Research

Prevalence and predictors of primary nonadherence to medications prescribed in primary care

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Abstract

Background: Most research on medication adherence has focused on secondary nonadherence and persistence to therapy. Medication prescriptions that are never filled by patients (primary nonadherence) remain understudied in the general population.

Methods: We linked prescribing data from primary care electronic medical records to comprehensive pharmacy dispensing claims between January 2013 and April 2019 in British Columbia (BC) to estimate primary nonadherence, defined as failure to dispense a new medication or its equivalent within 6 months of the prescription date. We used hierarchical multivariable logistic regression to determine prescriber, patient and medication factors associated with primary nonadherence among community-dwelling patients in primary care.

Results: Among 150 565 new prescriptions to 34 243 patients, 17% of prescriptions were never filled. Primary nonadherence was highest for drugs prescribed mostly on an as-needed basis, including topical corticosteroids (35.1%) and antihistamines (23.4%). In multivariable analysis, primary nonadherence was lower for prescriptions issued by male prescribers (odds ratio [OR] 0.66, 95% confidence interval [CI] 0.50–0.88). Primary nonadherence decreased with patient age (OR 0.91, 95% CI 0.90–0.92 for each additional 10 years) but increased with polypharmacy among patients aged 65 years or older. Patients filled more than 82% of their medication prescriptions within 2 weeks after their primary care provider visit.

Interpretation: The prevalence of primary nonadherence to new prescriptions was 17%. Interventions to address primary nonadherence could target older patients with multiple medication use and within the first 2 weeks of the prescription issue date.

Pharmacologic therapy initiation, compliance and continuation are important components of disease management.[1] Medication nonadherence is a complex, multidimensional and multifaceted problem that contributes to suboptimal health outcomes and poses substantial challenges and financial burdens on the health care system.[2–6] It is estimated that as much as 50% of patients worldwide do not take their medications as prescribed.[7] Although the causes are well understood, improving medication adherence has proven difficult.[8] Primary and secondary nonadherence are separate subsets of medication nonadherence. Unlike secondary nonadherence — which occurs when patients fill or refill the prescription but do not use it as prescribed — in primary nonadherence, patients do not fill the initial prescription or an appropriate alternative within a clinically acceptable time period.[9,10]

Most studies of medication nonadherence that rely on claims data for dispensed prescriptions measure secondary adherence, persistence or discontinuation to pharmacotherapy, but fail to account for medication initiation.[10] Research examining primary nonadherence is limited,[11] with most studies relying on self-reported measures of nonadherence to incident prescriptions via surveys,[12,13] which are hampered by methodologic limitations such as small sample sizes and self-reporting bias.[14] Other studies rely on electronic prescriptions of patients discharged from hospital,[5,15,16] which constitute a subsample of patients with higher comorbidities and a distinct, short-lived patient–clinician relationship. Relatively recent shifts from paper prescriptions to electronic systems make studying primary nonadherence more feasible on larger and more representative samples.[17]

The literature has reported substantial variation in primary nonadherence, with estimates ranging from as little as 1.94% of incident prescriptions never filled to as much as 75%.[10] These studies varied widely in their operational definition of primary nonadherence, unit of measure (patient v. prescription level), disease group, study design and health care settings,[18–23] which exacerbated the methodological challenges in synthesizing these study findings.[1,24,25] Despite the heterogeneity of these studies, common factors associated with primary nonadherence included younger age, number of concurrent medications and higher out-of-pocket costs.[25]

In Canada, primary nonadherence constitutes a major research gap, and the behaviour of not filling prescriptions for new medications is not well understood. An early study on primary nonadherence was conducted in primary care in Quebec and found that nearly one-third of incident prescriptions remain unfilled.[26] Others were limited to investigating primary nonadherence in disease-specific cohorts.[27,28] Understanding primary nonadherence is important as it is the first point at which patients fail to initiate their medication therapy and could lead to substantial health implications. Nevertheless, this behaviour may be appropriate for some medications prescribed on an as-needed basis, including the "wait-and-see approach." We sought to assess primary nonadherence among community-dwelling patients in British Columbia (BC) and explore its predictors using a novel linkage of prescribing data sets from electronic medical records with pharmacy dispensing data sets.

Methods

Data sources and study design

We used linked electronic medical records and administrative data sets from Population Data BC using unique encoded identifiers, including prescribing data sets from the electronic medical records of the BC Canadian Primary Care Sentinel Surveillance Network (BC CPCSSN) database,[29] the BC PharmaNet prescription drug claims database[30] and the BC Medical Services Plan consolidation files.[31] These data sets are described in further detail in Appendix 1A, available at www.cmaj.ca/lookup/doi/10.1503/cmaj.221018/tab-related-content. We also used the Health Canada Drug Product Database[32] to retrieve medication information such as active ingredient (AIG) codes and the anatomic classification system.

Data from CPCSSN are used for surveillance and research and are considered moderately representative of the Canadian patient population, with slight skewness to older adults and female patients.[33,34] The prescribing data from CPCSSN recorded all prescriptions issued by CPCSSN providers (e.g., family physicians, nurse practitioners) regardless of whether they were eventually filled. Data from CPCSSN included information on demographic characteristics of providers, primary care encounters and medications prescribed. The dispensing claims from PharmaNet included data on prescriptions that patients filled and, as such, constituted a subset of prescriptions written by CPCSSN providers.

Finally, we used the Medical Services Plan consolidation files to obtain patients' sociodemographic characteristics and registration status with the provincial Medical Services Plan.

Study population and time period

The study cohort included all individuals who had a documented visit to their primary care provider and who were written at least 1 medication prescription between Jan. 1, 2013, and Apr. 31, 2019. We included all individuals registered for at least 1 full year with the Medical Services Plan, unless they were newborns or had died. We excluded those receiving drug coverage through the federal government, such as First Nations people (on reserve) and veterans, for whom data were unavailable. We also excluded CPCSSN records with missing data in the medication field and duplicate records. Informed by known factors from the literature and Andersen's framework of health service use,[35] we hypothesized that primary nonadherence was associated with predisposing factors of patients and prescribers (sex and age), enabling resources (socioeconomic status) and need characteristics (drug type and concurrent medication use).

Outcomes and measures

Throughout this study, we defined primary nonadherence as failure to fill a new prescription or its equivalent within 6 months of the prescription issue date. As illustrated in Appendix 1, Figure S1, a new prescription was a medication defined by Health Canada AIG codes that had not been prescribed within the past 12 months. For each identified new medication prescribed by a CPCSSN provider, we searched, by AIG code, for a medication match in the dispensing claims for up to 6 months of the prescription issue date. We defined equivalent prescriptions as those with the same first 7 digits of the AIG code. This would include the same active ingredient or combination of ingredients from different manufacturers to cover generic medications. We chose the 6-month window to give patients enough time to fill their prescriptions (Appendix 1, Figure S1). The unit of analysis was prescription, and every match found constituted a count of adherence for the respective prescription. We measured primary nonadherence for patients who had 1 or more new prescriptions. The prevalence of primary nonadherence was expressed as the number of new prescriptions that were not filled divided by the total number of new prescriptions written. For filled prescriptions, we estimated the number of days to dispense a medication prescription written by a primary care provider.

Statistical analysis

We generated descriptive summary statistics and estimated the binary association between primary nonadherence and the characteristics of prescribers, patients and medications. We used a multivariable hierarchical logistic regression analysis to examine which prescriber, patient and medication covariates at the time of prescription issue were associated with primary nonadherence, while adjusting for clustering of observations within each nesting level.[36–38] Data were structured in multiple levels with patients naturally nested within unique primary care providers

(i.e., no crossover). We included 2 sets of random effects at both the prescriber and patient levels and assumed flexible covariance structures for residuals, and we calculated the conditional correlation coefficients (Appendix 1B).[37] We tested for suspected interaction terms between patient age and the variables for neighbourhood income quintile, number of medications prescribed in the past year and therapeutic category, as well as patient sex and prescriber sex. We retained only interactions that reached statistical significance ($p < 0.05$). We conducted all analyses using SAS version 9.4 (SAS Institute Inc.).

Ethics approval

We received ethics approval from the Behavioural Research Ethics Board at the University of British Columbia (H18–00059).

Results

Analytical cohort

Figure 1 shows the analytical cohort selection. After we applied our exclusion criteria, 419 723 prescriptions were left; of these, 150 565 were considered new prescriptions written by CPCSSN providers to 34 243 patients and constituted the primary study cohort (Figure 1).

Prevalence and predictors of primary nonadherence

The study cohort included 57 primary care providers and 34 243 patients. Among both providers and patients, 60% were female and mean age was mid-40s (Table 1). Of 150 565 new prescriptions, 25 649 were not filled within 6 months of the prescription issue date, representing an overall prevalence of primary nonadherence of 17.0%. These prescriptions were issued to 15 134 patients (44.2%) who failed to fill at least 1 prescription written for them over the study period. On the other hand, the remaining 124 916 prescriptions (83.0%) were filled by 30 896 patients (90.2%) (Figure 1). Patients who received more than 1 new prescription could be in both groups.

In unadjusted comparisons, primary nonadherence was lowest for prescriptions issued by prescribers aged 35 years or younger (17.1%) and male prescribers (15.1%) (Table 2). Although prevalence of primary nonadherence was similar between male and female patients, it was slightly higher among male versus female patients of female providers (20.7% v. 18.9%, $p < 0.001$) and among female versus male patients of male providers (15.4% v. 14.7%, $p = 0.01$) (Appendix 1, Table S1). Primary nonadherence decreased with age, with patients in older age groups more likely to fill new prescriptions. Primary

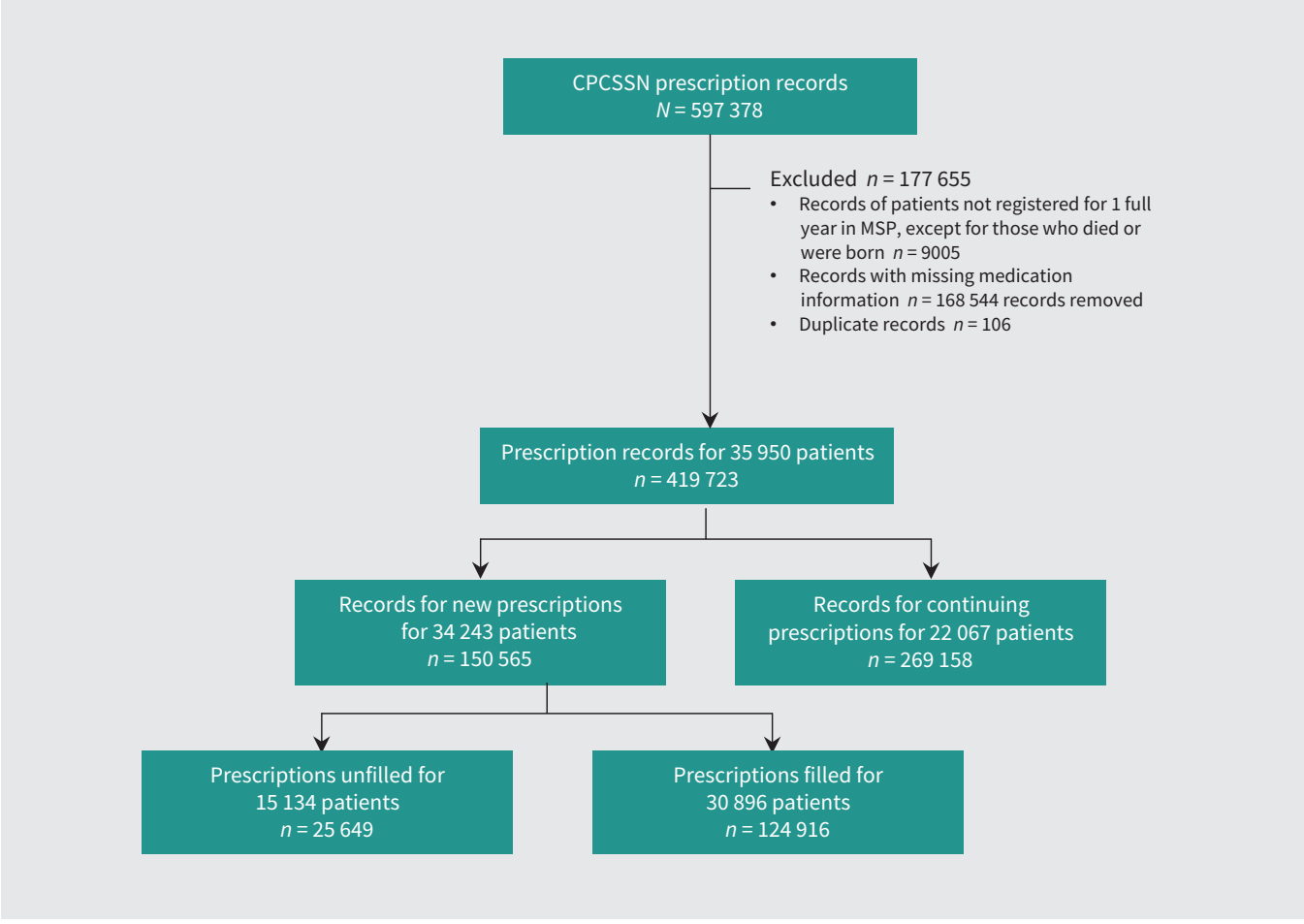

Figure 1: Flow diagram showing identification of the analytical cohort of new prescriptions written by Canadian Primary Care Sentinel Surveillance Network (CPCSSN) providers to patients. Note: MSP = Medical Services Plan.

Table 1: Characteristics of patients written new prescriptions and their primary care providers in British Columbia

Characteristic	Total no. (%)* of patients and their primary care providers	No. (%)* of patients who filled all their prescriptions and their primary care providers	No. (%)* of patients who failed to fill at least 1 prescription and their primary care providers
Primary care providers	***n* = 57**	***n* = 57**	***n* = 56**
Sex			
Female	34 (59.7)	34 (60.0)	33 (58.9)
Male	23 (40.3)	23 (40.3)	23 (41.1)
Age, mean ± SD, yr	43.1 ± 8.7	43.0 ± 8.6	43.9 ± 9.0
Age group, yr			
≤ 35	8–13 (14–22.8)	8–3 (14–22.8)	6–11 (10.7–19.6)
36–54	20 (35.1)	20 (42.9)	24 (42.9)
≥ 55	< 6 (< 10.5)	< 6 (< 10.5)	< 6 (< 10.5)
Missing	24 (42.1)	24 (42.1)	23 (41.1)
Patients	***n* = 34 243**	***n* = 30 896**	***n* = 15 134**
Sex			
Female	20 528 (59.9)	18 656 (60.4)	9568 (63.2)
Male	13 619 (39.8)	12 155 (39.3)	5529 (36.5)
Unknown	96 (0.3)	85 (0.3)	37 (0.2)
Age, mean ± SD, yr	44.1 ± 23.6	45.6 ± 23.1	44.7 ± 23.9
Age group, yr			
≤ 18	5905 (17.2)	4663 (15.1)	2465 (16.3)
19–44	11 300 (33.0)	10 127 (32.8)	5050 (33.4)
45–64	9385 (27.4)	8773 (23.7)	4034 (26.7)
≥ 65	7653 (22.4)	7333 (23.7)	3585 (23.7)
Neighbourhood income quintile			
1 (lowest income quintile)	4864 (14.2)	4324 (14.0)	2246 (14.8)
2	7002 (20.4)	6359 (20.6)	3071 (20.3)
3	7018 (20.5)	6321 (20.5)	3063 (20.2)
4	7596 (22.2)	6866 (22.2)	3370 (22.3)
5 (highest income quintile)	7477 (21.9)	6781 (22.0)	3232 (21.4)
Missing or NA	286 (0.8)	245 (0.8)	152 (1.0)
Health authority			
Interior	6606 (19.3)	6228 (20.2)	2360 (15.6)
Fraser	12 556 (36.7)	11 383 (36.8)	6113 (40.4)
Vancouver Coastal	13 037 (38.1)	11 409 (36.9)	5876 (38.8)
Vancouver Island	1914 (5.6)	1763 (5.7)	730 (4.8)
Northern	94 (0.3)	79 (0.26)	36 (0.24)
Missing or NA	36 (0.1)	34 (0.1)	19 (0.1)

Note: NA = not applicable, SD = standard deviation.
*Unless otherwise specified.

nonadherence prevalence was heterogeneous across therapeutic drug categories, with the highest prevalence among dermatological drugs (27.0%) and the lowest among cardiovascular medications (9.1%) (Table 2). Primary nonadherence prevalence was higher for drugs that could be prescribed for rapid symptom relief or on an as-needed basis, such as topical corticosteroids (35.1%) and antihistamines (23.4%) (Appendix 1, Table S2). Most new prescriptions (82.1%) were dispensed within 2 weeks, with more than two-thirds dispensed within 3 days of the prescription issue date (Figure 2).

Table 2: Unadjusted primary nonadherence prevalence by primary care provider, patient and medication characteristics in British Columbia

Characteristic	No. (%) of all new prescriptions *n* = 150 565	No. of new prescriptions unfilled *n* = 25 649	Frequency of primary nonadherence (%)
Primary care providers			
Sex			
Female	69 879 (46.4)	13 490	19.3
Male	80 686 (53.6)	12 159	15.1
Age group, yr			
≤ 35	14 015 (9.3)	2395	17.1
36–54	57 652 (38.3)	10 313	17.9
≥ 55	26 688 (17.7)	4754	17.8
Missing	52 210 (34.7)	8187	15.7
Patients			
Sex			
Female	95 852 (63.7)	16 657	17.4
Male	54 403 (36.1)	8946	16.4
Unknown	310 (0.2)	46	14.8
Age group, yr			
≤ 18	11 854 (7.8)	3255	27.5
19–44	40 016 (26.6)	8095	20.2
45–64	47 044 (31.2)	7350	15.6
≥ 65	51 651 (34.3)	6949	13.5
Neighbourhood income quintile			
1 (lowest income quintile)	22 347 (14.8)	4005	17.9
2	31 113 (20.7)	5293	17
3	31 019 (20.6)	5125	16.5
4	32 214 (21.4)	5556	17.3
5 (highest income quintile)	32 744 (21.8)	5417	16.5
Missing or NA	1128 (0.7)	253	22.4
Health authority			
Interior	27 463 (18.2)	3653	13.3
Fraser	65 287 (43.4)	11 328	17.4
Vancouver Coastal	49 433 (32.8)	9448	19.1
Vancouver Island	7961 (5.3)	1139	14.3
Northern	294 (0.2)	56	19.1
Missing or NA	127 (0.1)	25	19.7
No. of medications prescribed in the past 12 months			
0	62 715 (41.7)	10 933	17.4
1–3	46 960 (29.9)	7800	17.4
4–6	16 701 (11.1)	2750	16.5
≥ 7	26 189 (17.4)	4166	15.9
Drug therapeutic category			
Alimentary tract	11 663 (7.8)	2041	17.5
Cardiovascular	19 405 (12.9)	1758	9.1
Dermatological	14 334 (9.5)	3872	27.0
Genitourinary and sex hormones	12 937 (8.6)	2154	16.7
Anti-infectives	22 633 (15.0)	4947	21.9
Central nervous system	28 662 (19.0)	3745	13.1
Respiratory system	18 196 (12.1)	3363	18.5
Other*	22 735 (15.1)	3763	16.5

Note: NA = not applicable.
*Blood agents, hormones, antineoplastics, musculoskeletal, antiparasitic, sensory organs and various categories.

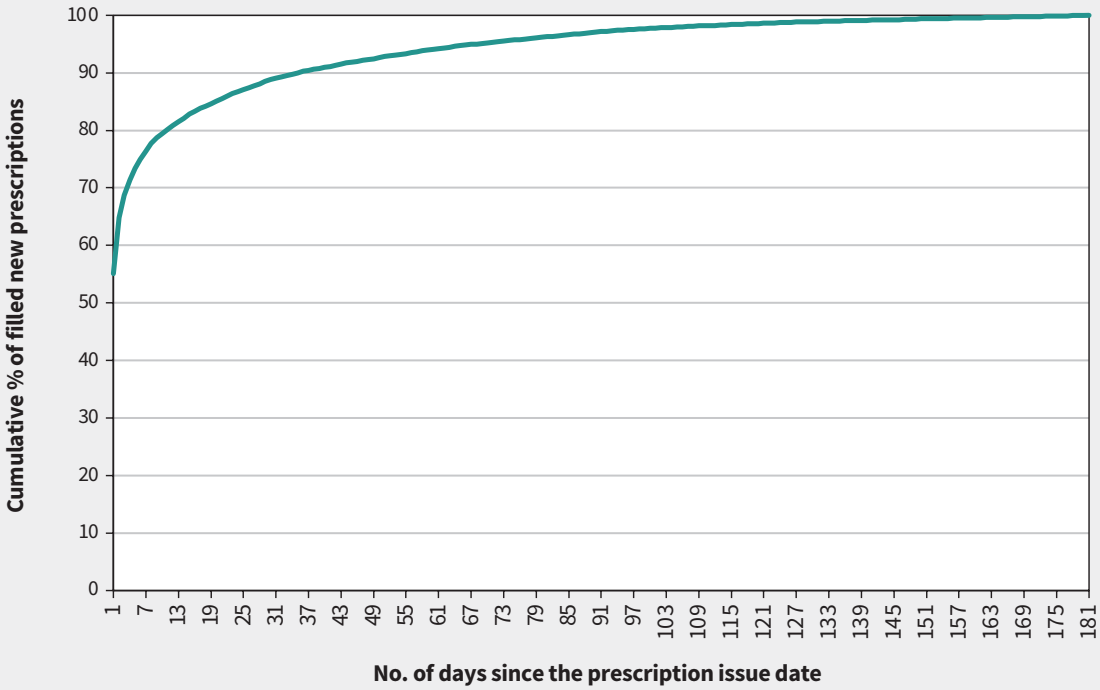

Figure 2: Cumulative frequency of filled new prescriptions written by Canadian Primary Care Sentinel Surveillance Network primary care providers in British Columbia.

Results of multivariable hierarchical logistic regression

Odds of primary nonadherence were lower for prescriptions issued by male providers (odds ratio [OR] 0.66, 95% confidence interval [CI] 0.50–0.88) (Table 3). Among patient characteristics, primary nonadherence decreased with increasing patient age (OR 0.91, 95% CI 0.90–0.92 for each additional 10 years). After multivariable adjustment, patient–provider sex discordance was not significantly associated with primary nonadherence (p = 0.19). Compared with anti-infectives, primary nonadherence was significantly greater for dermatological agents (OR 1.36, 95% CI 1.28–1.45) and the lowest for cardiovascular agents (OR 0.46, 95% CI 0.42–0.50).

Associations of neighbourhood income quintile, number of medications prescribed in the past 12 months, and therapeutic category with primary nonadherence differed across patient age. Among patients younger than 65 years, compared with those residing in the highest neighbourhood income quintile, those residing in the second lowest quintile had slightly higher odds of primary nonadherence (OR 1.06, 95% CI 0.99–1.14), although not statistically significant. This association was not observed among patients aged 65 years and older (OR 0.92, 95% CI 0.80–1.05; p for interaction between patient age and income quintile = 0.004). Among patients aged 65 years and older, compared with those prescribed no other medications in the past year, primary nonadherence was higher among those prescribed 1–3 (OR 1.16, 95% CI 1.05–1.29), 4–6 (OR 1.25, 95% CI 1.11–1.41), or 7 or more medications (OR 1.26, 95% CI 1.14–1.40). In contrast, this association was not statistically significant for patients younger than 65 years (p for interaction between patient age and number of medications prescribed in the past 12 months < 0.0001). Except for respiratory agents, the odds of primary nonadherence for those aged 65 years and older were lower across therapeutic drug categories than those younger than 65 years (p for interaction between patient age and therapeutic category < 0.0001).

Interpretation

In this study of primary care prescriptions, we found that 17% of new prescriptions were never filled. The odds of primary nonadherence were higher for younger patients, those who received primary care services from female prescribers, and older patients who were prescribed more medications. Across therapeutic categories, the odds of primary nonadherence were lowest for cardiovascular system agents and highest for dermatological agents. We leveraged novel data linkages to present substantial evidence on the extent of nonadherence to incident prescriptions and its predictors in primary care in BC.

The CPCSSN is the first and only pan-Canadian multidisease electronic medical records surveillance system that tracks prescription records across the province, and BC PharmaNet is the largest and most comprehensive population-based data system on prescription drug dispensing in Canada. The ability to link prescribing data to filled claims in BC is advantageous because pharmacy dispensing data in other jurisdictions are often not complete and often reflective of drugs on the public formulary. More than 80% of new prescriptions were dispensed in 2 weeks, which suggests that developing interventions to encourage patients to initiate their therapy within this time frame could improve primary adherence.

Table 3: Association of primary nonadherence with primary care provider, patient and medication characteristics in the overall study cohort and across patient age

	Overall study cohort		Patients aged ≥ 65 yr		Patients aged < 65 yr	
Characteristic	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Provider sex						
Female	1	–	1	–	1	–
Male	0.66	0.50–0.88	0.68	0.49–0.96	0.68	0.52–0.88
Odds per 10-year increase in provider age	1.05	0.97–1.13	1.05	0.92–1.19	1.02	0.94–1.11
Patient sex						
Female	1	–	1	–	1	–
Male	1.03	0.98–1.08	1.1	1.00–1.21	0.99	0.94–1.04
Odds per 10-year increase in patient age	0.91	0.90– 0.92	1.05	1.00– 1.10	0.89	0.88–0.90
Neighbourhood income quintile						
5 (highest income quintile)	1	–	1	–	1	–
4	1.06	0.99–1.13	1.06	0.93–1.21	1.06	0.98–1.13
3	1.03	0.97–1.10	0.95	0.84–1.08	1.05	0.98–1.13
2	1.03	0.96–1.10	0.92	0.80–1.05	1.06	0.99–1.14
1 (lowest income quintile)	1.04	0.97–1.11	1.03	0.89–1.19	1.04	0.96–1.12
No. of medications prescribed in the past year						
No other medication	1	–	1	–	1	–
1–3	1.01	0.97–1.06	1.16	1.05–1.29	0.98	0.93–1.03
4–6	1.11	1.04–1.18	1.25	1.11–1.41	1.05	0.98–1.14
≥ 7	1.11	1.04–1.18	1.26	1.14–1.40	1.02	0.94–1.10
Drug therapeutic category						
Anti-infectives	1	–	1	–	1	–
Alimentary tract	0.89	0.83–0.96	0.63	0.55–0.73	1.04	0.95–1.14
Cardiovascular	0.46	0.42–0.50	0.37	0.33–0.42	0.55	0.49–0.61
Dermatological	1.36	1.28–1.45	1.29	1.12–1.48	1.39	1.29–1.49
Genitourinary and sex hormones	0.71	0.66–0.77	0.65	0.54–0.78	0.74	0.68–0.80
Nervous system	0.56	0.53–0.60	0.51	0.45–0.58	0.59	0.55–0.63
Respiratory	0.82	0.77–0.88	0.86	0.76–0.99	0.81	0.75–0.87
Other*	0.75	0.70–0.79	0.64	0.57–0.73	0.8	0.74–0.86

Note: CI = confidence interval, OR = odds ratio from hierarchical logistic regression.
*Blood agents, hormones, antineoplastics, musculoskeletal, antiparasitic, sensory organs and various categories.

To date, the lack of a standardized terminology, operational definition and measurement methods of primary nonadherence has limited our understanding of the extent to which patients do not avail themselves of prescriber-ordered pharmaceutical treatment and has exacerbated the challenges with comparing its prevalence across different health care settings.[9,10,39] Our study findings are consistent with those of a meta-analysis of primary nonadherence in common chronic diseases, which estimated a similar prevalence for primary nonadherence in North America.[39] In contrast, another meta-analysis reported a lower rate of primary nonadherence to prescriptions, but Cheen and colleagues' estimate was higher when measured at the patient level.[25] Similarly, we reported higher primary nonadherence prevalence when patients were the unit of measure assessed, as opposed to prescriptions. This variability highlights specific medication attributes, patients' clinical characteristics and disease features associated with this behaviour. This may present, to a certain degree, either the perspective of patients regarding the value they place on the treatment offered to them by prescribers, or the weight they place on their concerns about medication adverse effects relative to the value of anticipated treatment benefits.

Primary nonadherence odds were higher when prescriptions were written by female prescribers, a finding that highlights the primary care provider's role in initiating medicines and suggests that lack of trust or confidence in the prescriber may be an important mechanism of primary nonadherence. This finding concurs with a previous study that found that prescriptions written by female providers were less likely to be filled.[40] This association, however, was not found in other studies, and the discrepancies could be explained by other unmeasured provider-based confounding factors, such as provider characteristics and patient–provider communication.

Patients' biological sex was not an important factor for primary nonadherence in our study population, but about two-thirds of our study cohort were females. This is in line with previous primary care research suggesting that females are more likely to seek care[41] for themselves and their children more frequently than males.

Although socioeconomic disadvantages are likely to increase primary nonadherence, particularly among older people,[13] we did not detect significant differences in primary nonadherence by neighbourhood income quintiles. This indicator is a proxy measure of area-level income and may not necessarily reflect individual socioeconomic status. In literature, patient sex and socioeconomic status have not been consistently associated with medication adherence.[42] In concordance with our study findings, lower odds of primary nonadherence have been reported among older patients.[43] Interestingly, we found that patients aged 65 years and older who were prescribed a higher number of other drugs were less likely to initiate their treatment, but this association was not observed for patients younger than 65 years. Multiple medication use presents an additional barrier to medication adherence,[44] translated into increased health care costs and regimen complexity,[45] and has previously shown associations with lower primary adherence among older patients.[5] The observed differences with polypharmacy are likely also related to out-of-pocket costs, which constitute a substantial barrier to treatment adherence[46] and initiation.[47] Our study could not directly measure access to drug coverage and the effects of out-of-pocket costs, which constitute potential confounding for not having these data. However, previous research found primary nonadherence to monotonically increase with out-of-pocket expenditures,[48] with younger patients and those with newly diagnosed chronic conditions being more price-sensitive and less likely to start medication therapy.[47,48]

The nonadherence prevalence varied by therapeutic classes and subgroups,[49] which could reflect patients' preferences for lifestyle changes or medications that provide immediate symptom relief rather than clinical benefits. The relatively higher observed primary nonadherence in dermatological agents and anti-infectives could partly reflect that these prescriptions were written on an as-needed approach or prescribed for minor conditions. A lesser degree of nonadherence and, notably, more than 1 in 10 medications for mostly preventive common chronic medical conditions — such as diabetes, hypertension and dyslipidemia — were never filled. These findings are remarkable as they likely reflect the asymptomatic nature of these conditions, the medical predisposition of patients and the duration of their pharmaceutical therapy, which require clinical, behavioural and financial commitments, respectively. Previous qualitative research highlighted additional barriers, such as patients' preferences for alternative management of hypertension through lifestyle balance and complementary medications.[50]

Our study estimated that 1 in 6 newly prescribed medications in primary care are never filled. This finding suggests that medication nonadherence measures that do not account for medication initiation tend to underestimate the overall prevalence of medication nonadherence. Although there is no gold standard of what would constitute adequate adherence,[42] our estimate of primary nonadherence for chronic medical conditions in primary care may be concerning, particularly given that 44% of the Canadian adult population consist of patients with at least 1 chronic condition.[51] The effects of primary nonadherence for common chronic conditions on the use of health care resources are unknown. We do not yet understand how it is related to adverse health outcomes and patient-reported outcomes[1] and whether these patients adopt their recommended pharmacotherapy later.

Limitations

Secondary data not primarily collected for research purposes might be missing information important for comprehensively understanding adherence to new medications. As such, we cannot rule out residual confounding or selection effects that may influence primary nonadherence. For example, we could not capture information on patients' demographics, such as Indigenous identity, race or ethnicity, which are possible confounders. In our study setting, we were not able to measure patients' perceptions about the value or preferences for their treatment, their concerns about adverse effects of medications, trust and communication with primary care providers, and primary health care continuity,[42,52] when these factors might be related to unidentified confounding factors to medication adherence.

Moreover, we were not able to describe how medication costs and insurance coverage were associated with primary nonadherence, because cost-related data were available only in the dispensing claims for prescriptions classified as adherent. A further limitation of our data is that we were unable to measure whether patients had access to supplemental private drug insurance that would have reduced their out-of-pocket costs. Finally, the study cohort was limited to patients who sought health services from sentinel primary care providers contributing to CPCSSN. Although these patients are reasonably representative of the Canadian population, with slight overrepresentation of older adults and female patients, providers are likely less representative of family physicians.[33,53] This may limit the generalizability of these results to providers in other primary care practices.

Conclusion

The unique prospect of data linkages between electronic medical records prescribing data and administrative pharmacy dispensing data enabled us to measure primary nonadherence in primary care. We found that 17% of new prescriptions remain unfilled in this population of patients. Interventions to address

primary nonadherence could prioritize targeting older patients with multiple medication use and within the first 2 weeks of the prescription order. Future research should examine the impact of primary nonadherence to chronic medications on patient outcomes and health system effects.

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