The role of adiposity and lifestyle in the relationship between family history of diabetes and 20-year incidence of type 2 diabetes in U.S. women

Esther van ’t Riet, MSc 1,2,3; Jacqueline M. Dekker, PhD 2,3; Qi Sun, PhD 1; Giel Nijpels, MD, PhD 2,4 Frank B. Hu, MD, PhD 1,5,6; Rob. M. van Dam, PhD 1,5,6

1 Dept. of Nutrition, Harvard School of Public Health, Boston, MA 02115, United States
2 EMGO Institute for Health and Care Research, VU University Medical Center, Amsterdam, The Netherlands
3 Dept. of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands
4 Dept. of General Practice, VU University Medical Center, Amsterdam, The Netherlands
5 Dept. of Epidemiology, Harvard School of Public Health, Boston, MA 02115, United States
6 Channing Laboratory, Department of Medicine, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA 02115, United States

Correspondence:
Esther van ’t Riet
Email: e.vantriet@vumc.nl
or
Rob van Dam:
Email : rvandam@hsph.harvard.edu

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Objective: To evaluate to what extent the association between family history of diabetes and risk of type 2 diabetes can be explained by excess adiposity and lifestyle risk factors.

Research design and methods: We analyzed data from 73,227 women who participated in the Nurses’ Health Study cohort. A family history of diabetes was defined as having at least one first degree family member with diabetes. Lifestyle factors, weight and height were assessed by using validated questionnaires, and body mass index (BMI) was calculated. The relative risk of type 2 diabetes was estimated using Cox proportional hazards analysis.

Results: We documented 5101 cases of type 2 diabetes during 20 years of follow-up. The age-adjusted relative risk of type 2 diabetes in participants with a family history was 2.27 (95% CI 2.14-2.40) as compared with those without a family history of diabetes. Participants with a family history of diabetes had a higher BMI and were more likely to have a parental history of obesity. BMI explained 21.1% (95% CI 19.4-22.9) of the association between family history of diabetes and risk of type 2 diabetes. Intakes of red meat, alcohol and sugar-sweetened beverages explained 1.1% (95% CI 0.8-1.3), 4.8% (95% CI 4.3-5.3) and 2.8% (95% CI 2.4-3.2) of this association respectively.

Conclusions: These results suggest that excess adiposity and, to a lesser extent, specific dietary habits can explain a substantial part of the association between having a family history of diabetes and risk of type 2 diabetes.
One of the major risk factors for type 2 diabetes is a positive family history of diabetes. In prospective studies, a family history of diabetes has consistently been associated with a higher risk of type 2 diabetes (1,2), but the reason for this association remains largely unknown. Recent studies have shown that currently identified genetic risk variants do not explain a substantial part of this association between family history of diabetes and risk of type 2 diabetes (3,4).

The clustering of body fatness in families, which can be due to both shared genetic and shared environmental influences, may also contribute to the relationship between family history and the development of type 2 diabetes. In cross-sectional studies, greater adiposity, was observed in persons with a family history of diabetes than in those without a positive family history (5-7). However, the contribution of lifestyle risk factors and excess adiposity to the association between family history of diabetes and risk of type 2 diabetes has not been examined in prospective studies. Therefore, we prospectively evaluated the following hypothesis in the Nurses’ Health Study: 1) a large proportion of the association between family history of diabetes and risk of type 2 diabetes can be explained by greater adiposity 2). To a lesser extent, specific lifestyle factors can explain part of the association between family history of diabetes and risk of type 2 diabetes.

METHODS

Study design and population for analysis: The Nurses’ Health Study (NHS) was started in 1976 when 121,700 married female registered nurses aged 30-55 years received a questionnaire on health status and potential risk factors for major chronic diseases. Ever since, participants were sent questionnaires biennially and the response rates have been approximately 90% (8). The NHS was approved by the institutional review board of the Brigham and Women’s Hospital (Boston, MA).

For the present analysis, we used the return of the 1984 questionnaire, which was completed by 97,510 participants, as baseline because information for family history was first collected in 1982 and the first extended food frequency questionnaire (FFQ) was administered in 1984. In this 1984 questionnaire, complete dietary information was available for 81,757 women. Women with a history of type 2 diabetes at baseline (N=329) were excluded. Furthermore, we excluded participants with cancer (except for non-melanoma skin cancer) or cardiovascular diseases at baseline (N= 4934), because the diagnosis of these diseases could have interfered with self-reports of lifestyle and family history. Women with incident types of diabetes other then type 2 diabetes or unconfirmed type 2 diabetes were also excluded (N=1480). Moreover, women with missing information for diabetes status, family history of diabetes, date of birth, weight or height were excluded (N=1787). As a result, 73,227 women remained for the present analysis. There were no differences between the total study population (N=81,757) and the population included for this analysis (N=73,227) for baseline characteristics, except for slight differences in mean age (50.6 and 50.2 years], the proportion of participants with obesity (13.3% and 12.3% ), mean weight change since age 18 years (28.3 and 27.6 kg] and the proportion of participants reporting to drink no alcohol (31.5% and 30.6% ) or over 10 grams of alcohol a day (23.6% and 24.0%).

Assessment of family history of diabetes and parental body size: Women were asked to report if any of their first degree family members (father, mother and/or siblings) ever had diabetes in the questionnaires mailed in
1982, 1988 and 1992. No questions about the type of diabetes in family members were included.

To assess obesity in the parents, a series of pictograms of body shape were included in the 1988 questionnaire (9). The pictograms estimate relative obesity, with values ranging from one (very thin) to nine (very obese). Women were asked to choose the pictogram that best described the body shape of their natural mother and their natural father at age 50 years. Previous research has shown that these pictograms can provide a reasonably accurate estimate of measured BMI of the parents 15 years in the past (r=0.74 for mothers and 0.63 for fathers) (9). According to the chosen image, both father and mother were categorized as non-obese (image 1-5) or obese (image 6-9).

**Assessment of lifestyle, socio-economic status, race and adiposity:** Dietary information was collected using a semi-quantitative FFQ included in the questionnaires mailed to the participants every 2-4 years. The reported portions were converted to gram weights per serving, and intakes of nutrients were computed by multiplying the frequency of consumption by the nutrient content in grams. The FFQ has been validated against biomarkers and diet records (10,11). Physical activity was assessed every 2-4 years asking about the time spent on vigorous and moderate physical activity on an average day in the last month. Information on cigarette smoking was assessed every 2 years. Information on the highest educational degree of the participant and their husband, father and mother’s occupation and race were assessed in the 1992 questionnaire.

Height was assessed in the baseline questionnaire and body weight every 2 years. Body mass index (BMI) was calculated as weight in kilograms divided by the height in meters squared (kg/m²). In 1980, women were asked to report their weight at age 18 years, which we used to calculate BMI at age 18 and weight change since age 18. In 1986, 1996 and 2000, waist and hip circumference was assessed by questionnaires that included measurement instructions and a tape measure. The validity of self-reported weight and circumference measurements was assessed in 140 participants from the Nurses’ Health Study aged 41-65 years. Pearson correlations between self-reported and technician-measured weight, waist circumference and hip circumference were high (r=0.97, 0.89 and 0.84 respectively) (12).

**Ascertainment of type 2 diabetes:** Women who reported to have diabetes in the biennial questionnaires were mailed a supplemental questionnaire to receive more information on diagnosis and treatment. The National Diabetes Data Group criteria (13) were used to confirm diagnosis of diabetes according to 1). an elevated glucose concentration (fasting plasma glucose of ≥7.8 mmol/l, random plasma glucose of ≥11.1 mmol/l, or plasma glucose ≥11.1 mmol/l after an oral glucose load), and at least one symptom related to diabetes (excessive thirst, polyuria, weight loss, or hunger); 2). no symptoms, but elevated glucose concentrations on two occasions; or 3). treatment with insulin or oral hypoglycemic medication. For cases of type 2 diabetes identified after 1998, the American Diabetes Association criteria (14) were used, lowering the cut-off point for fasting plasma glucose concentrations to 7.0 mmol/l. In a subsample, type 2 diabetes which was confirmed by the supplementary questionnaire was consistent with medical record reviews by an endocrinologist in 98% of the cases (15).

**Statistical analysis:** Person-time for each participant was calculated from the date of return of the 1984 questionnaire to the date of diagnosis of type 2 diabetes, death, or June 2004, whichever came first. Cox proportional hazard analysis was used to estimate the relative risk for type 2 diabetes according to
To evaluate the contribution of different covariates on the association between family history and diabetes risk, we used multivariate models with the following adjustments: 1). Age. 2). Age, socioeconomic status (SES; occupation of the father, occupation of the mother, husband’s highest degree, and participants highest degree) and race. 3). Age, SES, race, and lifestyle (smoking, physical activity, polyunsaturated-to-saturated fat intake ratio and intakes of coffee, alcohol, fruit, vegetables, sugar-sweetened beverages, whole grains, red meat, *trans*-fat, and total energy). 4). Age, SES, race, lifestyle, and BMI. Additional analyses were performed to evaluate whether inclusion of waist circumference or a combination of BMI at age 18 and weight change since age 18 in the statistical model would alter the results. In addition, we conducted a sensitivity analysis evaluating the effect of blood glucose testing on the results. Since 1998, women were asked biennially to report whether they had been screened for fasting blood glucose in the previous two years. We repeated our analysis for follow-up cycles from 1996 to 2004 restricted to women who reported to have been tested for blood glucose during a 2-year follow-up period.

All covariates were updated during follow-up whenever new information was obtained. For dietary variables we used cumulative updating to reduce within-person variation (16). The proportion of the association explained by including different covariates into the model was calculated based on the change in regression coefficients, using the method by Lin et al. (17) to calculate the 95% confidence intervals.

All P-values were two tailed, and values less than 0.05 were considered statistically significant. Inclusion of multiplicative interaction terms between time and family history in the multivariate models suggested that the proportional hazard assumption was not violated. The SAS statistical program version 9.1 (SAS Institute Inc., Cary, North Carolina) was used for all analyses.

**RESULTS**
We documented 5101 cases of incident type 2 diabetes during 1,365,617 person-years of follow-up. In women without and with a family history of diabetes, the incidences of type 2 diabetes were 26 and 68 per 10,000 person-years respectively.

**Baseline characteristics:** We evaluated baseline characteristics according to family history of diabetes. As compared with participants without a family history, participants with a family history were slightly older, had a higher BMI and waist circumference, were more likely to have parents with obesity, and had a lower alcohol intake and a higher intake of red meat and sugar-sweetened beverages (Online Appendix Table A1 which is available at [http://care.diabetesjournals.org](http://care.diabetesjournals.org)).

**Family history, lifestyle and adiposity, and risk of type 2 diabetes:** Table 2 presents the risk of type 2 diabetes in different categories of a family history of diabetes. After adjusting for age, the relative risk of type 2 diabetes in participants with a family history was 2.27 (95% confidence interval [CI] 2.14-2.40) as compared with participants without a family history. The relative risk of type 2 diabetes was similar for having a maternal or paternal history of diabetes.

We evaluated whether various diabetes risk factors could explain the association between family history and risk of type 2 diabetes. Adjustment for socioeconomic status and race did not substantially change the association between family history and diabetes risk, whereas adjustment for lifestyle explained part of the association (Table 1). To further evaluate this, we included all factors separately into the model.
Consumption of alcohol, red meat and sugar-sweetened beverages explained 4.8% (95% CI 4.3-5.3), 1.1% (95% CI 0.8-1.3) and 2.8 (95% CI 2.4-3.2) respectively of the association between family history of diabetes and risk of type 2 diabetes, whereas other lifestyle variables did not significantly contribute to explaining the association. Adjustment for BMI also weakened the association between family history of diabetes and risk of type 2 diabetes (Table 1) explaining 21.1% (95% CI 19.4-22.9) of the association.

We conducted a sensitivity analysis restricted to women who underwent blood glucose screening for the 1996 to 2004 period in which this information was available. Among the screened women the effect of additionally adjusting for SES and race, lifestyle, and adiposity was essentially the same as for the complete study population (Online Appendix Table A2).

To further explore the role of adiposity in the association between a family history of diabetes and incident diabetes, we ran various models adjusting for waist and hip circumference or adolescent BMI and adult weight change (Table 2). Neither considering measures of body fat distribution nor adolescent BMI explained a substantially greater proportion of the association between family history and diabetes risk as compared with the model that only included BMI.

**Body size of the parents, family history and incident diabetes:** In women who had at least one parent with obesity, the baseline prevalence of overweight (BMI 25.0-29.9 kg/m²) was 30% and the prevalence of obesity (BMI ≥ 30.0 kg/m²) was 17% as compared with 25% and 10% respectively in women who did not have parents with obesity (p < 0.0001). Table 3 shows the risk of type 2 diabetes according to four categories of diabetes and obesity in the parents. Compared with women without a parental history of diabetes or obesity, the relative risk of type 2 diabetes was similar for women with a parental history of both obesity and diabetes and those with only a parental history of diabetes, but substantially weaker for women with only a parental history of obesity. The association between having only a parental history of obesity and risk of type 2 diabetes was fully explained by the higher BMI of the participants (Table 3).

**DISCUSSION**

In this prospective cohort study of 73,227 women with 20 years of follow-up, we observed a direct association between a family history of diabetes and incidence of type 2 diabetes, which was similar for having a paternal or a maternal history of diabetes. A substantial part of this association could be explained by the higher BMI in persons with a family history of diabetes. Lower alcohol consumption and higher consumption of red meat and sugar-sweetened beverages modestly contributed to explaining the association between family history of diabetes and risk of type 2 diabetes.

Consistent with our findings, earlier research reported relatives risks of type 2 diabetes in individuals with self-reported parental history of diabetes ranging from 1.87 to 2.26 (1-3). In NHANES, adjustment for sex, race, age, hypertension, household income and education had no appreciable effect on the association between family history of diabetes and prevalence of type 2 diabetes, but adjustment for BMI did weaken the association (18). In our study generalized adiposity as reflected by BMI rather than circumference measures of fat distribution contributed to the association between family history of diabetes and prevalence of type 2 diabetes, but adjustment for BMI did weaken the association (18). In our study generalized adiposity as reflected by BMI rather than circumference measures of fat distribution contributed to the association between family history of diabetes and diabetes risk. This agrees with studies in which having a family history of diabetes was associated with a higher BMI, but not independently with a higher waist-to-hip ratio (5-7). Furthermore, the Quebec Family Study revealed that total body fat, but not fat distribution, shared common familial determinants (19).
In addition to adiposity, we examined the role of lifestyle factors. Consumption of red meat consumption, sugar-sweetened beverages and alcohol explained part of the association between family history of diabetes and risk of type 2 diabetes. Higher consumption of red meat and sugar-sweetened beverages and alcohol abstinence (as compared with moderate alcohol consumption) have been associated with a higher risk of type 2 diabetes (20-22). Consistent with the current finding, a parental history of diabetes was associated with lower alcohol consumption in a population-based study in the Netherlands (5). Higher consumption of red meat and sugar-sweetened beverages and alcohol abstinence (instead of moderate consumption) may thus modestly contribute to the higher risk of type 2 diabetes in persons with a family history of diabetes.

For a factor to explain a proportion of the association between a family history of diabetes and incident type 2 diabetes, it has to be both associated with risk of type 2 diabetes and shared by family members. In our study, established risk factors for diabetes such as smoking and lack of physical activity (2) did not contribute to the association between a family history and incident type 2 diabetes, suggesting that these factors did not cluster strongly within families at the age studied. This, however, does not imply that individuals with a family history of diabetes cannot benefit from adopting these lifestyle factors to lower their risk of developing type 2 diabetes (23).

Our study had several strengths. The large sample size increased the precision of our estimates. Furthermore, the prospective design limited the probability of differential misclassification of risk factors and selection bias was limited due to the high response rates for the follow-up questionnaires. Our study also had several potential limitations. First, diabetes was assessed by self-report which may have led to misclassification. However, our validation study using medical records indicated that the reporting of diabetes was accurate in this medically knowledgeable population. Second, individuals with a family history of diabetes have a higher probability of being tested for diabetes as compared with the general population (24), which increases their chance of having diabetes detected once it develops. However, in a sensitivity analysis restricted to women who underwent blood glucose testing the effects of adjustment for lifestyle factors and adiposity were essentially the same as for the complete study population. Third, family history of diabetes was not specific to type 2 diabetes, which might have influenced our results. Fourth, some measurement error in the assessment of adiposity, family history, and lifestyle is likely to have occurred. This has probably led to an underestimation of the proportion of the association between family history of diabetes and risk of type 2 diabetes that can be explained by adiposity and lifestyle factors. However, we cannot completely exclude the possibility that correlated error in the assessment of adiposity and lifestyle and the assessment of family history of obesity and diabetes has led to an overestimation of the explained proportions of the association between family history and risk of type 2 diabetes. Finally, our study only included registered nurses which limited the variation in SES and, to a lesser extent, lifestyle behaviors. In more diverse populations, SES, lifestyle factors, and adiposity may explain a greater proportion of the association between family history of diabetes and diabetes risk.

To conclude, our prospective findings confirm that having a first-degree family member with diabetes is a strong risk factor for type 2 diabetes with a similar risk associated with having a maternal and a paternal history of diabetes. A substantial part of the association between having a family history of diabetes and 20-year incidence of
type 2 diabetes could be explained by excess adiposity, while dietary factors including consumption of alcohol, red meat and sugar-sweetened beverages might also play a role. Further studies on this topic with more detailed measures of family history of diabetes, adiposity, and lifestyle factors are warranted. However, the current findings in combination with recent studies of genetic risk variants (3,4) suggest that most of the association between family history of diabetes and diabetes risk remains unexplained.

Further research on novel genetic and lifestyle risk factors, lifestyle in other periods of life, epigenetic risk factors, and specific gene-environment interactions is warranted to identify additional factors that mediate the strong association between having a family history of diabetes and personal risk of type 2 diabetes.

ACKNOWLEDGEMENTS
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REFERENCES


Table 1. Relative risk of type 2 diabetes according to family history of diabetes during 20 year follow-up (1984-2004)

<table>
<thead>
<tr>
<th></th>
<th>No family history</th>
<th>Family history</th>
<th>Father only</th>
<th>Mother only</th>
<th>Sibling only</th>
<th>&gt; 1 family member</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>3132</td>
<td>1969</td>
<td>517</td>
<td>727</td>
<td>240</td>
<td>485</td>
</tr>
<tr>
<td>Person-years</td>
<td>1,075,728</td>
<td>289,889</td>
<td>90,785</td>
<td>111,880</td>
<td>42,423</td>
<td>44,800</td>
</tr>
<tr>
<td><strong>Adjusted relative risk (95% CI)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1 (ref.)</td>
<td>2.27 (2.14-2.40)</td>
<td>2.04 (1.86-2.24)</td>
<td>2.18 (2.01-2.36)</td>
<td>1.72 (1.51-1.97)</td>
<td>3.42 (3.11-3.77)</td>
</tr>
<tr>
<td>SES/race</td>
<td>1 (ref.)</td>
<td>2.26 (2.13-2.39)</td>
<td>2.08 (1.89-2.29)</td>
<td>2.16 (1.99-2.35)</td>
<td>1.69 (1.48-1.93)</td>
<td>3.36 (3.05-3.71)</td>
</tr>
<tr>
<td>Lifestyle</td>
<td>1 (ref.)</td>
<td>2.13 (2.01-2.26)</td>
<td>1.97 (1.79-2.16)</td>
<td>2.05 (1.89-2.22)</td>
<td>1.64 (1.44-1.88)</td>
<td>3.06 (2.77-3.37)</td>
</tr>
<tr>
<td>BMI</td>
<td>1 (ref.)</td>
<td>1.91 (1.80-2.02)</td>
<td>1.78 (1.61-1.95)</td>
<td>1.85 (1.70-2.01)</td>
<td>1.47 (1.29-1.69)</td>
<td>2.62 (2.37-2.89)</td>
</tr>
</tbody>
</table>

95% CI denotes 95% confidence interval; BMI denotes body mass index; SES denotes socio-economic status. A family history of diabetes denotes diabetes in one or more first-degree family members.

1 Adjusted for age (continuous in months)

2 Model 1 additionally adjusted for occupation father (none, professional/managerial, clerical/sales/services), occupation mother (none; professional/managerial; clerical/sales/services), husband's highest degree (< high school, some HS, HS gad, college grad, grad school), participants highest degree (registered nurse, bachelor, master, doctoral), race (white, black, Asian, other)

3 Model 2 additionally adjusted for smoking (never, past, current smokers: $\leq 14, 15-24, \geq 25$ cigs/day), physical activity (< 1.0, 1.0-1.9, 2.0-3.9, 4.0-6.9, $\geq 7.0$ hours/week), intake of coffee (0, 0.1-0.9, 1.0-1.9, 2.0-3.9, 4.0-5.9, $\geq 6$ cups/day), alcohol (0, 0.1-4.9, 5.0-9.9, $\geq 10.0$ g/day), fruit (quintiles), vegetables (quintiles), sugar-sweetened beverages (quintiles), whole grain (quintiles), red meat (quintiles), trans-fat (quintiles), total energy (quintiles), and polyunsaturated-to-saturated fat ratio (quintiles)

4 Model 3 additionally adjusted for BMI (<21, 21-23, 23-25,25-27,27-30,30-33,33-35,35-40,$\geq 40$ kg/m²)
Table 2. Relative risk of type 2 diabetes according to family history of diabetes adjusted for various measures of body fatness

<table>
<thead>
<tr>
<th>Adjustment for adolescent BMI (1984-2004)</th>
<th>No family history</th>
<th>Family history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>1 (ref.)</td>
<td>2.14 (2.01-2.27)</td>
</tr>
<tr>
<td>Model 1 &amp; BMI</td>
<td>1 (ref.)</td>
<td>1.96 (1.85-2.09)</td>
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<tr>
<td>Model 1 &amp; BMI and BMI at age 18 yrs</td>
<td>1 (ref.)</td>
<td>1.99 (1.87-2.11)</td>
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<tr>
<td>Model 1 &amp; BMI at age 18 yrs and weight change</td>
<td>1 (ref.)</td>
<td>2.00 (1.88-2.12)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjustment for body fat distribution (1986-2004)</th>
<th>No family history</th>
<th>Family history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>1 (ref.)</td>
<td>2.18 (2.03-2.34)</td>
</tr>
<tr>
<td>Model 1 &amp; BMI</td>
<td>1 (ref.)</td>
<td>1.99 (1.85-2.14)</td>
</tr>
<tr>
<td>Model 1 &amp; waist and hip circumference</td>
<td>1 (ref.)</td>
<td>2.01 (1.87-2.16)</td>
</tr>
<tr>
<td>Model 1 &amp; BMI and waist and hip circumference</td>
<td>1 (ref.)</td>
<td>1.97 (1.83-2.12)</td>
</tr>
</tbody>
</table>

95% CI denotes 95% confidence interval; BMI denotes body mass index; family history of diabetes denotes diabetes in one or more first-degree family members; weight change denotes weight change since age 18 yrs. All anthropometric variables were modeled as continuous variables: BMI (kg/m²), waist circumference (cm), hip circumference (cm), weight change (kg)

1 Restricted to participants with complete data on BMI at age 18 years (4822 diabetes events during 1,295,965 person-years of follow-up)

2 Adjusted for age, race, socio-economic status, and lifestyle as described in the footnotes to Table 1.

3 Restricted to participants with complete data on waist and hip circumference with follow-up starting in 1986 when data on waist and hip circumference were first collected (3201 diabetes events during 834,231 person-years of follow-up).

Table 3. Relative risk of type 2 diabetes according to a parental history of diabetes and obesity.

<table>
<thead>
<tr>
<th>Parental history of diabetes and obesity*</th>
<th>DM- Obese-</th>
<th>DM- Obese+</th>
<th>DM+ Obese-</th>
<th>DM+ Obese+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>1620</td>
<td>1170</td>
<td>806</td>
<td>760</td>
</tr>
<tr>
<td>Person-years of follow-up</td>
<td>630,244</td>
<td>330,599</td>
<td>120,408</td>
<td>102,783</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adjusted relative risks (95% CI)†</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1 (ref.)</td>
<td>1.37 (1.27-1.48)</td>
<td>2.61 (2.40-2.84)</td>
<td>2.81 (2.57-3.06)</td>
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<tr>
<td>SES/race</td>
<td>1 (ref.)</td>
<td>1.36 (1.26-1.46)</td>
<td>2.58 (2.37-2.81)</td>
<td>2.73 (2.50-2.98)</td>
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<tr>
<td>Lifestyle</td>
<td>1 (ref.)</td>
<td>1.30 (1.20-1.40)</td>
<td>2.43 (2.23-2.65)</td>
<td>2.48 (2.27-2.71)</td>
</tr>
<tr>
<td>BMI</td>
<td>1 (ref.)</td>
<td>0.98 (0.91-1.06)</td>
<td>2.21 (2.03-2.41)</td>
<td>1.77 (1.62-1.93)</td>
</tr>
</tbody>
</table>

DM denotes diabetes mellitus; 95% CI denotes 95% confidence interval; BMI denotes body mass index

* History of diabetes mellitus and/or obesity in either the father or the mother.

† Multivariate models are described in the footnotes to Table 2.