Patient Age, Ethnicity, Medical History, and Risk Factor Profile, but Not Drug Insurance Coverage, Predict Successful Attainment of Glycemic Targets

Time 2 Do More Quality Enhancement Research Initiative (T2DM QUERI)

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OBJECTIVE — To identify factors in patients with type 2 diabetes and A1C >7.0% associated with attainment of A1C ≤7.0%.

RESEARCH DESIGN AND METHODS — We used a prospective registry of 5,280 Canadian patients in primary care settings enrolled in a 12-month glycemic pharmacotherapy optimization strategy based on national guidelines.

RESULTS — At close out, median A1C was 7.1% (vs. 7.8% at baseline) with 48% of subjects achieving A1C ≤7.0% ($P < 0.0001$). Older patients of Asian or black origin, those with longer diabetes duration, those with lower baseline A1C, BMI, LDL cholesterol, and blood pressure, and those on angiotensin receptor blockers and a lower number of antihyperglycemic agents, were more likely to achieve A1C ≤7.0% at some point during the study (all $P < 0.0235$). Access to private versus public drug coverage did not impact glycemic target realization.

CONCLUSIONS — Patient demography, cardiometabolic health, and ongoing pharmacotherapy, but not access to private drug insurance coverage, contribute to the care gap in type 2 diabetes.

Diabetes Care **33:2558–2560, 2010**

Treatment gaps in achieving A1C targets persist (1,2). Our goal was to identify, in a type 2 diabetic patient registry, factors that contribute to attaining the A1C target of ≤7.0% recommended by the 2003 Canadian Diabetes Association (CDA) clinical practice guidelines (3).

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Received 8 March and accepted 27 August 2010. Published ahead of print at http://care.diabetesjournals.org on 7 September 2010. DOI: 10.2337/dc10-0440.
*A list of participating T2DM QUERI investigators may be found in the online appendix available at http://care.diabetesjournals.org/cgi/content/full/dc10-0440/DC1.

RESEARCH DESIGN AND METHODS

— The "Time 2 Do More" (T2DM) protocol underwent ethics approval. Physicians were educated on the 2003 CDA guidelines, which focused on A1C ≤7.0%, fasting plasma glucose ≤7.0 mmol/l, LDL cholesterol ≤2.5 mmol/l, total-to-HDL cholesterol ratio <4.0, and blood pressure ≤130/80 mmHg.

The final 5,280 insulin-naive patients, enrolled from 378 primary care practices across nine Canadian provinces between March 2006 and September 2007, had A1C >7.0% and a clinical diagnosis of type 2 diabetes. Participation was voluntary, and written informed consent was mandatory. Protocol subclassification into private (unencumbered access to any antihyperglycemic agent [AHA]) or public (access only to AHA approved by provincial formulary programs) insurance groups was met by 4,797 patients (376 sites, nine provinces).

Physicians monitored and directed therapies using their best clinical judgment. The protocol neither mandated the frequency or timing of clinical visits nor dictated the specific medications or doses to be prescribed. Subjects not at A1C target at follow-up were encouraged to have their antihyperglycemic treatment intensified. Detailed feedback provided after visit two allowed physicians to identify those not at target and/or not receiving guideline-recommended treatments. Laboratory values were obtained as part of routine clinical care.

A generalized estimating equation model was fitted to assess the association between increase in number of prescribed AHAs at each visit and changes in A1C target achievement. Model selection was based on the quasi-likelihood under the independence model criterion (4). The final model was used to assess the association between drug insurance coverage and changes in target achievement.

Table 1—*Factors associated with temporal changes in A1C ≤7.0% achievement*

	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Men vs. women	0.996 (0.992–1.076)	0.93		
Age (per 5 years higher)	1.029 (1.012–1.045)	0.0006	1.024 (1.003–1.046)	0.0235
Ethnicity (Caucasian as reference)				
East and South-East Asian	0.764 (0.667–0.874)	<0.0001	0.715 (0.606–0.842)	<0.0001
South Asian	0.592 (0.500–0.701)	<0.0001	0.641 (0.528–0.779)	<0.0001
Black	0.651 (0.519–0.816)	0.0002	0.71 (0.548–0.920)	0.0095
Aboriginal Canadian native/Inuit	0.699 (0.517–0.945)	0.02	0.867 (0.604–1.244)	0.44
Others	0.945 (0.710–1.260)	0.701	0.903 (0.657–1.241)	0.53
Unknown	0.670 (0.512–0.876)	0.0035	0.651 (0.464–0.913)	0.0129
Insurance coverage (private vs. public)	0.979 (0.895–1.070)	0.64		
Baseline A1C (per 1% lower)	1.368 (1.301–1.438)	<0.0001	1.344 (1.273–1.419)	<0.0001
LDL cholesterol (per 1 mmol/l lower)*	1.412 (1.340–1.487)	<0.0001	1.349 (1.275–1.427)	<0.0001
Systolic blood pressure (per 10 mmHg lower)*	1.121 (1.093–1.151)	<0.0001	1.101 (1.063–1.140)	<0.0001
Diastolic blood pressure (per 10 mmHg lower)*	1.202 (1.154–1.251)	<0.0001	1.09 (1.031–1.153)	0.0024
Baseline BMI (per 5 kg/m^2 lower)	1.041 (1.013–1.071)	0.0044	1.044 (1.008–1.081)	0.0158
Duration of type 2 diabetes (per 5 years lower)	1.239 (1.193–1.287)	<0.0001	1.451 (1.375–1.532)	<0.0001
Smoker (No vs. Yes)	1.071 (0.948–1.210)	0.27		
Exercise vs. sedentary lifestyle	1.033 (0.956–1.115)	0.41		
Family history of diabetes (No vs. Yes)	1.086 (1.007–1.172)	0.033		
Pharmacotherapy				
Number of AHAs (per unit lower)*	1.176 (1.129–1.224)	<0.0001	1.326 (1.256–1.399)	<0.0001
Statin (Yes vs. No)	1.223 (1.112–1.344)	<0.0001		
ACE inhibitor (Yes vs. No)	1.052 (0.976–1.135)	0.19		
ARB (Yes vs. No)*	1.241 (1.145–1.346)	<0.0001	1.246 (1.133–1.370)	<0.0001
β-blocker (Yes vs. No)	1.090 (0.993–1.198)	0.072		

*Time-dependent variables. OR, odds ratio.

RESULTS — The cohort was 58.2% men and 74.9% Caucasian. Median age, baseline A1C, LDL cholesterol, and blood pressure were 60 years, 7.8%, 2.3 mmol/l, and 130/80 mmHg, respectively. Median duration of diabetes was 6 years with 18, 5.5, and 4.8% of the cohort reporting prior coronary artery, peripheral vascular, and cerebrovascular disease events, respectively. Sequential declines in A1C (median 7.1% at close out; $P < 0.0001$) paralleled progressive increases in A1C ≤7.0% attainments ($P < 0.0001$; supplementary Table 1 available at http://care.diabetesjournals.org/cgi/content/full/dc10-0440/DC1). Of the 3,122 patients who had A1C measured at all four visits, 35.9% did not achieve A1C ≤7.0% at any time during the study. Median fasting plasma glucose, lipid levels, and blood pressure improved temporally, as did the percentages of patients optimally managed (supplementary Table 1).

The number of patients on multiple AHAs increased whereas the number on monotherapy decreased during the study (supplementary Table 2). After adjusting for age and the covariates that were significant in the multivariable model, the number of AHAs prescribed at each previous visit remained significantly associated with target achievement during the study (Table 1). Older patients of Asian origin or blacks, those with longer diabetes duration, those with lower baseline A1C, BMI, LDL cholesterol, or blood pressure, and patients on angiotensin receptor blockers (ARBs) and with a lower number of AHAs prescribed, were more likely to achieve A1C target at some period during the study (all $P < 0.0235$). Differential access to drug insurance coverage was not associated with changes in glycemic target achievement in univariate ($P = 0.64$) and multivariable ($P = 0.24$) analyses.

CONCLUSIONS — In this physician practice–optimization strategy focused on optimizing AHA regimens, <50% of the patients recorded A1C ≤7.0% 12 months after entering the study. Multivariable analysis revealed that A1C ≤7.0% was associated with age, ethnicity, baseline A1C, LDL cholesterol, blood pressure, duration of diabetes, use of ARBs, and number of AHAs prescribed.

Although the predictive values of demography and cardiometabolic health on A1C improvements were not unexpected, the suboptimal success in A1C realization is intriguing because a quarter of the patients were already or subsequently placed on three or more AHAs at baseline. Clinical inertia (5,6) in the form of delayed insulin introduction was likely contributory. At the time of the study, although there was evidence that tight glycemic control can ameliorate microvascular complications (7,8), there were no similar data for macrovascular risk, which may have factored into physician decision making. The paradox that patients on a lower number of AHAs were more likely to achieve the A1C target probably stemmed from patients with "more severe" diabetes being more likely to be prescribed multiple AHAs.

Our finding that private insurance–enabled unencumbered access to any AHA did not impact on A1C ≤7.0% achievement must be interpreted cautiously because at the time of this study, thiazolidinediones were the only major class of AHAs not covered by the majority of Canadian provincial formularies. Notably, patients with public-only coverage were less likely than those with private insurance to be on thiazolidinediones at the beginning of the study, but this discrepancy was no longer evident after visit two.

This study has several limitations. An element of physician selection bias is likely because a quarter of the patients at baseline either were already on or were subsequently placed on three or more AHAs. Although only 59% of the patients had complete data for all four visits, study participation may have triggered improvements. Neither lifestyle modifications and social support systems nor comanagement by a specialist was

documented. Information on AHA prescriptions and therapeutic profiles was drawn from case report forms rather than pharmacy records.

Our study nonetheless has notable strengths. The data were from a large cohort that included both sexes and various ethnicities with differential drug insurance coverage. The longitudinal registry design resembles a "real world" setting without the typical clinical trial selection bias. Our study was initiated and completed before the results of the major outcome trials that have fuelled the controversies of how intensive glycemic lowering impacts severe hypoglycemia and cardiovascular events (9–12) were published and thus may serve as a useful benchmark for future comparisons of how practice patterns may evolve.

In conclusion, in a large Canadian cohort of type 2 diabetic patients not meeting glycemic targets, nearly 50% achieved the guideline-recommended A1C ≤7.0% target after 12 months in a physician-based practice optimization strategy. Success in realizing target A1C was associated with patient age, ethnicity, baseline A1C, LDL cholesterol, blood pressure, duration of diabetes, number of AHAs prescribed, and use of ARBs, but not with the type of drug insurance coverage.

Acknowledgments— The T2DM project was conceived, designed, and coordinated by the Canadian Heart Research Centre (CHRC), a federally incorporated, not-for-profit, academic research organization.

D.D. has received research grant support and/or speaker/consulting honoraria from ALTANA, AstraZeneca, Biovail, Bristol-Myers Squibb, Boehringer Ingelheim, GlaxoSmithKline, Merck, Novartis, Pfizer, sanofi-aventis, SERVIER, Solvay Pharmaceuticals, and Unilever. S.G.G. has received research grant support and/or speaker/consulting honoraria from AstraZeneca, Bayer, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Hoffmann-La Roche, Johnson & Johnson, Merck, sanofi-aventis, and Pfizer. S.B.H. has received research grant support and/or speaker/consulting honoraria from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Hoffmann-La Roche, Merck, Novo Nordisk, and sanofi-aventis. A.L. has received research grant support and/or speaker/consulting honoraria from AstraZeneca, GlaxoSmithKline, Merck, Pfizer, and sanofi-aventis. E.U. has received research grant support and/or speaker/consulting honoraria from GlaxoSmithKline, Merck, Novartis, Novo Nordisk, and sanofi-aventis. A.Y. has received speaker/consulting honoraria from sanofi-aventis and Bristol-Myers Squibb. L.A.L. has received research grant support and/or speaker/consulting honoraria from AstraZeneca, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Hoffmann-La Roche, Merck, Novartis, Novo Nordisk, Pfizer, sanofi-aventis, and SERVIER. GlaxoSmithKline Canada supported this study and had no role in the collection, management, analysis, or interpretation of the data; in the preparation, review, or approval of the manuscript; and in the decision of submitting the manuscript for publication or the target journal. No other potential conflicts of interest relevant to this article were reported.

H.T. wrote the manuscript, researched the data, contributed to the discussion, and reviewed/edited the manuscript. M.F.B.B. contributed to the discussion and reviewed/edited the manuscript. A.C. researched the data, contributed to the discussion, and reviewed/edited the manuscript. D.D. reviewed/edited the manuscript. S.G.G. designed the protocol, researched the data, contributed to the discussion, and reviewed/edited the manuscript. S.B.H. reviewed/edited the manuscript. A.L. designed the protocol, researched the data, contributed to the discussion, and reviewed/edited the manuscript. M.K.T. researched the data, contributed to the discussion, and reviewed/edited the manuscript. E.U. reviewed/edited the manuscript. A.T.Y. researched the data, contributed to the discussion, and reviewed/edited the manuscript. B.Z. reviewed/edited the manuscript. L.A.L. designed the protocol, wrote the manuscript, researched the data, contributed to the discussion, and reviewed/edited the manuscript.

Parts of this study were presented in abstract form at the Canadian Cardiovascular Congress, Edmonton, Alberta, Canada, 24–28 October 2009, and at the 20th International Diabetes Federation World Diabetes Congress, Montreal, Québec, Canada, 18–22 October 2009.

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