

**Question:** “What proportion of prescriptions are unfilled or not picked up by patients?”

**Team name:** MOXXI-McGill

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### **Data and analysis:**

#### **Data custodian organization(s) and data sources**

This study used data from The Medical Office of the XXIst Century (MOXXI)<sup>1</sup>. Designed by researchers at McGill University, MOXXI is a unique community-based electronic health record system that links electronic prescription information with health services data from the Quebec health insurance agency (Régie de l'Assurance Maladie du Québec [RAMQ]), including beneficiary and pharmacy claims data.

#### **List of datasets used**

Prescriptions were identified using the database of electronic prescriptions in the MOXXI system. Dispensed drugs were identified by linking patients to pharmacy claims data from RAMQ, which identified all drugs dispensed from any Quebec pharmacy to all residents registered in the public drug insurance plan. Approximately 50% of all Quebec residents (including seniors, social assistance recipients, and residents without private drug insurance) are registered in the public drug insurance plan.

**Data timeframe:** All prescriptions written between 01 January 2006 and 31 December 2012.

#### **Exclusions**

- Patients not registered in the public drug insurance plan on the day of the prescription or at any time in the past year (since information on dispensed drugs was unavailable for these patients).
- Patients younger than 18 years of age.
- Drugs with limited or no coverage under the public drug insurance plan (e.g. clopidogrel, sitagliptine) and over-the-counter medications (e.g. acetaminophen, acetylsalicylic acid, calcium).
- Prescriptions where the same drug (defined by generic ingredient code) had been prescribed or dispensed to the patient in the past year (e.g. prescription renewals).

#### **Nature and size of the MOXXI cohort**

Eligible physicians for MOXXI were primary care physicians in community-based, fee-for-service practices around two major urban centers in Quebec (Montreal and Quebec City). Eligible patients were all community-dwelling individuals who visited a MOXXI physician during the study period. Approximately 175 physicians and 90,000 patients consented to participate in the MOXXI research program during the study period, representing approximately 25% of eligible physicians and 30% of eligible patients. Compared to non-participants, MOXXI physicians were younger and MOXXI patients were older with more health complexities.

## **Summary of analysis methodology**

The unit of analysis was the prescription. Patients could contribute multiple prescriptions to the analysis. The primary nonadherence rate was defined as the proportion of prescriptions for new treatment where the prescribed drug was not dispensed to the patient within 30 days. Sensitivity analyses were conducted by extending the follow-up period to 90 and 270 days.

Sub-group analyses of 30-day primary nonadherence were conducted by therapeutic class and several patient characteristics, including sex, age, and co-payment status for drugs. Drugs were grouped into therapeutic classes based on the American Hospital Formulary Service (AHFS) classification system (Appendix). Multivariable alternating logistic regression methods<sup>2</sup> were used to calculate the independent association (via the odds ratio) of each factor with 30-day primary nonadherence while accounting for non-independence of the outcome among multiple prescriptions for the same patient and among multiple patients with the same physician.

## **Findings:**

### **Key statistics**

A total of 98,493 prescriptions for new treatment (representing 7.6% of all prescriptions written during the study period) met the inclusion criteria. These prescriptions were written for 27,279 patients. Within 30 days, 25,702 prescriptions were not dispensed, representing 26.1% of all prescriptions for new treatment. When the observation period was extended to 90 and 270 days, the primary nonadherence rate decreased to 22.3% and 19.4%, respectively (Table 1).

### *Sub-group analyses*

Primary nonadherence was similar among females (25.8%) and males (26.6%). Primary nonadherence was significantly lower among patients aged 75 years and older (20.6%) compared to patients under 55 years of age (32.7%) (adjusted odds ratio [OR] 0.47, 95% confidence interval [CI] 0.43-0.51). Patient co-payment status for drugs had the biggest impact, with primary nonadherence being significantly higher among patients who had to pay the maximum co-payment (32.0%) compared to patients with no co-payments (14.7%) (OR YY, 95% CI YY-ZZ) (Table 2).

Compared to cardiovascular agents, primary nonadherence was significantly lower for three therapeutic classes: 1) antidiabetic agents, excluding insulins (OR 0.64, 95% CI 0.57-0.72); 2) anti-infectives (OR 0.73, 95% CI 0.65-0.81), and 3) blood formation, coagulation, and thrombosis agents (OR 0.82, 95% CI 0.70-0.95). Primary nonadherence was significantly higher than cardiovascular agents for seven therapeutic classes: 1) insulins (OR 2.01, 95% 1.32-3.04), 2) pulmonary inhalers (OR 1.63, 95% CI 1.50-1.77), 3) contraceptives (OR 1.59, 95% 1.28-1.97), 4) skin and mucous membrane agents (OR 1.53, 95% CI 1.36-1.72), 5) ear, eye, neck, and throat preparations (OR 1.45, 95% 1.30-1.61), 6) analgesics and antipyretics (OR 1.23, 95% CI 1.10-1.38), and 7) gastrointestinal agents (OR 1.19, 95% CI 1.11-1.27) (Table 2).

### **Summary of findings**

In this study, approximately 1 in 4 prescriptions for new treatments were not dispensed to patients within 30 days. The primary nonadherence rate differed by therapeutic class, with lower rates for antidiabetic agents excluding insulins, anti-infectives, and blood formation, coagulation, and thrombosis agents (essential medications). Patient co-payment status for drugs had the greatest impact on whether patients filled their prescriptions.

### **Key limitations**

This study did not include prescriptions written by specialists, prescriptions for patients with private drug insurance, and drugs with no or limited coverage under the public drug insurance plan. Due to the legal context in Quebec where patients must bring paper prescriptions to pharmacies to get them filled, we were not able to identify prescriptions that reached pharmacies but were not dispensed. In order to identify such prescriptions, access to pharmacy databases or electronic transmission of prescriptions is required.

### **Additional insights**

The primary nonadherence rate in this study was high compared to a study conducted by Kaiser Permanente Southern California, which found that 9.8% of prescriptions for new treatment were not filled within 14 days<sup>3</sup>. In this integrated healthcare setting, all prescriptions were electronically transmitted from prescribers to Kaiser pharmacies, which may have increased primary adherence.

### **Policy implications of findings**

In an effort to improve medication adherence, several jurisdictions are experimenting with drug policies that provide patients with free access to essential medications. This study highlights the implications of these drug co-payment policies and their importance in enabling medication adherence. The lower primary nonadherence rate in the Kaiser setting highlights the potential benefits of implementing technologies that connect prescribers with pharmacists. Such technologies would allow clinicians to monitor unfilled prescriptions and be proactive in managing medication use among their patients.

### **References**

1. Tamblyn R, Huang A, Kawasumi Y, et al. The Development and Evaluation of an Integrated Electronic Prescribing and Drug Management System for Primary Care. *J Am Med Inform Assoc JAMIA*. 2006;13(2):148-159. doi:10.1197/jamia.M1887.
2. Carey V, Zeger SL, Diggle P. Modelling Multivariate Binary Data with Alternating Logistic Regressions. *Biometrika*. 1993;80(3):517-526. doi:10.2307/2337173.
3. Shin J, McCombs JS, Sanchez RJ, Udall M, Deminski MC, Cheetham TC. Primary nonadherence to medications in an integrated healthcare setting. *Am J Manag Care*. 2012;18(8):426-434.

**Table 1. Primary nonadherence at 30, 90, and 270 days, overall and by therapeutic class**

Therapeutic class	No. of prescriptions	Primary nonadherence, N (%)			Δ in primary nonadherence from 30 to 270 days, %
		30 days	90 days	270 days	
Antidiabetic agents, excluding insulin	2,010	354 (17.6)	276 (13.7)	247 (12.3)	-5.3
Anti-infectives	15,981	2,874 (18.0)	2,605 (16.3)	2,331 (14.6)	-3.4
Blood formation, coagulation, and thrombosis agents	1,136	222 (19.5)	179 (15.8)	156 (13.7)	-5.8
Corticosteroids	1,811	356 (19.7)	312 (17.2)	269 (14.9)	-4.8
Muscle relaxants	1,231	278 (22.6)	248 (20.2)	226 (18.4)	-4.2
Other therapeutic classes	1,542	362 (23.5)	284 (18.4)	251 (16.3)	-7.2
Central nervous system agents	14,714	3,478 (23.6)	2,943 (20.0)	2,583 (17.6)	-6.1
Cardiovascular agents	16,212	4,311 (26.6)	3,444 (21.2)	2,946 (18.2)	-8.4
Analgesics and antipyretics	9,755	2,629 (27.0)	2,318 (23.8)	2,089 (21.4)	-5.5
Bone resorption inhibitors	1,828	493 (27.0)	369 (20.2)	314 (17.2)	-9.8
Gastrointestinal agents	6,579	1,814 (27.6)	1,517 (23.1)	1,313 (20.0)	-7.6
Hormone-related agents	2,224	691 (31.1)	573 (25.8)	513 (23.1)	-8.0
Skin and mucous membrane agents	10,865	3,393 (31.2)	3,033 (27.9)	2,672 (24.6)	-6.6
Ear, eye, neck, and throat preparations	5,052	1,674 (33.1)	1,465 (29.0)	1,292 (25.6)	-7.6
Pulmonary Inhalers	6,653	2,324 (34.9)	1,995 (30.0)	1,610 (24.2)	-10.7
Insulins	228	89 (39.0)	78 (34.2)	66 (29.0)	-10.1
Contraceptives	672	360 (53.6)	297 (44.2)	259 (38.5)	-15.0
<b>ALL CLASSES</b>	<b>98,493</b>	<b>25,702 (26.1)</b>	<b>21,936 (22.3)</b>	<b>19,137 (19.4)</b>	<b>-6.7</b>

Table 2. Patient and drug characteristics associated with 30-day primary nonadherence

Characteristic	No. of prescriptions	30-day primary nonadherence, %	Adjusted OR* (95% CI)
<b>Patients</b>			
Sex			
Female	64,152	25.8	1.00 [Reference]
Male	34,341	26.6	0.99 (0.94-1.04)
Age, years			
<55	23,018	32.7	1.00 [Reference]
55-64	19,106	25.1	0.67 (0.63-0.71)
65-74	30,172	26.5	0.59 (0.54-0.65)
75+	26,197	20.6	0.47 (0.43-0.51)
Co-payment status for drugs			
No co-payment (free medication)	19,659	14.7	1.00 [Reference]
Partial copayment	21,281	20.8	1.99 (1.82-2.19)
Maximum copayment	57,544	32.0	2.47 (2.27-2.69)
<b>Drugs</b>			
Therapeutic class			
Antidiabetic agents, excluding insulin	2,010	17.6	0.64 (0.57-0.72)
Anti-infectives	15,981	18.0	0.73 (0.65-0.81)
Blood formation, coagulation, and thrombosis agents	1,136	19.5	0.82 (0.70-0.95)
Corticosteroids	1,811	19.7	1.02 (0.85-1.21)
Muscle relaxants	1,231	22.6	0.92 (0.81-1.05)
Other therapeutic classes	1,542	23.5	0.98 (0.87-1.10)
Central nervous system agents	14,714	23.6	0.97 (0.90-1.04)
Cardiovascular agents	16,212	26.6	1.00 [Reference]
Analgesics and antipyretics	9,755	27.0	1.23 (1.10-1.38)
Bone resorption inhibitors	1,828	27.0	1.03 (0.93-1.15)
Gastrointestinal agents	6,579	27.6	1.19 (1.11-1.27)
Hormone-related agents	2,224	31.1	1.08 (0.94-1.23)
Skin and mucous membrane agents	10,865	31.2	1.53 (1.36-1.72)
Ear, eye, neck, and throat preparations	5,052	33.1	1.45 (1.30-1.61)
Pulmonary Inhalers	6,653	34.9	1.63 (1.50-1.77)
Insulins	228	39.0	2.01 (1.32-3.04)
Contraceptives	672	53.6	1.59 (1.28-1.97)

Abbreviations: OR = odds ratio, CI = confidence interval

\*From an alternating logistic regression model including the following covariates: therapeutic class, patient sex, patient age, and patient co-payment status for drugs.

Information on patient co-payment status was missing for 9 prescriptions. These 9 prescriptions were excluded from the multivariable alternating logistic regression model.

## Appendix. Therapeutic and pharmacological classes of drugs included in the study

Therapeutic class	Pharmacological class*
Analgesics and antipyretics	<i>Formulation: Oral, rectal, transdermal, or injectable</i> Non-Steroidal antiinflammatory agents Opiates Other analgesics and antipyretics agents
Anti-infectives	<i>Formulation: Oral or injectable</i> Antibacterials Antivirals Antifungal Other antiinfectives
Antidiabetic agents, excluding insulins	<i>Formulation: Oral</i> Biguanides Sulfonyureas Other antidiabetic agents
Blood formation, coagulation, thrombosis	<i>Formulation: Oral or injectable</i> Anticoagulants Antianemia agents Antihemorrhagic agents
Cardiovascular agents	<i>Formulation: Oral, transdermal or injectable</i> Cardiac agents Hypotensive agents Antilipemic agents Vasodilating agents Other cardiovascular agents
Bone resorption inhibitors	<i>Formulation: Oral or injectable</i> Biphosphonates
Central nervous system agents	<i>Formulation: Oral, transdermal, rectal or injectable</i> Antidepressants Anxiolytics, sedative and hypnotics Anticonvulants Antiparkinson Antimigraine agents Antipsychotics Lithium
Corticosteroids	<i>Formulation: Oral, rectal or injectable</i> Corticosteroid agents
Gastrointestinal agents	<i>Formulation: Oral or rectal</i> Digestants Antiemetics Antiulcer and acid suppressants Prokinetic agents Antiinflammatory agents
Muscle relaxants	<i>Formulation: Oral</i> Skeletal muscle relaxants Smooth muscle relaxants
Hormone-related agents, excluding contraceptives	<i>Formulation: Oral, transdermal or injectable</i> Androgens Estrogens & Antiestrogens Thyroid & Antithyroid agents Progestins

\*Includes pharmacological classes of drugs that were prescribed and covered under the public drug insurance plan. 507 different medications were prescribed. Drugs were grouped into therapeutic groups based on the American Hospital Formulary Service classification system.

## Appendix (cont'd). Therapeutic and pharmacological classes of drugs included in the study

Therapeutic class	Pharmacological class*
Contraceptives	<i>Formulation: Oral, transdermal, implant or injectable</i> Hormonal contraceptive agents
Skin and mucous membrane agents	<i>Formulation: Topical</i> Antiinfectives Antiinflammatory agents Antipruritics Other skin and mucous membrane agents
Inhalers	<i>Formulation: Pulmonary inhalers</i> Long and short acting beta-agonists Inhaled corticosteroids Inhaled anticholinergic agents
Ear, Eye, Nose and Throat (EENT) Preparations	<i>Formulation: Drops, nasal inhalers</i> Antiinfectives Corticosteroids Anticholinergic Antiglaucoma agents Other EENT preparations
Other	Antihistamine agents Antineoplastic agents Cholinesterase inhibitors Leukotrien antagonists Opiate antagonists 5alphareductase inhibitors Antigout agents

\*Includes pharmacological classes of drugs that were prescribed and covered under the public drug insurance plan. 507 different medications were prescribed. Drugs were grouped into therapeutic groups based on the American Hospital Formulary Service classification system.