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Insulin Resistance and Truncal Obesity as Important Determinants of the Greater Incidence of Diabetes in Indian Asians and African Caribbeans Compared With Europeans

The Southall And Brent REvisited (SABRE) cohort

OBJECTIVE—To determine the extent of, and reasons for, ethnic differences in type 2 diabetes incidence in the U.K.

RESEARCH DESIGN AND METHODS—Population-based triethnic cohort. Participants were without diabetes, aged 40–69 at baseline (1989–1991), and followed-up for 20 years. Baseline measurements included fasting and postglucose bloods, anthropometry, and lifestyle questionnaire. Incident diabetes was identified from medical records and participant recall. Ethnic differences in diabetes incidence were examined using competing risks regression.

RESULTS—Incident diabetes was identified in 196 of 1,354 (14%) Europeans, 282 of 839 (34%) Indian Asians, and 100 of 335 (30%) African Caribbeans. All Indian Asians and African Caribbeans were first-generation migrants. Compared with Europeans, age-adjusted subhazard ratios (SHRs [95% CI]) for men and women, respectively, were 2.88 (95%, 2.36–3.53; P < 0.001) and 1.91 (1.18–3.10; P = 0.008) in Indian Asians, and 2.23 (1.64–3.03; P < 0.001) and 2.51 (1.63–3.87; P < 0.001) in African Caribbeans. Differences in baseline insulin resistance and truncal obesity largely attenuated the ethnic minority excess in women (adjusted SHRs: Indian Asians 0.77 [0.49–1.22]; P = 0.3; African Caribbeans 1.48 [0.89–2.45]; P = 0.13), but not in men (adjusted SHRs: Indian Asians 1.98 [1.52–2.58]; P < 0.001 and African Caribbeans, 2.05 [1.46–2.89; P < 0.001]).

CONCLUSIONS—Insulin resistance and truncal obesity account for the twofold excess incidence of diabetes in Indian Asian and African Caribbean women, but not men. Explanations for the excess diabetes risk in ethnic minority men remain unclear. Further study requires more precise measures of conventional risk factors and identification of novel risk factors.

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Ethnicity and incident diabetes

been published (9). Participants aged 40–69 years at baseline (1988–1991) were randomly selected from age- and sex-stratified primary care physician lists (n = 4,063) and workplaces (n = 795) in the London districts of Southall and Brent (Fig. 1). Because primary care registration is free and the gateway to all health services in the U.K., this forms a representative and comprehensive sampling frame. The study was designed to investigate cardiometabolic risk in different ethnic groups, primarily in men.

All Indian Asians and African Caribbeans were first-generation migrants. Ethnicity was interviewer-recorded based on parental origins and appearance and was subsequently confirmed by participants. Indian Asians originated from the Indian subcontinent. African Caribbeans originated from the Caribbean (91.5%) or from West Africa. At baseline, participants underwent fasting blood tests, blood pressure measurements, and anthropometry, and completed a health and lifestyle questionnaire. Those whose diabetes status was unknown underwent oral glucose tolerance testing (OGTT).

During 2008–2011, survivors were invited to participate in a morbidity follow-up, including a health and lifestyle questionnaire, primary care medical record review, and/or attendance at clinic at St. Mary’s Hospital, London. Clinic attendees fasted overnight and underwent measurements as at baseline, including OGTT.

All participants gave written informed consent. Approval for the baseline study was obtained from Ealing, Hounslow and Spelthorne, Parkside, and University College London research ethics committees, and at follow-up from St. Mary’s Hospital Research Ethics Committee (reference 07/H0712/109).

Identifying baseline and incident diabetes

Physician diagnosis or World Health Organization 1999 criteria (10) for fasting and OGTT blood glucose measurements defined baseline diabetes. Incident diabetes was identified from a positive report from one of the following sources:

Direct follow-up: Primary care medical record review: recorded diagnosis of diabetes or prescription of antidiabetic medications.

Participant questionnaire: recall of physician-diagnosed diabetes plus either year of diagnosis or receipt of named antidiabetic medication.

Clinical follow-up at 20 years: fasting or OGTT plasma glucose results meeting World Health Organization 1999 criteria (10). Plasma glucose was measured using hexokinase/NADP methods (Abbott Diagnostics).

Indirect follow-up: Hospital episode statistics (HES) or death certificates: diagnosis of diabetes at hospital discharge or diabetes listed as an underlying or contributory cause of death (ICD9 codes: 2500–2509; ICD10 codes: E100-E149) for sensitivity analyses only.

Age at diagnosis was identified at first report of diabetes in primary care medical

![Figure 1 — Follow-up of SABRE cohort, 1988–2011.](image-url)
records or age at follow-up for the 86 (15%) cases identified at follow-up clinic.

**Baseline risk factor measurements**

Height was measured using a stadiometer. Body fat included circumferences around the waist (halfway between costal margin and iliac crest), hip (over greater trochanter), and midthigh, and was measured using a fiberglass tape with a spring balance set to a constant tension of 600 g. Holtain Harpenden calipers were used to standard protocol to measure skinfold thicknesses. Subcutaneous truncal fat was estimated by addition of subscapular and suprailiac skinfold thicknesses.

For OGTT, plasma glucose and insulin were measured 2 h after 75 g oral glucose (9). Blood was analyzed at the same hospital laboratory (5). Glycated hemoglobin was measured in stored blood samples (Southall center only) using an immunoassay on a clinically validated automated analyzer (c311; Roche, Burgess Hill, U.K.); the high and low coefficients of variation were 2.9 and 3.3%. Baseline insulin resistance (IR) as a measure of hepatic IR and percentage β-cell function (HOMA2-B) were approximated using the HOMA2 calculator (11). The formula derived by Matsuda et al. (12) incorporates both fasting and postload measures, thus approximating both hepatic and peripheral IR \( \left( \text{fasting glucose \times 2-h glucose(mg/dL)} \times \text{fasting insulin \times 2 h insulin(\mu U/mL)} \times 10,000 \right) \).

Sitting blood pressure was the mean of two resting measurements using a random zero sphygmomanometer (Hawksley, Lancing, U.K.).

Physical activity was assessed by questionnaire. Methods based on the Allied Dunbar Fitness survey (13) were used to calculate energy expenditure for leisure activity, giving a summary estimate of total weekly energy expenditure (MJ) in sport, walking, cycling, and strenuous activities. An index of physical activity at work was generated (Supplementary Data).

**Statistical analyses**

Primary analyses relate to data obtained from direct follow-up sources for people without baseline diabetes. Indirect data (HES) and death certification data were not used for primary analyses because date of diagnosis could not be established. We amalgamated direct data sources to identify incident diabetes and found no evidence of heterogeneity between sources using a meta-analysis approach. Baseline characteristics by incident diabetes status were compared using parametric (Student t) or nonparametric (Wilcoxon rank sum/\( \chi^2 \)) tests, as appropriate.

Competing risks regression (competing risk = death) based on Fine and Gray proportional subhazards methods (14) was used to describe ethnic differences in diabetes incidence and to examine baseline characteristics representing a series of prespecified parameters (anthropometric, metabolic, blood pressure, lifestyle, socioeconomic position) as predictors of incident diabetes in univariate models. Those predictors that most substantially and significantly altered the subhazard ratio (SHR) for ethnic difference were included in multivariate models. Interactions between ethnicity and baseline risk factors chosen for multivariate models were examined.

We tested interactions between follow-up time and each covariate. The small number of covariates in which the proportional hazards assumption was violated was included as time-varying covariates. We plotted cumulative incidence curves for each ethnic–sex group and examined Schoenfeld-like residuals. All analyses are accepted as two-sided and statistical significance was accepted as \( P < 0.05 \).

**RESULTS**

Of those without baseline diabetes (N = 4,202), 3,908 (93%) were traced to a U.K. address. Direct follow-up data were available for 1,354 (66%), 839 (65%), and 335 (61%) of traced Europeans, Indian Asians, and African Caribbeans, respectively. Proportions with any follow-up data increased to 91, 87, and 92% of traced Europeans, Indian Asians, and African Caribbeans when HES and deaths data were included (Fig. 1).

Diabetes developed in 14% of Europeans, 33% of Indian Asians, and 30% of African Caribbeans between baseline (mean age, 51.8 ± 7.0 years) and follow-up (mean age, 70.5 ± 6.3 years). Cumulative incidence by age at follow-up is illustrated (Fig. 2).

**Diabetes risk and determinants in men**

Indian Asians who had development of diabetes had lower BMI at baseline but were more centrally obese than Europeans (Table 1). Although baseline fasting and postload glucose did not differ, Indian Asians had higher fasting insulin, more adverse measures of insulin resistance, and higher calculated β-cell function than Europeans. In contrast, only the

![Figure 2](https://example.com/image2.png)

**Figure 2**—Cumulative incidence of diabetes during 20 years of follow-up.
|                               | Incident diabetes | No diabetes |
|-------------------------------|-------------------|-------------|
|                               | European          | Indian Asian | African Caribbean | P* | European | Indian Asian | P** | African Caribbean | P** |
| Age                           | 51.6 ± 6.3        | 49.9 ± 6.5   | 53.8 ± 5.3       | 0.008 | 52.6 ± 7.2 | 50.9 ± 7.1 | <0.001 | 53.3 ± 6.2        | 0.27 |
| Smoking, % never/ex/current   | 23/36/40          | 66/12/22     | 60/20/20         | <0.001 | 29/40/31 | 78/9/13 | <0.001 | 54/20/26         | <0.001 |
| Years of education            | 10.4 ± 2.1        | 12.3 ± 3.6   | 10.8 ± 3.0       | 0.22 | 10.8 ± 2.6 | 12.6 ± 3.6 | <0.001 | 10.9 ± 2.7        | 0.61 |
| Manual occupation             | 94 (60%)          | 193 (76%)    | 46 (82%)         | 0.002 | 541 (60%) | 339 (75%) | <0.001 | 108 (81%)         | <0.001 |
| Years lived in U.K.           | —                 | 22.5 ± 6.4   | 29.8 ± 4.5       | —    | 22.8 ± 6.3 | —         | —     | 29.5 ± 3.9        | —    |
| BMI, kg/m²                    | 28.1 ± 4.3        | 26.5 ± 3.0   | 27.3 ± 3.3       | 0.27  | 25.6 ± 3.4 | 25.0 ± 3.4 | 0.003  | 25.7 ± 3.1        | 0.44 |
| Waist, cm                     | 96.9 ± 11.3       | 95.5 ± 9.2   | 91.8 ± 9.4       | 0.003 | 90.2 ± 10.0 | 90.3 ± 9.4 | 0.77  | 87.5 ± 9.3        | 0.003 |
| Thigh circumference, cm       | 58.6 ± 5.0        | 55.7 ± 4.3   | 60.2 ± 4.5       | <0.001 | 56.4 ± 4.2 | 56.4 ± 4.2 | <0.001 | 57.8 ± 4.5        | <0.001 |
| Waist-to-hip ratio            | 0.97 ± 0.06       | 1.00 ± 0.06  | 0.95 ± 0.05      | 0.048 | 0.93 ± 0.06 | 0.97 ± 0.06 | <0.001 | 0.93 ± 0.06       | 0.36 |
| Waist-to-height ratio         | 0.56 ± 0.06       | 0.56 ± 0.05  | 0.53 ± 0.05      | 0.15  | 0.52 ± 0.06 | 0.53 ± 0.05 | <0.001 | 0.51 ± 0.05       | 0.087 |
| Truncal skinfold thickness, cm| 4.2 (4.0–4.5)     | 4.9 (4.7–5.1) | 4.5 (4.2–5.1) | 0.178 | 3.5 (3.4–3.6) | 4.2 (4.1–4.4) | <0.001 | 3.7 (3.4–3.9)     | 0.23 |
| Systolic blood pressure, mmHg | 122 ± 14          | 125 ± 17     | 129 ± 14         | 0.001 | 122 ± 16 | 123 ± 17 | 0.039 | 126 ± 15         | 0.003 |
| Diastolic blood pressure, mmHg | 77 ± 10           | 82 ± 11      | 84 ± 11          | <0.001 | 77 ± 11 | 80 ± 10 | <0.001 | 80 ± 12          | <0.001 |
| Fasting blood glucose, mmol/L | 5.7 (5.6–5.8)     | 5.6 (5.6–5.7) | 5.9 (5.7–6.1)   | 0.21  | 5.4 (5.3–5.4) | 5.3 (5.3–5.4) | 0.092 | 5.4 (5.3–5.5)     | 0.79 |
| Fasting insulin, pmol/L       | 57.9 (52.9–63.3)  | 71.2 (66.4–76.3) | <0.001 | 51.2 (43.6–60.2) | 0.18  | 40.5 (39.0–42.1) | 52.8 (50.1–55.6) | <0.001 | 42.4 (38.0–47.4) | 0.40 |
| 2-h postchallenge glucose, mmol/L | 5.4 (5.2–5.6) | 5.6 (5.4–5.8) | 6.2 (5.7–6.8) | 0.001 | 4.8 (4.7–4.9) | 5.0 (4.9–5.1) | 0.009 | 5.3 (5.1–5.6)     | <0.001 |
| 2-h postchallenge insulin, pmol/L | 184.6 (161.6–210.8) | 312.7 (282.5–346.1) | 0.26 | 213.9 (173.4–263.7) | <0.001 | 111.8 (106.2–117.7) | 211.7 (196.4–228.2) | 0.057 | 128.4 (113.9–144.7) | <0.001 |
| HOMA2-IR                      | 1.1 (1.0–1.2)     | 0.8 (0.8–0.8) | 1.0 (0.8–1.2)   | 0.23  | 0.8 (0.7–0.8) | 1.0 (0.9–1.1) | <0.001 | 0.8 (0.8–0.9)     | 0.45 |
| HOMA2 estimate of % β-cell function | 76.8 (72.0–82.0) | 91.2 (86.5–96.2) | <0.001 | 67.4 (59.8–75.9) | 0.048 | 68.6 (66.8–70.5) | 83.7 (80.8–86.8) | <0.001 | 70.6 (65.1–76.5) | 0.47 |
| Matsuda index of insulin resistance | 0.17 (0.15–0.19) | 0.25 (0.23–0.27) | <0.001 | 0.19 (0.16–0.23) | 0.40  | 0.10 (0.10–0.11) | 0.16 (0.15–0.17) | <0.001 | 0.10 (0.09–0.11) | 0.020 |
| HbA1c, %                      | 5.7 ± 0.4         | 5.9 ± 0.5    | 5.5 ± 0.3        | <0.001 | 5.7 ± 0.4 | 5.7 ± 0.4 | <0.001 | —               | —    |
| Total cholesterol, mmol/L     | 6.1 (5.9–6.2)     | 5.9 (5.8–6.1) | 5.6 (5.3–5.9)   | 0.006  | 5.9 (59–6.0) | 5.8 (5.7–5.9) | 0.116 | 5.4 (5.2–5.6)     | <0.001 |

Continued on p. 387
Table 1—Continued

|                         | European | Indian | African | p*          | European | Indian | p**          | African | p**          |
|-------------------------|----------|--------|---------|-------------|----------|--------|-------------|---------|-------------|
| Triglycerides, mmol/L   | 1.9 (1.8–2.1) | 2.0 (1.8–2.1) | 0.88 | 1.1 (1.0–1.2) | <0.001   | 1.4 (1.4–1.5) | 1.6 (1.5–1.7) | 0.26   | 1.1 (1.0–1.1) | <0.001   |
| HDL cholesterol, mmol/L | 1.1 (1.1–1.2) | 1.1 (1.2–1.2) | 0.76 | 14 (1.3–1.4) | <0.001   | 1.3 (1.3–1.3) | 12 (1.2–1.2) | <0.001 | 1.4 (1.4–1.5) | <0.001   |
| Family history of diabetes | 36 (31%) | 111 (57%) |   <0.001   | 22 (50%) | 0.026   | 112 (19%) | 111 (34%) | <0.001   | 26 (28%) | 0.033   |
| Physical activity: median (25th, 75th percentiles), MJ/wk | 4.0 (1.5–7.1) | 3.5 (1.0–4.0) |   <0.001   | 3.3 (1.2–4.5) | 0.065   | 4.0 (1.5–6.0) | 3.5 (1.0–4.0) | <0.001 | 3.7 (1.2–4.7) | 0.060   |
| Physical activity at work, n (%) in most active group§ | 42 (31%) | 74 (37%) | 0.28 | 7 (17%) | 0.068   | 202 (27%) | 130 (36%) | 0.001   | 29 (31%) | 0.45   |
| Women without baseline diabetes | 40 (13%) | 29 (21%) | 44 (30%) | 262 | 107 | 102 |               |          |           |
| Age                     | 51.9 ± 6.1 | 51.3 ± 5.9 | 0.72 | 51.8 ± 6.3 | 0.98   | 52.7 ± 7.1 | 49.0 ± 6.4 | <0.001 | 52.8 ± 6.2 | 0.75   |
| Smoking, % never/ex/current | 55/15/30 | 100/0/0 |   <0.001   | 86/2/11 | 0.005   | 46/25/29 | 96/1/3 | <0.001   | 78/10/12 | <0.001   |
| Years of education      | 10.6 ± 2.6 | 11.4 ± 4.1 | 0.35 | 10.8 ± 3.2 | 0.76   | 10.7 ± 2.9 | 10.8 ± 3.6 | 0.65   | 10.8 ± 3.1 | 0.60   |
| Manual occupation       | 18 (45%) | 17 (59%) | 0.086 | 84 (63%) | 0.66   | 126 (50%) | 66 (69%) | 0.001   | 54 (53%) | 0.42   |
| Years lived in the U.K. |           |         |          |           |         |         |           |         |           |
| BMI, kg/m²              | 25.2 ± 5.8 | 28.5 ± 4.7 | 0.59 | 31.7 ± 5.6 | 0.055   | 25.2 ± 4.3 | 26.5 ± 4.1 | 0.004   | 28.6 ± 4.9 | <0.001   |
| Waist, cm               | 89.1 ± 14.4 | 87.5 ± 11.2 | 0.72 | 94.5 ± 12.8 | 0.059   | 77.8 ± 10.6 | 82.9 ± 9.9 | <0.001 | 85.3 ± 10.4 | <0.001   |
| Thigh circumference, cm | 61.6 ± 6.6 | 60.4 ± 5.5 | 0.43 | 65.1 ± 7.4 | 0.027   | 57.4 ± 5.2 | 58.7 ± 5.6 | 0.033   | 62.9 ± 7.0 | <0.001   |
| Waist-to-hip ratio      | 0.85 ± 0.08 | 0.87 ± 0.08 | 0.26 | 0.88 ± 0.08 | 0.040   | 0.79 ± 0.07 | 0.84 ± 0.08 | <0.001 | 0.83 ± 0.06 | <0.001   |
| Waist-to-height ratio   | 0.55 ± 0.09 | 0.56 ± 0.08 |   <0.001   | 0.59 ± 0.09 | 0.042   | 0.48 ± 0.07 | 0.54 ± 0.07 | 0.32   | 0.53 ± 0.06 | <0.001   |
| Truncal skinfold thickness, cm | 4.8 (4.0–5.7) | 7.3 (6.7–7.8) |   <0.001   | 5.9 (5.2–6.6) | 0.044   | 3.4 (3.3–3.6) | 6.3 (6.0–6.6) | <0.001 | 4.6 (4.2–5.0) | <0.001   |
| Systolic blood pressure, mmHg | 123 ± 22 | 128 ± 23 | 0.32 | 132 ± 18 | 0.042   | 118 ± 16 | 122 ± 22 | 0.127   | 127 ± 15 | <0.001   |
| Diastolic blood pressure, mmHg | 76 ± 13 | 80 ± 11 | 0.23 | 81 ± 12 | <0.001   | 74 ± 9 | 76 ± 10 | 0.080   | 82 ± 11 | 0.033   |

Continued on p. 388
Table 1—Continued

|                                     | Incident diabetes | No diabetes |                 |               |                 |                 |                 |                 |
|-------------------------------------|-------------------|-------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                                     | European          | Indian Asian| p*             | African Caribbean | p*             | European          | Indian Asian | p**             | African Caribbean | p**             |
| Fasting blood glucose, mmol/L       | 5.6 (5.4–5.8)     | 5.3 (5.1–5.4) | 0.009          | 5.6 (5.5–5.8) | 0.89           | 5.2 (5.2–5.3)     | 4.9 (4.8–5.0) | <0.001          | 5.3 (5.2–5.4)     | 0.139           |
| Fasting insulin, pmol/L             | 41.4 (33.8–50.8)  | 49.5 (41.5–59.0) | 0.21           | 59.9 (50.8–70.6) | 0.006          | 29.9 (27.8–32.3) | 39.8 (36.4–43.4) | <0.001          | 53.2 (47.8–59.1) | <0.001          |
| 2-h postchallenge glucose, mmol/L   | 6.1 (5.6–6.6)     | 6.4 (5.9–6.9) | 0.36           | 7.2 (6.7–7.7) | 0.003          | 5.6 (5.4–5.7)     | 5.3 (5.1–5.5) | 0.098           | 6.0 (5.8–6.3)     | 0.005           |
| 2-h postchallenge insulin, pmol/L   | 208.3 (160.8–269.8) | 355.1 (275.4–457.9) | 0.005          | 269.8 (218.6–332.9) | <0.001          | 129.0 (119.6–139.2) | 227.0 (197.2–261.2) | 0.118          | 204.2 (181.6–229.6) | <0.001          |
| HOMA-IR                             | 0.8 (0.7–1.0)     | 0.9 (0.8–1.0) | 0.71           | 1.2 (1.0–1.4) | 0.034          | 0.6 (0.5–0.6)     | 0.7 (0.7–0.8) | 0.005           | 1.0 (0.9–1.1)     | <0.001          |
| HOMA estimate of β-cell function    | 63.8 (55.5–73.2)  | 81.8 (75.6–86.6) | 0.016          | 83.8 (77.7–90.4) | 0.011          | 58.7 (55.7–61.8) | 81.1 (75.9–86.6) | <0.001          | 80.0 (71.6–89.3) | <0.001          |
| Matsuda index of insulin resistance | 0.17 (0.13–0.21)  | 0.23 (0.18–0.28) | 0.058          | 0.24 (0.20–0.28) | 0.0183         | 0.10 (0.10–0.11) | 0.16 (0.15–0.17) | <0.001          | 0.12 (0.11–0.13) | 0.020           |
| HbA1c, %                            | 5.6 ± 0.6         | 6.0 ± 0.3    | 0.007          | —              | —              | 5.5 ± 0.3         | 5.6 ± 0.4    | 0.039           | —              | —              |
| Total cholesterol, mmol/L           | 6.1 (5.8–6.4)     | 5.8 (5.5–6.1) | 0.24           | 5.5 (5.1–5.5) | 0.034          | 6.0 (5.8–6.1)     | 5.6 (5.4–5.8) | 0.008           | 5.3 (5.1–5.5)     | <0.001          |
| Triglycerides, mmol/L               | 1.6 (1.4–1.8)     | 1.4 (1.2–1.7) | 0.41           | 1.2 (1.0–1.4) | <0.001         | 1.2 (1.1–1.3)     | 1.3 (1.2–1.4) | 0.26            | 0.9 (0.9–1.0)     | <0.001          |
| HDL cholesterol, mmol/L             | 1.4 (1.3–1.6)     | 1.4 (1.3–1.5) | 0.64           | 1.5 (1.4–1.6) | 0.39           | 1.6 (1.6–1.7)     | 1.4 (1.4–1.5) | <0.001          | 1.6 (1.6–1.7)     | 0.75            |
| Family history of diabetes, n       | 14 (40%)          | 15 (60%)    | 0.126          | 26 (65%)       | 0.030          | 48 (26%)          | 28 (34%)     | 0.182           | 39 (48%)         | <0.001          |
| Physical activity: leisure time, median (25th, 75th percentiles), MJ/wk† | 1.9 (1.2–4.2)     | 1.0 (1.0–3.5) | <0.011         | 3.8 (1.2–4.1) | 0.33           | 3.7 (1.5–5.0)     | 1.0 (1.0–3.5) | <0.001          | 3.7 (1.2–4.3)     | 0.57            |
| Physical activity at work, n (%) in most active group‡ | 6 (20%)          | 4 (33%)     | 0.36           | 9 (32%)        | 0.29           | 44 (25%)          | 27 (44%)     | 0.007           | 29 (42%)         | 0.010           |

Data are mean ± SD or geometric means (95% CI) unless otherwise stated. *P relates to comparison with Europeans with incident diabetes. **P relates to comparison with Europeans who did not develop diabetes. †Walking, cycling, sporting, and strenuous activities. ‡Percentage based on those employed.
All women in Europeans and Indian Asians who had development of diabetes (Table 1). Fasting HDL cholesterol was lower and triglyceride levels were higher in African Caribbeans who had development of diabetes. Leisure time energy expenditure was lower in Indian Asians and African Caribbeans regardless of diabetes status. African Caribbeans who had development of diabetes were also less active at work than Europeans. Smoking predicted diabetes incidence in European and Indian Asian men.

Indian Asian men were nearly three times more likely to have development of diabetes than European men (Table 2) and were younger at diagnosis (median, 62 vs. 67 years; \( P < 0.001 \)). Adjustment for baseline smoking increased the SHR for Indian Asians versus Europeans to 3.37 (95% CI, 2.67–4.26; \( P < 0.001 \)).

The Matsuda index of IR most attenuated, but did not abolish, the Indian Asian excess risk of diabetes (adjusted SHR, 2.16; 95% CI, 1.68–2.78; \( P < 0.001 \)). Multivariate adjustment slightly further attenuated the ethnic differential (SHR, 1.98; 95% CI, 1.52–2.58; \( P < 0.001 \)) unadjusted the ethnic differential (SHR, 1.98; 95% CI, 1.52–2.58; \( P < 0.001 \)).

Table 2—Ethnic group differences in incidence of diabetes adjusted for baseline risk factors

| Risk factor | Indian Asians vs. Europeans | African Caribbeans vs. Europeans |
|-------------|------------------------------|---------------------------------|
| Unadjusted  | 2.82 (2.29–3.46), \( P < 0.001 \) | 2.46 (1.79–3.37), \( P < 0.001 \) |
| Adjusted for age | 2.88 (2.36–3.53), \( P < 0.001 \) | 2.23 (1.64–3.03), \( P < 0.001 \) |
| Adjusted for age and smoking | 3.37 (2.67–4.26), \( P < 0.001 \) | 2.27 (1.66–3.11), \( P < 0.001 \) |
| Adjusted for age, smoking, and years of education | 3.55 (2.79–4.32), \( P < 0.001 \) | 2.34 (1.71–3.21), \( P < 0.001 \) |
| Adjusted for age, smoking, and physical activity (leisure time and work group) | 3.37 (2.64–4.31), \( P < 0.001 \) | 2.33 (1.69–3.21), \( P < 0.001 \) |
| Adjusted for age, smoking, and BMI | 3.59 (2.83–4.56), \( P < 0.001 \) | 2.19 (1.60–3.00), \( P < 0.001 \) |
| Adjusted for age, smoking, and waist-to-height ratio | 2.98 (2.35–3.79), \( P < 0.001 \) | 2.43 (1.78–3.33), \( P < 0.001 \) |
| Adjusted for age, smoking, and height | 3.42 (2.67–4.38), \( P < 0.001 \) | 2.26 (1.64–3.10), \( P < 0.001 \) |
| Adjusted for age, smoking, height, and truncal skinfold thickness | 2.82 (2.20–3.60), \( P < 0.001 \) | 1.84 (1.31–2.58), \( P < 0.001 \) |
| Adjusted for age, smoking, height, and waist-to-hip ratio | 2.70 (2.10–3.49), \( P < 0.001 \) | 2.38 (1.73–3.26), \( P < 0.001 \) |
| Adjusted for age, smoking, fasting, and postload glucose/insulin | 2.36 (1.83–3.05), \( P < 0.001 \) | 1.96 (1.44–2.68), \( P < 0.001 \) |
| Adjusted for age, smoking, and Matsuda index of IR | 2.16 (1.68–2.78), \( P < 0.001 \) | 1.98 (1.45–2.69), \( P < 0.001 \) |
| Adjusted for age, smoking, and HOMA2-IR | 2.64 (2.06–3.38), \( P < 0.001 \) | 2.28 (1.66–3.12), \( P < 0.001 \) |
| Adjusted for age, smoking, and HOMA2-B | 3.08 (2.41–3.94), \( P < 0.001 \) | 2.40 (1.74–3.30), \( P < 0.001 \) |
| Adjusted for age, smoking and HDL cholesterol | 3.15 (2.47–4.01), \( P < 0.001 \) | 2.52 (1.80–3.55), \( P < 0.001 \) |
| Adjusted for age, smoking and triglycerides | 2.99 (2.34–3.83), \( P < 0.001 \) | 2.98 (2.13–4.16), \( P < 0.001 \) |
| Adjusted for age, smoking, Matsuda index of IR, HDL cholesterol, waist-to-height ratio, and truncal skinfold thickness | 1.98 (1.52–2.58), \( P < 0.001 \) | — |
| Adjusted for age, smoking, Matsuda index of IR, triglycerides, and truncal skinfold thickness | — | 2.28 (1.61–3.21), \( P < 0.001 \) |

SHR (95% CI) derived from competing risks proportional hazards regression (death = competing risk).
Ethnicity and incident diabetes

Pattern for women were similar to those for men with the following exceptions (Table 1). African Caribbean women were the most centrally obese. The sex difference in truncal skinfolds differed markedly by ethnicity in those who had development of diabetes. Baseline truncal skinfold was 0.6 cm greater in European women than in European men, but 2.4 cm greater in Indian Asian women and 1.4 cm greater in African Caribbean women than in men of the same ethnicity. Fasting insulin and HOMA-IR were highest in African Caribbean women and lowest in European women. Asian Indians and African Caribbeans had similarly elevated levels of Matsuda IR compared with Europeans. Fasting HDL cholesterol was lower and triglycerides were higher in European and African Caribbean women who later had development of diabetes, whereas there was no significant diabetes-related difference in lipid profiles in Indian Asian women. Leisure time physical activity was lowest in Indian Asian women, whereas African Caribbean and Indian Asian women were more active at work, regardless of diabetes status. Age at diagnosis of diabetes did not differ by ethnicity in women.

The ethnic differential in incident diabetes was less marked between Indian Asian and European women and disappeared on adjustment for truncal skinfold thickness (adjusted SHR, 1.08; 95% CI, 0.61–1.89; \( P = 0.79 \)). Waist-to-height ratio and Matsuda IR also had a similarly marked attenuating effect (Table 2). Only truncal skinfold thickness (\( P = 0.041 \)) and Matsuda IR (\( P < 0.001 \)) were independent predictors.

African Caribbean women were 2.5 times more likely to have development of diabetes than European women. Adjustment for truncal or abdominal obesity partially attenuated the ethnic differential, but the Matsuda IR index had the greatest attenuating effect. In the multivariate model, the SHR was 1.48 (95% CI, 0.89–2.45) (Table 2). Only Matsuda IR (\( P < 0.001 \)) and waist-to-height ratio (\( P = 0.016 \)) were independent predictors.

No other baseline risk factor, including family history, physical activity, socioeconomic markers, medication use, and age at migration, further altered the excess diabetes risk in men and women of either ethnicity.

Sensitivity analyses

Hospital discharge (HES) data, based on 2,996 people without baseline diabetes, demonstrated incident diabetes in 11 and 8% of European men and women, 26 and 14% of Indian Asian men and women, and 21 and 15% of African Caribbean men and women. Findings from analyses of ethnic group differences in diabetes incidence were similar when we used logistic regression to compare HES data added to direct follow-up (\( n = 3,679 \)) versus direct follow-up alone.

Smoking was unusual in Indian Asian and African Caribbean women; however, these analyses repeated in never-smoking women demonstrated similar ethnic differentials.

CONCLUSIONS—In this British population-based triethnic cohort with more than 20 years of follow-up, diabetes incidence is substantially elevated in people of African Caribbean and Indian Asian origin compared with Europeans. By age 80, 40–50% of British Indian Asian and African Caribbean men and women have diabetes, at least twice the prevalence observed in Europeans of the same age. Midlife measures of IR and of upper body fat deposition were already unfavorable in people who had development of diabetes approximately one decade later and were more adverse in the ethnic minorities. The Matsuda IR index contributed most to explaining the minority excess of diabetes in both sexes. Of obesity measures, adjustment for truncal fat provided the most consistent and independent attenuation of the ethnic differentials in both sexes. Adjustment for these risk factors in women largely abolished the ethnic minority difference in diabetes incidence. In men, however, a twofold excess remained for both ethnic minority groups. ARIC (6) and NHANES (7,8) both suggest that their available lifestyle and adiposity measures could determine some of the African American excess in diabetes in women, but not in men. However, these previous studies did not use the OGTT, and a significant proportion of cases are diagnosed on postload values alone. Further, the role of measures of insulin resistance and ectopic fat deposition, beyond abdominal fat, were not explored, as we have performed here. Inequalities in access to health care may adversely affect risks of incident diabetes in African Americans; this is not an issue in the U.K., where health care is free at the point of delivery. There are no previous longitudinal studies comparing Indian Asians with Europeans.

Direct measures of insulin sensitivity are not feasible for epidemiological studies, which therefore need to rely on surrogates. There are many surrogates and no clear consensus regarding which works best. This reflects the choice of clamp technique used, the population studied, methods of validation used, and the purpose of prediction. In general, surrogate measures of IR that incorporate both fasting and postload values are stronger predictors of future diabetes than fasting levels alone (15–17), although beyond that the choice is less clear. Of the surrogates at our disposal, the Matsuda index mapped most closely to the ethnic/sex gradient in diabetes incidence and provided
the most complete explanation for ethnic differences in risk. Comparison of OGTT-derived values of IR with hyperinsulinemic euglycemic clamp values suggests that they are valid markers of clamp-derived IR within Indian Asians (18) and within people of Black African descent (19), although these largely tested HOMA and not Matsuda indices. Calculated β-cell function at baseline was particularly low in African Caribbean men and lowest in those who had development of diabetes during follow-up. It is tempting to speculate that inadequate β-cell function explains elevated postchallenge glucose in African Caribbeans not matched by equivalently elevated postload insulin. However, smaller studies report C-peptide levels, a direct measure of β-cell function, that are similar in people of Black African descent in the U.K., U.S., or Africa compared with those of European origin; further, the acute insulin response to a glucose load is greater (20–22), even in those with established diabetes (23). In African Caribbeans, plasma insulin levels may be particularly affected by reduced hepatic insulin extraction and reduced insulin clearance (20,22,24), which could explain differences between variation in β-cell function and insulin concentrations. The pathogenesis of type 2 diabetes involves a prolonged period of insulin resistance initially compensated by increased β-cell function but latterly involving progressive β-cell deficit (25). European and Asian Indian men who would have development of type 2 diabetes had relatively elevated β-cell function, whereas among African Caribbean men and women there was no such increase. These findings suggest differences in the stage of pathogenesis reached in the groups at baseline. Our findings imply that, overall, IR was the principal driver of diabetes; however, in the absence of more detailed evaluations of β-cell function, this conclusion is tentative.

The greater visceral obesity of Indian Asians is an obvious candidate to account for the observed excess diabetes (26). However, others have suggested that deep subcutaneous truncal fat with larger hypertrophic adipocytes may be of key importance (27). We extend this observation by showing that truncal fat plays an independent role in accounting for the Indian Asian male excess in diabetes. Adjustment for truncal skinfolds provided the most consistent attenuation in the ethnic minority excess of diabetes incidence for men and women (although not independent of the Matsuda index in the comparison between African Caribbean and European women). We confirm the excess truncal obesity in people of Black African descent despite, in men at least, less visceral fat (28), and its strong predictive ability for diabetes incidence (8). Excess truncal fat in both Indian Asians and people of Black African descent is observed in youth and, in both cases, the growth trajectory for truncal skinfolds appears more rapid for the ethnic minority groups (29,30). Whereas the greater truncal fat despite less abdominal fat in women has been previously noted (31), it is striking here that the sex difference in truncal obesity is more marked in the ethnic minority groups than in Europeans.

Adjustment for IR provided more complete attenuation in the ethnic difference in diabetes incidence in women compared with men. Others have reported sex differences in response to the OGTT such that, in some studies at least, women are more likely to be classified as having impaired glucose tolerance and men are more likely to exhibit impaired fasting glucose (32,33). Impaired fasting glucose may be more strongly associated with β-cell failure (33,34). Thus, the weaker ability of HOMA-IR and Matsuda IR indices to account for ethnic differences in diabetes incidence in men may, speculatively, reflect the imprecision of their characterization of β-cell function, which may play a more important role in the onset of diabetes in men.

Underlying explanations for the greater predisposition to IR in people of ethnic minority descent or, perhaps more importantly, the protection from IR in individuals of European origin who, despite escalating levels of obesity, remain at lowest risk of diabetes are unknown. Changes in fat distribution over the life-course appear to differ by ethnicity (29,30). Although a genetic susceptibility may be an obvious explanation for ethnic differences in metabolic and obesity characteristics, and for the different trajectories over the life-course, it is notable that total energy intake is higher compared with British Europeans in largely first-generation Indian Asian migrants to the U.K. (35) and in Indian Asian children in the U.K. (36). Within India, migrants from rural to urban areas also have higher energy intakes compared with those of the rural population (37). This is associated with greater obesity, ectopic fat distribution, and IR. Further, age-related changes in adverse patterns of IR are more marked in Indian Asian migrant populations compared with Indian Asian nonmigrant populations (35). Such rapid changes in metabolic characteristics are likely to be environmentally rather than genetically driven. It is notable that dietary intake comparisons between rural and urban Cameroonians and British Jamaicans and Caribbeans do not suggest greater calorie or saturated fat intake in the latter (38); however, physical activity levels have been shown to be lower in migrant populations (39).

Strengths and limitations

To our knowledge, this is the largest triethnic cohort in the U.K. with lengthy (20-year) follow-up between middle and older age, thus providing unique prospective ethnicity-specific information on diabetes incidence. Loss to direct follow-up has occurred in one-third of all ethnic groups. However, in sensitivity analyses, the addition of hospital discharge (HES) data to those from direct follow-up provides diabetes status for more than 91% of traced individuals. Results of analyses based on these more complete data were similar to analyses based on direct follow-up. Baseline measurements are limited to those performed on only one occasion 20 years ago, meaning that we cannot account for changes in risk factors during the follow-up period or in earlier life. We have addressed lifestyle and socioeconomic status using the available baseline data on smoking habits, physical activity, years of education, and occupational status, but we acknowledge that these cannot capture all the complexities of the nonmetabolic explanations for ethnic differentials in diabetes incidence.

In conclusion, Indian Asian and African Caribbean migrants to the U.K. have at least twice the risk of development of diabetes compared with British Europeans, even in older age, broadly reflecting patterns observed in younger populations worldwide. Given the increasing life expectancies for those with type 2 diabetes (40), this presents a public health challenge. Measures of insulin resistance and ectopic fat deposition, particularly truncal, account for excess diabetes risk in Indian Asian and African Caribbean women but only make a contribution to the excess risk in ethnic minority men. Strikingly, we show that despite our comprehensive measures, the ethnic minority excess of incident diabetes in men (both Indian Asians and African Caribbeans) cannot be explained, whereas it can be explained for women. We would have anticipated otherwise, and our findings in a different geographical setting than the
Ethnicity and incident diabetes

U.S. and in two different ethnic groups strongly indicate that better assessment of risk factors and/or a search for novel factors are required if we are to understand why ethnic minority groups are at such high risk for diabetes.

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T.T. conducted primary statistical analyses and wrote the first draft of the manuscript. All authors contributed to study design and data interpretation. A.D.H., I.F.G., P.Wh., N.G.F., N.S., P.Wc., P.M.M., and N.C. commented on the draft manuscript and approved this version. T.T. is the guarantor of this work and, as such, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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