Medication nonadherence: Time for a proactive approach by pharmacists

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As a country, in 2019, Canada expected to spend $34,300,000,000 on prescribed drugs, with public drug programs accounting for 43.6% of this amount. Since publicly funded drug programs are paid for by Canadian taxpayers, it behooves us to ensure that the spending on drug treatment achieves the outcome it is intended to: achieving therapeutic goals, improving quality of life, maintaining productivity and decreasing avoidable use of the health care system, especially hospitalization. However, widespread nonadherence to medications deters us from achieving these goals. Up to 50% of patients are not adherent to their medications. As Dr. C. Everett Koop, the 13th Surgeon General of the United States, wisely noted, “Drugs don’t work in patients who don’t take them.” Therefore, improving medication adherence improves use of the health care system and decreases costs. Indeed, based on the results of a systematic review of interventions to improve adherence, the World Health Organization postulated that “increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments.”

Unfortunately, nonadherence rates have not improved over the past 15 years. One of the reasons for continuing nonadherence is its inherent complexity. Not only are there various types of nonadherence (Table 1), but there also exists a multitude of complex reasons for nonadherence (Figure 1) and means of measuring adherence (Table 2). However, it is not considered an insurmountable problem, as shown by the plethora of medication-dispensing aids on the market and emerging technology providing health care providers and caregivers with the ability to monitor medication intake in real time.

As health care providers with the most comprehensive access to medication-dispensing records, pharmacists are most ideally placed to proactively address medication nonadherence. At our disposal are the primary means by which medication adherence is measured. Mean possession ratio (MPR) and pill counts are frequently used to determine adherence. Furthermore, an MPR of 80% as a cutoff between adherence and nonadherence can predict hospitalization across chronic conditions. Interventions delivered by pharmacists are significantly more effective at improving adherence than those from other health care professionals, especially when delivered in person with patients at pharmacy counters. A proactive approach to address nonadherence in pharmacies should be undertaken by the following:

1. **Investigating why a patient is nonadherent**

   Patients may be nonadherent to 1 or more of their medications. There are many reasons a patient may be nonadherent (Figure 1). Intentional nonadherence emerges when a patient actively weighs the pros and cons of taking a medication. They may have misconceptions about the severity of their condition or the progression of disease. They may have a fear of adverse effects or of developing a dependence that outweighs the expected benefits. They may distrust their health care providers, or there may be stigma associated with taking the medication. Patients may also be nonadherent unintentionally due to physical and cognitive limitations, complexity of medication regimens, polypharmacy or cost of medications. Patients may be illiterate or face language barriers. While one factor may be driving nonadherence in some patients, in others, multiple factors may be at play.

   A crucial first step in determining why a patient is nonadherent is a candid, yet nonjudgmental, conversation about their medications in a private space with limited interruptions.
### Table 1: Taxonomy of adherence\(^2,^3,^{11,16}\)

| Term                     | Definitions/description                                                                                                                                 |
|--------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|
| Adherence                | Adherence is defined as the extent to which a person’s medication-taking behaviour corresponds to recommendations from a health care provider. It refers to how well a patient initiates, implements and discontinues dosing recommendations.\(^2,^{16}\) Adherence to medications indicates taking the right dose of the right medication at the right time(s) for the right duration.\(^3\) Nonadherence arises when patients alter the dosing regimen, adjust the dose taken, change the time of administration or discontinue the medication too early. Patients may skip doses or take too many doses. |
| Intentional nonadherence | Intentional nonadherence refers to an active decision by the patient to not take their medications as directed or recommended.\(^11\) This may be due to adverse effects, mistrust of medications or lack of belief in need or effect. |
| Unintentional nonadherence| Unintentional nonadherence indicates a passive, unplanned process by which the patient does not take their medications as recommended.\(^11\) It may result from forgetfulness or complexity in organizing regimens, among others. |
| Overadherence            | Overadherence arises when a patient actively or passively takes more medication than recommended in a period of time.                                                  |
| Compliance               | Extent to which a person follows the recommendations provided by a prescriber.\(^2,^{11}\) The term compliance is differentiated from the term adherence by the nature of the decision-making process provided for medication taking. Compliance implies that the patient complies with the instructions provided by the prescriber instead of participating in the collaborative decision-making process.\(^11\) |
| Concordance              | The term concordance refers to a decision-making process between the prescriber and patient where there is agreement on the purpose and use of the medication.\(^11\) |
| Persistence              | The length of time between the first and last dose. Refers to how long a patient stays on treatment.\(^11,^{16}\) |

**Figure 1** Factors driving medication adherence and assessment of nonadherence\(^2,^{17}\)
Some have suggested motivational interviewing as a strategy to examine the factors that may be driving nonadherence. Pharmacists often cite time limitations as a reason for not pursuing interventions. If time is an issue, there are a number of validated self-report measures that patients can complete to identify the barriers to adherence (Table 3). By being proactive, pharmacists can gauge and address potential problems with adherence for new prescriptions or ongoing therapy.

### 2. Tailoring a patient-specific strategy to address nonadherence

Due to the numerous reasons for nonadherence, there is no one solution that is effective for every patient or even for every instance

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**TABLE 2 Measuring adherence**

| Measures                                      | Description                                                                                                                                                                                                 |
|-----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| **Direct measures**                           |                                                                                                                                                                                                            |
| Directly observed therapy                     | Patient receives and takes medication doses in a pharmacy or health care facility in the presence of a health care provider.                                                                                     |
| Drug concentrations                           | The concentration of a drug or its metabolite is measured in the blood or urine of the patient.                                                                                                             |
| **Indirect measures**                         |                                                                                                                                                                                                            |
| Rates of pharmacy refills                     | Adherence is measured by examining rates of pharmacy refills of chronic medications over a period of time. Examples include mean possession ratio (MPR), medication refill adherence (MRA) and proportion of days covered (PDC). Usually measures ratios of days supply to number of days in the observation period. |
| Pill counts                                   | Counting the number of pills remaining in the prescription vial                                                                                                                                             |
| Self-report                                   | Patient provides medication intake information over a period of time in response to questions posed by health care providers or through validated medication adherence questionnaires or medication diaries. |
| Electronic or cloud-based medication-dispensing device | Tracks the number of times a medication dose is dispensed by the number of times the device is opened or dose automatically dispensed                                                                   |

**TABLE 3 Selected examples of self-report measures of adherence**

| Questionnaire                                      | Number of items in questionnaire                                                                                           |
|----------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Self-Reported Adherence (SERAD) Questionnaire      | 3 components with a 13-item section examining reasons for nonadherence                                                   |
| Simplified Medication Adherence Questionnaire       | 6                                                                                                                          |
| Visual analog scale (VAS)                          | 1                                                                                                                          |
| Brief Adherence Self-Report Questionnaire (ASRQ)   | 6                                                                                                                          |
| Voils Measures of Extent and Reasons for Medication Nonadherence | 3 items examining extent of nonadherence and 21 on reasons for nonadherence                           |
| Medication Therapy Adherence Scale (ITAS-M)        | 4                                                                                                                          |
| Brief Adherence Rating Scale (BARS)                | 4                                                                                                                          |
| Adherence to Refills and Medication Scale (ARMS)   | 12                                                                |
| Brief Medication Questionnaire (BMQ)               | 9                                                                                                                          |
| Medication Adherence Scale (MAS)                   | 32 (with subscales examining knowledge, attitudes and barriers)                                                          |
| Morisky Adherence Questionnaire                     | 4 or 8                                                               |
of nonadherence in any one individual patient over time.\textsuperscript{3,6,11,13} Effective communication and counselling is key to alleviating misconceived fears of adverse effects, dependence and mistrust of expected need or benefits of medications.\textsuperscript{3,6,13} However, where fears are not driven by misinformation, an even greater collaboration may be required to assist the patient. Such interventions include assisting the patient by weighing the pros and cons of a specific medication to make an informed decision; identifying safer alternatives, whether pharmacological or nonpharmacological; addressing clinically significant drug interactions or devising a plan to address and manage adverse effects.\textsuperscript{3,11,14}

To address nonadherence that rises from dosing of multiple drugs multiple times per day, pharmacists can simplify medication regimens by eliminating duplicate medications, dispensing combination pills for stable conditions and decreasing the number of times a patient has to take their medications in a day, as long as it is reasonable to do so. Initiating a blister packaging service can eliminate the need for the patient to organize their medication taking.\textsuperscript{6,11}

Forgetfulness is one the most cited reasons for nonadherence. This can be addressed by collaboratively identifying storage locations that can remind patients about their medications or developing a medication-taking routine.\textsuperscript{3} Additionally, there are multiple electronic dispensing devices with embedded alarms that can be set to specific times. One can set up notifications to be delivered to patients through emerging dispensing technology that provides real-time monitoring of medication intake.\textsuperscript{6,8,11}

If a physical limitation is impeding appropriate medication taking, appropriate strategies can be implemented based on the type of physical limitation—whether it is replacing safety lids with easy-open lids, increasing the font on the prescription label or colour coding the prescription vials. Dispensing in pill packs or easy-open blister packaging may also address this problem.\textsuperscript{11}

3. Monitoring continuously and changing strategy as needed
Factors driving nonadherence may change over time or with medication.\textsuperscript{14} Therefore, proactive and continuous monitoring of medication adherence is key in timely identification of nonadherence. Pharmacies could devise monthly checks on dispensing of chronic medications or set dispensing thresholds for certain medications for patients, below which would necessitate an investigation. Patient-specific tailored interventions may need to change as a patient’s reason for nonadherence evolves.

By implementing these 3 steps, pharmacists can identify nonadherent patients, investigate the causes and strategize collaboratively with patients to improve medication adherence. To address the challenge of nonadherence, in this and upcoming issues, we will discuss features and characteristics of smart medication dispensing products,\textsuperscript{8} provide strategies for proactive case finding of nonadherent patients and present a clinician guide that pharmacists can use to recommend electronic medication dispensing aids.\textsuperscript{15}

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