Intensification of Diabetes Therapy and Time Until A1C Goal Attainment Among Patients With Newly Diagnosed Type 2 Diabetes Who Fail Metformin Monotherapy Within a Large Integrated Health System

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OBJECTIVE

"Clinical inertia" has been used to describe the delay in the intensification of type 2 diabetes treatment among patients with poor glycemic control. Previous studies may have exaggerated the prevalence of clinical inertia by failing to adequately monitor drug dose changes and nonmedication interventions. This project evaluated the intensification of diabetes therapy and hemoglobin A_{1c} (A1C) goal attainment among patients with newly diagnosed type 2 diabetes when metformin monotherapy failed.

RESEARCH DESIGN AND METHODS

The electronic health record at Cleveland Clinic was used to identify patients with newly diagnosed type 2 diabetes between 2005 and 2013 who failed to reach the A1C goal after 3 months of metformin monotherapy. A time-dependent survival analysis was used to compare the time until A1C goal attainment in patients who received early intensification of therapy (within 6 months of metformin failure) or late intensification. The analysis was performed for A1C goals of 7% (*n* = 1,168), 7.5% (*n* = 679), and 8% (*n* = 429).

RESULTS

Treatment was intensified early in 62%, 69%, and 72% of patients when poor glycemic control was defined as an A1C >7%, >7.5%, and >8%, respectively. The probability of undergoing an early intensification was greater the higher the A1C category. Time until A1C goal attainment was shorter among patients who received early intensification regardless of the A1C goal (all $P < 0.05$).

CONCLUSIONS

A substantial number of patients with newly diagnosed type 2 diabetes fail to undergo intensification of therapy within 6 months of metformin monotherapy failure. Early intervention in patients when metformin monotherapy failed resulted in more rapid attainment of A1C goals.

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Despite clinical practice guidelines that recommend frequent monitoring of hemoglobin A_{1c} (A1C) and aggressive escalation of antidiabetic therapies to reach glycemic targets (1,2), research using the United States National Health and Nutrition Examination Survey database reported that from 2007 to 2010, only 52.5% of people with diabetes achieved an A1C of $<$7.0% (3). Metformin, in the absence of contraindications or intolerability, is generally the recommended first-line therapy to manage hyperglycemia in patients with type 2 diabetes (1,2). However, further intensification of therapy, with the initiation of additional antidiabetic medication, is often inappropriately delayed. Recent studies revealed that the median time to treatment intensification among those in whom metformin monotherapy failed exceeded 1 year and that the median time to treatment intensification was 14.0 months overall (4).

There are many challenges in achieving glycemic targets in patients with type 2 diabetes: the progressive deterioration in blood glucose control related to ongoing β-cell failure (5,6), the lack of medications that address all of the underlying pathophysiologic defects of type 2 diabetes (7), poor glycemic durability among the antidiabetic agents (8,9), and patient-related factors, including concern about the potential for medication-related adverse effects (10), medication complexity, tolerability, and/or affordability (8,11), and poor adherence to lifestyle modifications (8). Clinical inertia (failure to initiate or intensify therapy when indicated) also appears to be a very strong driving force behind the failure to obtain glycemic control (12). According to Phillips et al. (13), clinical inertia is due to at least three problems: overestimation of care provided, use of "soft" reasons to avoid intensification of therapy, and lack of education, training, and practice organization aimed at achieving therapeutic goals.

Although the time to treatment intensification and/or lack of intensification when clinically indicated (clinical inertia) has been studied in the overall prevalent population of patients with type 2 diabetes (4), there are no data in the literature regarding this topic in patients with newly diagnosed type 2 diabetes. Guidelines are clear on the need to aggressively intensify therapy in patients with newly diagnosed type 2 diabetes to get to the A1C goal, but patients and physicians may feel less urgency early in the course of the disease. The objectives of this study were to evaluate the prevalence of clinical inertia, identify factors associated with clinical inertia, and quantify the time until intensification and time until A1C control in patients with newly diagnosed type 2 diabetes who did not achieve glycemic targets after at least 3 months of metformin monotherapy.

RESEARCH DESIGN AND METHODS

Data Source

The enterprise-wide electronic health record (EHR) system at Cleveland Clinic was used to identify patients with newly diagnosed type 2 diabetes. Cleveland Clinic uses EPIC My Practice across the entire organization (installed in 1998). The EHR includes patient demographics; social, medical, family, and surgical history; vital signs; imaging data and pathology reports; and rich longitudinal clinical data (diagnosis, procedures, etc.) from inpatient and outpatient records. It contains discrete data linkage with Cleveland Clinic laboratory records and detailed information on medication use information. In 2014, Cleveland Clinic set a new annual record for outpatient visits (almost 6 million), and has $>$1 million active patients ($\geq$2 encounters within the past 12 months).

Inclusion and Exclusion Criteria

From 2005 to 2013, patients with newly diagnosed diabetes were identified by requiring at least two office encounters with a primary care provider or endocrinologist within the Cleveland Clinic Health System before the first structured diagnosis of diabetes (ICD-9 code 250.xx). This requirement helped to limit the inclusion of patients with preexisting diabetes who were being referred to Cleveland Clinic specifically for diabetes management. Excluded were patients with any structured evidence of diabetes $>$12 months before the date of diagnosis, determined by antidiabetic medication, ICD-9 code, or laboratory values consistent with having diabetes (elevated fasting or random blood glucose or elevated A1C). In a further attempt to exclude patients who potentially may have been receiving diabetes care elsewhere, patients in whom the time between the second prediagnosis of diabetes encounter and the subsequent diagnosis of diabetes was $\geq$2 years were excluded. Also excluded were patients without a subsequent outpatient encounter for type 2 diabetes after the date of diagnosis within the EHR, patients with documentation of an ICD9 code specific for type 1 diabetes at any time, and patients with gestational diabetes.

The study population was further restricted to patients with newly diagnosed type 2 diabetes who received at least 3 months of first-line metformin monotherapy. The first A1C after 3 months of metformin monotherapy was recorded as the initial/baseline A1C. If the initial/baseline A1C exceeded 1 year after the end of the 3-month course of metformin monotherapy, the patient was excluded because the patient was assumed to be lost to follow-up and was no longer being managed at the Cleveland Clinic. Because the baseline A1C is a measure of the effectiveness of the metformin monotherapy, the patient had to be on metformin monotherapy until the first A1C measurement and was excluded if any additional antidiabetic medication was added before the initial/baseline A1C assessment. Clinical inertia was defined as a lack of intervention within 6 months after an elevated baseline A1C ($>$7%, $>$7.5%, or $>$8%).

Statistical Analysis

A cross-sectional summary of patient characteristics was made for the entire cohort and then stratified by the baseline A1C category $>$7% (53 mmol/mol), $>$7.5% (58 mmol/mol), and $>$8% (64 mmol/mol).

Separate Kaplan-Meier analyses were performed for time until intervention for patients with baseline A1C $>$7% (n = 1,168), $>$7.5% (n = 679), and $>$8% (n = 429). These three discrete A1C cut points were chosen for evaluation to try to avoid overestimating the prevalence of clinical inertia because many patients may have had a higher A1C target ($>$7%), in line with recent guidelines that have recommended an individualized approach to diabetes management. "Intervention" included the addition of antidiabetic medication, prescription for a weight loss medication, change in metformin dose or regimen, or referral to a dietitian or nutritionist. The log-rank test was used to evaluate the difference between each stratified level within the Kaplan-Meier plots.

Time-dependent Cox regression analyses were constructed for time until A1C goal attainment. Because different patients may have different but appropriate A1C goals, the analysis was repeated for A1C goals of 7%, 7.5%, and 8%. A time-dependent analysis was used to account for the heterogeneity in the elapsed time between the initial A1C measurement and the initial intervention. To control for potential confounding variables in the relationship between early intervention and goal attainment, the Cox models included the covariates of age, race, sex, the Deyo-modified Charlson comorbidity index, the number of active nondiabetic medications, smoking status, and the number of preventative examinations of baseline A1C within the past 3 years. Because the time of the intervention occurs after the initial A1C, the intervention is therefore dependent on follow-up time and incorporated into a Cox regression as a time-dependent variable. Without this adjustment, there would be a bias of shorter follow-up times being associated with earlier interventions.

To identify factors/patient characteristics that were associated with clinical inertia, descriptive statistics for the groups with and without inertia were compared using χ^2 tests for the categorical variables and the Wilcoxon sign rank test for the continuous variables.

Record Review

A record review was conducted of 20 random patients with identified clinical inertia to determine the patient and physician contributions to the development of clinical inertia and to identify the reasons an intensification of therapy failed to occur when indicated. The patients' entire EHR was reviewed, with a particular focus on the information contained within the free-text progress notes and compliance with provider appointments.

RESULTS

From 2005 to 2013, 5,239 patients met the outlined inclusion and exclusion criteria: having newly diagnosed type 2 diabetes and having been treated with metformin monotherapy for at least 3 months. The patient population was ~50% female, 77% Caucasian, and 14% smokers, and 77% had private or Medicare insurance. The median age was 58 years. Patients with a baseline A1C >8% tended to be younger, male, and non-Caucasian. Table 1 provides the descriptive statistics for the entire cohort.

Baseline A1C Assessment

The median (interquartile range [IQR]) baseline A1C (first A1C within 1 year after being on a metformin monotherapy for at least 3 months) for the entire cohort (N = 5,239) was 6.4% (6.0, 6.9) (46 mmol/mol [42, 52]). The number (%) of patients with a baseline A1C >7%, >7.5%, and > 8%, were 1,168 (22%), 679 (13%), and 429 (8%), respectively. The median (IQR) baseline A1C for those patients with a baseline A1C >7%, >7.5%, or >8% who underwent an early intervention was 7.9% (7.3, 9.0) (63 mmol/mol [56, 75]), 8.5% (7.9, 9.9) (69 mmol/mol [63, 85]), and 9.2% (8.5, 10.8) (77 mmol/mol [69, 95]), respectively. The median (IQR) baseline A1C for those patients with a baseline A1C >7%, >7.5%, or >8% who underwent a late (or no) intervention was 7.5% (7.2, 8.1) (58 mmol/mol [55, 65]), 8.2% (7.8, 9.4) (66 mmol/mol [62, 79]), and 9.2% (8.4, 10.2) (77 mmol/mol [68, 88]), respectively. The median (IQR) time until baseline A1C assessment was 2.8 months (1.0, 6.0). Table 2 summarizes the data provided.

Follow-up A1C Assessment

The vast majority of patients had a follow-up A1C measurement (4,686 of 5,239 [89%]), defined as the first A1C after the baseline A1C. The median (IQR) time to follow-up A1C for the entire cohort was 5.9 months (3.7, 9.3). The median (IQR) time to follow-up A1C assessment in those patients with a baseline A1C >7%, >7.5% and >8% was 5.0 (3.2, 8.6), 4.9 (3.1, 9.0), and 5.0 months (3.1, 9.3), respectively. The median (IQR) follow-up A1C level in those patients who underwent an early intervention, with a baseline A1C >7%, >7.5%, and >8%, was 7.4% (6.9, 8.5) (57 mmol/mol [52, 69]), 7.8% (7.1, 9.3) (62 mmol/mol [54, 78]), and 8.3% (7.3, 9.8) (67 mmol/mol [56, 84]). The median (IQR) follow-up A1C level in those patients who underwent a late (or no) intervention with a baseline A1C >7%, >7.5%, and >8% was 7.4% (6.9, 8.5) (57 mmol/mol [52, 69]), 8.1% (7.1, 9.3) (65 mmol/mol [54, 78]), and 8.7% (7.3, 10.0) (72 mmol/mol [56, 86]), respectively (Table 2). The vast majority of patients, 4,138 (79%), also had a return visit with a primary care provider or endocrinologist within the Cleveland Clinic Health System.

Time From Baseline A1C Measurement Until Time of Intervention

The median time until intervention in the overall cohort was 1.18 years (~14 months). The percentage of patients with a baseline A1C >7%, >7.5%, and >8% who experienced clinical inertia (did not receive an intervention within 6 months of a baseline elevated A1C) was 38%, 31%, and 28%, respectively. Figure 1 shows the Kaplan-Meier curves for the time until intervention according to the different A1C cutoffs.

Patients with higher baseline A1C levels were more likely to receive an additional medication as the initial intervention. Table 3 reports the types of initial interventions according to baseline A1C.

Analysis of Time Until A1C Was Under Control

The time until A1C was under control was evaluated based on the initial/baseline A1C category after at least 3 months of metformin monotherapy (>7%, >7.5%, >8%) and then stratified into two subsets of patients: those who were observed to undergo an early intervention (≤6 months of the initial/baseline A1C) or late intervention (>6 months or never). Across all A1C categories, patients who underwent an early intervention had a lower probability of not having their A1C under control versus those who underwent a late or no intervention. (Fig. 2). In the adjusted time-dependent model, patients who underwent an early intervention had a lower probability of not having their A1C under control versus those who underwent a late or no intervention (initial/baseline A1C >7%: hazard ratio [HR] 0.57, 95% CI 0.22–0.91, P = 0.001; initial/baseline A1C >7.5%: HR 0.25, 95% CI 0.05–0.44, P = 0.01; initial/baseline A1C >8%: HR 0.25, 95% CI 0.00–0.49, P = 0.04).

Factors Associated With Clinical Inertia

The 443 patients (38%) who experienced clinical inertia, that is, did not undergo an intervention within 6 months of the elevated baseline A1C (>7%) versus the 725 (62%) who underwent early intervention, were slightly older, with a median (IQR) age of 56.0 (46.6, 64.8) vs.

Table 1—Descriptive statistics for the entire cohort and patients with a baseline A1C >7%, >7.5%, or >8%

Variables	All *N* = 5,239 (100%)	Initial A1C >7% *n* = 1,168 (22%)	Initial A1C >7.5% *n* = 679 (13%)	Initial A1C >8% *n* = 429 (8%)
Age, years	58 (49, 67)	54 (46, 62)	53 (44, 61)	52 (43, 59)
Sex				
Male	2,367 (45)	587 (50)	347 (51)	222 (52)
Female	2,872 (55)	581 (50)	332 (49)	207 (48)
Race				
White/Caucasian	4,017 (77)	873 (75)	490 (72)	307 (72)
Black/African American	889 (17)	227 (20)	149 (22)	98 (23)
Other	146 (3)	29 (2)	14 (2)	9 (2)
Missing	187 (3)	39 (3)	26 (4)	15 (3)
Insurance				
Medicaid	225 (4)	69 (6)	49 (7)	39 (9)
Medicare	2,059 (39)	394 (34)	223 (33)	132 (31)
Private	1,981 (38)	497 (43)	279 (41)	173 (40)
Other	215 (4)	52 (4)	26 (4)	18 (4)
Missing	759 (15)	156 (13)	102 (15)	67 (16)
Smoking status				
Never	2,390 (46)	496 (42)	291 (43)	189 (44)
Former	1,813 (35)	360 (31)	185 (27)	101 (24)
Current	754 (14)	217 (19)	138 (20)	94 (22)
Missing	282 (5)	95 (8)	65 (10)	45 (10)
DCSI	0 (0, 2)	0 (0, 2)	0 (0, 2)	0 (0, 2)
eGFR (mL/min/1.73 m^2)	68.3 (13.9, 92.6)	76.2 (14.9, 98.9)	76.9 (15.7, 99.8)	82.6 (16.0, 102.1)
Deyo-modified Charlson comorbidity index	2 (1, 3)	1 (1, 3)	1 (1, 3)	1 (1, 3)
Number of active nondiabetic prescription medications	3 (2, 5)	3 (2, 4)	3 (2, 4)	3 (2, 4)
Preventive exams in the past 3 years (V70.0)*	1,989 (38)	398 (34)	206 (30)	110 (26)
Coronary heart disease	665 (13)	124 (11)	60 (9)	31 (7)
Cerebrovascular accident	422 (8)	66 (6)	40 (6)	25 (6)
Heart failure	233 (4)	51 (4)	29 (4)	19 (4)
Hypertension	3,607 (69)	776 (66)	437 (64)	261 (61)

Data are presented as the median (IQR) or as *n* (%). DCSI, Diabetes Complication and Severity Index; eGFR, estimated glomerular filtration rate (calculated via Chronic Kidney Disease Epidemiology Collaboration equation). *ICD-9 diagnosis code for a general medical examination at a health care facility.

54.2 (47.0, 61.3) years (P = 0.038). No differences were observed for the following patient characteristics/variables between the patients who underwent early versus late (or no) intervention: race, insurance status (Medicaid, Medicare, or private), smoking status, Diabetes Complication and Severity Index, estimated glomerular filtration rate, Deyo-modified Charlson comorbidity index, number of active nondiabetes-related prescription medications, preventative examinations within the past 3 years, history of coronary artery disease, cerebral vascular accident, heart failure, or hypertension, and whether they had a specialist encounter.

Record Review

The record review that was conducted of 20 random patients with identified clinical inertia revealed that inertia, or lack of intensification, was patient-driven in 11 and physician-driven in the remaining 9. Every patient with inertia demonstrated multiple noncompliance behaviors, including missed appointments (clinical, laboratory, or nutrition consultations) and nonadherence to treatment regimens (medications, diet, or exercise). Instances of physician inertia were simply related to the physician's failure to intensify therapy as indicated to address an A1C elevation.

CONCLUSIONS

Research using the United States National Health and Nutrition Examination Survey database reported that from 2007 to 2010, only 52.5% of people with diabetes achieved an A1C <7.0% (3). This may be partly because in clinical practice, health care providers (and patients) fail to intensify therapy when it is indicated. Recent literature has noted that the median time to treatment intensification among those in whom metformin monotherapy fails, the preferred first-line agent, was greater than 1 year. In addition, the study noted that intensification occurred more quickly in those with higher A1Cs than those with A1Cs closer to goal (<7%) (4). This suggests that clinicians (and patients) may not be as aggressive with the intensification of treatment when a patient is closer to an A1C of 7%, a worrisome observation, because residual A1C elevation above 7% still increases the risk of diabetes-related complications. An additional study using the General Electric Centricity Electronic Medical Record database evaluated the effect of time to treatment intensification on glycemic goal attainment in patients in whom metformin monotherapy failed, and reported an adjusted odds ratio (OR) for glycemic goal attainment of 1.36 (95% CI 1.09–1.72) comparing early add-on to late add-on treatment. This association was stronger among patients with a higher trigger A1C at baseline, with ORs of 1.53 (95% CI 1.08–2.19) for

Table 2—Baseline and follow-up A1C, stratified by baseline A1C and intervention status and time to follow-up A1C

	N	Intervention ≤6 months no clinical inertia	No intervention ≤6 months clinical inertia
Baseline A1C >7%	1,168	725 (62)	443 (38)
Baseline A1C (%)		7.9 (7.3, 9.0)	7.5 (7.2, 8.1)
Baseline A1C (mmol/mol)		63 (56, 75)	58 (55, 65)
Follow-up A1C (%)		7.4 (6.9, 8.5)	7.4 (6.9, 8.5)
Follow-up A1C (mmol/mol)		57 (52, 69)	57 (52, 69)
Time to follow-up A1C (months)		5.0 (3.2, 8.6)	
Baseline A1C >7.5%	679	469 (69)	210 (31)
Baseline A1C (%)		8.5 (7.9, 9.9)	8.2 (7.8, 9.4)
Baseline A1C (mmol/mol)		69 (63, 85)	66 (62, 79)
Follow-up A1C (%)		7.8 (7.1, 9.3)	8.1 (7.1, 9.3)
Follow-up A1C (mmol/mol)		62 (54, 78)	65 (54, 78)
Time to follow-up A1C (months)		4.9 (3.1, 9.0)	
Baseline A1C >8%	429	309 (72)	120 (28)
Baseline A1C (%)		9.2 (8.5, 10.8)	9.2 (8.4, 10.2)
Baseline A1C (mmol/mol)		77 (69, 95)	77 (68, 88)
Follow-up A1C (%)		8.3 (7.3, 9.8)	8.7 (7.3, 10.0)
Follow-up A1C (mmol/mol)		67 (56, 84)	72 (56, 86)
Time to follow-up A1C (months)		5.0 (3.1, 9.3)	

Data are presented as *n* (%) or median (IQR).

A1C ≥8% and 2.63 (95% CI 1.40–5.27) for A1C ≥9% (14).

However, the results of these studies may not be generalizable to the population of patients with newly diagnosed type 2 diabetes. This study is unique in that it evaluated the concepts of clinical inertia, the time until intervention based on the A1C after at least 3 months of metformin monotherapy, and the time until A1C is under control with early versus a late (or no) intervention, in patients with newly diagnosed type 2 diabetes. Until this report, the literature pertaining to these concepts has been limited to the prevalent population of patients with type 2 diabetes.

The results of this study highlight many important aspects of clinical practice in the management of patients with type 2 diabetes. First, many patients with residual A1C elevation after at least 3 months of metformin monotherapy do not undergo an intervention/intensification of therapy within 6 months of the first A1C assessment (i.e., the initial/baseline A1C after at least 3 months of metformin monotherapy). The current study noted that in those with a residual A1C elevation of >7%, >7.5%, or >8%, 38%, 31%, and 28%, respectively, failed to undergo an intervention to further improve glycemic control within 6 months. These patients, by definition, experienced clinical inertia, the lack of intensification despite a reason to do so (i.e., an A1C above goal). Although many of these patients did eventually undergo an intervention to improve glycemia within 2 years of the initial/baseline A1C, this is a longer period than would be desired. A delay in treatment intensification by 1 year, in conjunction with poor glycemic control, has been reported to significantly increase the risk of macrovascular events (15). Patients with type 2 diabetes are often highly motivated near the time of diagnosis, so it would seem important to leverage this motivation and intervene to improve glycemic control early on in the disease process and not allow for time to pass and perhaps risk losing the patient to follow-up.

Secondly, this study highlights that the time until intervention is significantly affected by the initial/baseline A1C. The time until intervention was lower in those with higher initial/baseline A1Cs; that is, higher A1Cs appear to have encouraged the clinician and patient to intervene sooner, as indicated, and intensify the therapeutic approach. This suggests that "borderline" or A1C levels that are slightly above goal are less likely to be addressed in a timely manner versus those that clearly remain too high (>8%).

Lastly, and most importantly, the analysis found that the probability of a patient having his or her A1C under control is higher in those who undergo an early intervention (within 6 months) than in those who undergo a later (or no) intervention and that this persisted moving forward in time (Fig. 2). Thus, failure to intervene early, when it is indicated, may have a lasting effect on the ability to attain glycemic control. This is a worrisome finding, because glycemic control early in the course of disease has "a legacy effect" on the development of future diabetes-related complications (16).

In addition to the baseline A1C, patient age was the only additional variable associated with clinical inertia. Older patients were less likely to undergo an early intervention. This may be because older patients often have more comorbidities and additional social issues (insurance coverage, fixed income, etc.) that may serve as barriers to intensification or they may have had higher individualized A1C goals. The development of clinical inertia was not influenced by provider type (specialist vs. primary care). The percentage of patients with a specialist encounter was similar between patients with an A1C >7% who underwent an early intervention (10%) versus a late (or no) intervention (8%) (P = 0.25). Thus, the results of our report appear generalizable to the population of patients with newly diagnosed type 2 diabetes managed by primary care, irrespective of their access to specialty care.

At first glance, the median follow-up A1C data appears similar whether an early intervention occurred or not; however, when the median follow-up A1C values are compared with their respective baseline A1C values, stratified by intervention status and baseline A1C category (Table 2), an improvement in A1C in those who underwent an early intervention versus a late (or no) intervention was observed. Those who underwent early intensification were observed to have a higher median baseline A1C. This supports the assertion that the baseline A1C value is a factor behind the development of clinical inertia: the closer the A1C is to goal (<7% in general), the more likely a patient is to experience inertia.

The population appeared to be relatively well controlled at baseline: only 22% of the subjects had an A1C >7% and only 8% had an A1C >8%. The

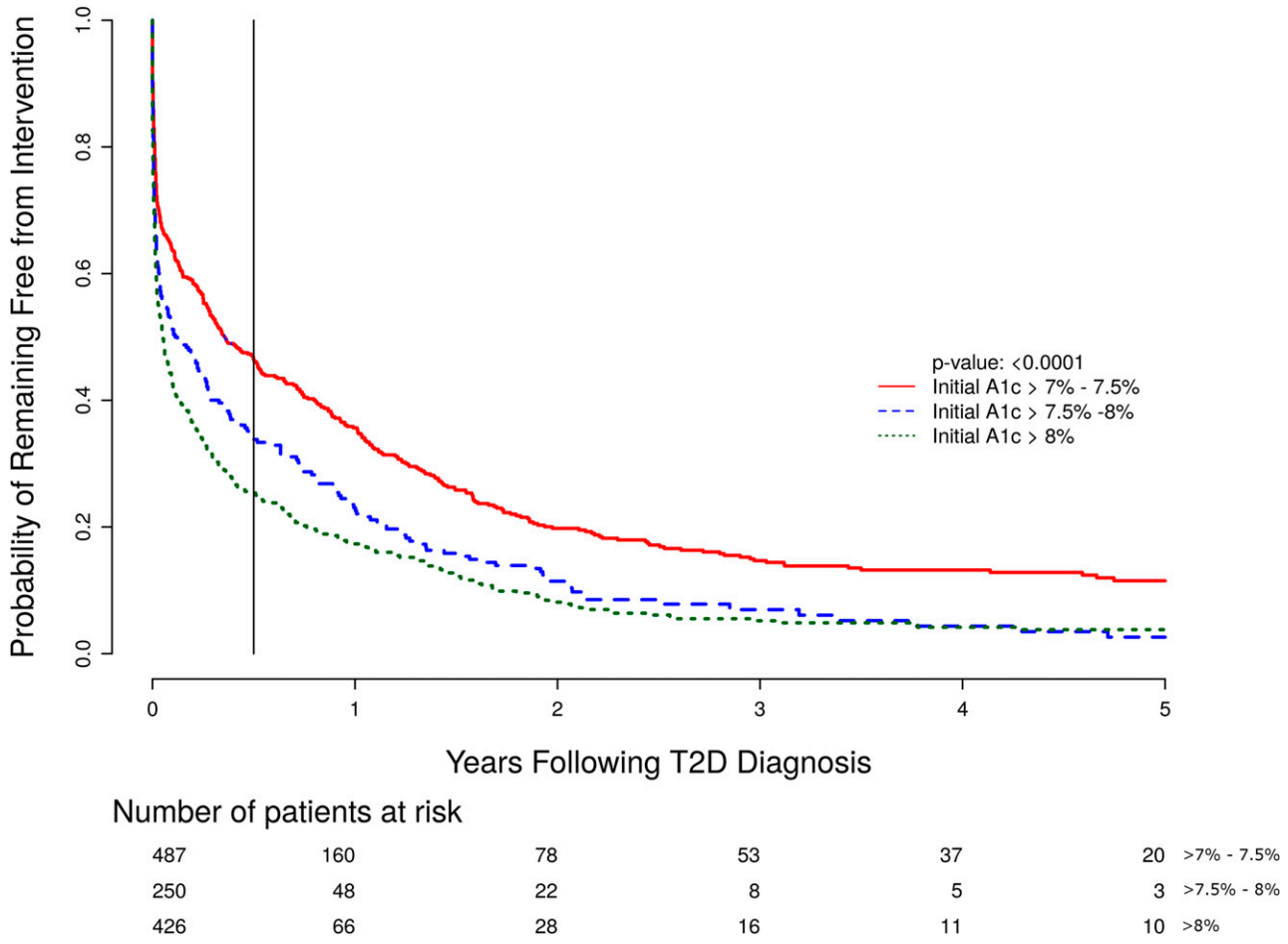

Figure 1—Kaplan-Meier curves for measuring time until intervention, stratified by initial A1C >7–7.5%, >7.5–8%, and >8%, where each bin is mutually exclusive. The *x*-axis is presented in years, and the *y*-axis is presented as the cumulative probability of not experiencing an intervention. The horizontal black line indicates 6 months, where 54% (100% − 46%) had an intervention for patients with an initial A1C >7–7.5%, 66% (100% − 34%) had an intervention for patients with an initial A1C >7.5–8%, and 75% (100% − 25%) had an intervention for patients with an initial A1C >8%. T2D, type 2 diabetes. $P < 0.0001$. The numbers at the bottom of the plot indicate how many patients are at risk for each time point between each stratified level.

relatively good control observed at baseline may possibly be a reflection of the nature of the Cleveland Clinic Health System (an integrated delivery system), patient access to specialty care, or perhaps simply because the study was focused on a population of patients with newly diagnosed type 2 diabetes. Of the 5,239 patients included in this report, 4703 (90%), were seen by primary care and only 536 (10%) were seen by an endocrinologist. Thus, access to specialty care does not appear to explain the relatively good glycemic control observed at baseline. In addition, in the population of patients with an A1C >7% at baseline, where an intensification of management was indicated, there were no statistically significant differences between the percentages of patients seen by a specialist versus a primary

Table 3—First intervention according to baseline A1C

	A1C >7% (*n* = 1,168)*		A1C >7.5% (*n* = 679)**		A1C >8% (*n* = 429)***	
Intervention	Within 6 months *n* = 725 (62.1%)	After 6 months *n* = 305 (26.1%)	Within 6 months *n* = 469 (69.1%)	After 6 months *n* = 149 (21.9%)	Within 6 months *n* = 309 (72.0%)	After 6 months *n* = 86 (20.0%)
Additional diabetic medication	336 (46.3)	145 (47.5)	245 (52.2)	76 (51.0)	174 (56.3)	44 (51.2)
Addition of a weight loss medication	2 (0.3)	1 (0.3)	2 (0.4)	1 (0.7)	1 (0.3)	0 (0)
Diet consultation/referral to nutritionist	53 (7.3)	38 (12.5)	35 (7.5)	18 (12.1)	27 (8.7)	11 (12.8)
Titration of metformin dosage	334 (46.1)	121 (39.7)	187 (39.9)	54 (36.2)	107 (34.6)	31 (36.0)

Data are presented as *n* (%). Within 6 months is limited to patients who received one of these interventions within the first 6 months. After 6 months is limited to patients who received their first intervention after 6 months. *138 (11.8%) did not receive any intervention. **61 (9.0%) did not receive any intervention. ***34 (7.9%) did not receive any intervention.

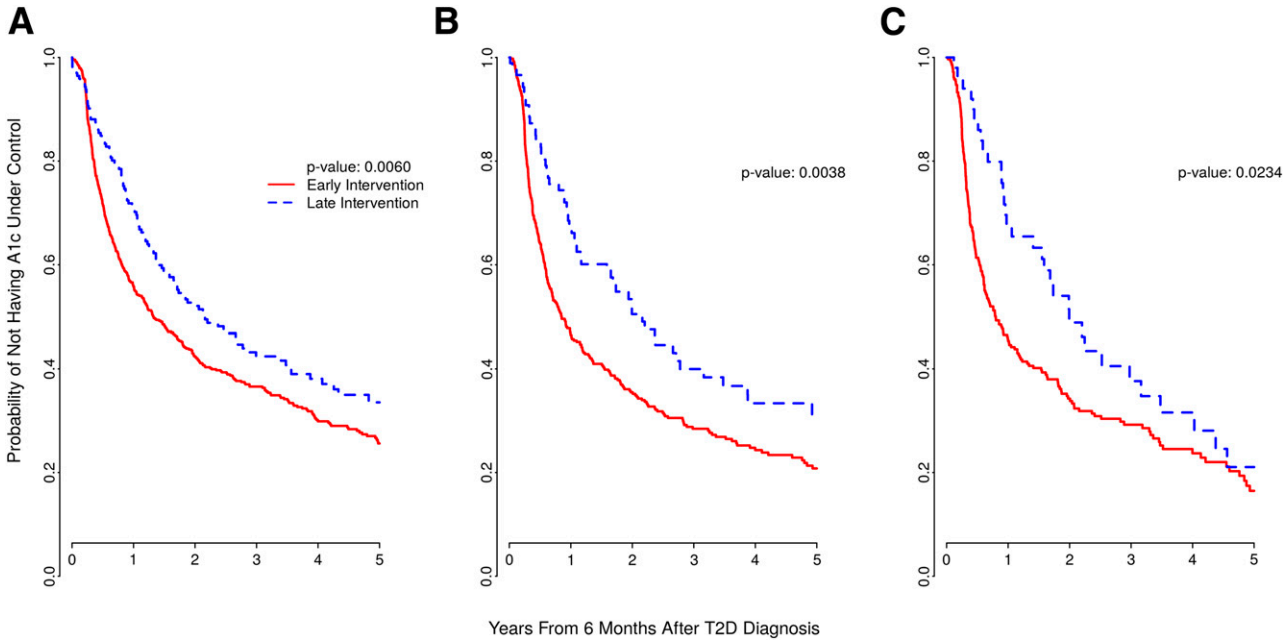

Figure 2—Kaplan-Meier curves of time until A1C is under control for initial/baseline A1C >7% (*A*), >7.5% (*B*), and >8% (*C*), and subset by early intervention (intervention on or before 6 months after to the initial A1C) and late or no intervention (intervention after 6 months). T2D, type 2 diabetes.

care provider, stratified by early versus late (or no) intervention. This suggests that the likelihood of an early intervention is independent of provider type. Accordingly, the findings of this report appear to be very generalizable to the population of patients with type 2 diabetes without access to specialty care.

Although the current clinical standard of care is reassessing A1C in 3 months and adjusting therapy accordingly, the decision was made to use a 6-month period to allow for an intervention because use of the shorter time may have resulted in an overestimation of the problem. If a patient did not undergo an intervention within 6 months, it would be very clear that the patient was inappropriately not undergoing treatment intensification.

The record review of 20 random patients with clinical inertia revealed that clinical inertia in 55% of the patients was patient driven. Every patient with "patient inertia" demonstrated multiple noncompliance behaviors. Most instances of physician inertia were simply related to the physician's failure to intensify therapy where indicated.

The strengths of this study include the large number of patients with newly diagnosed type 2 diabetes that were included in the analysis, a novel approach, and the large amount of clinical information that was available for those patients included in the analysis. Unlike other studies that have evaluated the various concepts of clinical inertia (4,14,15), the current analysis included numerous interventions in the definition of intensification rather than simply defining an intervention as the addition of another antidiabetic agent, which may not always be the modality by which a treatment intensification occurs. Moreover, follow-up A1C information was available on most of the subjects, which allowed an analysis of the effects of an intervention on glycemic control and, more importantly, the timing of that intervention on long-term glycemic goal attainment.

This study is not without limitations. A patient's personal A1C goal may have been different or individualized in accordance with the most recent American Diabetes Association/European Association for the Study of Diabetes guidelines (1), but such individual goals were not obtainable from the structured EHR data. However, it is unlikely that very many patients have an individualized A1C goal >8%; thus, the results at this A1C cut point would appear to be very generalizable to the population with newly diagnosed type 2 diabetes. A switch from metformin to extended-release metformin, which is often better tolerated than immediate-release metformin, was also not counted as an intervention.

The current study was unable to explore the relationship between early intensification and the development of complications related to type 2 diabetes and other long-term health outcomes, because this would have required more than the few years of follow-up information that was available for these patients at the time of the analysis. Certainly, this would be an area of future study to pursue once the follow-up and health outcomes of these patients with newly diagnosed type 2 diabetes accrue within the EHR. Future studies assessing treatment adherence and evaluating its effect on A1C goal attainment and health outcomes would also be of interest. These issues could not be evaluated in the present report given the short-duration of follow-up and lack of pharmacy fill-data of the prescribed medications for all the patients included in the analysis (both additional limitations). Lastly, although the additional information obtained from the EHR review was interesting, the relatively small number of records reviewed is a limitation.

The results of this study would seem to provide support for the most recent American Association of Clinical Endocrinologists guidelines (2), which recommend aggressive intensification of antidiabetic therapy after 3 months of monotherapy failure as well as after 3 months of dual-therapy failure. Failure to make these early interventions, as these results suggest, have a significant effect on the patients' long-term attainment of glycemic control. The UK Prospective Diabetes Study 10-year follow-up of intensive glucose control in patients with type 2 diabetes demonstrated the importance of early glycemic control on the development of long-term diabetes-related complications. The results of this study demonstrate that to obtain glycemic control, clinicians and patients need to escalate the therapeutic interventions earlier in the disease course and in a timelier manner.

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