Health Care Costs in People With Diabetes and Their Association With Glycemic Control and Kidney Function

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OBJECTIVE—To determine the association between laboratory-derived measures of glycemic control (HbA_{1c}) and the presence of renal complications (measured by proteinuria and estimated glomerular filtration rate [eGFR]) with the 5-year costs of caring for people with diabetes.

RESEARCH DESIGN AND METHODS—We estimated the cumulative 5-year cost of caring for people with diabetes using a province-wide cohort of adults with diabetes as of 1 May 2004. Costs included physician visits, hospitalizations, ambulatory care (emergency room visits, day surgery, and day medicine), and drug costs for people >65 years of age. Using linked laboratory and administrative clinical and costing data, we determined the association between baseline glycemic control (HbA_{1c}), proteinuria, and kidney function (eGFR) and 5-year costs, controlling for age, socioeconomic status, duration of diabetes, and comorbid illness.

RESULTS—We identified 138,662 adults with diabetes. The mean 5-year cost of diabetes in the overall cohort was $26,978 per patient, excluding drug costs. The mean 5-year cost for the subset of people >65 years of age, including drug costs, was $44,511 (Canadian dollars). Cost increased with worsening kidney function, presence of proteinuria, and suboptimal glycemic control (HbA_{1c} >7.9%). Increasing age, Aboriginal status, socioeconomic status, duration of diabetes, and comorbid illness were also associated with increasing cost.

CONCLUSIONS—The cost of caring for people with diabetes is substantial and is associated with suboptimal glycemic control, abnormal kidney function, and proteinuria. Future studies should assess if improvements in the management of diabetes, assessed with laboratory-derived measurements, result in cost reductions.

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Between 6 and 9% of North American adults have diabetes (1–3) and are at risk for diabetes-related complications, including both macro- and microvascular disease. Compared with adults without diabetes, adults with diabetes are three times as likely to be hospitalized with cardiovascular disease and six times as likely to be hospitalized with chronic kidney disease (1).

The economic burden of diabetes was estimated to be $12.2 billion (Canadian dollars [CDN]) in 2010 (4). In one province in Canada, where only 3.6% of the population had diabetes, medical costs for this group accounted for 15% of total health care spending (5). Patients with diabetes who have complications incur higher costs (4–8) and an estimated one-third of the direct medical cost of diabetes can be attributed to the management of complications (5). Cardiovascular illnesses account for the majority of this spending.

Suboptimal glycemic control (measured using HbA_{1c}), proteinuria (measured using urinalysis), and reduced kidney function (measured using the estimated glomerular filtration rate [eGFR]) are independent predictors of adverse clinical outcomes, including cardiovascular morbidity and mortality, in people with diabetes (9–11). Although the cost of diabetes is known to be higher for patients with comorbid illness, the link between cost and the laboratory measures noted above has not been firmly established or quantified. HbA_{1c} was associated with costs in the U.S. health maintenance organization (HMO) setting (12–15); however, these findings may not be transferable to other settings. Given the emphasis that diabetes clinical practice guidelines place on the use of laboratory measures to monitor and optimize care (16,17), it is important to understand whether these measures are associated with increased health care resource use in people with diabetes.

We have determined current medical costs over a 5-year time period for a province-wide cohort of patients with diabetes. We have also determined the association between laboratory-derived measures of glycemic control (HbA_{1c}) and presence of renal complications (proteinuria and reduced eGFR) with the 5-year costs of caring for people with diabetes.

RESEARCH DESIGN AND METHODS

Data sources

We used population-level data from the Alberta Kidney Disease Network (AKDN; www.akdn.info). The AKDN is a province-wide network that captures laboratory measurements, including serum creatinine, lipid profile, HbA_{1c}, and measures of urine protein (18). These data are linked to Alberta Health administrative data, which captures resource utilization for all provincial residents with public health insurance. All residents of Alberta are eligible for public health insurance, and >99% of residents participate in the government-sponsored insurance plan. Public health insurance covers the cost of all medically necessary

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Table 1—*Baseline characteristics for the cohort*

	Entire cohort	Age ≤65	Age >65	
	Mean (SD)/% (number)	Mean (SD)/% (number)	Mean (SD)/% (number)	*P* value‡
n	138,662	80,772	57,890	
Age	60.8 (15.3)	50.4 (10.5)	75.3 (6.91)	<0.001
Sex (female)	47.8 (66,286)	46.9 (37,865)	49.1 (28,421)	<0.001
Duration of diabetes (years)	5.4 (3.29)	5.0 (3.24)	5.9 (3.28)	<0.001
Aboriginal	4.7 (6,530)	6.5 (5,260)	2.2 (1,270)	<0.001
Socioeconomic status				
High income*	NA*	56.4 (28,583)	NA*	NA
Low income*	NA*	34.9 (28,161)	NA*	NA
Income support	11.0 (15,287)	16.7 (8,479)	4.8 (2,762)	<0.001
Comorbidities				
History of MI	4.9 (6,825)	3.3 (2,622)	7.3 (4,203)	<0.001
History of stroke	3.7 (5,134)	1.6 (1,311)	6.6 (3,823)	<0.001
History of CHF	12.8 (17,767)	5.4 (4,346)	23.2 (13,421)	<0.001
Hypertension	60.5 (83,926)	47.1 (38,011)	79.3 (45,915)	<0.001
On dialysis	0.77 (917)	0.65 (522)	0.68 (395)	0.061
History of cancer	7.4 (10,314)	4.4 (3,522)	11.7 (6,792)	<0.001
Charlson score ≤1	58.5 (81,061)	68.0 (54,935)	45.1 (26,126)	<0.001
Charlson score 2–3	28.9 (40,040)	25.4 (20,486)	33.8 (19,554)	<0.001
Charlson score >3	12.7 (17,561)	6.6 (5,351)	21.1 (12,210)	<0.001
Medications at baseline†				
No diabetes medication	NA	NA	31.8 (18,435)	NA
Oral antidiabetic	NA	NA	50.7 (29,367)	NA
Insulin	NA	NA	5.9 (3,414)	NA
Oral antidiabetic and insulin	NA	NA	11.5 (6,674)	NA
Statin	NA	NA	52.8 (30,584)	NA
Other cholesterol lowering	NA	NA	4.9 (2,841)	NA
Antihypertensive	NA	NA	78.4 (45,433)	NA
Laboratory values				
Kidney function: eGFR (mL/min/1.73 m^2)				
≥90	24.5 (34,009)	38.1 (30,760)	5.6 (3,249)	<0.001
60−89.9	34.9 (48,362)	28.8 (23,248)	43.4 (25,114)	<0.001
45−59.9	9.3 (12,857)	3.2 (2,581)	17.8 (10,276)	<0.001
30−44.9	4.8 (6,599)	1.2 (967)	9.7 (5,632)	<0.001
15−29.9	1.7 (2,370)	0.48 (384)	3.4 (1,986)	<0.001
<15 nondialysis	0.25 (347)	0.14 (111)	0.41 (236)	<0.001
Not measured	26.4 (34,118)	28.1 (22,721)	19.7 (11,397)	<0.001
Proteinuria				<0.001
Normal	48.9 (67,776)	50.6 (40,904)	46.4 (26,872)	<0.001
Mild	13.5 (18,649)	11.5 (9,284)	16.2 (9,365)	<0.001
Heavy	4.1 (5,691)	3.4 (2,782)	5.0 (2,909)	<0.001
Not measured	33.6 (46,546)	34.4 (27,802)	32.4 (18,744)	<0.001
Glycemic control (HbA_{1c})				
Good (≤7%)	38.3 (53,070)	34.2 (27,664)	43.9 (25,406)	<0.001
Fair (7.1−7.9%)	15.3 (21,189)	14.1 (11,412)	16.9 (9,777)	<0.001
Poor (8−9%)	9.6 (13,252)	10.0 (8,111)	8.9 (5,141)	<0.001
Inadequate (>9%)	9.8 (13,585)	12.4 (10,014)	6.2 (3,571)	<0.001
Not measured	27.1 (37,566)	29.2 (23,571)	24.2 (13,995)	<0.001

NA, not applicable. *High income, ≥$39,250; low income, <$39,250. There is no marker to distinguish between high and low income in residents >65 years of age. †Drug data were only available for the subgroup >65 years of age. ‡For comparison between all patients and >65 years of age.

physician visits, hospitalizations, investigations, and procedures. In addition, drug insurance is provided for all residents >65 years of age. Alberta Health data capture all health care utilization paid for through the provincial insurance plan. Vital statistics and health insurance registry data were also obtained from Alberta Health. Since public health insurance does not provide universal drug coverage for residents <65 years of age, drug costs are only available for patients >65 years of age. Physician visit, hospitalization, and ambulatory care costs are available for the entire cohort.

Cohort

A cohort of patients 18 years of age and older with prevalent diabetes as of 1 May 2004 was identified from Alberta Health administrative data (18). Cases of diabetes were defined based on health care encounters incurred between 1 April 1995 and the date of cohort entry, 1 May 2004. We used the validated National Diabetes Surveillance System definition: two or more physician claims for diabetes (ICD-9 code 250.x) within 2 years, or one or more hospitalizations with an ICD-9 code of 250.x, selected from all available diagnostic codes on the Hospital Discharge Abstract prior to 31 March 2002 or equivalent ICD-10 codes (E10–14) after 31 March 2002 (19,20). Due to the use of a single diagnostic code for diabetes, it is often not possible to reliably distinguish between type 1 and type 2 diabetes using administrative data. Approximately 90% of prevalent diabetes cases are type 2 diabetes (1); therefore, all cost estimates based on this cohort are heavily weighted toward type 2 diabetes. The cohort was followed for 5 years, from 1 May 2004 to 30 April 2009.

Age, sex, Aboriginal status, and measures of socioeconomic status were determined from the registry file. These factors were included because they are known modifiers of health care utilization (21,22). Aboriginal race/ethnicity was defined by First Nations status. Socioeconomic status was categorized as high income (annual adjusted taxable family income ≥CDN $39,250), low income (annual adjusted taxable family income <CDN $39,250), and income support (provided to people and families with disabilities or with incomes below specified thresholds, e.g., CDN $14,880 for a two-parent family with three children) according to the Alberta health insurance registry (23). The duration of diabetes was calculated as time from diagnosis to 1 May 2004. Comorbidities were defined using administrative data for health care encounters during the 3 years prior to cohort entry. We calculated the Charlson comorbidity index (24,25), a weighted score of 17 comorbid conditions that has been shown to predict mortality (24,25). We also determined the proportion of patients having a history of cardiovascular disease, hypertension, coronary revascularization, cancer, or end-stage renal disease (ESRD).

Baseline laboratory-derived measures relevant to patients with diabetes

Outpatient measures for HbA_{1c}, eGFR, and proteinuria (urine microalbumin-to-creatinine

Table 2—*Baseline characteristics stratified by category of glycemic control*

							<65 years of age		>65 years of age		
	Entire cohort	Good (≤7%)	Fair (7.1–7.9%)	Poor (8–9%)	Inadequate (>9%)	Not measured	Measured	Not measured	Measured	Not measured with diabetes meds	Not measured without diabetes meds
n	138,662	53,070	21,189	13,252	13,585	37,566	57,201	23,571	43,895	6,615	7,380
Mean age (SD)	60.8 (15.3)	63.2	62.7	60.1	55.8	58.3	51.6	47.5	74.9	74.7	78.1
Female (*n*, %)	66,286 (47.8)	48.0	45.7	45.2	43.9	51.1	44.9	51.7	48.8	47.0	52.5
Duration of diabetes (years)	5.4 (3.29)	4.5	6.0	6.6	6.4	5.3	4.9	5.1	6.0	5.9	5.3
Aboriginal (%)	4.7 (6,530)	4.1	3.3	4.5	8.8	4.9	6.4	6.7	2.3	1.5	2.4
Socioeconomic status (%)											
<65 years, high income*	56.4 (28,583)	48.6	48.3	50.1	49.3	51.5	42.5	44.7	NA	NA	NA
<65 years, low income*	17.9 (9,070)	36.7	37.4	34.3	31.2	33.3	35.5	33.3	NA	NA	NA
Income support	11.0 (15,287)	9.8	9.8	11.7	16.5	11.2	15.6	15.2	4.9	4.8	3.9
Comorbidities (%)											
History of MI	4.9 (6,825)	4.9	5.7	5.9	5.5	3.9	3.7	2.2	7.4	5.9	7.6
History of stroke	3.7 (5,134)	4.2	3.8	3.6	2.8	3.3	1.8	1.2	6.5	4.5	9.0
History of CHF	12.8 (17,767)	13.8	13.8	13.5	10.9	11.4	6.0	3.8	22.8	18.7	29.3
Hypertension	60.5 (83,926)	67.4	67.0	62.7	53.7	48.8	52.6	33.7	81.0	75.4	73.0
Dialysis	0.77 (917)	0.9	0.7	0.8	0.5	0.3	0.5	0.2	1.1	0.2	0.7
History of cancer	7.4 (10,314)	8.7	7.8	7.1	5.6	6.2	4.8	3.3	11.9	9.7	12.5
Charlson score ≤1	58.5 (81,061)	54.3	55.2	55.0	57.3	67.7	64.1	77.6	43.2	53.4	49.0
Charlson score 2–3	28.9 (40,040)	30.7	31.1	30.9	31.0	23.5	28.0	18.8	34.5	33.9	29.2
Charlson score >3	12.7 (17,561)	15.0	13.7	14.1	11.5	8.7	7.9	3.6	22.2	12.7	21.8

NA, not applicable. *High income, ≥$39,250; low income, <$39,250. There is no marker to distinguish between high and low income in residents >65 years of age.

ratio [ACR] and urine dipstick) were included from 2 years prior to 6 months past the index date. For those patients not on dialysis at baseline, the eGFR was estimated from serum creatinine using the validated CKD-EPI equation (26). The mean of the two outpatient eGFR measurements made closest to the index date (May 1, 2004) was used to categorize patients into standard eGFR categories (eGFR >90, 60–90, 45–60, 30–45, 15–30, and <15 mL/min/m^2 not requiring dialysis) (27). Patients on dialysis were classified separately, and the eGFR was not considered for this subset. Proteinuria was assessed using the median measurement for urine protein. The ACR was used as the primary measure of proteinuria, supplemented by urine dipstick measurement when ACR was not available. Proteinuria was categorized into three levels: normal (ACR <30 mg/g or dipstick negative), mild (ACR 30–300 mg/g or dipstick 1+ or trace), and heavy (ACR >300 mg/g or dipstick ≥2+). We used the mean of the two HbA_{1c} measurements made closest to the index date to classify patients according to glycemic control: good (HbA_{1c} ≤7%), fair (7.1–7.9%), poor (8–9%), or inadequate (>9%).

Outcomes

The primary outcome was 5-year cumulative health care costs for the entire cohort. Drug costs were excluded for all patients in this primary outcome. As a secondary outcome, we studied 5-year cumulative costs for the subset of patients >65 years of age, including drug costs. We adopted the perspective of the health care payer; therefore, nonmedical costs (i.e., patient time and travel costs, as well as costs related to lost productivity) were not included. All costs are reported in 2010 CDN dollars. To inform the generalizability of our results, we determined the incidence of clinical outcomes (myocardial infarction, stroke, congestive heart failure, coronary revascularization, ESRD, and death) over the 5-year follow-up period, enabling a qualitative comparison with rates observed in other diabetes cohorts.

Statistical analysis

All analyses were performed for the cohort as a whole and for the subgroup >65 years of age (in whom drug costs were included). The mean 5-year direct medical costs of diabetes were determined in both cases. Since <3% of patients were lost to follow-up due to outmigration, imputation for missing costs was not required. Costs were further categorized according to baseline demographic and clinical characteristics, including comorbid illness and laboratory measurements.

The association between measures of baseline glycemic control, kidney function (including a separate category for people with ESRD on dialysis at baseline), proteinuria, and 5-year cost was determined using multivariate linear regression, controlling for age, sex, Aboriginal status, socioeconomic status, duration of diabetes, and Charlson index score. Given its ease of interpretation and to facilitate communication, we used a linear regression model using ordinary least squares estimation to assess factors associated with cost, and to estimate the adjusted mean 5-year cost for each category. We compared the fit of the linear regression model against that of four other candidate models, linear regression on log total costs with smearing retransformation (28) and three generalized linear models using the negative binomial (gamma) and inverse Gaussian distributions, and found

Table 3—*Mean total 5-year unadjusted costs per patient with diabetes, overall and by subgroup*

	All patients, without drug costs ($) (IQR)	≤65 years, without drug costs ($) (IQR)	>65 years, without drug costs ($) (IQR)	>65 years, with drug costs ($) (IQR)
All patients	26,978 (3,401–30,141)	21,336 (2,575–19,844)	34,849 (5,911–44,692)	44,511 (13,758–56,333)
Age (years)				
<50	17,736 (2,072–15,551)	17,736 (2,072–15,551)	NA	NA
50–65	23,882 (3,304–23,547)	23,882 (3,304–23,547)	NA	NA
>65	34,849 (5,911–44,692)	NA	NA	NA
Male	27,348 (2,939–30,700)	21,379 (2,140–19,302)	36,038 (5,913–46,139)	45,638 (13,774–57,425)
Female	26,573 (3,967–29,526)	21,286 (3,175–20,348)	33,617 (5,909–43,351)	43,343 (13,745–55,294)
Aboriginal	38,186 (4,444–39,166)	35,049 (4,009–32,008)	51,179 (8,394–71,201)	56,997 (12,565–78,888)
Socioeconomic status				
High income* (age <65 years only)	14,624 (2,034–13,636)	14,624 (2,034–13,636)	NA*	NA*
Low income* (age <65 years only)	19,373 (2,752–19,305)	19,373 (2,752–19,305)	NA*	NA*
Income support	39,383 (4,906–43,772)	38,652 (4,674–40,878)	42,699 (6,294–55,470)	54,183 (15,046–69,179)
Duration of diabetes (years)				
<1	20,986 (2,877–22,996)	16,743 (2,381–16,829)	29,611 (5,090–38,714)	37,800 (11,442–48,227)
1–5	22,127 (2,895–24,444)	17,199 (2,283–16,737)	30,701 (5,188–39,615)	39,567 (12,224–50,031)
>5	31,857 (4,078–36,414)	26,304 (2,975–24,218)	37,990 (6,559–48,885)	48,324 (15,302–61,045)
History of MI	44,411 (7,619–55,031)	40,809 (4,981–43,863)	46,658 (10,240–60,105)	57,957 (19,385–73,736)
History of stroke	44,216 (7,485–56,085)	49,742 (6,633–58,265)	42,321 (7,922–55,491)	51,301 (14,623–66,727)
History of CHF	53,224 (10,650–67,543)	61,997 (8,572–73,919)	50,383 (11,466–66,001)	60,816 (19,426–78,920)
Hypertension	32,900 (4,714–38,707)	27,929 (3,454–26,622)	37,016 (6,553–47,706)	47,430 (15,365–59,654)
Dialysis	193,533 (54,785–314,785)	161,621 (29,717–251,234)	167,166 (46,885–261,328)	197,273 (66,419–390,034)
History of cancer	39,039 (7,326–48,279)	34,431 (5,238–36,614)	41,428 (9,206–52,772)	51,042 (16,763–64,631)

All values are in 2010 CDN (multiply by 1.072 to convert to 2010 U.S. dollars). *High income, ≥$39,250; low income, <$39,250. There is no marker to distinguish between high and low income in residents >65 years of age.

Table 4—*The cost of managing patients with diabetes, stratified by category of glycemic control*

	Entire cohort	Good (≤7%)	Fair (7.1–7.9%)	Poor (8–9%)	Inadequate (>9%)	Not measured	<65 years of age		>65 years of age		
	Mean (SD)/% (*n*)	Mean/%	Mean/%	Mean/%	Mean/%	Mean/%	Measured	Not measured	Measured	Not measured with diabetes meds	Not measured without diabetes meds
n	138,662	53,070	21,189	13,252	13,585	37,566	57,201	23,571	43,895	6,615	7,380
Hospitalization cost, $	14,587	14,832	15,014	16,327	18,848	11,844	11,220	7,796	21,321	20,971	16,594
Physician cost, $	6,253	6,600	6,642	7,028	7,484	4,825	6,048	4,412	7,742	6,659	5,359
Drug cost (age >65), $	9,662	9,860	11,240	11,613	10,607	7,240	NA	NA	10,434	9,770	4,975
Ambulatory care cost, $	6,138	6,618	6,487	7,502	7,701	4,217	6,411	3,711	7,426	5,755	4,453
Total cost without drugs, $	26,978	28,050	28,144	30,857	34,032	20,886	23,679	15,649	36,690	33,385	26,406
Total cost with drugs (age >65), $	44,511	44,959	46,772	51,956	54,071	36,945	NA	NA	46,923	43,153	31,381

Costs are expressed in CDN$.

that the linear regression model performed well based on mean absolute error, root mean squared error, Lin concordance, pseudo *R* squared, probability plots, quantile-quantile plots, and predicted versus observed mean costs. Ethics approval for the study was obtained from the conjoint health ethics review board at the University of Calgary. All analyses were undertaken using STATA, version 11.2 (College Station, TX).

RESULTS

Baseline characteristics

Overall 138,662 patients with prevalent diabetes as of 1 May 2004 were included in the cohort. The cohort was 47.8% female, 41.7% of patients were >65 years of age, and the mean duration of diabetes was 5.3 years (Table 1). The most common comorbid condition was hypertension (60.5%), and all comorbidities increased with age. In patients >65 years of age, two-thirds had filled a prescription for one or more oral antidiabetic medication at baseline (62.2%), and approximately one-fifth (17.4%) of patients were on insulin. Over three-quarters (78.4%) filled a prescription for an antihypertensive agent, and approximately one-half had filled a prescription for a statin (52.8%). Compared with patients <65 years of age, patients >65 years of age were less likely to be Aboriginal (6.5 vs. 2.2%), less likely to be on income support (16.7 vs. 4.8%), had a longer average duration of diabetes (5.0 vs. 5.9 years), and had a higher burden of disease measured by a Charlson score of >3 (6.6 vs. 21.1%) (Table 1).

Laboratory measurements

Laboratory measurements were available for the majority of the cohort: 73% for HbA_{1c}, 66% for proteinuria, and 84% for eGFR. These measurements revealed that 2.6% of the cohort had an eGFR <30, indicating severe renal impairment, 4.1% had heavy proteinuria, and 9.8% had inadequate glycemic control (>9% HbA_{1c}) (Table 1). Patients >65 years of age had a higher proportion of people with low eGFR and proteinuria but had better overall glycemic control. In all, 16% of the cohort did not have any of the three measurements. Patients without laboratory measurements tended to be younger (mean age 56.4 vs. 61.6 years) and had a lower burden of disease, measured by a Charlson score of >3 (4.6 vs. 14.2%) (Table 1).

Patient characteristics varied across strata of glycemic control and whether or not they had an HbA_{1c} measurement (Table 2). Those with inadequate glycemic control were younger, had a higher proportion with Aboriginal status and low socioeconomic status, and had less comorbid disease at baseline. To explore the notion that patients without HbA_{1c} measurements may have been misclassified, we compared patients under and over 65 years of age separately (Table 2). Among patients <65 years of age, those with unmeasured HbA_{1c} were less likely to have comorbid illness, possibly suggesting that some of the unmeasured patients were misclassified. Among those >65 years of age with unmeasured HbA_{1c}, some were taking diabetes medications. Those not taking diabetes medications were older and had more comorbid illness, indicating that rather than being misclassified, patients in this category may in fact be at a stage of illness where glycemic control has become less important. Although speculative, taken together, these findings suggest that patients without HbA_{1c} measurements represent a heterogeneous group comprised of misclassified patients, those with very mild disease, as well as frail older patients not being actively managed for their diabetes.

Five-year costs

Unadjusted 5-year costs are presented in Table 3. The mean cumulative 5-year cost of caring for patients with diabetes in Alberta, excluding drug costs was CDN $26,978 per patient (IQR $3,401–30,141). Costs increased with age, Aboriginal status, lower socioeconomic status, longer duration of diabetes, and comorbidity. Medications accounted for $10,000 or approximately one-quarter of the 5-year medical costs for people >65 years of age; the mean cumulative 5-year cost for this group, including drug costs, was CDN $44,511 (IQR $13,758–56,333) per patient. Excluding drug costs, patients >65 years of age had consistently higher costs.

Association between glycemic control, proteinuria, and kidney function and 5-year costs

After stratification by kidney function, the adjusted cost of caring for patients with diabetes varied from $25,316 (for patients with eGFR >90 mL/min) to $115,348 (for patients not on dialysis with eGFR <15 mL/min) (Fig. 1). Patients who had no proteinuria had an adjusted mean cost of $24,531 per patient compared with $46,836 for patients with heavy proteinuria. Patients with good glycemic control had an adjusted mean cost of $27,064 per patient compared with $32,629 for patients with inadequate control. Similar trends were noted in the subgroup of patients >65 years of age when drug costs were included. Adjusted costs demonstrated a consistent trend of increasing cost with increasing severity of disease, as assessed by laboratory measures (Fig. 1).

The mean unadjusted costs for patients without an eGFR or proteinuria measurement were slightly higher compared with the normal categories. In contrast, patients without an HbA_{1c} measurement had lower mean costs than those with HbA_{1c} ≤7%. When unadjusted costs were examined by level of glycemic control, we noted a similar pattern across all categories of cost (Table 4); those with good control cost less across all categories of health care spending.

The coefficients and *P* values for the linear regression model for the overall cohort are presented in Table 5. In addition to the laboratory parameters described above, worsening socioeconomic status, Aboriginal status, and increasing Charlson index score were associated with increased 5-year costs. When kidney function was considered, people with progressively lower levels of kidney function had significantly higher costs. The model estimates that patients with an eGFR of <15 mL/min have average 5-year costs $91,419 higher compared with a patient with no renal impairment (eGFR >90 mL/min), patients with heavy proteinuria have costs $22,305 higher per patient compared with those with no proteinuria, and patients with inadequate glycemic control had costs $5,565 higher per patient compared with those with good glycemic control.

CONCLUSIONS—The mean 5-year cost of diabetes in Alberta was CDN $26,978 per patient, excluding drug costs, and CDN $44,511 per patient for

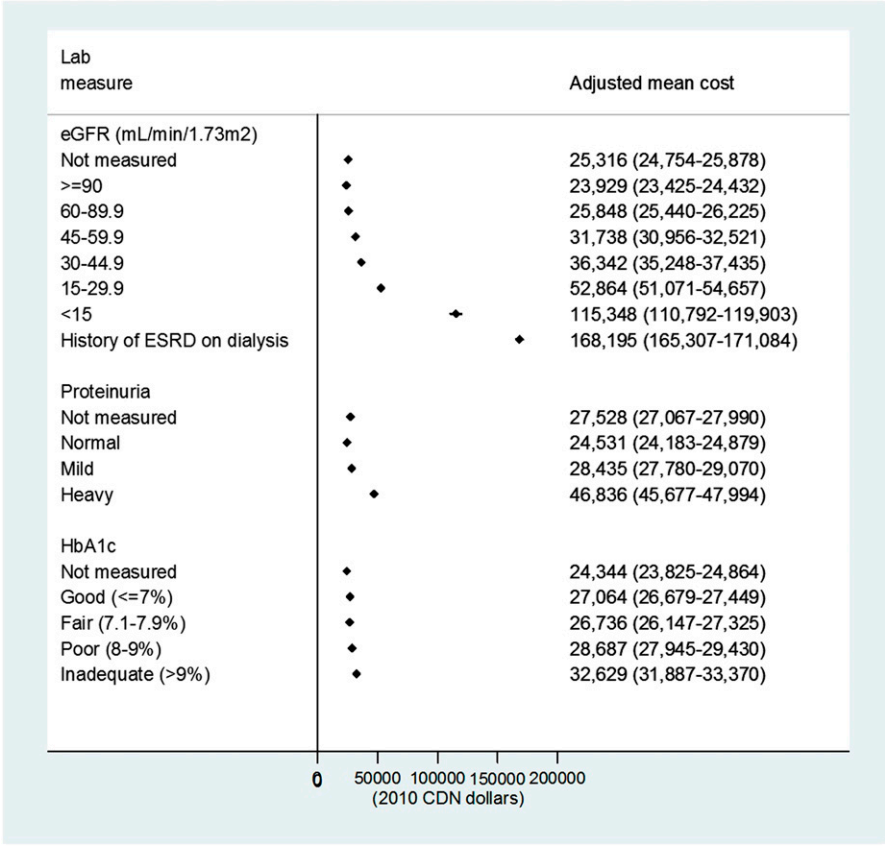

Figure 1—*Adjusted mean cost per patient, stratified by laboratory measure of relevance to patients with diabetes.*

Table 5—*Ordinary least squares regression analysis examining the demographic, clinical, and laboratory factors associated with mean total 5-year costs per patient in people with diabetes*

	Coefficient*	*P* value
Age (comparator <50 years)		
50–65 years	2,698	<0.001
65–80 years	6,670	<0.001
>80 years	2,728	<0.001
Female	−771	0.001
Socioeconomic status		
Low income	3,626	<0.001
Income support	15,824	<0.001
Aboriginal	14,398	<0.001
Duration of diabetes (comparator <1 year)		
1–5 years	663	0.094
>5 years	4,861	<0.001
Charlson comorbidity index (comparator ≤1)		
Charlson index 2–3	10,485	<0.001
Charlson index ≥4	26,155	<0.001
Kidney function: eGFR (comparator >90 mL/min/1.73 m^2)		
Not measured	1,388	<0.001
60–89.9 mL/min/1.73 m^2	1,919	<0.001
45–59.9 mL/min/1.73 m^2	7,810	<0.001
30–44.9 mL/min/1.73 m^2	12,413	<0.001
15–29.9 mL/min/1.73 m^2	28,936	<0.001
<15 mL/min/1.73 m^2 nondialysis	91,419	<0.001
History of ESRD on dialysis	142,158	<0.001
Proteinuria (comparator no proteinuria)		
Not measured	2,998	<0.001
Mild	3,904	<0.001
Heavy	22,305	<0.001
HbA_{1c} (comparator ≤7%)		
Not measured	−2,720	<0.001
7.1–7.9%	−328	0.351
8–9%	1,623	<0.001
>9%	5,565	<0.001
Constant†	4,065	<0.001

*The coefficient represents the additive cost for each covariate, compared with baseline. †The constant represents the baseline cost for a person <50 years of age, duration of diabetes <1 year, Charlson index ≤1, eGFR >90 mL/min, proteinuria normal, and HbA_{1c} ≤7%.

patients >65 years of age, including drug costs. Our analysis demonstrates that after adjusting for sex, age, duration of diabetes, Aboriginal status, socioeconomic status, and comorbid illness, costs increased with worsening kidney function, higher levels of proteinuria, and worsening glycemic control. Adjusted costs increased fivefold for people with eGFR <15 mL/min/m^2 compared with eGFR >90 mL/min/m^2 ($115,348 vs. $25,316) and were twice as high in patients with heavy proteinuria compared with those with no proteinuria ($46,836 vs. $24,531). Costs increased less dramatically as glycemic control worsened; patients with inadequate glycemic control ($32,629 for patients with HbA_{1c} >9%) had 20% higher costs compared with patients with good control ($27,064 for HbA_{1c} <7%). Costs were also positively associated with age, Aboriginal status, lower socioeconomic status, duration of diabetes, and Charlson comorbidity index.

It is estimated that 2.8 million Canadians will have diabetes in 2012, and our analysis suggests that health care funders will spend approximately CDN $25 billion per year on the care of people with diabetes. This represents ~12.5% of total health care spending in Canada, which was estimated at $200 billion annually in 2011 (29). This may be an underestimation of the costs of diabetes, given that we have not accounted for incident cases of diabetes in our 5-year projections nor have we included the cost of people with undiagnosed diabetes.

Other studies have noted an association between poor glycemic control (measured by HbA_{1c}) and cost (12–15); however, all were based on U.S. HMO populations and therefore may not have reflected patients at all socioeconomic levels. By differentiating HbA_{1c} levels into four distinct categories, we were able to show that costs do not appear to rise until HbA_{1c} increases beyond 7.9%. Similarly, Gilmer et al. (14) found that in HMO patients, higher HbA_{1c} was predictive of costs in patients with HbA_{1c} >7.5% but not in patients with HbA_{1c} of <7.5%. Our analysis further demonstrates that costs are associated with two other laboratory measures of direct relevance to patients with diabetes, namely eGFR, a marker of kidney function and proteinuria.

Although this study does not provide direct evidence that improvements in diabetes management would lead to cost reductions, our findings demonstrate a clear association between increased cost and suboptimal glycemic control and markers of kidney disease. It is plausible that better glycemic control in patients with HbA_{1c} >8% might delay or moderate the increasing costs associated with duration of diabetes through a reduction in diabetes complications (30–32). Wagner et al. (33) studied the association between improvement in glycemic control and cost in a retrospective cohort analysis and found that in patients with high baseline HbA_{1c} (≥10%) whose glycemic control improved, statistically significant cost savings were achieved. In addition, the optimized use of ACE inhibitors and angiotensin II receptor blockers or improved management of hypertension, through delaying the decline in kidney function (34–41), may lead not only to improvements in health but also to moderation of medical costs.

Mean 5-year costs were lower in patients who were not on oral antidiabetic medications or insulin at baseline (in those >65 years of age) and in patients who did not have laboratory testing during the 2 years prior to and 6 months past the index date. We are unable to determine the reasons why patients in these groups did not fill a prescription for diabetes medication or have laboratory testing within the measured time frame, and there are likely many factors involved. Our regression model included a "not

measured" category for each laboratory marker, which is reflected in the adjusted cost estimates. Our data demonstrated that the "not measured" category was comprised of a heterogeneous group of patients with respect to demographics and comorbid illness, both of which were accounted for in the adjusted analyses. We did not adjust for medication use since this information was not available for the entire cohort, nor were we able to adjust for unknown factors, such as mild diabetes, misclassification, and more specific socioeconomic characteristics.

Our study was an observational cohort study and was therefore limited by potential confounding and by the data available. Although we controlled for all available confounders, including age, sex, socioeconomic status, and comorbid illness, we were not able to control for other potentially important variables, including ethnicity and education. In addition, although we found a strong association between glycemic control, proteinuria, and kidney function and costs, it is unknown whether improved management would in fact lead to a decrease in health care costs. Economic evaluations alongside controlled intervention studies are needed to draw definitive conclusions. In addition, we used an administrative definition of diabetes to define our cohort and, although this definition has been shown to perform well, some cases may have been misclassified. Finally, the cohort was representative of the population of Alberta. Although this may not be generalizable to all other settings, we expect that the relative differences in costs that we observed across different categories of laboratory measures would hold in other jurisdictions.

Our study also has many strengths. The large dataset makes it unlikely that any of the associations found between patient factors and cost were due to chance alone. Furthermore, our unique dataset included access to linked laboratory, clinical, and costing data, enabling us to study the association between disease severity markers and cost.

In summary, we have generated updated values for the 5-year cost of caring for patients with diabetes in a universal health care system, which will aid decision makers in planning future resource allocation. After controlling for clinical and demographic factors, we found that the cost of caring for people with diabetes increased with suboptimal glycemic control, proteinuria, and worsening kidney function. Future studies should assess whether strategies to improve these laboratory measures lead to reduced costs.

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K.A.M., B.J.M., and F.C. were involved in the concept and design, performed statistical analysis, interpreted results, and drafted the manuscript. B.C. and N.W. performed statistical analysis. S.W.K. and D.R. interpreted results. P.R. performed statistical analysis and interpreted results. B.H. acquired data and interpreted results. F.A. acquired data and performed statistical analysis. All authors reviewed the final manuscript. F.C. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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References

1. Report from the National Diabetes Surveillance System. *Diabetes in Canada, 2009*. Public Health Agency of Canada, 2009
2. Centers for Disease Control and Prevention. *National Diabetes Fact Sheet: National Estimates and General Information on Diabetes and Prediabetes in the United States, 2011*. Atlanta, GA, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2011
3. Lipscombe LL, Hux JE. Trends in diabetes prevalence, incidence, and mortality in Ontario, Canada 1995-2005: a population-based study. Lancet 2007;369:750–756
4. Fu AZ, Qiu Y, Radican L, Wells BJ. Health care and productivity costs associated with diabetic patients with macrovascular comorbid conditions. Diabetes Care 2009;32:2187–2192
5. Simpson SH, Corabian P, Jacobs P, Johnson JA. The cost of major comorbidity in people with diabetes mellitus. CMAJ 2003;168:1661–1667
6. Brandle M, Zhou H, Smith BR, et al. The direct medical cost of type 2 diabetes. Diabetes Care 2003;26:2300–2304
7. O'Brien JA, Patrick AR, Caro JJ. Cost of managing complications resulting from type 2 diabetes mellitus in Canada. BMC Health Serv Res 2003;3:7
8. Pelletier EM, Shim B, Ben-Joseph R, Caro JJ. Economic outcomes associated with microvascular complications of type 2 diabetes mellitus: results from a US claims data analysis. Pharmacoeconomics 2009;27:479–490
9. Rosenson RS, Fioretto P, Dodson PM. Does microvascular disease predict macrovascular events in type 2 diabetes? Atherosclerosis 2011;218:13–18
10. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;321:405–412
11. Targher G, Zoppini G, Chonchol M, et al. Glomerular filtration rate, albuminuria and risk of cardiovascular and all-cause mortality in type 2 diabetic individuals. Nutr Metab Cardiovasc Dis 2011;21:294–301
12. Aagren M, Luo W. Association between glycemic control and short-term healthcare costs among commercially insured diabetes patients in the United States. J Media Econ 2011;14:108–114
13. Gilmer TP, O'Connor PJ, Manning WG, Rush WA. The cost to health plans of poor glycemic control. Diabetes Care 1997;20:1847–1853
14. Gilmer TP, O'Connor PJ, Rush WA, et al. Predictors of health care costs in adults with diabetes. Diabetes Care 2005;28:59–64
15. Oglesby AK, Secnik K, Barron J, Al-Zakwani I, Lage MJ. The association between diabetes related medical costs and glycemic control: a retrospective analysis. Cost Eff Resour Alloc 2006;4:1
16. American Diabetes Association. Standards of medical care in diabetes—2012. Diabetes Care 2012;35(Suppl. 1):S11–S63
17. Canadian Diabetes Association. Clinical practice guidelines for the prevention and management of diabetes in Canada. Canadian Journal of Diabetes 2008;32(Suppl. 1):S1–S201
18. Hemmelgarn BR, Clement F, Manns BJ, et al. Overview of the Alberta Kidney Disease Network. BMC Nephrol 2009;10:30
19. Blanchard JF, Ludwig S, Wajda A, et al. Incidence and prevalence of diabetes in Manitoba, 1986-1991. Diabetes Care 1996;19:807–811
20. Hux JE, Ivis F, Flintoft V, Bica A. Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. Diabetes Care 2002;25:512–516
21. Johnson D, Jin Y, Truman C. Influence of aboriginal and socioeconomic status on birth outcome and maternal morbidity. J Obstet Gynaecol Can 2002;24:633–640

22. Pohar SL, Johnson JA. Health care utilization and costs in Saskatchewan's registered Indian population with diabetes. BMC Health Serv Res 2007;7:126
23. Government of Alberta-Health and Wellness. Premium assistance program: premium subsidy [Internet]. Available from http://www.health.alberta.ca/AHCIP/premium-subsidy.html. Accessed 4 April 2011
24. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–383
25. Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43:1130–1139
26. Levey AS, Stevens LA, Schmid CH, et al; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–612
27. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis 2002;39(Suppl. 1):S1–S266
28. Duan N. Smearing estimate: a nonparametric retransformation method. J Am Stat Assoc 1983;78:605–610
29. National Health Expenditure Trends, 1975 to 2011. Ottawa, Ontario, 2011, CIHI2011
30. Bennett WL, Wilson LM, Bolen S, Maruthur N, Singh S, Chatterjee R, Marinopoulos SS, Puhan MA, Ranasinghe P, Nicholson WK, Block L, Odelola O, Dalal DS, Ogbeche GE, Chandrasekhar A, Hutfless S, Bass EB, Segal JB. 2011 Mar.
31. Goudswaard AN, Furlong NJ, Rutten GE, Stolk RP, Valk GD. Insulin monotherapy versus combinations of insulin with oral hypoglycaemic agents in patients with type 2 diabetes mellitus. Cochrane Database Syst Rev 2004 (4):CD003418
32. McIntosh B, Cameron C, Singh SR, et al. Second-line therapy in patients with type 2 diabetes inadequately controlled with metformin monotherapy: a systematic review and mixed-treatment comparison meta-analysis. Open Med 2011;5:e35–e48
33. Wagner EH, Sandhu N, Newton KM, McCulloch DK, Ramsey SD, Grothaus LC. Effect of improved glycemic control on health care costs and utilization. JAMA 2001;285:182–189
34. Brenner BM, Cooper ME, de Zeeuw D, et al.; RENAAL Study Investigators. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001;345:861–869
35. de Galan BE, Perkovic V, Ninomiya T, et al.; ADVANCE Collaborative Group. Lowering blood pressure reduces renal events in type 2 diabetes. J Am Soc Nephrol 2009;20:883–892
36. Kasiske BL, Kalil RS, Ma JZ, Liao M, Keane WF. Effect of antihypertensive therapy on the kidney in patients with diabetes: a meta-regression analysis. Ann Intern Med 1993;118:129–138
37. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD; The Collaborative Study Group. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. N Engl J Med 1993;329:1456–1462
38. Lewis EJ, Hunsicker LG, Clarke WR, et al.; Collaborative Study Group. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001;345:851–860
39. Parving HH, Lehnert H, Bröchner-Mortensen J, Gomis R, Andersen S, Arner P; Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria Study Group. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. N Engl J Med 2001;345:870–878
40. Patel A, MacMahon S, Chalmers J, et al.; ADVANCE Collaborative Group. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. Lancet 2007;370:829–840
41. Strippoli GF, Craig MC, Schena FP, Craig JC. Role of blood pressure targets and specific antihypertensive agents used to prevent diabetic nephropathy and delay its progression. J Am Soc Nephrol 2006;17(Suppl. 2):S153–S155