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RESEARCH

# Factors associated with early nonpersistence among patients experiencing side effects from a new medication

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ABSTRACT

*Background:* Drug discontinuation (i.e., nonpersistence) is often attributed to the emergence of adverse effects. However, it is not known whether other factors increase the risk of nonpersistence when adverse effects occur.

*Objectives:* To identify factors associated with early nonpersistence among patients experiencing adverse effects from newly prescribed medications.

*Methods:* A questionnaire was mailed to new users of antihypertensive, antihyperglycemic, and lipid-lowering medications in Saskatchewan, Canada, between 2019 and 2020. Only respondents experiencing adverse effects were included. Responses were compared between the nonpersistent group (i.e., people who had discontinued their medication) and the persistent group (i.e., those who were taking their medication at the time of the survey). Statistically significant factors were tested in multivariable logistic regression models. Odds ratios (ORs) and 95% CIs were reported.

*Results:* Of the 3973 returned questionnaires, 813 respondents experienced adverse -effects from their new medication and were included in the study. Of these, 143 respondents (17.5%) had stopped their medication at the time of survey completion; most discontinuations (72.1%) occurred within 1 month of the first dose. Nonpersistent patients were older, had lower income, and were less likely to be taking an antihyperglycemic medication. After covariate adjustment, 6 factors were independently associated with nonpersistence: age less than 65 years (OR 1.56 [95% CI 1.01–2.41]), female sex (1.67 [1.08–2.59]), health condition not considered dangerous (2.09 [1.25–3.51]), medication not considered important for health (6.90 [4.40–10.84]), failure to expect adverse effects before starting medication (2.67 [1.74–4.10]), and taking 2 or more medications (0.45 [0.27–0.73]).

*Conclusion:* Despite the strong link between the emergence of adverse effects and early nonpersistence, our findings confirm that this association is highly influenced by several factors external to the physical experiences caused by the new medication.



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**Key Points**

**Background:**

- For newly prescribed medications, nonadherence often manifests as complete drug discontinuation in the early stages of treatment.
- Adverse effects have been identified as a major risk factor for medication discontinuation.

**Findings:**

- Beliefs and expectations about medications substantially impact the probability that a drug will be discontinued if adverse effects occur early in therapy.
- Management of patients experiencing adverse effects should include an assessment of attitudes and beliefs in addition to strategies such as dosage reduction.

## Background

Nonadherence to chronic medications is widely recognized as a threat to individual health and health care sustainability.[1] Major patterns of nonadherence include (1) primary nonadherence, where a newly prescribed medication is never picked up from the pharmacy;[2] (2) poor execution (or noncompliance), where patients skip/forget doses frequently during the course of treatment;[3,4] and (3) nonpersistence, where patients discontinue a medication during a period of observation.[2,4,5] Ultimately, underuse of chronic medications, regardless of the pattern, can result in poor disease control and higher risks for hospitalization and even death.[6,7] In the United States alone, nonadherence has been estimated to cost $100-$500 billion in avoidable health care costs.[8]

Several research studies have shown that complete medication discontinuation (i.e., nonpersistence) is extremely common, especially in the early days after starting treatment. For example, our research group examined refill patterns for 52,039 residents of Saskatchewan, Canada, who were newly prescribed antihypertensive medications.[9] Of all patients classified as nonadherent during the first year (25,812 or 49.6%), almost half (10,081) had discontinued after the very first dispensation. Similar findings have been observed in other populations taking chronic medications,[10,11] including 27,329 patients with diabetes starting either antihyperglycemics, lipid-lowering, or antihypertensives in California.[10]

Medication-induced adverse effects have been strongly associated with nonadherence[12,13] and are a commonly cited factor in the development of early medication discontinuation (i.e., early nonpersistence).[14-16] Although serious adverse events warrant medication discontinuation, the high prevalence of early nonpersistence suggests that minor adverse effects must be the primary trigger in the vast majority of cases. As a result, the issue may be more complicated than the ability to withstand physical or sensory symptoms from a new drug. Patients who are worried about their condition or are optimistic about their treatment may be more likely to continue medications even when adverse effects occur.[13,17,18] Although tolerability concerns are very common during the first few months of therapy, the extent to which other factors might magnify or diminish the perceived seriousness of an adverse effect is not known. Given the high prevalence of early nonpersistence and the frequency with which adverse effects have been identified as the main cause, further research is needed to understand the interplay between adverse effects and other mediating factors. We used survey data from a population-based sample of adults initiating prescription medications for chronic conditions to determine the extent to which patient or provider level factors may modify the response to medication adverse effects.

## Methods

### *Data source—questionnaire design*

The present study is based on data collected from a questionnaire mailed to residents in the province of Saskatchewan, Canada, as part of a larger research program entitled Major Determinants of Non-adherence in Saskatchewan (the MD-NAS Study). The questionnaire was designed to capture patient-reported information that could be integrated with health-administrative data to help predict nonadherence among a cohort of new users of chronic medications. Future linkage of this questionnaire to administrative data will take place after a minimum of 1-year follow-up has been completed on each subject in the cohort and data are available for processing. In the interim, the MD-NAS questionnaire will be used to investigate barriers to optimal adherence in the early phases of treatment such as the study presented here.

The MD-NAS questionnaire was designed to collect patient-reported data on a wide breadth of adherence barriers not available in administrative databases. As a result, information on numerous domains of adherence determinants included patient-related factors (e.g., knowledge attitudes, beliefs), therapy-related factors (e.g., adverse effects), health care system/health care team factors (e.g., appointment length, relationship/trust), and social/economic factors (e.g., income, cost-related nonadherence). Although validated scales are available for many of these factors individually, the requirement for breadth restricted the utility of published scales owing to the risk of responder fatigue. Thus, questions from existing tools were often modified, and additional questions were developed by the research team.

The final questionnaire (Appendix 1) contained 58 items divided into 9 sections (i.e., sections A to I). The first 3 sections (Section A through C) contained questions about consent (Q1–Q3), confirmation of recently receiving a new medication (Q4–Q7), and the setting of the new prescription (i.e., prescribed in hospital, duration of appointment, etc) (Q8–Q13). These questions were primarily created by the study team based on the original study design, target population (i.e., new users), the health system environment, and ethical requirements. Section D (Q 14–Q19) contained questions about health care provider interactions (Q14, Q17, Q18, Q19) that were based on studies focusing on physician-patient communication.[19,20] This section also contained questions about specific medication knowledge (Q15,Q16) that were developed from published medication adherence surveys.[21,22]

Section E (Q20–Q25) contained questions about medication beliefs (Q20–Q24) that were based primarily on the work of McHorney[23] and Horne et al.[24] Section F (Q26–Q36) asked about the patient experiences with the new medications including direct questions about adverse effects with the new medication developed by the study team (Q28–Q30) as well as questions about forgetfulness (Q33,Q34) and physical limitations regarding bottle caps and written labels (Q35, Q36). Section G focused on cost and included a single item used previously to identify cost-related nonadherence (Q38).[25] Section H focused on adherence/persistence to the new medication (Q40–Q45). Questions about duration of time before stopping (Q41), physician knowledge about stopping the medication (Q42, Q43), and reasons for stopping (Q44) were developed by the study team to help provide more details about nonpersistent cases because they are not usually available in large scale studies. Question 45 was a standard visual analog scale to report adherence with wording tailored by the research team. Finally, section I contained questions about general demographics and health (Q46–Q57). Demographic and ethnic background were adapted from surveys produced by Statistics Canada. The first question following consent checkboxes was, "In the past 4 months, has your doctor prescribed you a new medication that you have not taken before?" Only respondents answering "YES" are asked to complete the rest of the questionnaire.

The final questionnaire draft was achieved using principles of scale development and survey research,[26] and members of the research team edited questions for flow and internal consistency. The initial draft questionnaire was reviewed by 10 experts in practice-based research and survey design, and changes in wording and relevance of selected items were recommended to improve content validity. To pretest the document, 15 patients who were newly prescribed chronic medications were recruited from the Saskatchewan Health Authority Cardiac Rehabilitation Program. On the basis of the comments received, the survey was revised to improve readability and question flow. The updated survey was piloted on 66 additional subjects who met study criteria as new users of chronic medications. We also conducted reliability testing on our sample of respondents. A total of 74 responders agreed to complete a second survey, with 68 available for assessment. For the vast majority of questions, retest items matched the original response over 80% of the time. Allowing 1 unit above or below the original Likert scale options, test-retest agreement was typically over 95%.

### *Questionnaire dissemination*

The government of Saskatchewan administers a provincial drug benefit program that covers approximately 90% of the population (approximately 1.1 million residents) regardless of age or socioeconomic status. Eligible patients of the MD-NAS study were beneficiaries of the provincial drug benefit program who were at least 30 years of age and had at least 2 years of continuous registration at the time of screening. Drug Plan personnel who were not part of the study team developed an automated process to identify patients with a new medication for either an antihypertensive, cholesterol-lowering, or antihyperglycemic medication. To be classified as a new user, patients could not have a claim for any drug under these general categories in the past 2 years. All beneficiaries meeting these criteria were mailed the questionnaire directly from the drug plan without researcher involvement. The questionnaire was distributed following the Dillman approach[27]; it included an invitation letter, cover letter with informed consent package, and reminder postcard. To ensure timely delivery of the questionnaire relative to the date of receiving a first dispensation for the medication, screening and subsequent mailout of questionnaires were conducted on 6 separate occasions: (1) September 2019; (2) October 2019; (3) November 2019; (4) December 2019; (5) January 2020; (6) February 2020. Thus, the delivery date of each mailout (i.e., the invitation letter) occurred within 4-6 weeks of the first dispensation for eligible individuals. For individuals receiving more than 1 eligible medication class, the earliest drug claim recorded during the screening period was selected. Although additional mailouts were planned, the onset of the coronavirus disease 2019 pandemic demanded prioritization to public health activities. This study was approved by the University of Saskatchewan Committee for Ethics in Human Research. No patient information other than survey responses were available to researchers during the mailout process.

### *Participants and comparator groups*

The present study is based on responses from a subset of the total number of responders to the MD-NAS questionnaire. Subjects were included if they met the following criteria: (1) consented to participate in the study; (2) confirmed initiating a new antihypertensive, cholesterol-lowering, or antihyperglycemic medication prescription within the past 4 months; and (3) reported experiencing adverse effects after starting their new medication (i.e., "Did you experience side effects from your new medicine? Yes/no"). Subjects were excluded if they denied receiving a new medication or reported a new medication from a different class other than antihypertensive, cholesterol-lowering, or antihyperglycemic. For patients who selected "do not know" for the class of their new medication or if their answer was missing, we manually reviewed their written response for the name of the medication and included them if they were using a drug of interest.

Responders who experienced adverse effects were classified into 2 groups on the basis of their answer to the following question: "*Are you still taking the new medicine prescribed to you*?" For those who responded "no" (i.e., nonpersistence), we described their responses to items directed only to the nonpersistent patients including the duration of treatment before discontinuation, whether the physician was aware of the discontinuation, who decided to discontinue the drug (i.e., physician or patient or both), and the reasons why patients discontinued. The entire sample of respondents (i.e., nonpersistent and persistent) was compared for the remaining items of interest.

### *Factors associated with early nonpersistence*

A total of 26 items from the original survey were identified as possible determinants of early nonpersistence. Because of the risk of multicollinearity between items in the survey asking about similar topics, each item was initially categorized into mutually exclusive constructs on the basis of the

conceptual framework developed by the World Health Organization.[1] However, only 2 of the initial constructs identified strong internal consistency: health care provider support (Cronbach's alpha 0.82), and knowledge about medications (Cronbach's alpha 0.77). Low consistency was observed for the remaining constructs, even after recategorization to improve their scores. As a result, items that were not included in a construct were tested individually between nonpersistent and persistent patients. The 2 constructs were represented in the analysis by calculating the sum of all responses scored as 1-5 on the basis of their Likert scale as outlined by McHorney.[23] The first construct, health care provider support, included 5 questions (questions 14, 17, 18, 19, 25) for a total possible score of 25 points. Higher scores represented greater support from a health care provider. The second construct (knowledge about medications) contained 2 questions (questions 15 and 16) for a total score of 10. Again, a higher score represented better knowledge about the medication. Summary scores for the 2 constructs were converted into binary variables (i.e., high vs. low) because the distribution was highly skewed. The threshold for a high score in each construct was set at the upper quartile boundary (75th percentile).

*Data analysis*

Baseline characteristics of responders were described and stratified by those who reported nonpersistence and those who did not. Missing values for individual items were censored. Univariate analyses of differences between the 2 groups were tested using a chi-square test of independence for categorical and ordinal variables.

Logistic regression analysis was used to test univariate associations between each variable and the outcome of nonpersistence; unadjusted odds ratios (ORs) were estimated along with 95% CIs. All variables with a significance level of $P < 0.10$ were assessed for multicollinearity using the variance inflation factor (VIF). Any variables with VIF > 2.5 were identified and removed from the group of eligible covariates. An initial multivariable logistic regression model was constructed with demographic variables (age < 65 or ≥ 65 years and sex). Other variables were added to the model in a stepwise fashion; they were retained if they produced a statistically significant improvement in discriminating nonpersistence from persistence compared with the model without the given variable. Improvement was measured by the difference in the integrated discrimination improvement.[28] For each new model, we also measured the discrimination performance using the c statistic (i.e., area under the receiver operating characteristic curve).[29] All analyses were conducted using IBM SPSS version 28.0 and SAS Software v 9.4 (SAS Institute Inc, Cary, NC).

## Results

Questionnaires were mailed to 11,970 eligible patients. From these, 3973 completed and returned the questionnaire for a response rate of 33.2%. Of the 3973 respondents, 813 (20.5%) reported experiencing adverse effects after starting their new medication (Figure 1). For this subgroup, the mean age was 60 years (SD 12.3 years), 43.9% (n = 357) were male, 66.7% (n = 543) had pursued education after high school, and the vast majority were Caucasian (87.2%, n = 709) (Table 1). Among these respondents who had experienced an adverse effect, 17.5% (n = 143) reported discontinuing their medications at the time of completing the survey. Over one-quarter of nonpersistent responders (n = 41, 28.7%) had stopped their medication within the first week, and 104 (72.1%) had stopped within the first month (Table 2); the vast majority identified the adverse effect as the reason for discontinuation (n = 122, 85.3%). A total of 30 (21.0%) indicated not feeling safe, and 14 (9.8%) indicated that they did not need the medication anymore. Only 2 people (1.4%) indicated that the medicine was too costly, and one indicated that it was inconvenient to take (0.7%). In almost half of the cases of nonpersistence, the physician was aware of the discontinuation; in one-third of cases (46/143, 32.2%), the physician agreed with discontinuing (according to the respondent).

No statistically significant differences were observed for physical activity, smoking, and a healthy diet between nonpersistent and persistent individuals. Only one-quarter of all study respondents indicated receiving help with their adverse effects (26.6%, n = 217), and no statistically significant was observed for this variable between groups. In contrast, nonpersistent patients were older (i.e., percentage of patients over 65 years: 43.3% vs. 31.7%, $P = 0.08$), more likely to be female (63.6% vs. 53.2%, $P = 0.02$), had lower income (percentage reporting < $25,000 per year: 21.6% vs. 12.3%, $P = 0.003$), less likely to be taking an antihyperglycemic medication (15.3% vs. 27.0%, $P = 0.004$), and less likely to be taking multiple medications (≥: 63.6% vs. 83.8%, $P < 0.01$) versus those who were still taking their medication. In addition, nonpersistent (versus persistent) responders scored lower in the health provider support score (i.e., percentage of respondents with high score: 17.4% vs 30.9%, $P = 0.001$) as well as knowledge about medications (percentage of patients with high score: 26.5% vs. 48.4%, $P<0.01$).

Differences between nonpersistent and persistent patients were also observed in their perceptions about medications and conditions. Only 67.1% (96/143) of nonpersistent patients felt that their condition was a danger to their health, compared with 88.5% (593/670) of those who were still taking their medication ($P < 0.01$). In addition, only 43.3% (62/143) of nonpersistent patients thought that the new medication was important for their health (vs. 85.2% (571/670) of persistent patients, $P < 0.01$). Interestingly, respondents who were taking antihyperglycemic medications indicated that their medication was important to their health more often than those taking antihypertensives or cholesterol-lowering medications (85.1%[172/202] vs. 76.4% (433/567) respectively, $P = 0.005$). Nonpersistent patients were less likely to expect adverse effects before they started taking the medication (36.3% vs. 58.6%, $P < 0.01$). Finally, a higher percentage of nonpersistent responders felt that their medication would do more harm than good (60.1% (86/143) versus 16.2% 109/670, $P < 0.01$); however, given that adverse effects had already occurred before responding to this question, this item was not included in the multivariate analysis as it may not have reflected their beliefs before starting the drug.

The initial regression model containing age and sex only enabled very modest discrimination between persistent and nonpersistent responders (i.e., c statistic = 0.588). However, performance of the final model was substantially improved

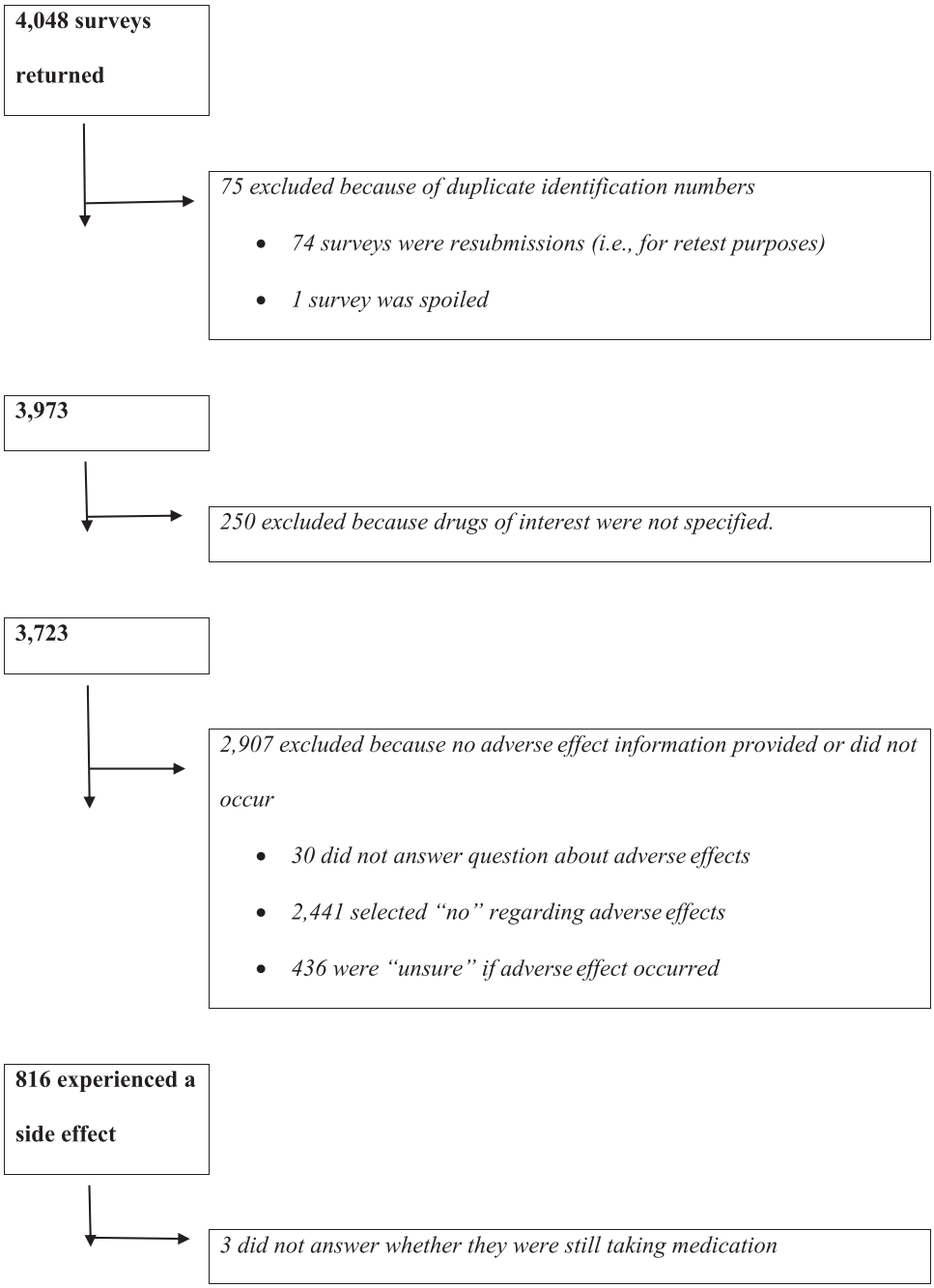


**Figure 1.** Surveys excluded during selection of study sample.

(c statistic = 0.818). Statistically significant increases in the odds of nonpersistence were observed with 5 variables: age less than 65 years (OR 1.56 [95% CI 1.01–2.41]), female sex (1.67 [1.08–2.59]), health condition not considered dangerous (2.09 [1.25–3.51]), medication not considered important for health (6.90 [4.40–10.84]), and failure to expect adverse effects before starting medication (2.67 [1.74–4.10]) (Table 3). In contrast, taking 2 or more medications daily (i.e., vs. only one) was associated with lower odds of nonpersistence (0.45 [0.27–0.73]).

## Discussion

We conducted a population-level survey to understand the factors associated with early nonpersistence among new users of chronic medications experiencing adverse effects. One in 6 respondents (i.e., with adverse effects) who recently started a new medication discontinued it, generally within 1 month after the first dose. The vast majority identified the adverse effect as the primary reason for discontinuation, whereas cost, convenience, and the healthy adherer phenomenon appeared

**Table 1**
Baseline characteristics of new medication users who experienced adverse effects

| Variable | Overall group, n (%) | Persistent, n (%) | Nonpersistent, n (%) | *P* value |
|---|---|---|---|---|
| All respondents | 813 (100) | 670 (100) | 143 (100) | — |
| Age, y | | | | 0.008 |
| <65 | 532 (65.4) | 452 (67.4) | 80 (55.9) | |
| ≥65 | 275 (33.8) | 213 (31.7) | 62 (43.3) | |
| Missing | 6 (0.7) | 5 (0.7) | 1 (0.6) | |
| Sex | | | | 0.026 |
| Male | 357 (43.9) | 306 (45.6) | 51 (35.7) | |
| Female | 448 (55.1) | 357 (53.2) | 91 (63.6) | |
| Missing | 8 (1.0) | 7 (1.0) | 1 (0.7) | |
| Education | | | | 0.040 |
| ≤High school | 265 (32.5) | 208 (31.0) | 57 (39.8) | |
| >High school | 543 (66.7) | 458 (68.3) | 85 (59.4) | |
| Missing | 5 (0.6) | 4 (0.5) | 1 (0.6) | |
| Race | | | | 0.993 |
| White or Caucasian | 709 (87.2) | 585 (87.0) | 124 (86.7) | |
| Other | 97 (11.9) | 80 (11.9) | 17 (11.8) | |
| Missing | 7 (0.8) | 5 (0.7) | 2 (1.3) | |
| Marital status | | | | 0.192 |
| Married | 581 (71.4) | 484 (72.2) | 97 (67.8) | |
| Single | 223 (27.4) | 177 (26.4) | 46 (32.1) | |
| Missing | 9 (1.1) | 9 (1.3) | 0 (0.0) | |
| Income | | | | 0.003 |
| <$25,000 | 114 (14.0) | 83 (12.3) | 31 (21.6) | |
| ≥$25,000 | 662 (81.4) | 558 (83.2) | 104 (72.7) | |
| Missing | 37 (4.5) | 29 (4.3) | 8 (5.5) | |
| Discount | | | | 0.837 |
| Yes | 567 (69.7) | 468 (69.8) | 99 (69.2) | |
| No or Not sure | 238 (29.2) | 195 (29.1) | 43 (30.0) | |
| Missing | 8 (0.9) | 7 (1.0) | 1 (0.6) | |
| Cost Related Non-Adherence | | | | 0.072 |
| Yes | 18 (2.2) | 12 (1.7) | 6 (4.1) | |
| No or Not sure | 791 (97.8) | 656 (97.9) | 135 (94.4) | |
| Missing | 4 (0.5) | 2 (0.2) | 2 (1.3) | |
| Was the medication prescribed in the hospital? | | | | 0.417 |
| Yes | 113 (13.9) | 97 (14.5) | 16 (11.2) | |
| No | 697 (85.7) | 570 (85.1) | 127 (88.8) | |
| Missing | 3 (0.4) | 3 (0.4) | 0 (0.0) | |
| Did you receive help to deal with the adverse effect(s) of your new medicine? | | | | 0.075 |
| Yes | 217 (26.6) | 171 (25.5) | 46 (32.1) | |
| No or not sure | 587 (72.2) | 494 (73.7) | 93 (65.0) | |
| Missing | 9 (1.1) | 5 (0.7) | 4 (2.7) | |
| Did you go back to see your doctor to discuss the new medicine after you started taking it? | | | | 0.309 |
| Yes | 350 (43.0) | 284 (42.3) | 66 (46.1) | |
| No or not sure | 447 (54.9) | 375 (55.9) | 72 (50.3) | |
| Missing | 16 (1.9) | 11 (1.6) | 5 (3.4) | |
| Do you have a regular family doctor? | | | | 0.985 |
| Yes | 754 (92.7) | 621 (92.7) | 133 (93.0) | |
| No | 57 (9.2) | 47 (7.0) | 10 (7.0) | |
| Missing | 2 (0.2) | 2 (0.3) | 0 (0.0) | |
| Medication | | | | 0.021 |
| Lipid lowering | 229 (28.2) | 181 (27.0) | 48 (33.6) | |
| Antihyperglycemic | 292 (35.9) | 255 (38.0) | 37 (25.9) | |
| Antihypertensive | 292 (35.9) | 234 (34.9) | 58 (40.6) | |
| No. Medications | | | | <0.001 |
| 1 medication | 147 (18.0) | 108 (16.1) | 39 (27.2) | |
| ≥2 medications | 648 (79.7) | 557 (83.8) | 91 (63.6) | |
| Missing | 18 (2.2) | 5 (0.7) | 13 (9.0) | |
| Your new medicine is for a condition that is a danger to your health. | | | | <0.001 |
| Strongly agree and agree | 689 (84.7) | 593 (88.5) | 96 (67.1) | |
| Not sure or Disagree and Strongly disagree | 121 (14.8) | 74 (11.0) | 47 (32.8) | |
| Missing | 3 (0.3) | 3 (0.4) | 0 (0.0) | |
| You are convinced that your new medicine is important for your health. | | | | <0.001 |

**Table 1** (*continued*)

| Variable | Overall group, n (%) | Persistent, n (%) | Nonpersistent, n (%) | *P* value |
|---|---|---|---|---|
| Strongly agree and Agree | 633 (77.8) | 571 (85.2) | 62 (43.3) | |
| Not sure or disagree and strongly disagree | 175 (21.5) | 94 (14.0) | 81 (56.6) | |
| Missing | 5 (0.6) | 5 (0.7) | 0 (0.0) | |
| You worry that your new medicine will do more harm than good. | | | | <0.001 |
| Strongly agree and agree | 195 (23.9) | 109 (16.2) | 86 (60.1) | |
| Not sure or disagree and strongly disagree | 612 (75.2) | 557 (83.1) | 55 (38.4) | |
| Missing | 6 (0.7) | 4 (0.5) | 2 (1.3) | |
| You expected to get adverse effects from this new medicine before you started taking it. | | | | <0.001 |
| Strongly agree and agree | 445 (54.7) | 393 (58.6) | 52 (36.3) | |
| Not sure or disagree and strongly disagree | 365 (44.8) | 274 (40.8) | 91 (63.6) | |
| Missing | 3 (0.3) | 3 (0.4) | 0 (0.0) | |
| In general, would you say your health is: | | | | 0.208 |
| Excellent/Very good/Good | 657 (80.8) | 547 (81.6) | 110 (76.9) | |
| Fair/Poor | 152 (18.6) | 120 (17.9) | 32 (22.3) | |
| Missing | 4 (0.4) | 3 (0.4) | 1(0.6) | |
| In general, would you say your mental health is: | | | | 0.455 |
| Excellent/Very good/Good | 716 (88.4) | 587 (87.6) | 129 (90.2) | |
| Fair/Poor | 94 (11.6) | 80 (11.9) | 14 (9.7) | |
| Missing | 3 (0.4) | 3 (0.4) | 0 (0.0) | |
| Physically active | | | | 0.406 |
| Yes | 556 (68.4) | 456 (68.1) | 100 (69.9) | |
| No | 244 (30.0) | 206 (30.7) | 38 (26.6) | |
| Missing | 13 (1.6) | 8 (1.2) | 5 (3.5) | |
| Healthy diet | | | | 0.939 |
| Yes | 735 (90.4) | 605 (90.3) | 130 (90.9) | |
| No | 75 (9.2) | 62 (9.3) | 13 (9.1) | |
| Missing | 3 (0.4) | 3 (0.4) | 0 (0.0) | |
| Tobacco use | | | | 0.847 |
| Yes, I use tobacco products daily | 76 (9.3) | 61 (9.1) | 15 (10.5) | |
| Yes, I use tobacco products occasionally | 32 (3.9) | 27 (4.0) | 5 (3.4) | |
| No, I do not use tobacco product at all | 704 (86.6) | 581 (86.7) | 123 (86.0) | |
| Missing | 1 (0.1) | 1 (0.1) | 0 (0.0) | |
| Health care provider support score | | | | 0.001 |
| ≥19 | 232 (28.5) | 207 (30.9) | 25 (17.4) | |
| <19 | 580 (71.3) | 462 (69.1) | 118 (82.5) | |
| Missing | 1 (0.1) | 1 (0.1) | 0 (0.0) | |
| Knowledge about medications | | | | <0.001 |
| ≥8 | 360 (44.2) | 322 (48.4) | 38 (26.5) | |
| <8 | 445 (54.7) | 343 (51.6) | 102 (71.3) | |
| Missing | 8 (0.9) | 5 (0.7) | 3 (2.0) | |

to play a minor role at best. Of all factors associated with early nonpersistence, patient perceptions and beliefs appeared to dominate. Although our sample was restricted to respondents taking medications for a potentially life-threatening problem (i.e., antihyperglycemic, lipid-lowering, or antihypertensive medication), many believed that their condition posed minimal health risks, and this belief appeared to decrease their willingness to continue taking the medication in the face of adverse effects. Interestingly, antihyperglycemic medications were perceived as important for health more often than lipid-lowering or antihypertensives and were also associated with a lower risk of early nonpersistence in the unadjusted analysis. Although beliefs about medications have been linked to general cases of nonadherence previously, the present study confirms that they play a major role in the occurrence of early nonpersistence when adverse effects occur.

Willingness to take a medication is thought to be a product of necessity versus concern,[17,30] and patient concerns leading to nonadherence are often focused on drug safety.[31-33] Indeed, the emergence of adverse effects during the early phases of treatment can shift the perspectives of patients about drug safety.[32] However, our study suggests that drug intolerance may be highly influenced by unconscious bias and perhaps even induced by negative baseline beliefs about medications and health status. Wood and colleagues have previously demonstrated that 90% of the adverse effect burden reported in statin-intolerant patients could be elicited by placebo.[34] These findings do not suggest that adverse effect complaints are an excuse to avoid treatment, but patients are undoubtedly expressing genuine concerns that should not be discounted. In contrast, unresolved concerns about safety or necessity of a drug may sensitize people toward physical or psychological stimuli occurring during the early phase of treatment. This scenario may be more problematic for the treatment of asymptomatic conditions such as hypertension, hyperlipidemia, and, possibly, hyperglycemia. Although the need to educate about the importance of controlling asymptomatic conditions is well recognized by health care providers, our

**Table 2**
Characteristics of nonpersistent responders (n = 143)

| Variable | n (%) |
|---|---|
| How long did you take your new medicine for before stopping? | |
| I stopped taking it after 1 day | 4 (2.8) |
| I stopped taking it between 2-6 days | 41 (28.7) |
| I stopped taking it between 1 wk and 1 mo | 59 (41.3) |
| I stopped taking it after more than 1 mo | 35 (24.5) |
| Not sure | 3 (2.1) |
| Missing | 1 (0.7) |
| Does your doctor know you stopped taking your new medicine? | |
| Yes | 65 (45.5) |
| No | 65 (45.5) |
| Not sure | 9 (6.3) |
| Missing | 4 (2.8) |
| Whose decision was it to stop taking your new medicine? | |
| It was my decision to stop | 95 (66.4) |
| It was my doctor's decision to stop | 15 (10.5) |
| My doctor and I both decided I should stop | 31 (21.7) |
| I am not sure (or I don't remember) | 1 (0.7) |
| Missing | 1 (0.7) |
| I had an adverse effect that bothered me | |
| Yes | 122 (85.3) |
| No | 19 (13.3) |
| Missing | 2 (1.4) |
| I did not need the medicine anymore | |
| Yes | 14 (9.8) |
| No | 127 (88.8) |
| Missing | 2 (1.4) |
| I did not feel safe on this medicine | |
| Yes | 30 (21.0) |
| No | 111 (77.6) |
| Missing | 2 (1.4) |
| The medicine was too costly | |
| Yes | 2 (1.4) |
| No | 139 (97.2) |
| Missing | 2 (1.4) |
| The medicine was too inconvenient to take | |
| Yes | 1 (0.7) |
| No | 140 (97.9) |
| Missing | 2 (1.4) |
| Stopped for other reasons | |
| Yes | 30 (21.0) |
| No | 111 (77.6) |
| Missing | 2 (1.4) |

findings suggest that patients who do not accept or recognize the necessity of treatment are at a very high risk for nonpersistence when adverse effects occur.

Prevention of early nonpersistence has traditionally focused on minimizing adverse effect burden by initiating medications at low doses.[16,35-39] Although high dose medications have been associated with lower adherence in some studies,[16,36,39] other studies have failed to confirm the association[35] or have found that high doses led to better adherence.[37] Another study found medium doses of duloxetine to be associated with higher adherence than either low or high dosing strategies.[38] These inconsistent findings relating to the association between drug dosage, adverse effects, and nonpersistence are likely a result of the major confounding influence of patient attitudes and beliefs identified in our study. Ultimately, health care providers must recognize that cases of drug intolerance will often require more than direct, physical measures such as lowering the dose of the offending agent. In our study, a relatively high number of respondents reported that their physician either instructed the medication discontinuation or knew about it. Although medication discontinuation may be appropriate within months of initiation in some cases, true contraindications to treatment (i.e., condition resolution or serious adverse events) are expected to be rare among people starting antihypertensives, antihyperglycemics, or lipid-lowering drugs. Thus, some cases of physician-prescribed discontinuation may have resulted from a failure of conventional support measures such as dosage reduction to resolve the reported adverse effects. Ultimately, improving the effectiveness of strategies to support people with medication adverse effects may help prevent some cases of nonpersistence.

The influence of health care providers on the occurrence of early nonpersistence is an important consideration in adherence research. Although patient beliefs were ultimately the most powerful predictors in our adjusted analysis, crude differences observed from our baseline comparisons may still be relevant. Only one-quarter of our entire sample of respondents reported receiving any help in dealing with their adverse effects, and failure to expect adverse effects before starting the medication was associated with early nonpersistence. Perhaps this corresponds with observations from the unadjusted analysis finding lower levels of medication knowledge and lower levels of health care provider support for nonpersistent versus persistent responders. One of 10 people who were nonpersistent felt that they did not need their medication anymore, an unexpected response, given the types of medications included in this study (i.e., antihypertensive, lipid-lowering, and antihyperglycemics).

Although it might seem logical that additional efforts directed toward patient counseling are needed, it is already known that simple educational interventions do not improve adherence on their own.[33] Moreover, patient education has been a priority of front-line health care providers for decades[40]; thus, it is possible that patient education was provided to many of our respondents but perhaps was not remembered or accepted. The nuances of dealing with adverse effect messaging is a difficult area for health care providers. Some feel that too much information will dissuade people from taking it.[41,42] Others may fear accusations of failure to disclose if not enough information is provided. At the very least, there are wide discrepancies in how health care providers and patients perceive adverse effect risk and what degree of adverse effect disclosure is reasonable.[43-45] Perhaps the high number of nonpersistent individuals failing to anticipate adverse effects in our study represents an unintended consequence of health care providers reassuring the patients that adverse effects are unlikely. Although reassurance is considered an important aspect of patient support,[41,46] our findings suggest that awareness about the possibility of adverse effects is important.

Our study had several strengths, including a population-based sample of new medication users, all of whom recently started a new medication (i.e., antihyperglycemic, lipid-lowering, or antihypertensive) and completed an extensive questionnaire. However, several limitations must be acknowledged. First, we cannot verify the outcome of early nonpersistence, and we cannot assess the impact of

**Table 3**
Factors associated with early nonpersistence among new users of chronic medications who experienced adverse effects

| Factor | Adjusted OR | 95% CI | *P* value |
|---|---|---|---|
| Age, y | | | |
| ≥65 (Reference) | | | |
| <65 | 1.56 | 1.01–2.41 | 0.046 |
| Sex | | | |
| Male (reference) | | | |
| Female | 1.67 | 1.08–2.59 | 0.022 |
| No. medications, n (%) | | | |
| One medication (Reference) | | | |
| ≥2 medications | 0.45 | 0.27–0.73 | 0.002 |
| Your new medicine is for a condition that is a danger to your health. | | | |
| Strongly agree and agree (Reference) | | | |
| Not sure or disagree and strongly disagree | 2.09 | 1.25–3.51 | 0.005 |
| You are convinced that your new medicine is important for your health. | | | |
| Strongly agree and agree (Reference) | | | |
| Not sure or disagree and strongly disagree | 6.90 | 4.40–10.84 | < 0.001 |
| You expected to get adverse effects from this new medicine before you started taking it. | | | |
| Strongly agree and agree (Reference) | | | |
| Not sure or disagree and Strongly disagree | 2.67 | 1.74–4.10 | < 0.001 |

Abbreviation used: CI, confidence Interval; OR, odds ratio.

nonresponse bias. Second, we did not capture the severity of adverse effects among respondents. Third, our survey was mailed to patients soon after starting a new medication; thus, additional cases of nonpersistence would be expected with longer follow-up. Fourth, the cross-sectional nature of the survey makes it difficult to confirm which of these beliefs were present at baseline (i.e., before starting the drug) versus being formed during the causal pathway.

## Conclusion

Despite the seemingly strong link between the emergence of adverse effects and early nonpersistence, our findings confirm that this association is strongly influenced by factors beyond the physical experiences with a given drug. Beliefs and expectations about medications affect the willingness of patients to persist with medications if adverse effects occur early in the course of therapy. Therefore, health care providers must be aware of the possibility that medication intolerance may have origins in an individual's baseline beliefs and attitudes about the drug or their health condition in general.

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## References

1. World Health Organization. Adherence to long-term therapies: evidence for action. Available at: https://apps.who.int/iris/bitstream/handle/10665/42682/9241545992.pdf. Accessed December 27, 2021.
2. Raebel MA, Schmittdiel J, Karter AJ, Konieczny JL, Steiner JF. Standardizing terminology and definitions of medication adherence and persistence in research employing electronic databases. *Med Care*. 2013;51(8 Suppl 3):S11–S21.
3. Vrijens B, Vincze G, Kristanto P, Urquhart J, Burnier M. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. *BMJ*. 2008;336(7653):1114–1117.
4. Cramer JA, Roy A, Burrell A, et al. Medication compliance and persistence: terminology and definitions. *Value Health*. 2008;11(1):44–47.
5. Hess LM, Raebel MA, Conner DA, Malone DC. Measurement of adherence in pharmacy administrative databases: a proposal for standard definitions and preferred measures. *Ann Pharmacother*. 2006;40(7–8):1280–1288.
6. Korhonen MJ, Robinson JG, Annis IE, et al. Adherence tradeoff to multiple preventive therapies and all-cause mortality after acute myocardial infarction. *J Am Coll Cardiol*. 2017;70(13):1543–1554.
7. Rodriguez F, Maron DJ, Knowles JW, Virani SS, Lin S, Heidenreich PA. Association of statin adherence with mortality in patients with atherosclerotic cardiovascular disease. *JAMA Cardiol*. 2019;4(3):206–213.
8. Simon ST, Kini V, Levy AE, Ho PM. Medication adherence in cardiovascular medicine. *BMJ*. 2021;374:n1493.
9. Evans CD, Eurich DT, Remillard AJ, Shevchuk YM, Blackburn D. First-fill medication discontinuations and nonadherence to antihypertensive therapy: an observational study. *Am J Hypertens*. 2012;25(2):195–203.
10. Karter AJ, Parker MM, Moffet HH, Ahmed AT, Schmittdiel JA, Selby JV. New prescription medication gaps: a comprehensive measure of adherence to new prescriptions. *Health Serv Res*. 2009;44(5 Pt 1):1640–1661.
11. Pedan A, Varasteh L, Schneeweiss S. Analysis of factors associated with statin adherence in a hierarchical model considering physician, pharmacy, patient, and prescription characteristics. *J Manag Care Pharm*. 2007;13(6):487–496.
12. Leporini C, De Sarro G, Russo E. Adherence to therapy and adverse drug reactions: is there a link? *Expert Opin Drug Saf*. 2014;13(Suppl 1):S41–S55.
13. Rief W, Avorn J, Barsky AJ. Medication-attributed adverse effects in placebo groups: implications for assessment of adverse effects. *Arch Intern Med*. 2006;166(2):155–160.
14. Navar AM, Roe MT, White JA, et al. Medication discontinuation in the IMPROVE-IT trial. *Circ Cardiovasc Qual Outcomes*. 2019;12(1), e005041.
15. Nabieva N, Fehm T, Häberle L, et al. Influence of side-effects on early therapy persistence with letrozole in post-menopausal patients with early breast cancer: results of the prospective EvAluate-TM study. *Eur J Cancer*. 2018;96(1):82–90.
16. Flory JH, Keating SJ, Siscovick D, Mushlin AI. Identifying prevalence and risk factors for metformin non-persistence: a retrospective cohort study using an electronic health record. *BMJ Open*. 2018;8(7), e021505.
17. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res*. 1999;47(6):555–567.

18. Oladimeji O, Farris KB, Urmie JG, Doucette WR. Risk factors for self-reported adverse drug events among medicare enrollees. *Ann Pharmacother*. 2008;42(1):53–61.
19. Bultman DC, Svarstad BL. Effects of physician communication style on client medication beliefs and adherence with antidepressant treatment. *Patient Educ Couns*. 2000;40(2):173–185.
20. Ledford CJW, Villagran MM, Kreps GL, et al. "Practicing medicine": patient perceptions of physician communication and the process of prescription. *Patient Educ Couns*. 2010;80(3):384–392.
21. Simpson SH, Johnson JA, Farris KB, Tsuyuki RT. Development and validation of a survey to assess barriers to drug use in patients with chronic heart failure. *Pharmacotherapy*. 2002;22(9):1163–1172.
22. McGinnis B, Olson KL, Magid D, et al. Factors related to adherence to statin therapy. *Ann Pharmacother*. 2007;41(11):1805–1811.
23. McHorney CA. The Adherence Estimator: a brief, proximal screener for patient propensity to adhere to prescription medications for chronic disease. *Curr Med Res Opin*. 2009;25(1):215–238.
24. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health*. 1999;14(1):1–24.
25. Law MR, Cheng L, Dhalla IA, Heard D, Morgan SG. The effect of cost on adherence to prescription medications in Canada. *CMAJ*. 2012;184(3):297–302.
26. Boateng GO, et al. Devleloping and validating scales for health, social, and behavioural reserach: a primer. *Front Public Health*. 2018;6:149.
27. Dillman DA, Smyth JD, Christian LM. *Internet, Mail, and Mixed-Mode: the Tailored Design Method*. 3rd ed. Hoboken, NJ: John Wiley; 2009.
28. Pencina MJ, D'Agostino RB, Steyerberg EW. Extensions of net reclassification improvement calculations to measure usefulness of new biomarkers. *Stat Med*. 2011;30(1):11–21.
29. Pencina MJ, D'Agostino Sr RB. Evaluating discrimination of risk prediction models: the C statistic. *JAMA*. 2015;314(10):1063–1064.
30. Sipos M, Farcas A, Prodan N, Mogosan C. Relationship between beliefs about medicines and adherence in elderly patients with cardiovascular and respiratory diseases: a cross-sectional study in Romania. *Patient Educ Couns*. 2021;104(4):911–918.
31. Mohammed MA, Moles RJ, Chen TF. Medication-related burden and patients' lived experience with medicine: a systematic review and meta-synthesis of qualitative studies. *BMJ Open*. 2016;6(2), e010035.
32. Pound P, Britten N, Morgan M, et al. Resisting medicines: a synthesis of qualitative studies of medicine taking. *Soc Sci Med*. 2005;61(1):133–155.
33. Marshall IJ, Wolfe CDA, McKevitt C. Lay perspectives on hypertension and drug adherence: systematic review of qualitative research. *BMJ*. 2012;345, e3953.
34. Wood FA, Howard JP, Finegold JA, et al. *N*-of-1 trial of a statin, placebo, or no treatment to assess side effects. *N Engl J Med*. 2020;383(22):2182–2184.
35. Kerr AJ, Mitnala S, Lee M, White HD. Utilisation and maintenance of high-intensity statins following acute coronary syndrome and coronary angiography: opportunities to improve care (ANZACS-QI 26). *N. Z. Med J*. 2020;133(1511):21–40.
36. Chung PW, Yoon BW, Lee YB, et al. Medication adherence of statin users after acute ischemic stroke. *Eur Neurol*. 2018;80(1–2):106–114.
37. Alfian SD, Worawutputtapong P, Schuiling-Veninga CCM, et al. Pharmacy-based predictors of non-persistence with and non-adherence to statin treatment among patients on oral diabetes medication in the Netherlands. *Curr Med Res Opin*. 2018;34(6):1013–1019.
38. Liu X, Gelwicks S, Faries DE, Able SL. Initial duloxetine prescription dose and treatment adherence and persistence in patients with major depressive disorder. *Int Clin Psychopharmacol*. 2010;25(6):315–322.
39. Virani SS, Woodard LD, Akeroyd JM, Ramsey DJ, Ballantyne CM, Petersen LA. Is high-intensity statin therapy associated with lower statin adherence compared with *low*- to moderate-Intensity statin therapy? Implications of the 2013 American College of Cardiology/American Heart Association cholesterol management guidelines. *Clin Cardiol*. 2014;37(11):653–659.
40. Tarn DM, Paterniti DA, Williams BR, Cipri CS, Wenger NS. Which providers should communicate which critical information about a new medication? Patient, pharmacists, and physician perspectives. *J Am Geriatr Soc*. 2009;57(3):462–469.
41. Wells RE, Kaptchuk TJ. To tell the truth, the whole truth, may do patients harm: the problem of the nocebo effect for informed consent. *Am J Bioeth*. 2012;12(3):22–29.
42. Barnes K, Faasse K, Geers AL, et al. Can positive framing reduce Nocebo side effects? Current evidence and recommendation for future research. *Front Pharmacol*. 2019;10, 167–167.
43. Berry DC, Holden W, Bersellini E. Interpretation of recommended risk terms: differences between doctors and lay people. *Int J Pharm Pract*. 2004;12(3):117–124.
44. Sleath B, Roter D, Chewning B, Svarstad B. Asking questions about medication: analysis of physician-patient interactions and physician perceptions. *Med Care*. 1999;37(11):1169–1173.
45. Ziegler DK, Mosier MC, Buenaver M, Okuyemi K. How much information about adverse effects of medication do patients want from physicians? *Arch Intern Med*. 2001;161(5):706–713.
46. Izuka NJ, Alexander MAW, Balasooriya-Smeekens C, Mant J, De Simoni A. How do stroke survivors and their carers use practitioners' advice on secondary prevention medications? Qualitative study of an online forum. *Fam Pract*. 2017;34(5):612–620.

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**Appendix 1**

Survey: Prescription drugs used by people in Saskatchewan
Please use a pen to clearly mark your answers with an "X."

***Example question:***

1. You are:
   x Male
   o Female

If you have any questions, please feel free to contact us at **306-966-2081**.

Your answers will remain anonymous. In other words, we will **NEVER** find out your name or address unless you choose to provide it to us.

Once you have completed the survey, please mail it back in the envelope provided. You will NOT need stamps.

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**Section A:**

**In this first section, we would like to find out whether you agree to participate in this study.**

1. I have read the Participant Information and Consent Form and understand it.
   ▫ Yes
   ▫ No
2. I agree to fill out the survey and drop it in the mail.
   ▫ Yes
   ▫ No (Note: You can throw the survey away if you choose this option)
3. I give permission to the Saskatchewan Ministry of Health to give the researchers some information from records in the provincial health databases but not my name, address or telephone number.
   ▫ Yes
   ▫ No

**Section B:**

**In this section, we would like to find out whether you were prescribed a new medicine recently. If you were prescribed several new medicines lately, we will ask some questions to help you pick ONE only.**

4. In the past 4 months, has your doctor prescribed you a new medicine that you have not taken before?
   ¨ NO – I have NOT received any new prescriptions in the past 4 months
   § *If you selected "NO," you are finished the survey. Please return this questionnaire to us by mail.*
   ¨ Yes, I have been prescribed 1 new medicine in the past 4 months
   ¨ Yes, I have been prescribed MORE THAN 1 new medicine in the past 4 months
5. What types of NEW MEDICINE(S) have you started taking within the past 4 months? Select as many boxes as necessary.
   ¨ Medicine(s) for cholesterol ★★★★★(5)
   ¨ Medicine(s) for diabetes or high sugar ★★★★(4)
   ¨ Medicine(s) for high blood pressure ★★★(3)
   ¨ Medicine(s) for other conditions not listed ★★(2)
   Please specify_____
   _____
   ¨ I don't know what my new medicine(s) are for ★(1)
6. Looking at the medicine(s) you picked in the last question, which ONE has the most stars beside it?
   ▫ Medicine(s) for cholesterol
   ▫ Medicine(s) for diabetes or high sugar
   ▫ Medicine(s) for blood pressure
   ▫ Medicine(s) for other conditions not listed
   ▫ I don't know what my medicine(s) are for
7. Please write down the name of the ONE new medicine you selected in Question #3. This name can be found on the label of your pill bottle.
   _____

**Please continue to the next page**

**Section C:**

**Now that you have picked ONE new medicine, we would like to know how you got it.**

8. Were you prescribed this new medicine while you were in the hospital?
   ¨ Yes Go to Question #7
   ¨ No Continue to Question #6
9. On the day the doctor wrote your new prescription, how long did your appointment last?
   ▫ Less than 10 minutes
   ▫ 10-20 minutes
   ▫ More than 20 minutes
   ▫ Not sure
10. Who prescribed your new medicine?
    ▫ My regular doctor
    ▫ A "specialist" doctor that you had visited before
    ▫ A "specialist" doctor that you had never visited before
    ▫ A doctor who took care of me in the hospital
    ▫ Not sure
    ▫ Other (please specify) _____
11. Before the doctor prescribed your new medicine, did he/she ask if you would be willing to take it?
    ▫ Yes
    ▫ No o Not sure
12. What was the date that you started taking your new medicine (approximately)?
    (DD/MM/Year)_____
13. Did your doctor give you free samples of your new medicine before you started getting it from the pharmacy?
    ▫ Yes
    ▫ No

**Section D:**

**In this section, we would like to find out how much you were told about your new medicine. Please select whether you strongly agree, agree, disagree, or strongly disagree with the following statements.**

14. You were given a chance to ask questions about your new prescription to the doctor that prescribed it.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Disagree
    - ▫ Strongly disagree17k
15. You know what this new medicine is used for.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Disagree
    - ▫ Strongly disagree
16. You know the reasons why this new medicine is good for you.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Disagree
    - ▫ Strongly disagree
17. Before you started taking your new medicine, you were told about the side effects that it could cause.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Disagree
    - ▫ Strongly disagree
18. The doctor took the time to help you understand the new medicine.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Disagree
    - ▫ Strongly disagree
19. A pharmacist or nurse took the time to help you understand the new medicine.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Disagree
    - ▫ Strongly disagree

**Please continue to the next page.**

**Section E:**

**In this section, we would like to know what you think about your new medicine. Please select whether you strongly agree, agree, not sure, disagree, or strongly disagree with the following statements.**

20. Your new medicine is for a condition that is a danger to your health.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Not sure
    - ▫ Disagree
    - ▫ Strongly disagree
21. You are convinced that your new medicine is important for your health.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Not sure
    - ▫ Disagree
    - ▫ Strongly disagree
22. You worry that your new medicine will do more harm than good.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Not sure
    - ▫ Disagree
    - ▫ Strongly disagree

**Please continue to the next page.**

23. You expected this new medicine to be difficult to take exactly as prescribed by the doctor.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Not sure
    - ▫ Disagree
    - ▫ Strongly disagree
24. You expected to get side effects from this new medicine before you started taking it.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Not sure
    - ▫ Disagree
    - ▫ Strongly disagree
25. Overall, you trust the doctor that prescribed your new medicine.
    - ▫ Strongly agree
    - ▫ Agree
    - ▫ Not sure
    - ▫ Disagree
    - ▫ Strongly disagree

**Please continue to the next page.**

**Section F:**

**In this section, we would like to know what it is like to take your new medicine.**

26. For how long are you supposed to take your new medicine?
    - ▫ Less than 6 months
    - ▫ More than 6 months but less than 1 year
    - ▫ For at least 1 year or longer
    - ▫ Not sure
27. How many pills of your new medicine are you supposed to take each day?
    - ▫ half a pill per day
    - ▫ 1 pill per day
    - ▫ 1 pill EVERY SECOND day
    - ▫ 2 pills per day
    - ▫ 3 pills per day
    - ▫ 4 pills per day
    - ▫ 1 pill every week
    - ▫ 1 pill every month
    - ▫ Other (please specify _____)
28. Did you experience side effect(s) from your new medicine?
    - ¨ Yes Continue to Question #26
    - ¨ No Go to Question #28

¨ Not sure Continue to question #26

**Please continue to the next page.**

29. Did you receive help to deal with the side effect(s) of your new medicine?
    - ¤ Yes
    - ¤ No
    - ¤ Not sure
30. Did the side effect(s) of your new medicine prevent you from taking it as prescribed?
    - ¤ Yes
    - ¤ No
    - ¤ Not sure
31. Did you go back to see your doctor to discuss the new medicine after you started taking it?
    - ¤ Yes
    - ¤ No
    - ¤ Not sure
32. When you take your new medicine, how does it make you feel?
    - ¤ I feel better when I take it
    - ¤ I don't feel any different when I take it
    - ¤ I feel worse when I take it
    - ¤ I am not sure how it makes me feel
33. How often do you forget to take your new medicine?
    - ¤ I always forget
    - ¤ I sometimes forget
    - ¤ I rarely forget
    - ¤ I never forget

    **Please continue to the next page. You are over half-way finished!**
34. How do you remember to take your new medicine regularly? You may select MORE than one answer for this question.
    - ¨ A friend or family member helps me
    - ¨ I use a pill pack or bubble pack
    - ¨ I do not need help to remember
    - ¨ Other (please specify _____)
35. Do you have difficulty opening your medicine bottles?
    - ¤ Yes
    - ¤ No
    - ¤ Not sure
36. Do you have difficulty reading the instructions on your medicine bottles?
    - ¤ Yes
    - ¤ No
    - ¤ Not sure

**Section G:**

**In this section, we'd like to know how costly your new medicine is.**

37. Do you get a discount on your medicine costs? Select 'yes' if you do not pay full price.
    - ¤ Yes
    - ¤ No
    - ¤ Not sure
38. In the past few months, because of the cost, did you do anything to make your new medicine last longer?
    - ¤ Yes
    - ¤ No
    - ¤ Not sure
39. What is your best estimate of the total income received by all household members, from all sources, before taxes and deductions, in the past 12 months?
    - ¤ Less than $10 000
    - ¤ $10 000-24 999
    - ¤ $25 000-49 999
    - ¤ $50 000-74 999
    - ¤ $75 000-99 999
    - ¤ More than $100 000

**Section H:**

**In this section, we'd like to know how often you take your new medicine. We know that many people quit taking their new medications so please feel free to give us your honest answers. Your doctor will never know you took this survey and we will never be told your name.**

40. Are you still taking the new medicine prescribed to you?
    - ¨ Yes Go to Question #42
    - ¨ No Continue to Question #38

**Please continue to next page.**

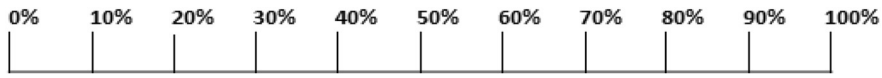
41. Approximately how long did you take your new medicine for before stopping?
    - ¤ I stopped taking it after 1 day
    - ¤ I stopped taking it between 2 to 6 days
    - ¤ I stopped taking it between 1 week and 1 month
    - ¤ I stopped taking it after more than 1 month
    - ¤ Not sure
42. Does your doctor know you stopped taking your new medicine?
    - ¤ Yes
    - ¤ No
    - ¤ Not sure
43. Whose decision was it to stop taking your new medicine?
    - ¤ It was my decision to stop
    - ¤ It was my doctor's decision to stop
    - ¤ My doctor and I both decided I should stop
    - ¤ I am not sure (or I don't remember)
44. Which of the following statements best describes why you stopped taking your new medicine? You may select MORE than one answer for this question.
    - ¤ I had a side effect that bothered me
    - ¤ I did not need the medicine anymore
    - ¤ I did not feel safe on this medicine
    - ¤ The medicine was too costly
    - ¤ The medicine was too inconvenient to take
    - ¤ Other - please specify _____
45. Many of us do not always take our medicines regularly. Please put an "X" on the line below to show your best estimate about how much of your new medicine you have taken since you started taking it.

    For example:

    0% means you have taken NONE of your new medicine

    50% means you have taken your medicine HALF as often as prescribed

    100% means you have taken your new medicine exactly as prescribed.




**Section I:**

**In this section, we would like to find out a little more about you.**

46. Do you have a regular family doctor?
    - ▫ Yes
    - ▫ No
47. How many different prescription medicines do you have to take every day (including your new medicine)?
    - ▫ 1
    - ▫ 2
    - ▫ 3
    - ▫ 4
    - ▫ 5
    - ▫ 6 or more

**Please continue to the next page.**

48. In general, would you say your health is:
    - ▫ Excellent
    - ▫ Very good
    - ▫ Good
    - ▫ Fair
    - ▫ Poor
49. In general, would you say your mental health is:
    - ▫ Excellent
    - ▫ Very good
    - ▫ Good
    - ▫ Fair
    - ▫ Poor
50. In general, would you say you are physically active?
    - ▫ Yes
    - ▫ No
51. In general, would you say you try to eat a healthy diet?
    - ▫ Yes
    - ▫ No
52. At the present time, do you use tobacco products (including cigarettes, cigars, a pipe, snuff or chewing tobacco)?
    - ▫ Yes, I use tobacco products daily
    - ▫ Yes, I use tobacco products occasionally
    - ▫ No, I do not use tobacco product at all
53. You are:
    - ▫ Male
    - ▫ Female
54. What year were you born? _____
55. What is the highest grade or level of school that you have completed?
    - ▫ 8th grade or lower
    - ▫ Grade 9-13
    - ▫ Trade certificate or diploma from a vocational school or apprenticeship training OR certificate or diploma from a community college, CEGEP, school of nursing
    - ▫ Bachelor's degree
    - ▫ University degree or certificate above bachelor's degree
56. Which of the following best describes your racial background? You may select MORE than one answer for this question.
    - ▫ White or Caucasian
    - ▫ Chinese
    - ▫ South Asian (e.g., East Indian, Pakistani, Sri Lankan)
    - ▫ Black
    - ▫ Filipino
    - ▫ Latin American
    - ▫ Southeast Asian (e.g., Cambodian, Indonesian, Laotian, Vietnamese)
    - ▫ Arab
    - ▫ West Asian (e.g., Afghan, Iranian)
    - ▫ Japanese
    - ▫ Korean
    - ▫ Aboriginal
    - ▫ Other
57. What is your marital status?
    - ▫ Married
    - ▫ Living common-law
    - ▫ Widowed
    - ▫ Separated
    - ▫ Divorced
    - ▫ Single, never married

**LAST QUESTION!**

58. Would you consider taking this same survey again in 1 month so we can check if your opinions about this new medication have changed?
    - ▫ YES (If you choose yes, the Ministry of Health will send you this SAME survey again)
    - ▫ NO (If you choose NO, they will NOT you send another survey)

**You have finished!**

**Thank you very much for taking part in this important study! If you have any questions or concerns, please feel free to phone me.**

Place this survey in the return envelope and drop it in a mailbox.

DO NOT write your name or address. It is important that we do not find out who you are or where you live. You will NOT need stamps.

Sincerely,
David Blackburn
College of Pharmacy & Nutrition
University of Saskatchewan
Phone number: 306-966-2081