EPIDEMIOLOGY/HEALTH SERVICES RESEARCH

Variations in Diabetes Prevalence in Low-, Middle-, and High-Income Countries: Results From the Prospective Urban and Rural Epidemiological Study

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OBJECTIVE

The goal of this study was to assess whether diabetes prevalence varies by countries at different economic levels and whether this can be explained by known risk factors.

RESEARCH DESIGN AND METHODS

The prevalence of diabetes, defined as self-reported or fasting glycemia ≥7 mmol/L, was documented in 119,666 adults from three high-income (HIC), seven upper-middle-income (UMIC), four lower-middle-income (LMIC), and four low-income (LIC) countries. Relationships between diabetes and its risk factors within these country groupings were assessed using multivariable analyses.

RESULTS

Age- and sex-adjusted diabetes prevalences were highest in the poorer countries and lowest in the wealthiest countries (LIC 12.3%, UMIC 11.1%, LMIC 8.7%, and HIC 6.6%; $P < 0.0001$). In the overall population, diabetes risk was higher with a 5-year increase in age (odds ratio 1.29 [95% CI 1.28–1.31]), male sex (1.19 [1.13–1.25]), urban residency (1.24 [1.11–1.38]), low versus high education level (1.10 [1.02–1.19]), low versus high physical activity (1.28 [1.20–1.38]), family history of diabetes (3.15 [3.00–3.31]), higher waist-to-hip ratio (highest vs. lowest quartile; 3.63 [3.33–3.96]), and BMI (≥35 vs. <25 kg/m^2; 2.76 [2.52–3.03]). The relationship between diabetes prevalence and both BMI and family history of diabetes differed in higher- versus lower-income country groups (P for interaction < 0.0001). After adjustment for all risk factors and ethnicity, diabetes prevalences continued to show a gradient (LIC 14.0%, LMIC 10.1%, UMIC 10.9%, and HIC 5.6%).

CONCLUSIONS

Conventional risk factors do not fully account for the higher prevalence of diabetes in LIC countries. These findings suggest that other factors are responsible for the higher prevalence of diabetes in LIC countries.

The International Diabetes Federation estimated that 8.3% (382 million) of adults worldwide had diabetes in 2013 and that the prevalences vary across different countries (1). These differences between countries may be the because of differences in the distributions of known risk factors among countries, such as ethnicity,

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age, family history of diabetes, birth weight, obesity, socioeconomic status, and the degree of westernization (2–22). They may also be the result of variations in the relationship between these risk factors and diabetes among countries with varying degrees of economic development. Thus, socioeconomic factors such as education, rapid industrialization, urbanization, international trade with high-income countries (HICs), migration from rural to urban centers, and lifestyle changes (e.g., calorie-dense diets, reduced physical activity, and tobacco use) may affect diabetes differently in developed versus developing countries (3–22). For example, diabetes has been reported to be more frequent among residents of urban than those of rural regions in developing countries and in adults with lower education levels in developed countries. Variations such as these may be real, or they may seem to occur because they were based on studies conducted in different countries at different periods of time using different methodological approaches. Whether the differences in diabetes prevalence between countries with different economies persist after adjusting for variations in known risk factors is not known.

The Prospective Urban and Rural Epidemiological (PURE) study is an international, population-based evaluation of risk factors and noncommunicable diseases that is being conducted in several countries (23–25). At the first visit, 119,666 adults provided a blood sample for fasting glucose and were asked about their diabetes status and diabetes-specific medications. In this article, we report differences in diabetes prevalence between countries grouped according to income and explore whether these differences can be explained by known diabetes risk factors.

RESEARCH DESIGN AND METHODS

Study Design and Population

The design, recruitment, and participant characteristics of the PURE study have been published (23–25). In brief, the choice of the countries reflects a balance between a large number of communities in countries at different economic levels with substantially heterogeneous socioeconomic status and the feasibility of the collaborating research center in each country to successfully achieve long-term follow-up. The participating countries were grouped according to the 2006 World Bank Income classifications based on gross national product per capita and included four low-income countries (LICs) (Bangladesh, India, Pakistan, and Zimbabwe), three lower-middle-income countries (LMICs) (China, Colombia, and Iran) and one occupied territory (Palestine), seven upper-middle-income countries (UMICs) (Argentina, Brazil, Chile, Malaysia, Poland, South Africa, and Turkey), and three HICs (Canada, Sweden, and the United Arab Emirates). To obtain distinct social and economic environments as well as access to different types of health care, we recruited households in cities and rural regions. In cities, communities from low-, middle-, and high-income areas were chosen based on known information of the geographical area, such as a set of contiguous postal codes or groups of streets, to obtain some representative population in each income area. Rural communities were villages at least 50 km from the cities.

Eligibility criteria included men and women aged between 35 to 70 years, who intended to remain at the same address for the next 4 years and who gave their informed consent to participate in the long-term PURE study. Recruitment of households began in Karnataka, India, in 2003 as a vanguard phase, and overall enrollment was mostly done between January 2005 and December 2009. The PURE study enrolled 156,502 adults aged 35 to 70 years. Of these, 119,666 had a fasting plasma glucose measure and compose the current study population. Details on the approach to enrollment to ensure an unbiased sample from each community, the high response rates (78%), and the comparability of demographics and mortality rates with national statistics have been previously reported (23–25). The PURE study was approved by the research ethics committees in the participating countries.

Diabetes Definitions and Baseline Measurements

Participants were considered to have diabetes if they were told by a health professional that they had diabetes, reported taking a glucose-lowering agent, or had a fasting plasma glucose concentration ≥7.0 mmol/L. Before the venous puncture, the health professional verified that the participant fasted for at least 8 h (no food or beverages, excluding water). Fasting blood was centrifuged within 2 h of collection at the local site. Samples were kept on ice until centrifugation. Plasma was either immediately analyzed for glucose locally or stored at −20° to −70°C, and was subsequently shipped in temperature-controlled containers for central measurement at either the national coordinating center or—for Bangladesh, Brazil, Colombia, Pakistan, Poland, South Africa, the United Arab Emirates, and Zimbabwe—at the Clinical Research and Clinical Trials Laboratory in Hamilton, Canada. Plasma glucose was measured by standardized enzymatic methods using hexokinase or glucose oxidase. National laboratory centers and glucose determinations are reported in Supplementary Appendix 1.

At entry into the study, all participants answered standardized questionnaires on diabetes, demographics, ethnicity,

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family medical history, physical activity, diet, smoking, education levels, income, and medical history (including medications used); they underwent blood pressure measurements, electrocardiography, and venipuncture to collect blood samples. Family history of diabetes included a father, mother, brother, and/or sister having diabetes as reported by the participants. Total physical activity levels during the previous week were determined using the International Physical Activity Questionnaire (26) and reported in MET-min. Activity levels were considered to be low if it was less than 600 MET-min/week, moderate if it was between 600 and 3,000 MET-min/week, or high if above 3,000 MET-min/week. Smoking included cigarettes, pipe, cigars, beedis, and any other type of tobacco used. Current smokers were individuals who smoked any tobacco at entry in the study, and included those who had quit within the previous year. Former smokers were those who had quit for more than a year. Never smokers were those who responded that they had never smoked. Education level was based on the number of years at school, categorized as none or primary (first 6 years), secondary (7–11 years), and college, trade school, or university (>11 years). Participants' habitual food intake was recorded using country-specific validated food frequency questionnaires as reported in the PURE study (27). The global diet quality assessment for this report is based on an adaptation of the Alternate Healthy Eating Index (AHEI), which is known to be predictive of cardiovascular disease risk (28). Six of the nine food items included in the AHEI were measured. Of these, five variables were identical (vegetables, fruits, nuts and soy protein, whole-grain cereal fiber, ratio of white to red meat, and ratio of polyunsaturated to saturated fatty acid) and one item was comparable (deep-fried foods instead of *trans* fats). Scoring of the modified AHEI has been described previously. In this study, scores varied between 6.2 and 70.0, with higher scores indicating more frequent intake of healthy food choices (e.g., eating vegetables, fruits, nuts, fish). The population was stratified into three groups as eating an unhealthy, less healthy, and healthy diet, and cut points were based on tertile scores of 30.9 and 37.8; a score <30.9 indicated unhealthy eating.

Weight, height, and waist and hip circumferences were measured by trained research staff with participants wearing light indoor clothes without shoes. Waist-to-hip ratios were divided into separate quartiles for men and women; the highest quartile (fourth) was >0.96 for men and >0.89 for women. BMI was calculated as weight in kilograms divided by the square of height in meters, and was subdivided as <25, 25–29.9, 30–34.9, and ≥35 kg/m^2. The numbers of people for whom risk factor data were unavailable are noted in Table 1.

Statistical Methods

Continuous variables were summarized as means and standard deviations, and categorical variables as numbers and percentages. Age-adjusted diabetes prevalences were compared between urban and rural residence and between male and female sex for each country using the GLIMMIX procedure in SAS. Multilevel logistic regression models were used to assess the difference in diabetes prevalences and risk factor levels according to the following variables: age, sex, residency location, BMI, waist-to-hip ratio, physical activity levels, AHEI score, combined former and current smoking, education level, family history of diabetes, and ethnicity. In multilevel structure models, we considered individual participants nested in communities and communities nested in countries. Odds ratios (ORs) are shown with 95% CI, and a *P* value <0.05 was considered significant for the multilevel regression models. The possibility that differences in prevalence by region were the result of regional differences in the relationship between risk factors and diabetes prevalence was assessed by including region × risk factor interaction terms in the models assessing each risk factor and setting a *P* value suggesting an interaction at <0.1. However, ethnicity was not included with the other risk factors in the model for interaction according to country groupings because of the strong relationship between ethnicity and country groupings, as shown in Supplementary Appendix 2. All analyses were done in SAS version 9.2 (SAS Inc., Cary, NC).

RESULTS

Baseline Characteristics

Baseline characteristics of the 119,666 individuals in this report were generally similar to the characteristics of the 156,502 participants in the overall PURE study (see Supplementary Appendix 3). Of the 119,666 participants, 13,206 (11.0%) were recorded as having diabetes; 9,279 (70%) had self-reported diabetes or were taking a glucose-lowering agent; and 3,927 (30%) had an elevated fasting plasma glucose concentration (≥7.0 mmol/L) and for analyses were classified as having newly diagnosed diabetes. Compared with participants without diabetes, those with diabetes were older, more often male, obese, less educated, and less physically active; had a higher rate of family history of diabetes and a poorer diet; resided more often in cities than in rural communities; and smoked less (Table 1).

Differences in Diabetes Prevalences and Risk Factors

The crude prevalence of diabetes varied between country income groups. Age- and sex-adjusted prevalence of diabetes (95% CI) was highest in LICs (12.3% [10.9–13.9%]), followed by UMICs (11.1% [9.7–12.6%]) and LMICs (8.7% [7.9–9.6%]), and was lowest in HICs (6.6% [5.7–7.7%]) (*P* for trend <0.0001). The percentage of the population with self-reported diabetes or taking a glucose-lowering agent and with a plasma glucose concentration ≥7 mmol/L was 54.7% in HICs, 52.3% in UMICs, 56.0% in LMICs, and 59.5% in LICs. At the same BMI categories, diabetes prevalences adjusted for age, sex, and residency location varied markedly, especially at low BMI values, with the highest prevalence of diabetes among LICs. Such variations are observed among the different quartiles of waist-to hip ratio but are less pronounced (Fig. 1).

The multivariable adjusted ORs of risk factors associated with diabetes in the overall country income groups are shown in Fig. 2. For all country groups, 5-year increases in age category, increased BMI and waist-to-hip ratio, male sex, family history of diabetes, urban versus rural residence, low versus high physical activity levels, and low versus high education level were related to increased diabetes risk. However, smoking status and diet quality based on the AHEI were not related to diabetes prevalence. There was a significant interaction between country grouping and family

Table 1—Characteristics of participants with diabetes compared with those of participants without diabetes

	Participants without diabetes (*n* = 106,460)	Participants with diabetes (*n* = 13,206)	*P* value
Age, years	50.21 ± 9.68	54.97 ± 9.01	<0.0001
Male sex	44,872 (42.1)	5,887 (44.6)	<0.0001
Residency location			
Urban	55,299 (51.9)	8,120 (61.5)	<0.0001
Rural	51,161 (48.1)	5,086 (38.5)	
Education level			
Less than high school (primary)	43,370 (40.7)	5,624 (42.6)	<0.0001
High school (secondary)	40,947 (38.5)	5,068 (38.4)	
Some college or more	21,880 (20.6)	2,472 (18.7)	
Missing	263 (0.2)	42 (0.3)	
Family history of diabetes	19,422 (18.2)	5,172 (39.2)	<0.0001
Missing	10,375 (9.7)	1,837 (13.9)	
Waist-to-hip ratio	0.87 ± 0.08	0.92 ± 0.08	<0.0001
BMI (kg/m^2)	25.61 ± 5.01	27.83 ± 5.69	<0.0001
Obesity (BMI ≥30)	16,862 (15.8)	3,744 (28.4)	<0.0001
Missing for BMI and waist-to-hip ratio	1,401 (1.3)	160 (1.2)	
Physical activity level			
Low	14,236 (13.4)	2,340 (17.7)	<0.0001
Medium	37,985 (35.7)	4,901 (37.1)	
High	46,435 (43.6)	4,809 (36.4)	
Missing	7,804 (7.3)	1,156 (8.8)	
Tobacco use			
Never	70,115 (65.9)	8,864 (67.1)	<0.0001
Former	13,416 (12.6)	2,011 (15.2)	
Current	22,371 (21.0)	2,264 (17.1)	
Missing	558 (0.5)	67 (0.5)	
AHEI			
Low tertile	35,148 (33.0)	4,256 (32.2)	<0.0001
Middle tertile	33,244 (31.2)	4,218 (31.9)	
High tertile	33,640 (31.6)	4,015 (30.4)	
Missing	4,428 (4.2)	717 (5.4)	

Data are mean ± SD or *n* (%).

history of diabetes, BMI, and (to a lesser extent) AHEI (Fig. 2 and Supplementary Appendix 4). After adjusting for other risk factors, the ORs of having diabetes with family history of diabetes were 2.76 in HICs, 2.62 in UMICs, 3.86 in LMICs, and 2.86 in LICs (*P* for trend <0.0001). For BMI ≥35 vs. <25 kg/m^2, fully adjusted ORs of diabetes were 2.62 including all country income groups, 5.57 in HICs, 3.12 in UMICs, 1.93 in LMICs, and 1.34 in LICs (*P* for trend <0.001). The association of AHEI with diabetes was modestly significant in UMICs (1.20) but reversed in LMICs (0.89), whereas no association was found in HICs and LICs. When adjusted for age and sex, and for each additional risk factor as well as ethnicity, there was still variability in diabetes prevalences in most country income categories; the highest prevalence was documented in LICs (*P* for trend <0.0001) (Table 2).

CONCLUSIONS

Our study has two main findings. First, diabetes prevalence was unexpectedly higher in LICs. Second, the higher rate in LICs is not fully explained by the conventional risk factors such as age, family history of diabetes, urban residency, low education level, low physical activity levels, tobacco consumption, unhealthy diet, increased BMI and waist-to-hip ratio, and ethnicity; this suggests that other factors associated with a country's income level are likely to contribute to the differences in diabetes prevalence.

Studies have shown a higher prevalence with older age (2,4–6), high versus low waist-to-hip ratio and BMI (3–10,14,15), family history of diabetes (3–5), urban versus rural residence (3–6,21,22), low versus high education level (3,14–22), low versus high physical activity levels (3,4,11), smoking (3,11,12), and unhealthy diet (3,4,28–33). These factors are reported in various countries but often differ in their prevalence and the degree of association with diabetes. For example, Southeast Asians have a higher rate of diabetes at a younger age despite much lower BMI levels compared with North Americans (5–8). In this study, all the described factors except smoking increased the risk of diabetes across the country income groups, even after multivariable adjustments. The absence of an impact of current and/or former smoking contrasts with previous findings related to diabetes incidence (3,11,12) and may be attributed to several factors, particularly the small number of smokers, different tobaccos, the quantity consume and the duration of consumption, and the cross-sectional nature of our study. The AHEI had no impact except in UMICs and LMICs, where the diet quality had an opposite effect; AHEI is largely related to fruits

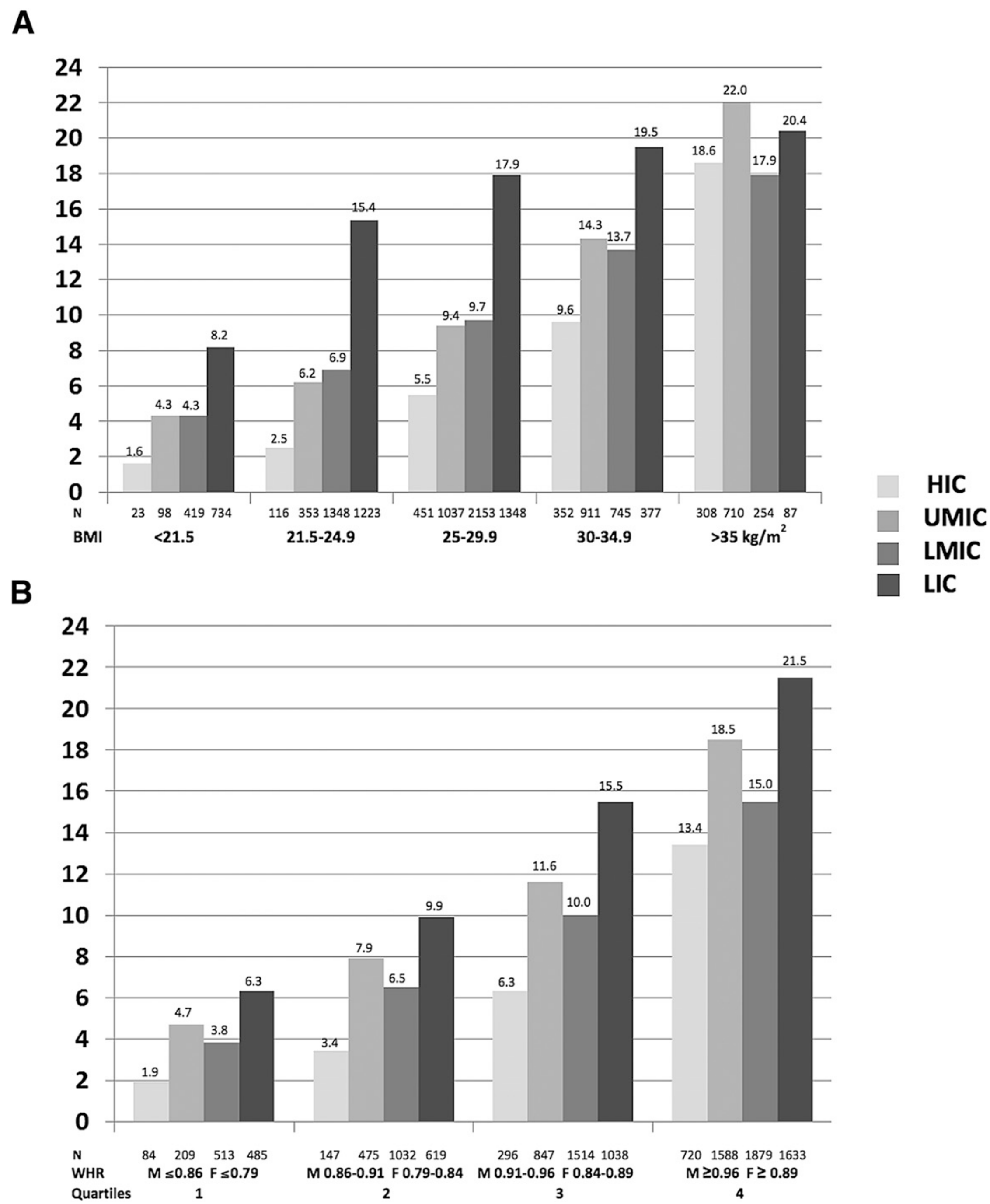

Figure 1—Adjusted diabetes prevalences (percentages) among income country groups according to BMI (*A*) and waist-to-hip ratio (WHR) (*B*). F, values for women; M, values for men.

and vegetables and fats but does not take into account the amount of refined carbohydrates consumed, which are known to be associated with higher diabetes risk (30,34). Further prospective research is needed to examine the impact of the quantity and duration of different tobacco consumption, as well as of the diet (e.g., dietary glycemic index), across countries with different income levels (29).

We found no evidence of heterogeneity with increasing age, male sex, residency location, education levels, waist-to-hip ratio, and physical activity levels. All these factors act similarly to increase the risk of diabetes and did not contribute to the variability in diabetes prevalence across countries with different economies. Although family history of diabetes and dietary pattern seemed to be differentially associated by country income groups, no consistent pattern was observed. By contrast, the significant interaction between groups at different BMI versus diabetes rates varied by the economic levels of the country groups. The reasons for this interaction remain unclear and may be the result of confounding with unmeasured factors that are influenced by a country's income or by chance. Alternatively, populations that are particularly susceptible to one risk

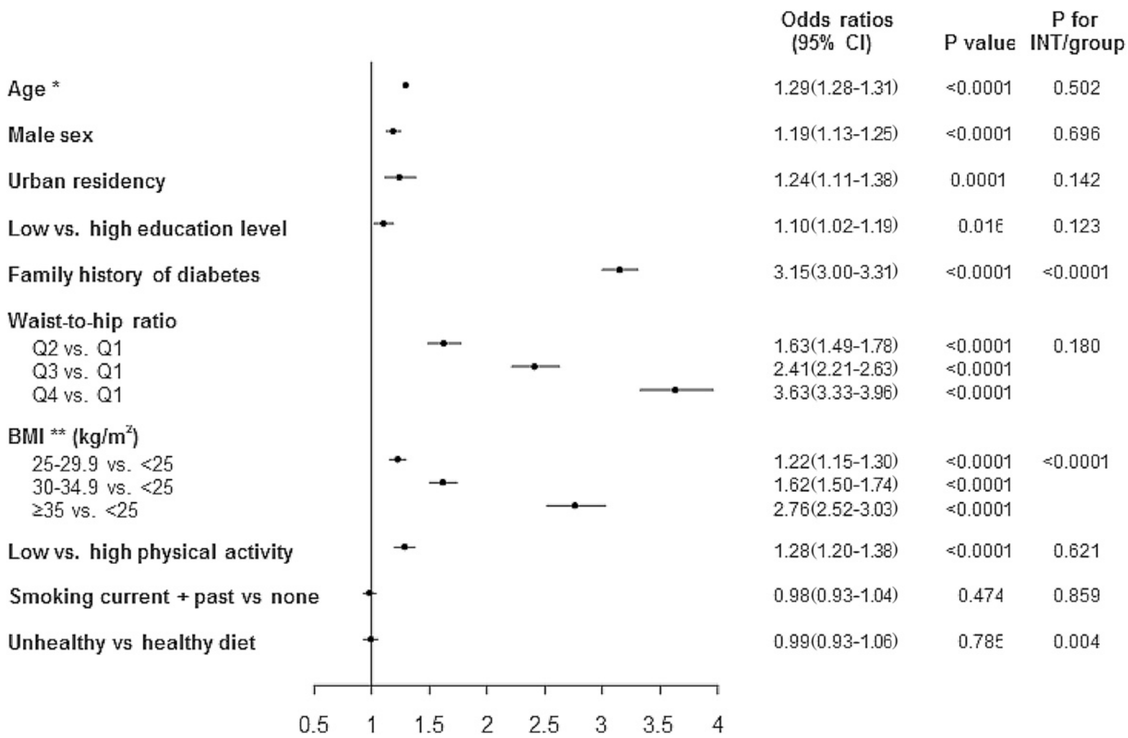

Figure 2—Multivariable adjusted ORs of risk factors associated with diabetes in the countries overall. The model included the following covariates: age, sex, residency location, BMI, waist-to-hip ratio, physical activity level, AHEI, combined former and current smoking, education level, and family history of diabetes. INT, interaction. *The OR for age is for every 5-year increase. **BMI. The waist-to-hip ratio quartiles (Q) represent different cut points for women (Q1 <0.79; Q2 0.79–0.84; Q3 0.84–0.89; Q4 >0.89) and for men (Q1 <0.86; Q2 0.86–0.91; Q3 0.91–0.96; Q4 >0.96). Low physical activity is equivalent to <600 MET-min/week; high physical activity equates to ≥3,000 MET-min/week. An unhealthy diet is based on the AHEI.

factor may develop diabetes at a lower level or threshold than other populations. This may indeed be the case for BMI in this study, which is strongly linked to diabetes at lower thresholds in LICs than in HICs (Fig. 1). Ethnicity could thus be an important factor explaining the variability of diabetes prevalence in each country category.

When adjusted for ethnicity and all the risk factors, the differences in the diabetes prevalence by country income group were modified, but the variability persisted. This underscores that the higher prevalence in LICs is not fully explained by the measured conventional risk factors and ethnicity. Other factors not measured in this study—such as genetic factors, fetal and early-life nutritional

Table 2—Diabetes prevalences adjusted by risk factors overall and each country grouping

Total participants/adjusted diabetes rates (*n*)	Overall	HIC	UMIC	LMIC	LIC
	119,666	14,757	26,088	55,430	23,391
1) Adjusted for age and sex*	9.45 (8.87–10.06)	6.62 (5.69–7.70)	11.08 (9.72–12.60)	8.73 (7.94–9.60)	12.34 (10.90–13.94)
2) Adjusted for *1*) + BMI	8.73 (8.21–9.29)	5.18 (4.52–5.93)	8.07 (7.17–9.07)	8.22 (7.56–8.92)	15.54 (13.99–17.23)
3) Adjusted for *2*) + waist-to-hip ratio	8.00 (7.51–8.51)	4.96 (4.32–5.70)	7.70 (6.82–8.67)	7.43 (6.82–8.09)	13.59 (12.18–15.13)
4) Adjusted for *3*) + low physical activity	8.19 (7.70–8.72)	5.12 (4.46–5.88)	7.89 (7.00–8.89)	7.60 (6.98–8.26)	13.96 (12.51–15.55)
5) Adjusted for *4*) + urban residency	8.16 (7.67–8.68)	4.82 (4.20–5.53)	7.94 (7.07–8.92)	7.65 (7.05–8.30)	13.97 (12.55–15.51)
6) Adjusted for *5*) + low education level	8.10 (7.62–8.62)	4.82 (4.20–5.53)	7.95 (7.07–8.92)	7.63 (7.03–8.28)	13.96 (12.54–15.51)
7) Adjusted for *6*) + unhealthy diet**	8.02 (7.54–8.54)	4.70 (4.09–5.39)	7.84 (6.97–8.81)	7.57 (6.97–8.21)	13.98 (12.54–15.54)
8) Adjusted for *7*) + smoking	8.02 (7.53–8.53)	4.71 (4.10–5.41)	7.85 (6.98–8.83)	7.58 (6.98–8.23)	13.93 (12.49–15.50)
9) Adjusted for *8*) + family history of diabetes	9.56 (8.99–10.16)	5.49 (4.83–6.24)	8.85 (7.95–9.84)	9.86 (9.15–10.62)	19.07 (16.94–21.39)
10) Adjusted for *9*) + ethnicity group	9.85 (9.35–10.38)	5.64 (4.85–6.56)	10.68 (9.45–12.05)	10.06 (9.03–11.20)	13.98 (10.57–18.26)

Data are % (95% CI). Community-level cluster was included as a random effect in the models. *Age is for every 5-year increase. **Unhealthy diet is based on the AHEI.

status, weight cycling, metabolic factors contributing to a low threshold for age, dietary factors including glycemic load, preventive attitude and behavior particularly in those with a family history of diabetes, psychosocial and social factors, and unrecognized or unmeasured environmental toxins or factors—may have contributed to the increased risk among LICs. Further studies are needed to determine the reasons for the increasing prevalence of diabetes with lower national income.

Although our study was not designed to assess the national prevalence of diabetes in the 18 countries individually, it documents diabetes in relatively unbiased samples of different segments of the population identified according to age, sex, and household location in groups of countries with different economy levels; however, caution is needed in extrapolating our information as being representative of each country. Methodological and/or biological factors may contribute to the variable rates. Although we did not measure plasma glucose in a central laboratory, it is unlikely that glucose analysis between centers explains the variability in diabetes prevalence between country income groups. The diabetes criteria used here underestimate the diabetes rates, since we neither measured hemoglobin A_{1c} nor performed oral glucose tolerance tests. Although we used a standardized approach for evaluating diet and physical activity, these markers are based on recall and are not assessed quantitatively as part of lifestyle over several years. Among the strengths of our study are the large population assessed during the same time period and the use of uniform methodology in countries with different economies. It generates new findings regarding diabetes prevalences and risk factor variability among people living in countries with different income levels.

In conclusion, adults living in poorer countries have higher rates of diabetes. Conventional risk factors do not fully account for the higher prevalence of diabetes in LICs. Future analyses of regional differences in diabetes prevalence and incidence should focus on identifying novel epidemiological and biological reasons for such differences.

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Author Contributions. G.R.D. initiated and designed the study, analyzed the data, and wrote the manuscript. H.C.G. designed the study, analyzed the data, and wrote the manuscript. X.Z. performed the statistical analyses. S.R. collected data. S.Y. designed the study and analyzed the data. All authors were responsible for the measurements and data acquisition in their center, and they read and approved the final version of the manuscript. The PURE project office staff, national coordinators, investigators, and key staff are listed in Supplementary Appendix 6. G.R.D. is the guarantor of this work and, as such, had full access to all 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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