Editor's key points

- Primary medication nonadherence—when a patient does not fill their initial prescription—increases adverse clinical events, morbidity, mortality, and overall health care costs. Nonadherence is a critical barrier to treatment success and a challenge for health care providers. This study aimed to offer a robust picture of drug initiation and adherence in an adult primary care population, where treatment is often started.
- The authors analyzed primary nonadherence across several medication classes for chronic and acute conditions commonly treated in primary care, where nonadherence may affect health outcomes.
- This study was unable to identify a consistent pattern of association between primary nonadherence and patient demographic, clinical, or provider characteristics.

Primary medication nonadherence in a large primary care population

Observational study from Manitoba

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Abstract

Objective To analyze primary medication nonadherence across several prescription indications and test the predictors of drug nonadherence in an adult primary care population.

Design Retrospective observational study using primary care provider prescriptions linked to pharmacy-based dispensing data from 2012 to 2014.

Setting Manitoba.

Participants Patients in the Manitoba Primary Care Research Network.

Main outcome measures Prevalence of primary medication nonadherence by drug class. Multivariable logistic regression models were used to test the associations of patient demographic and clinical or provider characteristics with primary medication nonadherence. The C statistic was used to assess the models' discriminative performance.

Results A total of 91,660 unique prescriptions were assessed from a cohort of more than 200,000 patients. Primary medication nonadherence ranged from 13.7% (antidepressants) to 30.3% (antihypertensives). In conditions that typically present symptomatically (eg, infections, anxiety) nonadherence ranged from 13.7% to 17.5%. The range was 21.2% to 30.0% for medications related to asymptomatic conditions or those typically detected by screening. The discriminative performance of the models based on patient demographic, clinical, or provider characteristics was weak.

Conclusion Primary medication nonadherence is common, occurring more often in asymptomatic conditions. The poor predictability of the models suggests that caution is required when considering characteristic-based interventions or prediction tools to improve primary medication nonadherence.

Non-adhésion primaire à la médication dans une population nombreuse en soins primaires

Étude observationnelle au Manitoba

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Résumé

Objectif Analyser la non-adhésion primaire à la médication parmi plusieurs prescriptions indiquées et mettre à l'essai des facteurs de prédiction de la non-adhésion dans une population adulte en soins primaires.

Type d'étude Une étude observationnelle rétrospective à l'aide des ordonnances prescrites par des professionnels de la santé reliés à une pharmacie qui a fourni des données de 2012 à 2014.

Contexte Manitoba.

Participants Des patients dans le Réseau de recherche en soins primaires du Manitoba.

Principaux paramètres à l'étude La prévalence de la non-adhésion primaire selon la classe de médicaments. Des modèles de régression logistique à variables multiples ont servi pour mettre à l'essai les associations entre les renseignements démographiques des patients, les caractéristiques cliniques ou les caractéristiques propres aux professionnels, et la non-adhésion primaire à la médication. La statistique C a été utilisée pour évaluer le rendement discriminant du modèle.

Résultats Un total de 91 660 ordonnances individuelles prescrites à plus de 200 000 patients ont été évaluées. La non-adhésion primaire à la médication variait de 13,7 % (antidépresseurs) à 30,3 % (antihypertenseurs). Pour les problèmes typiquement symptomatiques (p. ex. infections, anxiété), la non-adhésion variait de 13,7 à 17,5 %. Elle se situait entre 21,2 et 30,0 % pour les médicaments associés à des problèmes asymptomatiques ou à ceux habituellement détectés par dépistage. Le rendement discriminant des modèles fondés sur les données démographiques des patients, les caractéristiques cliniques ou les caractéristiques propres aux professionnels était faible.

Conclusion La non-adhésion primaire à la médication est fréquente et se produit plus souvent dans le cas des problèmes asymptomatiques. La faible prévisibilité des modèles fait valoir qu'il faut user de prudence lorsque sont envisagées des interventions fondées sur des caractéristiques ou des outils de prédiction pour réduire la non-adhésion primaire à la médication.

Points de repère du rédacteur

- La non-adhésion primaire à la médication, c'est-à-dire lorsqu'un patient ne fait pas remplir sa première ordonnance, augmente les événements cliniques indésirables, la morbidité, la mortalité et les coûts globaux en soins de santé. La non-adhésion est un obstacle majeur à la réussite du traitement et un défi pour les professionnels de la santé. Cette étude visait à brosser un tableau probant du démarrage d'une médication et de l'adhésion au médicament au sein d'une population adulte en soins primaires, un milieu où un traitement est souvent amorcé.
- Les auteurs ont analysé la non-adhésion primaire dans le cas de diverses classes de médicaments pour des problèmes chroniques et aigus couramment traités en soins primaires, lorsque la non-adhésion peut nuire aux résultats sur le plan de la santé.
- Cette étude n'a pas réussi à cerner un modèle uniforme d'associations entre la non-adhésion primaire et les données démographiques des patients et d'autres caractéristiques cliniques ou particulières aux professionnels.

Primary medication nonadherence—when a patient does not fill their initial prescription—is common.[1] Several studies indicate that poor medication adherence increases adverse clinical events, morbidity, mortality, and overall health care costs.[1-8] Nonadherence is a critical barrier to treatment success and a considerable challenge for health care providers.[9] Being aware of the extent to which nonadherence occurs in specific conditions is the first step to addressing it.[5,10]

Primary medication nonadherence is distinct from secondary medication nonadherence, where medications are filled but not taken as prescribed.[1] We focused on primary medication nonadherence because, until recently, many of the studies evaluating primary nonadherence to medication were limited by small sample sizes, suboptimal methodologies, or surrogate measures of adherence behaviour.[5,8] The recent availability of electronic medical record (EMR) prescribing information linked to medication dispensation information available from provincial health administrative data offers a more complete picture of drug initiation and adherence behaviour, particularly in primary care where treatment is often initiated.[1,5,8,11]

Rates of primary nonadherence have been shown to vary between 2.4% and 30.7%.[1] Several factors related to the patient, provider, social context, and medical condition have demonstrated associations with higher rates of nonadherence. However, the influence of specific characteristics and their relevance as predictors of primary medication nonadherence vary greatly.[1,3,10,12-14] Additionally, much of the research on primary medication nonadherence has focused on specific chronic disease populations (eg, diabetes, hypertension) and, therefore, a more comprehensive approach is warranted.[2,15-20] The objective of this study was to analyze primary nonadherence across several prescription indications and test the predictors of drug adherence behaviour in an adult primary care patient population in Manitoba.

Methods

In Canada, health care delivery is a provincial and territorial responsibility; medical services are provided in hospitals and community settings via single-payer, publicly funded insurance. Provinces and territories must meet standards described in the Canada Health Act to receive federal funding. Administrative health records are stored and maintained by provincial and territorial government bodies. We performed a retrospective observational study with primary care provider prescriptions linked to pharmacy-based dispensations data from the Manitoba Population Research Data Repository at the Manitoba Centre for Health Policy (MCHP). The MCHP Population Research Data Repository contains population-based de-identified administrative records submitted to the Manitoba government to report health and social service use by residents of Manitoba and includes data on emergency department visits (Emergency Department Information System) and all prescriptions filled in Manitoba pharmacies (Drug Program Information Network [DPIN]).[21-23]

The MCHP data repository also holds clinical data from the Manitoba Primary Care Research Network (MaPCReN), which includes a database of de-identified primary care EMR data from community-based primary care practices. Primary care providers who have consented to participate in MaPCReN include family physicians, nurse practitioners, and community pediatricians. It is one of the networks participating in the Canadian Primary Care Sentinel Surveillance Network, which also has 10 other regional networks. Prior studies have demonstrated that patient populations within Canadian Primary Care Sentinel Surveillance Network and MaPCReN practices are representative in terms of disease prevalence and prescribing rates when compared with other national data sources.[24,25] At the time of this study, MaPCReN included 44 primary care clinics representing 241 providers (including approximately 20% of the family physicians in Manitoba) caring for more than 200,000 patients aged 18 years or older.

Prescriptions written from April 1, 2012, to December 31, 2014, from the MaPCReN database were linked to Manitoba's DPIN. The DPIN contains data for all prescriptions dispensed by community pharmacies in the province of Manitoba. We included medication classes indicated for common chronic and acute conditions often treated in primary care and where nonadherence may affect health outcomes.

A separate study cohort was produced for each medication class and indication pairing listed in **Table 1**. **Table 1** also provides the corresponding World Health Organization's Anatomical Therapeutic Chemical codes used to define each medication in the grouping.

The main outcome, primary medication nonadherence, was defined as the absence of a dispensing record (in DPIN) after a new prescription (in MaPCReN) within 90 days of the date the prescription was written. New prescriptions were defined as those not dispensed to the patient within the previous 365 days.

Multivariable logistic regression models were used to test the association of patient demographic and clinical or provider characteristics with primary medication nonadherence. The specific covariates for the models were calculated using standard definitions,[22,23,26] and those included in the models are described in appendices available from **CFPlus.*** A mixed-effects multivariable logistic regression model, which included a random intercept for provider, was also fit to the data to assess

*Appendices outlining specific covariates included in the models are available from **https://www.cfp.ca**. Go to the full text of the article online and click on the **CFPlus** tab.

Table 1. Medications, typical indications, and corresponding Anatomic Therapeutic Chemical codes selected for the study

MEDICATION CLASS	TYPICAL INDICATIONS	CODES
Antibiotics	Infection	J01, G04A
Antidepressants	Depression	N06A
Antihypertensives	Hypertension	C02, C03, C04, C05, C07, C08, C09
Benzodiazepines	Anxiety	N05BA, N03AE
Bisphosphonates	Osteoporosis	M05B
Hypoglycemics	Diabetes	A10
Lipid-lowering agents	Cardiovascular disease, hyperlipidemia	C10

the magnitude of clustering of patients among providers. The intraclass correlation was used to provide a measure of the clustering effect; it has a lower bound of 0 and an upper bound of 1, with higher values indicating a stronger clustering effect.

The C statistic was used to describe the discriminative performance of the models for each medication class. A model with a C statistic greater than 0.7 is considered to have reasonable discriminative performance, while a model with a C statistic greater than 0.8 is considered to have strong discriminative performance.[27]

All data management, programming, and analyses were conducted using SAS, version 9.4. This research was approved by the University of Manitoba Health Research Ethics Board and by the province's Health Information Privacy Committee.

Results

The demographic characteristics of the study cohorts are described in **Table 2**. Overall, there were 91,660 unique prescriptions from more than 200,000 active patients. The smallest number of prescriptions was for bisphosphonates (N=670) and the largest grouping was antibiotics, which included 37,402 prescriptions. Most prescriptions were provided to female patients in all medication class cohorts, with the exception of lipid-lowering agents. Most prescriptions were for patients in the younger age groupings (18 to 44, 45 to 64), with the exception of bisphosphonates, which were mostly started in the 65 to 74 age grouping. The distribution of prescriptions within the income quintiles was fairly even, falling within a range of 14.4% to 22.8% in each category.

The range of primary medication nonadherence was 13.7% (antidepressants) to 30.3% (antihypertensives). In conditions that typically present symptomatically, such as infections, depression, and anxiety, nonadherence ranged from 13.7% to 17.5%. Medications related to asymptomatic conditions or those typically detected by screening, such as hypertension, osteoporosis, and diabetes, demonstrated nonadherence rates from 21.2% to 30.3%. The exception to this trend was medications used for hyperlipidemia and cardiovascular disease (lipid-lowering agents), which had a primary nonadherence rate of 15.2%. **Table 3** describes overall primary nonadherence by medication class, age group, and sex.

The intraclass correlation was very low for the multivariable mixed-effects logistic regression model that included a random intercept for provider, suggesting minimal clustering effects. Therefore, subsequent models fit to the data were based on the assumption of independence of observations.

The C statistic provided for each medication class cohort (**Table 4**)[28] indicates how well patient demographic and clinical characteristics predicted primary medication nonadherence. In general, the models demonstrated weak discriminative performance. In addition, there was little consistency in the association of the model covariates with primary nonadherence for each medication class.

Discussion

While our results closely follow the upper range of primary medication nonadherence reported in other studies (prevalence estimates ranging from 13.7% to 30.3%),[1,14] they still add important information for clinical practice. Medications related to chronic, typically asymptomatic conditions had rates of primary medication nonadherence that were 10 to 20 percentage points higher compared with symptomatic conditions (eg, depression, anxiety, infection). Our data demonstrate the intuitive notion that patients not experiencing symptoms may be less motivated to take medication to treat their conditions. Prescribers should consider this for conditions such as diabetes or hypertension and, particularly, for a new diagnosis or change in medication management. For symptomatic conditions, most patients filled their incident prescriptions. However, the literature suggests that this may be different for secondary adherence, where a prescription is filled but not taken as prescribed.[6,29-34]

Within the literature, a recent meta-analysis by Lemstra et al pooled 24 studies that considered 550,485 prescriptions and reported a combined primary nonadherence rate of 14.6% (95% CI 13.1% to 16.2%) when considering antihypertensives, lipid-lowering agents, hypoglycemics, and antidepressants.[35] In the same paper, the nonadherence rate for lipid-lowering agents was 17.0% (95% CI 14.4% to 19.5%), which closely reflects the rate observed in our study.[35] We found that lipid-lowering agents (eg, statin medication) had a relatively low nonadherence rate (15.2%), despite being used for asymptomatic conditions such as hyperlipidemia and cardiovascular disease. This may be owing to

Table 2. Demographic characteristics by medication class

CHARACTERISTIC	ANTIBIOTICS, n (%) (N=37,402)*	ANTI-DEPRESSANTS, n (%) (N=14,257)*	ANTI-HYPERTENSIVES, n (%) (N=18,609)*	BENZODIAZEPINES, n (%) (N=4448)*	BISPHOSPHONATES, n (%) (N=670)*	HYPOGLYCEMICS, n (%) (N=11,294)*	LIPID-LOWERING AGENTS, n (%) (N=4980)*
Sex							
• Male	11,623 (31.1)	4596 (32.2)	8463 (45.5)	1414 (31.8)	79 (11.8)	4609 (40.8)	2733 (54.9)
• Female	25,779 (68.9)	9661 (67.8)	10,146 (54.5)	3034 (68.2)	591 (88.2)	6685 (59.2)	2247 (45.1)
Age group, y							
• 18-44	14,980 (40.1)	6815 (47.8)	2981 (16.0)	1681 (37.8)	35 (5.2)	3436 (30.4)	394 (7.9)
• 45-64	13,421 (35.9)	5179 (36.3)	7912 (42.5)	1774 (39.9)	159 (23.7)	4554 (40.3)	2673 (53.7)
• 65-74	4634 (12.4)	1200 (8.4)	3964 (21.3)	579 (13.0)	203 (30.3)	1745 (15.5)	1304 (26.2)
• ≥75	4367 (11.7)	1063 (7.5)	3752 (20.2)	414 (9.3)	273 (40.7)	1,559 (13.8)	609 (12.2)
Income quintile							
• Q1 (lowest)	6911 (18.5)	2710 (19.0)	3309 (17.8)	639 (14.4)	135 (20.1)	2045 (18.1)	799 (16.0)
• Q2	7083 (18.9)	2845 (20.0)	3453 (18.5)	812 (18.3)	139 (20.7)	2156 (19.1)	969 (19.5)
• Q3	7274 (19.4)	2835 (19.9)	3777 (20.3)	878 (19.7)	130 (19.4)	2116 (18.7)	982 (19.7)
• Q4	8225 (22.0)	2997 (21.0)	4056 (21.8)	1035 (23.3)	122 (18.2)	2549 (22.6)	1136 (22.8)
• Q5 (highest)	6604 (17.7)	2451 (17.2)	3425 (18.4)	940 (21.1)	123 (18.4)	2062 (18.3)	990 (19.9)
• Missing	1305 (3.5)	419 (2.9)	589 (3.2)	144 (3.2)	21 (3.1)	366 (3.2)	104 (2.1)

*N represents the no. of prescriptions in each grouping.

Table 3. Primary nonadherence rates for the study cohorts by medication class, sex, and age group

	NONADHERENCE, n (%)*						
VARIABLE	ANTIBIOTICS	ANTI-DEPRESSANTS	ANTI-HYPERTENSIVES	BENZODIAZEPINES	BISPHOSPHONATES	HYPOGLYCEMICS	LIPID-LOWERING AGENTS
Total	**6552 (17.5)**	**1956 (13.7)**	**5634 (30.3)**	**694 (15.7)**	**185 (27.6)**	**881 (21.2)**	**775 (15.2)**
Sex							
• Male	1827 (4.9)	642 (4.5)	2607 (14.0)	220 (5.0)	27 (4.0)	452 (10.9)	408 (8.2)
• Female	4725 (12.6)	1314 (9.2)	3027 (16.3)	474 (10.7)	158 (23.6)	429 (10.3)	347 (7.0)
Age group, y							
• 18-44	3070 (8.2)	959 (6.7)	934 (5.0)	232 (5.2)	31 (4.6)	168 (4.0)	62 (1.2)
• 45-64	2204 (5.9)	724 (5.1)	2266 (12.2)	293 (6.6)	49 (7.3)	436 (10.5)	342 (6.9)
• 65-74	701 (1.9)	152 (1.1)	1244 (6.7)	95 (2.1)	42 (6.3)	186 (4.5)	224 (4.5)
• ≥75	577 (1.5)	121 (0.9)	1190 (6.4)	74 (1.7)	63 (9.4)	91 (2.2)	127 (2.6)

*N represents the no. of prescriptions in each grouping.

patients preferring medication over dietary changes[36] or, as Casula et al suggested, a difference in counseling, patients' motivation, or the perceived benefit of particular medications.[37] While the underlying reasons for nonadherence are beyond the scope of our study, our results confirmed the variability of patient characteristics as predictors of primary medication nonadherence.[2,13,38] Our models were unable to determine provider characteristics that predict primary medication nonadherence, reinforcing the concept of complex patient-provider interactions.

Our study did demonstrate patient demographic and clinical factors associated with primary medication nonadherence, including having pre-existing polypharmacy, frequently presenting to hospital, and having comorbidities. Still, the significant associations were not consistent across various indications. These findings diverge from the literature; Davidson et al found that an increasing number of medications was associated with improved medication adherence,[12] and a review by Seal et al noted several studies where primary medication nonadherence was associated with comorbidity and poorer health status.[13]

Table 4. Primary nonadherence C statistics, ORs, and 95% CIs for patient demographic and clinical characteristics by medication class: *Statistically significant differences are presented in boldface.*

	MEDICATION CLASS						
VARIABLE	ANTIBIOTICS (N=37,402)*	ANTI-DEPRESSANTS (N=14,257)*	ANTI-HYPERTENSIVES (N=18,609)*	BENZODIAZEPINES (N=4448)*	BISPHOSPHONATES (N=670)*	HYPOGLYCEMICS (N=11,294)*	LIPID-LOWERING AGENTS (N=4980)*
C statistic	0.59	0.56	0.57	0.61	0.69	0.62	0.59
Sex, OR (95% CI)							
• Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref
• Female	**0.87 (0.82-0.93)**	0.99 (0.89-1.10)	**1.08 (1.01-1.15)**	0.94 (0.78-1.12)	0.94 (0.78-1.12)	**1.23 (1.14-1.33)**	0.99 (0.84-1.16)
Age group, y, OR (95% CI)							
• 18-44	**0.55 (0.49-0.61)**	**0.78 (0.63-0.97)**	0.93 (0.83-1.04)	1.19 (0.87-1.63)	**0.04 (0.01-1.12)**	**1.29 (1.12-1.47)**	1.35 (0.96-1.91)
• 45-64	**0.74 (0.67-0.82)**	**0.79 (0.64-0.98)**	**1.11 (1.02-1.22)**	1.08 (0.80-1.44)	0.69 (0.43-1.12)	**1.38 (1.22-1.56)**	**1.74 (1.38-2.21)**
• 65-74	**0.81 (0.72-0.91)**	0.89 (0.69-1.15)	1.02 (0.92-1.12)	1.14 (0.81-1.60)	1.26 (0.49-2.01)	**1.18 (1.02-1.36)**	1.26 (0.98-1.61)
• ≥75	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Income quintile, OR (95% CI)							
• Q1 (lowest)	**0.85 (0.78-0.93)**	1.10 (0.94-1.30)	**1.23 (1.11-1.37)**	1.31 (0.98-1.75)	1.55 (0.84-2.86)	1.12 (0.99-1.28)	0.88 (0.68-1.15)
• Q2	0.97 (0.89-1.06)	1.00 (0.85-1.17)	**1.15 (1.04-1.27)**	0.87 (0.68-1.12)	1.18 (0.67-2.11)	1.11 (0.98-1.26)	0.91 (0.71-1.17)
• Q3	1.04 (0.95-1.14)	0.99 (0.84-1.15)	**1.32 (1.19-1.46)**	1.29 (0.99-1.67)	1.36 (0.75-2.46)	1.13 (1.00-1.29)	0.98 (0.76-1.26)
• Q4	1.10 (1.00-1.20)	1.05 (0.90-1.23)	**1.14 (1.03-1.25)**	1.20 (0.93-1.53)	1.06 (0.58-1.90)	1.02 (0.90-1.15)	1.01 (0.79-1.29)
• Q5 (highest)	Ref	Ref	Ref	Ref	Ref	Ref	Ref
• Missing	**1.22 (1.03-1.44)**	1.00 (0.74-1.35)	1.05 (0.87-1.27)	**0.65 (0.42-0.99)**	1.26 (0.41-3.86)	0.89 (0.71-1.12)	1.94 (0.95-3.95)
No. of hospitalizations,† OR (95% CI)							
• 0	Ref	Ref	Ref	Ref	Ref	Ref	Ref
• 1-2	0.99 (0.90-1.09)	1.06 (0.90-1.26)	1.02 (0.91-1.14)	**1.40 (1.01-1.93)**	1.58 (0.87-2.86)	**0.85 (0.74-0.98)**	0.96 (0.72-1.29)
• ≥3	1.03 (0.77-1.38)	0.80 (0.51-1.27)	1.03 (0.75-1.40)	1.13 (0.44-2.89)	0.33 (0.04-2.67)	0.77 (0.52-1.13)	0.65 (0.28-1.52)
No. of ambulatory visits,† OR (95% CI)							
• 0	Ref	Ref	Ref	Ref	Ref	Ref	Ref
• 1-2	1.04 (0.93-1.16)	1.17 (0.95-1.43)	0.96 (0.81-1.12)	1.21 (0.84-1.76)	1.12 (0.31-4.07)	1.06 (0.88-1.27)	1.31 (0.92-1.86)
• 3-9	1.09 (0.98-1.22)	1.14 (0.94-1.39)	0.88 (0.75-1.03)	1.13 (0.91-1.85)	1.03 (0.30-3.52)	0.94 (0.79-1.12)	1.34 (0.96-1.88)
• ≥10	1.13 (1.00-1.29)	1.05 (0.84-1.32)	0.89 (0.75-1.05)	**1.57 (1.04-2.38)**	1.11 (0.30-4.06)	1.03 (0.85-1.25)	1.05 (0.71-1.56)

Table 4 *continued on page 526*

Table 4 *continued from page 525*

VARIABLE	MEDICATION CLASS						
	ANTIBIOTICS (N=37,402)*	ANTI-DEPRESSANTS (N=14,257)*	ANTI-HYPERTENSIVES (N=18,609)*	BENZODIAZEPINES (N=4448)*	BISPHOSPHONATES (N=670)*	HYPOGLYCEMICS (N=11,294)*	LIPID-LOWERING AGENTS (N=4980)*
No. of ED visits,† OR (95% CI)							
• 0	Ref	Ref	Ref	Ref	Ref	Ref	Ref
• 1-2	**0.79 (0.72-0.87)**	1.01 (0.87-1.18)	**1.26 (1.12-1.41)**	1.09 (0.81-1.46)	1.57 (0.86-2.86)	1.09 (0.96-1.25)	1.12 (0.84-1.50)
• ≥3	**0.61 (0.51-0.72)**	0.76 (0.58-1.00)	1.25 (0.97-1.60)	0.93 (0.52-1.65)	1.53 (0.51-4.56)	0.99 (0.75-1.30)	1.92 (0.85-4.34)
No. of prescriptions,† OR (95% CI)							
• 0-2	Ref	Ref	Ref	Ref	Ref	Ref	Ref
• 3-5	0.99 (0.92-1.07)	**1.22 (1.07-1.38)**	**0.75 (0.69-0.82)**	1.10 (0.89-1.37)	0.78 (0.45-1.34)	0.96 (0.86-1.07)	1.06 (0.86-1.31)
• ≥6	0.97 (0.89-1.06)	**1.42 (1.23-1.65)**	**0.69 (0.63-0.76)**	1.21 (0.94-1.56)	0.65 (0.36-1.15)	0.91 (0.81-1.03)	1.14 (0.90-1.45)
Charlson Comorbidity Index,[28] OR (95% CI)							
• 0	Ref	Ref	Ref	Ref	Ref	Ref	Ref
• 1-2	**1.20 (1.11-1.29)**	0.98 (0.86-1.12)	1.13 (1.05-1.22)	**0.80 (0.65-1.00)**	1.20 (0.77-1.86)	**0.88 (0.79-0.97)**	0.91 (0.75-1.09)
• ≥3	1.07 (0.91-1.25)	**0.72 (0.54-0.95)**	0.99 (0.84-1.15)	**0.56 (0.34-0.91)**	1.03 (0.48-2.23)	**0.71 (0.58-0.88)**	0.76 (0.52-1.11)

ED—emergency department, OR—odds ratio, Ref—reference category.
*N represents the number of prescriptions in each grouping.
†Based on the 365 days prior to the index date.

However, since much of the existing literature has focused exclusively on a specific setting or single disease population, our study adds a more comprehensive view of drug initiation and adherence within primary care.

The results of our study share an important similarity with other medication nonadherence literature. Much of the literature suggests a compelling driver of the patient's decision to fill their prescription is having insurance that covers the cost of the medication.[1,39] In our models, several medication classes indicated an increased likelihood of adherence in the most-affluent income quintile; however, this finding was not consistent. Nonetheless, while drug coverage deductibles are lower in less-affluent income quintiles, these costs may still present a barrier for patients with limited financial means. Thus, the results of this study continue to reinforce the important role of the primary care provider in working with patients to consider sustainable drug management or alternative plans.[14,40]

Our findings suggest that providers may not be able to use particular attributes to predict which patients will or will not fill a new prescription, adding to the notion that primary medication nonadherence is complex and often influenced by varied and competing influences.[2,38,41] Based on the poor predictability of our models, caution is required when considering characteristic-based interventions or prediction tools to improve primary medication nonadherence. Rather, an individual approach based on knowledge of the patient and their values is preferable in order to understand the influences and motivations associated with primary medication nonadherence and address the issue.

Limitations

This study had several key limitations. First, since we used medication dispensing information from administrative data linked only to EMR prescribing data of consenting providers, it may not be fully representative of the entire population, despite the large numbers of prescriptions assessed. Further, we were unable to include the cost of individual medication or copayment amounts in our analyses. We also cannot be certain of the exact indication for each prescription or the clinical circumstances related to the interaction that led to the prescription because a review of narrative text was outside the scope of this study. Finally, we did not study the causes of primary medication nonadherence.

Conclusion

Primary medication nonadherence is common, occurring more often with asymptomatic conditions. Overall, we were unable to identify a consistent pattern of association related to patient demographic, clinical, or provider

characteristics and primary nonadherence, indicating the need for individual, patient-centred approaches to improving primary medication nonadherence.

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Contributors

All authors contributed to the concept and design of the study; data gathering, analysis, and interpretation; and preparing the manuscript for submission.

Competing interests

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