Ethnicity and Sex Affect Diabetes Incidence and Outcomes

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OBJECTIVE — Diabetes guidelines recommend aggressive screening for type 2 diabetes in Asian patients because they are considered to have a higher risk of developing diabetes and potentially worse prognosis. We determined incidence of diabetes and risk of death or macrovascular complications by sex among major Asian subgroups, South Asian and Chinese, and white patients with newly diagnosed diabetes.

RESEARCH DESIGN AND METHODS — Using population-based administrative data from British Columbia and Alberta, Canada (1997–1998 to 2006–2007), we identified patients with newly diagnosed diabetes aged ≥35 years and followed them for up to 10 years for death, acute myocardial infarction, stroke, or hospitalization for heart failure. Ethnicity was determined using validated surname algorithms.

RESULTS — There were 15,066 South Asian, 17,754 Chinese, and 244,017 white patients with newly diagnosed diabetes. Chinese women and men had the lowest incidence of diabetes relative to that of white or South Asian patients, who had the highest incidence. Mortality in those with newly diagnosed diabetes was lower in South Asian (hazard ratio 0.69 [95% CI 0.62–0.76], $P < 0.001$) and Chinese patients (0.69 [0.63–0.74], $P < 0.001$) then in white patients. Risk of acute myocardial infarction, stroke, or heart failure was similar or lower in the ethnic groups relative to that of white patients and varied by sex.

CONCLUSIONS — The incidence of diagnosed diabetes varies significantly among ethnic groups. Mortality was substantially lower in South Asian and Chinese patients with newly diagnosed diabetes than in white patients.

Diabetes Care 34:96–101, 2011

Over the past 20 years, we have seen an explosive increase in the number of cases of diabetes worldwide. The number of individuals with diabetes is expected to more than double by the year 2025. This will have a tremendous public health impact given the high rates of acute myocardial infarction [AMI], heart failure, stroke, and death that follow diabetes.

Along with advancing age and increases in obesity prevalence, one putative factor thought to be contributing to this global epidemic is an escalation in the population of nonwhite groups at higher risk for diabetes. The largest increases in diabetes worldwide are occurring in developing countries. The prevalence of diabetes in urban areas of India is as high as 18% (1) and a recent study shows a threefold increase in diabetes prevalence in certain areas of China (2). South Asian and Chinese groups may have a greater susceptibility to developing diabetes due to a predisposition to insulin resistance in the presence of environmental factors including diet and physical inactivity. Differences in health care systems, limited access to health services, and social deprivation can further compound the risk of developing diabetes and its complications.

Our current understanding of the incidence and prognosis of diabetes in South Asian and Chinese men and women is limited. There is a paucity of ethnicity- and sex-stratified longitudinal population-based studies. Incidence has only been estimated from prevalence data in cross-sectional studies under various health care systems. General practitioner clinic and general population surveys in Western countries uniformly observe a higher prevalence of diabetes in South Asian respondents compared with that in the general population (3,4). Results among Chinese migrants are inconsistent, with prevalence rates up to 14% (5). Further, it is unclear whether these groups also have a greater susceptibility to developing complications of diabetes. We conducted a large, population-based study in two Canadian provinces to determine the incidence of diabetes and the risk of death and macrovascular complications including AMI, heart failure, and stroke among South Asian, Chinese, and white women and men up to 10 years after a new diagnosis of diabetes.

RESEARCH DESIGN AND METHODS

Data sources

We used administrative data from two Canadian provinces (British Columbia 1993–2006 and Alberta 1994–2007) that comprise 44% of all Chinese and 34% of all South Asian people in Canada (6). Physician claims files contain information for each hospital and outpatient encounter for each patient. Hospital discharge abstracts include all inpatient services for all hospitals within these provinces and contain primary and secondary discharge diagnosis codes of the ICD-9 and ICD-10, with up to 25 diagnosis fields per individual admission. Physician claims and hospital discharge data are updated daily and include all patients with provincial health

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Received 5 May 2010 and accepted 11 October 2010. Published ahead of print at http://care.diabetesjournals.org on 26 October 2010. DOI: 10.2337/dc10-0865.

insurance. Under a universal health care system, virtually all residents of these provinces are covered by health insurance ensuring completeness of data. The provincial population registry contains surname, birth date, sex, and postal code on residents of the province. Population counts from provincial registries correspond to census population estimates (7), but, unlike census data, provide actual counts in inter-census years. All deaths are reported to the Vital Statistics database, and date of death was obtained by linking to Vital Statistics via a unique personal health number.

Study population

All residents of these provinces with a physician diagnosis of diabetes were included. Individuals with diabetes were defined as those with an ICD-9 or ICD-10 code for diabetes (ICD-9-CM: 250.x; ICD-10: E109, E119, E139, E149, E101, E111, E131, E141, E105, E115, E135, and E145) for at least one hospital discharge abstract or two physician claims within 2 years. Patients aged <35 years were excluded to reduce the misclassification of type 2 diabetes as type 1 diabetes. Patients with gestational diabetes mellitus, identified with coding for an obstetrical event within 5 months of diabetes diagnosis were also excluded. This coding algorithm was extensively validated against physician diagnosis of diabetes across sex, age-groups, and rural/urban residents and among those with and without comorbid conditions with a sensitivity of 92.3%, specificity of 96.9%, and a positive predictive value (PPV) of 77% (8,9).

Categorizing ethnic group

Self-reported ethnicity is not documented in administrative data in Canada. We used validated surname analysis to categorize patients as South Asian (from Pakistan, India, or Bangladesh) or Chinese (from China, Taiwan, or Hong Kong) using surnames recorded in provincial registries. Compared with self-report, the sensitivity for the Quan surname algorithm for Chinese ethnicity was 78%, specificity was 99.7%, and PPV was 81% (10). For the Nam Pehchan algorithm for South Asian ethnicity, the sensitivity was 90–94%, specificity was 99.4%, and PPV was 63–96% (11–13). All remaining patients are referred to as "white" because this group is largely (93.2%) composed of white, nonvisible minority individuals (6).

Procedures

To determine incident cases, we identified all patients in whom diabetes was diagnosed at each fiscal year. Patients with incident cases had a minimum of 3 previous years without any coding for diabetes in hospital or physicians claims files to minimize misclassifying prevalent cases as incident (98.9% of patients in each ethnic group still had nondiabetes physician visits in this time period). Thus, incident cases are determined for 1997–2003. To avoid falsely attributing the absence of diabetes diagnosis to newly arrived immigrants, we only included those patients with health insurance registration for at least 3 years before their diabetes diagnosis.

To control for severity of illness at the time of diagnosis of diabetes, we measured clinical variables from the Charlson Comorbidity Index validated to predict mortality in patients with type 2 diabetes (14). Socioeconomic status (SES) was assessed using area level median income based on the patient's postal code. SES data were missing for 11,665 patients (2.5% Chinese, 2.9% South Asian, and 4.4% white). A missing value was assigned to these patients and retained in all models.

Outcomes

Time to death after diabetes diagnosis was the primary outcome. Secondary outcomes included hospitalization for AMI, acute stroke, or heart failure and were determined using validated coding algorithms in hospital discharge abstracts: AMI (ICD-9 410; ICD-10 I21), PPV 0.95 (15); stroke (ICD-9 430, 431, 434, and 436; ICD-10 I60-I62, I63.3-I63.5, I63.8, I63.9, and I64), PPV 0.85–0.98 (16); and heart failure (ICD-9 428.x; ICD-10 I5O), PPV 0.84 (17). Time to event was assessed up to 31 March 2006 for British Columbia and to 31 March 2007 for Alberta with up to 10 years follow-up (median 4.0 years). Patients were censored if they moved out of the province or reached the end of the observation period.

Statistical analysis

We determined age-specific (reported for the most recent fiscal year, 2003–2004) and age-standardized incidence of diagnosed diabetes for each ethnic and sex group. Yearly incidence of diagnosed diabetes (per 1,000 population) was calculated using new cases of diabetes for each group as the numerator with the corresponding population count as the denominator for the most recent 5-year time period (1999–2003). Annual population counts for each ethnic and sex group were determined by applying the surname algorithms to the annual provincial registry population counts, minimizing denominator bias. We used direct age standardization for each group with the total provincial population in the same fiscal year as the reference group. Poisson regression analysis was used to compare incidence rates between ethnic and sex groups and linear regression was used to determine change in incidence over time.

Categorical variables were compared using the χ^2 test. Cox proportional hazards models were constructed and stratified by sex, with adjustment for province, SES quintile, age in 5-year categories, previous history of AMI, heart failure, cerebrovascular disease, peripheral arterial disease, renal impairment, cancer, dementia, chronic pulmonary disease, hypertension, rheumatic disease, peptic ulcer disease, liver disease, hemiplegia, metastatic carcinoma, and AIDS/HIV. We also conducted sensitivity analyses using the British Columbia cohort by additionally adjusting for insulin, metformin, statin, or ACE inhibitor prescribing within 5 years of diagnosis using a province-wide prescription drug database (PharmaNet) only available in British Columbia.

All analyses were conducted with SAS (version 9.1.3) and graphs were plotted using R. This study was approved by the local ethics institutional review boards.

RESULTS — There were 555,206 patients who met the coding definition for diabetes. After exclusion of 18,037 patients aged <35 years, 17,602 with gestational diabetes, 199,592 patients without a minimum 3-year period of observation without a diabetes diagnosis, and 43,138 patients without insurance registration within 3 years before diabetes diagnosis, 276,837 remaining patients were identified as having incident cases of diagnosed diabetes (15,066 [5.4%] South Asian, 17,754 [6.4%] Chinese, and 244,017 [88.1%] white patients).

South Asian patients were 4.6 years younger on average than Chinese and white patients at diagnosis of diabetes (Table 1). White patients were more likely to have cardiovascular disease and cancer relative to the ethnic groups.

Diabetes incidence

From Table 2, incidence of diagnosed diabetes was higher among men relative

Table 1—*Baseline characteristics among diabetic patients aged ≥35 years*

Characteristics	Chinese	South Asian	White	*P* value
n	17,754	15,066	244,017	
Age at diagnosis				
Age (years)	59.7 ± 12.8	56.5 ± 12.3	61.3 ± 13.1	<0.001
35–49 years	4,390 (24.7)	4,753 (31.6)	50,082 (20.5)	<0.001
50–64 years	6,680 (37.6)	6,307 (41.9)	94,788 (38.8)	
65–79 years	5,507 (31.0)	3,424 (22.7)	76,717 (31.4)	
≥80 years	1,177 (6.6)	582 (3.9)	22,430 (9.2)	
Female sex	8,458 (47.6)	6,672 (44.3)	110,142 (45.1)	<0.001
Province: British Columbia	14,084 (79.3)	9,529 (63.3)	143,630 (58.9)	<0.001
Socioeconomic quintile				
First quintile (low)	4,370 (24.6)	3,208 (21.3)	56,915 (23.3)	<0.001
Second quintile	3,908 (22.0)	3,498 (23.2)	49,138 (20.1)	
Third quintile	2,990 (16.8)	3,051 (20.3)	46,377 (19.0)	
Fourth quintile	2,814 (15.9)	2,730 (18.1)	42,607 (17.5)	
Fifth quintile (high)	3,223 (18.2)	2,147 (14.3)	38,196 (15.7)	
Unknown	449 (2.5)	432 (2.9)	10,784 (4.4)	
Comorbid conditions				
Hypertension	7,308 (41.2)	5,612 (37.3)	99,578 (40.8)	<0.001
Myocardial infarction	266 (1.5)	473 (3.1)	10,152 (4.2)	<0.001
Congestive heart failure	444 (2.5)	498 (3.3)	14,578 (6.0)	<0.001
Peripheral vascular disease	245 (1.4)	155 (1.0)	6,234 (2.6)	<0.001
Cerebrovascular disease	447 (2.5)	358 (2.4)	9,318 (3.8)	<0.001
Dementia	121 (0.7)	106 (0.7)	4,103 (1.7)	<0.001
Chronic pulmonary disease	1,394 (7.9)	1,794 (11.9)	31,032 (12.7)	<0.001
Renal disease	324 (1.8)	194 (1.3)	5,090 (2.1)	<0.001
Cancer	593 (3.3)	372 (2.5)	14,127 (5.8)	<0.001
Oral hypoglycemic agent*	4,619 (32.8)	3,731 (39.1)	52,590 (36.6)	<0.001
Insulin*	149 (1.1)	130 (1.36)	4,092 (2.85)	<0.001

Data are means ± SD or *n* (%). *Medication prescribed within 1 year of diagnosis in British Columbia patients only.

to women for all ethnic groups. Overall, South Asian patients had the highest age-adjusted incidence of diabetes, whereas Chinese patients had the lowest (Fig. 1). In the age-specific incidence, South Asian patients had the highest incidence of diabetes in all young to middle-aged categories. However, after the age of 65, the incidence of diabetes was highest among white patients. Diabetes incidence for white patients and Chinese men increased during the observation period but remained stable for South Asian patients and Chinese women (Fig. 1).

Mortality and macrovascular complications

Total mortality was substantially lower in South Asian and Chinese men and women than in white men and women (Table 3). Even after adjustment for baseline characteristics, mortality remained substantially lower in South Asian and Chinese patients. Additional adjustment for use of insulin, metformin, ACE inhibitors, or statin therapy in the sensitivity analysis did not materially affect these results. These differences were seen across different age subgroups, within each province, and among those with and without comorbid conditions.

Macrovascular complications among ethnic groups varied by sex. South Asian and white women had a similar risk of developing macrovascular complications. However, Chinese women had a substantially lower risk of AMI and heart failure. South Asian and Chinese men had a lower risk of stroke and heart failure relative to that of white men. Chinese men had the lowest risk for AMI whereas South Asian and white men had a similar risk of AMI.

CONCLUSIONS — South Asian patients had the highest incidence of diagnosed diabetes, whereas Chinese patients had the lowest incidence. Mortality was also lower for South Asian and Chinese patients compared with that for white patients with newly diagnosed diabetes, for both men and women. However, macrovascular complications varied by ethnicity and sex.

There is a disproportionately high rate of new cases of diabetes among young to middle-aged, South Asian patients. Our findings affirm estimates from numerous prevalence studies (3,4). The age-

Table 2—*Age-specific incidence of diagnosed diabetes by ethnicity and sex (per 1,000 population) in fiscal year 2003–2004*

	Chinese				South Asian				White		
Age	New cases	Pop*	Incidence (95% CI)	*P* value	New cases	Pop*	Incidence (95% CI)	*P* value	New cases	Pop	Incidence (95% CI)
Women											
35–44 years	128	61,099	2.1 (1.7–2.5)	0.006	129	27,846	4.6 (3.8–5.4)	<0.001	1,367	506,420	2.7 (2.6–2.8)
45–54 years	292	50,900	5.7 (5.1–6.4)	0.99	205	22,069	9.3 (8.0–10.6)	<0.001	2,757	480,861	5.7 (5.5–6.0)
55–64 years	214	23,479	9.1 (7.9–10.3)	0.04	257	16,795	15.3 (13.5–17.2)	<0.001	3,424	323,964	10.6 (10.2–10.9)
>65 years	464	40,374	11.5 (10.5–12.5)	0.004	240	19,257	12.5 (10.9–14.0)	0.4	5,787	438,246	13.2 (12.9–13.5)
Men											
35–44 years	154	53,886	2.9 (2.4–3.3)	0.1	257	30,600	8.4 (7.4–9.4)	<0.001	1,622	502,421	3.2 (3.1–3.4)
45–54 years	339	50,521	6.7 (6.0–7.4)	0.02	277	22,760	12.2 (10.8–13.6)	<0.001	3,704	482,218	7.7 (7.4–7.9)
55–64 years	290	23,681	12.3 (10.9–13.7)	0.02	288	16,709	17.2 (15.3–19.2)	<0.001	4,572	324,698	14.1 (13.7–14.5)
>65 years	411	35,126	11.7 (10.6–12.8)	<0.001	228	17,768	12.8 (11.2–14.5)	<0.001	5,940	354,004	16.8 (16.4–17.2)

*2003–2004 population.

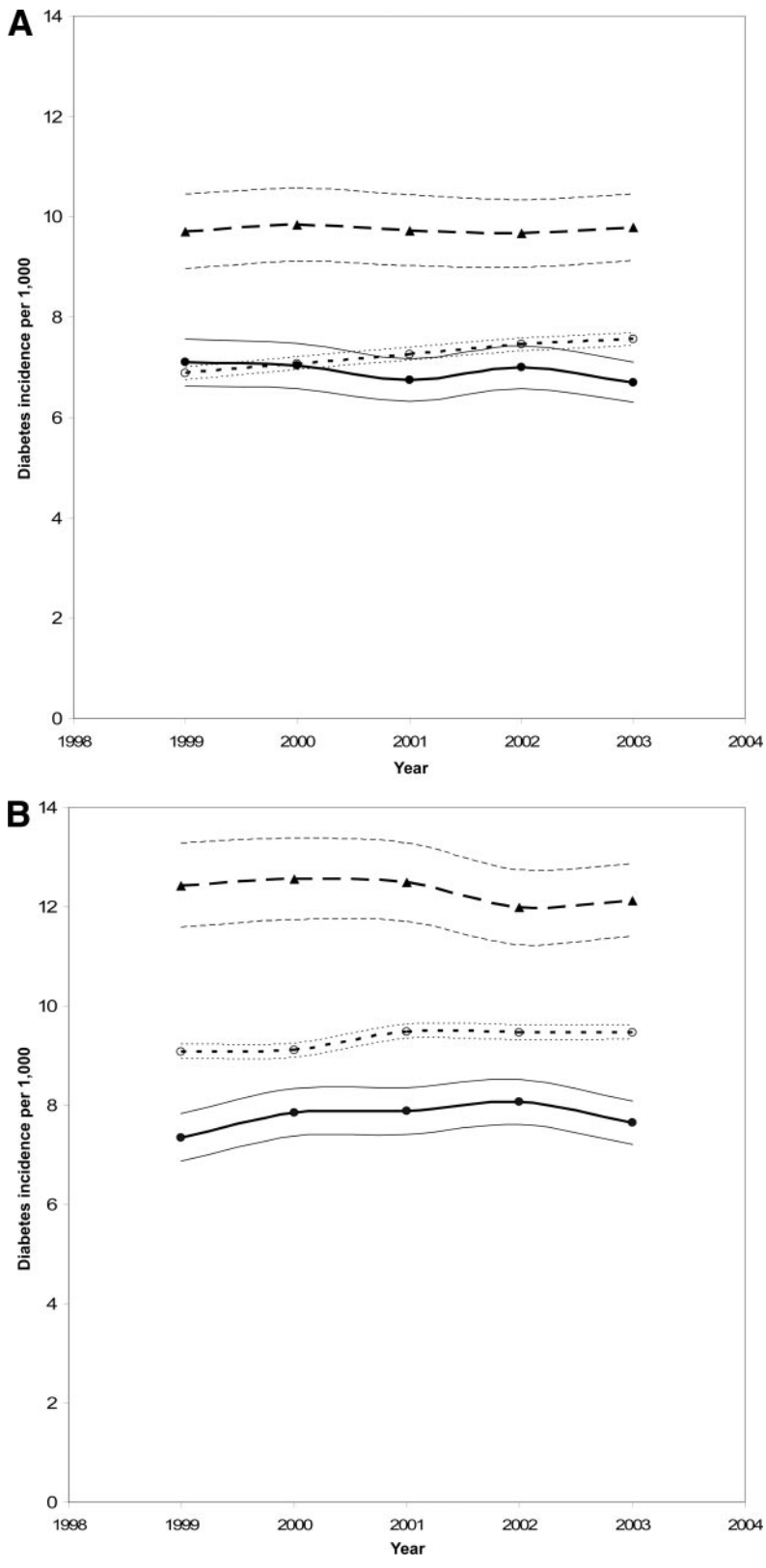

Figure 1—A*: Age-adjusted incidence of diagnosed diabetes by ethnicity in women aged ≥35 years (1999–2003).* B*: Age-adjusted incidence of diagnosed diabetes by ethnicity in men aged ≥35 years.* ▲*, South Asian;* ○*, white;* ●*, Chinese.*

and sex-specific incidence pattern of diabetes among white patients is also consistent with general population incidence rates (8). The observed lower incidence of diabetes in Chinese patients contrasts with that in a small study reporting a similar incidence between Chinese and other patients in the U.S.; however, age-adjusted incidence was not determined (18).

Diabetes guidelines generally recommend initial screening for diabetes at age 45 years, although a younger threshold is recommended for patients of Asian descent. The optimal age at which to start early surveillance in South Asians is unclear. It is also not known whether early surveillance would benefit other Asian groups (e.g., Chinese). This study identified an alarmingly high incidence of diabetes in South Asian patients, particularly in men aged 35–44 years, indicating that screening as early as 35 years may be warranted. Our findings also suggest that Chinese patients do not necessarily share this early proclivity for developing diabetes.

Despite a greater predilection for developing diabetes, we found a paradoxically lower mortality among South Asians than among white patients. Chinese patients also had a significantly lower mortality. Although South Asian patients were considerably younger and both South Asian and Chinese patients possessed fewer comorbid conditions at the onset of diabetes, the mortality benefit persisted after adjustment for these differences. Our findings are consistent with results from several smaller studies of diabetic patients (19,20), and general population mortality rates also indicate lower all-cause mortality for South Asian and Chinese patients compared with white patients living in North America (21). Our results, however, contrast with those for the Southall Diabetes Survey cohort, which reported a nonsignificant trend toward increased mortality in South Asian patients compared with their white counterparts using prevalent rather than incident cases (22). However, mortality rates for all groups were substantially higher compared with general population mortality rates for Chinese, South Asian, and white patients living in North America (21). This observation suggests that the presence of diabetes confers a greater risk of death regardless of ethnicity.

The reasons for the ethnic and sex differences in mortality and macrovascular complications of diabetes are unclear, and

Table 3—*Age-standardized and -adjusted outcomes by ethnicity in diabetic women and men aged ≥35 years*

	Age standardized events/1,000 patient years			Hazard ratio (95% CI),* *P* value	
Outcome	Chinese	South Asian	White	Chinese vs. white	South Asian vs. white
Women					
n	8,458	6,672	110,142		
Mortality	18.6	20.7	30.9	0.69 (0.63–0.74) $P < 0.001$	0.69 (0.62–0.76) $P < 0.001$
Stroke	4.1	5.3	4.7	0.91 (0.76–1.08) $P = 0.26$	1.06 (0.88–1.29) $P = 0.54$
AMI	1.5	5.4	4.5	0.34 (0.26–0.46) $P < 0.001$	1.19 (0.99–1.44) $P = 0.06$
Heart failure	2.3	6.0	6.3	0.42 (0.34–0.54) $P < 0.01$	0.95 (0.79–1.15) $P = 0.6$
Men					
n	9,296	8,394	133,875		
Mortality	17.8	20.5	32.6	0.61 (0.60–0.66) $P < 0.001$	0.68 (0.63–0.74) $P < 0.001$
Stroke	4.2	4.3	5.1	0.81 (0.69–0.96) $P = 0.01$	0.82 (0.68–0.99) $P = 0.04$
AMI	2.8	7.9	7.9	0.37 (0.31–0.45) $P < 0.001$	1.05 (0.92–1.19) $P = 0.49$
Heart failure	2.0	4.4	6.4	0.38 (0.30–0.48) $P < 0.01$	0.71 (0.56–0.92) $P < 0.01$

*Hazard ratios are adjusted for age, SES, province, and comorbid conditions including previous history of AMI, heart failure, cerebrovascular disease, peripheral arterial disease, renal impairment, cancer, dementia, chronic pulmonary disease, hypertension, connective tissue disease-rheumatic disease, peptic ulcer disease, mild liver disease, paraplegia and hemiplegia, moderate or severe liver disease, metastatic carcinoma, and AIDS/HIV.

we can speculate on possible mechanisms. South Asian and Chinese patients, particularly men, may have their diabetes diagnosed earlier along the course of disease and may receive more aggressive care. However, even after we adjusted for metformin, statin, and ACE inhibitor prescribing, the mortality benefit in South Asian and Chinese patients persisted. Alternatively, some ethnic patients may not have accessed medical care and were therefore not included in the study population. These individuals with undiagnosed diabetes may be more likely to experience early mortality. However, a national survey in Canada found that visible minority and white patients reported a similarly high frequency of physician visits (23). Chinese and South Asian patients have lower rates of smoking and BMI, potentially contributing to their survival advantage. However, these differences are unlikely to account for all the benefit. In a U.S. study, despite adjustment for these differences, a lower risk of AMI, stroke, and heart failure was identified in Asian patients with newly diagnosed diabetes (24); however, South Asian and Chinese subgroups were not analyzed separately. In our analysis, white patients had higher rates of cardiovascular complications and therefore may have higher rates of cardiovascular death. Consistent with a general population study, white patients may also have higher rates of noncardiovascular death, including deaths due to cancer (21), collectively contributing to their higher all-cause mortality. Ethnic differences in macrovascular complications were largely attenuated in women. This observation may reflect fewer differences in diabetes management among women of different ethnic backgrounds. A study of 9,833 diabetic patients identified similar service delivery and intermediate outcomes including A1C levels and systolic blood pressure among Scottish and South Asian women (25). The lower rates of cardiovascular complications in the ethnic groups may reflect possible differences in chronic disease management including increased adherence to medication and strong family supports. Some of these influences such as family support and caregiving may also differ by sex within cultural groups.

The strengths of this study include the use of population-based data for a large, ethnically diverse area using coding algorithms extensively validated against physician diagnosis in the same geographic region. However, there are several limitations. First, we used surname algorithms alone to categorize ethnicity rather than self-report. Although the specificities of these algorithms were high, there is potential for some misclassification of ethnic categories that would underestimate differences among ethnic categories. Second, we could not differentiate type 1 and type 2 diabetes, although from our sensitivity analysis in British Columbia, <3% of patients received insulin within 1 year of diabetes diagnosis. Third, we were only able to identify physician-diagnosed diabetes, underestimating the true incidence of diabetes. Fourth, observational studies are susceptible to bias from residual confounding including confounding by age. There may be residual confounding by age. We were unable to control for differences in smoking, BMI, visceral fat, and diabetes control. We did not have information on year of immigration, but because the majority of immigration to Canada by these ethnic groups has occurred in the past 25 years (6), this population would largely be composed of first-generation immigrants. Finally, we used broad ethnic categories, and there is likely some heterogeneity among smaller subgroups within each ethnic category.

In summary, diabetes incidence and outcomes are heavily influenced by ethnicity and sex. South Asian patients have a significantly higher incidence of physician-diagnosed diabetes that is concentrated at young and middle ages, whereas Chinese patients do not. These results may have implications for screening and timing of culturally sensitive interventions to reduce this epidemic. We also observed a paradoxical finding that despite a high incidence of diabetes, mortality was lower in South Asian patients than in the general diabetic population and macrovascular complication occurrence further varied by sex. Mortality was similarly low in Chinese patients. Further studies are needed to confirm this paradoxical finding and elucidate underlying mechanisms for differences in diabetes risk and outcomes by ethnicity and sex.

Acknowledgments— This study was funded by the Canadian Institutes of Health Research

(CIHR). N.A.K. is a CIHR New Investigator, a GENESIS (Sex and Sex Determinants of Cardiovascular Disease, funded by CIHR and Heart and Stroke Foundation Canada) scholar, and a St. Paul's Hospital Physician Scholar. H.Q. is a CIHR New Investigator and a senior population health investigator at the Alberta Heritage Foundation for Medical Research. S.A. holds the Michael G. DeGroote Heart and Stroke Foundation of Ontario Chair in Population Health and the Eli Lilly May Cohen Chair in Women's Health Research at McMaster University. L.P. holds a career investigator award from the Fonds de la recherche en santé du Québec and the William Dawson Chair of Medicine at McGill University.

The study sponsor had no role whatsoever in study design; in the collection, analyses, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

No potential conflicts of interest relevant to this article were reported.

N.A.K. and H.Q. developed the study design, contributed to data collection, conducted data analysis, contributed to data interpretation, and wrote the manuscript. H.W. conducted data analysis, contributed to data interpretation, and wrote the manuscript. S.A. and N.R.C.C. developed the study design, contributed to data interpretation, and wrote the manuscript. Y.J. contributed to data collection, contributed to data interpretation, and wrote the manuscript. L.P. contributed to data interpretation and wrote the manuscript.

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