Quantifying Social Reinforcement Among Family Members on Adherence to Medications for Chronic Conditions: a US-Based Retrospective Cohort Study

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BACKGROUND: More than 50% of patients are non-adherent to medications, often without an easily identifiable reason to clinicians. No study has quantified the extent to which health behaviors like medication-taking are correlated within families using national or routinely collected data for a range of conditions.
OBJECTIVE: To examine how an individual's health behaviors are influenced by those of their family members, particularly in adherence to medications for chronic conditions.
DESIGN: Retrospective cohort study.
PATIENTS: Using claims from a large nationwide insurer, we identified patients initiating medications for one of five chronic conditions with a family member who also recently filled one of these medications.
MAIN MEASURES: The primary exposure was whether family members were fully adherent (defined as a proportion of days covered ≥ 80%) before the patient's date of initiation. The outcome of interest was whether patients were fully adherent in the 12 months after initiation. Baseline demographic and clinical characteristics were also measured before initiation. We used multivariable modified Poisson regression to examine the association between prior family adherence and subsequent patient adherence.
KEY RESULTS: Among 254,144 patients, rates of full adherence among patients whose family members were and were not fully adherent were 37.3% and 26.9%, respectively (adjusted relative risk [aRR] 1.29, 95%CI 1.28–1.31). The association was stronger when both used cardiometabolic medications (aRR 1.35, 95%CI 1.32–1.37). Similarly, patients were also 38% more likely to be adherent if they and their family members used a medication for the same condition (aRR 1.38, 95%CI 1.35–1.40).
CONCLUSIONS: Adherence among family members appeared to be highly correlated, suggesting positive reinforcement by family or the sharing of unmeasured behaviors or characteristics associated with better adherence. Regardless, information about prior adherence among family members from routinely collected data could potentially inform adherence prediction or intervention efforts.

KEY WORDS: medication adherence; social contagion; social reinforcement; chronic disease; health behavior.

J Gen Intern Med 34(6):855–61
DOI: 10.1007/s11606-018-4654-9

BACKGROUND

Understanding the extent to which an individual's behaviors are influenced by those of their family members is critically important, particularly for health behaviors that must be sustained.[1] Several studies have found that support from family members or friends is thought to positively impact several health behaviors.[2, 3] This type of social reinforcement appears to be critical in the development and maintenance of health behaviors such as exercise or diet,[2, 4] likely through the provision of practical or emotional assistance, rather than mere cohabitation.[3, 5]

One example of a critically important and easily quantifiable health behavior is adherence to medications, defined by healthcare organizations as the extent to which patients take their medications as prescribed.[6–8] Poor medication adherence imposes significant clinical and financial burdens on the healthcare system.[8–10] On average, less than half of patients regularly take medications for common chronic conditions despite starting them, a behavior often called "secondary" non-adherence.[11, 12] There are many known barriers to adherence, including motivation, beliefs, forgetfulness, health literacy, out-of-pocket costs, or access-related barriers.[6, 13] These low rates have persisted despite extensive efforts to identify and predict patients at risk of poor secondary adherence, develop and test interventions to improve adherence, and to create clinician incentives for better performance by including adherence as a quality measure.[13–16]

One of the reasons that adherence remains consistently low may be that the true factors leading to non-adherence behaviors, such as social reinforcement from family members, are not being sufficiently addressed with these approaches.[1, 14, 17]

Electronic supplementary material *The online version of this article (https://doi.org/10.1007/s11606-018-4654-9) contains supplementary material, which is available to authorized users.*

Received October 30, 2017
Revised March 20, 2018
Accepted August 17, 2018
Published online November 7, 2018

For medication adherence, this may mean that a family member's experience, established routines, or observing someone else take medications may be mediators of the impact of social support on consistent medication use. Social reinforcement by family could be a key unexplored factor for adherence behaviors.

Quantifying the degree to which social forces influence habit formation in medication adherence, especially among immediate family members, could lead to impactful interventions for chronic disease management.[9, 10, 18] However, little is known about how specific shared behaviors in family members, like adherence, may directly or indirectly influence patients starting medications for chronic diseases. The data that do exist about the role of social support in adherence have largely relied on self-report, which may not easily scale or could be subject to social desirability bias.[3, 5, 17, 19] Conversely, to our knowledge, no study has used routinely collected data to quantify the extent to which behaviors like medication-taking are correlated among family members and the strength of these effects across different diseases. Accordingly, the objective was to examine the association between prior secondary adherence among family members and subsequent secondary adherence among patients initiating treatments for five conditions (i.e., diabetes, hypertension, hyperlipidemia, hypothyroidism, and mental health).

METHODS

Data Source and Patient Population

In this retrospective cohort study, we used administrative claims data for commercially insured individuals receiving benefits through a large national US health insurer (Fig. 1). These data include HIPAA-limited patient-level claims for medical inpatient and outpatient procedures, hospitalizations, emergency room visits, office visits, and outpatient pharmacy prescription drug dispensations linked to plan enrollment data using scrambled patient identifiers. Family identifiers were available for 100% of health plans allowing for linkages in the same family. The Institutional Review Board of Brigham and Women's Hospital approved this study.

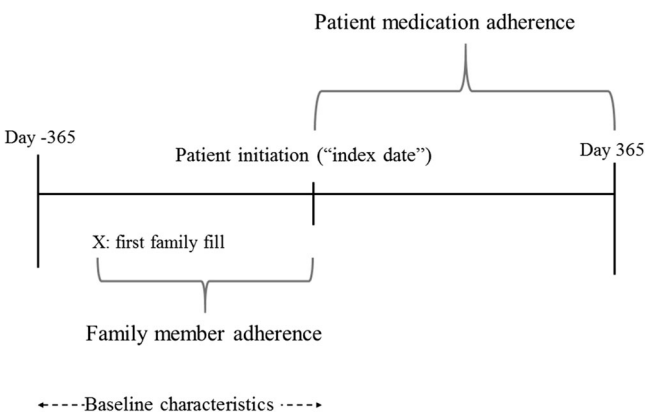

Fig. 1 Study design.

Patient and Family Member Identification

Our study cohort consisted of patients who initiated an oral medication between 01/01/2011 and 09/30/2015 for one of five conditions: diabetes, hypertension, hyperlipidemia, hypothyroidism, or mental health (i.e., depression or anxiety). These medications were chosen because they are for highly prevalent, medically managed conditions with varying clinical courses (Online Appendix Table 1).[20–22] We chose initiation of a medication as our inclusion criteria, because receipt of a chronic medication may be a better indicator of a condition than administrative claims diagnosis codes.[21] The date of this first prescription was defined as the "index date," and initiation was defined as not filling a medication for that condition in the 365 days before the index date.

To be included, patients had to (1) be ≥ 18 years of age, (2) maintain continuous enrollment in the 365-day period before the index date, and (3) have a family member who filled a medication for any of the five conditions (Online Appendix Table 1) before the patient's index date (Fig. 1); family members could be < 18 years of age. If patients initiated multiple medications in the study period, we included only the first in which the patient satisfied the inclusion criteria above. If the patient had multiple family members with eligible medications (< 2% of the cohort), we examined the member with the earliest fill date.

Medication Adherence

The outcome of interest was adherence to the medications of interest. To generate this outcome, we created a drug supply diary for each patient beginning on the date of their first prescription fill for a study drug until 365 days after the index date. For each family member, we generated a drug supply diary beginning on their first fill in the 365 days before the patient's index date until the index date. To enhance generalizability, we allowed for the first family member fill to be anytime in the 365 days before the patient's index date for the primary analyses. These supply diaries linked all prescription fills of the initiated medication based on dispensing date and days supplied, where the supply for overlapping fills could accumulate up to 180 days of excess supply. Switching was allowed across medications for the same chronic condition (e.g., among all hypertensive drug classes). If a patient's family member had more than one eligible medication, we created separate supply diaries for each.

From these supply diaries, we calculated the proportion of days that patients had medications available, or the proportion of days covered (PDC), by dividing the number of days with medications available by the number of days during the follow-up period. We defined patients as fully adherent if they had a PDC of ≥ 80%, the level of adherence often believed to be necessary to achieve clinically-important effects.[21, 22] We

performed the same calculations for family members. If the patient had a family member with multiple eligible medications, we took the average PDC in the 365 days before the patient's index date and calculated optimal adherence based upon this average.[23]

Baseline Characteristics

We measured patient characteristics in the 365 days before medication initiation. Demographic characteristics, including age and sex, were obtained from enrollment files at initiation. Other characteristics were measured using International Classification of Diseases 9th edition (ICD-9) codes or Current Procedural Terminology (CPT) codes, including clinical comorbidities, a combined comorbidity score (a measure of overall health status based on comorbidities)[24], number of outpatient physician office visits, number of days hospitalized, number of unique medications filled (e.g., therapeutic complexity), and markers of healthy behaviors measurable in claims (influenza vaccine, receipt of a colonoscopy and mammogram/prostate specific antigen test among eligible patients).[25, 26] We measured characteristics of the initiated medications, including patients' copayments and brand name status, from the outpatient prescription claims. We also measured family member characteristics, including medications filled, copayment and therapeutic class, and demographic characteristics like age and sex.

Statistical Analysis

We first described the characteristics and medication adherence of patients and their family members. Absolute standardized differences (ASD), indexes that measure effect size between groups, were used to assess differences in baseline characteristics by family member adherence; a significant difference is usually characterized by an ASD > 0.10 (approximately equivalent to $p < 0.05$).[27]

We then used multivariable modified Poisson regression models, adjusting for all patient baseline characteristics listed in Table 1, to estimate the association between family members being fully adherent (PDC ≥ 80%) and patients being fully adherent after initiation. These models generate the estimated relative risks (RRs) with robust standard errors and are considered to be appropriate when the outcomes are common (e.g., incidences of ≥ 10%).[28]

In our primary analyses, we consider full adherence for any of the conditions. In secondary analyses, we restricted to (a) patients and family members who both filled medications for cardiometabolic conditions, defined by diabetes, hypertension, and hyperlipidemia, and (b) patients initiating medications for the same condition (e.g., hypertension) as their family member. We also repeated analyses among subgroups by condition.[29] We conducted these two additional analyses because we hypothesized that the associations may be stronger if patients and their family members have conditions with similar etiology and management.

To explore whether certain social situations were more influential on adherence, we repeated analyses among key pre-specified subgroups of patients by sex, age, and baseline therapeutic complexity. We also explored whether discordance between patients and family members in age (defined by ≥ 5 years difference), sex (e.g., male-female or female-male) or number of baseline medications (defined by ≥ 3 additional or fewer medications) influenced patients' adherence by evaluating potential interactions between baseline family member adherence ("main effect") and these factors. We hypothesized that discordance may modify the strength of the relationship.

We also conducted several sensitivity analyses, including restricting to patients with family members who had filled their medication ≥ 180 days before the patient's index date to ensure enough time to evaluate PDC.[23] We restricted to those ≥ 26 years and also to age differences ≤ 15 years to limit the possibility of patients or family members being dependents. In other sensitivity analyses, we excluded mental health (to focus on non-episodic chronic conditions), patients and family ≥ 65 years of age (to exclude older adults), and family ≤ 18 years of age (to exclude minors), and modified utilization covariates included in analyses to evaluate the robustness of findings across different populations.

All analyses were conducted using SAS 9.4 (Cary, NC).

RESULTS

The cohort consisted of 254,144 patients newly initiating a medication for a chronic condition (Online Appendix Table 2). Their mean age was 48.6 years (SD: 14.5), and 52.3% were female. Baseline characteristics are shown in Table 1, stratified by family member adherence at baseline. Except for fewer patients with adherent family members filling their initial medications with days' supplies > 30 days, no characteristics significantly differed between groups. Regarding family concordance, 84.6% of female patients had male family members, and 92.2% of male patients had female family members. The median (IQR) age difference between patients and their family was 4 years (1–10 years).

Rates of adherence by family members and patients are shown in Online Appendix Table 3. Overall, 49.2% of family members were fully adherent to their medications before patient initiation. Patient adherence differed slightly by chronic condition; patients initiating medications for hypothyroidism had the highest levels of adherence.

In the year after initiating treatment, patients with family members who were previously adherent had higher levels of medication adherence than those whose family members were non-adherent (Fig. 2). On average, 37.3% of patients whose family members were fully adherent were themselves adherent, compared to 26.9% of patients with poorly adherent family members (adjusted relative risk [aRR] 1.29, 95% CI 1.28–1.31) (Table 2). The association was also strong among patients who filled a medication for a related cardiometabolic

Table 1 Baseline Characteristics of the Cohort

Characteristic, %	Patients			Family members	
	Fully adherent* family members	Poorly adherent* family members	Absolute standardized difference	Fully adherent*	Poorly adherent*
	(*N* = 124,534)	(*N* = 129,610)		(*N* = 124,534)	(*n* = 129,610)
Demographic					
Female, %	53.9	50.7	0.07	48.3	54.4
Age, mean (SD)	50.1 (14.9)	47.1 (14.0)	0.01	53.0 (11.6)	47.2 (13.5)
Region %					
West	17.7	17.9	0.01	17.7	17.9
South	45.7	49.4	0.09	45.8	49.4
Midwest	28.0	24.9	0.09	28.0	24.9
Northeast	8.3	7.6	0.03	8.3	7.6
Clinical					
Coronary artery disease, %	1.5	1.3	0.02	1.6	0.9
Congestive heart failure, %	0.5	0.4	0.02	0.6	0.4
Chronic kidney disease, %	2.9	2.4	0.04	4.1	2.6
COPD/Asthma, %	11.6	11.0	0.03	11.5	11.4
Dementia, %	0.9	0.7	0.03	0.8	0.7
Depression, %	17.2	18.2	0.03	15.9	19.6
Diabetes, %	13.4	13.4	0.00	19.8	15.3
Hypertension, %	44.8	42.9	0.04	58.6	41.7
Hyperlipidemia, %	46.2	43.2	0.07	56.9	46.2
Liver disease, %	3.6	3.5	0.01	4.0	3.9
Stroke/TIA, %	0.5	0.4	0.02	0.4	0.3
Combined comorbidity, mean (SD)	0.3 (1.3)	0.2 (1.2)	0.02	0.3 (1.1)	0.3 (1.0)
Health resource utilization					
Office visits, mean (SD)	6.1 (5.4)	5.8 (5.2)	0.01	6.7 (5.8)	6.2 (5.6)
Hospital days, mean (SD)	0.7 (3.9)	0.7 (4.7)	0.00	0.6 (4.1)	0.8 (4.6)
Flu shot, %	19.2	16.9	0.08	18.9	16.5
Colonoscopy, %	7.3	6.3	0.05	8.8	7.1
Mammogram/PSA, %	31.8	29.0	0.07	35.9	27.9
No. unique drugs, mean (SD)	7.3 (5.3)	7.0 (5.1)	0.01	8.2 (5.5)	7.5 (5.4)
Index medication					
Brand name medication, %	9.3	9.3	0.00	14.1	13.3
Copayment, Mean (SD)	12.1 (17.4)	12.0 (16.5)	0.00	17.1 (24.2)	14.5 (20.2)
Days supplied ≤ 30 days, %	84.9	89.6	0.14	n/a	n/a

SD, standard deviation; COPD, chronic obstructive pulmonary disease; TIA, transient ischemic attack; PSA, prostate specific antigen test
**Fully adherent (PDC ≥ 0.8) and poorly adherent (PDC < 0.8) defined in days 1–365 after the date of initiation*

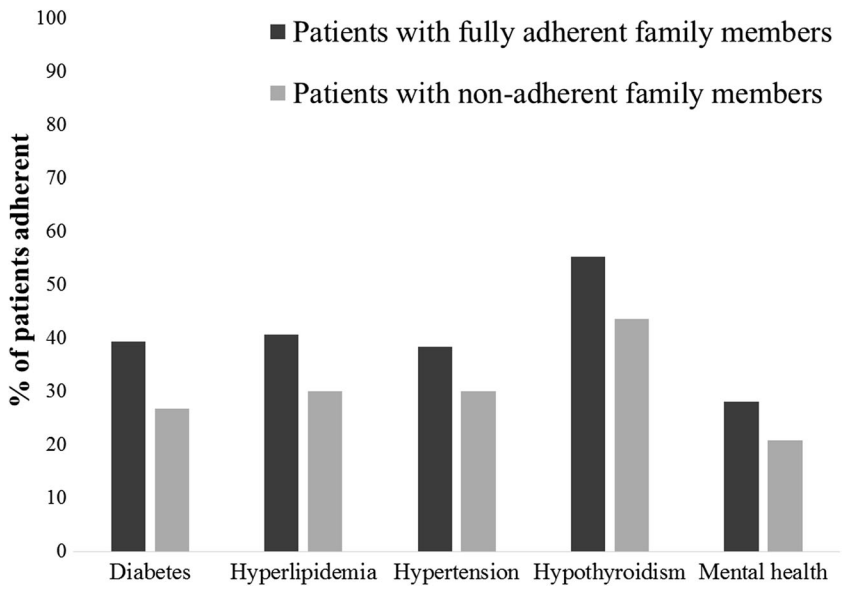

Fig. 2 Unadjusted patient adherence to chronic medications in the 12 months after initiation.

Table 2 Association Between Full Family Member Adherence and Subsequent Patient Adherence to Chronic Medications

Adherence measure	No. of patients	Relative risk of full adherence (95% CI)*
All patients	254,144	1.29 (1.28–1.31)
Patients with related cardiometabolic disease	119,790	1.35 (1.32–1.37)
Patients with same chronic disease	91,726	1.38 (1.35–1.40)
Diabetes	4673	1.42 (1.29–1.56)
Hyperlipidemia	24,229	1.50 (1.45–1.56)
Hypertension	42,819	1.30 (1.27–1.34)
Hypothyroidism	3604	1.29 (1.21–1.39)
Mental health	16,401	1.40 (1.32–1.48)

CI, confidence interval

condition as their family members (aRR 1.35, 95% CI 1.32–1.37). When filling medications for the same condition (i.e., diabetes), the association was similar (aRR 1.38, 95% CI 1.35–1.40) (Table 2). Finally, we evaluated the potential effect of adherence among family members with the same disease in subgroups by disease. We observed strong effects among all disease subgroups with the highest among family units with hyperlipidemia (aRR: 1.50, 95% CI: 1.45–1.56).

Figure 3 shows the estimated association between prior family adherence and subsequent patient adherence among subgroups of patient age, sex, and therapeutic complexity and concordance of age, sex, and therapeutic complexity between patients and their family members. The associations were significantly stronger among younger adults (age < 50 years) and patients who had filled fewer medications at baseline (< 6 medications). There was no significant effect modification by differences by patient sex. In addition, subgroups based on age, sex, or therapeutic complexity concordance did not significantly impact the relationship (Fig. 3).

Finally, all the sensitivity analyses by age, condition, or adjusted covariates did not differ substantially from the original results (Online Appendix Table 4).

DISCUSSION

To our knowledge, this is the first study to use routinely collected administrative claims data to evaluate how medication adherence among a patient's family members was associated with whether they will take newly initiated chronic medications as prescribed. Across a range of chronic conditions, we estimated that patients with family members who had demonstrated high levels of adherence were 29% more likely to be adherent themselves than patients whose family members were not adherent. These differences were even stronger for patients starting medications for the same or similar chronic cardiometabolic condition as family members.

In the management of chronic conditions, adherence to medications has become a key measure of healthcare quality and patient outcomes for providers, insurers and other healthcare organizations.[30] Despite widespread research, long-term adherence remains persistently low.[12, 31] One potential reason may be that patient behavioral factors are not being sufficiently identified in prior approaches.[1, 17, 32] In fact, the relative differences in adherence between patients with poorly adherent and optimally adherent family members observed in this study are larger than adherence-improving interventions widely considered to be effective, such as eliminating copayments, case management, and intensive behavioral support.[32]

There are several possible mechanisms to explain the observed associations. For example, adherence among family members could be the result of positive reinforcement. This positive reinforcement could take the form of providing encouragement, sharing knowledge about managing a condition, or supplying practical assistance with daily routines for disease management.[3] Other literature suggests that patients with family who provide practical or emotional support, rather than just structural support, positively influence medication-taking behaviors of patients.[3, 5] The stronger associations among family units using medications for the same disease could indicate

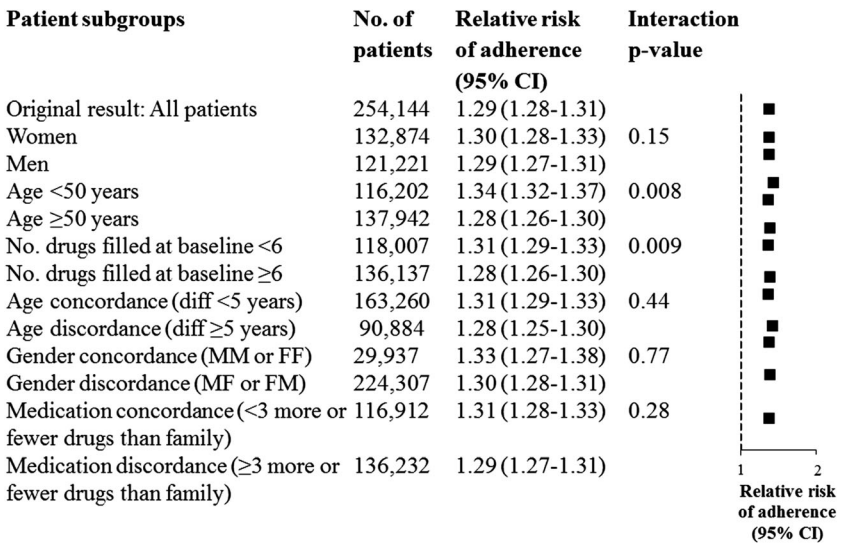

Fig. 3 Potential modifiers of the relationship between full family member adherence and subsequent patient adherence to chronic medications: subgroup analyses.

some degree of practical guidance in health management. Conversely, family members may share unmeasurable behaviors or characteristics, such as educational attainment or race/ethnicity, that are associated with better adherence. Moreover, there could also have been negative reinforcement, in that poorly adherent family members could have discouraged patients from optimal adherence. It is not possible from the study data to distinguish which of these explanations is most likely.

The degree to which social support can be leveraged into interventions is still largely unknown, although several studies have investigated the use of peer networks or mentors, though not necessarily with family members.[33–35] To our knowledge, the few interventional studies of social support on adherence have largely focused on patients with HIV or other communicable diseases.[3, 36] These interventions involved peer support groups or formal educational sessions with partners; partner-facing ones were more successful.[3] In addition, a few directly observed therapy (DOT) interventions, where another individual watches the patient take medications, for tuberculosis management involving family members have been found to be as successful as health workers.[36] Conversely, one of the largest social support interventions for non-communicable diseases to date found no differences in adherence.[35] However, social support was just one component and involved medication technology that primarily informed designated family members or friends of missed doses. Across these studies, one-on-one engagement, particularly in-person and among family members, was found to be more successful at improving adherence versus other approaches.[3, 37]

These findings suggest several avenues for interventions. For example, organizations or healthcare providers in integrated delivery systems might consider providing additional interventional support for patients initiating medications if there are indications of poor adherence by family members. Organizations without access to claims data could potentially measure self-reported adherence with validated scales or use electronic health records to evaluate consistency of medication refill requests among family units or caregivers.[38, 39] In research, investigators could potentially measure family members' prior adherence to chronic medications as predictor variables to attempt to explain behavioral or environmental differences between patients. Measuring prior family member adherence among patients newly initiating medications in observational studies could help control for healthy user bias, by providing additional information about the patient environment or socioeconomic characteristics that are not traditionally captured.[40, 41] Given the correlated behaviors, developing and evaluating family-based programs, like family medication synchronization programs or behavioral interventions, may also be potential strategies. Further research should also investigate whether improving adherence among family members translates into improvements in patients.

Our findings should be considered in light of several limitations. First, this is a study based on administrative data, and some bias is possible because of inadequately or incompletely measured covariates, such as race/ethnicity, which are not available in commercial claims data. Given the nature of the data, medication adherence was measured indirectly using days supply, a validated method that has been shown to correlate well with electronic records and patient self-report.[42] This measure is also used by health plans and the Centers for Medicare and Medicaid Services.[43] Any medication discontinuation that may have occurred could also be clinically appropriate but is likely to be non-differential. Patients could also have initiated medications for other indications, but we expect this to be non-differential. We also could not elucidate the specific reason why behaviors were correlated, whether a family member was a partner or child, or type of social support; some families may have better access to medications and lower deductibles (although there were no observed differences in out-of-pocket copayments), or barriers like forgetfulness could have been reduced through synchronizing medication-taking. The subgroup analyses are also exploratory and have the potential for multiple testing.

Regarding generalizability, our data source also only includes patients who are commercially insured or have Medicare Advantage, so they may not be representative of all patients. We also focused on secondary adherence, rather than medication initiation (e.g., primary adherence). Additionally, we examined each patient's first medication that met criteria to capture initial behaviors; patients with more complex regimens may have different adherence. However, more than 60% of study patients initiated only one eligible medication. We also did not examine insulin, as PDC is less reliable.[44]

Adherence to newly initiated medications for chronic conditions was associated with prior medication adherence among family members in real-world data. These findings suggest that positive social reinforcement for medication-taking occurs between family members or that family members share behavior or characteristics that are associated with better adherence, both of which are indicative of social support. Information about prior adherence among family members collected from routinely collected data may be able to inform adherence intervention or prediction efforts by providers, plans, and other healthcare organizations.

Acknowledgements: *A portion of this research was presented at the Annual Conference for the International Society for Pharmacoepidemiology in 2017 (Montreal, Canada).*

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Compliance with Ethical Standards:

Conflict of Interest: *Julie Lauffenburger has received salary support for unrestricted research grants from Sanofi and Astra Zeneca and is supported by the NIH (K01HL141538-01). Niteesh Choudhry has received unrestricted research grants from Sanofi, Astra Zeneca, Merck, CVS Health, PhRMA Foundation, the Arnold Foundation, and Medisafe. He is also a consultant to and holds equity in Ontiq, Inc. Nazleen Khan and Greg Brill report no conflicts.*

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