Continuity of Care and Changes in Medication Adherence Among Patients With Newly Diagnosed Diabetes

Chi-Chen Chen, PhD, and Shou-Hsia Cheng, PhD

ABSTRACT

Objectives: Recent studies have revealed significant variation in medication adherence among patients with chronic conditions. Little is known about the effect of continuity of care (COC) on changes in medication adherence. This study aims to identify medication adherence trajectories among patients with newly diagnosed diabetes, as well as to examine the association of COC and medication adherence among various adherence trajectories.

Methods: This study utilized a longitudinal design with a 6-year follow-up, from 2002 to 2008, under a universal health insurance program in Taiwan. Subjects 18 years or older with type 2 diabetes that was newly diagnosed in 2002 were included in the study. The main outcome was medication adherence measured by medication possession ratio each year. Group-based trajectory models were used for analysis.

Results: Four medication adherence trajectories were identified: persistent adherence (39.9%), increasing adherence (27.5%), decreasing adherence (12.0%), and nonadherence (20.6%). Patients with high or medium COC index scores were more likely to be adherent to medications than those with low COC index scores in all of the trajectory adherence groups.

Conclusions: This study demonstrated the heterogeneity in patients' medication adherence and identified 4 distinct trajectories of medication adherences among those with newly diagnosed type 2 diabetes. Improving COC may lead to better medication adherence in all of the adherence trajectory groups.

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Diabetes is a prevalent condition characterized by significant complications and serious consequences.[1] Medication adherence is the most important determinant of diabetes management; its effects are greater than those of dietary control or lifestyle changes.[2] However, medication adherence rates vary markedly, from 36% to 93%, among patients with diabetes.[3] Nonadherence to medications is associated with worse glycemic control, which, in turn, can increase micro- or macrovascular complications and healthcare utilization.[4] Therefore, improving adherence to medications is an important task for policy makers worldwide. Medication adherence is also one of the main issues considered in value-based insurance design.[5]

Although the issues that affect medication adherence have been examined, 2 gaps remain in our knowledge about this issue. First, the majority of studies concerning medication adherence have used a static measure of medication adherence (ie, at a single point in time).[6-10] The few studies that have used a longitudinal design either did not focus on the dynamic changes in medication adherence,[11-14] or only focused on the changes between 2 time points.[15,16] Furthermore, studies focusing on the changes between 2 time points could not capture the heterogeneity in medication adherence changes that occur after the second time point. Until now, only 2 studies utilized advanced dynamic measurement, capturing the short-term heterogeneity in medication adherence and examining the factors affecting the trajectory patterns of medication adherence.[17,18]

Continuity of care (COC) is significantly associated with favorable health outcomes, especially among patients with chronic conditions.[19,20] These patients usually receive care from several physicians and have complex medication regimens that often result in fragmented care. The medical home demonstration project in the United States intends to improve care coordination among various healthcare pro-

viders, and thus improve COC between patients and their physicians.[21] However, the majority of previous studies have focused on the effects of COC on healthcare utilization and patient satisfaction.[22] There is limited and inconclusive evidence regarding the effects of COC on medication adherence.[13,14,23-25] Furthermore, to the best of our knowledge, the effects of COC on medication adherence among patients with various adherence trajectories have been relatively unexplored.

Take-Away Points

This study employed longitudinal data to identify medication adherence trajectories among patients with newly diagnosed diabetes and to examine the relationship between continuity of care (COC) and medication adherence among various adherence trajectories.

- This study demonstrated the heterogeneity in medication adherence and identified 4 distinct trajectories of medication adherence: persistently high, increasing, decreasing, and nonadherence.
- Better COC between patients and their physicians was consistently associated with higher medication adherence in every trajectory adherence group.
- More attention should be directed toward designing new strategies to improve COC.

Group-based trajectory models may provide an alternative approach to modeling the change of outcomes and individual differences in changes of outcomes.[26] Its purpose is to discover distinctive patterns of individuals with homogeneous longitudinal trajectories within the population and to explain individual-level differences at the group level.[27,28] Using group-based trajectory analysis, this study aimed to identify medication adherence trajectories within 6 years after the initial diagnosis of diabetes, and to examine the association of COC and long-term medication adherence among patients with various adherence trajectories.

Healthcare Delivery in Taiwan

Healthcare systems in Taiwan and in many Asian and Central and Eastern European countries largely focus on specialist and hospital care. There is no referral requirement; patients are free to visit physicians at community clinics or hospital outpatient departments for each episode according to individual preference.[29] Since the implementation of the compulsory National Health Insurance (NHI) program in Taiwan in 1995, empirical studies have found that the NHI has significantly improved general access to healthcare.[30] The average number of annual physician visits in Taiwan is one of the highest in the world, with approximately 13 visits per person in 2010; patients are often criticized for their doctor-shopping behavior.[31] Therefore, the features of having free choice of providers for every visit without referral requirement and a very high number of physician visits under the NHI program might hamper information sharing or mutual trust between patients and their physicians; this can subsequently result in the deterioration of COC and poor patient adherence to medications. The easy access to ambulatory care and comprehensive claims data under the universal health insurance system facilitates the need for investigations into the effects of COC on medication adherence among patients with diabetes.

METHODS

Data Source and Subjects

The NHI claims data set from 1999 to 2008 was obtained from the National Health Research Institutes of Taiwan. A longitudinal study design was used for this study. We identified patients with type 2 diabetes (T2D) according to the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) codes of 250.xx, excluding the type 1 diabetes codes of 250.x1 and 250.x3, in the claims data. First, we defined the index date of the first claim with the diagnosis of T2D for each patient in the year 2002. New patients with T2D were identified by their lack of T2D-related claims over the 3 years (1999-2002) before the index date of diagnosis in 2002.

Patients were then included in the analysis if they: 1) were aged at least 18 years on the index date; 2) were alive throughout the study period to ensure comprehensive follow-up observations; 3) had at least 3 physician visits in every year of the study period given the inapplicability of COC indicators in patients with very few visits (this criterion has been adopted in previous studies[32-34]); 4) had a prescription for 1 or more oral antihyperglycemic medication on the index date of the initial diagnosis to capture the appropriate timing of initial prescriptions for new patients[15]; 5) had at least 1 prescription for an oral antihyperglycemic medication in every year of the study period to ensure that the patients included in the study were those who required ongoing pharmacological therapy; and 6) had no insulin prescriptions during any of the years in the study period. The unit of analysis was patient-years. As a result, a total of 12,123 patients and 72,738 patient-years were included in the analysis.

Variables of Interests

Continuity of care. COC was the main independent variable in this study. This study calculated the COC score based on outpatient services only. Considering the varia-

tion and very high number of physician visits in Taiwan, we chose the continuity of care index (COCI) as our predictor variable because the COCI is minimally sensitive to the number of physician visits by patients.[35] The COCI was composed of the number of different physicians seen and the number of visits to each physician. The COCI value ranges between 0 and 1, with a higher value representing better COC. The equation for the COCI was as follows:

$$COCI = \frac{\sum_{j=1}^{M} n_j^2 - N}{N(N-1)}$$

N represents the total number of physician visits, n_j is the number of visits to the same physician (j), j is a given physician, and M is the number of physicians. In a study by Bice and Boxerman (1977),[36] the summation term in the numerator was the sum of the number of unreferred physicians. Because of the lack of referral arrangements in Taiwan, we used the total number of physician visits in the analysis. Also, because the COCI values have no inherent clinical meaning, we categorized them into 3 equal tertiles (low [0-0.23], intermediate [0.24-0.43], and high [0.44-1.00]) according to the distribution of scores across the entire study population for each year.

Medication adherence trajectory. Medication adherence was defined using the medication possession ratio (MPR), which was calculated as the ratio of the total days with a supply of a prescribed medication divided by the total number of days in each year during the 6 years following the index date. The MPR calculation also included medication days based on refill visits for oral antihyperglycemic drugs.

Antihyperglycemic drugs were identified by their anatomical therapeutic chemical codes and included biguanides (A10BA), sulfonamides or urea derivatives (A10BB), combinations of oral blood glucose–lowering drugs (A10BD), alpha glucosidase inhibitors (A10BF), thiazolidinediones (A10BG), dipeptidyl peptidase 4 (DPP-4) inhibitors (A10BH), and other blood glucose-lowering drugs, excluding insulin (A10BX). When the patients were hospitalized, the days on which they took the prescribed medications were excluded from the denominator in the MPR calculation. In addition, the patients may have received multiple medications for different numbers of days during a visit; therefore, the calculation of MPR was based on the prescription that covered the longest days (usually for chronic conditions such as diabetes). In this study, patients were considered to be adherent to oral antihyperglycemic medications if the MPR was between 80% and 120% for each year.[37,38] The trajectories of medication adherence were constructed using the adherence statuses in the 6 years after the initial diagnosis of diabetes.

Covariates

Several confounding factors were controlled for in the regression models. The time-varying variables were health status measures, including: 1) hospitalization in the previous year; 2) the diabetes complication severity index (DCSI)[39]; 3) the chronic illness with complexity index (CICI)[40]; and 4) multiple medications in a prescription. The DCSI was used to adjust for the severity of diabetes complications and consisted of scores from 7 categories of complications: cardiovascular complications, nephropathy, retinopathy, peripheral vascular disease, stroke, neuropathy, and metabolic disorders. The CICI was used to adjust for comorbidity in patients with multiple chronic diseases. We excluded diabetes-related complications to avoid duplicating the comorbidity effect presented by the DCSI. In the analysis, we counted the number of comorbidities based on the CICI scores. The multiple medications per prescription were dichotomized by 3 medications or more.

The time-constant variables were the patient's sex, age, and the location of residence (rural or urban) in the baseline year. Due to a lack of information on a patient's residence in the NHI claim data, we took 2 steps to approximate the residence for each patient. First, we identified 3 types of beneficiaries who were enrolled into NHI via occupational unions or local government agencies—farmers and fishermen/members of occupational unions, low-income families, and local residents who were enrolled via household registry office—where the zip code of enrollment organization was considered as the proxy for patient's residence. For the abovementioned subjects, this study only included the NHI policy holders and their spouses because they were presumably living together. For the remaining subjects, we used the zip code of the most frequently visited clinic/hospital for minor illnesses (*ICD-9-CM* codes 460-466, 480-487) as proxies. Rural-urban designations were based on the population density of the township of the patient's residence. Those townships with the lowest 30% of population density were defined as a rural area in Taiwan.

Statistical Analysis

We used a semi-parametric, group-based trajectory model to identify distinct subgroups of individuals who followed similar patterns of medication adherence over time.[26,41] This model was performed with the SAS version 9.2 PROC TRAJ procedure (SAS Institute, Cary, North Carolina).

We employed the Bayesian information criterion (BIC) to determine the optimal number of trajectories. Because of the large sample size in this study, we anticipated that

Table 1. Characteristics of the Study Subjects With Newly Diagnosed Type 2 Diabetes in the Baseline Year

Characteristics	Study Sample	
Total	12,123	
Adherence to oral antihyperglycemic medications		
MPR (mean, SD)	75.18	32.91
80% ≤ MPR ≤120% (n, %)	6398	52.78
COCI (mean, SD)	0.39	0.25
Age, years (mean, SD)	55.62	11.34
Sex (n, %)		
Male	6403	52.82
Female	5713	47.13
Missing	7	0.06
Low-income status (n, %)	90	0.74
DCSI score (n, %)		
Score 0	7354	60.66
Score 1	2876	23.72
Score 2+	1893	15.61
CICI score (n, %)		
Score 0	4514	37.24
Score 1	4686	38.65
Score 2+	2923	24.11
Hospitalization in the previous year (n, %)	2081	17.17
Multiple medications per prescription, 3+ (n, %)	7545	62.24
Patient's resident area (n, %)		
Urban areas	7041	58.08
Rural areas	3014	24.86
Missing	2068	17.06

CICI indicates chronic illness with complexity index; COCI, continuity of care index; DCSI, diabetes complication severity index; MPR, medication possession ratio.

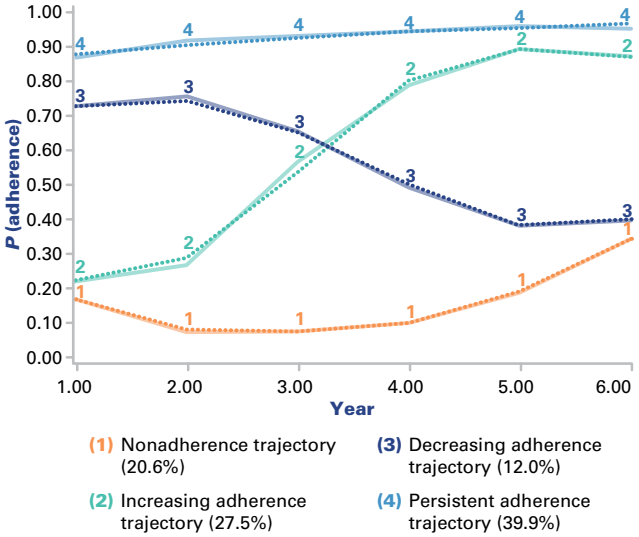
the BIC value might decrease along with the increase in the number of trajectories; nonetheless, we only considered 1 to 4 trajectories to facilitate the interpretation of the adherence patterns from a practical perspective. Then, we determined the shape of the trajectories by testing the cubic terms of time for each trajectory first, indicating the use of cubic terms of time to model the probability that a patient within each trajectory would be adherent. To ensure the principle of parsimony, if the cubic and quadratic terms were not significant in a given model, subsequent analysis was performed with constant and linear terms.[42] Once the optimal number and shape of the trajectories were chosen, we estimated the group membership probability for each subject and assigned each subject to the specific trajectory group with the highest group membership probability. Because the distribution of medication adherence was binary, we fit a logit model to examine the relationship between COC and medication adherence while taking into account the time-constant and time-varying covariates.

RESULTS

Table 1 presents the characteristics of the study subjects with newly diagnosed T2D in 2002. The mean MPR value was 75.18% and the COCI score was 0.39; the mean age was 55.62 years and males comprised 52.82% of the sample. Regarding health status, the rate of hospitalization in the previous year was 17.17%; 60.66% of the subjects had a DCSI score of 0 and 15.61% had a score of 2 or higher.

Using the group-based trajectory model, we identified 4 distinct medication adherence trajectories based on the BIC scores (eAppendix 1 and eAppendix 2 [eAppendices available at **www.ajmc.com**]). As shown in the Figure, the persistent adherence trajectory accounted for 39.9% of the subjects, and their medication adherence was constantly high. The increasing adherence trajectory accounted for 27.5% of the subjects, who showed an increasing trend in their adherence status over time, whereas the decreasing adherence trajectory included 12% of the subjects who showed a continuous declining trend in their medication adherence. The nonadherence trajectory accounted for

Figure. The 4 Groups of Longitudinal Trajectories for Adherence to Oral Antihyperglycemic Medications in the First 6 Years After the Initial Diagnosis of Diabetes



The solid lines indicate the observed proportion of subjects who are adherent in each group.
The dotted lines indicate the predicted probability of adherence in each group.

Table 2. Adherence Trajectory Models Predicted by Continuity of Care and Other Time-Constant and Time-Varying Covariates

	Nonadherence Trajectory		Increasing Adherence Trajectory		Decreasing Adherence Trajectory		Persistent Adherence Trajectory	
Variables	**Estimate**	***P***	**Estimate**	***P***	**Estimate**	***P***	**Estimate**	***P***
Intercept	–0.499	.180	–1.201	<.001	–0.733	.062	1.018	<.001
Linear	–2.478	<.001	–1.665	<.001	1.697	<.001	0.259	<.001
Quadratic	0.619	<.001	0.901	<.001	–0.659	<.001	–	–
Cubic	–0.039	.004	–0.092	<.001	0.061	<.001	–	–
Time-varying covariates								
COCI (ref group = low)								
Medium	0.338	<.001	0.600	<.001	0.249	.013	0.587	<.001
High	0.559	<.001	0.802	<.001	0.506	<.001	1.062	<.001
DCSI score (ref group = score 0)								
Score 1	0.303	<.001	0.225	.001	0.307	.004	0.170	.043
Score 2+	0.715	<.001	0.549	<.001	0.334	.005	0.055	.558
CICI score (ref group = score 0)								
Score 1	0.267	.005	–0.084	.274	0.323	.007	–0.044	.635
Score 2+	0.136	.085	–0.060	.345	0.183	.044	0.001	.998
Hospitalization in the previous year	0.366	<.001	0.346	<.001	–0.160	.174	–0.090	.363
Multiple medications per prescription, 3+	0.096	.196	0.183	.002	0.121	.197	0.322	<.001
Time-constant covariates								
Constant	–	–	–3.386	<.001	–3.665	<.001	–5.067	<.001
Log of age at baseline	–	–	0.912	<.001	0.817	.001	1.443	<.001
Female	–	–	0.213	.004	0.022	.835	0.302	<.001
Rural area	–	–	–0.019	.804	–0.542	<.001	–0.474	<.001

CICI indicates chronic illness with complexity index; COCI, continuity of care index; DCSI, diabetes complication severity index; ref, reference.

20.6% of the subjects, and this group consistently had the lowest probability of medication adherence.

Table 2 presents the relationship between COC and the likelihood of medication adherence among various adherence trajectories. The COCI score estimate was positively and significantly associated with medication adherence in each trajectory group. This association implies that patients with high or medium COCI scores were more likely to adhere to medication use compared with patients with low COCI scores, regardless of their trajectory groups. In addition, older patients or female patients were less likely to be in the nonadherence trajectory group than in other groups. Patients living in the rural area were more likely to be in the nonadherence trajectory group than in other groups.

DISCUSSION

The objective of this study was to construct trajectories of medication adherence among patients with newly diagnosed T2D first, and then to examine the association between COC and medication adherence among the various adherence trajectories.

Previous studies that constructed medication trajectories were restricted to short-term follow-up. Riegel et al (2012) examined the trajectories of medication nonadherence in adults with heart failure over a 6-month period and identified 2 distinct trajectories,[17] and Franklin et al (2013) described patients' adherence to the lipid-lowering medication "statin" during the 15 months following the first prescription.[18]

The present study identified 4 distinct medication adherence trajectories (persistent, increasing, decreasing, and nonadherence) during the 6-year follow-up period after the initial diagnosis of diabetes. We noticed that only 39.9% of the subjects were always adherent to medication and that 20.6% of the subjects were consistently nonadherent during these 6 years. We also found that older patients were less likely to be in the nonadherence trajectory group. The

findings were consistent with previous studies which suggested that adherence increases with age.[43,44] In addition, this study revealed that patients living in the rural area were more likely to be in the nonadherence trajectory. On the contrary, Egede et al (2011) reported that adherence to antidiabetic medication was higher among rural versus urban veterans; however, when accounting for the effect of race/ethnicity on medication adherence, they identified that rural-dwelling Hispanic veterans had lower medication adherence compared with their urban counterparts.[45] The factors associated with the medication adherence patterns deserve further investigation.

Among the 4 medication adherence trajectories, we found that medication adherence was positively associated with the degree of COC. The findings of this study are consistent with those of previous studies[13,14,23]; however, Robels and Anderson (2011) found that a positive association between COC and adherence to antihypertensive drugs may exist only within a limited range of illness severity.[25] This positive association between COC and medication adherence may be attributable to better information sharing and better goal alignment between patients and physicians, as suggested by Donaldson (2001).[46]

Better information sharing implies that physicians are more familiar with the patients' prognosis and medication use over time. Better alignment between goals and treatments may increase the interpersonal relationship between patients and physicians, which, in turn, increases the patients' trust.[47,48] Increased communication and trust may, subsequently, improve patients' medication management by improving adherence to medications, for example. This finding suggests that COC is an important factor that influences medication adherence for patients with T2D, regardless of the type of medication adherence trajectory.

Strategies that aim to increase the COC between patients and physicians should be encouraged; for example, the introduction of the medical home project in the United States[21] to enhance coordinated care for patients might improve the COC for project enrollees.

Limitations

This study has several limitations. First, this study did not include unobserved (eg, health-seeking behavior) or unavailable (eg, illness severity) characteristics in the regression models. We included several proxy indicators for illness severity in the regression model, such as the DCSI score, which might reduce the bias related to the confounders that were not incorporated into the models. Second, MPR only indicates medication possession rather than medication consumption, which may lead to an overestimation of medication adherence. Nevertheless, MPR has been commonly used in previous studies to quantify medication adherence and is a valid predictor of healthcare outcomes.[6-10,37,38] Third, patients without medication prescription at the first time of diabetes diagnosis and patients who received insulin treatment in any of the years during the study period were excluded from the analysis, which might lessen the representativeness of the study subjects. Finally, there are certain unique aspects of Taiwan's healthcare system, such as free choice of providers for every visit without referral requirements, which may limit the generalizability of the findings to other healthcare systems.

CONCLUSIONS

This study demonstrated the heterogeneity in medication adherence and identified 4 distinct trajectories of medication adherence for patients with newly diagnosed T2D. Better COC between patients and their physicians was consistently associated with higher medication adherence in the 4 trajectory adherence groups. More attention should be directed toward designing new strategies to improve COC after the diagnosis of diabetes.

Author Affiliations: Department of Public Health, College of Medicine, Fu Jen Catholic University (CCC), New Taipei City, Taiwan; Institute of Health Policy and Management, College of Public Health, National Taiwan University (SHC), Taipei City, Taiwan.

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Address correspondence to: Shou-Hsia Cheng, PhD; Institute of Health Policy and Management, College of Public Health, National Taiwan University, 17 Xu-Zhou Rd, Taipei, Taiwan, 100. E-mail: shcheng@ntu.edu.tw.

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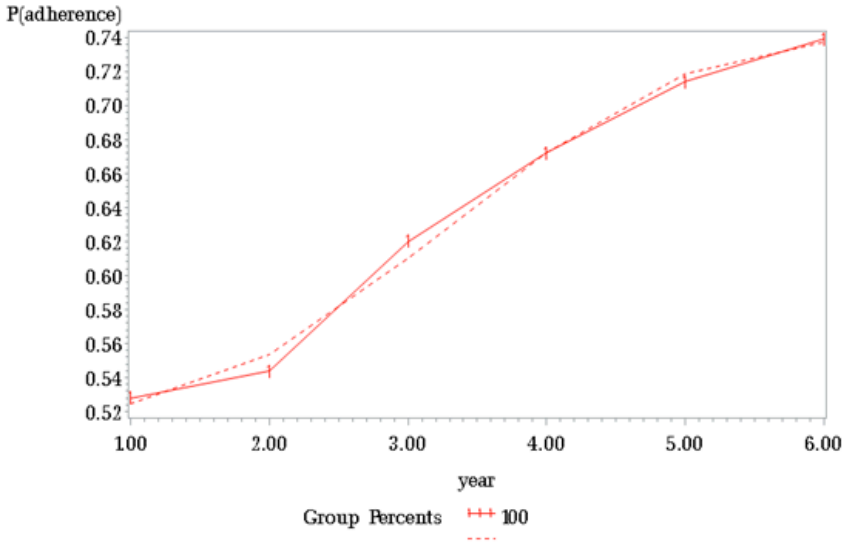
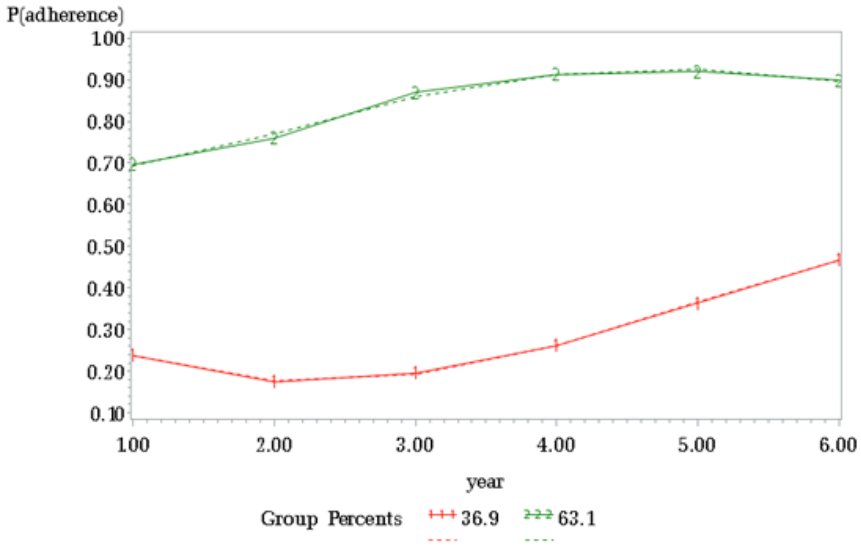
eAppendix 1. Model Fit Statistics for the Adherence Trajectory Models Using 1-4 Groups

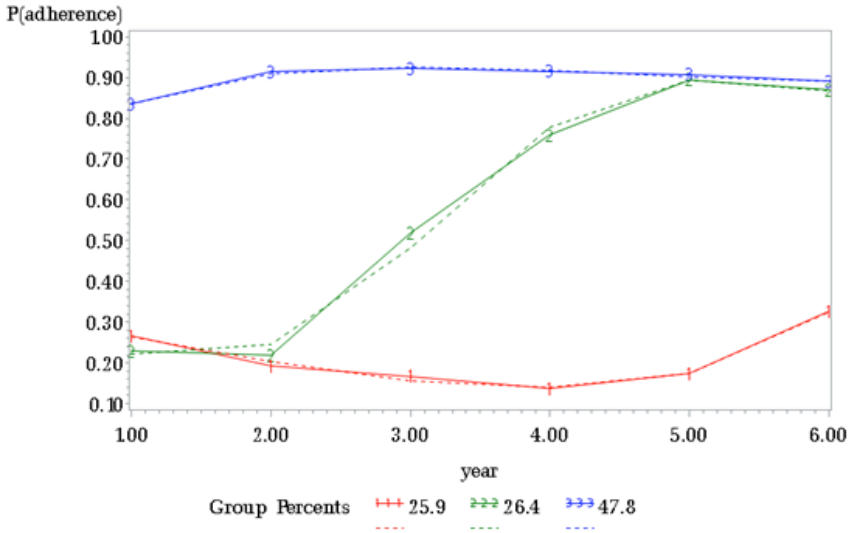
Number of Groups	**BIC** (N = 72,738)	**BIC** (N = 12,123)
1	–46708.22	–46704.64
2	–40303.81	–40295.75
3	–39474.64	–39462.09
4	–39110.71	–39093.69

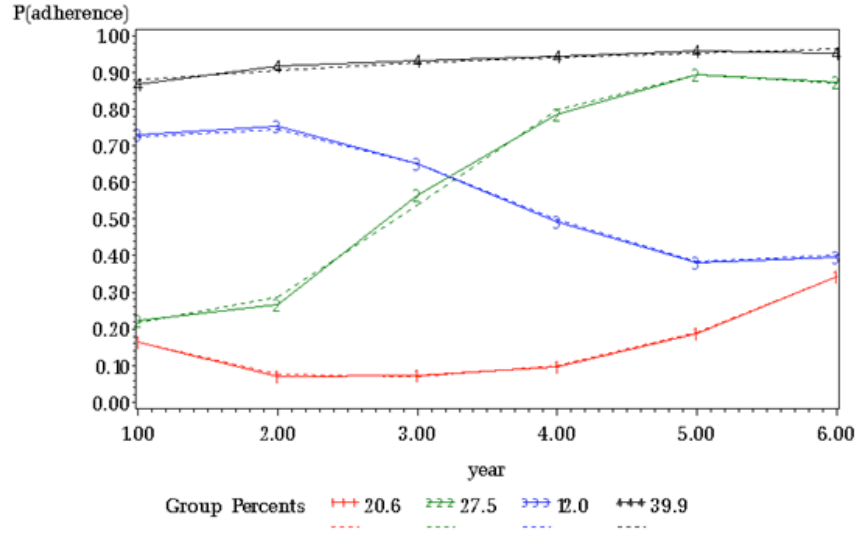
BIC indicates Bayesian information criterion

eAppendix 2. Adherence Trajectory Models Using 1-4 Groups









The solid lines indicate the observed proportion of subjects who were adherent in each group. The dotted lines indicate the predicted probability of adherence for each group.