

## Effects of conformance to type 2 diabetes guidelines on health care resource utilization, clinical outcomes, and cost: A retrospective claims analysis

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### ABSTRACT

**Objectives:** To determine if there is a difference in the outcomes of diabetes patients managed with high, intermediate, or low conformance to diabetes guidelines.

**Study design:** Retrospective database analysis.

**Methods:** This was a retrospective database analysis of adults diagnosed with type 2 diabetes and with glycated hemoglobin (HbA1c)  $\geq 7\%$  (53 mmol/mol) who were commercially insured by, or receiving Medicare benefits through, Aetna. Subjects were classified as having high, intermediate, or low conformance to current guidelines. Six, 12, and 18 months later, health care resource utilization, clinical outcomes, and costs were assessed using multivariable regression analysis to determine whether differences existed between patients with high, intermediate, and low conformance. Regression models were adjusted using pre-index variables, and the results were expressed as incidence rate ratios (IRRs) with 95% confidence intervals (CIs).

**Results:** A total of 21,171 individuals were included in the analysis. In analyses of patients with low versus high conformance, pharmacy costs were significantly lower over 18 months of outcome assessment ( $P < 0.001$ ), but diabetes-related outpatient costs were significantly higher ( $P < 0.001$ ). In analyses of patients with intermediate versus high conformance, diabetes-related outpatient costs were significantly greater at 12 and 18 months ( $P < 0.001$  for both).

**Conclusions:** Reduced conformance to guidelines leads to higher diabetes-related costs.

### Introduction

According to the Centers for Disease Control, 12.3% of the adult US population has diabetes mellitus, mostly type 2 [1]. In addition to lifestyle modifications in diet and exercise, maintaining healthy blood glucose levels is the primary focus of type 2 diabetes management. The American Diabetes Association (ADA) has established a target of  $< 7.0\%$  (53 mmol/mol) glycated hemoglobin (HbA1c) for most adults with type 2 diabetes, with more stringent targets for patients with short-duration, treatment-amenable disease in the context of good cardiovascular health, and less stringent targets for patients with a history of hypoglycemia, limited life expectancy, and cardiovascular comorbidities [2]. Based on data from 1.7 million privately insured and Medicare patients, between 50% and 60% of type 2 diabetes patients achieved HbA1c  $< 7.0\%$  (53 mmol/mol) in the years 2006–2013 in the United States [3].

A variety of pharmacotherapies are available to help type 2 diabetes

patients achieve their HbA1c target. The ADA guidelines recommend regimen intensification (e.g., increased dosage of oral antidiabetic (OAD) agents, add-on pharmacotherapy, or switching to basal or other insulin) and/or closer glucose monitoring (e.g., follow-up HbA1c testing or additional diabetes-related provider visits) for patients with poor glycemic control [2]. Timely intensification of pharmacotherapy results in better glycemic control [4–6] with no increase, or even reductions, in health care costs [5,6]. However, studies of clinical and economic outcomes after regimen intensification [4–13] have to date focused primarily on comparisons between intensified regimens [5,8,10,12,13], without incorporating closer glucose monitoring into their assessments of intensification. We sought to investigate the effect of both elements of type 2 diabetes management.

The objective of this study was thus to determine if there is a significant difference in the clinical and economic outcomes of insured US adults with type 2 diabetes whose disease management was highly conformant to the ADA guidelines (i.e., in agreement with or adherent

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to the standards set by the guidelines), in terms of both regimen intensification and glucose monitoring, compared to patients managed at intermediate or low levels of conformance.

## Methods

### Study design and data source

This was a retrospective analysis of the medical and pharmacy claims of members of Aetna's fully insured commercial or Medicare Advantage plans using Aetna's claims, Medical Case, and Health Profile databases. The claims data include diagnoses and procedures rendered during inpatient, outpatient, and covered skilled facility encounters, derived from International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) and ICD 10th Revision (ICD-10) codes; professional encounters, derived from current procedural terminology (CPT) codes; use of durable medical equipment, derived from Healthcare Common Procedure Coding System (HCPCS) codes; administered and dispensed pharmaceuticals, derived from HCPCS and national drug codes (NDCs), respectively; the presence of laboratory, pathology, and imaging services; and allowable costs of health care services. Allowable costs represent the total amount reimbursed to the service provider from all sources—health plan (including any secondary insurers) and patient. Lab results (e.g., HbA1c) were available for tests performed at contracted laboratories.

Study data were accessed in compliance with the Health Insurance Portability and Accountability Act of 1996. As a retrospective analysis, the study was approved by the Sterling Institutional Review Board. Informed consent was not required as no contact with human subjects was involved, and subject identifiers were not released by Aetna.

### Study sample

The study population included patients aged  $\geq 18$  with a diagnosis of type 2 diabetes and an HbA1c test result  $\geq 7.0\%$  (53 mmol/mol) during an index period ranging from July 1, 2014 to August 31, 2015. The date of the HbA1c test result was defined as the index date. Type 2 diabetes was defined as one or more of the following: at least 1 hospitalization with an ICD claim for type 2 diabetes; at least 1 emergency room (ER) visit with an ICD claim for type 2 diabetes; at least 2 ICD claims for type 2 diabetes at least 30 days apart within a 12-month period; or at least one pharmacy claim for a non-insulin injectable, or an OAD agent except metformin, or a metformin pharmacy claim without a diagnosis code for pre-diabetes or polycystic ovary syndrome (Table A.1). Inclusion also required continuous medical and pharmacy coverage for  $\geq 6$  months before and  $\geq 18$  months after the index date. Patients with ICD claims indicating type 1 diabetes treated only with insulin, gestational diabetes, steroid-induced diabetes, metastatic cancer; or in a skilled nursing facility or hospice care; or enrolled in Aetna's Compassionate Care Program, were excluded from the analysis.

### Study periods

In addition to the index period, baseline and outcome assessment periods, as well as a conformance assessment period, were defined (Fig. A.1). The baseline period consisted of the 6 months immediately prior to the index date. Conformance assessment was carried out during the 12 months immediately after the index date. The outcome assessment period began 12 months following the index date and lasted at least 6 months but not  $> 18$  months. Data collection officially ended on April 30, 2017.

### Conformance assessment

Conformance cohorts (high, intermediate, and low) were defined based on a combination of glycemic control and physician action

(Fig. 1). In brief, high conformance was defined as evidence of effective action being taken given the level of glycemic control. Low conformance was identified in cases where no action was taken despite poor glycemic control. Intermediate conformance described situations falling into neither the high nor low categories in which there was opportunity for additional engagement. Therefore, a patient with the combination of good control and either "action" or "mixed action" or a patient with poor control and "action" was in the high conformance cohort. A patient with good control and "no action" or poor control and "mixed action" was assigned to the intermediate cohort. Finally, a patient with poor control and "no action" was in the low conformance cohort. Physician action was weighted more heavily than glycemic control in the assignment of conformance cohorts. For instance, if the physician took action, but glycemic control was poor, the patient was assigned to the high conformance cohort.

Good glycemic control was defined as a subsequent HbA1c test result  $< 7.0\%$  (53 mmol/mol); poor control was a test result  $\geq 7.0\%$  (53 mmol/mol). If the only HbA1c measurement available was the index value ( $\geq 7.0\%$  (53 mmol/mol) by definition), the patient was classified as having poor control. However, if the patient had subsequent HbA1c measurements in the 12 months following the index date (the conformance assessment period), the patient was assigned to a conformance cohort according to the preponderance of their glycemic control. A preponderance of good control was defined as having  $\geq 50\%$  of the post-index HbA1c measurements  $< 7.0\%$  (53 mmol/mol), whereas if  $< 50\%$  of measurements were  $< 7.0\%$  (53 mmol/mol), the patient was classified as having poor control.

Physician action was defined as an indication in the claims of a follow-up HbA1c test, a medication class change, the addition of another medication, or a diabetes-related visit to a primary care provider. Physician action was determined within the 4-month period after each HbA1c measurement  $\geq 7.0\%$  (53 mmol/mol), including the index measurement and any additional measurements. As for glycemic control, physician action was classified according to the preponderance of evidence. Thus, if action was taken  $> 50\%$  of the time, the patient was classified as having physician "action", whereas for action taken  $< 50\%$  of the time, the classification was "no action." If action was taken exactly 50% of the time, the patient was classified as having "mixed" physician action.

### Outcome assessment

The outcomes assessed during the outcome assessment period were (A) all-cause health care resource use (HCRU) further categorized by inpatient, outpatient, and ER utilization; (B) diabetes-related HCRU further categorized by inpatient, outpatient, and ER utilization; (C) clinical outcomes defined as a composite of glycemic events (hyperglycemic and hypoglycemic) and microvascular (defined as an ICD-9 or ICD-10 diagnosis code on a medical claim indicating type 2 diabetes with nephropathy, neuropathy, or retinopathy) and macrovascular (defined as an ICD-9 or ICD-10 diagnosis code on a medical claim indicating cerebrovascular accident, coronary artery disease, peripheral artery disease, or transient ischemic attack) complications; and (D) costs for each type of HCRU (inpatient, outpatient, and ER) as well as pharmacy costs. Unadjusted rates of HCRU and individual clinical outcomes, as well as mean cost per member per year, were calculated at 6, 12, and 18 months in the outcome assessment period.

### Statistical analysis

Demographic characteristics of the study population during the baseline period were analyzed descriptively as numbers and percentages for categorical variables and as means (with standard deviation) or medians (with interquartile range) for continuous variables. Baseline demographic (age, sex, health plan type, median income, and geographic location of residence) and clinical characteristics (retrospective

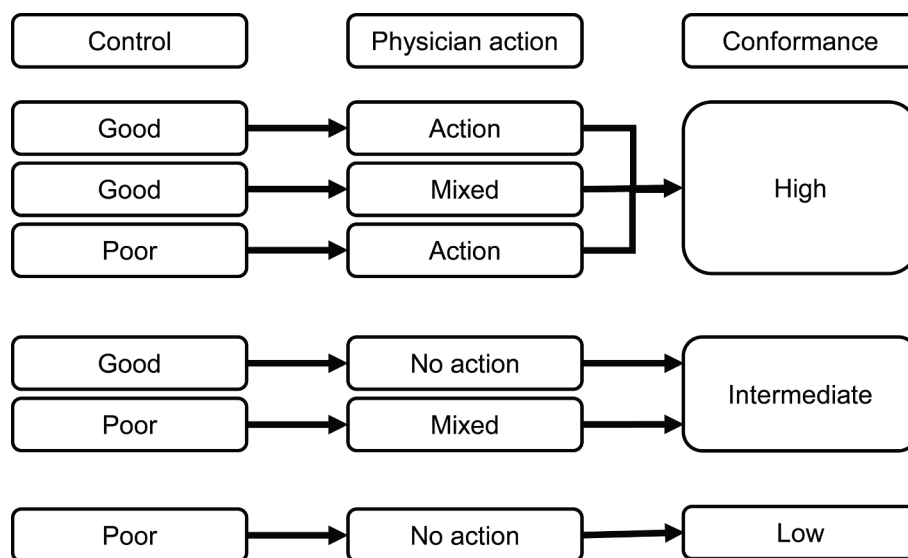


Fig. 1. Conformance cohort assignment.

episode risk group (ERG) score [14], comorbidities, retinal exams, HbA1c testing and test results, outpatient visits, nephropathy screening, and low-density lipoprotein cholesterol testing) were compared across the conformance cohorts using Chi-square tests for categorical variables and ANOVA for continuous variables (or Kruskal-Wallis tests for skewed data, if appropriate).

To identify variables that might affect the study outcomes (HCRU, clinical outcomes, and costs), bivariate analyses were used to determine the association of each baseline variable with each outcome. The association of continuous variables was tested by Spearman rank-order correlation, and that of categorical variables by Wilcoxon rank sum or Kruskal-Wallis tests. In addition, all independent variables were tested for multicollinearity. Independent variables found to be significantly associated with the study outcomes ( $P < 0.01$ ) in the bivariate analyses were adjusted in the subsequent multivariable regression analyses.

A negative binomial distribution model with log link function was used for regression models of HCRU and composite clinical outcomes, and a gamma distribution with log link function for the models of cost. Backward elimination removed those variables not statistically significantly associated with each outcome ( $P > 0.1$ ). The result was a fully reduced multivariable model with statistically significant independent predictors of HCRU, clinical outcomes, and cost at 6, 12, and 18 months of outcome assessment. The models produced incidence rate ratios (IRRs) and 95% confidence intervals (CIs) that expressed the relative difference in the rate of each outcome (for HCRU and clinical outcomes), or the relative difference in costs for patients, in the low versus high (or intermediate versus high) conformance cohorts.

## Results

### Description of the study population

A total of 21,171 Aetna health plan members met the inclusion criteria and were included in the analysis (Fig. B.2). The mean age of the study population was 60 years, and 45% of the subjects were female (Table 1). Approximately two thirds of the population were white (66%), had commercial insurance (67%), and resided in the Atlantic region of the United States (67%).

### Assessment of conformance subgroups

Among the 21,171 included subjects, 16,859 (80%) had high conformance, 1933 (9%) had intermediate conformance, and 2379 (11%) had low conformance (Table 1). Age decreased with increasing conformance ( $P < 0.001$ ), as did the percentage of patients on Medicare ( $P < 0.001$ ) and their median household income ( $P < 0.01$ ; Table 1). The ERG score increased from 1.93 to 2.05 from the low to the high conformance cohort ( $P < 0.001$ ). Comorbidities were similarly prevalent among the cohorts, with hyperlipidemia and hypertension occurring in  $\geq 80\%$  of subjects (Table 1). The rate of testing for HbA1c and LDL-C increased with increasing conformance ( $P < 0.001$  for both).

### Health care resource use, clinical outcomes, and costs

The percentage of members with all-cause and diabetes-related inpatient, outpatient, and ER visits increased with increasing follow-up time (Fig. 2A and B). At 18 months of follow-up, rates of HCRU for the low, intermediate, and high conformance cohorts were 16%, 17%, and 14%, respectively, for all-cause inpatient visits; 58%, 60%, and 64%, respectively, for all-cause outpatient visits; and 28%, 27%, and 26%, respectively, for ER visits. The rate of outpatient visits (both all-cause and diabetes-related) varied significantly with conformance status at each follow-up time point, with the highest rates in members with high conformance (Fig. 2A and B).

The rates of hyperglycemic, hypoglycemic, microvascular, and macrovascular events also increased with follow-up time (Fig. 2C). By 18 months of outcome assessment, event rates for the low, intermediate, and high conformance cohorts were 4.1%, 4.9%, and 4.4%, respectively, for hyperglycemic events; 0.4%, 0.7%, and 0.7%, respectively, for hypoglycemic events; 27.6%, 30.6%, and 33.4%, respectively, for microvascular events; and 15.9%, 15.0%, and 14.5%, respectively, for macrovascular events. The rate of microvascular events varied significantly with conformance status at each time point; members with high conformance experienced the highest rates of microvascular events (Fig. 2C).

Costs associated with all-cause and diabetes-related inpatient, outpatient, and ER visits are shown in Fig. 3. In the high conformance

**Table 1**  
Demographic and clinical characteristics of the study population in the baseline period<sup>a</sup>.

	All (N = 21,171)	High conformance (N = 16,859)	Intermediate conformance (N = 1,933)	Low conformance (N = 2,379)	P value <sup>b</sup>
<b>Demographic</b>					
Age, mean years (SD)	60.2 (12.3)	59.92 (12.1)	61.07 (12.5)	61.46 (13.0)	< 0.001
Female	45%	45%	47%	44%	0.09
Ethnicity <sup>c</sup>					
White	66%	65%	64%	69%	0.02
Black	16%	17%	16%	15%	
Hispanic/Latino	7%	7%	6%	6%	
Asian	5%	5%	6%	4%	
Other/mixed	7%	7%	8%	7%	
Plan type					
Commercial	67%	67%	65%	63%	< 0.001
Medicare	33%	33%	35%	37%	
Income, median (IQR)	\$62,647 (49,026–81,564)	\$62,579 (48,735–81,472)	\$63,844 (50,436–82,029)	\$64,123 (50,436–83,298)	< 0.01
Geographic location <sup>d</sup>					
Atlantic	67%	59%	62%	53%	
Midwest	6%	6%	6%	4%	
Central South	14%	15%	13%	9%	
Rocky Mountain	1%	10%	8%	5%	
Pacific	12%	12%	17%	11%	
<b>Clinical</b>					
ERG score, median (IQR)	2.03 (1.10–3.92)	2.05 (1.12–4.0)	1.96 (1.05–3.64)	1.93 (0.99–3.71)	< 0.001
Comorbidities					
Hyperlipidemia	87%	88%	87%	82%	< 0.0001
Hypertension	83%	84%	82%	80%	< 0.0001
Gastritis/dyspepsia	29%	30%	29%	25%	< 0.0001
Obesity	26%	27%	23%	19%	< 0.0001
Low back pain	20%	20%	18%	16%	< 0.0001
Ischemic heart disease	20%	19%	20%	21%	0.1764
Chronic thyroid disorders	18%	19%	19%	17%	0.3032
Cataract	18%	18%	18%	19%	0.4416
Osteoarthritis	14%	14%	14%	12%	0.0178
Glaucoma	13%	13%	13%	12%	0.4698
Chronic renal failure	12%	12%	12%	11%	0.0476
Retinal exam	21%	22%	20%	21%	0.08
HbA1c test	18%	16%	14%	9%	< 0.001
HbA1c at index date, median (IQR)	7.8 [62 mmol/mol] (7.2–9.2)	7.8 [62 mmol/mol] (7.2–9.3)	7.6 [60 mmol/mol] (7.2–8.8)	7.7 [61 mmol/mol] (7.2–8.8)	< 0.001
Outpatient visit	60%	62%	61%	59%	0.06
Nephropathy screening	52%	52%	53%	52%	0.64
LDL cholesterol test	16%	17%	13%	10%	< 0.001

ERG, episode risk group; IQR, interquartile range; LDL, low-density lipoprotein; N/A, not available; SD, standard deviation

<sup>a</sup> Values are presented as percentages unless otherwise indicated.

<sup>b</sup> Comparisons are between the three conformance cohorts.

<sup>c</sup> Percentages are calculated for those with known ethnic background (N = 11,601).

<sup>d</sup> Geographic data missing for 0.1% of the population.

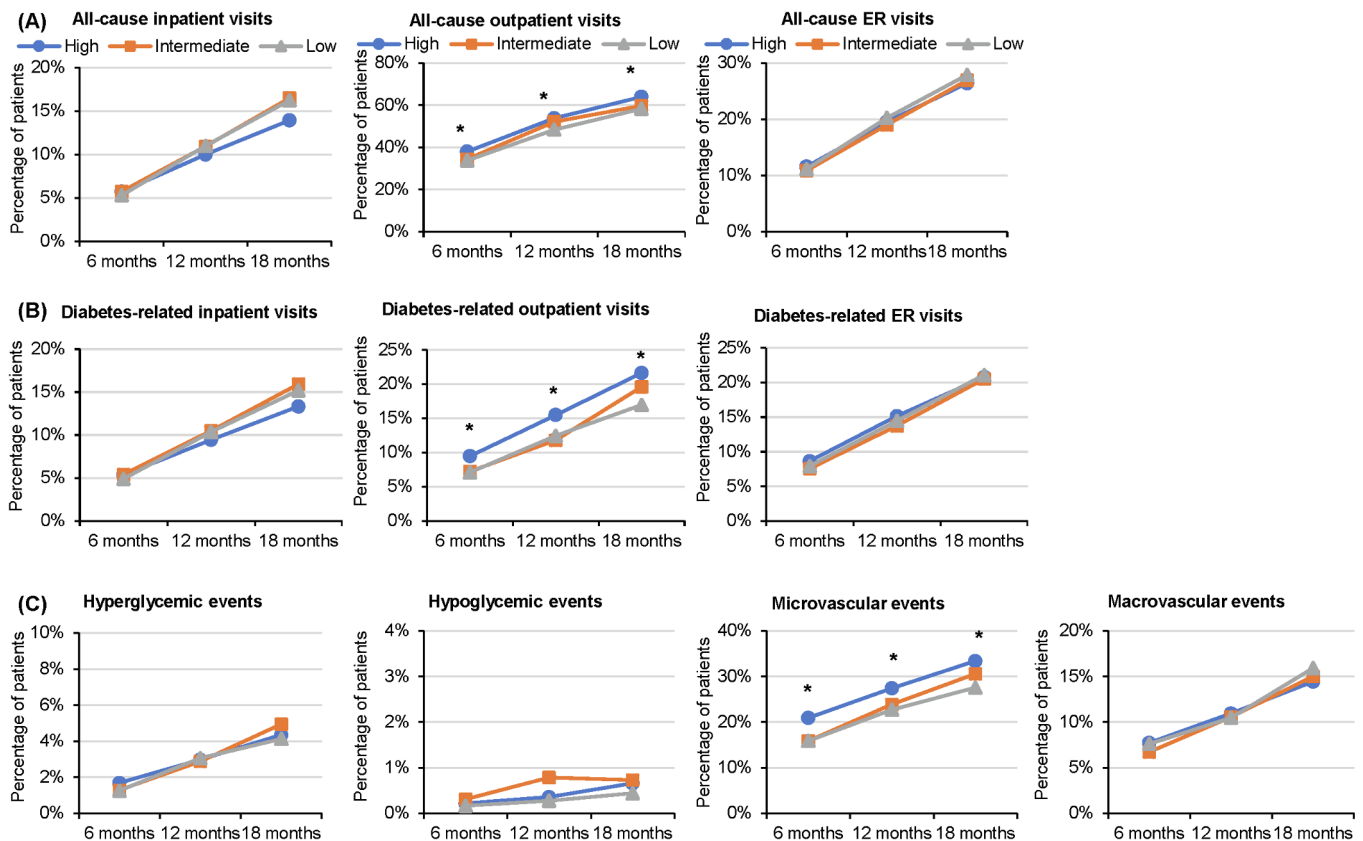
cohort, all-cause costs per member per year totaled \$3005 for inpatient visits, \$961 for outpatient visits, and \$644 for ER visits at 18 months of follow-up. For comparison, the corresponding all-cause costs per member per year in the low conformance cohort were \$3593 for inpatient visits, \$733 for outpatient visits, and \$580 for ER visits.

#### Effect of conformance on health care resource use, clinical outcomes, and costs

In covariate-adjusted regression analyses of members with low versus high conformance (Table 2), the only resource use that varied significantly was diabetes-related outpatient visits, the rate of which was 18% lower at 6 months of follow-up in members with low conformance (IRR 0.82, 95% CI 0.69–0.98;  $P < 0.05$ ). The rate of clinical outcomes—a composite variable including hyperglycemic, hypoglycemic, microvascular, and macrovascular events—was also significantly lower at 6 months of follow-up in members with low conformance (IRR 0.79, 95% CI 0.71–0.89;  $P < 0.001$ ). At 6 months, all-

cause and diabetes-related inpatient costs, diabetes-related ER costs, and pharmacy costs were lower in members with low versus high conformance, while diabetes-related outpatient costs were higher (Table 2). However, of these, only pharmacy costs and diabetes-related outpatient costs remained significantly different at 18 months of outcome assessment, with a 13% reduction in pharmacy costs (IRR 0.87, 95% CI 0.81–0.93,  $P < 0.001$ ) and a 60% increase in diabetes-related outpatient costs (IRR 1.60, 95% CI 1.32–1.95,  $P < 0.001$ ) in members with low conformance. Interestingly, all-cause inpatient costs were significantly lower in members with low conformance at 6 months (IRR 0.84, 95% CI 0.74–0.96,  $P < 0.01$ ), but became significantly higher by the 18-month time point (IRR 1.28, 95% CI 1.00–1.63,  $P < 0.05$ ).

In covariate-adjusted regression analyses of members with intermediate versus high conformance (Table 2), the only resource use that varied significantly was the rate of diabetes-related outpatient visits, which was 22% lower at 6 months of follow-up (IRR 0.78, 95% CI 0.64–0.95;  $P < 0.05$ ) and 18% lower at 12 months of follow-up in members with intermediate conformance (IRR 0.82, 95% CI 0.66–1.00;



**Fig. 2.** Unadjusted (A) all-cause and (B) diabetes-related HCRU and (C) clinical outcomes in the outcome assessment period ER, emergency room Asterisks represent a statistically significant difference between the three conformance cohorts. All-cause outpatient visits were significantly different at 6, 12, and 18 months with P values of  $P < 0.0001$ ,  $P < 0.001$ , and  $P < 0.01$ , respectively. Diabetes-related outpatient visits were significantly different at 6, 12, and 18 months with P values of  $P < 0.0001$ ,  $P < 0.0001$ , and  $P < 0.05$ , respectively. Microvascular events were significantly different at 6, 12, and 18 months with P values of  $P < 0.0001$ , and  $P < 0.01$ , respectively.

$P < 0.05$ ). Clinical outcomes did not differ significantly between members with intermediate and high conformance. Both all-cause and diabetes-related ER costs were higher in members with intermediate conformance at 6 months of follow-up (Table 2); however, these differences were not significant at later time points. In contrast, all-cause outpatient costs were significantly higher in members with intermediate conformance at all three follow-up times, with a differential of 66% at 12 months (IRR 1.66, 95% CI 1.45–1.90;  $P < 0.001$ ). Diabetes-related outpatient costs were significantly lower in members with intermediate conformance at 6 months of follow-up (IRR 0.72, 95% CI 0.65–0.80;  $P < 0.001$ ), but became significantly higher at 12 months (IRR 1.49, 95% CI 1.29–1.72;  $P < 0.001$ ), reaching a 2.59-fold difference by 18 months (IRR 2.59, 95% CI 2.10–3.18;  $P < 0.001$ ).

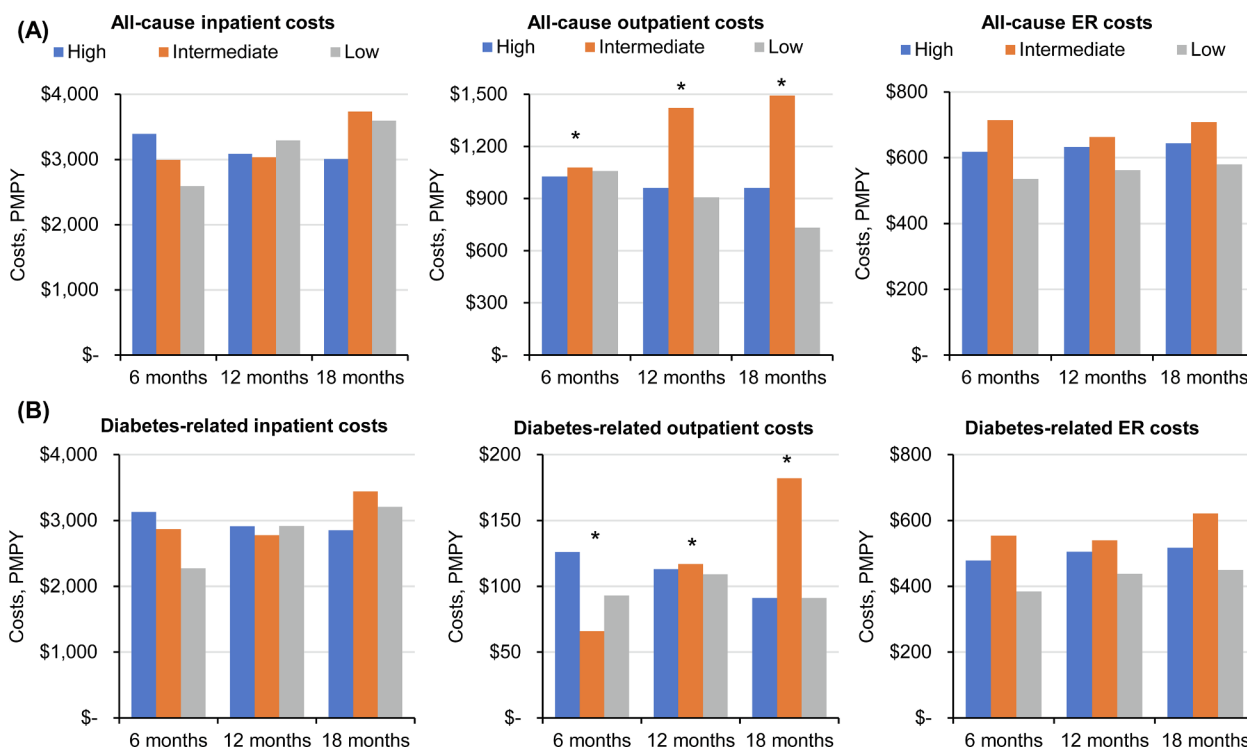
## Discussion

This analysis of insured US adults with type 2 diabetes showed that HCRU and clinical outcomes such as hypoglycemia did not vary significantly over time with low versus high conformance to diabetes guidelines, but medical and pharmacy costs did. Pharmacy costs were consistently lower in members with low conformance, whereas diabetes-related outpatient costs were consistently higher, at 6, 12, and 18 months of outcome assessment.

Previous US studies of health care costs after regimen intensification have found that some regimens result in higher costs, while other result

in lower costs. In type 2 diabetes patients treated with 2 OADs, adding a third OAD or a glucagon-like peptide-1 receptor agonist resulted in higher post-intensification costs, whereas adding basal insulin reduced costs [7]. Similarly, post-intensification health care costs were shown to decrease in type 2 diabetes patients starting basal insulin after use of 1, 2, or 3 OADs [5] and in patients adding rapid-acting insulin to basal insulin [9]. In each of these studies, an increase in pharmacy costs after regimen intensification was offset by decreased inpatient and/or outpatient costs. Based on the results of these studies, we expected to find similar results. Our finding that low conformance, a designation which includes both regimen intensification and glucose monitoring, was associated with lower pharmacy costs but higher outpatient and inpatient costs is consistent with these previous reports.

The IRR for all-cause inpatient costs in Aetna members with low conformance went from significantly lower than high-conformance members at 6 months to significantly higher by the 18-month time point. A similar reversal in IRR was seen for diabetes-related outpatient costs in members with intermediate conformance. Together these findings suggest that the full economic effects of conformance may become evident only over a multi-year time frame. This is consistent with the conclusions of Sullivan et al., who found that HbA1c reductions were greater but costs were higher over a 1-year time period in type 2 diabetes patients who received counseling/educational support versus those without support [15]. They explained the discrepancy between their results and those of previous studies, which had reported



**Fig. 3.** Unadjusted (A) all-cause and (B) diabetes-related costs in the outcome assessment period ER, emergency room; PMPY, per member per year Asterisks represent a statistically significant difference between the three conformance cohorts. All-cause outpatient costs were significantly different at 6, 12, and 18 months with P values of  $P < 0.0001$ ,  $P < 0.001$ , and  $P < 0.05$ , respectively. Diabetes-related outpatient costs were significantly different at 6, 12, and 18 months with P values of  $P < 0.0001$ ,  $P < 0.001$ , and  $P < 0.05$ , respectively.

cost savings in patients receiving educational interventions for 3–5 years [16,17], as a product of the shorter time horizon. Similarly, US studies showing cost reductions with improved HbA1c have assessed 2–5 years' worth of data [18,19]. However, at least 2 previous studies have reported decreased costs associated with HbA1c reductions, even over a relatively short follow-up time (1 year) [20,21]. As an example, Aagren et al. found, based on 1 year of claims data in type 2 diabetes patients, that a 1-percentage-point decrease in HbA1c was associated with a decrease in diabetes-related costs of 4.2% [20]. Thus, it is important to study cost in relation to conformance or regimen intensification over an extended time horizon, as was done in the current study.

#### Limitations

One limitation of the current study is that the analysis sample was heavily weighted toward high conformance, which is not entirely consistent with published evidence for lack of attainment of HbA1c goals [3] and for clinical inertia (i.e., failure by health care providers to initiate or intensify treatment when glycemic targets have not been met) [22,23]. Reported rates of clinical inertia range from 33% to 50% [22,23], and may be driven by provider age and specialty, patients' HbA1c levels, and providers' fear of inducing hypoglycemia [22–24]. Our definition of conformance encompassed a broad range of criteria, including both indicators of regimen intensification and actions such as HbA1c testing, and thus more patients would be classified as conformant by this definition than by a definition that included only markers of regimen intensification. In addition, the universal application of  $< 7.0\%$  (53 mmol/mol) as the glycemic target may have affected the conformance distribution, since ADA guidelines allow for

personalized targets depending on the clinical situation of the patient [2]. Less stringent A1C goals may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, or long-standing diabetes in whom the goal is difficult to achieve [2]. Our definition of conformance did not take into account these exceptions.

Other limitations include the fact that individuals with commercial health insurance or Medicare coverage may not be representative of type 2 diabetes patients with other insurance or those who are uninsured. In terms of study design, claims data are known to be susceptible to coding errors and/or underreporting, which may affect the findings. In particular, the composite clinical events were subject to detection bias, which would limit the number of events we were able to detect using claims data. In addition, information on individual education level, health beliefs, support systems, and health priorities, factors that may affect conformance to diabetes guidelines were not available in the claims data. Finally, the participation of patients in counseling/educational support programs was not included in the definition of conformance, even though such programs have been shown to improve glycemic control [15].

#### Conclusion

In conclusion, the results of this analysis of insured type 2 diabetes patients in the United States showed that reduced conformance to diabetes guidelines led to lower pharmacy costs but higher diabetes-related outpatient costs over the course of 18 months.

#### Declaration of Competing Interest

At the time of the study, Rajesh R. Mehta, Alison M. Edwards, Ajay

**Table 2**  
Multivariable modeling of the relationship of low versus high and intermediate versus high conformance to resource use, clinical outcomes, and cost<sup>a</sup>.

	6 months	12 months	18 months
<b>Low versus high conformance</b>			
<b>Resource use</b>			
All-cause inpatient visits	0.96 (0.78–1.18)	1.14 (0.95–1.38)	1.21 (0.96–1.52)
Diabetes-related inpatient visits	0.93 (0.75–1.15)	1.11 (0.92–1.35)	1.12 (0.89–1.43)
All-cause outpatient visits	0.97 (0.89–1.05)	0.94 (0.86–1.03)	0.94 (0.83–1.06)
Diabetes-related outpatient visits	0.82 (0.69–0.98) ***	1.05 (0.88–1.25)	1.06 (0.85–1.33)
All-cause ER visits	1.05 (0.92–1.20)	1.08 (0.94–1.23)	1.17 (0.99–1.38)
Diabetes-related ER visits	0.98 (0.83–1.15)	0.99 (0.84–1.15)	1.11 (0.92–1.34)
Clinical outcomes	0.79 (0.71–0.89) *	0.94 (0.82–1.06)	0.99 (0.83–1.17)
<b>Costs</b>			
All-cause inpatient costs	0.84 (0.74–0.96) **	1.04 (0.88–1.22)	1.28 (1.00–1.63) ***
Diabetes-related inpatient costs	0.80 (0.71–0.91) *	0.97 (0.82–1.14)	1.21 (0.95–1.55) ***
All-cause outpatient costs	0.98 (0.89–1.08)	0.93 (0.83–1.05)	0.81 (0.68–0.96) ***
Diabetes-related outpatient costs	1.21 (1.10–1.33) *	1.72 (1.52–1.95) *	1.60 (1.32–1.95) *
All-cause ER costs	0.96 (0.86–1.07)	1.06 (0.93–1.22)	1.15 (0.94–1.41)
Diabetes-related ER costs	0.84 (0.75–0.93) **	1.00 (0.87–1.15)	1.10 (0.90–1.35)
Pharmacy costs	0.90 (0.86–0.95) *	0.88 (0.84–0.93) *	0.87 (0.81–0.93) *
<b>Intermediate versus high conformance</b>			
<b>Resource use</b>			
All-cause inpatient visits	1.04 (0.84–1.30)	1.10 (0.89–1.36)	1.19 (0.93–1.53)
Diabetes-related inpatient visits	1.07 (0.85–1.34)	1.10 (0.89–1.37)	1.18 (0.92–1.53)
All-cause outpatient visits	1.04 (0.95–1.14)	1.09 (0.99–1.21)	1.10 (0.97–1.25)
Diabetes-related outpatient visits	0.78 (0.64–0.95) ***	0.82 (0.66–1.00) ***	1.00 (0.79–1.27)
All-cause ER visits	1.09 (0.94–1.26)	1.04 (0.90–1.21)	1.07 (0.89–1.29)
Diabetes-related ER visits	1.05 (0.89–1.25)	1.02 (0.86–1.21)	1.11 (0.90–1.37)
Clinical outcomes	0.93 (0.83–1.05)	1.00 (0.87–1.14)	1.12 (0.93–1.34)
<b>Costs</b>			
All-cause inpatient costs	1.04 (0.91–1.20)	0.99 (0.83–1.19)	1.25 (0.96–1.63)
Diabetes-related inpatient costs	1.09 (0.95–1.25)	1.00 (0.84–1.20)	1.17 (0.90–1.51)
All-cause outpatient costs	1.31 (1.17–1.45) *	1.66 (1.45–1.90) *	1.54 (1.27–1.87) *
Diabetes-related outpatient costs	0.72 (0.65–0.80) *	1.49 (1.29–1.72) *	2.59 (2.10–3.18) *
All-cause ER costs	1.24 (1.11–1.40) *	1.09 (0.94–1.28)	1.17 (0.94–1.46)
Diabetes-related ER costs	1.18 (1.05–1.33) **	1.11 (0.95–1.29)	1.21 (0.96–1.51)
Pharmacy costs	0.98 (0.93–1.03)	1.01 (0.95–1.08)	1.02 (0.94–1.10)

ER, emergency room.

<sup>a</sup> Data are presented as the incident rate ratio and 95% confidence intervals. Comparisons are between the two conformance cohorts listed in the title. P values indicated with symbols: \* P < 0.001, \*\* P < 0.01, \*\*\* P < 0.05. Independent variables considered for each model were: insurance type (commercial versus Medicare), household income, geographical region, age, sex, number of comorbidities (a count of the top 10 in study sample), retrospective ERG score, OAD use, number of OAD classes, use of ACE inhibitors, angiotensin II receptor blockers (ARBs), glucagon-like peptide-1 (GLP-1) inhibitors, insulin, retinal screening during baseline, and number of providers seen.

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#### Author contributions

R.R.M. participated in the conception and design of the study; acquisition of the data; analysis and interpretation of the data; drafting the manuscript; and critically revised the manuscript.

A.M.E. participated in the conception and design of the study; analysis and interpretation of the data; and critically revised the manuscript.

S.R. participated in the conception and design of the study; interpretation of the data; and critically revised the manuscript.

A.S. participated in the analysis and interpretation of the data; and critically revised the manuscript.

K.J.S. participated in the conception and design of the study; analysis and interpretation of the data; and drafting the manuscript.

K.I. participated in the conception and design of the study; interpretation of the data; and critically revised the manuscript.

All authors approved the final version of the manuscript.

#### Appendix A. Supplementary data

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#### References

- [1] Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States; 2014 [cited KIA1C/. Available from: <https://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf>.
- [2] American Diabetes Association. Standards of Medical Care in Diabetes-2017. *Diabetes Care*. 2017; 40 (Suppl 1):S1-S135. 10.2337/dc17-S003.
- [3] Lipska KJ, Yao X, Herrin J, McCoy RG, Ross JS, Steinman MA, et al. Trends in Drug Utilization, Glycemic Control, and Rates of Severe Hypoglycemia, 2006–2013. *Diabetes Care* 2017;40(4):468–75. <https://doi.org/10.2337/dc16-0985>.
- [4] Watson L, Das R, Farquhar R, Langerman H, Barnett AH. Consequences of delaying treatment intensification in type 2 diabetes: evidence from a UK database. *Curr Med Res Opin* 2016;32(9):1465–75. <https://doi.org/10.1185/03007995.2016.1157462>.

- [5] Levin PA, Zhou S, Gill J, Wei W. Health outcomes associated with initiation of basal insulin After 1, 2, or  $\geq 3$  oral antidiabetes drug(s) among managed care patients with type 2 diabetes. *J Manag Care Special Pharm* 2015;21(12):1172–81. <https://doi.org/10.18553/jmcp.2015.21.12.1172>.
- [6] Bhattacharya R, Zhou S, Wei W, Ajmera M, Sambamoorthi U. A real-world study of the effect of timing of insulin initiation on outcomes in older medicare beneficiaries with type 2 diabetes mellitus. *J Am Geriatr Soc* 2015;63(5):893–901. <https://doi.org/10.1111/jgs.13388>.
- [7] Levin PA, Wei W, Zhou S, Xie L, Baser O. Outcomes and treatment patterns of adding a third agent to 2 OADs in patients with type 2 diabetes. *J Manag Care Special Pharm* 2014;20(5):501–12. <https://doi.org/10.18553/jmcp.2014.20.5.501>.
- [8] Bell K, Parasuraman S, Raju A, Shah M, Graham J, Denno M. Resource utilization and costs associated with using insulin therapy within a newly diagnosed type 2 diabetes mellitus population. *J Manag Care Special Pharm* 2015;21(3). <https://doi.org/10.18553/jmcp.2015.21.3.220>. 220–8a.
- [9] Aagren M, Luo W, Moes E. Healthcare utilization changes in relation to treatment intensification with insulin aspart in patients with type 2 diabetes. Data from a large US managed-care organization. *J Med Econ* 2010;13(1):16–22. <https://doi.org/10.3111/13696990903485154>.
- [10] Levin P, Fan T, Song X, Nero D, Davis B, Chu BC. Comparing clinical outcomes and costs for different treatment intensification approaches in patients with type 2 diabetes uncontrolled on basal insulin: adding glucagon-link peptide 1 receptor agonists versus adding rapid-acting insulin or increasing basal insulin dose. *Endocr Pract* 2017;23(11):1316–24. <https://doi.org/10.4158/ep171769.Or>.
- [11] Perez-Nieves M, Kabul S, Desai U, Ivanova JI, Kirson NY, Cummings AK, et al. Basal insulin persistence, associated factors, and outcomes after treatment initiation among people with type 2 diabetes mellitus in the US. *Curr Med Res Opin* 2016;32(4):669–80. <https://doi.org/10.1185/03007995.2015.1135789>.
- [12] Thayer S, Wei W, Buysman E, Brekke L, Crown W, Grabner M, et al. The INITIATOR study: pilot data on real-world clinical and economic outcomes in US patients with type 2 diabetes initiating injectable therapy. *Adv Ther* 2013;30(12):1128–40. <https://doi.org/10.1007/s12325-013-0074-8>.
- [13] Miao R, Wei W, Baser O, Xie L. Real world outcomes of adding rapid-acting insulin versus switching to analog premix insulin among US patients with type 2 diabetes treated with insulin glargine. *Patient Prefer Adherence*. 2013; 7: 951–60. 10.2147/PPA.S49287.
- [14] Optum. Episode Treatment Groups 2015 [cited KIA1C/. Available from: <https://etg.optum.com/etg-links/episode-treatment-groups/>.
- [15] Sullivan SD, Dalal MR, Burke JP. The impact of diabetes counseling and education: clinical and cost outcomes from a large population of US managed care patients with type 2 diabetes. *Diabetes Educat*: 2013; 39 (4): 523-31. 10.1177/0145721713486525.
- [16] Duncan I, Birkmeyer C, Coughlin S, Li QE, Sherr D, Boren S. Assessing the value of diabetes education. *Diabetes Educat* 2009;35(5):752–60. <https://doi.org/10.1177/0145721709343609>.
- [17] Robbins JM, Thatcher GE, Webb DA, Valdmanis VG. Nutritionist visits, diabetes classes, and hospitalization rates and charges: the Urban Diabetes Study. *Diabetes Care* 2008;31(4):655–60. <https://doi.org/10.2337/dc07-1871>.
- [18] Menzin J, Korn JR, Cohen J, Lobo F, Zhang B, Friedman M, et al. Relationship between glycemic control and diabetes-related hospital costs in patients with type 1 or type 2 diabetes mellitus. *J Manag Care Pharm JMCP*. 2010;16(4):264–75. <https://doi.org/10.18553/jmcp.2010.16.4.264>.
- [19] Oglesby AK, Secnik K, Barron J, Al-Zakwani I, Lage MJ. The association between diabetes related medical costs and glycemic control: a retrospective analysis. *Cost Eff Resour Alloc* 2006;4:1. <https://doi.org/10.1186/1478-7547-4-1>.
- [20] Aagren M, Luo W. Association between glycemic control and short-term healthcare costs among commercially insured diabetes patients in the United States. *J Med Econ* 2011;14(1):108–14. <https://doi.org/10.3111/13696998.2010.548432>.
- [21] Shetty S, Secnik K, Oglesby AK. Relationship of glycemic control to total diabetes-related costs for managed care health plan members with type 2 diabetes. *J Manag Care Pharm JMCP*. 2005;11(7):559–64. <https://doi.org/10.18553/jmcp.2005.11.7.559>.
- [22] Mahabaleshwar R, Gohs F, Mulder H, Wilkins N, DeSantis A, Anderson WE, et al. Patient and Provider Factors Affecting Clinical Inertia in Patients With Type 2 Diabetes on Metformin Monotherapy. *Clin Therap* 2017; 39 (8): 1658-70.e6. 10.1016/j.clinthera.2017.06.011.
- [23] Mata-Cases M, Benito-Badorrey B, Roura-Olmeda P, Franch-Nadal J, Pepio-Vilaubi JM, Saez M, et al. Clinical inertia in the treatment of hyperglycemia in type 2 diabetes patients in primary care. *Curr Med Res Opin* 2013;29(11):1495–502. <https://doi.org/10.1185/03007995.2013.833089>.
- [24] Escalada J, Orozco-Beltran D, Morillas C, Alvarez-Guisasola F, Gomez-Peralta F, Mata-Cases M, et al. Attitudes towards insulin initiation in type 2 diabetes patients among healthcare providers: a survey research. *Diabetes Res Clin Pract* 2016;122:46–53. <https://doi.org/10.1016/j.diabres.2016.10.003>.