

# The Darkening Cloud of Diabetes

## Do trends in cardiovascular risk management provide a silver lining?

DEAN T. EURICH, PHD<sup>1</sup>  
JOHN-MICHAEL GAMBLE, MSC<sup>1</sup>

SCOT H. SIMPSON, MSC<sup>2</sup>  
JEFFREY A. JOHNSON, PHD<sup>1</sup>

**OBJECTIVE** — We aimed to evaluate the changes in cardiovascular-related health care utilization (drug therapies, hospitalizations) and mortality for the diabetic population during a 9-year period in Saskatchewan, Canada.

**RESEARCH DESIGN AND METHODS** — We identified annual diabetes prevalence rates for people aged  $\geq 30$  years between 1993 and 2001 from the administrative databases of Saskatchewan Health. Annual rates of evidence-based drug therapies (antihypertensives, ACE inhibitors,  $\beta$ -blockers, calcium channel blockers, 3-hydroxy-3-metaglutaril coenzyme A reductase inhibitors [statins]), hospitalizations for cerebrovascular and cardiac events, and all-cause mortality were estimated. Rates were direct age and sex standardized using the 2001 Canadian population, and trends over time were assessed using Joinpoint regression.

**RESULTS** — From 1993 to 2001, diabetes prevalence increased 34% (4.7–6.5%,  $P < 0.001$ ) with the highest rates in men and those aged  $\geq 65$  years. The rate of increase in diabetes prevalence appeared to slow in those aged  $< 65$  years ( $P < 0.01$  for trend). Significant increased use of evidence-based drug therapies was observed (41% increase in antihypertensive agents, 97% increase in ACE inhibitors, 223% increase in statin therapies; all  $P < 0.05$  for trend). During this period, both cerebrovascular and cardiac-related hospitalizations declined by 36% (9.5 vs. 6.1 per 1,000) and 19% (38.0 vs. 30.6 per 1,000) ( $P < 0.05$  for trends), respectively, with similar reductions regardless of sex. No change in all-cause mortality was observed (17.7 vs. 17.8 deaths per 1,000;  $P > 0.05$ ).

**CONCLUSIONS** — During our period of study, there was an increase in the utilization of evidenced-based drug therapies in people with diabetes and reductions in cardiovascular-related hospitalizations. Despite this, we observed no change in all-cause mortality.

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**D** iabetes represents a major public health burden, both locally and globally (1). From 1985 to 2000, the number of people living with diabetes globally rose from 30 million to  $\sim 171$  million (1). Future projections have estimated the prevalence of diabetes to exceed 300 million cases by 2030, with the majority of growth occurring in developing countries (1). Recent estimates, however, suggest that these projections may grossly underestimate the true prevalence (2).

It is well known that diabetes is associated with significant morbidity and mortality. It is estimated that there are six

deaths every minute attributable to the complications of diabetes, with cardiovascular disease being responsible for the vast majority (3). Not surprisingly, diabetes and its complications place an enormous burden on both patients and the health care system, with direct health care costs ranging from 2.5 to 15% of annual health care budgets (4). Given the expected rise in diabetes cases, this economic burden will also increase.

For these reasons, considerable resources have been invested to improve diabetes management. In addition to lifestyle changes, a cornerstone of this management scheme has been the use of

evidence-based drug therapies for vascular protection (5). Large trials have demonstrated that aggressive pharmacologic management of cardiovascular risks can reduce both morbidity and mortality in patients with diabetes (5). It would also appear that the diabetic community is incorporating this evidence into the daily management of diabetic patients. Several studies (6–9) have reported significant increases in the use of evidence-based drug therapies in people with diabetes. However, previous studies have largely focused on antihyperglycemic management (7,8) or have been restricted to specific subpopulations of patients with diabetes (e.g., aged  $\geq 65$  years) (6,9).

The increased prevalence of diabetes has been attributed not only to an increase in incidence but also to reduced mortality rates (2,10). A decrease in mortality rates over time in people with diabetes has been reported in both Canada and the U.S. (2,10–14). It remains uncertain, however, whether concurrent changes in utilization rates of evidence-based drug therapies over time has resulted in substantial improvements in the health of people with diabetes at the population level. We are unaware of studies that have simultaneously evaluated the trends in health care utilization and subsequent changes in mortality in people with diabetes. Therefore, our objective was to explore both health care utilization patterns (i.e., evidence-based drug therapies and hospitalizations) and mortality rates over a 9-year period in an unselected population of patients with diabetes.

### RESEARCH DESIGN AND METHODS

— Data were compiled from the provincial administrative databases for Saskatchewan Health. These databases have been extensively described elsewhere and are considered to be both high quality and comprehensive (15). Saskatchewan Health provides universal health coverage to 99% of the  $\sim 1$  million people in Saskatchewan, Canada (15). These databases include a demographic and vital statistics population registry, outpatient prescription drugs, hospital separation data, and physician services and are linkable through unique patient

From the <sup>1</sup>School of Public Health, University of Alberta, Edmonton, Alberta, Canada; and the <sup>2</sup>Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta, Canada.

Corresponding author: Dr. Dean Eurich, [deurich@ualberta.ca](mailto:deurich@ualberta.ca).

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Table 1—Prevalence of diabetes in 1993 and 2001

	All	Men	Women	Aged <65 years	Aged ≥65 years
1993					
Covered population (n)	539,024	263,112	275,912	397,471	141,553
People with diabetes (n)	27,014	14,431	12,583	11,094	15,920
Crude rate (%)	5.0	5.5	4.6	2.8	11.2
Adjusted rate (%)	4.7*	5.2†	4.2†	2.9*	11.2*
2001					
Covered population (n)	558,085	271,504	286,581	412,739	145,346
People with diabetes (n)	40,098	21,363	18,735	17,448	22,650
Crude rate (%)	7.2	7.9	6.5	4.2	15.6
Adjusted rate (%)	6.5*	7.2†	5.9†	4.2*	15.3*

\*Age and sex adjusted to 2001 Canadian population; †age adjusted to 2001 Canadian population.

identifiers. Importantly, unlike other linked administrative datasets in most jurisdictions, the Saskatchewan Health data include prescription drug information for all ages (i.e., it is not restricted to the age >65 years subgroup). For these analyses, registered Indians were excluded, as their prescription drug benefits are provided by the federal government and are not included in these datasets. Ethical approval was obtained from the health ethics research board of the University of Alberta.

### Outcome assessment

Beneficiaries eligible for provincial prescription drug benefits, aged ≥30 years with diabetes, were identified using the previously validated Canadian National Diabetes Surveillance System criteria (16). Any individual having two physician visits on 2 different days within a 2-year period or one hospitalization with a diagnosis of diabetes (ICD-9 code 250) were identified as having diabetes (2,16). Point prevalence on 31 December of each year was used to determine annual diabetes prevalence and all-cause mortality rates.

Hospital separation records were used to identify subjects with at least one hospitalization for any reason (all cause) or for cardiovascular reasons per calendar year. A hospitalization was categorized as cardiovascular-related if the primary or most responsible diagnosis was coded as a cardiac disorder (ICD-9 codes 410–414 and 425–429) or a cerebrovascular disorder (ICD-9 codes 430–438). Prescription drug use was defined as one or more prescription claims for a medication within a class during the calendar year. Evidence-based drug therapies of interest included the use of any antihypertensive medications (e.g., diuretics, β-blockers, ACE inhibitors, angiotensin receptor II blockers,

calcium channel blockers [CCBs], or α-blockers; the use of ACE inhibitors, β-blockers, or CCBs, specifically; and, the use of 3-hydroxy-3-metaglutaric coenzyme A reductase inhibitors [statins]).

### Statistical analyses

All rates were direct age and sex standardized using the 2001 Canadian census data to facilitate comparisons over time (2). For yearly diabetes prevalence, all subjects diagnosed with diabetes and alive at any point in the year were included in the numerator. The denominator was calculated as the total number of people aged ≥30 years in Saskatchewan who were eligible for benefits within the province as of 30 June of the calendar year. Similar calculations were used for hospitalizations, prescription claims, and mortality, with the numerator representing the total number of people with diabetes who had the event of interest (hospitalization, prescription claim, or death) within the year and the denominators representing all subjects diagnosed with diabetes and were alive at any point within the year. Results are presented for both men and women as well as for those aged <65 and ≥65 years.

All age and sex standardized rates and associated SEs were calculated using Stata Intercooled, version 10 (Stata, College Station, TX). Trends in age- and sex-standardized rates were calculated using Joinpoint regression (<http://srab.cancer.gov/software/software.html>). This form of regression analysis has been used in numerous evaluations of trend data and has been previously described in detail (17). Briefly, this analysis begins by assuming that there are no joinpoints (i.e., a simple linear line) and, through a series of permutations, tests whether the addition of joinpoints (up to two joinpoints were

considered) results in a statistically significant linear change in direction or magnitude of the rates. Parameter estimates for each trend include the annual percentage of change (APC) in rates and associated 95% CI according to generalized linear models that assumed a Poisson distribution.

**RESULTS** — Between 1993 and 2001, crude diabetes prevalence steadily increased by 44% (from 5.0 to 7.2%) (Table 1). After age and sex standardization, the adjusted rates increased 34% (from 4.7 to 6.5%), with an APC increase of 4.3% (95% CI 3.8–4.8) ( $P < 0.001$ ) (Table 1 and Table 2). The difference in crude and adjusted rates suggests that part of the observed increase in diabetes is related to the increasing age of the population.

Although men had a higher prevalence of diabetes compared with women in 1993 (standardized rate ratio [sRR] 1.23 [95% CI 1.20–1.26]) and in 2001 (1.21 [1.19–1.24]), the APC increase was similar between sexes (Table 2). Similarly, people aged ≥65 years had a much higher prevalence of diabetes compared with those aged <65 years in 1993 (sRR 3.84 [3.76–3.94]) and in 2001 (sRR 3.67 [3.59–3.74]), although the APC increase was similar between age-groups (Table 2). Interestingly, in people aged <65 years, the increase in diabetes rates slowed significantly after 1998; 5.4% APC before 1998 and 3.6% APC after 1998 (Table 2) ( $P < 0.001$  for rate change).

### Drug utilization

Between 1993 and 2001, the number of people with at least one prescription claim for an antihypertensive agent increased significantly from 345.8 to 487.1 per 1,000 people with diabetes, respec-

Table 2—Annual percentage change in diabetes prevalence, prescription claims, hospitalizations, and mortality between 1993 and 2001

Outcome	Rates per 1,000			Overall trend			Period-specific trends*						
	1993–2001		Period	APC (95% CI)		Period	Trend 1		Trend 2		Period	APC (95% CI)	
	1993	2001		APC	(95% CI)		APC	(95% CI)	APC	(95% CI)		APC	(95% CI)
<b>Diabetes prevalence</b>													
Overall (age and sex adjusted)	4.7	6.5	1993–2001	4.3	(3.8–4.8)†	—	—	—	—	—	—	—	—
Men (age adjusted)	5.2	7.2	1993–2001	4.2	(3.9–4.6)†	—	—	—	—	—	—	—	—
Women (age adjusted)	4.2	5.9	1993–2001	4.5	(4.1–4.8)†	—	—	—	—	—	—	—	—
Age <65 years (age and sex adjusted)	2.9	4.2	1993–2001	4.7	(4.3–5.2)†	1993–1998	5.4	(4.5–6.4)†	1998–2001	3.6	(2.0–5.2)†	—	—
Aged ≥65 years (age and sex adjusted)	11.2	15.3	1993–2001	4.0	(3.7–4.3)†	—	—	—	—	—	—	—	—
<b>Antihypertensive use</b>													
Overall (age and sex adjusted)	345.8	487.1	1993–2001	4.8	(3.8–5.9)†	1993–1996	1.5	(-0.6 to 3.6)	1996–2001	6.3	(5.5–7.0)†	—	—
Men (age adjusted)	301.5	468.3	1993–2001	6.3	(5.0–7.5)†	1993–1997	3.5	(1.1–6.0)†	1997–2001	8.5	(6.6–10.6)†	—	—
Women (age adjusted)	386.5	504.3	1993–2001	3.7	(2.9–4.6)†	1993–1995	-0.8	(-6.3 to 5.0)	1995–2001	4.6	(3.8–5.4)†	—	—
Age <65 years (age and sex adjusted)	290.8	425.8	1993–2001	5.5	(4.2–6.9)†	1993–1996	1.0	(-1.36 to 3.32)	1996–2001	7.4	(6.5–8.2)	—	—
Aged ≥65 years (age and sex adjusted)	550.8	715.3	1993–2001	3.5	(3.1–3.9)†	—	—	—	—	—	—	—	—
<b>ACE inhibitor use</b>													
Overall (age and sex adjusted)	166.9	328.6	1993–2001	9.2	(8.5–9.9)†	—	—	—	—	—	—	—	—
Men (age adjusted)	155.5	347.8	1993–2001	11.3	(10.5–12.1)†	—	—	—	—	—	—	—	—
Women (age adjusted)	178.5	311.8	1993–2001	7.4	(6.8–8.0)†	—	—	—	—	—	—	—	—
Age <65 years (age and sex adjusted)	146.8	299.9	1993–2001	9.9	(9.0–10.9)†	1993–1997	7.8	(5.1–10.5)†	1997–2001	11.5	(9.6–13.4)†	—	—
Aged ≥65 years (age and sex adjusted)	241.9	435.4	1993–2001	7.6	(7.1–8.2)†	—	—	—	—	—	—	—	—
<b>β-Blocker use</b>													
Overall (age and sex adjusted)	80.3	112.5	1993–2001	5.2	(3.7–6.8)†	1993–1996	-0.1	(-3.0 to 2.9)	1996–2001	7.3	(6.3–8.4)†	—	—
Men (age adjusted)	74.8	111.6	1993–2001	6.6	(4.5–8.7)†	1993–1996	-0.6	(-6.4 to 5.7)	1996–2001	9.4	(7.3–11.6)†	—	—
Women (age adjusted)	85.5	113.4	1993–2001	4.1	(2.9–5.4)†	1993–1995	-2.2	(-11.5 to 8.1)	1995–2001	5.3	(3.9–6.6)†	—	—
Age <65 years (age and sex adjusted)	71.6	86.4	1993–2001	3.3	(1.5–5.1)†	1993–1996	-2.9	(-5.6 to -0.1)†	1996–2001	5.9	(4.8–7.0)†	—	—
Aged ≥65 years (age and sex adjusted)	113.0	210.1	1993–2001	8.7	(7.6–9.9)†	—	—	—	—	—	—	—	—
<b>CCB use</b>													
Overall (age and sex adjusted)	119.1	129.2	1993–2001	0.8	(0.4–2.0)†	1993–1998	-1.2	(-1.5 to -0.8)†	1998–2001	4.3	(3.6–5.0)†	—	—
Men (age adjusted)	117.2	124.0	1993–2001	0.54	(-0.8 to 1.9)	1993–1998	-1.7	(-2.4 to -1.0)†	1998–2001	4.7	(3.2–6.2)†	—	—
Women (age adjusted)	120.8	134.1	1993–2001	1.1	(-0.1 to 2.2)	1993–1999	-0.3	(-0.8 to 0.3)	1999–2001	6.0	(3.1–9.0)†	—	—
Age <65 years (age and sex adjusted)	95.0	95.8	1993–2001	0.0	(-1.6 to 1.6)	1993–1998	-2.6	(-3.0 to -2.2)†	1998–2001	4.8	(3.9–5.6)†	—	—
Aged ≥65 years (age and sex adjusted)	208.8	254.1	1993–2001	2.0	(1.2–2.8)†	1993–1999	1.2	(0.1–2.3)†	1999–2001	5.1	(-0.45 to 11.0)	—	—
<b>Statin use</b>													
Overall (age and sex adjusted)	54.8	177.1	1993–2001	17.9	(15.0–20.8)†	1993–1997	10.5	(7.8–13.3)†	1997–2001	22.6	(20.0–24.4)†	—	—
Men (age adjusted)	59.5	191.9	1993–2001	17.4	(15.2–19.7)†	1996–2001	9.0	(1.5–17.1)†	1996–2001	20.2	(18.0–22.4)†	—	—
Women (age adjusted)	50.3	163.4	1993–2001	18.4	(14.1–22.9)†	—	—	—	—	—	—	—	—
Age <65 years (age and sex adjusted)	55.1	165.4	1993–2001	16.8	(13.4–20.4)†	1993–1997	8.4	(5.5–11.4)†	1997–2001	22.6	(20.7–24.6)†	—	—
Aged ≥65 years (age and sex adjusted)	53.5	220.8	1993–2001	20.8	(19.0–22.6)†	—	—	—	—	—	—	—	—
<b>All-cause hospitalization</b>													
Overall age-sex adjusted	300.3	252.7	1993–2001	-1.6	(-2.1 to -1.1)†	—	—	—	—	—	—	—	—
Men (age adjusted)	275.8	231.6	1993–2001	-1.8	(-2.4 to -1.3)†	—	—	—	—	—	—	—	—
Women (age adjusted)	322.9	272.1	1993–2001	-1.5	(-2.2 to -0.9)†	—	—	—	—	—	—	—	—

Aged <65 years (age and sex adjusted)	269.3	219.3	1993–2001	–2.2 (–2.7 to –1.6)†				
Aged ≥65 years (age and sex adjusted)	416.0	376.9	1993–2001	–0.6 (–1.5 to 0.2)				
Cerebrovascular-related hospitalization								
Overall (age and sex adjusted)	9.5	6.1	1993–2001	–5.4 (–6.7 to –3.7)†				
Men (age adjusted)	10.0	6.0	1993–2001	–6.0 (–8.5 to –3.5)†				
Women (age adjusted)	9.0	6.1	1993–2001	–5.0 (–6.5 to –3.5)†				
Aged <65 years (age and sex adjusted)	4.6	3.1	1993–2001	–6.4 (–11 to –1.4)†				
Aged ≥65 years (age and sex adjusted)	27.7	17.1	1993–2001	–4.7 (–6.1 to –3.3)†				
Cardiac-related hospitalization								
Overall (age and sex adjusted)	38.0	30.6	1993–2001	–2.0 (–3.2 to –0.8)†				
Men (age adjusted)	42.6	33.4	1993–2001	–2.2 (–3.2 to –1.1)†				
Women (age adjusted)	33.8	28.0	1993–2001	–1.8 (–4.1 to 0.6)				
Aged <65 years (age and sex adjusted)	24.1	18.7	1993–2001	–2.3 (–3.9 to –0.7)†				
Aged ≥65 years (age and sex adjusted)	89.8	75.2	1993–2001	–1.6 (–2.8 to –0.5)†				
All-cause mortality								
Overall (age and sex adjusted)	17.7	17.8	1993–2001	–0.1 (–1.4 to 1.3)				
Men (age adjusted)	18.1	17.7	1993–2001	–0.7 (–3.1 to 1.7)				
Women (age adjusted)	17.3	17.9	1993–2001	0.4 (–1.3 to 2.2)				
Aged <65 years (age and sex adjusted)	8.0	7.2	1993–2001	–3.7 (–9.2 to 2.1)				
Aged ≥65 years (age and sex adjusted)	54.4	57.3	1993–2001	1.1 (–0.4 to 2.5)				

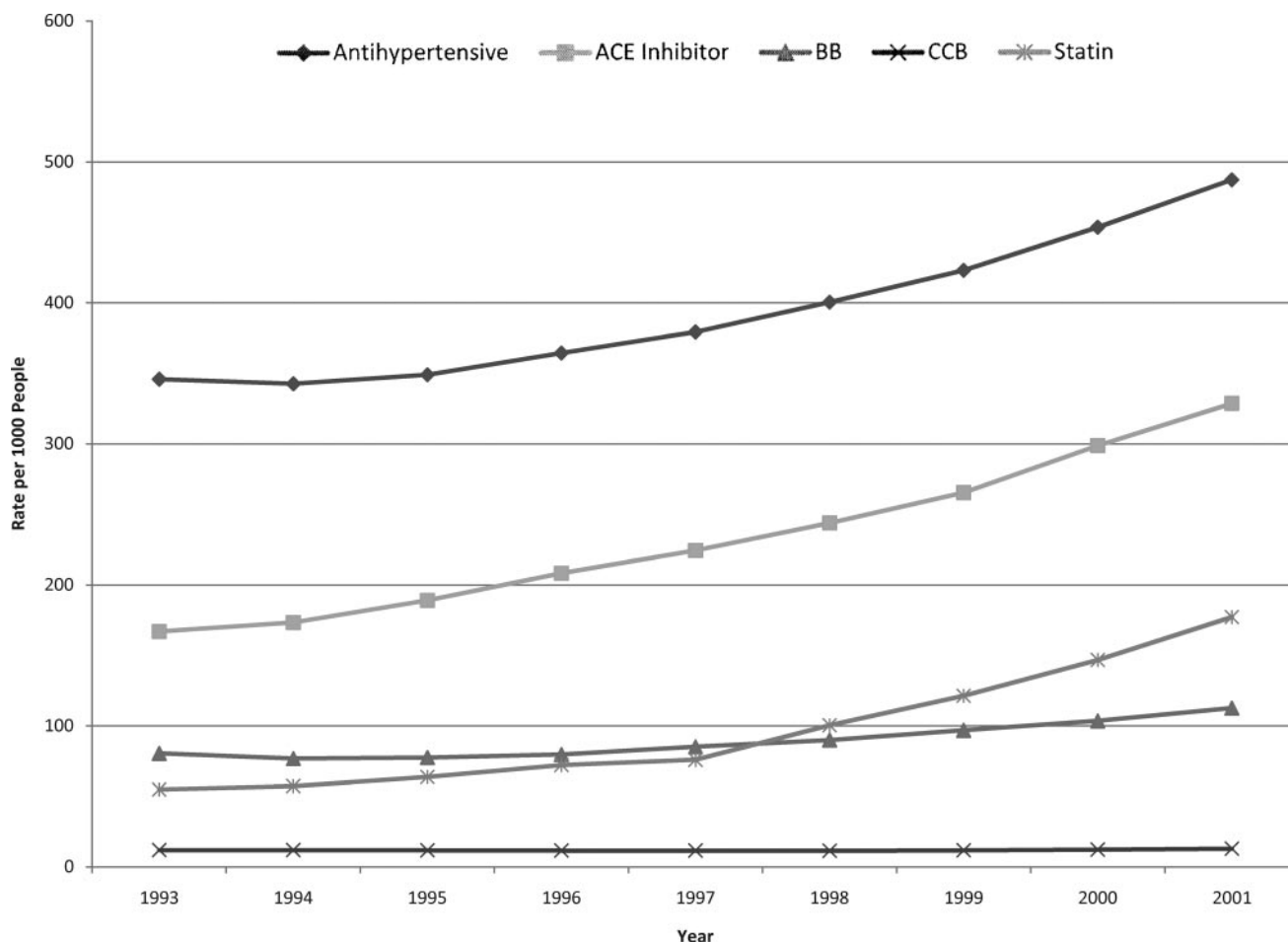
\*Only outcomes assessed that had a statistically significant linear difference from the overall trend in direction or magnitude are presented. †APC differs significantly from zero ( $P < 0.05$ ).

tively (Table 2) (Fig. 1). Although overall utilization increased during this period, utilization remained fairly constant between 1993 and 1996 (APC increase 1.5%,  $P > 0.05$  for trend), but thereafter rates of antihypertensive use changed significantly with an APC increase of 6.3% ( $P < 0.001$  for trend) (Table 2). The rate of change differed, however, by sex and age. Men had a substantially greater APC increase in utilization compared with women (6.3 vs. 3.7%), although overall utilization rates remained significantly lower for men in 2001 (sRR 0.92 [95% CI 0.89–0.96]) (Table 2). Similarly, higher utilization rates were observed in people aged  $\geq 65$  years irrespective of time period; however, those aged  $< 65$  years had a substantially greater APC increase compared with those aged  $\geq 65$  years (5.5 vs. 3.5%) (Table 2).

The use of ACE inhibitor therapy nearly doubled between 1993 and 2001, with an APC increase of 9.2% ( $P < 0.001$ ) (Table 2) (Fig. 1). The largest APC increase in ACE inhibitor utilization was observed in men, which was 35% greater than the increase observed in women (11.3 vs. 7.4%). Despite lower utilization in 1993, men were more likely to use an ACE inhibitor in 2001 compared with women (34.8 vs. 31.2%,  $P < 0.05$ ) (Table 2). The rates of ACE inhibitor utilization also increased more significantly in people with diabetes aged  $< 65$  years compared with those aged  $\geq 65$  years (APC increase 9.9 vs. 7.6), with the highest utilization increase occurring between 1997 and 2001 (Table 2).

$\beta$ -Blocker utilization initially decreased between 1993 and 1996 before significantly increasing in the remaining years (Table 2) (Fig. 1). Men and women showed a similar pattern of utilization. People aged  $\geq 65$  years were much more likely to use a  $\beta$ -blocker compared with those aged  $< 65$  years, irrespective of time period. In fact, the rate of increase of  $\beta$ -blockers was over twofold higher in those aged  $\geq 65$  years compared with those aged  $< 65$  years from 1993 to 2001 (APC 8.7 vs. 3.3%) (Table 2).

The use of CCBs remained similar in 2001 compared with 1993, with only a slight increase in utilization. Like  $\beta$ -blockers, however, CCB use significantly decreased from 1993 to 1998 before rapidly increasing from 1998 to 2001 (Fig. 1). Similar patterns of utilization were observed among the groups, with the exception of those aged  $\geq 65$  years, which showed both the highest utilization



**Figure 1**—Overall direct age- and sex-standardized prescription rates between 1993 and 2001.

of CCBs and the highest APC increase (Table 2). The largest increase in utilization occurred with statin therapy, with a 223% relative increase in utilization between 1993 and 2001 (Fig. 1). Overall, the APC increase in statin use was 17.9% with a twofold increase in utilization rates between 1997 and 2001 compared with 1993 and 1997 (Table 2). Similar increases in utilization rates were observed regardless of age or sex, with men and those aged  $\geq 65$  years more likely to receive statin therapy over the study period.

#### All-cause hospitalization

Hospitalization rates decreased by 16%, from 300.3 per 1,000 in 1993 to 252.7 per 1,000 in 2001 ( $P < 0.05$ ). Similar declines were observed in men, women, and in those aged  $< 65$  years. Although a decline was also observed in those aged  $\geq 65$  years, the rate of decline was not as large compared with the other groups examined and was not statistically significant (Table 2). The largest reduction in hospitalization rates occurred for cerebrovascular-related hospitalizations, with

a significant 5.4% APC decrease between 1993 and 2001 (Table 2). Importantly, the largest reductions were observed in those aged  $\leq 65$  years (APC decrease of 6.4%), with similar reductions being observed in both men and women (Table 2). Rates of cardiac-related hospitalizations also declined significantly by 2% annually during this period. Few differences existed between sex or age-groups, however. Men had higher rates of cardiac-related admission than women (sRR 1.2,  $P < 0.05$ ), as did those aged  $\geq 65$  years compared with aged  $< 65$  years (sRR 4.0,  $P < 0.05$ ).

#### All-cause mortality

Despite increased utilization of evidence-based drug therapies and observed declines in hospital-related morbidity from 1993 to 2001, mortality rates remained remarkably stable during this period (Table 2), irrespective of sex or age. Although slightly larger rates of decline were observed in people with diabetes aged  $< 65$  years, there was no statistical difference in

the rates observed in 1993 compared with those in 2001 for this group ( $P > 0.05$ ).

**CONCLUSIONS**— The adjusted prevalence of diabetes in Saskatchewan, Canada increased by 34% from 1993 to 2001, with a consistent annual percentage increase of 4.3%. Although these results are similar to other studies, the overall rate of increase appears lower. For example, in a large study (2) conducted in Ontario, Canada, from 1995 to 2000, the adjusted prevalence of diabetes increased from 5.2 to 6.9%, representing a 33% relative increase. During that same time (i.e., 1995 and 2000), our observed increase of 25% (5.2–6.5%, respectively) in prevalence is 24% lower than that observed in Ontario. Furthermore, the Ontario study included all people aged  $\geq 20$  years, whereas our study was restricted to only those aged  $\geq 30$  years and thus likely at higher overall risk for diabetes; the difference in observed rates would likely be larger if the previous study were to be restricted to only those people aged  $\geq 30$  years. Regardless, our data highlight the

disturbing trend of increasing diabetes rates and is consistent with studies in both Canada and the U.S. (2,18). Importantly, however, our data also suggest that in people aged <65 years, the rate of increase in diabetes prevalence significantly slowed between 1998 and 2001. The reason for this change and whether this is a trend continued in more recent years is unknown.

An increase in prescription claims for select evidence-based drug therapies suggests that both providers and patients are moving toward more aggressive management of cardiovascular risk factors in diabetes. Significant increases in the utilization of antihypertensive therapies from 1993 to 2001 resulted in almost half of all people with diabetes using an antihypertensive agent in 2001. In contrast to previous studies (6,19,20), we found higher utilization rates among women, although the gap between sexes significantly narrowed during our study period. Similar to previous studies (6), the largest increase occurred with ACE inhibitor therapy, with one-third of all diabetic patients receiving ACE inhibitors. Men, however, were more likely to receive ACE inhibitor therapy than women, and it has been speculated that this differential prescribing may result from either an increased recognition of atherosclerotic risk in men or concerns for adverse effects in women (e.g., teratogenic risk) (6). Interestingly, although decreases in both  $\beta$ -blocker and CCB therapy during the overall period were observed, utilization within both classes significantly increased in the later 1990s. This coincides with the publication of several antihypertensive trials that may have influenced physician prescribing and overall utilization (5). Similarly, statin use significantly increased after 1997, corresponding to the publication of several landmark clinical trials of statins (5).

Several studies (11,21–23) have failed to demonstrate a consistent trend with respect to cardiovascular-related events in patients with diabetes. Our results suggest that significant improvements in the morbidity of diabetes occurred, demonstrated by significant reductions in both the rates of all-cause hospitalization and cardiovascular-related events. Overall, rates of cerebrovascular and cardiac-related hospitalizations declined by 36 and 19%, respectively, during this period. Moreover, unlike previous studies (11,21) that observed reductions in men only, we observed simi-

lar reductions in cardiovascular-related events among both sexes. Although the reason for these trends is unknown, one would assume that improvements in patient awareness of diabetes complications, improvements in overall patient management, and more aggressive evidence-based drug therapies aimed at cardiovascular risk reduction likely played a role (19,20,24).

Despite substantial improvements in the utilization of evidence-based drug therapies and reductions in morbidity in patients with diabetes, we did not observe reductions in mortality during the study period. This is in contrast to several recent reports (2,10–14). Lipscombe et al. (2) reported a 25% decrease in the adjusted mortality rate in people with diabetes between 1995 and 2005 in Ontario, Canada. Other studies, however, have reported no significant change in overall mortality (11) or even increased cardiovascular-related mortality rates in people with diabetes (22,23). Studies have also suggested, however, that sex-related differences in mortality may exist, with several studies (11,14,21) observing changes favoring men.

The reason for the discrepancies in mortality between studies is not known, but several possible explanations exist. First, despite our large population, imprecision in the adjusted mortality rates may have precluded identification of small but clinically important reductions in mortality, particularly in the <65 years age-group. Second, rates of undiagnosed diabetes may have affected our results if these rates were substantially higher in 1993 than 2000. If so, mortality events misclassified to those with undiagnosed diabetes may have artificially lowered the diabetes mortality rates in 1993 and negate any observed mortality benefit. Although data on undiagnosed diabetes is not available in the administrative data, estimates from the U.S. suggest that undiagnosed diabetes rates have remained constant throughout our period of study (25). Finally, it is possible our time period was insufficient to observe the longer-term benefits on mortality associated with improved prescribing of evidence-based therapies. Moreover, our outcome was restricted to all-cause mortality, and it is therefore possible that reductions in cause-specific mortality may have occurred during the time period that we were unable to capture. However, as previously shown, the majority of mortality

in patients with diabetes is cardiovascular related (11,21).

Our study has several strengths, including the use of large, comprehensive, administrative health data of an unselected population of patients with diabetes for our estimates; inclusion of all adult age-groups; and the long duration of follow-up. There are some limitations, however. First, although a previously validated algorithm was used to identify diabetes (16), it is possible that some cases may have been missed due to the administrative nature of the data. Second, we were unable to evaluate the impact of changes in diagnostic criteria for diabetes that have occurred during our period of study. It is possible that the observed increase in diabetes prevalence may be partially related to more stringent diagnostic criteria for glucose tolerance; on the other hand, the rate of increase in prevalence was more or less constant. Third, we are unable to make any assertions about the appropriateness of the health services delivered (pharmacological or hospitalizations). Fourth, we did not have data on clinical parameters and, perhaps more importantly, patient self-care behaviors. It is possible that medication nonadherence or weight gain, for example, may negate benefits of increased dispensation of evidence-based therapies. If this was the case, however, we would also expect to see increased rates of hospitalizations for important clinical events, which we did not observe.

The results of this study have important public health implications for the management of diabetes both near and long term. While many studies have criticized the prescribing rates of evidence-based drug therapies in patients with diabetes, both patients and providers should be commended for the significant improvements that have already occurred. Diabetes is a multifaceted, complex disease, and although more work is required, current trends suggest that treatment gaps in patients with diabetes are indeed narrowing. Although one cannot say for certain, it would appear that the mounting clinical evidence and guideline endorsements have resulted in significant positive changes in prescribing at the population level, with more intensive utilization of pharmacological therapies. While we did not observe reductions in mortality, significant improvement in the use of evidence-based drug therapies and declines in major cardiovascular co-

morbidity suggests that despite the increasing dark cloud of diabetes, there may indeed be a silver lining.

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All authors took part in the planning and design of the study. D.T.E. and J.A.J. obtained the data. D.T.E. conducted the statistical analyses. All authors had access to the data and participated in the interpretation of the data. D.T.E. and J.-M.G. wrote the first draft of the report. All authors reviewed and revised the paper for important intellectual content and gave approval for the version to be published.

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