INSPQ INSTITUT NATIONAL DE SANTÉ PUBLIQUE DU QUÉBEC

Preventing Intentional OTC Drug Overdoses

Québec

AUTHORS (in alphabetical order)

Louise Marie Bouchard, Scientific Advisor
Direction du développement des individus et des communautés

Élise Chartrand, Scientific Advisor
Unité Évaluation de l'organisation des soins et services

Pierre-André Dubé, Pharmacist-Toxicologist
Direction de la santé environnementale et de la toxicologie

Dominique Gagné, Scientific Advisor
Direction du développement des individus et des communautés

Mathieu Gagné, Scientific Advisor
Bureau d'information et d'études en santé des populations

Gilles Légaré, Scientific Advisor
Bureau d'information et d'études en santé des populations

Pierre Maurice, Medical Specialist
Direction du développement des individus et des communautés

Anne-Claire Panneton, Pharmacist
Direction de la santé environnementale et de la toxicologie

UNDER THE COORDINATION OF

Pierre-André Dubé, Pharmacist-Toxicologist
Direction de la santé environnementale et de la toxicologie

Pierre Maurice, Medical Specialist, Unité Sécurité et prévention des traumatismes
Direction du développement des individus et des communautés

WITH THE COLLABORATION OF

Charles Cardinal, Librarian
Centre for Research and Intervention on Suicide and Euthanasia (CRISE), Université du Québec à Montréal

Elham Rahme, Associate Professor
Faculty of Medicine, McGill University

LAYOUT

Florence Niquet, Administrative Officer
Direction du développement des individus et des communautés

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Stéphanie Mercier, Pharmacist, Member of the Comité consultatif scientifique en matière de conditions et modalités de vente des médicaments, Office des professions du Québec

Vicky Tessier, Librarian
Institut national de santé publique du Québec

External Panel of Experts

René Blais, Medical Director
Centre antipoison du Québec

Ian Bourgoin, Pharmacist, Pharmaceutical Affairs Advisor, Association québécoise des pharmaciens propriétaires

Michel Caron, Pharmacist, adjoint professionnel à la direction générale, Ordre des pharmaciens du Québec

Claudine Laurier, Pharmacist, Full Professor,
Faculté de pharmacie, Université de Montréal

Brian Mishara, Director
Centre for Research and Intervention on Suicide and Euthanasia (CRISE)

Denis Roy, Senior Director, Professional Affairs
Association des bannières et des chaînes de pharmacie du Québec

European Expert Consulted

Keith Hawton, Professor of Psychiatry
Centre for Suicide Research, University of Oxford

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Preface

The range of possible interventions to prevent suicide deaths and suicide attempts, including intentional overdoses with over-the-counter drugs, must include actions at various levels, from promoting mental health to reducing access to means to proper treatment of depression, early screening for high-risk situations, and the implementation of sentinel training programs in the workplace and the community.

As part of the mandate given by the Ministère de la Santé et des Services sociaux (*Ministry of Health and Social Services*), this opinion focuses specifically on the use of over-the-counter drugs as a means of committing suicide.

Table of contents

The appendices to this document are available (in French only) at:

https://www.inspq.qc.ca/sites/default/files/publications/2117_intoxications_volotaires_medicaments_annexes.pdf.

Appendices

List of initialisms and acronyms

ASA	Acetylsalicylic acid
INSPQ	Institut national de santé publique du Québec (*Quebec National Institute of Public Health*)
MPS	Maximum package size
MQS	Maximum quantity per sale
MUD	Maximum unit dose
NAPRA	National Association of Pharmacy Regulatory Authorities
NDSAC	National Drug Scheduling Advisory Committee
NSAID	Non-steroidal anti-inflammatory drug
OTC	Over-the-counter
PD	Prescription drug

Key messages

- Each year in Québec, approximately 174 people commit suicide by drug overdose, of which at least 15 are the result of over-the-counter (OTC) drug overdoses.
- A substantial number of suicides and suicide attempts by overdose involve more than one substance.
- The number of suicides by OTC medication is underestimated, since in cases where several drugs have been ingested, only the substance that is presumed to have caused the death is considered when determining the most likely cause of death.
- Acetaminophen is by far the most common drug involved in intentional OTC drug overdoses, followed by salicylates, non-steroidal anti-inflammatories, and antihistamines. Depending on the ingested drug and dose, these medications can have serious adverse health effects.
- Unlike in a number of European countries, Canada (including Québec) has no restrictions on the maximum quantity per OTC pack sold in pharmacies, particularly for acetaminophen, ibuprofen and naproxen.
- The intervention strategy most often studied to reduce intentional OTC drug overdoses involves acetaminophen and consists of reducing the number of tablets per container and per purchase. The results of studies in the United Kingdom indicate that this type of measure has significantly reduced the number of suicides and attempted suicides involving acetaminophen, as well as accidental intoxications with the drug. However, there are few studies on the subject and numerous methodological constraints. It is difficult to conclude with certainty that such a measure has any impact on the rate of intentional acetaminophen overdoses, although a number of studies have suggested benefits.
- Other measures for reducing acetaminophen overdoses described in the scientific literature generally involve expert opinions. These focus on packaging, reducing the dose per tablet, labelling, public education, restricting sale sites, allowing sale by prescription only, and the addition of another active ingredient in the products to reduce liver toxicity.
- In the light of the scientific literature consulted and the deliberations of the experts panel, a number of measures are recommended for Québec, namely:
  - Set a maximum package size for OTC acetaminophen under Schedule III of the Regulation respecting the terms and conditions for the sale of medications.
  - Urge the public and health care professionals to contact the poison centre (Centre antipoison du Québec) for any overdose, intentional or otherwise.
  - Include the problem of intentional OTC drug overdose in any integrated suicide prevention strategy.
- Other measures may also be considered, including:
  - Greater public awareness and information on the safe use of OTC drugs while taking care to craft the messages in such a way that these medications are not seen as a means of suicide.
  - Set up an official Québec program to collect and safely dispose of expired or unused medication.
  - Limit the maximum unit dose for some OTC medications.
  - Set a maximum package size for medications other than acetaminophen.
  - Set a maximum quantity per sale for some OTC medications.
  - Reclassify some OTC drugs while maintaining their accessibility (make them Schedule II under the pharmacist's control – behind-the-counter).

Summary

This opinion was prepared at the request of the Ministère de la Santé et des Services sociaux. Its purpose is primarily to examine all the strategies available for preventing intentional over-the-counter (OTC) drug overdoses and determine which of them would be desirable and applicable in Québec.

To that end, the following objectives were pursued:

- Describe the scope and characteristics of the problem of intentional OTC drug overdoses in Québec and compare this with what has been observed in some other jurisdictions.
- Describe the legislation in place at the provincial, national and international levels that limits access to OTC drugs for use in humans.
- Synthesize knowledge of interventions that are effective at preventing intentional OTC drug overdose identified in the scientific literature and in grey literature and isolate the key underlying theoretical models.
- Determine measures applicable in Québec that provide the greatest benefit with the fewest drawbacks.

Legislation regulating access to OTC drugs for use in humans

In Canada, in accordance with the *Food and Drugs Act* and the *Food and Drug Regulations*, the federal government determines which drugs must be available by prescription and which can be dispensed over-the-counter. It is up to each provincial and territorial government to enact stricter regulations regarding OTC drugs, if necessary. In Québec in 1998, the Office des professions du Québec adopted the Regulation respecting the terms and conditions for the sale of medications. Under these regulations and the *Pharmacy Act* (chapter P-10, s. 37.1), drugs for use in humans are divided into categories in the form of schedules (schedules I, II and III, and unscheduled drugs). Each category determines the terms and conditions of drug sales.

The four OTC drugs most often involved in intentional drug overdoses are acetaminophen, ibuprofen, naproxen and acetylsalicylic acid (ASA). A comparative analysis of access to these drugs was produced in a number of jurisdictions, including Canada, and more specifically Québec, as well as other socioeconomically comparable countries. While acetaminophen, ibuprofen and ASA are accessible under certain conditions outside of pharmacies in most countries, including Canada, some European countries, such as France, Germany and Finland, restrict access to pharmacies only. Only the United States does not place any specific conditions on the sale of these products, apart from a maximum unit dose for ibuprofen sold outside of pharmacies. Unlike most of the targeted countries, Canada (including Québec) and the United States do not impose any maximum packaging size for most OTC drugs sold in pharmacies, whether they are on the shelves or under the pharmacist's control.

Scope of the problem

It is difficult to determine with any accuracy which drug is most often used to commit suicide, given the tendency to use more than one drug when committing suicide. The available statistics show that each year, at least 174 Québecers commit suicide by drug overdose, 15 of whom take OTC drugs. The actual number is likely higher, since in cases where several medications are taken, only the substance found in toxicology screening by the coroner is considered when determining the most likely cause of death. OTC drugs also cause 750 hospitalizations annually for intentional overdoses, most often caused by acetaminophen. In addition, it is estimated that between 6,000 and 7,300 people a year visit the emergency department for intentional OTC drug overdoses, with acetaminophen again the predominant culprit. A study conducted in two Montréal hospitals showed that 40% of patients visiting emergency departments for intentional acetaminophen poisoning had purchased the drug for the express purpose of overdosing, while the remainder had used the tablets they had available at home. Young people and women were most often hospitalized or treated in emergency departments for non-intentional OTC drug overdoses.

Effective interventions

The most studied intentional OTC drug overdose reduction strategies in the scientific literature focus on acetaminophen. Eight strategies were identified:

- Setting maximum package sizes and quantities per sale.
- Packaging: using blister packs rather than bottles.
- Reducing the maximum unit dose.
- Adding ingredients in each tablet to decrease liver toxicity.
- Overdose warnings on the label.
- Public education on the dangers of acetaminophen poisoning.
- Restricting points of sale to pharmacies only.
- Making acetaminophen available by prescription only.

Of these strategies, the most studied was restricting the number of tablets per container and per purchase. Its effectiveness has been difficult to gauge with certainty, given the many methodological problems encountered. These difficulties play a major role in the variability of results observed in the studies. In any event, studies on legislation limiting the number of tablets per sale in the United Kingdom have shown some reduction in the number of cases of acetaminophen poisoning.

Despite the conflicting opinions, Keith Hawton, head of the Centre for Suicide Research at Oxford University (England) and author and co-author of several studies and publications on acetaminophen poisoning, feels that the U.K. legislation has helped to reduce the number of overdoses. The researcher and his colleagues conducted a study in England and Wales in 2013 that attempted to control a number of the limitations observed in other studies. The researchers observed a significant reduction (42%) in acetaminophen-related deaths, with 765 fewer deaths by suicide or indeterminate cause and 975 fewer deaths if non-intentional deaths are factored in. Nonetheless, given that the rate of severe acetaminophen poisoning remains high in the United Kingdom, Hawton and his colleagues suggested a further reduction in the number of tablets per pack.

Given the difficulty of enforcing merchant compliance with such legislation, methods such as programming cash registers and offender monitoring have been suggested.

Lastly, to maximize the impact of legislation on acetaminophen consumption and minimize the substitution effect, it is advisable that the same rules apply to the sale of all OTC pain relievers (e.g., ibuprofen, ASA).

The other strategies identified are less well documented than the first. They have been described for the most part through qualitative studies conducted primarily via interviews of patients who attempted suicide by acetaminophen overdose. They have been recognized by some authors as possibly preventing acetaminophen poisoning. As for adding ingredients to decrease liver toxicity, this measure is generally rejected owing to the anticipated side effects.

Interventions applicable in Québec

A deliberative process was used to determine which preventive measures would be applicable in Québec. A consensus was reached on a number of desirable measures, namely: 1) setting a maximum package size for Schedule III OTC acetaminophen; 2) promoting the use of the poison centre (Centre antipoison du Québec), by disseminating the telephone number to professionals and the public to ensure rapid response to overdoses, whether intentional or otherwise; and 3) incorporate the problem of intentional OTC drug overdoses into any suicide prevention strategy.

Other measures in addition to those above have been suggested but are not the subject of a consensus. These are:

- Implementing an information strategy focused on safe acetaminophen use by means of better product labelling.[1] This strategy is in place in the United States and is being planned by Health Canada. It will emphasize morbidity rather than the risk of death (and by implication, suicide). This measure does not

[1] Health Canada, Incident Report. [http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2015/54178a-eng.php pages consulted on July 9, 2015].

have unanimous support because it could lead those with mental health problems or who are in crisis to see this type of medication as a suicide method.

- Implementing an official provincial program to collect expired or unused medication for safe disposal so that the practice can be better overseen, standardized and centralized. The program should be accompanied by ongoing public awareness on the public-health benefits of the practice (e.g., fewer drugs available in the home for abuse or intentional overdose by youth).[2] This measure is controversial owing to the lack of evidence of its effectiveness.

The panel of experts was also unable to reach a consensus on other methods for controlling access to OTC medications, such as limiting unit doses and maximum quantities per sale. The experts were divided between the need to institute some of these measures in Québec and the reluctance around the constraints they would impose on users and the pharmaceutical sector.

It is in this context that the decision was made to present a number of measures that could be implemented alone or in combination and set out the pros and cons of each. Apart from the status quo, these measures are:

- limiting the maximum unit dose;
- setting a maximum package size for OTC medications other than acetaminophen;
- setting a maximum quantity per sale; and
- rescheduling certain OTC drugs while maintaining their accessibility (e.g., Schedule II).

[2] This type of measure is discussed in Ouellet N, Dubé PA. Retour des médicaments périmés ou inutilisés aux fins de destruction du point de vue de la santé publique. *Bulletin d'information toxicologique* 2014;30(2):47-65. [Online, available in French only] https://www.inspq.qc.ca/toxicologie-clinique/retour-des-medicaments-perimes-ou-inutilises-aux-fins-de-destruction-du-point-de-vue-de-la-sante-publique

1 Introduction

Suicide is often an impulsive act committed in a moment of crisis or in response to a trigger event. Under such circumstances, quick access to a means of committing suicide increases the risk of a suicide attempt and, depending on the lethality of the chosen method, the risk of death from such an attempt (Mishara and Tousignant, 2004). For this reason, the World Health Organization feels that a strategy aimed at controlling access to means should be part of any national suicide prevention plan (World Health Organization, 2014).

This opinion focuses on this strategy, which is in line with the 2008-2012 Québec Public Health Program, which calls for closer oversight of medication access as a means of reducing Québec's suicide rate. Depending on the substance and dose ingested, OTC drugs like acetaminophen, ibuprofen and ASA can have serious health consequences, such as liver and kidney damage, cardiopulmonary disorders, coma and death.[3]

According to the systematic review by Mann et al. (2005), the implementation of strategies aimed at reducing drug accessibility is an effective way to reduce the total number of intentional overdoses, a number of which result in suicide. Strategies for reducing the risk of intentional drug overdoses include reducing the quantity of readily accessible medication, reducing toxicity or substituting less toxic products (Mann et al., 2005). The drugs most often involved in intentional overdoses include some OTC medications. In order to reduce overdoses of these medications, some countries, including the United Kingdom, have passed legislation to tighten control over accessibility.

It is in this context that this opinion was prepared at the request of the Ministère de la Santé et des Services sociaux (*Ministry of Health and Social Services*). Its purpose is to examine all existing strategies for preventing intentional OTC drug overdoses and determine which strategies are appropriate and applicable in Québec.

2 Objectives

To achieve the stated goal, the following objectives were set:

- Describe the scope and characteristics of the intentional OTC drug overdoses problem in Québec and compare this to findings in some other jurisdictions.
- Describe legislation enacted at the provincial, national and international levels to limit access to OTC drugs for use in humans.
- Synthesize knowledge of interventions that are effective at preventing intentional OTC drug overdoses, as set out in scientific and grey literature.[4]
- Identify measures applicable to Québec that confer the greatest benefits with the fewest drawbacks.

The preparation of this opinion required producing a number of supporting documents and tools. These are presented in the appendices.[5]

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[3] See Appendix 1 for the potential medical consequences of intentional OTC drug overdoses with one or more of the most common drugs, divided into three levels of severity.

[4] "Grey literature stands for manifold document types produced on all levels of government, academics, business and industry in print and electronic formats that are protected by intellectual property rights, of sufficient quality to be collected and preserved by library holdings or institutional repositories, but not controlled by commercial publishers." (Schöpfel, 2012)

[5] Avis sur la prévention des intoxications volontaires par médicaments accessibles sans ordonnance: annexes https://www.inspq.qc.ca/sites/default/files/publications/2117_intoxications_volotaires_medicaments_annexes.pdf [available in French only]

3 Methodology

3.1 Conceptual framework

Two conceptual frameworks were used in this process. The first, described by Florentine and Crane (2010), involves the steps in the suicidal process, from a triggering event through distress, suicidal ideation, a suicide attempt, and finally to suicide death. This framework was helpful in properly situating the access-to-means strategy within the range of suicide prevention measures.

The second framework was described by Haddon (1980). Its purpose is to support the identification of a set of potential prevention strategies to reduce the number of intentional OTC drug overdose cases by means of a matrix. Consisting of two axes, the matrix made it possible to target potential interventions in four categories of factors: human (e.g., modifying consumer behaviour); technological (e.g., packaging); environmental (e.g., environment that lends itself to supervision by a pharmacist); and economic or socio-legal environmental factors (e.g., list of medications on one of the schedules of the Regulation respecting the terms and conditions for the sale of medications). The vertical axis of the matrix is made up of three phases defined in reference to an event, namely: the pre-event phases (preventing the ingestion of a drug); peri-event (reducing the toxicity of the ingested dose); and post-event (access to rapid and appropriate emergency care).

In this opinion, the event is defined as the intentional consumption of a potentially toxic dose of one or more OTC drugs. In order to focus our efforts on prevention, the pre- and peri-event phases were given priority.

3.2 Legislation governing access to medications for use in humans

A number of regulatory body websites were consulted to collect information about the federal and provincial legislative frameworks governing OTC drugs for use in humans in Canada. First, the Health Canada site was consulted to obtain information about federal legislation. From that site, links provided access to the texts of Canadian statutes and Health Canada Therapeutic Products Directorate guidelines. The site also mentioned the involvement of the National Association of Pharmacy Regulatory Authorities (NAPRA). The NAPRA site contained information about drug classification and the implementation status, in each Canadian province and territory, of the proposed national model. Further links provided access to the sites of the various orders of pharmacists across Canada.

The Ordre des pharmaciens du Québec (*Quebec College of Pharmacists*) and Office des professions du Québec websites were consulted to access legislation governing the terms and conditions of the sale of drugs for use in humans in Québec. Lastly, a member of the Office des professions du Québec scientific advisory committee on the terms and conditions of the sale of medications was consulted for further information, including the workings of the committee in charge of making recommendations on drug classification decision rules in Québec.

3.3 Scope and characteristics of the problem

Estimates of intentional overdoses[6] and the substances used were made using a number of data sources for the Québec population aged 10 and over. The number of deaths and suicides were taken from the computerized database registry of the Québec coroner's office (Bureau du coroner du Québec) for 2001 through 2010. The number of hospitalizations for overdoses was taken from the Med-Echo sheets for six years from 2006-2007 through 2011-2012. Figures for all intentional overdoses (suicides and suicide attempts) and overdoses with unknown intent[7] were taken from these two databases.

The number of overdose cases involving hospital emergency department visits was estimated based on the Ontario rates for the most recent years available. With regard to the substances used in overdose cases, these were determined using the data from a research project carried out in two Québec hospitals for 2009-2010 and an estimate of population health surveys. Lastly, the database of the poison centre (Centre

[6] Overdose is a physiological state resulting from the action of one or more toxic substances within the body. It is intentional when the person who overdosed did so with the deliberate intention of doing him/herself harm.

[7] See Appendix 2 for a detailed description of the data sources (reliability, inclusion, exclusion, etc.).

antipoison du Québec) was used to calculate the number of calls made for OTC drug overdoses.

3.4 Synthesis of knowledge of effective interventions

3.4.1 Published material

In winter 2014, the search for published material was carried out using two search engines (Ovid and EBSCO) available through the Institut national de santé publique du Québec (INSPQ). Some documents were identified by looking through the bibliographies of synthesis documents that were deemed the most relevant and the most recent materials.[8] To be selected, a document would have to focus on intentional OTC drug overdoses reduction strategies or on the risk of substitution when strategies were implemented to reduce access to a means of committing suicide.

The second phase of the document search was completed using the bibliographies of selected articles. The process was carried out in March 2015 using the Google Scholar and Scopus databases and consisted of identifying studies published in 2014 and 2015 that cited one or more of the studies listed in the bibliographies of the articles selected in the initial phase. Only articles that directly related to OTC drug controls for preventing intentional overdoses (or that appeared to do so based on their titles) were selected.[9]

In March 2015, a search of cited works in articles in the bibliographies of documents selected in the first phase was carried out using the Google Scholar and Scopus databases. This material search method made it possible to identify instances of the use of knowledge published in scientific journal articles published earlier. Because the initial search for published material was carried out in early 2014, only cited works published in 2014 and 2015 were considered.

3.4.2 Unpublished material

Three databases focusing specifically on or including dissertations and theses, i.e., Open Access Theses and Dissertations, ProQuest Dissertations and Theses, and PsycInfo, were searched. The search questions used were similar to those used in the published material search, with semantics adapted to each database. The grey literature sites recommended by the INSPQ were also consulted.[10] The results of these searches yielded little material that was relevant to this opinion. Unpublished documents were forwarded by colleagues or were identified during the material search and reading process.

3.5 Deliberative process with outside experts

A panel of external experts was set up to support the work of the INSPQ members, specifically with regard to:

- scientific material and grey literature about intentional OTC drug overdoses; and
- the legal context surrounding the sale of over-the-counter (OTC) drugs in Québec and Canada, as compared to other developed countries and the United States in particular.

The panel engaged in a deliberative process[11] to select the prevention strategies with the most benefits and fewest drawbacks in a Québec context.

To that end, four meetings were held. The first two involved presenting the key issues and discussing the control strategies identified in the scientific literature. To complement these two meetings, the task force consulted a European expert, Dr. Keith Hawton, author of several studies and publications on restricting access to acetaminophen in the United Kingdom.

In addition, in order to collect positions on preventive measures applicable in Québec, the experts were asked to complete a questionnaire. The questions centred on the following themes:

- Effective or promising measures tailored to the Québec reality targeting individuals, products, the environment and legislation to curb intentional OTC

8 See Appendix 3 for detailed information on the documentation search (Tables 2, Through 7).

9 The cited works and unpublished material search was performed by the Centre for Research and Intervention on Suicide and Euthanasia (CRISE).

10 See Appendix 4 for the grey literature sites recommended by the INSPQ.

11 "A deliberative process is a process allowing a group of actors to receive and exchange information, critically examine an issue, and to come to an agreement which will inform decision making." (Fearon, 1998) http://www.ncchpp.ca/docs/DeliberativeDoc1_EN_pdf.pdf

drug overdoses that did not focus solely on limiting means.

- The pros and cons of a measure aimed at reducing accessibility by limiting the quantity available, package size and places of sale.
- Relevance for Québec of adopting measures to limit access to some OTC drugs, such as acetaminophen, salicylates, first-generation antihistamines, ibuprofen, naproxen and dextromethorphan.

The results of this exercise were used to inform discussions in the fourth and final committee meeting.

4 Legislation governing access to drugs for use in humans

4.1 Canada

In Canada, under the *Food and Drugs Act* and the *Food and Drug Regulations*, the federal government determines which drugs must be dispensed by prescription and which are available over the counter. Each of the provincial and territorial governments is free to enact stricter regulations, as needed, with regard to OTC drugs.[12]

In May 1995, NAPRA proposed a national model of schedules for human drugs to harmonize drug sale conditions across Canada. The model consisted of three schedules or four categories of drugs for use in humans: schedules I (prescription drugs), II (drugs dispensed under pharmacist control – behind-the-counter) and III (drugs available under pharmacist supervision – over-the-counter), and unscheduled drugs. Each category determines the terms and conditions of sale of the drugs.[13] A National Drug Scheduling Advisory Committee (NSAC), made up of eight Canadian experts and representatives of the Consumers' Association of Canada and Health Canada's Therapeutic Products Directorate, issues recommendations to the provincial pharmaceutical regulatory authorities using procedures and inclusion factors that are established for each schedule.[14]

The model uses the principle of non-scheduling, meaning that a drug is first assessed using Schedule I criteria, then those of Schedule II, and finally Schedule III. If the drug does not meet the scheduling criteria for any of the schedules, it is considered unscheduled and may be sold at any point of sale without restriction. The schedule determines the conditions of sale of its listed drugs. This process ensures appropriate medication use and public safety.

The NDSAC makes drug scheduling recommendations at the request of manufacturers, the public or any other interested party requesting the rescheduling of a drug. Recommendations can also involve the approval of a new OTC drug or a request from the federal government to deregulate a given prescription drug.

NAPRA serves as a committee secretariat, sending scheduling recommendations to proponents, provincial regulatory bodies and other interested parties. All Canadian provinces and territories except Québec have adopted the NAPRA model.

4.2 Québec

In 1998, the Office des professions du Québec adopted the Regulation respecting the terms and conditions for the sale of medications. Under these and the *Pharmacy Act* (chapter P-10, s. 37.1), drugs for use in humans are also divided into schedules (schedules I, II and III, and unscheduled drugs). These schedules are the same as those set by Health Canada, but the list of drugs in each schedule may differ in that it may be more restrictive than what is set out in the federal government's basic conditions. The scientific advisory committee on the terms and conditions of drug sale (Comité consultatif scientifique en matière de conditions et modalités de vente des médicaments) consists of one physician, one pharmacist and one veterinarian. Its role is to assess drug rescheduling requests received by the Office using inclusion factors (currently under revision by the committee, last updated 2006-03-07).[15] The committee

[12] See Appendix 5 for elements pertaining to legislation of drugs for use in humans (Table 8).
[13] See Appendix 5 for Québec's Terms and Conditions for the Sale of Medications for Human Consumption (Table 9).
[14] See Appendix 6 for ANORP classification of drugs for use in humans.
[15] See Appendix 7 for information on the classification of drugs for use in humans by the Office des professions du Québec.

makes recommendations to the Office, which consults with the Institut national d'excellence en santé et en services sociaux (*National Institute of Excellence in Health and Social Services*), the Collège des médecins du Québec (*Quebec College of Physicians*), the Ordre des médecins vétérinaires du Québec (*Quebec College of veterinarians*) and the Ordre des pharmaciens du Québec (*Quebec College of Pharmacists*) before regulating the terms and conditions of sale.

The committee makes drug scheduling recommendations in response to business cases made to the Office by an interested person or persons. Most requests are made by manufacturers. Any regulation amendment decisions by the Office are published in the *Gazette officielle du Québec* and there is a 45-day period during which any person or persons can forward comments to the Office president. Once the comment period has passed, the provincial government is free to approve the regulation, with or without changes. The Office notifies the applicants of the decisions rendered.

4.3 Other countries

Legislation in selected countries, namely Germany, Australia, Denmark, the United States, Finland, France, Ireland, Norway, New Zealand, the United Kingdom and Sweden, was consulted to provide a general overview of OTC drug accessibility and compare this to the situation in Canada and Québec. Generally speaking, a drug is classified based on whether or not it is dispensed by prescription. In both cases, it is available through pharmacies under the direct or indirect control of the pharmacist. In some cases, OTC drugs can also be made available outside the pharmacy setting, in a setting with no pharmacist on duty. Depending on the country, sale outside of pharmacies—general sale—may require government authorization. For example, authorization must be obtained from the Danish government to allow qualified staff in a non-pharmacy point of sale to sell OTC drugs. In Canada and the United States, however, once general sale is authorized in any business, the presence of qualified staff is not required. In France and Finland, sales of drugs outside the pharmacy setting (general sale) is not allowed. Each country's legislation has its own unique characteristics. To compare the targeted countries to Canada and more specifically Québec, a summary of direct access to the four oral OTC drugs for human use most often involved in intentional overdoses was prepared.[16] It should be noted that remote access (e.g., via the Internet) was not examined as part of this opinion.

Overall, acetaminophen, ibuprofen and ASA are accessible without a prescription under certain conditions (maximum unit dose, maximum package size), outside of pharmacies in most countries, including Canada. Some European countries, such as France, Germany and Finland, restrict access to pharmacies only. Only the United States imposes no specific conditions for general sale of these products, apart from a maximum unit dose of 200 mg for ibuprofen, and package sizes are not limited to a maximum quantity of unit doses. In Ireland, as in Québec, ibuprofen and naproxen are only accessible in pharmacies. Some countries still do not authorize OTC sales of naproxen (Denmark and Finland). Unlike most of the selected countries, Canada (including Québec) and the United States do not impose any maximum package size for most OTC drugs sold in pharmacies, whether they are on the shelves or under the pharmacist's control.

5 Scope and characteristics of the intentional OTC drug overdose problem

Data on intentional OTC drug overdoses are presented by means of an injury severity model used in trauma assessment (Sahai et al., 2005). The data are divided into four sections: mortality, hospitalizations, emergency department visits and calls to the poison centre (Centre antipoison du Québec).

The estimated number of cases and their characteristics in terms of age, sex, and population totals are presented. The substances used in the overdose are described by broad drug category, with the main OTC drugs involved presented.[17] A fifth section compares Québec's overdose rates with those set out in Canadian and international scientific literature.

[16] See Appendix 5 for information about the accessibility of acetaminophen, ibuprofen, naproxen and acetylsalicylic acid (Table 10).

[17] See Appendix 8 for data tables.

5.1 Intentional OTC drug overdose related mortality

In Québec, between 2001 and 2010, 4,483 people died of overdoses.[18] Of those deaths, 1,743 were suicides[19] by medication overdose.[20] Of that number, 1,589 (91%) were primarily related to a prescription drug (PD) and 154 (8%) to an OTC drug.[21]

The rate of suicides primarily attributable to OTC drug overdoses is 0.2 per 100,000 people, for an annual average of 15 suicides (Table 1). Rates are similar for men and women. They do differ by age group, however, with the highest rates among people aged 35 to 49 and 50 to 64, at 0.3 and 0.4 per 100,000 people, respectively.

Table 1 Suicides by intentional OTC drug overdose by age and sex, Québec, 2001 to 2010

Characteristics	Number†	%	Death rate††
Total	154	100.0	0.2
Sex			
Men	67	43.5	0.2
Women	87	56.5	0.3
Age group			
10-19	4	2.6	0.0
20-34	19	12.3	0.1
35-49	54	35.1	0.3
50-64	58	37.7	0.4
65 and over	19	12.3	0.2

† Includes cases of undetermined intent.

†† Rate per 100,000 people.

Source: Office of the Québec coroner computerized database.

The prescription drugs most commonly involved were: opioids (51%); psychotropic drugs (primarily antidepressants) (25%); anxiolytic drugs (9%); and psychostimulants (4%). The most common OTC drugs were: acetaminophen, in more than half of all cases (54%); salicylates and non-steroidal anti-inflammatories (NSAIDs) (24%); and antihistamines (21%).[22]

5.2 Intentional OTC drug overdose related hospitalizations

For the six-year period of 2006-2007 to 2011-2012, there were 19,454 hospitalizations[23] for overdoses in Québec, of which 15,991 (82%) were related to intentional overdoses or those of undetermined intent. That number represents an average of 2,665 hospitalizations per year, for a rate of 38.1 hospitalizations per 100,000 people. The hospitalization rate for overdoses among women is higher than for men (44.7 vs. 31.3). With regard to age, the highest hospitalization rate was observed in those aged 35 to 49 (50.2), followed by those aged 50 to 64 (39.8), with a rate of 37.5 and 17.2, respectively, among those aged 10 to 19 and 65 and over.[24]

Of the intentional overdoses or those of undetermined intent, more than three-quarters (76.4%) involved at least one PD, and 32.4% at least one OTC drug. Drugs were involved in 7.4% of these hospitalizations.[25]

In total, 21,937 drugs were recorded during these hospitalizations. PDs accounted for 76.0% of medications ingested (N = 16,596). Drugs affecting the central nervous system made up the majority of these (81.9%).[26] Psychotropic drugs (N = 6,025, primarily antidepressants) were the most common drugs, followed by anxiety drugs (N = 4,305), analgesics (N = 1,363) and anticonvulsants (N = 1,038).[27]

18 A rate of 6.6 deaths per 100,000 people (Appendix 8, Table 11).

19 Includes intentional deaths and deaths of undetermined intent (see Appendix 8, Table 11).

20 Although suicides by overdose involve several substances, only the main substance assumed to have caused the death is considered when determining the cause of a suicide.

21 See Appendix 9 (Figure 1).

22 See Appendix 9 (Figure 1).

23 Data drawn from the Med-Echo database.

24 See Appendix 8 (Table 13).

25 See Appendix 8 (Table 13). The total for substances exceeds 100% because more than one drug may be involved in hospitalizations.

26 Several substances are generally involved in intentional overdoses. As a result the total for medications may exceed the number of cases in the tables and figures in appendices 8 and 9.

27 See Appendix 9 (Figure 2).

OTC drugs made up one-quarter (24%) of all medications involved in hospitalizations for intentional overdoses or those with undetermined intent. Over half (53%) of these 5,341 OTC drugs involved acetaminophen (N = 2,852), while 14% involved salicylates (N = 447) or other pain relievers (N = 289). NSAIDs accounted for 823 of the OTC drugs recorded, followed by muscle relaxers (N = 191) and gastrointestinal drugs (N = 179).[28]

5.2.1 Characteristics of persons hospitalized for intentional OTC drug overdose

The hospitalization rate for intentional overdoses involving OTC drugs was 10.7 per 100,000 people, for an average of 751 people per year (Table 2). The hospitalization rate for OTC drug overdoses was twice as high among women as among men, and was higher among those aged 10 to 19, decreasing with age to reach its lowest estimate among people aged 65 and over.

Table 2 Intentional OTC drug overdose hospitalizations by age and sex, Québec, 2006-2007 to 2011-2012

Characteristics	Number	%	Rate†
Total	**4,508**	**100**	**10.7**
Sex			
Men	1,448	32.12	7.0
Women	3,060	67.88	14.4
Age group			
10-19	1,093	24.25	19.5
20-34	1,053	23.36	11.4
35-49	1,134	25.16	10.9
50-64	917	20.34	9.4
65 and over	311	6.90	4.5

† Rate per 100,000 people.

Source: Med-Echo database.

5.2.2 Liver damage related to medication overdose

Some OTC drugs, including acetaminophen, can cause severe liver damage at high doses. Of the 4,508 people hospitalized for overdoses involving OTC drugs, 278 people (6.0%) had a diagnosis of toxic liver disease with necrosis or acute hepatitis, in some cases necessitating a liver transplant.[29, 30]

5.3 Estimates of emergency department visits

Québec does not currently have a functional database of emergency department visits that would make it possible to quantify overdose cases. To address this shortcoming, an overview of the literature on recent populational studies was done to estimate the number of ER visits for intentional overdoses.[31] An Ontario study produced by Bethell and Rhodes (2009) estimated the rate of visits related to suicide attempts at between 127 and 168 per 100,000 people for 2001-2002. Medication overdoses made up three-quarters of those visits. When those rates were applied to the 2013 Québec population aged 12 and over, the estimated number of emergency department visits for intentional drug overdoses (both prescription and OTC) ranged from 6,000 to 7,300 visits per year.

Another study by Rhodes (Rhodes et al., 2008) with the same population over the same period found a high frequency of overdose with multiple drugs (19%), with the most common medications being benzodiazepines (12%), acetaminophen (11%) and antidepressants (10%). The author noted that the rate of intentional OTC drug overdose was higher among young people than in older individuals, who tended to use prescription drugs instead.

5.3.1 Estimates via health studies

The 2008 Québec population health study on a large sample representing the population estimated a self-reported suicide attempt rate of 5 per thousand (5‰) over a one-year period (Infocentre de santé publique du Québec, 2015). The rate was significantly higher among women (7‰) than among men (2‰). According to the data, approximately 27,900 Québecers aged 15 and over attempted suicide in 2008. This rate of self-reported suicide attempts has been stable over time, as indicated in previous Québec population health studies conducted

[28] See Appendix 9 (Figure 2).

[29] Data drawn from the Med-Echo database.

[30] The list of the hepatic effects is available in Appendix 2. It is important to note that liver transplants in people who have made several suicide attempts are rare, since such attempts are a hindrance when selecting subjects to prioritize

[31] The definition and data sources used are presented in Appendix 2. A summary table of the six studies selected is available in Appendix 10.

in 1992 and 1998 (Boyer et al., 1993; Boyer et al., 2000). These studies showed that 38% of subjects reporting a suicide attempt in the preceding year, or 10,600 people, went to the emergency department. Overdose with medication (prescription or OTC) was cited in 57% of cases.

Based on these data, we can estimate that annually, approximately 6,000 Québecers aged 15 and over visit emergency departments for intentional drug overdose.

5.3.2 Description of intentional OTC drug overdoses based on emergency department admissions in two Montréal hospitals

A 2009 and 2010 Montréal-area study on cases of attempted suicide in emergency departments at two Montréal hospitals made it possible to detail the types of drugs reported in cases of intentional overdose in a sample of 181 patients (Rahme et al., to be published). The study showed that the distribution by subject sex was comparable to that of hospitalizations for intentional drug overdoses, with two-thirds of female patients and more than half of male patients among those aged 35 and under. Women who came to emergency departments for intentional drug overdoses were significantly younger than men who did so ($P < 0.01$). Hospitalization following the emergency department visit was required for 43.1% of patients. Hospital admission tended to be higher in men (51.7%) than in women (38.8%)[32] and increased significantly with age, from 21.2% in those aged 25 and under to 56.3% among those aged 50 and over.[33]

Forty-three percent of patients took more than one drug for self-poisoning, and this proportion did not vary by sex, but tended to increase with age. Nearly half (47%) of all patients reported having taken at least one OTC drug, and this proportion was significantly higher among women (54%) than among men (33%) ($P = 0.02$). Similarly, younger patients reported more OTC drugs (59% in those under 25 years) than did older patients (33% of those aged 50 years and over) ($P = 0.02$).[34] The distribution by age and sex of overdose patients who visited an emergency department were similar to those observed in the Ontario studies cited above (Rhodes et al., 2008; Bethell and Rhodes, 2009).

Intentional medication overdose is sometimes accompanied by the consumption of alcohol, illicit drugs or other substances. In total, concurrent alcohol and medication consumption was identified in 30.7% of patients, while illicit drug consumption was present in 20.8% of them. Cocaine and its derivatives were the most commonly used illicit drugs. Alcohol consumption was found to be substantially higher in men than in women, but this was not the case for illicit drugs. Alcohol use was also significantly higher in illicit drug users.[35] In addition, there was no significant difference in combined alcohol and drug consumption by patient age, and this type of consumption did not lead to a higher frequency of hospitalization following the emergency department visit.

In total, 325 substances were reported (and/or found in the toxicology screen report) by the 181 patients, for an average of 1.7 medications per person.[36] Over half of the patients (56.9%) reported having taken a single medication; 20.4% two medications; and 22.7% three medications or more.[37] Pain and fever relievers, as well as psychotropics, were reported by nearly half (55.1% and 46.1%) of the 181 patients, while anxyolitics, sedatives and hypnotics accounted for one-third of cases (33.1%). Of all the medications used, analgesics and antipyretics were the main class of drugs with 30.1% of the 325 substances reported, followed by psychotropics (25.2%), anxiolytics, sedatives and hypnotics (18.1%), and antihistamines (5.8%).[38]

More than one-third (36%) of medications reported during emergency department visits were OTC drugs. The proportion of OTC drugs reported by women (42%) was significantly higher than in men (24%) ($P = 0.002$). The proportion of OTC drugs reported by younger

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32 See Appendix 8 (Table 14).

33 These data were taken from an ongoing study by E. Rahme et al. at McGill University on suicide attempt patients treated in the emergency departments of two Montréal hospitals.

34 These data were taken from an ongoing study by E. Rahme et al. at McGill University on suicide attempt patients treated in the emergency departments of two Montréal hospitals.

35 See Appendix 8 (Table 15).

36 See Appendix 8 (Table 16).

37 See Appendix 8 (Table 14).

38 See Appendix 8 for the distribution of medications by therapeutic classification (Table 16).

patients was also proportionately higher than that reported by older patients ($P < 0.001$).[39]

Analgesics and antipyretics made up two-thirds of the reported OTC drugs. Antihistamines were the second most common class of OTC drugs (15%), followed by central nervous system drugs (7%) and other drugs.[40] Among the analgesics, acetaminophen alone accounted for 47% of reported OTC drugs, followed by diphenhydramine (12.2%), ibuprofen (8.7%) and acetylsalicylic acid (8.7%).[41]

The provenance of drugs used in overdoses was checked for all reported drugs. If was found that 80.4% of all drugs were available in the patient's home, while 12% were purchased for the purpose of self-harm and 6.7% were taken from someone else.[42] The proportion of OTC drugs, available at the patient's home was lower (68%) than that reported overall, while that of drugs purchased for the purpose of self-harm was higher (24%). Acetaminophen was purchased for the purpose of self-harm in 39% of cases.[43]

5.4 Calls to the poison centre

The poison centre produces statistics on the calls they receive about drug overdoses. For the period of 2008-2012, the Centre antipoison du Québec (Quebec Poison Centre) took 61,236 calls for actual or suspected medication overdoses in persons aged 10 and over. Of that number, half (49.5%) were intentional overdoses. In nearly two-thirds of cases (64.7%), the calls for intentional overdoses were made by women. With respect to age, calls about intentional overdoses primarily involved people aged 20 to 34 (29.6%), followed by those aged 35 to 49 (28.5%), teens aged 10 to 19 (21.8%), those aged 50 to 64 (16.7%) and seniors aged 65 and over (3.5%). OTC drug overdoses led to 17,720 calls, of which 9,506 (53.6%) involved intentional overdoses.[44]

Acetaminophen was the drug most often involved, with 4,424 calls, or nearly half of calls for intentional OTC drug overdoses. Ibuprofen (N = 2,280) was the second most often involved followed by antihistamines (N = 910).[45] Calls for intentional acetaminophen overdoses came primarily from women (71.4%) and were more frequent among adolescents (37.6%), decreasing with age to 3.3% among those aged 65 and over. Calls for intentional overdoses involving ASA and other salicylates (N = 851) and cold and flu medications (N = 463) were proportionately fewer, as were vitamins and minerals, dextromethorphan and natural health products (N = 578). Women were overrepresented in calls for OTC drug overdoses (proportions ranging from 62.3% to 74.7%) and calls involving teens aged 10 to 19.[46]

5.5 Canadian and international comparisons

Québec data on deaths by overdose were compared to those from the rest of Canada for the ten-year period from 2001 to 2010.[47] The rates of suicide by all medications (prescription and OTC) were 30% lower in Québec than in the rest of Canada,[48] while the rate of suicide by OTC drugs was even lower in Quebec (50% of that of the rest of Canada). All the differences were significant regardless of whether or not deaths of undetermined intent were factored in.

Among those who died of PD or OTC drug overdoses, there were few differences in death distributions by sex or age groups, between Québec and the rest of Canada. However, the rate of death of undetermined intent was

39 These data were taken from an ongoing study by E. Rahme et al. at McGill University on suicide attempt patients treated in the emergency departments of two Montréal hospitals.

40 See Appendix 9 (Figure 3).

41 See Appendix 8 (Table 17).

42 See Appendix 8 (Table 18).

43 These data were taken from an ongoing study by E. Rahme et al. at McGill University on suicide attempt patients treated in the emergency departments of two Montréal hospitals.

44 See Appendix 8 (Table 19).

45 See Appendix 9 for a selection of key OTC drugs, with a description of the types of overdose (Figure 4).

46 See Appendix 8 (Table 19).

47 See Appendix 8 (Tables 20, 21 and 22) and Appendix 8 (Figure 5).

48 See Appendix 8 (Table 23).

three times higher in the rest of Canada (43%) than it was in Québec (16%).

The Québec's rate of death by drug (either prescription or OTC) overdose was lower than that reported in the United States for the similar time period, while, its distribution by sex was comparable (CDC, 2013). The Québec rate of death by drug overdose was similar to that reported in France in the 1990s (Saviuc, Bedry and Flesh, 1999). However, it is difficult to compare the types of drugs used in suicide because of the different classifications used in the two countries. In a ten-year study in the Greater Toronto Area, 21% of suicides were attributable to an OTC drug (Sinyor et al., 2012). In the latter study, as in Québec, the most frequently used prescription drugs were opioids and tricyclic antidepressants.

The U.S. rate of hospitalizations for intentional overdose were higher (48/100,000 people) than those in Québec (38/100,000 people) with rates in women higher than in men in both regions (CDC, 2013). In the United States, medications remain the main means of intentional overdose in more than 80% of all cases. A recent Canadian study estimated the rate of hospitalizations for acetaminophen overdose at 14/100,000 people, with a majority of intentional overdoses. Young women aged 15 to 19 had the highest rate (Health Canada, 2014). It should be noted that hospitalizations for intentional overdoses were under-reported.

In the absence of Québec data on emergency department visits for suicide attempts, it was impossible to compare risks with other provinces or countries. However, the distributions by age and sex observed in the sample of the two Montréal hospitals were similar to those reported for Ontario, the United States and Great Britain, with women, teenagers and young adults making the most emergency department visits (Doshi et al., 2005; Hawton, Bergen et al., 2007; Bethell and Rhodes, 2009). In those three studies, as in Montréal, prescription drugs were primarily used by older patients, while young people generally took OTC drugs. Acetaminophen was the main OTC drug used in the United States, Ontario, Great Britain and Alberta (Myers, Li et al., 2007). Those studies found that 40% to 55% of subjects who presented at the emergency department for intentional overdoses had also consumed alcohol with the drugs; this proportion was higher than that estimated in the Montréal sample.

In conclusion, it is difficult to accurately determine which medication is most used in suicides, as medications are frequently combined when making a suicide attempt. The available statistics show that each year, at least 174 Québecers commit suicide by drug overdose, of which 15 do so using OTC drugs. This number is an underestimation of the number of deaths involving OTC drugs, since in cases where more than one drug or substance is consumed, only the substance found on the toxicology screening or the one the coroner considers most toxic is listed as being the most likely cause of death. OTC drugs cause 750 hospitalizations annually for intentional and undetermined-intent overdoses, most often involving acetaminophen. Moreover, an estimated 6,000 to 7,300 people aged 15 and over make an emergency department visit for intentional OTC drug overdoses, again primarily involving acetaminophen. The Montréal study showed that 40% of patients who went to the emergency department for intentional acetaminophen overdoses had purchased the drug for the purpose of self-harm, while the remainder had used the tablets they had at home (Rahme et al., to be published). Young people and women were the ones who most often went to the emergency department or were hospitalized for intentional OTC drug overdoses.

6 Effective interventions

6.1 Most studied OTC drug: acetaminophen

The most-studied intentional OTC drug overdose reduction strategies in the scientific literature focus on acetaminophen. Acetaminophen (or paracetamol in Europe) is one of the most commonly used pain relievers in Canada and worldwide. It is also frequently used in intentional overdoses (e.g., in Canada, Myers, Li and Shaheen, 2007). Overdoses with this drug can cause severe liver damage necessitating a liver transplant and possibly causing death. Ease of access is the main reason this OTC drug is used in intentional overdoses (Simkin et al., 2012; O'Rourke, Garland and McCormick, 2002; Hawton et al., 1995).

6.2 Strategies for reducing intentional acetaminophen overdoses

Eight categories of intentional acetaminophen overdose reduction strategies were identified.[49] The following sections focus on what is known about each strategy category.

6.2.1 Setting maximum package sizes and maximum quantity per sale for acetaminophen

Restricting access to acetaminophen by setting a maximum package size (MPS) and maximum quantity per purchase (maximum quantity per sale – MQS) is the most commonly examined strategy in the scientific literature. The rationale for this type of restriction stems from studies showing that a substantial proportion of intentional overdoses with pain relievers are impulsive, often involving the ingestion of drugs that are readily accessible or already available in the home (Hawton, 2002).

The size and configuration of OTC acetaminophen packs vary by country and generally within each country (McNeil Consumer Healthcare, 2009). Packs sold outside the United States and Canada hold fewer tablets; in European countries, they contain between 12 and 32 tablets, and these mostly come in blister packs.

Thirty-seven quantitative studies on the impact of limited acetaminophen access on the risk of overdose were identified. These were conducted in various countries. They focus on:

- The impact of legislation in the United Kingdom (24 studies) and Ireland (3 studies).
- Changes to acetaminophen access in other countries (7 studies).
- Comparisons of acetaminophen overdoses in various countries (3 studies).

Thirty-four of the studies were included in one or more of the five literature reviews identified, including four systematic studies published between 2004 and 2010. The two most recent reviews are unpublished reports prepared by the Alberta Institute of Health Economics (Guo, Harstall and Chatterley, 2010) and by the research unit of an OTC pain reliever manufacturer (McNeil Consumer Healthcare, 2009). The other three reviews were published in scientific journals and focus exclusively on studies in the United Kingdom (Hawkins, Edwards and Dargan, 2007; Morgan and Majeed, 2005; Bateman, 2009).[50] All the authors came to the same conclusion: there is much variation in findings, with some studies reporting a link between overdose rates and acetaminophen access, while others reporting no link. The authors of five studies, particularly Guo et al. (2010), reported difficulty interpreting their findings owing to methodological limitations. More recently, Bateman (2014) reported the same problem.[51] As a result, there is a lack of evidence to show that restricting access to acetaminophen significantly reduces intentional overdose rates. Only three studies have been published since the most recent review (2010), and two showed no reduction in intentional overdoses.

6.2.1.1 Impact of legislation in the United Kingdom and Ireland

Owing to the high rate of intentional acetaminophen overdoses, the United Kingdom in 1998 and Ireland in 2001 passed legislation to reduce the number of tablets sold in and outside of pharmacies. Prior to 1998 in the United Kingdom, there were no limits placed on acetaminophen purchases in pharmacies; package sizes outside of pharmacies could hold a total quantity of up to 24,500 mg (Hawton, 2002).

In short, legislation on acetaminophen MPS and MQS in these two countries can be summed up as follows:

- 1998 legislation the United Kingdom:[52]
  - Reduce pharmacy MPS for acetaminophen to 32 tablets, with an MQS of 100 tablets or at the pharmacist's discretion.
  - Reduce acetaminophen MPS outside of pharmacies to a maximum of 16 tablets.
  - Include a warning on the package label and information insert.

[49] See Appendix 11 for a summary of these strategies (Table 25).

[50] See Appendix 12 for a Venn diagram illustrating overlaps between the studies identified in each of the five literature reviews (Figure 6).

[51] See Appendix 12 for a description of the methodological limitations.

[52] This legislation applies to acetaminophen and acetylsalicylic acid (aspirin).

- 2001 legislation in Ireland:
  - Reduce the pharmacy MPS for acetaminophen to a maximum of 24 tablets.
  - Reduce the MPS for acetaminophen outside of pharmacies to a maximum of 12 tablets.

A significant issue reported in the application of MQS legislation is getting merchants to follow it. One proposed method for facilitating supervision consists of programming cash registers to display a warning when acetaminophen is purchased in too large a quantity (Morgan and Majeed, 2005). This method is used for acetaminophen in the United Kingdom. In addition, Britain's Medicines and Healthcare Products Regulatory Agency (MHRA) exercises a certain level of vigilance by issuing warnings to violators (shops, websites).

A detailed analysis of the studies on the impact of legislation (see blue square below) concluded that, given the studies limitations, namely that they are uncontrolled quasi-experimental studies and are of questionable methodological quality, it cannot be stated with certainty that acetaminophen access restrictions resulted in a drop in overdoses. This observation is consistent with those in previous literature reviews on the question. However, given the results obtained, it is equally impossible to conclude that this measure is ineffective. The majority of studies have shown a reduction in acetaminophen overdoses following the introduction of access limitations in Great Britain.

However, the results are mixed for Scotland and Ireland. It is possible that the legislation is less stringently enforced in these countries than in England, primarily as regards to tablet sales outside of pharmacies (Laffoy, Scallan and Byrnel, 2001). However, the lack of any drop in overdoses observed in these studies may simply be related to the dubious reliability of the indicators used.

6.2.1.2 Substitution effect

Whenever the question of restricting access to a means of suicide is considered, the risk of substitution with another method has to be taken into account. As described in the methodological analysis of the identified studies, the substitution of other pain relievers is a real concern when debating restricting access to acetaminophen. Scientific literature on suicide prevention clearly demonstrates this phenomenon. Three main aspects must be taken into account: contextual factors, similarity of the means used and degree of lethality. The published data indicate that the risk of substitution varies depending on some contextual elements, such as: the means to which access will be limited (Daigle, 2005; Nordentoft et al., 2006; Nordentoft et al., 2007; Florentine and Crane, 2010; Lin and Lu, 2011; Lester, 2012); the country (Sarchiapone et al., 2011; Yip et al., 2012); and the individual's age (Yip et al., 2012) and sex (Daigle, 2005; Nordentoft, 2007; Yip et al., 2012). Some studies showed a substitution effect, in that a similar means would be employed when access to a commonly used method was restricted (Daigle, 2005; Florentine and Crane, 2010; Lester, 2012; Yip et al., 2012). For example, in the United Kingdom, an increase in the number of suicides by carbon monoxide poisoning from automobile exhaust was observed once the domestic gas commonly used for suicide was detoxified (Daigle, 2005; Florentine and Crane, 2010; Lester, 2012; Yip et al., 2012). The substitution effect disappears, however, when access to the alternate method is also restricted (Florentine and Crane, 2010; Sarchiapone et al., 2011). However, if a highly lethal means is restricted and the alternate method is less so, the chances of surviving a suicide attempt are better. Conversely, the reverse can occur if the alternate method is more lethal than the now-limited means. It is important to bear this in mind when considering restricting access to a means as a suicide prevention method (Nordentoft, 2007; Florentine and Crane, 2010; Sarchiapone et al., 2011; Lester, 2012; Yip et al., 2012).

Studies have shown an overdose substitution effect following acetaminophen access limitations, in favour of ibuprofen (Hawton et al., 2004) and acetylsalicylic acid (Balit et al., 2002). Overdoses of the latter two drugs cause gastrointestinal problems and increased risk of bleeding. While there is an antidote that can mitigate the harmful effects of acetaminophen in an overdose (acetylcysteine), this is not the case when treating overdoses of other OTC drugs (Hawkins, Edwards and Dargan, 2007). The substitution effect can be particularly problematic.

That said, the substitution effect with another drug is not always observed; for example, Gunnell et al. (2013) found that cases of gastric hemorrhage[53] did not really increase following the new legislation in the United Kingdom. According to the authors, this indicates the absence of substitution of ibuprofen or ASA for acetaminophen. A study was conducted on the withdrawal of Co-proxamol[MD], which is a compound of acetaminophen and propoxyphene (Hawton et al., 2012). This prescription analgesic, not marketed in Canada, was gradually withdrawn from the market in the United Kingdom beginning in 2005 and was completely eliminated in 2007. Other medications may contain propoxyphene. These were completely withdrawn from the Canadian and U.S. markets in 2010 because even a mild overdose could result in death (propoxyphene could cause severe cardiac arrhythmia). The results showed that in the six years following the medication's withdrawal in the United Kingdom, there was a substantial decrease in the number of deaths by overdose of this drug, with no apparent increase in deaths involving other pain relievers. This assumes that the medication withdrawal strategy did not cause a substitution effect and therefore contributed to an overall decline in the actual number of suicides by overdose.

[53] Gastric hemorrhages are generally caused by overdoses of ibuprofen or acetylsalicylic acid.

Detailed analysis of quantitative studies on limiting acetaminophen access

To further explore the findings reported in previous reviews on the decrease in acetaminophen overdoses following legislation changes in the United Kingdom and Ireland, a systematic methodological evaluation of the studies in question was carried out.

In total, 22 publications were selected. These were all quasi-experimental, uncontrolled studies. They focused on three different types of indicators, namely: hospitalizations or emergency department visits following an overdose; deaths by overdose; and admission to specialized liver disease or transplant wards (Prince et al., 2000; Robinson, Smith and Johnston, 2000; Turvill, Burroughs and Moore, 2000; Hawton et al., 2001; Laffoy, Scallan and Byrne, 2001; Newsome et al., 2001; Thomas and Jowett, 2001; Sheen et al., 2001; Sheen et al., 2002b; Wilkinson et al., 2002; Bateman et al., 2003; Hawton et al., 2003; Hugues et al., 2003; Langford, Arunam and Mutimer, 2003; Hawton et al., 2004; Inglis, 2004; Morgan, Griffiths and Majeed, 2005; O'Loughlin and Sherwood, 2005; Bateman et al., 2006; Morgan, Griffith and Majeed, 2007; Gorman et al., 2007; Hawton et al., 2013).

Five other publications identified dealt exclusively with calls made to poison control centres or with tablet sales (Laing et al., 2001; Donohoe and Tracey, 2001; Sheen et al., 2002a; Donohoe, Walsh and Tracey, 2006; Morgan et al., 2007). The latter were excluded from the methodological evaluation owing to limitations related to the use of such indicators. The number of calls to poison control centres is likely to rise following legislation-related public advertising. In addition, in these studies, discrepancy was noted betwwen the package size and the number of tablets sold.[54]

Distribution of methodological criteria

In order to assess the methodological quality of the 22 selected studies, an evaluation grid consisting of eleven criteria was used. Considerable variability was observed with regard to the studies' compliance with these methodological criteria.[55] Nearly three-quarters (73%) of the studies used an unlimited sample or a sufficiently long period of time after legislation was passed to observe an effect. More than half (59%) of the studies adjusted for confounders and effect modifiers. Half of the studies adjusted for sociodemographic variables or for two or more overdose indicators. Just under half of the studies (46%) measured the substitution effect or documented indicator reliability (41%). More than one-third (36%) of the studies specified whether the overdoses were intentional or not, used data for a minimum of three years before and three years after the legislation, or used measures to guard against detection bias. Lastly, only 23% of the studies used multivariate statistical analyses.

Overdose reductions and measure types

Assessing the methodological quality of the studies also involves categorizing their findings with regard to whether or not they indicate a drop in overdoses following the passing of legislation. Most studies found a drop in overdoses, both in terms of overall score (a drop in overdoses for at least one of the indicators used was observed in 18 studies (82%)), and for indicator type used. The smallest observed impact was related to the death rate (73%).[56]

However, while these results initially appeared to be overwhelmingly positive, they must be nuanced. With regard to hospitalizations and emergency department visits for overdoses, five of the 14 studies (36%) reporting a drop in overdoses observed either a subsequent increase in overdoses one to two years after the passing of legislation (3 studies), or too small a decline in the number of overdoses (1 study), or did not compare the observed differences statistically.

With regard to deaths by overdose, five of the eight studies (62%) reporting a drop in overdoses found either a subsequent increase in overdose deaths one or two years after the passing of legislation (3 studies), or a drop in concurrent overdoses with other, non-legislated drugs (2 studies).

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54 See Appendix 13 for the process used to assess the methodological quality of the 22 studies, the list of methodological criteria used, and a summary of the methodological assessment of each study, in chronological order of publication date (Tables 26 to 27).

55 See Appendix 13 for an illustration of the distribution of methodological criteria for all 22 studies analyzed (Figure 7).

56 See Appendix 13 for information about the presence or absence of a drop in overdoses according to the measures used (Figure 8).

Studies focusing on admissions to specialized liver disease or transplant units were more conclusive. Only one study among the six (17%) reporting a decrease in overdoses presented mixed results depending on the variables controlled for in the statistical analyses.

The four studies that reported no drop in overdoses for all measures were conducted in Scotland (three studies, two of which were published in 2001 and one in 2006) and Ireland (one study in 2001). Overall, half of the studies carried out in this region reported no drop, while all those from England, Wales or, more broadly, the United Kingdome, reported a drop.

Decrease in overdoses and methodological quality of the studies

Findings regarding the effect of legislation on overdoses were analyzed based on the studies' compliance with the 11 methodological criteria.[57] The studies that reported a decrease in overdoses (for at least one of the analyzed indicators), compared to those that found no decrease, appear to be:

- More likely to have:
- Documented reliability of the key indicators (50% and 0%, respectively).
- Controlled for changes other than those relating to legislation (67% and 25%, respectively).
- Measured the substitution effect (50% and 25%, respectively).
- Less likely to have considered:
  - A sufficiently long post-legislation period to observe an effect, i.e., more than one year following the passing of legislation (67% and 100%, respectively).
  - Adjustment for at least one sociodemographic variable (44% and 75%, respectively).

Conflict of interest

One study (5%) declared a potential conflict of interest indicating that the author had received an unrestricted educational grant from a pharmaceutical company. Absence of a conflict of interest was declared in eight studies (36%), while it was not mentioned in the 13 other studies (59%).

[57] See Appendix 13 for study compliance with methodological criteria according to findings (Table 28).

6.2.1.3 Changes to acetaminophen access in other countries

Seven studies worldwide focusing on the impact of changes to acetaminophen access were identified, three of which dealt with the lifting of sale restrictions and two with temporary product withdrawal. Some studies found no significant link between access and acetaminophen overdose rates.

In Canada, restrictions on acetaminophen sales (tablets of more than 325 mg per unit dose and packs of more than 24 tablets were sold in pharmacies only) were lifted in 1999 in some provinces (Ontario, New Brunswick, Manitoba, Yukon, Nunavut, the Northwest Territories), and in 2000 in others (Newfoundland, Saskatchewan, British Columbia), while other provinces had no restrictions (Alberta, Nova Scotia, Prince Edward Island). One study (Prior et al., 2004, McNeil Pharmaceutical Group) focused on comparing provincial rates of hospitalization for acetaminophen poisoning (intentional or otherwise) or liver toxicity, by presence and absence of restrictions and before and after their lifting where applicable (1995-2001). Unfortunately, Québec was not included in the study owing to the lack of data on poisonings. The findings nonetheless indicated that poisoning rates did not substantially increase once restrictions were lifted.

Two studies were carried out in Denmark, following the free sale of acetaminophen in January 1984 (no MPS, sold in pharmacies only) and since 2000, MPS of 10 tablets have been sold outside of pharmacies (Ott et al., 1990, Nordentoft et al., 2006). These studies showed no significant increase in hospital admission rates or acetaminophen poisoning death rates following the lifting of sale restrictions. In another study conducted in Norway (Lund et al., 2012) following the change to free sale outside of pharmacies (MPS of 10 g) in November 2003, the number of patients treated in hospitals for acetaminophen poisoning did not increase.

In Australia in 2000, pharmaceutical companies had to temporarily withdraw acetaminophen from the market (for two two-month periods) owing to product contamination. Two studies considered this incident as an opportunity to study the effect of restricted acetaminophen access on the risk of acetaminophen overdose. The first study found no drop in intentional overdoses, as measured by the number of calls to a poison control centre and by visits to toxicology centres (Balit et al., 2002). In the second study, the presence of many confounding factors made it impossible to conclude that the observed drop in hospitalizations for overdose were related to the drug's unavailability (Kisely, Lawrence and Preston, 2003). The short duration of the restriction makes it difficult to interpret the results of these studies.

6.2.1.4 Comparison of acetaminophen poisoning rates in various countries

Two of the three studies comparing acetaminophen poisonings in various countries found a link between the poisoning rate and the authorized number of acetaminophen tablets per purchase.

One study focused on a comparison between the United Kingdom and France prior to the 1998 legislation change in the U.K. (Gunnell et al., 1997). At the time, acetaminophen access was much broader in the United Kingdom than in France (8 g MPS was available only in pharmacies). Three sources of data were used: suicide death, non-fatal cases of acetaminophen poisonings, and drug sales (1974-1991). The results showed a trend indicating that suicide and poisoning rates were lower in France, but the study's limitations made it impossible to draw clear conclusions.

The same researchers (Gunnell, Murray and Hawton, 2000) conducted another study involving comparisons among 23 countries (not including Canada) in terms of the accessibility of acetaminophen and information about acetaminophen poisoning, i.e., the number of hospital visits, suicides and the number of calls made to poison control centres. Despite the limitations associated with a lack of standardization of measures, it seemed that acetaminophen-related mortality rates were higher in countries where limited quantities of acetaminophen can be purchased.

Another study compared acetaminophen overdose between England and Ireland (Hawton et al., 2011). The findings showed that the difference in MPS between England (32 tablets in pharmacies, 16 elsewhere) and Ireland (smallest quantity: 24 and 12 tablets) did not affect the number of acetaminophen overdoses or the number of tablets ingested, and that more packs were purchased in Ireland.

6.2.1.5 Summary

The link between acetaminophen accessibility and the rate of intentional acetaminophen overdoses is difficult to gauge, given the numerous methodological constraints encountered. These difficulties play a key role in the variability of the results observed in studies. Regardless, this analysis indicates that a substantial number of studies found some reduction in acetaminophen overdoses following the introduction of MPS and MQS legislation in the United Kingdom.

The only country to have conducted several studies with more stringent research methods is the United Kingdom. The results of those studies indicated that restricting acetaminophen accessibility has significantly reduced acetaminophen-related suicides and suicide attempts, as well as accidental overdoses. Despite conflicting opinions, Dr. Keith Hawton, head of the Centre for Suicide Research at Oxford University (England) and author and co-author of several studies on acetaminophen poisoning, feels that the United Kingdom's legislation has helped to reduce overdoses. The researcher and his colleagues conducted a study in 2013 in England and Wales, taking into account a broad range of the methodological limitations described previously. The time followed was 14 years (1995-2009). The findings underwent interrupted time series analysis and were controlled for all suicides and deaths related to acetaminophen overdose. Their findings indicated a substantial 43% drop in acetaminophen-related deaths, or 765 fewer deaths attributable to suicide and undetermined causes, and 975 fewer deaths if accidental deaths are included. They also observed a 61% drop in liver transplant requests, but that estimate varied depending on the analysis and is therefore less reliable.

Nonetheless, several authors acknowledge that the rate of serious acetaminophen poisonings continues to be too high in the United Kingdom (Hawton et al., 2013; Handley and Flanagan, 2014; Bailey and Wisniacki, 2014). For this reason, Hawton and his colleagues have advised further MPS reductions to match those of Ireland and Germany. Experts in the United Kingdom initially recommended setting the MPS for acetaminophen to 12 g (24 tablets of 500 mg) as part of the legislation, as this would be a non-fatal dose, but the suggestion was rejected (Bateman, 2014). The acetaminophen MPS for pharmacy sale (32 tablets) is still enough to cause severe liver damage.

Lastly, to maximize the impact of acetaminophen legislation and minimize the risk of the substitution effect, it would be best to apply the same sale restriction rules to other OTC pain relievers (e.g., ibuprofen, acetylsalicylic acid, naproxen).

The other acetaminophen overdose reduction strategies identified are not as well documented as this one. They are generally the subject of qualitative studies, including interviews with patients who attempted suicide by acetaminophen overdose.

6.2.2 Packaging: using blister packs instead of bottles

Researchers feel that individually packaged tablets would lengthen the time it would take to ingest the desired number of tablets for an overdose. If the attempt is an impulsive act in a time of crisis, the delay may give the person time to think about what they're doing and possible reduce the severity of the overdose (e.g., Chan, 1997; Chan, 2000; Hawkins, Edwards and Dargan, 2007). In the United Kingdom, acetaminophen MPS legislation has led to the use of blister packs. It is therefore difficult to distinguish the effect of the legislation from that of the packaging (McNeil Consumer Healthcare, 2009).

A U.S. study proposed using compliance packaging for all OTC pain relievers, thus targeting both intentional and non-intentional overdoses (Weiss, 2009). This type of packaging, in the form of blister packs, takes four criteria into account: 1) keeping the instructions for use, warnings and dosage attached to the blister pack card until it is empty; 2) maximizing packaging surface area to allow for larger type font and emphasis on the most important instructions and warnings; 3) placing tablets in a logical order in accordance with the recommended maximum daily dose; and 4) limiting the number of tablets per package size.[58] The study did not mention whether this type of packaging was ever actually used.

6.2.3 Reduction in unit dose

Hawton et al. (2013) suggested reducing the maximum unit dose (MUD) from 500 mg to 325 mg per tablet, as suggested by the U.S. Food and Drug Administration in

[58] See Appendix 14 for a compliance packaging prototype (Figures 9 and 10).

2011, for prescription drugs that combined acetaminophen and codeine. This strategy could diminish the severity of overdoses. However, they specified that it would be necessary to make sure that pain-relief effectiveness was not hindered by the dose decrease of 175 mg.

6.2.4 Adding ingredients to decrease liver toxicity

Another overdose reduction strategy involves adding ingredients to acetaminophen preparations. It was suggested that an emetic be added that would cause nausea and vomiting in overdose situations only, in order to reduce overdose-related dangers. However, the proposed measure was rejected because it would be impossible to apply the strategy without causing side effects with the ingestion of a therapeutic dose (Hawton, 2002).

Two other suggestions consisted of adding an antidote to liver damage. The addition of methionine, a natural amino acid synthesizer, could have a protective effect on the liver in an overdose. This approach was rejected, however, owing to carcinogenic and mutagenic risk (Hawton, 2002, citing Jones et al., 1997; Krenzelok, 1997) and side effects like unpleasant taste and gastrointestinal symptoms (Gunnel, Murray and Hawton, 2000). Adding substances would also raise production costs.

Adding acetylcysteine, which is also used as an antidote in acetaminophen overdoses (Andrus et al., 2001), could be considered because the product would not interfere with the drug's effectiveness and would be tasteless and odourless if correctly manufactured. However, there is little documentation to support this suggestion.

6.2.5 Label warnings about the dangers of product overdose

Serious and more visible package warnings about the dangers of exceeding the recommended dose could help some people avoid an overdose. However, there is little evidence that this method is effective. It seems that few people read the messages (Hawton et al., 1996) and that the warnings have no impact on the decision to proceed with an intentional overdose (Simkin et al., 2012). In addition, according to a consulted expert, the warnings might even encourage those truly wishing to commit suicide to use this method. However, since intentional overdose is not always associated with a genuine desire to die, instructions to get to a hospital as quickly as possible to have an antidote administered if needed, may be helpful in an overdose situation (O'Rourke, Garland and McCormick, 2002). It was also suggested that the number of a suicide prevention helpline be included[59] (Beauregard-Paultre et al., 2013).

6.2.6 Public education on the hazards of acetaminophen overdose

The general public would benefit from knowing some information about acetaminophen overdoses. A study of teens in the United Kingdom and the United States found that a substantial proportion of young people were unaware of the potentially fatal effects of even a small quantity of acetaminophen (Gunnell, Murray and Hawton, 2000 citing Gilbertson et al., 1996). Also, acetaminophen overdose does not cause loss of consciousness, and the harmful effects occur gradually. Studies on the reasons behind intentional overdoses found that although most patients were aware of the dangers of acetaminophen, most would not have chosen that method had they been aware of its consequences (O'Rourke, Garland and McCormick, 2002; Hawton et al., 1996). Being better informed of the dangers and effects experienced during acetaminophen overdoses might lead the person taking the drug, or those around him or her, to seek help sooner (Gunnell, Murray and Hawton, 2000). However, here again, showcasing the potentially lethal nature of acetaminophen overdose may encourage those who are seriously suicidal to choose this method.

6.2.7 Limiting points of sale: pharmacies only

Interviews with patients in the United Kingdom who were admitted to hospital following an intentional acetaminophen overdose found that at least half of patients had purchased tablets specifically for the overdose and that most had done so in non-pharmacy settings, such as supermarkets, convenience stores, service stations, and online (Simkin et al., 2012, O'Rourke, Garland and McCormick, 2002). Thus, limiting sales to pharmacies would make acetaminophen harder to access during a suicide crisis. However, according to Gunnell, Murray and Hawton (2000), this would pose an inconvenience to most users who are not at risk and lead to possible substitution with another, more toxic product. Moreover, there is little evidence on the

[59] In Quebec, people in distress or whose loved ones are in distress can call 1-866-Appelle at any time.

effectiveness of such a strategy. In some European countries, including France, Belgium and Germany, acetaminophen is sold solely in pharmacies (Journal de l'Ordre national des pharmaciens, 2014).

In 2009, Sweden authorized the sale of a number of medications, including acetaminophen, outside the pharmacy setting. However, when it was found that acetaminophen overdoses increased (calls to poison control centres and hospitalizations), the country reversed its decision and banned sales outside pharmacies in March 2015 (Haroche, 2014). Similarly, Denmark decided to return to prescription-only dispensation of large quantities of pain relievers, including acetaminophen (Sundhedsstyrelsen: Danish Health and Medicines Authority, 2013).

6.2.8 Prescription-only status for acetaminophen

Limiting acetaminophen to prescription-only would greatly reduce access of this drug for everyone, including those who use it for therapeutic purposes. However, this would place an undue burden on front-line services, increase health care costs, and inconvenience most users, who are not at risk of overdosing (Gunnell, Murray and Hawton, 2000; Hawkins, Edwards and Dargan, 2007).

7 Deliberative process with experts

The deliberative process made it possible to obtain the opinions of the panel of external experts on effective and promising intentional OTC drug overdose prevention measures, the pros and cons of such measures, and their relevance to the Québec context.[60]

The process made it possible to identify three measures that the experts agreed are applicable to Québec. Therefore, it is recommended that a MPS be set for Schedule III acetaminophen. It was also recommended that the use of the province's poison centre (Centre antipoison du Québec) be promoted among health care professionals and the public so that overdoses, whether intentional or otherwise, can be treated promptly. Also, whatever measures are chosen to deal with intentional OTC drug overdoses, the panel feels that this issue should be included in any integrated suicide prevention strategy.

Apart from the above measures, others were suggested but were not the subject of a consensus. These are:

- Implementing an information strategy on safe acetaminophen use via improved product labelling, among other measures.[61] This type of strategy is in place in the United States and is being planned by Health Canada. It is expected to emphasize morbidity rather than mortality risk (with its implication on suicide). This measure was not unanimously supported by the experts, some of whom feel that those in crisis or suffering from mental health disorders might use this type of medication as a suicide method.
- The implementation of an official provincial program to collect expired or unused drugs for safe disposal so that this practice can be better supported, standardized and centralized. This program should be associated with ongoing efforts to raise public awareness of this practice from a public health standpoint (e.g., less medication in the home that would be accessible to young people for abuse or intentional overdoses).[62]
- Implementation of further OTC drug access control measures, such as limits on unit doses and MQS. Opinions were divided between the need to institute some of these measures in Québec and because of the constraints they would place on users and the pharmaceutical field.

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60 See Appendix 15 for a synthesis of the deliberative process.

61 Health Canada, Incident Report. [http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2015/54178a-eng.php, pages consulted on July 9, 2015].

62 This type of measure is discussed in Ouellet N, Dubé PA. Retour des médicaments périmés ou inutilisés aux fins de destruction du point de vue de la santé publique. *Bulletin d'information toxicologique* 2014;30(2):47-65. [Online, in French only] https://www.inspq.qc.ca/toxicologie-clinique/retour-des-medicaments-perimes-ou-inutilises-aux-fins-de-destruction-du-point-de-vue-de-la-sante-publique.

8 OTC drug accessibility restriction measures applicable to Québec

Given the small number of studies on the effects of reducing OTC drug accessibility and the lack of a consensus on the applicability of such a strategy in Québec, it was deemed preferable to present a range of possible measures. These measures could be implemented on their own or in combination, taking into account the arguments for and against each of them, as described in the table below. Some measures were recently recommended by Health Canada (2014) in its report aimed at minimizing acetaminophen-related liver damage.[63]

MEASURES	ARGUMENTS		SPECIFIC CONDITIONS	COMMENTS
	FOR	AGAINST		
Status quo	Access is easier for those who do not have access to a physician and those who have chronic conditions. No changes required in the practice or management of medications in the pharmacy.	No expected improvement in terms of mortality and morbidity. No medical or pharmaceutical follow-up. Side effects go unidentified and unreported (post-market surveillance). Use of these drugs is seen as harmless. Anticipated overdoses owing to the marketing of package sizes previously reserved for repackaging[64] by the pharmacist.	N/A	The available data underestimate the actual intentional OTC drug overdose rate. Schedule-related restrictions are already in place (MPS for unscheduled OTC drugs). Québec is already the province with the most restrictions in Canada. Intentional overdoses generally involve a combination of prescription and/or OTC drugs. Limiting quantities will not prevent someone from stockpiling potentially toxic quantities at home, but it does make it more difficult. This is less of an issue in cases involving impulsive suicide attempts. Conclusive data are currently insufficient (few studies and multiple methodological limitations), although a number of studies have observed a drop in intentional OTC drug overdoses as a result of reduced access to means.

[63] This report examines all overdoses, intentional or otherwise, involving acetaminophen, and its suggestions include: 1) limiting the unit does to 325 mg per tablet for OTC drugs and to 500 mg for prescription drugs; 2) eliminating the combination of acetaminophen in prescription opioid preparations; and 3) reducing the maximum package size to 13 g for OTC drugs containing acetaminophen.

[64] In this context, repackaging means that the pharmacist removes a quantity of tablets from a large pack to dispense a smaller quantity in a pill bottle.

MEASURES	ARGUMENTS		SPECIFIC CONDITIONS	COMMENTS
	FOR	AGAINST		
Limit the maximum unit dose (MUD) For example, a maximum of X mg per unit dose	Maintains accessibility of OTC drugs. More difficult to stockpile toxic doses at home. Limits the ingestion of potentially toxic or lethal doses. Likely decrease in side effects. Potential decrease in overdoses, intentional or otherwise.	Limits accessibility without a prescription to a higher unit dose that may be clinically required. Impact on cost of treatment must be considered. Currently, conclusive evidence is lacking.		Opportunities for medical or pharmaceutical consultation (if treatment is ineffective or symptoms are poorly controlled). Could be combined with other measures.
Set a maximum package size (MPS) For example, a maximum of X tablets per pack	This measure appears to have been effective in England. Measure that does not appear to have created problems for users or pharmacists in England. Potential decrease in the number of overdoses, intentional or otherwise. Same as MUD.	Requires more frequent trips to the pharmacy to restock. Impact on treatment cost must be considered.	Must be applied to all OTC drugs most often involved in intentional overdoses and to combination drugs that contain them. To be effective, a MQS would also have to be established. Package sizes with larger number of tablets could be accessible under the control of a pharmacist or by prescription.	Opportunities for medical or pharmaceutical consultation (more effective use of drugs). May be combined with other measures. It should be noted that the panel of external experts reached a consensus in recommending an MPS for Schedule III acetaminophen. An MPS for the public does not prevent pharmacists from purchasing larger package sizes for repackaging.
Set a maximum quantity per sale (MQS) For example, a maximum of X packs of Y tablets each, per transaction	Same as MPS. The need for more frequent trips to the pharmacy can be alleviated by medical prescriptions for chronic disease cases. Potential decrease in overdoses, intentional or otherwise.	Requires monitoring sales at the cash register. Requires more frequent visits to the pharmacy to restock. Conclusive data are currently insufficient.	Requires the collaboration of merchants. To be effective, an MPS would also have to be established.	May be combined with other measures.

MEASURES	ARGUMENTS		SPECIFIC CONDITIONS	COMMENTS
	FOR	AGAINST		
Reschedule certain OTC drugs while maintaining accessibility For example, make package sizes exceeding X number of tablets or any packaging other than blister packs Schedule II drugs (under the control of a pharmacist)	Opportunities for medical or pharmaceutical consultation. Ability to limit larger sizes to Schedule II while maintaining accessibility. Potential decrease in overdoses, intentional and otherwise. Improved pharmaceutical follow-up by having the drug entered in the patient's file. Allows patients the possibility of obtaining larger quantities of medication.	Impact on treatment cost must be considered. The switch to Schedule II entails the drug being entered into the patient's file, the pharmacy being reorganized, and a heavier workload for pharmacists with no corresponding increase in remuneration.	Requires legislative changes (drug schedules) at the provincial government level. Must apply to all OTC drugs frequently involved in intentional overdoses and to combined drugs containing these ingredients.	Rescheduling by active ingredient or package size. A number of European countries that unscheduled drugs have reversed the decision to restrict sales to pharmacies only (e.g., Sweden, Denmark). Some countries limit drug sales solely to pharmacies (e.g., France, Germany, Belgium). The use of blister packs for unscheduled and Schedule III drugs does not make it impossible to sell large quantities under Schedule II, but makes it more difficult or limits the taking of large numbers of tablets as an impulsive action during a suicidal crisis.

9 Conclusion

The examination of all intentional OTC drug overdose prevention strategies and the identification of measures that are desirable and applicable to Québec required a thorough understanding of legislation governing access to drugs for use in humans, the scope and characteristics of the intentional OTC drug overdose issue, and effective interventions based on published and unpublished documentation.

An examination of OTC drug legislation showed that unlike most of the countries studied, Canada (including Québec) and the United States do not impose maximum package sizes for four OTC drugs sold in pharmacies, whether freely accessible or under the pharmacist's control. Generally speaking, Québec is the most stringent when it comes to OTC drug access (points of sale, MPS when sold outside of pharmacies, and maximum unit dose) as compared to Canada as a whole.

Our analysis of the data made it possible to conclude that drug overdoses account for a substantial proportion of the means used in suicide deaths and suicide attempts in Québec. These are most often the result of a combination of substances, including but not limited to OTC drugs. Among the latter are acetaminophen, ibuprofen, naproxen and ASA, which can cause severe complications depending on the substances and quantities absorbed. According to the data, acetaminophen is by far the most commonly used of the OTC drugs that cause deaths and hospitalizations.

Regarding desirable interventions for Québec, the consensus reached as part of the discussion process yielded the following recommendations: set a MPS for acetaminophen available under Schedule III; promote the use of the poison centre (Centre antipoison du Québec) to the population and health care professionals; and incorporate the intentional OTC drug overdose issue into any integrated suicide prevention strategy.

The literature consulted examined a number of prevention strategies but focused primarily on acetaminophen. The studies centred mainly on restricting acetaminophen accessibility in the United Kingdom (MPS and MQS). Selling all OTC drugs exclusively in blister packs should be considered, however this is not actually the case in Canada.

The only country where several studies with more sophisticated research methods were conducted is the United Kingdom. The results of those studies indicated that this type of measure significantly reduced suicide deaths and suicide attempts involving acetaminophen, as well as non-intentional overdoses with the drug. In addition, the studies recommended applying the same sale restriction rules to other OTC pain relievers (e.g., ibuprofen, ASA) in order to minimize substitution risk. However, considering the small number of studies on the subject and the numerous methodological constraints, it is difficult to conclude with certainty that any such measure would have an impact on the rate of intentional acetaminophen overdoses in countries other than England.

Other prevention strategies studied involved using blister packs rather than bottles as packaging and reducing the unit dose. Even though these strategies were recommended by some studies, they were based on expert opinions rather than epidemiological studies. Adding ingredients to tablets to mitigate acetaminophen toxicity faced great expert reluctance because of the potential side effects of these ingredients.

Given the context, it was deemed preferable to present to the reader a set of measures that may be implemented alone or in combination to limit OTC drug accessibility and to discuss the advantages and disadvantages of these measures under specific conditions that may be required for their implementation.

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