Gaps in Medication Monitoring May Contribute to Death

- Develop standardized processes for following up (at appropriate intervals) with patients who are taking medications for chronic conditions that require laboratory monitoring.
- Educate patients with chronic medical conditions about the importance of lifelong follow-up appointments. For those taking medications that require monitoring, emphasize the need to ensure that this monitoring takes place.
- Requests for prescription refill authorization should be scrutinized carefully by both pharmacists, prescribers to ensure that the medication and its dose continue to be appropriate and safe.
- Implement standardized processes for communicating test results, including definition of roles and responsibilities both internally, within the clinic/practice, and externally, with laboratories and other testing facilities.

Hypothyroidism, a chronic condition resulting from low thyroid activity, affects up to 4% of the population. Symptoms of hypothyroidism include fatigue, weight gain, and cold intolerance.1,2 Levothyroxine, a synthetic form of a thyroid hormone, is the drug of choice for replacement therapy to treat this condition. Although levothyroxine is generally well tolerated, regular blood work is required to monitor thyroid hormone levels and prevent serious adverse events.3

As part of ongoing collaboration with several provincial offices of the Chief Coroner or Medical Examiner, ISMP Canada received a report about the death of a woman who was taking levothyroxine but had not undergone monitoring for an extensive period. This bulletin describes the suboptimal follow-up and monitoring of this patient’s hypothyroidism and suggests strategies to overcome the challenges associated with the management of patients with chronic disorders.

Medication Incident

Levothyroxine was prescribed for a young adult with hypothyroidism. She took this medication once daily for at least 4 years before her death. Abnormal results on laboratory tests conducted 3 years before her death suggested that the levothyroxine dose was too high. However, there was no documentation of any follow-up related to these results and no indication that any additional investigations had been ordered. According to available records, it appears that the prescriber authorized refills of the levothyroxine prescription multiple times without seeing the patient and without ordering repeat thyroid function tests.

About 1 month before her death, the patient went to the hospital because of palpitations and shortness of breath. Thyroid function tests at that time yielded results indicative of hyperthyroidism, probably due to an excessive replacement dose of levothyroxine. Additional investigations revealed evidence of heart damage. The patient later experienced cardiac arrest and could not be resuscitated. Post-mortem
investigations suggested that excessive levothyroxine therapy over a prolonged period may have contributed to the development of cardiomypathy, which in turn led to her death.

**Background**

Monitoring of the level of thyroid-stimulating hormone (TSH) in the blood is required to ensure that the replacement dose of levothyroxine is correct. Guidelines recommend checking TSH levels in the blood 4–8 weeks after initiation of therapy and after every dose adjustment. Once the TSH level is stable and within normal limits, additional testing every 12 months is considered acceptable. If testing reveals an abnormal result, then more frequent monitoring is recommended, together with medication dose adjustments, as needed, until the TSH stabilizes in the normal range.

Hyperthyroidism is a condition reflecting excessive thyroid activity. Although hyperthyroidism can be caused by a number of diseases, it is commonly the result of an excessive dose of replacement thyroid hormone. Persistent hyperthyroidism can cause atrial fibrillation, heart damage, and dilated cardiomypathy. Proper monitoring of the levels of TSH and other thyroid hormones, coupled with appropriate clinical assessment and suitable dose adjustments, is necessary to ensure safe patient care.

**Discussion**

This case highlights that follow-up and laboratory monitoring are critical for patients who are taking prescription medications over the long term. For undetermined reasons, there was a lack of follow-up for this patient, even though test results, both from 3 years before her death and at the time of hospital admission, suggested that she had had hyperthyroidism for some time. Initial titration of the levothyroxine dose and regular monitoring could potentially have prevented the heart damage and her untimely death.

Multiple factors must be considered to minimize the risk of harm when patients are treated for conditions requiring long-term medications. These factors can be related to the individual patient, to the practitioner, or to the communication of information (Table 1).

**Table 1. Risk factors for harm related to long-term medications**

<table>
<thead>
<tr>
<th>FACTOR TYPE: <strong>Patient-related</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPECIFIC RISK FACTOR:</strong></td>
</tr>
<tr>
<td>• Financial and transportation concerns</td>
</tr>
<tr>
<td>• Presence of comorbid conditions (e.g., mental health)</td>
</tr>
<tr>
<td>• Difficulty in navigating a complex medical system</td>
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<tr>
<td>• Medication nonadherence</td>
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<table>
<thead>
<tr>
<th>FACTOR TYPE: <strong>Practitioner-related</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPECIFIC RISK FACTOR:</strong></td>
</tr>
<tr>
<td>• Time and workload constraints:</td>
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<tr>
<td>- may prevent monitoring for adherence with prescribed therapy</td>
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<tr>
<td>- may negatively affect the care of patients with chronic medical conditions</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>FACTOR TYPE: <strong>Communication failures</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPECIFIC RISK FACTOR:</strong></td>
</tr>
<tr>
<td>• Ineffective communication among a patient’s multiple care providers</td>
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<tr>
<td>- missed reports of laboratory results</td>
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<tr>
<td>- poor documentation</td>
</tr>
<tr>
<td>• Lack of documentation by the primary care physician regarding required follow-up</td>
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</tbody>
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**Recommendations**

Conversations with patients about their medications can be initiated with “5 Questions to Ask about Your Medications”, a tool that was developed collaboratively by patients and healthcare professionals (https://www.ismp-canada.org/medrec/5questions.htm). Effective communication and joint decision-making can improve patients’ adherence to treatment plans and their overall health outcomes.

The following recommendations are suggested to improve the monitoring of, and communication with, patients who are taking medications for chronic conditions.
Monitor for new side effects, drug interactions, and contraindications. Evaluate whether the frequency of refill requests is appropriate and safe. Prescribe only enough medication to last until the next assessment is due.

Community Pharmacists

When patients start new drug therapy for a chronic medical condition:
- Provide both written and verbal drug information about symptoms that may indicate over- or under-dosing of the medication and recommend follow-up with the primary care provider if those symptoms appear. Highlight symptoms that require medical attention or a visit to the emergency department.
- Educate patients about the importance of lifelong follow-up appointments and, if they are taking prescribed medications that require therapeutic monitoring, the importance of ensuring that this monitoring takes place. Include discussion about recommended intervals for monitoring, and ask whether the next appointment has been scheduled.
- When patients are refilling medications for a chronic medical condition:
  - Review monitoring parameters (e.g., side effects and symptom control) and address any concerns.
  - Ask patients when they were last assessed or monitored by the prescriber. If the interval is longer than recommended for that medication, contact the prescriber to determine whether the patient should undergo reassessment or laboratory testing before continuing the medication.
  - Review the appropriateness of refill authorization requests before faxing them to the prescriber. Ensure that automated processes such as telephone dial-in services and electronic requests (by email or through a website) do not bypass this step.
  - Ask for an original prescription at appropriate intervals, to support regular follow-up with the physician.
- Lobby jurisdictional pharmacy advocacy groups to seek integration with and access to central laboratory databases. Such integration allows...
Levothyroxine, a synthetic form of a thyroid hormone. Thyroid function tests at that time yielded abnormal results. About 1 month before her death, the patient went to the hospital because of palpitations and shortness of breath. Prescription multiple times without seeing the patient prescriber authorized refills of the levothyroxine. Follow-up related to these results and no indication of any medication dose adjustments, as needed, until the TSH level is stable and within normal limits, additional testing every 4–8 weeks after initiation of therapy and after each dose adjustment. Guidelines recommend checking TSH levels in the blood every dose adjustment. Once the TSH level is stable, this bulletin describes the suboptimal and contraindications. The case described here illustrates how lack of monitoring for a patient with a chronic condition can lead to harm, including death. It is essential that practitioners consider the circumstances that may contribute to failures in a system that is designed and intended to ensure patient well-being. In addition to highlighting barriers to the care of patients with chronic medical conditions, this bulletin suggests improvements to both the healthcare system and individual practitioners’ practices.

### References


### Acknowledgements

ISMP Canada extends appreciation to the family for allowing details of this medication incident to be shared and gratefully acknowledges expert review of this bulletin by the following individuals (in alphabetical order):

- Julie Coffey, Director, Centre for Education, Institute for Quality Management in Healthcare, Toronto, ON;
- Yi Min Huang, MD, CCFP, Family Physician, Grace Health Centre, Toronto, ON; Mika Ng, RPh, BScPhm, Richmond Hill, ON; Janice Nolan, Executive Director, Programs, Institute for Quality Management in Healthcare, Toronto, ON; R. Kent Stewart, Chief Coroner of Saskatchewan, Regina, SK; Adrienne Tors, MD, Family Physician, Toronto, ON.
therapy to treat this condition. Although Levothyroxine, a synthetic form of a thyroid hormone (TSH) in the blood is required to ensure that it stabilizes in the normal range.5

A low thyroid activity, affects up to 4% of the population and could not be resuscitated. Post-mortem investigations suggested that excessive levothyroxine medication dose adjustments, as needed, until the hormone dose is optimized.6,7

Multiple factors must be considered to minimize the risk of harm when patients are treated for conditions such as hypothyroidism and suggests strategies to overcome barriers to the care of patients with chronic medical conditions.8

As part of ongoing collaboration with several professional guidelines, that outline considerations for this patient, even though test results, both from prescription medications over the long term. For patients who are taking medications for chronic conditions, this bulletin suggests adjusting, is necessary to ensure safe patient care. Monitoring for a patient with a chronic condition can contribute to failures in a system that is designed and required monitoring is taking place, and identify contraindications.


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**Injectable Compounded Product Label Design for Safety**

Label content and design have been identified as contributing factors to numerous medication incidents. It is crucial to consider the intended use of the product and the needs of the end user when designing product labels.

ISMP Canada has developed the following checklists for the safe labelling of injectable compounded products:

- A general checklist (for injectable compounded products)
- An epidural checklist (specific to epidural medications)
- An intravenous opioid checklist (specific to intravenous opioid medications)

ISMP Canada is seeking consultation from compounded product providers including manufacturers and commercial compounds, and community pharmacy and hospital compounds, as well as any other interested stakeholders.

**Please provide your feedback!**

(https://www.ismp-canada.org/CompoundLabelling/feedback.htm)

We appreciate your participation in this consultation, and look forward to your input by **Friday, March 24th, 2017**.
Your Opinion Matters!

We would like to invite you to participate in a short survey about your experience using *5 Questions to Ask about your Medications* developed collaboratively by Canadian Patient Safety Institute, Patients for Patient Safety Canada, Canadian Society of Hospital Pharmacists, Canadian Pharmacists Association and the Institute for Safe Medication Practices Canada. Your input will be used to help us continue to improve medication safety resources for patients.

This survey will take less than 5 minutes to complete. Thank you for your participation.

**Take the Survey**
(http://survey.patientsafetyinstitute.ca/n/5qstoaskforpatients.aspx)

If you have any further questions, please contact us at: medrec@ismp-canada.org

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**CMIRPS**

Canadian Medication Incident Reporting and Prevention System

The Canadian Medication Incident Reporting and Prevention System (CMIRPS) is a collaborative pan-Canadian program of Health Canada, the Canadian Institute for Health Information (CIHI), the Institute for Safe Medication Practices Canada (ISMP Canada) and the Canadian Patient Safety Institute (CPSI). The goal of CMIRPS is to reduce and prevent harmful medication incidents in Canada.

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**HIROC**

The Healthcare Insurance Reciprocal of Canada (HIROC) provides support for the bulletin and is a member owned expert provider of professional and general liability coverage and risk management support.

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**ISMP Canada**

The Institute for Safe Medication Practices Canada (ISMP Canada) is an independent national not-for-profit organization committed to the advancement of medication safety in all healthcare settings. ISMP Canada’s mandate includes analyzing medication incidents, making recommendations for the prevention of harmful medication incidents, and facilitating quality improvement initiatives.

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**Report Medication Incidents**

(Including near misses)

**Online:** [www.ismp-canada.org/err_index.htm](http://www.ismp-canada.org/err_index.htm)

**Phone:** 1-866-544-7672

ISMP Canada strives to ensure confidentiality and security of information received, and respects the wishes of the reporter as to the level of detail to be included in publications. Medication Safety bulletins contribute to Global Patient Safety Alerts.

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This bulletin shares information about safe medication practices, is noncommercial, and is therefore exempt from Canadian anti-spam legislation.

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**Contact Us**

**Email:** cmirps@ismp-canada.org

**Phone:** 1-866-544-7672

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