73 [65.4, 78.7]*	67 [61.9, 73.4]*
Systolic BP (mmHg)	142 ± 17*	137 ± 18*	131 ± 20	128 ± 18
Diastolic BP (mmHg)	84 ± 10	82 ± 10	76 ± 9	77 ± 10
Actual hypertension (%)	73.3*	53.9*	63.6*	39.5*
Lipid-lowering agents (%)	8.3	11.3	15.2	9.6

Data are means ± SD, medians and 25 and 75 percentiles, or proportions.
*$P < 0.05$: *t*-tests, Mann–Whitney *U*-tests, or Fisher's exact tests.
†Women ≥ 20 g/day; men ≥ 40 g/day.
BMI, body mass index; BP, blood pressure; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment–insulin resistance; SES, socio-economic status.

MONICA Augsburg Surveys (Southern Germany), a standardized Type 2 diabetes incidence rate of 5.8 per 1000 PY in men and 4.0 per 1000 PY in women was observed [7]. However, these lower estimates were based on clinical diagnoses only and included a younger population (10-year difference in mean age). In the former East-German diabetes registry (German Democratic Republic), an almost complete assessment of all newly diagnosed diabetes cases was possible [14]. At the end of the registry period in 1987, the age-specific diabetes incidence rate (non-insulin-treated diabetes) was about 12 per 1000 PY in the elderly population (60–69 years), which was somewhat lower than in our study [14].

Estimates of Type 2 diabetes incidence in other European populations, which are based on OGTT, are rare. In the Bruneck Study (Northern Italy), Type 2 diabetes incidence in individuals aged 40–79 years was 7.6 per 1000 PY (follow-up period 1990–2000) [15]. In the Ely cohort study in Cambridgeshire (UK), which was also carried out from 1990 to 2000, a comparable diabetes incidence was found in a somewhat younger population (40–69 years: 7.3 per 1000 PY) [16]. The Asturias Study was a population-based follow-up study in Northern Spain (1998–2005), which reported a Type 2 diabetes incidence of 10.8 per 1000 PY (age group 30–75 years) [17]. A similar study was carried out in Southern Spain among subjects aged 18–65 years in 1997–1998 [18]. In 2003–2004, an incidence of 19.1 per 1000 PY was estimated. Study designs and response to follow-up in these studies were comparable to the KORA cohort. However, all Type 2 incidence estimates were based on small numbers of cases, which limited their precision. Nevertheless, the data indicate that there is a variation of Type 2 diabetes incidence in Europe. Our estimate from Southern Germany is among the highest in Europe to be reported so far. In line with most [7,17,18] but not all [15] previous European studies, we have found a higher Type 2 diabetes incidence in men than in women.

Both IFG and IGT, which represent different abnormalities (IFG: primarily impaired insulin secretion; IGT: primarily insulin resistance) [19], carried an increased Type 2 diabetes risk. As in previous studies, the combined presence of these glucose disorders was associated with a very high risk [17,18,20]. The 7-year cumulative Type 2 diabetes incidence was almost 50% among those with presumably both reduced insulin secretion and insulin sensitivity (IFG+IGT) in the present study. The OGTT appears to be useful to identify high-risk individuals. Both baseline fasting and 2-h glucose were independently related to

Table 4 Seven-year diabetes risk according to various risk factor categories in the elderly population (55–74 years at baseline): KORA S4/F4

	Odds ratio* (men)	Odds ratio* (women)	Total odds ratio*
Women	—	—	1.0
Men	—	—	1.9 (1.2, 2.9)
Age 55–64 years	1.0	1.0	1.0
Age 65–74 years	2.1 (1.2, 3.7)	1.5 (0.7, 3.1)	1.9 (1.2, 2.9)
Parental diabetes (no)	1.0	1.0	1.0
Parental diabetes (yes)	2.7 (1.5, 4.9)	2.0 (0.9, 4.3)	2.4 (1.5, 3.8)
BMI < 30 kg/m^2	1.0	1.0	1.0
BMI ≥ 30 kg/m^2	2.9 (1.6, 5.1)	2.5 (1.2, 5.2)	2.7 (1.7, 4.3)
Central obesity (no)†	1.0	1.0	1.0
Central obesity (yes)†	3.9 (2.2, 7.1)	4.2 (1.7, 10.6)	4.0 (2.5, 6.6)
Actual hypertension (no)	1.0	1.0	1.0
Actual hypertension (yes)	2.1 (1.1, 3.8)	2.4 (1.1, 5.1)	2.2 (1.4, 3.5)
Active during leisure time	1.0	1.0	1.0
Inactive during leisure time	1.8 (1.02, 3.3)	0.7 (0.4, 1.5)	1.3 (0.8, 2.0)
Never smokers	1.0	1.0	1.0
Ex-smokers	1.9 (0.99, 3.8)	1.1 (0.5, 2.7)	1.5 (0.9, 2.6)
Current smokers	2.3 (0.9, 5.7)	1.3 (0.4, 4.7)	1.8 (0.9, 3.6)
High alcohol intake‡ (no)	1.0	1.0	1.0
High alcohol intake‡ (yes)	1.3 (0.7, 2.4)	0.2 (0.02, 1.1)	0.9 (0.5, 1.5)

*Odds ratios (95% confidence interval) are age- and sex-adjusted (if appropriate).
†Central obesity: waist circumference men ≥ 102 cm, women ≥ 88 cm.
‡High: women ≥ 20 g/day; men ≥ 40 g/day.
BMI, body mass index.

Table 5 Predictors of incident Type 2 diabetes in the elderly population: multivariable logistic regression analysis (stepwise selection)

Variables	Odds ratio (men) (95% CI)	Odds ratio* (women) (95% CI)	Total odds ratio (95% CI)
Age (years)	1.6 (1.1, 2.4)*	1.4 (0.9, 2.2)	1.6 (1.2, 2.1)*
Sex (males)	—	—	0.9 (0.5, 1.8)
Parental diabetes	2.5 (1.1, 5.5)*	1.6 (0.7, 3.9)	1.8 (1.0, 3.3)*
BMI (kg/m^2)	1.9 (1.2, 2.8)*	1.1 (0.7, 1.6)	1.4 (1.1, 1.9)*
Fasting glucose (mmol/l)	1.8 (1.2, 2.6)*	1.4 (0.9, 2.2)	1.6 (1.2, 2.2)*
2-h glucose (mmol/l)	2.5 (1.8, 3.5)*	2.6 (1.7, 4.1)*	2.5 (1.9, 3.3)*
HbA_{1c} (%)	1.6 (1.1, 2.3)*	1.7 (1.1, 2.6)*	1.6 (1.2, 2.2)*
Serum uric acid (mmol/l)	1.5 (1.1, 2.2)*	2.2 (1.3, 3.9)*	1.7 (1.3, 2.3)*
Current smokers†	4.0 (1.2, 13.0)*	2.7 (0.6, 12.8)	3.6 (1.5, 8.9)*
Ex-smokers†	1.4 (0.6, 3.3)	1.6 (0.5, 4.5)	1.6 (0.8, 3.0)

Odds ratios for continuous variables were estimated for an increase by 1 SD of each continuous variable. Other variables not included in the final model: HDL-cholesterol, serum creatinine, actual hypertension, systolic blood pressure, adiponectin, fasting insulin, triglycerides.
Total model $R^2 = 0.20$.
*$P < 0.05$.
†Reference group: never smokers.
BMI, body mass index.

incident Type 2 diabetes in our study. The association between 2-h glucose and incident diabetes was somewhat stronger than the relationship between fasting glucose and diabetes in the present study. In addition, there was an indication for a higher diabetes incidence in I-IGT than in I-IFG. This observation is not supported by a recent meta-analysis of prospective studies, which found a similar diabetes risk in I-IFG and I-IGT [21]. However, only three studies with heterogeneous populations were included in the meta-analysis (Netherlanders, Han Chinese, Pima Indians). Thus, further studies are needed to investigate if I-IGT is a stronger risk predictor for Type 2 diabetes than I-IFG. Finally, HbA_{1c} was an independent risk predictor of future diabetes incidence in our study and may also be useful for estimating the individual diabetes risk in the elderly population [22].

We have investigated a population with a higher baseline age than in previous studies to determine the importance of known risk factors for Type 2 diabetes in the elderly population. In line with previous studies, (central) obesity, hypertension, parental

diabetes and serum uric acid were important risk factors [7], whereas physical inactivity and alcohol intake were not related to incident diabetes in the total study population. Data on the association of physical activity with incident diabetes in the elderly population are limited [23]. Previous studies have suggested that vigorous physical activity was most protective, but that moderate physical activity was also related to a decreased diabetes risk in the elderly [23]. In our study, only the total time of physical activity per week was recorded, which might explain why no significant benefit was found. Moderate alcohol consumption (one to three drinks per day) is associated with a decreased incidence of diabetes, whereas heavy consumption may be associated with an increased risk [24]. In our low-risk elderly population, alcohol consumption was not related to future diabetes risk in the total sample. In women only, increased alcohol intake was more often found among those who did not develop diabetes during follow-up. However, this analysis was based on very few cases.

A recent meta-analysis of observational studies has suggested an association between smoking and Type 2 diabetes [25]. However, the evidence that this association is causal is still considered preliminary [25]. Both causal and non-causal explanations have been discussed. In a previous analysis from the MONICA/KORA Augsburg study, a significant dose–response relationship between nicotine and tar intake and the development of Type 2 diabetes was observed in men [26]. There is also evidence from clinical studies that smoking may impair insulin sensitivity, the hallmark of Type 2 diabetes. Insulin-mediated glucose uptake is lower in smokers than in non-smokers [25,27]. The present study adds to this knowledge that the association between smoking and Type 2 diabetes was not explained by obesity, several metabolic risk markers and established lifestyle risk factors.

There are several limitations to our study. First, the follow-up was not complete for participants who were alive in 2006–2008. The comparison of baseline characteristics between attendees and non-attendees indicated a 'healthy participant effect'. Therefore, diabetes incidence may have been underestimated. In addition, (pre)diabetic subjects have an increased mortality, which yields a higher likelihood that they have been lost to follow-up. Although we adjusted our analyses for a range of confounders, some data were missing (e.g. diet) or insufficient (e.g. HOMA-IR instead of euglycaemic hyperinsulinaemic clamp). Thus, residual confounding may be present. The strength of our study is the well-defined population sample. Furthermore, in contrast to other prospective studies, diagnosis of diabetes was based on validated diagnoses and OGTT.

In conclusion, this longitudinal study has provided an up-to-date estimate of Type 2 diabetes incidence in a European population. It also shows that diabetes risk can be estimated by glucose measurements using the OGTT.

Competing interests

Nothing to declare.

Acknowledgements

The Diabetes Cohort Study was funded by a German Research Foundation project grant to the first author (DFG; RA 459/2-1). The German Diabetes Centre is funded by the German Federal Ministry of Health, and the Ministry of School, Science and Research of the State of North-Rhine-Westfalia. The KORA research platform and the KORA Augsburg studies are financed by the Helmholtz Zentrum München, German Research Centre for Environmental Health, which is funded by the German Federal Ministry of Education, Science, Research and Technology and by the State of Bavaria. We thank the field staff in Augsburg who were involved in the conduct of the studies.

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