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Type 2 diabetes mellitus unawareness, prevalence, trends and risk factors: National Health and Nutrition Examination Survey (NHANES) 1999–2010

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Abstract

Objectives: To determine whether the associations with key risk factors in patients with diagnosed and undiagnosed type 2 diabetes mellitus (T2DM) are different using data from the National Health and Nutrition Examination Survey (NHANES) from 1999 to 2010.

Methods: The study analysed the prevalence and association with risk factors of undiagnosed and diagnosed T2DM using a regression model and a multinomial logistic regression model. Data from the NHANES 1999–2010 were used for the analyses.

Results: The study analysed data from 10 570 individuals. The overall prevalence of diagnosed and undiagnosed T2DM increased significantly from 1999 to 2010. The prevalence of undiagnosed T2DM was significantly higher in non-Hispanic whites, in individuals <30 years old and in those with near optimal (130–159 mg/dl) or very high (≥220 mg/dl) non-high-density lipoprotein cholesterol levels compared with diagnosed T2DM. Body mass index, low economic status or low educational level had no effect on T2DM diagnosis rates. Though diagnosed T2DM was associated with favourable diet/carbohydrate intake behavioural changes, it had no effect on physical activity levels.

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Conclusion: The overall T2DM prevalence increased between 1999 and 2010, particularly for undiagnosed T2DM in patients that were formerly classified as low risk.

Keywords
Type 2 diabetes mellitus, NHANES, hypercholesterolaemia, hypertension, risk factors

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Introduction

In recent decades, the prevalence of type 2 diabetes mellitus (T2DM) has dramatically increased in the USA and worldwide.[1–3] Among individuals with T2DM, undiagnosed diabetes, which is shown to be associated with a body mass index (BMI) value $\geq 35\,kg/m^2$, is highly prevalent worldwide and is more likely to be associated with severe diabetic complications.[4] Another study noted that in the USA adolescent population, T2DM accounted for approximately half of adolescent diabetes and one-third of these cases were undiagnosed.[5] The economic costs associated with undiagnosed diabetes in the USA increased by 83% from 2007 to 2012, whereas the economic costs of diagnosed diabetes increased by 41% from 2007 to 2012.[6] During the period of undiagnosed diabetes, risks for micro- and macrovascular complications are elevated and it has been proposed that treating hyperglycaemia to prevent complications is more effective than treating these complications after they have developed.[7]

In other countries during the last decade, the percentage of patients with undiagnosed T2DM among all T2DM patients were reported to be 30% in Iran,[8] 50% in Germany[9] and about 75% in China.[10] According to the sixth edition of the Diabetes Atlas of International Diabetes Federation (2013), in some developing regions such as South-East Asia, Western Pacific, and Africa, the proportion of people with undiagnosed T2DM was equal to or greater than the population of patients diagnosed with T2DM.[11]

Risk factors for developing T2DM, including obesity and a sedentary lifestyle, play important roles in escalating the prevalence of diabetes.[12–14] In addition, behavioural and environmental factors have to be taken into consideration.[15,16] In particular, obesity at a young age is an important risk factor for T2DM.[17,18] Increased physical activity is associated with a reduced risk of diabetes in both men and women and even moderate activity is protective against T2DM.[19,20] Metabolic syndrome, a known precursor of T2DM, is characterized by insulin resistance and includes other metabolic abnormalities such as hypertension, hypercholesterolaemia and hypertriglyceridaemia.[21–23] The prevalence of metabolic syndrome has increased particularly in developing countries, perhaps as a result of the adoption of a Western diet (more processed foods), particularly in Asia.[24]

Although many risk factors for T2DM, such as BMI values $\geq 25\,kg/m^2$, have been investigated in the past, previous studies have not examined whether undiagnosed T2DM is correlated with other specifically identified risk factors and whether undiagnosed T2DM patients might be distinguished from diagnosed T2DM patients by these risk factors.

The objectives of the present study were to determine whether the associations with key risk factors in patients with diagnosed and undiagnosed T2DM are different, and to analyse the prevalence of diagnosed and

undiagnosed T2DM in groups defined by demographic characteristics and risk factors. Analysis of the National Health and Nutrition Examination Survey (NHANES) data from 1999 to 2010 should help to better describe the clinical profile of undiagnosed T2DM patients, which may serve as guidance for improving T2DM diagnosis in China.

Patients and methods

Study population

The NHANES is a cross-sectional health survey representing the noninstitutionalized USA population. NHANES was carried out by the National Center for Health Statistics, which is a branch of the Centers for Disease Control and Prevention. A complex, multistage, probability sampling strategy was used for data collection and subgroups of particular public interest were intensively sampled.[25] The study was approved by the National Center for Health Statistics Institutional Ethics Review Board and all adult participants provided written informed consent. In the current study, NHANES data were obtained from individuals interviewed between 1999 and 2010, which included men, and non-pregnant and non-lactating women (age range, 30–79 years). Participants answered questionnaires on demographics, lifestyle and medical factors. NHANES also obtained anthropometric measurements and biomarker data at mobile examination centres. This present study did not focus on adolescents and young adults because a young age of onset is a hallmark of type 1 diabetes.[26] Participants with missing exposure outcomes and covariate information were excluded from the study.

Type 2 diabetes mellitus status

Type 2 diabetes mellitus status (normoglycaemic, diagnosed diabetes, undiagnosed diabetes) was defined based on the fasting plasma glucose concentration, glycosylated haemoglobin (HbA1c) levels, and questionnaires. Diagnosed diabetes was defined by positive responses to one or more questions such as: ''Have you ever been told by a doctor that you have diabetes?'' and ''Are you now taking diabetic pills to lower your blood sugar?''. Undiagnosed diabetes was defined by negative responses to the questions above and a fasting glucose concentration $\geq$126 mg/dl ($\geq$7.0 mmol/l) or HbA1c $\geq$6.5%. Normoglycaemia was defined as fasting glucose <126 mg/dl and HbA1c <6.5% and no positive responses to the questionnaire.[27]

Risk factors

Hypertension was defined as a mean diastolic blood pressure $\geq$90 mmHg or a mean systolic blood pressure $\geq$140 mmHg or a positive response to the questions: ''Have you been told on two or more different visits that you had hypertension?'' or ''Are you taking prescribed medicine to lower blood pressure''. Prehypertension was defined as a mean diastolic blood pressure between 80 and 89 mmHg or a mean systolic blood pressure between 120 and 139 mmHg.[27,28] Physical activity was defined as the number of hours a subject spent on vigorous or moderate physical activity in a typical week.[29] Participants who claimed they carried out moderate or vigorous activity >120 h/week were considered implausible and excluded from the analysis. Hypercholesterolaemia was defined as a non-high-density lipoprotein cholesterol (non-HDL-C) level $\geq$130 mg/dl.[27] The levels of non-HDL-C were classified as follows based on the treatment goals recommended by the Adult Treatment Panel III final report: optimal <130 mg/dl; near optimal/above optimal 130–159 mg/dl; borderline high 160–189 mg/dl; high 190–219 mg/dl; and very high $\geq$220 mg/dl.[30]

Obesity categories were defined as follows: underweight (BMI $<18.5\,kg/m^2$); healthy (BMI 18.5–24.9 kg/m^2); overweight (BMI 25.0–29.9 kg/m^2); and obese (BMI $\geq$ 30.0 kg/m^2). Hypertriglyceridaemia was defined as triglyceride $\geq$150 mg/dl. Nutritional data were collected from 24-h dietary recall and were linked to a database of the nutrient composition of food for energy intake calculation. Energy intake was classified into four quartiles: first quartile (<1451.0 kcal); second quartile (1451.0–1912.9 kcal); third quartile (1913.0–2509.5 kcal); and fourth quartile ($\geq$2509.6 kcal). Carbohydrate intake was classified into four quartiles and the cut-off values were: first quartile (<175.0 g); second quartile (175.0–234.5 g); third quartile (234.6–310.0 g); and fourth quartile ($\geq$310.1 g). The cut-off values for categorizing physical activity into four quartiles were: first quartile (<0.23 h); second quartile (0.23–2.99 h); third quartile (3.00–8.99 h); and fourth quartile ($\geq$9.00 h).

Covariates

Race/ethnicity was determined by self-reported demographic questionnaires and categorized as 'Mexican American', 'Other Hispanic', 'Non-Hispanic White', 'Non-Hispanic Black', and 'other Race – including Multi-Racial'. Marital Status was categorized as 'Married', 'Widowed', 'Divorced', 'Separated', 'Never married', and 'Living with partner'. Family income-to-poverty ratio was determined by the family income and The Department of Health and Human Services' poverty guidelines. The cut-off values for the four quartiles of family income-to-poverty ratio were: first quartile (<1.20); second quartile (1.20–2.27); third quartile (2.28–4.20); and fourth quartile ($\geq$4.21). Education levels were determined by questions: 'What is highest degree or level of school completed or the highest degree received?' and categorized into 'Less than 9th grade', '9–11th grade (includes 12th grade with no diploma), 'high school graduation/General Educational Development or equivalent', 'some college or Associate of Arts degree', and 'college graduate or above'.

Insurance status was determined by responses to whether the participant was 'covered by health insurance or some other kind of health care plan, including health insurance obtained through employment or purchased directly, as well as government programmes like Medicare and Medicaid that provide medical care or help to pay for medical bills.

Statistical analyses

The prevalence of diagnosed or undiagnosed diabetes was established using SAS software version 9.3 (SAS Institute, Cary, NC, USA) to estimate percentage and 95% confidence intervals. The standard error was estimated by a Taylor series (linearization) method based on a complex sampling design. The Rao-Scott χ^2-test was a design-adjusted version of the Pearson χ^2-test, which was used for equality of prevalence for categorical variables. The two samples *t*-test was used in the PROC SURVEYREG (SAS Institute) to test for equality of continuous variables and two-proportion Z-tests were used to test proportions between diagnosed and undiagnosed diabetes groups. The PROC SURVEYREG described by NHANES tutorials, examined the age-adjusted prevalence of diagnosed and undiagnosed T2DM from 1999 to 2010, with the 2000 Census serving as the standard population. Linear trends of age-adjusted prevalence were assessed by regression models, with a 2-year survey cycle treated as a continuous variable. A *P*-value <0.05 was considered statistically significant.

Multinomial logistic regression was conducted using SAS software version 9.3 PROC SURVEYLOGISTIC (SAS Institute)

for each variable to assess the association between risk factors and diagnosed or undiagnosed diabetes. Model 1 was a logistic regression model to assess the association between diabetes status as a dependent variable and each risk factor as an independent variable. Model 2 was based on model 1 and adjusted according to socio-demographic variables including age, gender, race/ethnicity, education level, family income-to-poverty ratio, marital status, and insurance status. Model 3 was a multivariable logistic regression analysis of all variables from model 2 and adjusted for other risk factor variables including hypertension, hypercholesterolaemia, hypertriglyceridaemia, physical activity, carbohydrate intake and energy intake.

Results

This study included a cohort of adults from six NHANES 2-year survey cycles (1999–2010) consisting of 10 570 participants with clinical, demographic and laboratory data, which were divided into diagnosed diabetes, undiagnosed diabetes and normoglycaemic groups (Table 1). During the 12 years, participants with undiagnosed diabetes were significantly more likely to be male without insurance and have a higher carbohydrate and energy intake than those diagnosed with diabetes ($P < 0.05$ for all comparisons). Mean age, BMI, and the prevalence of hypertension, hypercholesterolaemia and hypertriglyceridaemia were similar between the diagnosed and undiagnosed groups (Table 1). Furthermore, the proportion of patients <30 years old was significantly higher in the undiagnosed than in the diagnosed diabetes group ($P = 0.0032$) (Table 2). Non-Hispanic white people comprised a significantly larger proportion of the undiagnosed diabetes group compared with the diagnosed diabetes group ($P = 0.0015$). Compared with diagnosed T2DM patients, individuals with undiagnosed T2DM were significantly more likely to have near optimal (130–159 mg/dl) or very high (≥220 mg/dl) non-HDL-C serum concentrations ($P < 0.05$ for both comparisons). A significantly higher proportion of diagnosed T2DM patients were in the first quartile and a significantly lower proportion were in the fourth quartile of energy and carbohydrate intakes compared with undiagnosed patients ($P < 0.05$ for all comparisons).

The overall age-adjusted prevalence for diagnosed diabetes and undiagnosed diabetes increased significantly from 4.96% and 3.45% in 1999 to 7.78% ($P = 0.008$) and 4.36% ($P = 0.041$) in 2010, respectively (Figure 1a). As expected, the prevalence of diagnosed diabetes was higher than undiagnosed diabetes in the total population and in the subgroups defined by risk factors (Figures 1a and 1b). The prevalence of diagnosed diabetes in non-Hispanic white and non-Hispanic blacks increased significantly during the 12 years ($P = 0.046$ and $P = 0.017$, respectively) and nearly doubled in 2009–2010 compared with 1999–2000. However, the increasing trend was not significant for undiagnosed diabetes in all race/ethnicity groups.

Among gender subgroups, females had a slightly lower prevalence than males for both diagnosed and undiagnosed diabetes in most years between 1999 and 2010 (Figure 1a). Neither diagnosed diabetes nor undiagnosed diabetes in gender subgroups exhibited significantly increasing trends. Both diagnosed diabetes and undiagnosed diabetes in participants with hypertension showed a significant increasing prevalence ($P = 0.009$ and $P = 0.004$, respectively) between 1999 and 2010 (Figure 1b). But the prevalence of diagnosed or undiagnosed diabetes did not change significantly over time for participants without hypertension. Similarly, participants with hypercholesterolaemia also displayed a significantly increasing prevalence for both

Table 1. Demographic and clinical characteristics of adult study participants ($n = 10\,570$) categorized as having diagnosed type 2 diabetes mellitus (T2DM), undiagnosed T2DM and being normoglycaemic from 1999 to 2010.

	Diagnosed T2DM ($n = 995$)	Undiagnosed T2DM ($n = 479$)	Normoglycaemic population ($n = 9096$)	Total study population ($n = 10\,570$)
Age, years	60.24 (59.05, 61.43)	58.90 (57.09, 60.71)	44.93 (44.30, 45.56)	46.45 (45.83, 47.07)
Family income-to-poverty ratio	2.66 (2.53, 2.79)	2.82 (2.63, 3.00)	3.10 (3.03, 3.17)	3.06 (2.99, 3.13)
Fibre intake, g	15.77 (15.05, 16.48)	15.63 (14.62, 16.65)	16.13 (15.79, 16.46)	16.08 (15.76, 16.41)
Carbohydrate intake, g	209.18 (202.46, 215.90)	241.35 (230.01, 252.70)*	267.10 (263.97, 270.23)	262.30 (259.21, 265.39)
Energy intake, kcal	1814.56 (1756.83, 1872.29)	2074.14(1979.21, 2169.07)*	2192.11 (2167.16, 2217.05)	2162.59 (2138.52, 2186.66)
Body mass index, kg/m^2	32.26 (31.69, 32.82)	32.56 (31.58, 33.54)	27.94 (27.76, 28.11)	28.39 (28.21, 28.57)
Physical activity, h	5.92 (4.49, 7.34)	6.49 (5.07, 7.90)	8.47 (8.03, 8.91)	8.23 (7.82, 8.64)
Male[a]	501 (49.35)	284 (60.95)*	4519 (48.62)	5304 (49.10)
Hypertension[a]	695 (66.08)	305 (61.86)	2994 (28.12)	3994 (31.86)
Hypercholesterolaemia[a]	788 (79.22)	399 (82.60)	6314 (68.92)	7501 (70.09)
Hypertriglyceridaemia[a]	443 (48.75)	247 (49.86)	2554 (27.68)	3244 (29.87)
Obesity[a]	548 (58.81)	255 (56.78)	2845 (29.85)	3648 (32.74)
Insurance[a]	870 (90.22)	388 (84.95)**	7025 (81.05)	8283 (81.81)

Data presented as mean (95% confidence interval) or *n* of patients (%).

[a]Percentage values are adjusted by sampling weights that results in disconcordance between raw frequencies and percentages due to uneven sampling weights among races.

*P-value < 0.01, a significant difference between diagnosed and undiagnosed T2DM; **P-value < 0.05, a significant difference between diagnosed and undiagnosed T2DM; two samples *t*-tests were used to test the equality of means and two-proportion Z-tests were used to test proportions between diagnosed and undiagnosed diabetes groups.

Table 2. Demographic characteristics of adult study participants categorized as having diagnosed type 2 diabetes mellitus (T2DM; $n = 995$) and undiagnosed T2DM ($n = 479$) stratified according to demographic, cardiometabolic and other variables.

	Diagnosed T2DM ($n = 995$)	Undiagnosed T2DM ($n = 479$)	Statistical significance[a]
Age, years			
<30	3 (0.36; 0.00, 0.83)	12 (2.58; 0.96, 4.21)	$P = 0.0032$
30–39	37 (6.43; 3.80, 9.06)	40 (9.44; 5.78, 13.11)	NS
40–49	129 (18.47; 14.48, 22.46)	60 (15.99; 11.11, 20.86)	NS
50–59	207 (23.10; 19.67, 26.52)	94 (25.61; 19.49, 31.73)	NS
60–69	327 (26.95; 23.65, 30.25)	134 (23.28; 18.87, 27.68)	NS
>70	292 (24.69; 21.36, 28.03)	139 (23.09; 18.46, 27.73)	NS
Race/ethnicity			
Mexican American	244 (8.38; 6.07, 10.69)	96 (7.24; 5.20, 9.28)	NS
Other Hispanic	73 (5.96; 3.12, 8.80)	27 (3.71; 1.66, 5.77)	NS
Non-Hispanic White	398 (62.67; 57.43, 67.92)	245 (72.43; 67.23, 77.64)	$P = 0.0015$
Non-Hispanic Black	241 (15.69; 12.51, 18.87)	97 (12.52; 9.66, 15.39)	NS
Other Race – including Multi-Racial	39 (7.29; 4.64, 9.95)	14 (4.09; 1.09, 7.09)	NS
Educational level			
Less than 9th grade	223 (13.68; 11.10, 16.26)	92 (10.76; 7.85, 13.67)	NS
9–11th grade (includes 12th grade with no diploma)	179 (14.24; 11.48, 16.99)	83 (13.51; 10.06, 16.67)	NS
High school graduation/ GED or equivalent	230 (27.07; 23.07, 31.08)	130 (31.79; 26.40, 37.18)	NS
Some college or AA degree	239 (28.79; 24.40, 33.18)	109 (25.21; 19.98, 30.43)	NS
College graduate or above	124 (16.22; 12.81, 19.63)	65 (18.73; 13.55, 23.90)	NS
Marital status			
Married	585 (62.15; 58.80, 65.50)	266 (58.44; 52.85, 64.03)	NS
Widowed	148 (12.54; 10.20, 14.89)	79 (12.80; 9.60, 16.00)	NS
Divorced	128 (12.77; 10.29, 15.24)	61 (13.89; 9.49, 18.29)	NS
Separated	38 (3.22; 1.84, 4.61)	11 (1.93; 0.70, 3.16)	NS
Never married	62 (5.87; 3.86, 7.88)	38 (8.02; 5.38, 10.67)	NS
Living with partner	34 (3.44; 2.05, 4.83)	24 (4.92; 2.52, 7.31)	NS
Family income-to-poverty ratio			
First quartile	280 (19.96; 17.16, 22.76)	121 (17.25; 13.06, 21.44)	NS
Second quartile	304 (29.16; 25.58, 32.75)	151 (28.94; 23.42, 34.46)	NS
Third quartile	240 (25.56; 21.33, 29.80)	107 (26.10; 20.34, 31.86)	NS
Fourth quartile	171 (25.31; 21.08, 29.55)	100 (27.71; 22.35, 33.08)	NS
Obesity			
Underweight	5 (0.32; 0.02, 0.62)	3 (0.32; 0.00, 0.71)	NS
Normal	139 (15.10; 11.97, 18.23)	71 (13.43; 9.92, 16.94)	NS
Overweight	305 (26.06; 22.44, 29.67)	150 (29.47; 24.67, 34.27)	NS
Obese	546 (58.52; 54.25, 62.79)	255 (56.78; 50.96, 62.60)	NS
Hypertension			
Normal	148 (17.46; 13.96, 20.97)	76 (18.45; 13.39, 23.51)	NS
Hypertension	695 (66.08; 62.03, 70.13)	305 (61.86; 56.12, 67.60)	NS
Prehypertension	152 (16.46; 13.54, 19.37)	98 (19.69; 15.60, 23.78)	NS

(continued)

Table 2. Continued.

	Diagnosed T2DM ($n = 995$)	Undiagnosed T2DM ($n = 479$)	Statistical significance[a]
Non-HDL-C level			
Optimal	177 (46.12; 41.77, 50.48)	39 (31.95; 26.59, 37.31)	$P < 0.0001$
Near optimal/ above optimal	275 (24.43; 20.94, 27.92)	99 (30.16; 26.01, 34.32)	$P = 0.0326$
Borderline high	253 (17.78; 14.79, 20.77)	144 (20.09; 15.20, 24.98)	NS
High	169 (6.82; 4.03, 9.60)	99 (8.27; 5.55, 11.00)	NS
Very high	121 (4.86; 3.09, 6.62)	98 (9.52; 6.48, 12.56)	$P = 0.0130$
Energy intake			
First quartile	394 (34.44; 30.33, 38.56)	140 (24.03; 19.82, 28.25)	$P = 0.0006$
Second quartile	277 (27.77; 24.04, 31.49)	119 (23.21; 18.68, 27.75)	NS
Third quartile	204 (23.36; 20.00, 26.71)	116 (25.32; 20.21, 30.42)	NS
Fourth quartile	120 (14.43; 11.69, 17.17)	104 (27.44; 21.44, 33.44)	$P = 0.0001$
Carbohydrate intake			
First quartile	385 (35.48; 31.71, 39.25)	152 (29.06; 23.69, 34.43)	$P = 0.0290$
Second quartile	299 (31.30; 27.94, 34.66)	124 (25.42; 20.30, 30.53)	$P = 0.0452$
Third quartile	211 (23.00; 19.63, 26.37)	104 (23.13; 18.46, 27.80)	NS
Fourth quartile	100 (10.22; 7.57, 12.86)	99 (22.39; 18.20, 26.59)	$P < 0.0001$
Physical activity			
First quartile	384 (31.61; 27.75, 35.47)	147 (28.38; 23.66, 33.11)	NS
Second quartile	245 (28.04; 24.96, 31.13)	124 (29.58; 24.80, 34.36)	NS
Third quartile	210 (22.96; 19.02, 26.91)	108 (20.84; 15.80, 25.89)	NS
Fourth quartile	156 (17.38; 14.08, 20.68)	100 (21.19; 16.13, 26.26)	NS

Data presented as *n* of patients (%; 95% confidence interval); percentage values are adjusted by sampling weights that results in disconcordance between raw frequencies and percentages due to uneven sampling weights among races.
[a]Group with diagnosed T2DM compared with the undiagnosed T2DM group; two-proportion Z-tests were used to test the equality of proportions between diagnosed and undiagnosed diabetes.
GED, General Educational Development; AA, Associate of Arts; Non-HDL-C, non-high-density lipoprotein cholesterol; NS, no significant between-group difference $P \geq 0.05$.

diagnosed ($P = 0.020$) and undiagnosed T2DM ($P = 0.046$), which was not observed in patients without hypercholesterolaemia.

The prevalence of diagnosed diabetes increased significantly in participants with and without hypertriglyceridaemia ($P = 0.040$ and $P = 0.030$, respectively), whereas hypertriglyceridaemia had no effect on participants with undiagnosed diabetes. The prevalence of diagnosed diabetes increased over the years in obese individuals and those covered by insurance ($P = 0.018$ and $P = 0.010$, respectively), but these factors did not influence changes in the prevalence of undiagnosed diabetes (Figure 1b).

Hypertension was associated with an increased risk of both diagnosed and undiagnosed diabetes (odd ratios [ORs] and 95% confidence interval [CI] were 4.98 [4.19, 5.92], $P < 0.0001$, and 4.15 [3.26, 5.27], $P < 0.0001$, respectively) (Table 3 and Table 4, model 1). After adjustment for sociodemographic and other risk factors, the ORs were somewhat attenuated (OR 1.69, 95% CI 1.29, 2.22, $P = 0.0001$ for diagnosed diabetes; and OR 1.86, 95% CI 1.31, 2.64, $P = 0.0005$ for undiagnosed diabetes; Table 3 and Table 4, model 3), but still significant. Similar to hypertension, participants with obesity and hypertriglyceridaemia also had

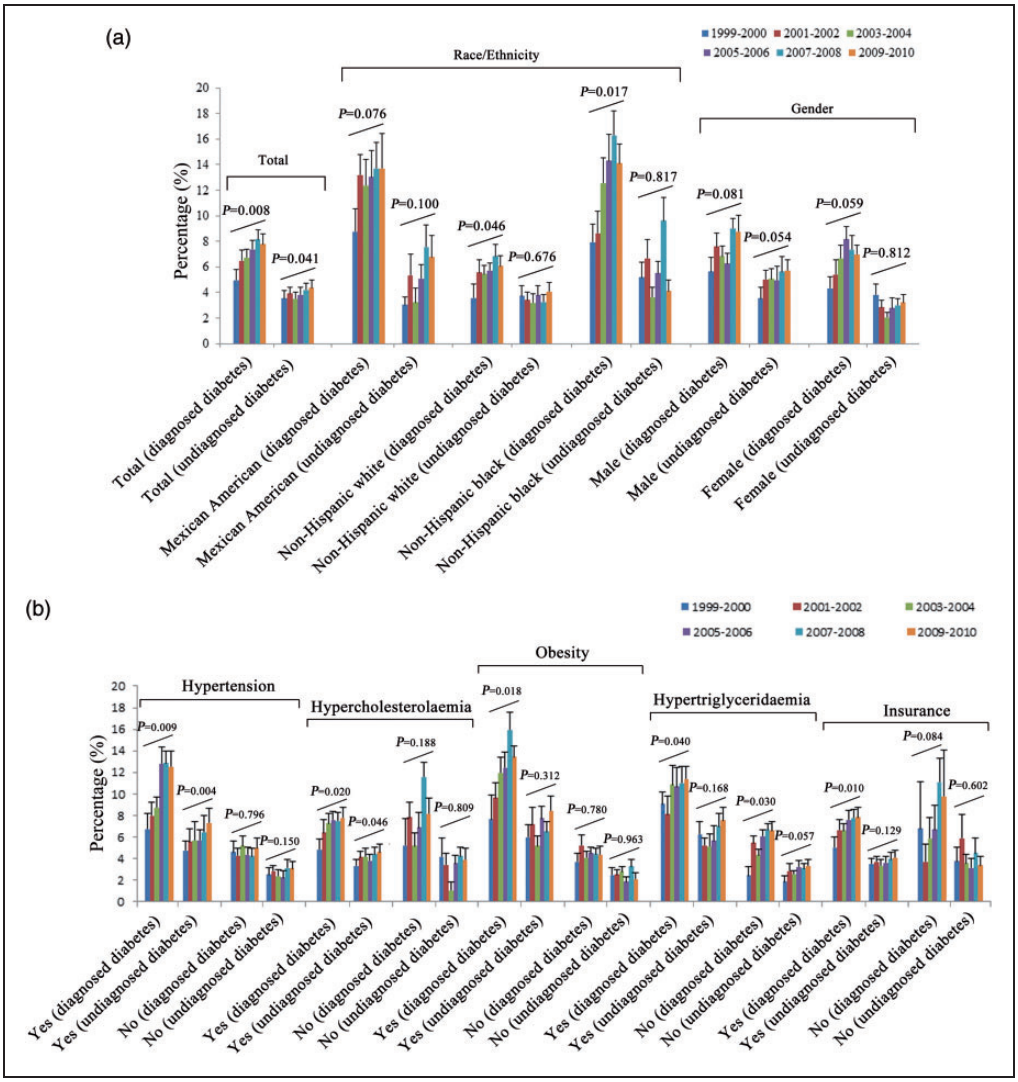

Figure 1. Age-adjusted prevalence of diagnosed and undiagnosed type 2 diabetes mellitus in the total population and in race/ethnicity as well as gender subgroups (a); and in hypertension, hypercholesterolaemia, obesity, hypertriglyceridaemia and insurance subgroups (b) from the National Health and Nutrition Examination Survey 1999 to 2010 (error bars are SE). NS, no significant between-group difference $P \geq 0.05$). The colour version of this figure is available at: http://imr.sagepub.com.

a significantly higher risk of being diagnosed with diabetes (OR and 95% CI were 3.00 [2.32, 3.89], $P < 0.0001$ for obesity; and 1.84 [1.40, 2.43], $P < 0.0001$ for hypertriglyceridaemia) and undiagnosed diabetes (OR and 95% CI were 2.49 [1.74, 3.58], $P < 0.0001$ for obesity; and 1.45 [1.06, 1.99], $P = 0.0213$ for hypertriglyceridaemia) (Table 3 and Table 4, model 3). Hypercholesterolaemia was significantly associated with both diagnosed diabetes and undiagnosed diabetes in the crude model (Table 3 and Table 4, model 1),

Table 3. Odd ratio (OR) and 95% confidence interval (95% CI) for the association between diagnosed type 2 diabetes mellitus (T2DM) and risk factors.

	Diagnosed T2DM					
	Model 1		Model 2		Model 3	
Risk factor	OR (95% CI)	Statistical significance	OR (95% CI)	Statistical significance	OR (95% CI)	Statistical significance
Hypertension	4.98 (4.19, 5.92)	$P < 0.0001$	2.28 (1.74, 2.97)	$P < 0.0001$	1.69 (1.29, 2.22)	$P = 0.0001$
Hypercholesterolaemia	1.72 (1.38, 2.15	$P < 0.0001$	1.17 (0.83, 1.66)	NS	0.86 (0.61, 1.21)	NS
Hypertriglyceridaemia	2.49 (2.08, 2.98)	$P < 0.0001$	2.00 (1.54, 2.60)	$P < 0.0001$	1.84 (1.40, 2.43)	$P < 0.0001$
Obesity	3.35 (2.81, 4.00)	$P < 0.0001$	3.51 (2.74, 4.48)	$P < 0.0001$	3.00 (2.32, 3.89)	$P < 0.0001$
Physical activity						
First quartile	Reference		Reference		Reference	
Second quartile	0.63 (0.51, 0.76)	$P < 0.0001$	1.01 (0.70, 1.47)	NS	1.05 (0.72, 1.53)	NS
Third quartile	0.45 (0.35, 0.57)	$P < 0.0001$	0.76 (0.55, 1.06)	NS	0.76 (0.53, 1.09)	NS
Fourth quartile	0.36 (0.28, 0.47)	$P < 0.0001$	0.57 (0.38, 0.87)	$P = 0.0096$	0.66 (0.42, 1.03)	NS
Carbohydrate intake						
First quartile	Reference		Reference		Reference	
Second quartile	0.78 (0.64, 0.96)	$P = 0.0187$	0.67 (0.50, 0.90)	$P = 0.0076$	0.65 (0.45, 0.96)	$P = 0.0292$
Third quartile	0.52 (0.41, 0.66)	$P < 0.0001$	0.52 (0.37, 0.74)	$P = 0.0002$	0.44 (0.28, 0.68)	$P = 0.0003$
Fourth quartile	0.21 (0.15, 0.28)	$P < 0.0001$	0.28 (0.18, 0.45)	$P < 0.0001$	0.21 (0.09, 0.48)	$P = 0.0002$
Energy intake						
First quartile	Reference		Reference		Reference	
Second quartile	0.68 (0.54, 0.86)	$P = 0.0011$	0.80 (0.58, 1.10)	NS	0.99 (0.67, 1.40)	NS
Third quartile	0.51 (0.41, 0.63)	$P < 0.0001$	0.55 (0.38, 0.81)	$P = 0.0024$	0.82 (0.52, 1.29)	NS
Fourth quartile	0.27 (0.21, 0.35)	$P < 0.0001$	0.44 (0.27, 0.71)	$P = 0.0008$	0.86 (0.42, 1.77)	NS

NS, no significant association ($P \geq 0.05$).

but the associations were attenuated and not statistically significant after sociodemographic and other factors were adjusted in the models (Table 3 and Table 4, models 2 and 3).

Compared with subjects with the lowest physical activity quartile 1 (Q1, reference), the ORs of having diagnosed diabetes and undiagnosed diabetes decreased in participants who underwent more physical activity (Q4 ORs and 95% CIs were 0.36 [0.28, 0.47], $P < 0.0001$ for diagnosed diabetes; and 0.49 [0.36, 0.68], $P < 0.0001$ for undiagnosed diabetes) (Table 3 and Table 4, model 1). After adjustment for sociodemographic factors, only the Q4 of physical activity was associated with diagnosed diabetes (OR and 95% CI 0.57 [0.38, 0.87], $P = 0.0096$) and the association was not significant in undiagnosed diabetes (OR and 95% CI 0.69 [0.42, 1.13]) (Table 3 and Table 4, model 2).

Subjects with a higher quartile of carbohydrate intake showed greater differences between diagnosed diabetes and undiagnosed diabetes. For example, the ORs of having diagnosed diabetes and undiagnosed diabetes were 0.65 and 0.64 respectively in Q2, but the ORs were 0.21 (95% CI 0.09, 0.48, $P = 0.0002$) and 0.82 (95% CI 0.41, 1.63) respectively in Q4 (Table 3 and Table 4, model 3). The higher quartile of the carbohydrate intake group had a lower risk of having diagnosed diabetes.

The sociodemographic factors adjusted ORs (95% CI) for energy intake in those with diagnosed diabetes were 0.80 (0.58,

Table 4. Odd ratio (OR) and 95% confidence interval (95% CI) for the association between undiagnosed type 2 diabetes mellitus (T2DM) and risk factors.

	Undiagnosed T2DM					
	Model 1		Model 2		Model 3	
Risk factor	OR (95% CI)	Statistical significance	OR (95% CI)	Statistical significance	OR (95% CI)	Statistical significance
Hypertension	4.15 (3.26, 5.27)	$P < 0.0001$	2.25 (1.55, 3.25)	$P < 0.0001$	1.86 (1.31, 2.64)	$P = 0.0005$
Hypercholesterolaemia	2.14 (1.61, 2.86)	$P < 0.0001$	1.34 (0.84, 2.12)	NS	1.06 (0.66, 1.71)	NS
Hypertriglyceridaemia	2.60 (2.08, 3.24)	$P < 0.0001$	1.71 (1.25, 2.35)	$P = 0.0008$	1.45 (1.06, 1.99)	$P = 0.0213$
Obesity	3.09 (2.43, 3.93)	$P < 0.0001$	2.87 (2.05, 4.03)	$P < 0.0001$	2.49 (1.74, 3.58)	$P < 0.0001$
Physical activity						
First quartile	Reference		Reference		Reference	
Second quartile	0.74 (0.55, 0.98)	$P = 0.0338$	0.84 (0.51, 1.37)	NS	0.88 (0.54, 1.45)	NS
Third quartile	0.45 (0.33, 0.63)	$P < 0.0001$	0.68 (0.43, 1.09)	NS	0.74 (0.45, 1.21)	NS
Fourth quartile	0.49 (0.36, 0.68)	$P < 0.0001$	0.69 (0.42, 1.13)	NS	0.81 (0.48–1.37)	NS
Carbohydrate intake						
First quartile	Reference		Reference		Reference	
Second quartile	0.78 (0.56, 1.07)	NS	0.61 (0.39, 0.96)	$P = 0.0323$	0.64 (0.39, 1.05)	NS
Third quartile	0.64 (0.47, 0.87)	$P = 0.0038$	0.66 (0.44, 0.99)	$P = 0.0457$	0.70 (0.40, 1.23)	NS
Fourth quartile	0.55 (0.41, 0.75)	$P = 0.0002$	0.75 (0.48, 1.18)	NS	0.82 (0.41, 1.63)	NS
Energy intake						
First quartile	Reference		Reference		Reference	
Second quartile	0.81 (0.62, 1.06)	NS	0.92 (0.63, 1.35)	NS	1.16 (0.78, 1.75)	NS
Third quartile	0.79 (0.58, 1.07)	NS	0.71 (0.48, 1.05)	NS	0.92 (0.53, 1.60)	NS
Fourth quartile	0.74 (0.54, 1.02)	NS	0.99 (0.57, 1.71)	NS	1.30 (0.60, 2.80)	NS

NS, no significant association ($P \geq 0.05$).

1.10) for Q2, 0.55 (0.38–0.81; $P = 0.0024$) for Q3, and 0.44 (0.27, 0.71; $P = 0.0008$) for Q4 (Table 3, model 2), but this was not found in higher quartiles of caloric intake for undiagnosed diabetes (Table 4, model 2).

Discussion

The proportion of undiagnosed diabetes remains high despite enhanced surveillance programmes, in particular national health programmes in the US,[31–34] which may in part be due to a lack of health-related quality of life deficits,[35] at least in the initial stages of undiagnosed diabetes. However, a recent study reported a prevalence of 32.55% of microvascular complications in asymptomatic newly diagnosed T2DM patients.[36] In an earlier study undertaken in 300 newly diagnosed T2DM patients, 38.6% had coronary heart disease and 17.7% had silent myocardial infarctions; with microvascular complications already present (neuropathy [27.5%], nephropathy [20.2%] and retinopathy [17.9%]), which had presumably developed during the asymptomatic preclinical phase of the disease.[37] Another study showed that among 1917 non-demented men and women, those with undiagnosed diabetes had the lowest cognitive performance.[38] In order to develop policies and strategies for improving the detection of T2DM, particularly in developing countries, noninvasive risk models for predicting undiagnosed prevalent diabetes mainly based on age, BMI, waist

circumference and hypertension have been developed.[39] A previous study noted that diabetes diagnosis in the US varied considerably between individuals with different BMIs.[4] In individuals with BMIs $\geq 35\,kg/m^2$, diagnosed diabetes increased markedly from 4.9% in 1960 to 8.6% during 1976–1980 and 15.1% in 1999–2000, whereas undiagnosed diabetes decreased from 12.5% during 1976–1980 to 3.2% in 1999–2000 in the same group.[4] In contrast, changes in prevalence within the BMI strata $\leq 35\,kg/m^2$ were modest and there was no increase in the percentage of total cases that were diagnosed.[4] The findings of the current study were similar since BMI and obesity were not associated with the prevalence of undiagnosed T2DM, which might reflect increased awareness rates amongst obese people (Table 2). However, BMI as a risk factor for developing T2DM has been shown to vary between ethnic groups[40] and the BMI threshold for T2DM screening of American Asians has been modified to $23\,kg/m^2$ by the American Diabetes Association.[41] Although the percentage of individuals covered by insurance was significantly lower in undiagnosed versus diagnosed T2DM patients in the present study, the family income-to-poverty ratio and educational status unexpectedly did not have any influence on whether T2DM was diagnosed or not, indicating that public health measures were effective for poorer people and those with lower levels of education.[42]

Non-Hispanic white people were the majority of the surveyed population and the only ethnic group with a significantly higher undiagnosed prevalence of T2DM. Although the prevalence of undiagnosed T2DM was lower in non-Hispanic whites compared with other ethnic groups (Figure 1a), the predominant proportion of non-Hispanic whites in the total undiagnosed T2DM population implies that this population deserves to be the major target for addressing T2DM unawareness. Low HDL-C levels have been noted to contribute to the pathophysiology of T2DM,[43,44] and a larger proportion of individuals with very high ($\geq$220 mg/dl) non-HDL-C had undiagnosed diabetes, which might reflect a lack of hypercholesterolaemia awareness. Unexpectedly, the rate was also higher in people with non-HDL-C levels of 130–159 mg/dl, which might have been a factor for not expecting a diagnosis of T2DM and thereby a reason for undiagnosed diabetes. In addition, compared with individuals with diagnosed diabetes, those individuals with undiagnosed diabetes comprised a larger proportion of the <30 years age group, indicating that younger people may care less about their health and therefore have a higher level of T2DM unawareness.

Several studies have reported that a high carbohydrate intake is associated with a risk of developing diabetes,[45–47] findings consistent with the results of the present study. In a fully adjusted model (model 3), carbohydrate intake was associated with diagnosed diabetes but not with undiagnosed diabetes (Table 3 and Table 4), and carbohydrate and energy uptake was lower in diagnosed patients (Table 2), indicating effective dietary lifestyle intervention in diagnosed T2DM patients.[12] In contrast, awareness of T2DM did not significantly drive physical activity changes among patients in different physical activity quartiles, which may imply that unlike dietary intake, T2DM awareness is not a determining factor for physical activity behaviour change. Among the cardio-metabolic factors, hypertension, hypertriglyceridaemia and obesity were strongly associated with both diagnosed and undiagnosed diabetes, although hypercholesterolaemia did not reach statistical significance after adjusting for covariates and confounders (Table 3 and Table 4). Physical activity displayed an inverse association with diabetes in the three models used in this present study, especially in

model 1, findings that were consistent with those of other research.[48]

The present research had several limitations. First, it was a cross-sectional survey study and directional cause–effect relationships between risk factors and diabetes risk cannot be inferred. Secondly, there were issues with dietary intake recall, since participants may have under-reported their food intake or changed their usual dietary pattern because they participated in the survey.[49] Thirdly, due to a change of the measuring method, some variables may display slight differences. It is also important to note that the prevalence, trends and possibly patient characteristics of undiagnosed T2DM patients in developing countries such as China may be distinct from those in the US. Thus, country-specific epidemiological studies need to be carried out to address the unmet T2DM unawareness, since the rate of undiagnosed diabetes is considerably higher in China then in the US.[10]

In conclusion, this present study investigated the differences in the prevalence rates of diagnosed and undiagnosed T2DM and the associations with risk factors using data from NHANES from 1999 to 2010. The overall prevalence rates of diagnosed and undiagnosed T2DM increased significantly from 1999 to 2010 and were associated with hypertension, hypertriglyceridaemia, obesity and hypercholesterolaemia. Subgroup analyses revealed increasing rates of hypertension, hypercholesterolaemia, obesity, hypertriglyceridaemia, and insurance coverage in diagnosed patients and increasing rates of hypertension and hypercholesterolaemia in undiagnosed T2DM patients from 1999 to 2010. The rate of undiagnosed T2DM was higher in males, in those younger than 30 years of age, non-Hispanic whites or those with very high non-HDL-C levels ($\geq$220 mg/dl). It was also higher in individuals with near optimal non-HDL-C levels of 130–159 mg/dl, as well as in patients without health insurance compared with patients diagnosed with T2DM. Since the rate of undiagnosed T2DM was high particularly in people that are considered to be at a low risk of developing T2DM, a Chinese approach for diabetes screening should involve general population surveillance, which is covered by public health insurance.

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Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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