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Association Between Method of Prescribing and Primary Nonadherence to Dermatologic Medication in an Urban Hospital Population

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IMPORTANCE Prescription underuse is associated with poorer clinical outcomes. A significant proportion of underuse is owing to primary nonadherence, defined as the rate at which patients fail to fill and pick up new prescriptions. Although electronic prescribing increases coordination of care and decreases errors, its effect on primary nonadherence is less certain.

OBJECTIVES To analyze factors associated with primary nonadherence to dermatologic medications and study whether electronic prescribing affects rates of primary nonadherence.

DESIGN, SETTING, AND PARTICIPANTS A retrospective review of medical records was conducted from January 1, 2011, to December 31, 2013, among a cohort of new patients prescribed dermatologic medications at a single, urban, safety-net hospital outpatient dermatology clinic.

MAIN OUTCOMES AND MEASURES The primary outcome was the overall rate of primary nonadherence, defined as filling and picking up all prescribed medications within a 1-year period, and the difference in primary nonadherence between patients who received electronic prescriptions and those who received paper prescriptions. Secondary outcomes included the association of primary nonadherence with sex, age, relationship status, primary language, race/ethnicity, and number of prescriptions.

RESULTS A total of 4318 prescriptions were written for 2496 patients (mean [SD] age, 47.7 [13.2] years; 849 men and 1647 women). The overall rate of primary nonadherence was 31.6% (n = 788). Based on multivariable analysis, the risk of primary nonadherence was 16 percentage points lower among patients given an electronic prescription (15.2%) than patients given a paper prescription (31.5%). Primary nonadherence decreased with age (<30 y, 38.9%; 30-49 y, 35.3%; and 50-69 y, 26.3%), and then increased in elderly patients 70 years and older (31.9%). Of patients who were given 1, 2, 3, 4, or 5 prescriptions, rates of primary nonadherence were 33.1%, 28.8%, 26.4%, 39.8%, and 38.1%, respectively. Primary nonadherence decreased with age but then increased in elderly patients. Patients identifying English as their primary language had the highest rate of primary nonadherence (33.9%) compared with Spanish (29%) or other speakers (20.4%).

CONCLUSIONS AND RELEVANCE Compared with paper prescriptions, electronic prescriptions were associated with less primary nonadherence. Number of prescriptions, language, race/ethnicity, and age were associated with increased rates of primary nonadherence. Efforts must be made to understand why primary nonadherence occurs, identify patients prone to primary nonadherence, and simplify medication regimens to maximize adherence and quality of care.

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As the health care system in the United States has increasingly moved to the use of electronic medical records, electronic prescribing (e-prescribing) has become an important part of improving quality of care and the patient experience. Electronic prescribing increases coordination between pharmacist and physician and can decrease prescription errors.[1,2] However, it is less certain how e-prescribing affects the rate at which patients fill (primary adherence) or do not fill (primary nonadherence) their new prescriptions.[3]

Although it may seem intuitive that primary adherence would increase by removing the patient from the prescription-to-pharmacy routing process, few studies have compared primary nonadherence of patients given traditional paper prescriptions vs e-prescriptions. Of these studies, there have been mixed results regarding the use of e-prescriptions, with some showing increased primary adherence, others showing decreased primary adherence, and still others showing no difference.[4-7]

Understanding the epidemiologic factors of prescriptions is important because underuse of prescription medications continues to be a problem. Underuse of prescription medications has been linked to poorer patient outcomes and increased health care costs.[8] Most studies examining nonadherence focus on medication use patterns among patients who have already filled their prescriptions.[9-14] Fewer studies focus strictly on primary nonadherence. In dermatology, only a few, mostly small studies have specifically investigated primary nonadherence.[15-17]

In this study, we measure primary nonadherence to dermatologic medications by examining prescription data from a large, urban county hospital system with an enclosed prescription environment. Patient and prescription characteristics were evaluated to assess factors associated with primary nonadherence.

Key Points

Question Are patients more likely to fill and pick up medications if they receive a paper prescription or an electronic prescription?

Findings In this record review of 2496 patients with a highly subsidized pharmaceutical benefit plan seen at the dermatology clinic of a county hospital, there was a 47% reduction in primary nonadherence if the prescription was in electronic format compared with a paper prescription.

Meaning Patients are more likely to fill and pick up medications if they are prescribed in an electronic format.

Methods

Patients on the Parkland Health Plus (PHP) program, a taxpayer-subsidized health insurance program for uninsured, low-income residents of Dallas County, Texas, were included in this study. As part of PHP, patients receive a prescription drug benefit at considerably reduced cost if they fill their prescriptions through a closed pharmacy system. Data from the closed pharmacy system were linked with the electronic medical record system of Parkland Health and Hospital System in Dallas, Texas, for this analysis. Only new patients at PHP seen by a dermatologist in the outpatient dermatology clinic at Parkland Memorial Hospital were included. New patients were defined by not having a visit to the clinic in the prior 3 years. The index visit was defined as a visit by a new patient occurring from January 1, 2011, to December 31, 2013, during which 1 or more dermatologic medications were prescribed. Patients were excluded if they did not have a medication prescribed at their visit. Nonformulary medications were excluded from the analysis. Patients' age, sex, self-reported race/ethnicity, relationship status (married, common law, or significant relationship [eg, domestic partnership or civil union] vs divorced, legally separated, single, or widowed), primary language spoken, number of dermatologic prescriptions, type of prescription given (electronic or paper), and date of medication pick-up were extracted from the linked electronic medical record and pharmacy record.

Primary nonadherence was defined as not filling and picking up all dermatologic prescriptions obtained during the index visit within 1 year of the prescription date. Adherence was further classified as full adherence (filling all prescriptions), some adherence (filling some but not all prescriptions), and complete nonadherence (filling none of the prescriptions). Demographic and prescription characteristics and their crude association with primary nonadherence were assessed using Mantel-Haenszel general association tests for categorical variables and analysis of variance for continuous variables. We used linear regression models (with identity and log link functions) to estimate crude and adjusted risk differences and risk ratios with 95% CIs for the risk of primary nonadherence among patients with e-prescriptions vs paper prescriptions. The variables included in the analysis were age, sex, race/ethnicity, marital status, and primary language spoken. Kaplan-Meier product limit survival curves were created for time (in days) until all prescriptions were filled. Data management and analysis was performed with SAS, version 9.3 (SAS Institute Inc).

The study was approved by the University of Texas Southwestern Medical Center Institutional Review Board. Owing to the retrospective nature of the study, patient consent was not necessary. A data use agreement was also approved for use of the de-identified data at The University of North Carolina at Chapel Hill.

Results

A total of 2496 patients met the inclusion criteria and were prescribed a total of 4318 medications for dermatologic conditions, at a mean of 1.7 prescriptions per patient. The mean (SD) age of patients was 47.7 (13.2) years, and the majority were women (1647 [66%]). Consistent with the population served by this health system, nearly half of patients (1220 [48.9%]) were Hispanic, and the rest were black (654 [26.2%]), white (443 [17.7%]), or other race/ethnicity (179 [7.2%]). The most common primary language was English (1468 [58.8%]), followed by Spanish (920 [36.9%]) (**Table 1**). Most encounters involved printed prescriptions (1693 [67.8%]). Overall, 3254

Table 1. Characteristics of the Study Population by Prescription Type

Characteristic	Electronic Prescription (n = 803)[a]	Paper Prescription (n = 1693)[a]	*P* Value[b]
Sex			
Female	532 (66.3)	1115 (65.9)	.85
Male	271 (33.7)	578 (34.1)	
Age, mean (SD), y	48.2 (13.3)	47.5 (13.1)	.18
Primary language			
English	480 (59.8)	988 (58.4)	.78
Spanish	290 (36.1)	630 (37.2)	
Other	33 (4.1)	75 (4.4)	
Race/ethnicity			
Non-Hispanic white	162 (20.2)	281 (16.6)	.12
Hispanic white	387 (48.2)	833 (49.2)	
Black	195 (24.3)	459 (27.1)	
Other	59 (7.3)	120 (7.1)	
Relationship status			
In a relationship	335 (41.7)	732 (43.2)	.47
Not in a relationship	468 (58.3)	961 (56.8)	

[a] Data are presented as number (percentage) of patients unless otherwise indicated.

[b] Mantel-Haenszel general association test for categorical variables and analysis of variance for continuous variables.

Table 2. Adherence by Patient and Prescription Characteristics

Characteristic	No. (%)			*P* Value[a]
	Adherent	Some Adherence	Completely Nonadherent	
Prescription type				
Paper	1064/1693 (62.8)	137/1693 (8.1)	492/1693 (29.1)	<.001
Electronic	644/803 (80.2)	32/803 (4.0)	127/803 (15.8)	
Age, y				
<30	142/231 (61.5)	22/231 (9.5)	67/231 (29.0)	<.001
30-49	712/1100 (64.7)	93/1100 (8.5)	295/1100 (26.8)	
50-69	807/1096 (73.6)	52/1096 (4.7)	237/1096 (21.6)	
≥70	47/69 (68.1)	2/69 (2.9)	20/69 (29.0)	
Sex				
Female	1117/1647 (67.8)	119/1647 (7.2)	411/1647 (25.0)	.41
Male	591/849 (69.6)	50/849 (5.9)	208/849 (24.5)	
Language				
English	969/1486 (66.0)	121/1486 (8.2)	378/1486 (25.7)	<.001
Spanish	653/920 (71.0)	46/920 (5.0)	221/920 (24.0)	
Other	86/108 (79.6)	2/108 (1.9)	20/108 (18.5)	
Race/ethnicity				
Non-Hispanic white	288/443 (65.0)	19/443 (4.3)	136/443 (30.7)	.007
Hispanic white	858/1220 (70.3)	79/1220 (6.5)	283/1220 (23.2)	
Black	437/654 (66.8)	57/654 (8.7)	160/654 (24.5)	
Other	125/179 (69.8)	14/179 (7.8)	40/179 (22.3)	
Relationship status				
In a relationship	752/1067 (70.5)	55/1067 (5.2)	260/1067 (24.4)	.01
Not in a relationship	956/1429 (66.9)	114/1429 (8.0)	359/1429 (25.1)	

[a] Mantel-Haenszel general association test.

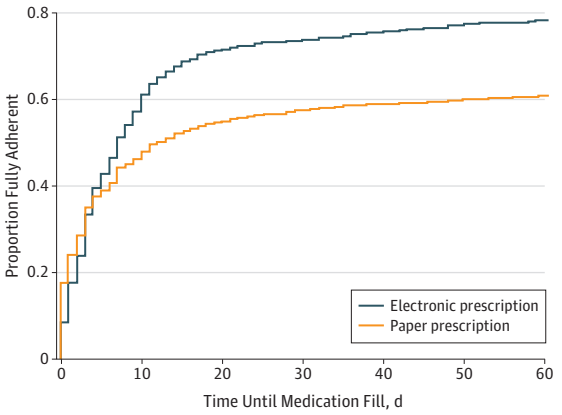
prescriptions (75.4%) were filled and picked up. The patient-level primary adherence rate was 68.4% (n = 1708). Of the patients who were nonadherent, 169 (6.8%) filled and picked up some of their prescriptions while 619 (24.8%) filled and picked up none.

Sex and relationship status were not associated with a difference in primary nonadherence. Rates of primary nonadherence decreased with increasing age (<30 years, 67 of 231 [29%]; 30-49 years, 295 of 1100 [26.8%]; 50-69 years, 237 of 1096 [21.6%]; and ≥70 years, 20 of 69 [29%]). Patients who did not speak English had lower rates of primary nonadherence (Spanish, 221 of 920 [24%]; other language, 20 of 108 [18.5%]) compared with those who identified English as their primary language (378 of 1468 [25.7%]). Hispanic patients had the highest full adherence rate (858 of 1220 [70.3%]) of any racial/ethnic group (**Table 2**).

Table 3. Number of Medications Filled According to the Number of Medications Prescribed

	Medications Filled, No. (%)							
Medications Prescribed, No.	0	1	2	3	4	5	6	7
1 (n = 1291)	427 (33.1)	864 (66.9)						
2 (n = 777)	142 (18.3)	82 (10.6)	553 (71.2)					
3 (n = 273)	34 (12.5)	8 (2.9)	30 (11.0)	201 (73.6)				
4 (n = 128)	15 (11.7)	0	6 (4.7)	30 (23.4)	77 (60.2)			
5 (n = 21)	1 (4.8)	0	0	1 (4.8)	6 (28.6)	13 (61.9)		
6 (n = 5)	0	0	0	1 (20.0)	0	4 (80.0)	0	
7 (n = 1)	0	0	0	0	0	0	1 (100)	0

Figure. Time Until Medication Fill for Fully Adherent Patients



Time until medication fill for fully adherent patients (patients filling all medications prescribed) for 60 days after the index visit. There was a statistically significant difference at 60 days (Wilcoxon test; $P < .001$).

The risk of primary nonadherence was 17 percentage points lower among patients given an e-prescription than patients given a paper prescription. This difference was 16 percentage points in the adjusted analysis. This finding represents a 47% reduction in the risk of primary nonadherence for patients who received an e-prescription vs those who received a paper prescription. Patients with paper prescriptions had a higher proportion of full adherence in the first 4 days after the prescription was issued, but after this point, patients with e-prescriptions were much more likely to be fully adherent (**Figure**).

Primary adherence was 66.9% (864 of 1291) when 1 prescription was given and increased to 71.2% (553 of 777) when 2 and 73.6% (201 of 273) when 3 prescriptions were given; however, primary adherence declined to 60.2% (77 of 128) when 4 prescriptions were given (**Table 3**).

Discussion

In this study measuring rates of primary nonadherence to medications prescribed by dermatologists, we found a 31.6% rate of primary nonadherence, defined as failing to fill and pick up all prescriptions within 1 year of receiving the prescriptions. This rate is slightly greater than the 20% to 30% rates of primary nonadherence reported in previous studies specifically investigating dermatologic medications.[15-17] However, some of these studies were limited by self-reported response bias, which could have underestimated the level of primary nonadherence. In fact, 1 study showed that, although patients self-reported a rate of primary nonadherence of 6.2%, when pharmacy records were queried for external validation, rates of primary nonadherence were 45% and 25% at 2 weeks and 6 months, respectively.[16] It is often difficult to compare adherence studies directly given different follow-up times, study populations, and reliability of outcomes measured (eg, surveys vs claims vs direct pharmacy data). Moreover, unlike many primary nonadherence studies, our unit of analysis for defining nonadherence was at the patient level, not the prescription level. When compared at the prescription level, our study population shows similar rates of nonadherence as reported in other studies. In our study, 24.6% of prescriptions went unfilled, which is lower than the rate of primary nonadherence to dermatological medications of 31.2% reported by Fischer et al,[18] 27.8% reported by Tamblyn et al,[19] and 29.2% reported by Storm et al.[17] This comparable level of primary nonadherence is remarkable given the low-income demographic of patients in our study. Patients with lower incomes are often more sensitive to prices, and our results are likely owing to the subsidized pharmacy benefit received by patients for their medications.

Similar to Anderson et al,[15] we found a decrease in primary nonadherence to dermatologic medication with use of e-prescriptions. We also found that, during the first 4 days from the index visit, patients with paper prescriptions had a higher rate of full adherence. Although this study was not designed to establish a cause, it is possible that having a paper prescription served as a tangible reminder for patients to fill and pick up their prescription in the short term. However, in the longer term, lost or misplaced paper prescriptions could have led to a diminished likelihood of full adherence.

The effect of e-prescribing on primary nonadherence has been variable, with studies showing increased, decreased, or unchanged rates of primary nonadherence.[4-7] For example, in a prospective study conducted in an emergency department, while pharmacy wait times and patient satisfaction improved, there was no difference in rates of primary nonadherence between e-prescriptions and paper prescriptions.[4] In another example, a large cross-sectional cohort study examining the characteristics of abandoned prescriptions showed that e-prescriptions were more likely to be abandoned at the pharmacy.[6] It is possible that the variability in primary non-

adherence is owing to different populations being studied or different study designs, such as reliance on patient self-reports, for measuring rates of primary nonadherence.

A notable finding of our study is the decrease in rates of primary nonadherence when patients are given between 1 and 3 prescriptions, followed by an increase in rates of primary nonadherence when they are given more than 3 prescriptions (Table 3). The number of dispensed drugs is associated with primary nonadherence.[20] Polypharmacy is a well-documented problem in patients' compliance with complex treatment regimens.[21,22] Patients on the PHP plan pay $5 per prescription, which could explain increased nonadherence beyond 3 prescriptions. Cost is a major consideration for many patients. Up to 32% of older patients take less medication than prescribed to reduce costs.[23] Although patients in our study are buffered from high medication costs, multiple medications can become financially burdensome.

Similar to other studies of primary nonadherence, we did not find a sex difference in rates of primary nonadherence; however, younger patients had higher rates of primary nonadherence.[15,18] In our study, Hispanic patients had among the lowest rate of primary nonadherence. This finding is in contrast to other reports that show higher rates of primary nonadherence among Hispanic patients.[24,25] However, a similar finding has been reported for rates of primary nonadherence to cardiac medications within the PHP population.[26] Adherence is multifactorial and complex, but it is possible that adherence of Hispanic patients is higher because Parkland Memorial Hospital has the infrastructure to accommodate the needs of its high volume of Spanish-speaking patients. Sociocultural differences of non–English-speaking patients in their trust of physician recommendations could also have positively influenced primary adherence.

Limitations

This study has some limitations. The insurance coverage environment allowed for direct study of nonadherence; however, this distinctiveness makes the study less generalizable as it exclusively encompasses a population of poor residents of Dallas County in one subspecialty clinic receiving a subsidized pharmacy benefit. Sixty-six percent of study participants were female, and the racial demographics included 48.9% Hispanic and 26.2% black patients, which may not be representative of other dermatology clinics. It is possible that there were other factors not captured in the data that could have resulted in the difference in adherence rates. Misclassification of medications as unfilled could have resulted if prescription adjustments were made by telephone after initial visit. Finally, while this study uncovered factors associated with primary nonadherence, it was not designed to understand the reasons for patient nonadherence.

Conclusions

Electronic prescribing has become one of the major criteria to evaluate meaningful use of electronic health records by health care professionals.[27] In this study, we demonstrated that e-prescribing is associated with reduced rates of primary nonadherence. As the health care system transitions from paper prescriptions to directly routed e-prescriptions, it will be important to understand how that experience affects patients, particularly their likelihood of filling the prescriptions. Primary nonadherence is a common and pervasive problem. Steps should be taken to better understand why primary nonadherence happens and how it can be improved.

ARTICLE INFORMATION

Correction: This article was corrected on November 16, 2016, to fix typographical errors in the Results sections of the Abstract and text and in the Discussion.

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Study concept and design: Adamson.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Adamson.
Critical revision of the manuscript for important intellectual content: All authors.
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Additional Contribution: Bhavin Patel, PharmD, MBA, Parkland Memorial Hospital Pharmacy Department, assisted with data acquisition. He was not compensated for his contribution.

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NOTABLE NOTES

The History of John Hans Menkes and Kinky Hair Syndrome

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John Hans Menkes was a pediatric neurologist, born in Vienna, Austria, in 1928. Following the German annexation of Austria, Menkes immigrated to the United States with his family in 1939 at the age of 11 years. He completed high school in California and subsequently earned undergraduate and graduate degrees in organic chemistry at the University of Southern California. Although he held a passion for writing and journalism, Menkes ultimately decided to follow the family tradition of studying medicine.[1] Following a pediatric neurology residency at Columbia-Presbyterian Medical Center in New York, Menkes went to the University of California, Los Angeles, where he spent the rest of his life advancing the field of pediatric neurology and having an impact on the fields of genetics and dermatology.

Menkes' chief contribution to medicine was his discovery of kinky hair syndrome or Menkes disease. In 1962, Menkes encountered a male infant who, while developmentally normal at birth, quickly developed floppy muscle tone, seizures, and coarse, brittle hair.[1,2] Menkes learned that the infant's 4 male siblings, also young children, had very similar physical manifestations, suggesting an X-linked genetic disorder. Through Menkes's further investigations and the contributions of other researchers, it is known today that Menkes disease results from a genetic mutation in the *ATP7A* gene, which is responsible for producing an enzyme that regulates copper levels in the body. This subsequent deficiency in copper transport across cells ultimately deprives the brain and other tissues of this important mineral, explaining the symptoms that Menkes observed.[3]

Menkes is famous for other medical achievements, such as describing the first known cases of maple syrup urine disease while he was an intern in 1954.[1] This autosomal recessive disorder is due to a disruption in the metabolism of branched-chain amino acids, leading to a buildup of isoleucyl ketoacid that gives the urine its characteristic odor.

Menkes's contributions to society were not limited to medicine, as he was also highly regarded for his contributions to the humanities. His passion for writing did not falter as he aged, and he wrote 3 novels and 3 plays that were produced in Los Angeles. One of these productions, titled *The Last Inquisitor*, was a Holocaust drama that won a prestigious Drama-Logue Award; this was a theater award for a play selected by theater critics of the Drama-Logue newspaper, a weekly west-coast theater trade publication. In addition, Menkes served as an expert witness for plaintiffs in trials involving damage resulting from vaccines and was appointed to the National Institute of Medicine's Forum for Vaccine Safety.[1]

Menkes was named the director of pediatric neurology at Los Angeles' Cedar-Sinai Medical Center in 1997. He died of colon cancer and complications of chemotherapy in November of 2008, 1 month from his 80th birthday.

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