Declining Trends of Cardiovascular-Renal Complications and Mortality in Type 2 Diabetes: The Hong Kong Diabetes Database

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OBJECTIVE

Nationwide studies on secular trends of diabetes complications are not available in Asia. We examined changes in risk factor control and incidence of complications from diabetes and death in a large longitudinal cohort of Chinese adults with type 2 diabetes in Hong Kong.

RESEARCH DESIGN AND METHODS

Between 1 January 2000 and 31 December 2012, 338,908 Chinese adults with type 2 diabetes underwent metabolic and complication assessment in 16 diabetes centers operated by Hong Kong Hospital Authority that provided care to a large majority of diagnosed patients. Patients were followed for incident acute myocardial infarction (AMI), stroke, end-stage renal disease (ESRD), and death until 31 December 2012. Risk factor levels between enrollment periods were compared. Incidence of clinical events, stratified by diabetes duration, was examined over time.

RESULTS

Incidence of complications from diabetes and death declined over the observation period in patients at varying disease duration. Among the high-risk group with diabetes for at least 15 years, crude incidence of AMI decreased from 8.7 to 5.8, stroke from 13.5 to 10.1, ESRD from 25.8 to 22.5, and death from 29.0 to 26.6 per 1,000 person-year between the periods 2000 to 2002 and 2010 to 2012. Improvements in levels of metabolic risk factors were detected. Proportion of patients achieving HbA_{1c} <7.0% (53 mmol/mol) was increased from 32.9 to 50.0%, blood pressure ≤130/80 mmHg from 24.7 to 30.7%, and LDL cholesterol <2.6 mmol/L from 25.8 to 38.1%.

CONCLUSIONS

From this territory-wide Hong Kong Diabetes Database, we observed decreases in incidence of cardiovascular-renal complications and death and corresponding improvements in risk factor control over a 13-year period.

Diabetes is an emerging pandemic of modern societies driven by obesity, aging population, and improved survival in those affected. A quarter of the world's population with diabetes comes from China, where industrialization and growing economy have contributed to obesogenic lifestyle and unprecedented rise in metabolic diseases (1,2).

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Diabetes is associated with disabling sequelae and premature death, which are preventable by rigorous control of risk factors (3–6). Secular changes in complications from diabetes have been reported in the U.S., Canada, and Sweden, and in these reports, rates of major clinical events declined over time, in line with improvements in care for diabetes (7–10). Similar data on trends in risk factor levels and incidence of complications are lacking in Asia.

Hong Kong is a special administrative region of China with a population of 7.3 million. The Hospital Authority (HA), a statutory body that governs all public hospitals and government outpatient clinics in Hong Kong, serves the majority of chronic disease care in the region. Since the deployment and obligatory use of electronic medical record in the HA in 1995, detailed clinical information of all Hong Kong residents using public services were being universally captured. As part of a quality-improvement program that started in 1999, regular structured assessment of metabolic control and vascular complications was offered to all patients with diabetes, the results of which were entered into the electronic system. The recording of comprehensive baseline clinical characteristics and outcomes offers a unique opportunity to study disease pattern, quality of care, and prognosis of a large representative sample of the population with diabetes in Hong Kong.

In the current article, we document the disease characteristics and incidences of cardiovascular-renal complications and all-cause death among Chinese adults with type 2 diabetes enrolled into the prospective territory-wide Hong Kong Diabetes Database. We examined the temporal changes in risk factor levels and incidence of complications according to period of enrollment.

RESEARCH DESIGN AND METHODS

Patients

The Hong Kong HA, established in 1990 and accountable to the Hong Kong Special Administrative Region Government, currently manages 42 public hospitals and institutions, 47 specialist outpatient clinics, and 73 general outpatient clinics. In a recent estimation, the HA provides 90% of total hospital bed days and 80% of outpatient visits. Clinical records of patients attending public hospitals and clinics were entered into the linked Central Computer System, which identifies patients by their unique Hong Kong Identity Card number compulsory for all Hong Kong residents. In 1999, a quality-improvement program comprising regular comprehensive assessment of metabolic control, micro-, and macrovascular complications of diabetes using a structured clinical protocol was implemented. Sources of referral included both hospital-based specialist outpatient clinics and community-based family medicine clinics in the public sector. There were no set criteria for referral, and patients with diabetes were referred for evaluation at the discretion of their treating physician. In 2009, the government set out initiatives to further promote chronic care, and with the additional funding support, the number of patients assessed has significantly increased since. Overall, between 50 and 60% of all patients with diabetes receiving care at the public clinics were assessed (W.-Y.S., personal communication).

The Hong Kong Diabetes Database consists of all patients who underwent metabolic and complication assessment between 1 January 2000 and 31 December 2012 in the HA. Patients were enrolled into the database at different disease durations, and for each patient, clinical measurements collected on the date of assessment were taken as baseline. The diagnosis and type of diabetes were confirmed by the referring physician. For this analysis, we included Chinese adults aged ≥18 years with type 2 diabetes. Patients with type 1 diabetes, gestational diabetes mellitus, or diabetes of unknown type were excluded. This study has been approved by the local Clinical Research Ethics Committees.

Clinical and Laboratory Measurements

Clinical assessment followed a structure protocol with documentation of demographic information, past medical history, medication prescription, and family history of diabetes. Blood pressures and anthropometric parameters were obtained. Patients were examined for presence of diabetic retinopathy using either direct fundoscopy or retina photography. Fundoscopy was performed by trained or in-training endocrinologists, and interpretation of retinal photo was undertaken by endocrinologists or optometrists. Peripheral sensory neuropathy was defined by fulfilling at least two out of three of reduce pinprick or monofilament sensation, reduced vibration sensation, and self-reported numbness on either foot. Laboratory measurements included HbA_{1c}, fasting plasma glucose, lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), renal function test, liver function test, complete blood count, and urine albuminuria. We used the abbreviated Modification of Diet in Renal Disease Study formula for estimation of glomerular filtration rate (GFR) (11). Microalbuminuria was defined as spot urine albumin-to-creatinine ratio (ACR) of 3.5–30 mg/mmol in female and 2.5–30 mg/mmol in male, 4-h albumin excretion rate 20–200 μg/min, or 24-h urine albumin 30–300 mg. Macroalbuminuria was defined as urine ACR >30 mg/mmol, albumin excretion rate >200 μg/min, or 24-h urine albumin >300 mg. For this analysis, we further defined hypertension as systolic blood pressure >130 mmHg, diastolic blood pressure >80 mmHg, or prevalent use of antihypertensive drugs. Dyslipidemia was defined as LDL-cholesterol ≥2.6 mmol/L or prevalent use of statins. Obesity was defined as BMI ≥25 kg/m^2 (12).

Outcome Ascertainment and Definition

All hospital discharges were coded according to ICD-9. Codes listed as principal diagnosis were used for outcome identification of acute myocardial infarction (AMI), ICD-9 code 410, and stroke, ICD-9 codes 430–438. End-stage renal disease (ESRD) was defined as requirement of dialysis (procedure code 39.95 or 54.98) or estimated GFR <15 mL/min/1.73 m^2. Information on death was obtained from the Hong Kong Death Registry, matched by Hong Kong Identity Card number. Patients were followed until death or the censored date of 31 December 2012.

Statistical Analysis

For descriptive analysis, continuous variables were expressed as mean ± SD or median (interquartile range), and categorical variables were expressed as percentages. The denominator of categorical variables was the number of patients with available data. Between-group comparison was tested using χ^2 test for categorical variables, *t* test for normally distributed continuous variables, and Kruskal-Wallis test for continuous variables with skewed distribution. Missing data were not imputed, and patients

with missing data for a variable would not be included in the analysis involving that particular variable.

We first compared the baseline clinical characteristics including demographics, metabolic profile, past complications, and medication use of the cohort separated by calendar periods of enrollment (2000–2003, 2004–2006, 2007–2009, and 2010–2012). We examined the changes of selected metabolic indices including HbA_{1c}, systolic blood pressures, and LDL-cholesterol as a function of disease duration and compared these changes across enrollment periods.

Next, we explored temporal changes in the incidences of complications from diabetes. Patients who were assessed during the subsequent years had shorter disease duration because of more liberal and earlier patient referral. To address potential confounding by changes in disease duration, we obtained incidence rates of complications according to duration of diabetes for each calendar period of enrollment. Multivariate Cox regression analysis was used to test the effect of year of enrollment on incident complications. Treating calendar year as a continuous variable, we derived hazard ratios (HRs) and 95% CIs for each outcome of AMI, stroke, ESRD, and all-cause death. Four models were constructed for each outcome: model 1, adjusted for assessment age, sex, and duration of diabetes; model 2, adjusted for the interaction term of calendar year of enrollment $\times$ duration of diabetes, in addition to variables in model 1; model 3, adjusted for HbA_{1c}, systolic blood pressure, LDL cholesterol, and BMI, in addition to variables in model 1; and model 4, adjusted for history of coronary heart disease (in the Cox model for stroke, ESRD, and death), stroke (in the model for AMI, ESRD, and death), and ESRD (in the model for AMI, stroke, and death), in addition to variables in model 3. The interaction term in model 2 was applied to test whether calendar year of enrollment modifies the relationship between disease duration and events. Patients with past history of coronary heart disease, stroke, or ESRD at baseline were excluded in the Cox regression analysis for the corresponding complication. A two-sided P value of <0.05 was considered significant. Analysis was performed using the Statistical Analysis System (version 9.3; SAS Institute, Cary, NC).

RESULTS

Between 1 January 2000 and 31 December 2012, 345,255 patients underwent clinical assessment for metabolic control and complications from diabetes. After excluding 4,604 with type 1 diabetes, 101 with gestational diabetes mellitus, and 1,642 with diabetes of unknown type, 338,908 patients were included for analysis.

Changes in Metabolic Risk Factors and Treatment Over Time

We compared baseline clinical parameters of patients enrolled in 2000–2003, 2004–2006, 2007–2009, and 2010–2012 (Table 1). Patients who presented in the subsequent periods were older but had shorter duration of diabetes. Glycemic control as assessed using HbA_{1c} and fasting plasma glucose improved over time, as did systolic blood pressures and LDL-cholesterol, whereas increases in BMI and waist circumferences were observed. Compared with patients who were enrolled later, those who presented earlier had higher background frequencies of micro- and macrovascular complications.

We derived mean estimates of HbA_{1c}, systolic blood pressures, and LDL cholesterol against the duration of diabetes as reported at baseline, separated by periods of enrollment. In all of the periods, HbA_{1c} declined sharply after diagnosis followed by a gradual ascent, although the absolute levels of HbA_{1c} remained lower in the subsequent compared with the earlier cohorts (Fig. 1). Systolic blood pressures (Fig. 2) increased as diabetes progressed with time; however, the absolute levels of blood pressures were lower in those enrolled later. Levels of LDL-cholesterol (Fig. 3) did not change with disease duration in the earlier cohorts enrolled between 2000 and 2003 and 2004 and 2006, whereas a decline was detected in patients who presented during the successive periods.

The prescription of antidiabetic drug regimen by duration of diabetes was examined across enrollment periods (Supplementary Table 1). The proportion of patients on diet-control only fell with increasing duration of diabetes across all examination periods. Among patients with diabetes for >10 years, up to 40% of those enrolled in 2000–2003 and 10–14% of those from 2010–2012 remained untreated. As diabetes progressed, the proportion of patients on oral antidiabetic monotherapy also decreased, whereas the proportion of patients using dual and triple oral antidiabetic therapy increased. Overall, the use of any noninsulin antidiabetic regimen was higher among patients enrolled during the later compared with earlier periods. A preference for metformin over sulfonylurea was observed in patients presented in recent years, whereas the reverse was noted in the earlier cohorts (Supplementary Table 2). With respect to insulin use, more patients from the earlier compared with subsequent cohorts were prescribed insulin alone or insulin with single oral antidiabetic drug, and patients enrolled in the later periods were more likely to be prescribed insulin with two oral agents. The use of antihypertensives, renin-angiotensin system (RAS) inhibitors, statins, and antiplatelet drugs was increased over time (Table 1).

Incidence of Cardiovascular-Renal Complications and Death

During a 1,374,977 person-year follow-up, AMI occurred in 5,376 patients, stroke in 11,321, and ESRD in 15,470 patients without these events at baseline, and 28,402 patients have died. We obtained crude incidence rates according to disease duration stratified by examination periods (Table 2). Incidences of all outcomes increased with increasing disease duration, and barring the estimates from the earliest period of 2000–2002, during which the number of patients enrolled was small, overall, rates of AMI, stroke, ESRD, and all-cause death declined with successive year of enrollment.

We conducted multivariate Cox regression analysis to test the changes in incident complications over time. Adjusted for age, sex, and diabetes duration, enrollment year was negatively related to incident AMI, stroke, ESRD, and all-cause death, denoting lower hazards of clinical events with subsequent year of presentation (Table 3). We detected significant interaction at a positive direction between enrollment year and disease duration for incident stroke (HR of interaction term: 1.001 [95% CI 1.000–1.002]; $P = 0.011$) and ESRD (HR of interaction term: 1.002 [95% CI 1.001–1.002]; $P < 0.001$). This indicates that enrollment year had moderating effects on the relationship between duration of diabetes and clinical events and that even as the risks of stroke and ESRD were reduced with each successive year of presentation, the difference in risks narrowed as disease duration lengthens

Table 1—Baseline clinical characteristics of 338,908 Chinese adults with type 2 diabetes stratified by calendar period of enrollment

		Period of enrollment			
	Total	2000–2003	2004–2006	2007–2009	2010–2012
Number	338,908	33,143	60,067	97,879	147,819
Demographics					
Age (years)	62.8 ± 12.2	60.9 ± 12.2	62.9 ± 12.2	63.0 ± 12.2	63.2 ± 12.2
Male (%)	48.7	47.3	46.9	49.4	49.3
Ex-/current smoker (%)	30.2	30.5	30.2	30.9	29.9
Family history of diabetes (%)	44.5	42.9	38.8	43.9	47.8
Duration of diabetes (years)	4.0 (8.0)	6.0 (8.0)	5.0 (8.0)	3.0 (8.0)	3.0 (7.0)
Metabolic control					
BMI (kg/m^2)	25.7 ± 4.1	25.4 ± 3.9	25.6 ± 4.0	25.8 ± 4.1	25.9 ± 4.1
Waist circumference (cm)					
Male	90.0 (12.0)	89.0 (13.0)	90.0 (12.0)	90.0 (12.0)	91.0 (12.0)
Female	87.0 (14.0)	85.0 (13.0)	86.0 (13.0)	87.0 (13.0)	88.0 (13.0)
Systolic blood pressure (mmHg)	137.5 ± 19.1	140.1 ± 21.5	138.0 ± 19.8	137.5 ± 19.0	136.6 ± 18.3
Diastolic blood pressure (mmHg)	76.0 ± 10.7	76.5 ± 10.7	75.3 ± 10.5	76.0 ± 10.5	76.2 ± 10.8
HbA_{1c} (% [mmol/mol])	7.6 ± 1.6 (60 ± 12.6)	7.8 ± 1.7 (62 ± 13.5)	7.8 ± 1.6 (62 ± 12.7)	7.6 ± 1.7 (60 ± 13.4)	7.3 ± 1.5 (56 ± 11.5)
Fasting plasma glucose (mmol/L)	7.8 ± 2.6	8.4 ± 2.9	8.2 ± 2.7	7.9 ± 2.6	7.4 ± 2.4
LDL cholesterol (mmol/L)	3.0 ± 0.9	3.2 ± 0.9	3.1 ± 0.9	3.1 ± 0.9	2.9 ± 0.9
Triglycerides (mmol/L)	1.4 (1.0)	1.5 (1.2)	1.4 (1.1)	1.5 (1.1)	1.3 (0.9)
HDL cholesterol (mmol/L)	1.2 ± 0.3	1.3 ± 0.4	1.3 ± 0.4	1.2 ± 0.3	1.3 ± 0.4
Estimated GFR (mL/min/1.73 m^2)	76.5 ± 22.8	72.9 ± 2.1	73.7 ± 21.9	76.1 ± 21.6	78.8 ± 22.0
Obesity (%)	53.6	50.7	51.4	53.8	55.0
Hypertension (%)	88.1	87.7	87.8	88.2	88.3
Dyslipidemia (%)	84.1	86.5	84.2	84.8	83.2
Diabetes-related complications					
Albuminuria (%)	34.2	39.1	37.6	32.5	33.7
Microalbuminuria	26.0	29.5	28.5	25.6	25.4
Macroalbuminuria	8.2	9.6	9.1	6.9	8.3
Chronic kidney disease (%)	18.1	20.2	21.1	18.0	16.4
ESRD (%)	0.5	0.6	0.6	0.5	0.4
Diabetic retinopathy (%)	29.7	30.4	21.9	26.0	33.5
History of coronary heart disease (%)	5.8	6.9	5.9	4.9	6.1
History of stroke (%)	4.9	5.9	5.0	4.1	5.1
Treatment					
Noninsulin antidiabetic drugs (%)	62.7	53.8	60.4	62.5	65.7
Metformin (%)	50.0	37.7	42.0	48.4	57.1
Sulfonylureas (%)	41.1	43.1	47.8	43.6	36.3
Thiazolidinediones (%)	0.4	0.2	0.5	0.5	0.3
Dipeptidyl peptidase 4 inhibitors (%)	0.3	0.0	0.0	0.0	0.7
Insulin (%)	5.0	9.0	7.1	4.3	3.7
Antihypertensive drugs (%)	59.1	42.5	52.1	56.7	67.4
RAS inhibitors (%)	28.3	22.2	24.6	26.7	32.2
Statins (%)	16.3	8.8	8.6	8.8	26.1
Antiplatelet drugs (%)	13.3	10.3	12.5	12.8	14.7
Target attainment					
HbA_{1c} <7.0% (53 mmol/mol) (%)	42.9	32.9	33.1	41.3	50.0
Blood pressure ≤130/80 mmHg (%)	29.3	24.7	28.1	29.5	30.7
LDL cholesterol <2.0 mmol/L (%)	11.9	8.2	8.7	10.0	14.4
LDL cholesterol <2.6 mmol/L (%)	33.1	25.8	26.6	29.3	38.1
At least one target (%)	40.0	36.2	37.9	41.4	40.7
At least two targets (%)	18.4	10.7	13.2	16.7	23.3
All three targets (%)	3.8	1.5	2.1	2.9	5.5

At least one target: attained at least one of HbA_{1c} <7.0% (53 mmol/mol), blood pressure ≤130/80 mmHg, or LDL cholesterol <2.6 mmol/L; at least two targets: attained at least two of HbA_{1c} <7.0% (53 mmol/mol), blood pressure ≤130/80 mmHg, or LDL cholesterol <2.6 mmol/L; and all three targets: attained HbA_{1c} <7.0% (53 mmol/mol), blood pressure ≤130/80 mmHg, and LDL cholesterol <2.6 mmol/L. $P < 0.05$ for comparison of all parameters between assessment periods.

(Supplementary Fig. 1*B* and *C*). The interaction term of enrollment year × duration of diabetes was not significant for incident AMI ($P = 0.551$) and all-cause death ($P = 0.700$), suggesting that enrollment year and disease duration were unrelated to each other in their respective association with AMI and all-cause death (Supplementary Fig. 1*A* and *D*).

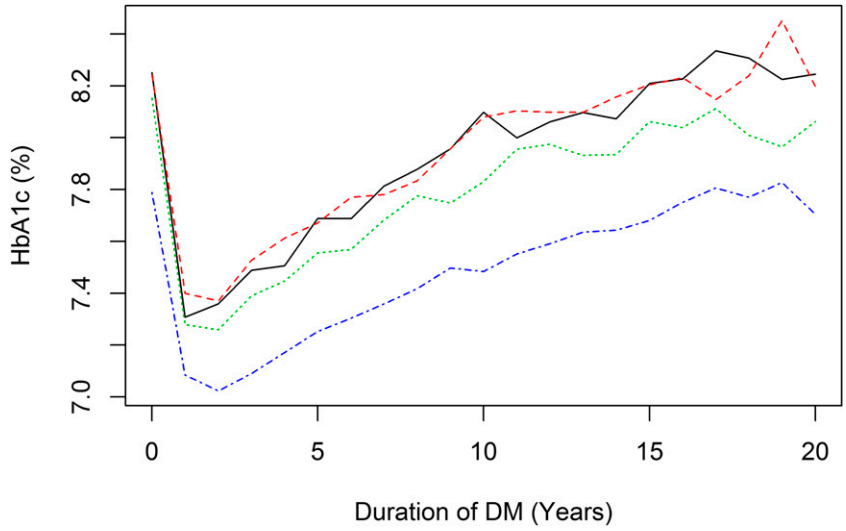

Figure 1—Trajectories of HbA_{1c} of patients with type 2 diabetes (DM) enrolled in 2000–2003, 2004–2006, 2007–2009, and 2010–2012. Black solid line, 2000–2003; red dashed line, 2004–2006; green dotted line, 2007–2009; and blue dashed and dotted line, 2010–2012.

When adjusted for modifiable risk factors for complications including HbA_{1c}, systolic blood pressures, LDL cholesterol, and BMI, the association between year of enrollment and diabetes outcomes except AMI remained significant. Further adjustment for baseline micro- and macrovascular complications had no appreciable impact on the association between enrollment year and remaining outcomes.

CONCLUSIONS

From this large longitudinal cohort of Chinese patients in Hong Kong with type 2 diabetes recruited over a 13-year period from 2000 to 2012 with detailed disease characterization and outcome capture, we observed significant declines in incidences of cardiovascular-renal complications and all-cause death over time. Improvements in metabolic profile were identified, in keeping with increases in the use of antidiabetic, antihypertensive, and lipid-lowering medications.

Temporal Changes in Cardiovascular-Renal Complications and Death

Work by others centering on trends of complications from diabetes in developed countries demonstrated temporal improvement in selected diabetes outcome (6–9,13,14). In the U.S., analysis of data accrued from multiple clinical sources and surveys showed remarkable falls in rates of AMI, stroke, lower limb amputation, ESRD, and death from hyperglycemic crisis among patients with diabetes over a two-decade period from 1990 to 2010, with the largest reduction in cardiovascular events and smallest in renal complication (7). In Canada, based on the Ontario Diabetes Database containing clinical information of >670,000 patients with diabetes, decreases in rates of AMI, stroke, and all-cause death were identified between 1992 and 1999 (9). In our population, we also detected declines in incidence of complications from diabetes particularly in stroke and ESRD. In the Cox regression analysis, adjustment for modifiable risk factors rendered the relationship between enrollment year and incident AMI nonsignificant but did not substantially attenuate the association of enrolment year with stroke, ESRD, and all-cause death. This suggests that reduction in the risks of AMI was mostly mediated by better metabolic control, whereas other unmeasured accomplishments in patient care, such as patient education, improved treatment adherence, and earlier screening for complications, might have contributed to favorable trends in the other outcomes.

Notably, patients who were enrolled during later periods had shorter duration of diabetes and correspondingly fewer micro- and macrovascular complications at baseline. We found that the relationship between year of enrollment and clinical events persisted despite adjustment for baseline complications, indicating that reduction in rates of major clinical events with time occurred independently to shifts in background complication profile.

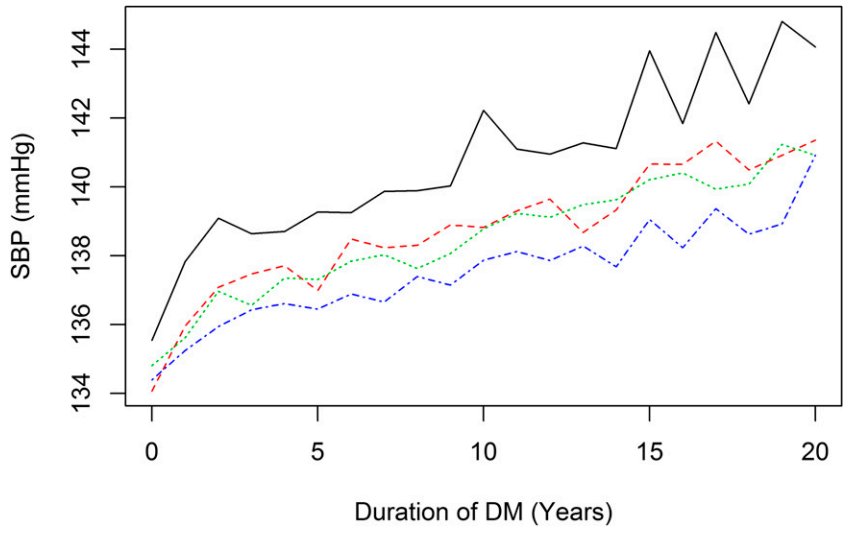

Figure 2—Trajectories of systolic blood pressures (SBP) of patients with type 2 diabetes (DM) enrolled in 2000–2003, 2004–2006, 2007–2009, and 2010–2012. Black solid line, 2000–2003; red dashed line, 2004–2006; green dotted line, 2007–2009; and blue dashed and dotted line, 2010–2012.

Trends in Metabolic Target Attainment and Treatment

Consistent with decreases in incidence of complications from diabetes, patients experienced improvements across a range of metabolic risk factors. Between the 2000–2003 and 2010–2012 periods, the proportion of patients achieving HbA_{1c} <7.0% (53 mmol/mol) was increased from 32.9 to 50.0%, blood pressure ≤130/80 mmHg, from 24.7 to 30.7%, and LDL cholesterol <2.6 mmol/L, from 25.8 to 38.1%. In a recent nationally

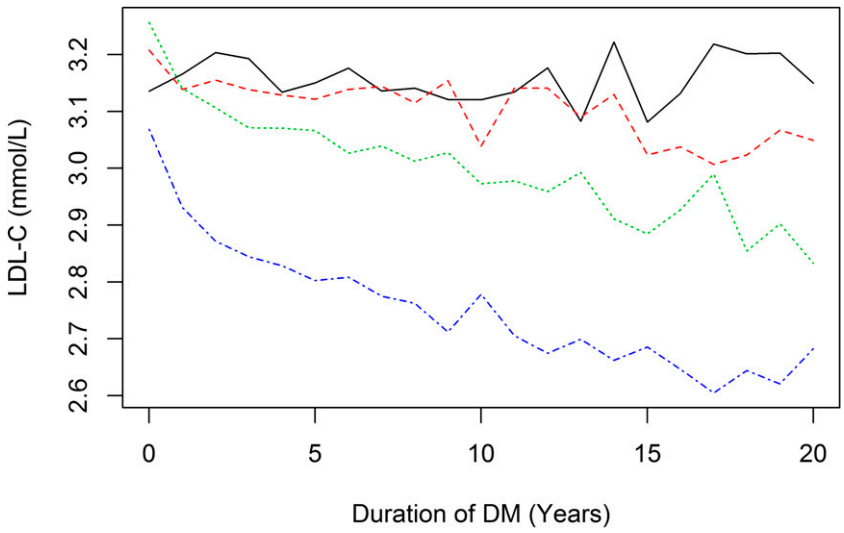

Figure 3—Trajectories of LDL cholesterol (LDL-C) of patients with type 2 diabetes (DM) enrolled in 2000–2003, 2004–2006, 2007–2009, and 2010–2012. Black solid line, 2000–2003; red dashed line, 2004–2006; green dotted line, 2007–2009; and blue dashed and dotted line, 2010–2012.

representative survey of 5,599 patients conducted in Taiwan, just over one-third of patients achieved glycemic goal, whereas blood pressure and LDL cholesterol targets were reached in 38 and 56% of patients, respectively (15). The GUIDANCE study, which enrolled 7,597 patients from eight European countries, reported attainment of glycemic target in 54%, blood pressure target in 19%, and LDL cholesterol target in 55% (16). From population-based statistics in the U.S., the respective figures were 52, 51, and 57%, among patients assessed between 2007 and 2010 (17). Glycemic control of our cohort enrolled in the 2010–2012 period measured favorably to Taiwan and was similar to rates reported in the U.S. and Europe, although disease duration was also shorter in our population. In contrast, attainment of blood pressure and lipid targets fared worse compared with the other regions.

We compared trajectories of HbA_{1c}, systolic blood pressure, and LDL cholesterol by enrollment periods. Following an initial decline, there was a steady rise in HbA_{1c} with increasing disease duration, consistent with gradual deterioration in insulin function as diabetes progresses. Nonetheless, levels of HbA_{1c} were overall lower in patients who presented later, and this correlated with greater use of antidiabetic drug therapy in particular

Table 2—Incidence of diabetes complications and all-cause death by diabetes duration and period of enrollment

	Period of enrollment			
Duration of diabetes	2000–2003	2004–2006	2007–2009	2010–2012
AMI, incidence (per 1,000 person-years [95% CI])				
≤2 years	1.31 (0.70–2.48)	1.49 (1.00–2.21)	1.86 (1.48–2.35)	1.85 (1.58–2.18)
3–5 years	3.56 (2.54–5.00)	2.40 (1.87–3.08)	2.33 (1.91–2.85)	2.17 (1.86–2.54)
6–8 years	2.86 (1.87–4.37)	2.94 (2.28–3.78)	3.26 (2.64–4.03)	3.21 (2.69–3.84)
9–11 years	5.40 (3.77–7.75)	4.10 (3.22–5.22)	4.15 (3.33–5.16)	3.82 (3.12–4.68)
12–14 years	4.57 (2.90–7.22)	4.94 (3.78–6.46)	3.92 (3.00–5.13)	5.24 (4.29–6.40)
≥15 years	8.68 (6.75–11.18)	6.83 (5.76–8.12)	7.19 (6.12–8.44)	5.76 (4.94–6.71)
Stroke, incidence (per 1,000 person-years [95% CI])				
≤2 years	6.97 (5.27–9.25)	7.07 (5.90–8.49)	5.74 (5.03–6.56)	4.09 (3.67–4.57)
3–5 years	7.35 (5.80–9.32)	8.18 (7.15–9.37)	7.12 (6.36–7.98)	4.86 (4.38–5.40)
6–8 years	10.32 (8.25–12.92)	9.43 (8.19–10.86)	9.33 (8.23–10.58)	6.86 (6.07–7.74)
9–11 years	10.58 (8.18–13.71)	10.43 (8.97–12.14)	11.31 (9.91–12.90)	8.73 (7.65–9.97)
12–14 years	11.37 (8.51–15.21)	12.00 (10.11–14.24)	12.58 (10.83–14.61)	7.63 (6.47–9.00)
≥15 years	13.53 (11.06–16.56)	13.99 (12.42–15.75)	14.01 (12.50–15.70)	10.13 (9.04–11.34)
ESRD, incidence (per 1,000 person-years [95% CI])				
≤2 years	4.44 (3.16–6.27)	4.19 (3.32–5.28)	4.03 (3.45–4.71)	3.48 (3.10–3.91)
3–5 years	5.57 (4.27–7.26)	6.69 (5.78–7.74)	5.53 (5.25–6.70)	4.47 (4.02–4.97)
6–8 years	8.40 (6.60–10.71)	10.06 (8.81–11.49)	8.91 (7.87–10.10)	7.24 (6.46–8.12)
9–11 years	12.79 (10.18–16.08)	13.00 (11.39–14.83)	12.95 (11.49–14.60)	9.72 (8.61–10.98)
12–14 years	19.31 (15.54–24.00)	17.12 (14.89–19.69)	14.89 (13.02–17.02)	14.09 (12.53–15.84)
≥15 years	25.75 (22.35–29.67)	29.25 (27.01–31.68)	25.96 (23.94–28.14)	22.46 (20.86–24.17)
All-cause death, incidence (per 1,000 person-years [95% CI])				
≤2 years	8.72 (6.82–11.15)	10.03 (8.64–11.65)	10.55 (9.58–11.61)	8.32 (7.72–8.97)
3–5 years	13.42 (11.31–15.92)	12.00 (10.77–13.38)	12.58 (11.57–13.67)	10.54 (9.84–11.29)
6–8 years	11.91 (9.73–14.59)	14.90 (13.37–16.60)	14.50 (13.16–15.98)	14.29 (13.17–15.50)
9–11 years	16.95 (13.92–20.66)	17.71 (15.83–19.80)	18.56 (16.81–20.50)	17.56 (16.05–19.22)
12–14 years	18.25 (14.64–22.78)	21.26 (18.79–24.07)	21.68 (19.43–24.19)	19.68 (17.84–21.71)
≥15 years	29.03 (25.46–33.11)	28.03 (25.89–30.36)	31.74 (29.54–34.10)	26.55 (24.84–28.38)

Table 3—Multivariate Cox regression analysis to show HRs of calendar year of assessment with major clinical outcomes

	AMI		Stroke		ESRD		All-cause death	
	HR (95% CI)*	*P* value	HR (95% CI)*	*P* value	HR (95% CI)*	*P* value	HR (95% CI)*	*P* value
Model 1	0.971 (0.960–0.984)	<0.001	0.929 (0.921–0.936)	<0.001	0.941 (0.935–0.948)	<0.001	0.953 (0.947–0.958)	<0.001
Model 2	0.975 (0.959–0.991)	0.002	0.920 (0.910–0.930)	<0.001	0.925 (0.916–0.934)	<0.001	0.953 (0.947–0.960)	<0.001
Model 3	0.985 (0.969–1.002)	0.077	0.926 (0.916–0.935)	<0.001	0.955 (0.946–0.964)	<0.001	0.960 (0.953–0.967)	<0.001
Model 4	0.987 (0.971–1.003)	0.110	0.926 (0.917–0.936)	<0.001	0.957 (0.948–0.966)	<0.001	0.963 (0.956–0.970)	<0.001

Model 1: adjusted for age, sex, duration of diabetes; model 2: adjusted for age, sex, duration of diabetes, and interaction term year of enrollment × duration of diabetes; model 3: adjusted for age, sex, duration of diabetes, HbA_{1c}, systolic blood pressure, LDL cholesterol, and BMI; and model 4: adjusted for age, sex, duration of diabetes, HbA_{1c}, systolic blood pressure, LDL cholesterol, BMI, history of coronary heart disease, stroke, and ESRD. *HR for outcome per calendar year of assessment from the previous calendar year.

more complex regimen. Systolic blood pressures increased with disease duration, which likely reflects age-related rise in blood pressures, although transition to diabetic kidney disease might also have worsened blood pressure control. Similar to the glycemic trend, patients enrolled during subsequent periods had better control of blood pressures. Levels of LDL cholesterol remained fairly static over time among patients assessed during the periods 2000–2003 and 2004–2006, but declined in those enrolled later. This may be explained by suboptimal use of statins in part because of restricted drug formulary in Hong Kong public clinics and hospitals in the earlier years when evidences for the use of these agents were only just being established. Advances in local practice guidelines have motivated wider prescription of statins as well as other ancillary agents such as RAS inhibitors, which benefitted risk factor control.

Strengths and Limitations

This study has a number of methodological strengths, including a large sample size with comprehensive characterization of patients at baseline, representativeness of the cohort, long follow-up duration, and high capture rate of hospitalization for major events and vitality. Our study is subjected to the following limitations: firstly, we have only registered patients who have undergone metabolic and complication assessment and have not included all patients with diabetes who attended the public health system. Nonetheless, we believe that our sample, which included patients attending both community outpatient and hospital-based specialist clinics of similar proportion to the case mix of patient population in the HA, was representative of population with diabetes in this sector, who make up the majority of the Hong Kong disease population. Secondly, we relied on ICD-9 codes on hospital discharges for outcome identification, and as such, our end points were opened to potential problem of misclassification. We have also only used principal diagnosis and thus might have missed major events that have occurred but were listed as secondary diagnoses. Thirdly, we were not able to capture clinical outcomes of patients who were admitted to hospitals in the private sector. Given the large differentials in medical costs between private and public, the vast majority of local residents seek care in the heavily subsidized public system. In a recent estimation, the HA provides >90% of total hospital bed days (18), and it is therefore unlikely that exclusion of patients who presented to the private sector have affected the results and conclusions of the study appreciably. Fourthly, clinical assessment procedures have not been consistent across sites. For instance, some centers used retina photography for evaluation of retinopathy, whereas others might rely on direct fundoscopy. In addition, laboratories at different hospitals have used different methods for biochemistry measurements including measurement of HbA_{1c}, and changes in methods have occurred over time. Lastly, duration of diabetes was significantly shorter in patients who were enrolled during the later years, and this might have contributed to lower observed rates of complications from diabetes in this subgroup. In order to dissect out potential confounding effects of disease duration, we derived incidence rates of complications by strata of disease duration and found that for similar disease duration, occurrence of complications remained lower in those who presented during subsequent periods. It is also possible that broader screening in recent years has resulted in patients being diagnosed sooner in their disease trajectory, which might similarly favor fewer complications in these subjects.

CONCLUSIONS

From this territory-wide prospective cohort of Chinese adults with type 2 diabetes in Hong Kong, we found reductions in incidence of major cardiovascular events, renal events, and all-cause death over the past decade. These trends were supported by parallel improvements in the control of modifiable risk factors and increases in uptake of pharmacological treatments of these conditions. Notwithstanding, there remain considerable gaps in the care of patients with diabetes, and up to 50–70% of our patients were not achieving goals. Insofar as risks of discrete complications have fallen, given the continuous rise in the number of existing cases of diabetes in Hong Kong, the disease burden will remain profound. Our results underscore the need to intensify health care efforts targeting disease awareness, broader screening, and aggressive risk factor management in this patient group in whom adverse outcomes are highly preventable.

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