Sustained Hyperglycemia Among Patients With Diabetes

What matters when action is needed?

Jennifer E. Lafata, phd[1]
Elizabeth A. Dobie, mph[1]
George W. Divine, phd[2]
Marianne E. Ulcickas Yood, dsc, mph[3]
Bruce D. McCarthy, md[4]

OBJECTIVE — To estimate prevalence of, and factors associated with, sustained periods of hyperglycemia among patients with diabetes and factors associated with receipt of appropriate care once A1C values are persistently elevated.

RESEARCH DESIGN AND METHODS — Among patients initiating oral monotherapy ($n = 5,070$), Kaplan-Meier and Cox proportional hazards methods were used to estimate time to, and factors associated with, sustained hyperglycemia (defined by two A1cs >8% and no recent medication intensification), and among those experiencing sustained hyperglycemia, time to, and factors associated with, appropriate receipt of care (i.e., medication intensification or achieving A1C ≤7%).

RESULTS — Within 1 year, 8% experienced sustained hyperglycemia, with the proportion rising to 38% within 5 years. Patients using sulfonylurea had greater risk of hyperglycemia (hazard ratio [HR] 1.47 [95% CI 1.30–1.66]) compared with those initiating metformin. Risk increased with age (1.89 [1.27–2.83]), was greater for African Americans (1.19 [1.05–1.36]), and increased with A1C levels >7%. Among individuals with sustained hyperglycemia ($n = 1,386$), mean time to appropriate care was 9.7 months, with 25% not receiving appropriate care within 1 year. Shorter delays to appropriate care receipt were associated with increasing income (1.03 [1.00–1.07]), A1C >9% (1.38 [1.06–1.79]) and >11% (1.65 [1.25–2.18]), increasing medication adherence (1.03 [1.01–1.04]), and visits to primary care (4.22 [3.65–4.88]) or endocrinology (3.89 [2.26–6.70]). Longer delays were associated with increasing drug copayments (0.96 [0.93–0.98]).

CONCLUSIONS — Patients incurring sustained hyperglycemia are at risk of further delays in appropriate management. Barriers to appropriate care include prescription drug copayments, few physician contacts, and other factors that are likely amenable to intervention.

Diabetes Care 32:1447–1452, 2009

Clinical inertia among patients with diabetes reflects the proportion of patients with elevated glycosylated hemoglobin (A1C) and no intensification of pharmacological therapy. Prior research has found that between 33 and 66% of patients with an elevated A1C do not have timely intensification of their medications (1–7). Numerous clinical trials have provided consistent evidence of the detriment of prolonged periods of hyperglycemia among adults with type 2 diabetes (8,9), and few would argue that once A1C values are substantially and consistently above target levels, intensification of pharmacological therapy is warranted.

Although the presence of poor control in diabetes has been documented, the extent to which patients with diabetes incur sustained periods of poor control and no recent medication intensification is not well quantified. Nor is it known what factors eventually facilitate the receipt of appropriate care once a patient incurs a sustained period of poor control. Among a cohort of patients initiating oral monotherapy, we report the risk of, and factors associated with, sustained hyperglycemia and evaluate factors associated with receipt of appropriate care among individuals with sustained hyperglycemia.

RESEARCH DESIGN AND METHODS

Setting and population

Study-eligible patients received care from a multispecialty group practice in southeast Michigan and were aged 18 years or older when initiating oral monotherapy between 2000 and 2005. Therapy initiation was defined as a dispensing for an oral antidiabetic agent preceded by 6 months in which no antidiabetic agent was dispensed. Eligible patients had continuous health plan enrollment during the 6-month period immediately before and after therapy initiation and had two or more A1C tests during follow-up.

Data sources

Automated administrative records were used to compile demographic information (i.e., age, sex, race, and marital status), dates and type of health plan enrollment (i.e., employer sponsored versus Medicare risk versus Medicare supplemental), a linear measure of prescription drug copayment, and residential street address. The latter was combined with data from the 2000 U.S. Census to construct estimates of median household income in the patient's census-block of residence (10). Medical claims data were used to capture information on ambulatory care visits, inpatient hospital admissions, and associated diagnostic codes (i.e., ICD-9-CM codes). Inpatient and outpatient diagnostic information was used to construct measures of comorbidities and complications associated with diabetes (i.e., amputation, carotid endarterectomy, end-stage renal disease, heart failure, hypertension, left ventricu-

From the [1]Center for Health Services Research, Henry Ford Health System, Detroit, Michigan; the [2]Department of Biostatistics and Research Epidemiology, Henry Ford Health System, Detroit, Michigan; the [3]School of Public Health, Yale University School of Medicine, New Haven, Connecticut; and the [4]Allina Medical Clinic, Minneapolis, Minnesota.
Corresponding author: Jennifer Elston Lafata, jlafata1@hfhs.org.
Received 11 November 2008 and accepted 7 May 2009.
DOI: 10.2337/dc08-2028

lar hypertrophy, and retinopathy). Inpatient discharge diagnoses and procedure codes were used to construct indicators reflective of cardiac events (i.e., angina, angiogram, bypass, myocardial infarction, peripheral vascular disease, stroke, and transient ischemic attack). Dates and results of all A1C testing were compiled from a clinical information system.

Pharmacy claims data were used to construct dichotomous flags of antidiabetic, antihypertensive, cholesterol-lowering, and antidepression medication use. We used days supply information from dispensing data to measure medication adherence (with a medication possession ratio) in the periods immediately after oral monotherapy initiation and immediately preceding the date of sustained hyperglycemia (11). Among the subgroup of patients with sustained hyperglycemia, we also used the latest dispensing information available between inception date and the date of the patient's second elevated A1C to determine whether the patient was still receiving monotherapy or had changed to combination oral therapy. For each of these measures, medications paid for by the health plan were known, regardless of the dispensing pharmacy.

Table 1—*Characteristics of the oral monotherapy and sustained hyperglycemia cohorts at time of oral monotherapy initiation*

	Oral (monotherapy cohort)	Sustained (hyperglycemia cohort)
n	5,070	1,358
Sociodemographic characteristics		
Age (years)	60 ± 13	58 ± 12
Female (%)	48	45
Race (%)		
White	57	50
African American	37	45
Other	5	5
Marital status (%)		
Married	67	65
Not married/unknown	33	35
Insurance type (%)		
Employer-sponsored	60	67
Medicare risk	23	21
Medicare complimentary	17	13
Prescription drug copayment (USD)	$5.00 (0, 35)	$3.00 (0, 35)
Household income (USD)*	$49,631 ± 22,133	$47,569 ± 20,890
Hyperglycemia medication therapy (%)		
Sulfonylurea	52	59
Metformin	45	38
Other monotherapy	4	3
Adherence (%)	83.1 ± 25.1	82.2 ± 24.9
Glycemic control (%)		
A1C level†	8.6 ± 2.2	9.6 ± 2.3
By category		
A1C <7%	19	6
7 ≤ A1C <8%	19	12
8 ≤ A1C <9%	13	16
9 ≤ A1C <11%	13	21
A1C ≥11%	11	18
Untested (%)	26	28
Length of observation		
Months‡	44.5 ± 17.2	52.7 ± 13.8

Data are means ± SD and median (min, max) unless otherwise indicated. *Geo-coded median household income by residential zip code. †A1C level is defined by the most recent value available in the preceding 3 months or subsequent 1 month. ‡Time in months from oral monotherapy initiation to first of disenrollment, insulin initiation, or 31 December 2005.

Study outcomes

Sustained hyperglycemia was defined when a second A1C test result >8% was recorded with at least 90 days between that result and the prior elevated result, with no intermediate test result ≤7% and no medication change in the 90 days preceding the second test. Among individuals facing sustained hyperglycemia, we constructed a measure reflecting time (in days) from the date of sustained hyperglycemia (i.e., second elevated A1C) to the first date the patient had a pharmaceutical dispensing indicating therapy intensification (i.e., time to therapy intensification). Therapy intensification included the addition of an oral agent, an increase in oral agent dose, a change in oral agent class, the addition of insulin, or any combination of these. We also constructed a measure reflecting time (in days) from the date of sustained hyperglycemia to the receipt of "appropriate care." Appropriate care was defined as either a pharmaceutical dispensing of a therapy intensification or an A1C test result ≤7% (6).

Statistical analysis

We used Kaplan-Meier methods to estimate mean time to sustained hyperglycemia and proportion facing sustained hyperglycemia annually from inception (i.e., initiation of oral monotherapy). We fit a Cox proportional hazards model to evaluate patient factors associated with sustained hyperglycemia. Prescription drug copayment, diabetic complications, and cardiac events were evaluated as time-varying covariates with diabetic complications and cardiac events treated as flags that turned on (and stayed on) as of the date of first occurrence. Patients were followed from therapy initiation through the first of health plan disenrollment, insulin initiation, or 31 December 2005. (Patients were censored at insulin initiation because of inherent challenges with using claims data alone to monitor changes in insulin dosing.)

Among the subset of eligible patients experiencing sustained hyperglycemia and no recent medication intensification during follow-up, we used Kaplan-Meier methods to describe time to medication intensification and appropriate care. For these estimates, patients were followed from the date of their second elevated A1C through the first of health plan disenrollment or medication intensification/appropriate care. Cox proportional hazards models were used to evaluate the factors associated with time to medication intensification and appropriate care.

Patient sociodemographic characteristics (age, race, sex, marital status, type of insurance coverage, household income) and lipid lowering, antihypertensive, and antidepressant medication use were evaluated at the time of sustained hyperglycemia. Antidiabetic medication use (i.e., oral mono- or combination therapy) was also assessed at the time of sustained hyperglycemia, as was the patient's recent 6-month adherence to this therapy. Prescription drug copayment, A1C level, diabetic complications, cardiac events, inpatient admissions, and visits to primary care, endocrinology, cardiology, and the emergency department were evaluated as time-varying covariates. Diabetic complications and cardiac events were treated as flags that turned on (and stayed on) as of date of first occurrence, whereas inpatient admission, emergency department visit, and office visit events were flagged on the date of each occurrence and remained flagged until 30 days after the date of the event.

All Cox proportional hazards models were fit with the robust variance estimation method in PROC PHREG in SAS (12) to account for the potential nonindependence of observations (i.e., patients) treated by the same physician. All models controlled for the year the patient initiated oral monotherapy and, in the case of appropriate care/intensification, the length of time between the two A1C tests defining the period of sustained hyperglycemia.

RESULTS

Cohort characteristics

Table 1 describes the cohort initiating oral monotherapy (n = 5,070) and the subset of this cohort who incurred a sustained period of hyperglycemia during follow-up (n = 1,386). The average age of the cohort was just over 60 years. A total of 48% were female and 37% were African American, whereas approximately two-thirds were married. The majority had their health plan coverage via an employer-sponsored plan, and the median prescription drug copayment faced was $5.00. Per the cohort inclusion criteria, all were dispensed oral monotherapy (most often a sulfonylurea or metformin) at baseline. Mean adherence in the 6-month period after dispensing was 83.1 ± 25.1% (means ± SD). At the time patients were dispensed the oral agent, 74% had an A1C measurement on record in the preceding 3 months or following 1 month. Among individuals with an A1C on record, mean A1C was 8.6 ± 2.3%. Patients were observed for an average of almost 4 years (45 months, range 6–73).

Table 2—*Factors associated with a sustained period of hyperglycemia among patients initiating oral monotherapy: Cox proportional hazards regression results* (n = 4,912)*

	Hazard ratio (95% CI)	*P*
Sociodemographic characteristics		
Age in decades	1.89 (1.27–2.83)	<0.01
Male	1.11 (0.99–1.24)	0.08
Race		
White	1.00	
African American	1.19 (1.05–1.36)	<0.01
Other	1.17 (0.91–1.50)	0.23
Married	0.84 (0.75–0.95)	<0.01
Insurance type		
Employer-sponsored	1.00	
Medicare risk	1.39 (1.13–1.71)	<0.01
Medicare complimentary	0.98 (0.78–1.23)	0.88
Income (in 10K USD increments)	0.97 (0.94–1.00)	0.05
Prescription drug copayment (USD)	0.94 (0.90–0.97)	<0.01
Medication use		
Hyperglycemia medication regimen		
Metformin	1.00	
Sulfonylurea	1.47 (1.30–1.66)	<0.01
Other monotherapy	1.04 (0.74–1.46)	0.82
Hyperglycemia medication adherence (in 10% increments)	0.98 (0.96–1.00)	0.04
Other current medications		
Antihypertensive agent	1.08 (0.95–1.23)	0.24
Cholesterol-lowering agent	1.20 (1.04–1.39)	0.01
Antidepressive agent	1.11 (0.94–1.32)	0.22
Comorbidities and complications		
Amputation	0.83 (0.27–2.58)	0.75
Cardiovascular event	0.99 (0.96–1.01)	0.23
Carotid endarterectomy	1.86 (0.66–5.19)	0.24
End-stage renal disease	0.55 (0.38–0.79)	<0.01
Heart failure	1.12 (0.77–1.64)	0.55
Hypertension	0.92 (0.80–1.06)	0.26
Left ventricular hypertrophy	0.49 (0.20–1.17)	0.11
Retinopathy	1.07 (0.87–1.32)	0.50
Glycemic control		
No test at therapy initiation	3.20 (2.53–4.06)	<0.01
A1C level		
<7%	1.00	
7–7.9%	2.44 (1.88–3.16)	<0.01
8–8.9%	4.58 (3.55–5.91)	<0.01
9–10.9%	5.97 (4.65–7.66)	<0.01
≥11%	5.94 (4.60–7.66)	<0.01

*A total of 153 patients did not have income and 5 did not have copay data available.

Prevalence of and factors associated with sustained hyperglycemia

Among the cohort, 1,386 patients were observed to have a period of sustained hyperglycemia and no recent medication intensification during follow-up. Just over one-third of individuals had been dispensed oral combination therapy before incurring sustained hyperglycemia. The mean adherence to antidiabetic medications in the 3-month period preceding sustained hyperglycemia was 64.4 ± 42.2%. Furthermore, at the time of sustained hyperglycemia, the mean A1C of the cohort was 9.7 ± 1.7%, with 38% incurring an A1C between 9 and 11% and 20% incurring an A1C >11%. Among in-

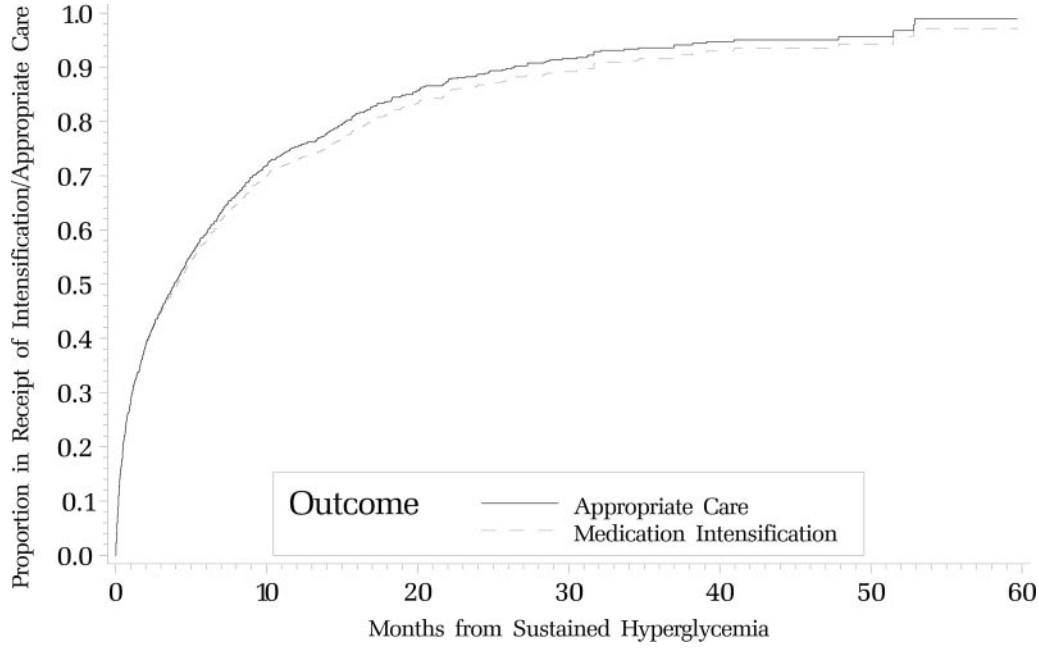

Figure 1—*Time to medication intensification (pharmaceutical dispensing indicating addition of oral agent, increase in oral agent dose, change in oral agent class, addition of insulin, or any combination of these) and appropriate care (medication intensification or A1C test result ≤7%) (n = 1,386) among individuals with sustained hyperglycemia.*

dividuals with sustained hyperglycemia, the mean length of observation from that date forward was 22 months (range 1–69).

Results from the Kaplan-Meier estimates of time from initiation of antidiabetic monotherapy to sustained hyperglycemia indicate that 8% of patients incurred sustained hyperglycemia within 12 months and that this proportion steadily rose over time, with 38% facing a period of sustained hyperglycemia within 5 years. The mean length of time between the two elevated A1C values used to define the sustained period (that is, the mean length of time the patient incurred hyperglycemia when labeled "sustained") was 7.6 ± 9.7 months (range 3–64). Of note among the Cox proportional hazards model findings (Table 2) was that the risk of incurring sustained hyperglycemia increased with increasing age and A1C levels >7%. Risk was also greater for African American patients and those who originally initiated a sulfonylurea (compared with those initiating metformin). On the other hand, risk decreased with increasing income and medication adherence.

Time to appropriate care

Once a patient with diabetes incurred sustained hyperglycemia, the median time to appropriate care was another 3.9 months. As illustrated in Fig. 1, whereas 59% of patients received appropriate care within 6 months, by the end of 12 months, 25% of patients had not received appropriate care, and at the end of 2 years, 11% still had not received appropriate care. If return to glycemic control is not considered (i.e., a medication intensification only), median time increases to 4.1 months and the proportion continuing to have an elevated A1C without an intensification is 42% at 6 months, 27% at 12 months, and 14% at 2 years. Of note is the fact that, without intensification, <5% of patients return to glycemic control when control is defined by 7%, and only an additional 4% return to control without intensification when control is defined by 8%.

Factors associated with appropriate care receipt after sustained hyperglycemia

Time to appropriate care significantly decreases as income increases (Table 3). Furthermore, appropriate care receipt is facilitated by patient medication adherence, recent hospital admission, and visits to primary care and endocrinology. Patients with an A1C value between 9 and 11%, as well as those with an A1C >11%, also have reduced delays in the receipt of appropriate care compared with individuals with A1C values between 8 and 9%. Delays are longer for those dispensed combination therapy and increase with increasing prescription drug copayments. Model findings and results do not differ substantively when time to medication intensification only is considered (data not shown).

CONCLUSIONS — Control of hyperglycemia has long been identified as a challenge in the care of patients with diabetes. Among patients initiating oral therapy, we found periods of hyperglycemia exceeding 3 months (and averaging almost 10 months) to be commonplace: 25% of patients incurred a sustained period of hyperglycemia within 3 years of initiating oral monotherapy. The risk of sustained hyperglycemia and no recent medication intensification was notably greater for African American patients as well as those dispensed a sulfonylurea and increased with increasing age and A1C levels. On the other hand, increasing income and medication adherence were protective of sustained hyperglycemia. Specific reasons behind some of these findings can only be speculated. For example, whereas it may be that clinicians are less aggressive in treating older and African American patients, it may be that older and African American patients prefer less aggressive treatment or some combination of these factors.

Furthermore, we found that 41% of patients experiencing sustained hyperglycemia did not receive appropriate care (as evidenced by an intensification of treat-

Table 3—*Factors associated with appropriate care receipt among patients with sustained hyperglycemia: Cox proportional hazards regression results* (n = *1,358*)*

	Hazard ratio (95% CI)	*P*
Sociodemographic characteristics		
Age in decades	0.94 (0.86–1.03)	0.19
Male	0.97 (0.85–1.11)	0.67
Race		
White	1.00	
African American	0.88 (0.76–1.02)	0.08
Other	0.90 (0.68–1.19)	0.47
Married	0.94 (0.82–1.08)	0.36
Insurance type		
Employer-sponsored	1.00	
Medicare risk	0.97 (0.77–1.23)	0.81
Medicare complimentary	0.99 (0.78–1.27)	0.96
Income (in 10K USD increments)	1.03 (1.00–1.07)	0.05
Prescription drug copayment (USD)	0.96 (0.93–0.98)	<0.01
Medication use		
Hyperglycemia medication regimen		
Oral monotherapy	1.00	
Oral combination therapy	0.82 (0.71–0.94)	<0.01
Hyperglycemia medication adherence (in 10% increments)	1.03 (1.01–1.04)	<0.01
Other current medications		
Antihypertensive agent	1.26 (1.09–1.47)	<0.01
Cholesterol-lowering agent	1.26 (1.08–1.46)	<0.01
Antidepressive agent	1.49 (1.19–1.87)	<0.01
Medical care visit event(s)		
Inpatient admission	1.68 (1.02–2.75)	0.04
Emergency department	1.19 (0.80–1.76)	0.40
Primary care	4.22 (3.65–4.88)	<0.01
Endocrinology	3.89 (2.26–6.70)	<0.01
Cardiology	0.99 (0.70–1.41)	0.97
Comorbidities and complications		
Amputation	0.62 (0.21–1.77)	0.37
Cardiovascular event	1.01 (0.81–1.25)	0.93
Carotid endarterectomy	1.40 (0.49–4.04)	0.53
End-stage renal disease	1.16 (0.84–1.59)	0.38
Heart failure	0.98 (0.67–1.44)	0.93
Hypertension	0.85 (0.71–1.02)	0.08
Left ventricular hypertrophy	1.73 (0.82–3.65)	0.15
Retinopathy	0.96 (0.79–1.18)	0.71
Glycemic control		
A1C level		
≤8%	1.00	
8–9%	0.94 (0.73–1.22)	0.64
9–11%	1.38 (1.06–1.79)	0.02
≥11%	1.65 (1.25–2.18)	<0.01

*A total of 28 patients did not have income data available.

ment or subsequent A1C <7%) within 6 months of their second elevated A1C. A quarter of the patients did not receive appropriate care 12 months later, and one in nine still had no evidence of appropriate care 2 years later. Such findings are troubling because multiple clinical trials have provided evidence of the detriment of sustained hyperglycemia among adults with type 2 diabetes (8,9).

We found delays in appropriate care decreased as the per capita income in the patient's community of residence increased and as the patient's prescription drug copayment decreased. These findings translate into substantive differences in the length of delays. For example, patients residing in communities with median household incomes of $20,000 have a hazard rate 22% less favorable than that for patients who reside in communities with median household incomes of $80,000. Furthermore, the Kaplan-Meier estimated median length of delay in appropriate care for patients facing a $5.00 prescription drug copayment was just under 4 months, whereas the median delay for those facing a $7.00 copayment was just over 6.5 months. Taken together, these findings call into question the merits of across-the-board increases in patient financial burdens. Instead, they support the recent movement among some employers toward "value-based insurance design" (13). Under such plans, copayments for some medications (including those used to treat diabetes care) are reduced explicitly to encourage appropriate use (14).

We also found that the likelihood of appropriate care increases substantially with a recent ambulatory care visit—regardless of whether the visit is to a primary care physician or an endocrinologist. Other studies have yielded similar results (6,15). While inpatient admissions also serve to shorten the time to appropriate care, one could speculate that at least some of these admissions might have been avoided if intensification occurred sooner.

Furthermore, we found that patients already dispensed combination oral therapy before incurring sustained hyperglycemia have an 18% less favorable hazard ratio for receipt of appropriate care than patients who remained on monotherapy. Whereas we cannot specifically link this finding to insulin initiation, it is consistent with the hypothesis that physicians and patients have psychological and other barriers to initiating insulin therapy (16–21).

As others have also observed, delays in appropriate care appear commonplace until A1C levels reach ≥9% (3,6,15,22,23). We cannot discern whether such inactivity below 9% is attributable to a failure to realize a likely need for therapy intensification, patient preferences, physician preferences, or a combination of these and other factors. Of note, however, is the fact that <5% of patients return to glycemic control without intensification.

Finally, we found delays in the receipt of appropriate care among those less adherent to hyperglycemia medications. Although not frequently studied, this finding is consistent with that of Grant et al. (4). Whereas intensification of therapy

for patients who are nonadherent to prescribed medications is rarely clinically indicated, there is growing evidence that physicians are often unaware of their patient's medication adherence status (24).

Our study is not without limitations. The use of pharmaceutical claims data to evaluate medication intensifications means that prescriptions provided to patients but never filled are not identified (as are those filled but paid for by another source) and assumes that medications dispensed were ingested. Likewise, because A1C testing is often supplemented with home glucose monitoring, the clinical control measure may be different from that known by patients and providers in practice. Furthermore, some patients may have clinical conditions that make medication change inappropriate. Yet, we focus on those patients with two elevated A1C test results—or those for whom an intensification is likely most warranted—and are able to control for medication adherence when evaluating factors associated with receipt of appropriate care. Furthermore, the small sample size may have contributed to some of the nonstatistically significant findings (particularly that of race and age) in the time-to-appropriate-care equation. Finally, care should be taken when generalizing findings to other populations, especially those that are uninsured.

Our study is one of few to quantify delays in appropriate care receipt among patients with diabetes and one of the first to evaluate simultaneously patient, physician, and system factors associated with appropriate care receipt. Findings highlight that no one person or thing is to blame when care quality falls short. Instead, receipt of quality care results from a complex system of factors. Although the decision to intensify diabetes medication is one usually associated with physicians, to be effective, interventions targeting improvements in pharmacological management should consider a broad array of factors. These include the financial barriers patients may face, the importance of access to routine visits, and possible psychological barriers to appropriate care. The good news is that many of these factors appear amenable to clinical and public policy changes.

Acknowledgments— This research was funded by sanofi-aventis. The funding agency had no role in the study design, analysis, or interpretation of data; decision regarding publication; or preparation of this article. J.E.L. is a member of the Abbott Health Policy Advisory Board and has current research funding from Teva Neuroscience. She previously received salary support from a grant from Novo Nordisk. E.A.D. currently receives salary support as part of a research grant from Teva Neuroscience and has received past salary support as part of a research grant from Novo Nordisk. G.W.D. previously received salary support as part of a research grant from Novo Nordisk. M.E.U.Y. has received research funding from Glaxo SmithKline. No other potential conflicts of interest relevant to this article were reported.

References

1. Wetzler HP, Snyder JW. Linking pharmacy and laboratory data to assess the appropriateness of care in patients with diabetes. Diabetes Care 2000;23:1637–1641
2. Grant RW, Cagliero E, Dubey AK, Gildesgame C, Chueh HC, Barry MJ, Singer DE, Nathan DM, Meigs JB. Clinical inertia in the management of type 2 diabetes metabolic risk factors. Diabet Med 2004;21:150–155
3. Grant RW, Buse JB, Meigs JB. Quality of diabetes care in U.S. academic medical centers: low rates of medical regimen change. Diabetes Care 2005;28:337–442
4. Grant R, Adams AS, Trinacty CM, Zhang F, Kleinman K, Soumerai SB, Meigs JB, Ross-Degnan D. Relationship between patient medication adherence and subsequent clinical inertia in type 2 diabetes glycemic management. Diabetes Care 2007;30:807–812
5. Shah BR, Hux JE, Laupacis A, Zinman B, van Walraven C. Clinical inertia in response to inadequate glycemic control: do specialists differ from primary care physicians? Diabetes Care 2005;28:600–606
6. Rodondi N, Peng T, Karter AJ, Bauer DC, Vittinghoff E, Tang S, Pettitt D, Kerr EA, Selby JV. Therapy modifications in response to poorly controlled hypertension, dyslipidemia, and diabetes mellitus. Ann Intern Med 2006;144:475–484
7. Yood MU, Lafata JE, Koro C, Wells KE, Pladevall M. Time to pharmacotherapy change in response to elevated HbA1c test results. Curr Med Res Opin 2006;22:1567–1574
8. Holman R, Paul S, Bethel M, Matthews D, Neil H. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008;359:1577–1589
9. Turner RC, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49): UK Prospective Diabetes Study (UKPDS) Group. JAMA 1999;281:2005–2012
10. Vine MF, Degnan D, Hanchette C. Geographic information systems: their use in environmental epidemiologic research. Environ Health Perspect 1997;105:598–605
11. Hess LM, Raebel MA, Conner DA, Malone DC. Measurement of adherence in pharmacy administrative databases: a proposal for standard definitions and preferred measures. Ann Pharmacother 2006;40:1280–1288
12. SAS Institute Inc.: *SAS/STAT Users Guide*. Cary, NC, SAS Institute Inc., 2004
13. Benefit-based copays in the real world: the employer perspective. Am J Manag Care 2006;12:S353–S358
14. Fuhrmans V: New Tack on Copays: Cutting Them. Employers, Insurers Bet That Covering More of the Cost of Drugs Can Save Money Over the Long Term for Chronic Conditions. *The Wall Street Journal*. 8 May 2007
15. Berlowitz DR, Ash AS, Glickman M, Friedman RH, Pogach LM, Nelson AL, Wong AT. Developing a quality measure for clinical inertia in diabetes care. Health Serv Res 2005;40:1836–1853
16. Sperl-Hillen J, O'Connor PJ, Carlson RR, Lawson TB, Halstenson C, Crowson T, Wuorenma J. Improving diabetes care in a large health care system: an enhanced primary care approach. Jt Comm J Qual Improv 2000;26:615–622
17. Okazaki K, Goto M, Yamamoto T, Tsujllm S, Ishll H. Barriers and facilitators in relation to starting insulin therapy in type 2 diabetes (Abstract). Diabetes 1999;48:A1319
18. Polonsky WH, Fisher L, Guzman S, Villa-Caballero L, Edelman SV. Psychological insulin resistance in patients with type 2 diabetes: the scope of the problem. Diabetes Care 2005;28:2543–2545
19. Peyrot M, Rubin RR, Lauritzen T, Skovlund SE, Snoek FJ, Matthews DR, Landgraf R, Kleinebreil L. Resistance to insulin therapy among patients and providers: results of the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) study. Diabetes Care 2005;28:2673–2679
20. Rubin RR, Peyrot M. Psychological issues and treatments for people with diabetes. J Clin Psychol 2001;57:457–478
21. O'Connor PJ. Improving diabetes care by combating clinical inertia. Health Serv Res 2005;40:1854–1861
22. Karter AJ, Moffet HH, Liu J, Parker MM, Ahmed AT, Ferrara A, Selby JV. Achieving good glycemic control: initiation of new antihyperglycemic therapies in patients with type 2 diabetes from the Kaiser Permanente Northern California Diabetes Registry. Am J Manag Care 2005;11:262–270
23. Brown JB, Nichols GA. Slow response to loss of glycemic control in type 2 diabetes mellitus. Am J Manag Care 2003;9:213–217
24. Schectman JM, Schorling JB, Nadkarni MM, Voss JD. Can prescription refill feedback to physicians improve patient adherence? Am J Med Sci 2004;327:19–24