Adverse reactions with cannabis products in Canada

CSTE Cannabis Subcommittee

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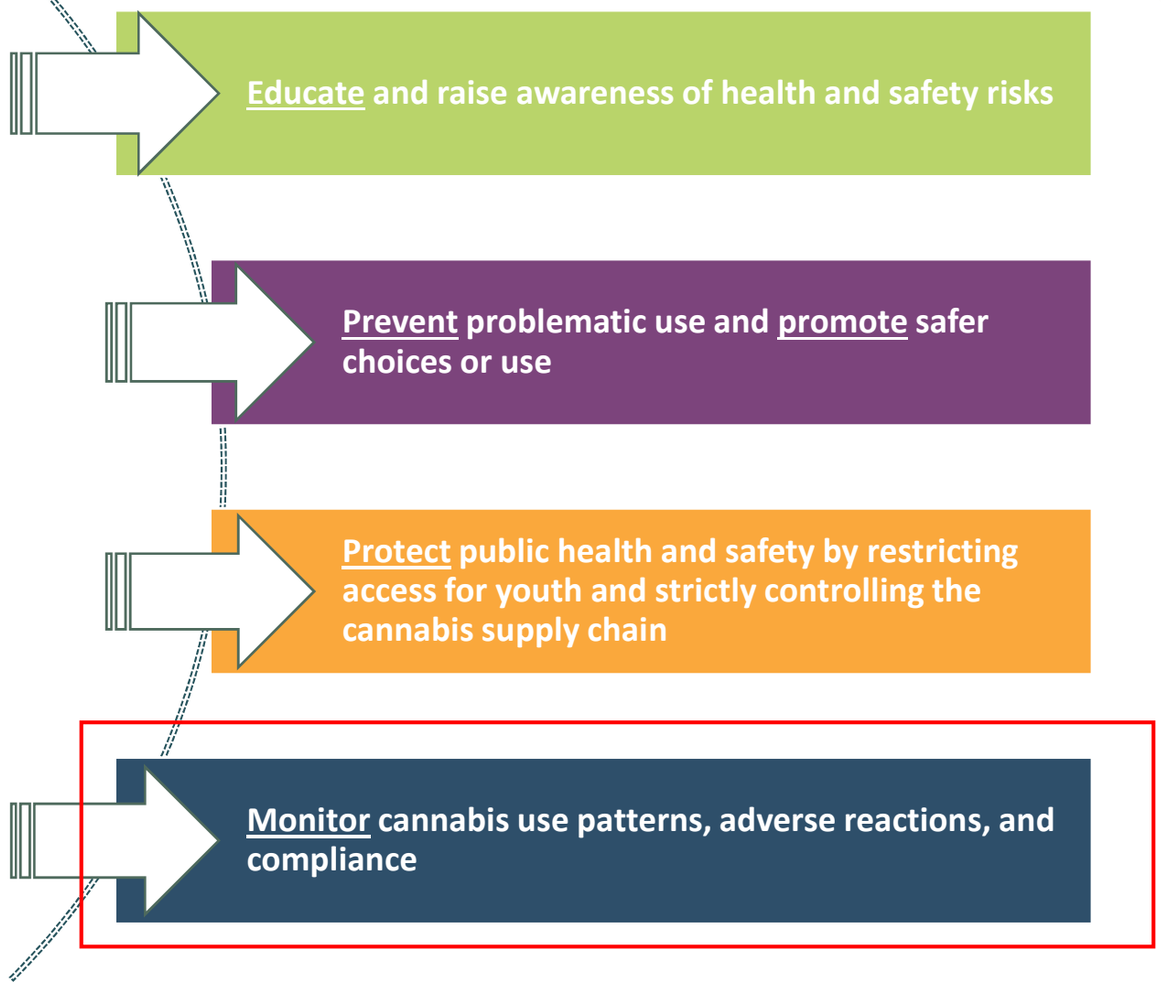
Purpose

- To provide a brief overview of the Vigilance Framework for Cannabis Products led by the Office of Cannabis Science and Surveillance.
- To provide an overview of the adverse reaction data collected by Health Canada during the second year since the coming into force of the *Cannabis Act* and its Regulations, covering the reporting period of January 1, 2020 to December 31, 2020, with comparisons to the first year of legalization (October 17, 2018 to December 31, 2019).

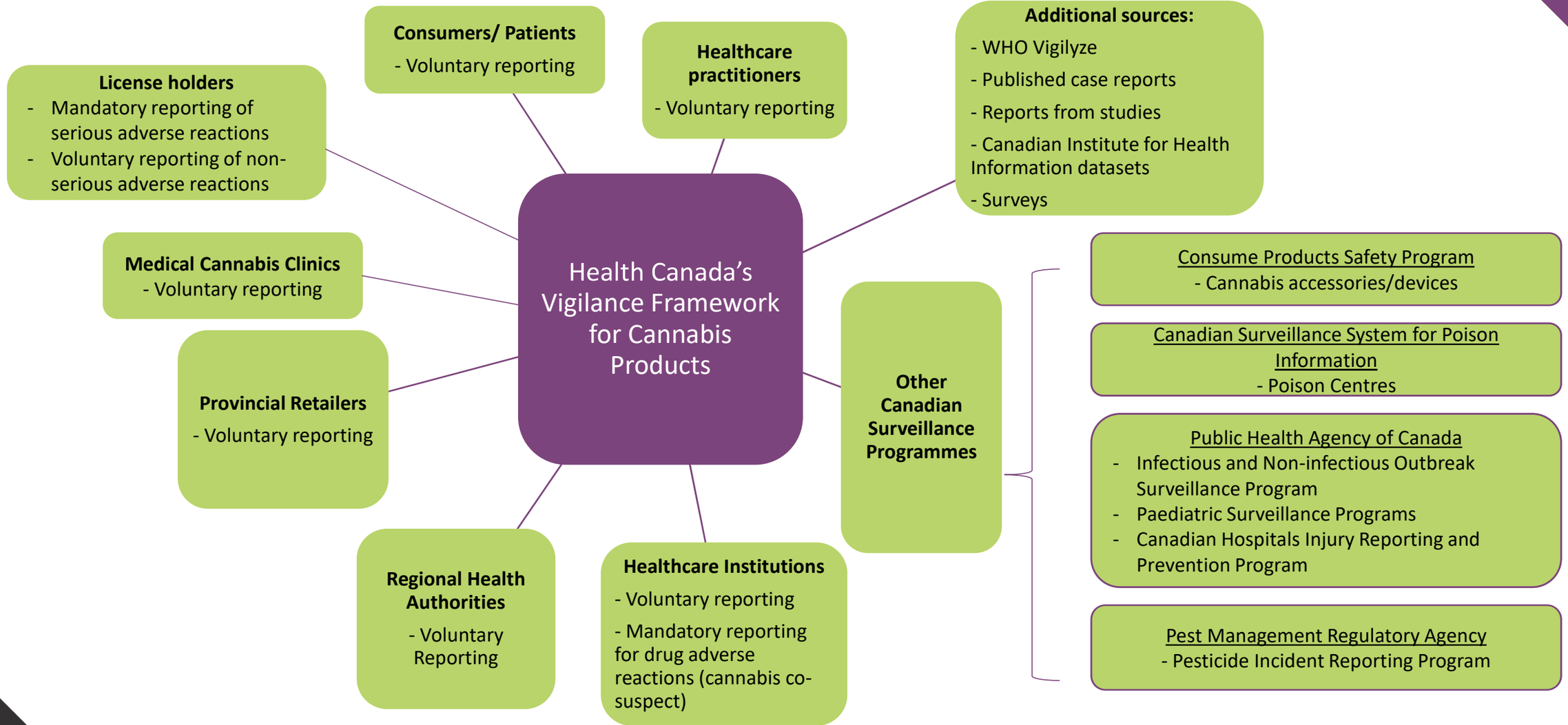
Vigilance Framework for Cannabis Products

- The Office of Cannabis Science and Surveillance (OCSS) at Health Canada leads the Vigilance Framework for Cannabis Products.
  - **Aim:** timely collection, monitoring, detection and assessment of adverse reactions to support decision-making, knowledge translation and communication of the safety of cannabis products to the public so they may make informed decisions.
- Supported by the Marketed Health Products Directorate for collection, housing and coding of adverse reaction reports in the Canada Vigilance Database.
- Enables the centralisation of adverse reaction data for health products and cannabis products in the same pharmacovigilance database – important for signals of mutual interest (e.g., cannabis-drug interactions).

Public Health Approach to Legalization and Regulation:



Sources of adverse reactions



Adverse reaction monitoring and assessment process

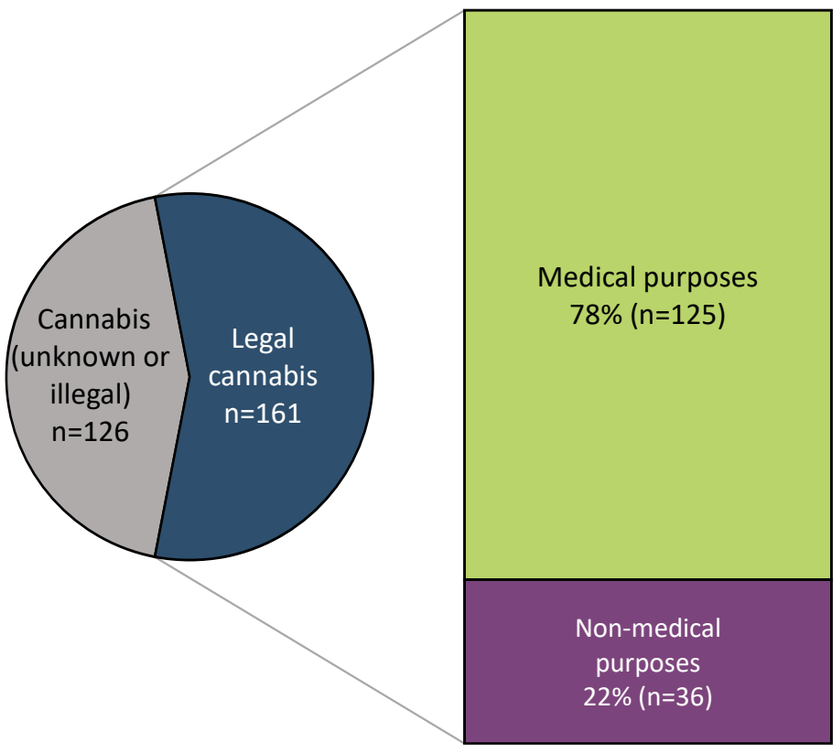
- Adverse reaction reports are submitted to Health Canada
- Adverse reaction reports are coded and collected in the Canada Vigilance Database
- Cases involving cannabis are monitored, screened and triaged on a near-time basis
- Serious (& medically important) adverse reaction cases with cannabis products are followed up and assessed for causality
- Two or more cases of interest may trigger signal prioritization and/or case series, which integrates other data such as foreign reports and scientific/medical literature
- Suspected product quality complaints in reports are referred to Compliance & Enforcement partners for Compliance Verification
- Adverse reaction data is aggregated, analysed and reported on an annual basis

Adverse reactions with legal cannabis products since legalization

A Snapshot

Total adverse reaction reports received in 2020

- A total of 287 adverse reaction reports* associated with cannabis as a suspect substance were reported to Health Canada's Canada Vigilance Database between January 1 to December 31, 2020.



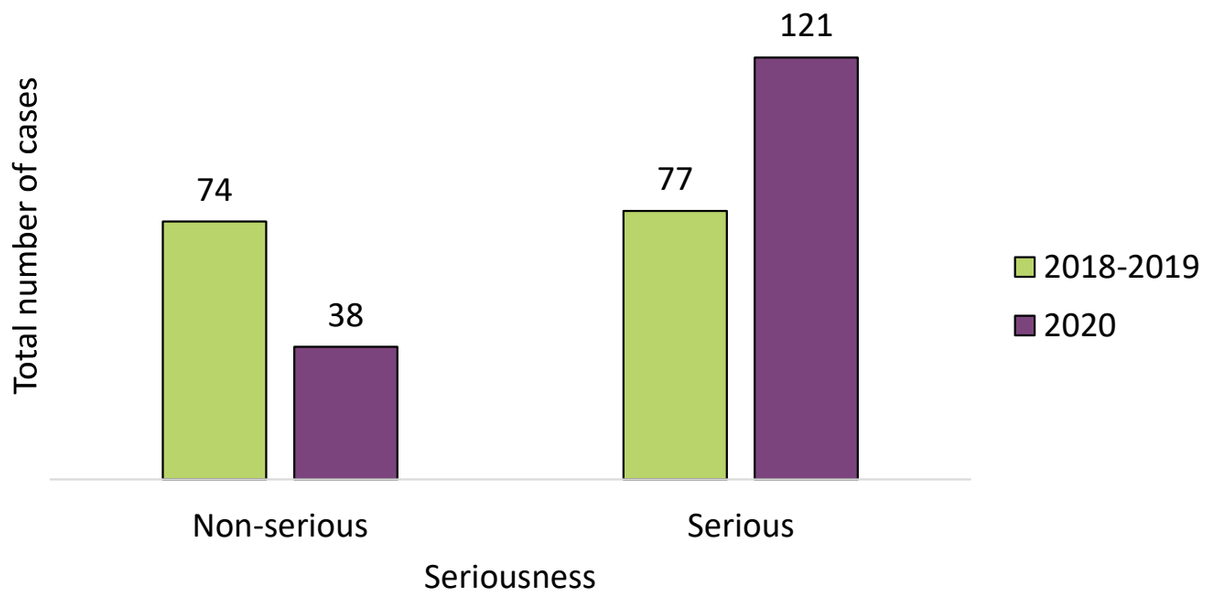
* Reports may originate from multiple sources (e.g., licence holders, consumers/patients, HCPs, medical cannabis clinics, retailers) and pertain to the same case

Cannabis adverse reactions outside the legal framework

- Three reports of suspected vaping-associated lung illness (VALI) involving cannabis were reported to Canada Vigilance in 2020.
  - One case was suspected of involving legal cannabis products while the other two were suspected of involving cannabis from an unknown or illegal source.
- The current reporting period included 44 pediatric reports of accidental ingestion of cannabis.
  - **All cases** involved cannabis from an unknown or illegal source.
- Many cases of polysubstance use.

Adverse reaction cases by number and seriousness

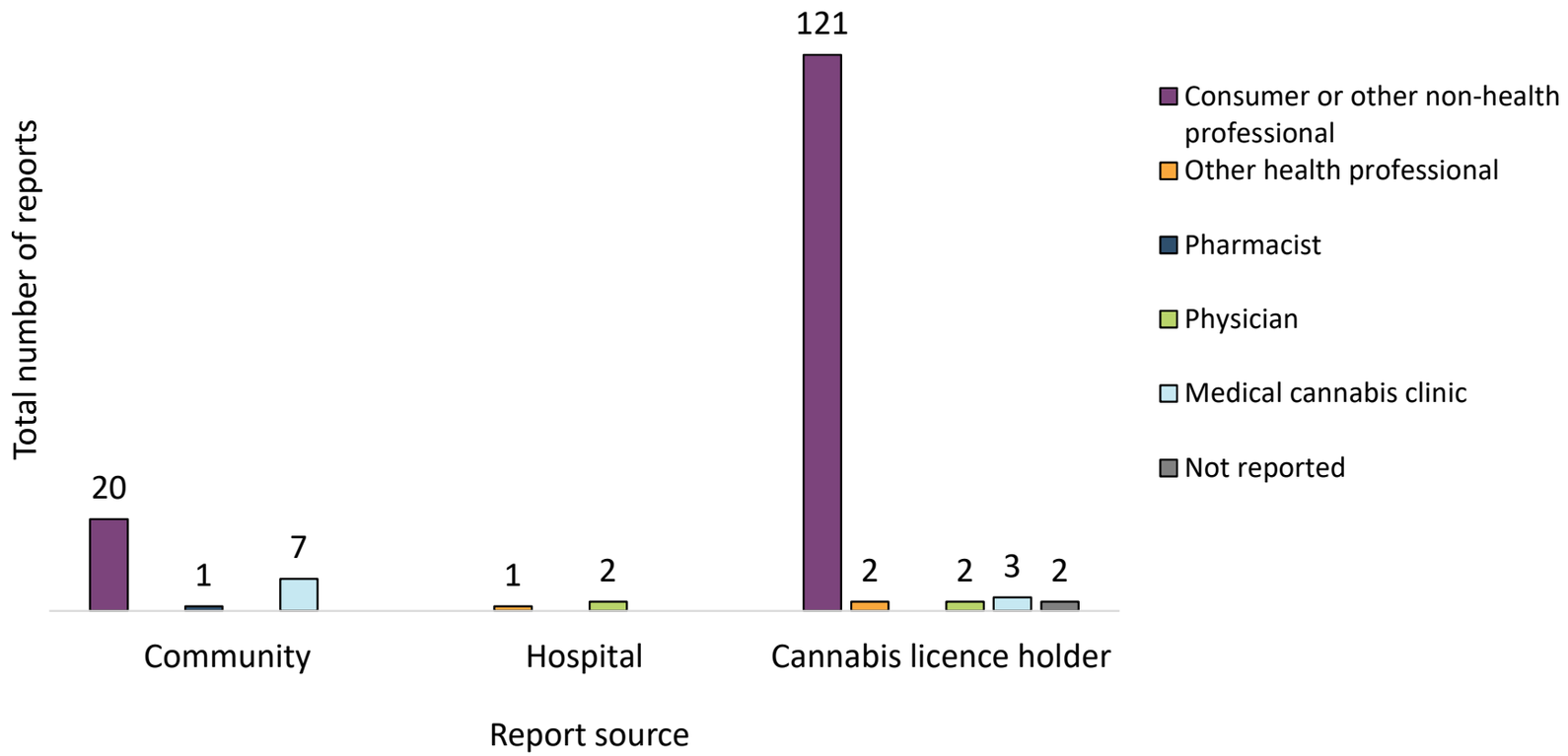
- Between January 1 and December 31, 2020, there were 159 unique adverse reaction cases associated with legal cannabis products submitted to the Canada Vigilance Database
  - A small increase from the previous reporting period (n=151)*
- Most cases were reported as serious (77%)
  - An increase from the previous reporting period (51%)



*Previous reporting period covers Oct 17, 2018 -Dec 31, 2019, when only initial classes of cannabis products were commercially available on the Canadian marketplace

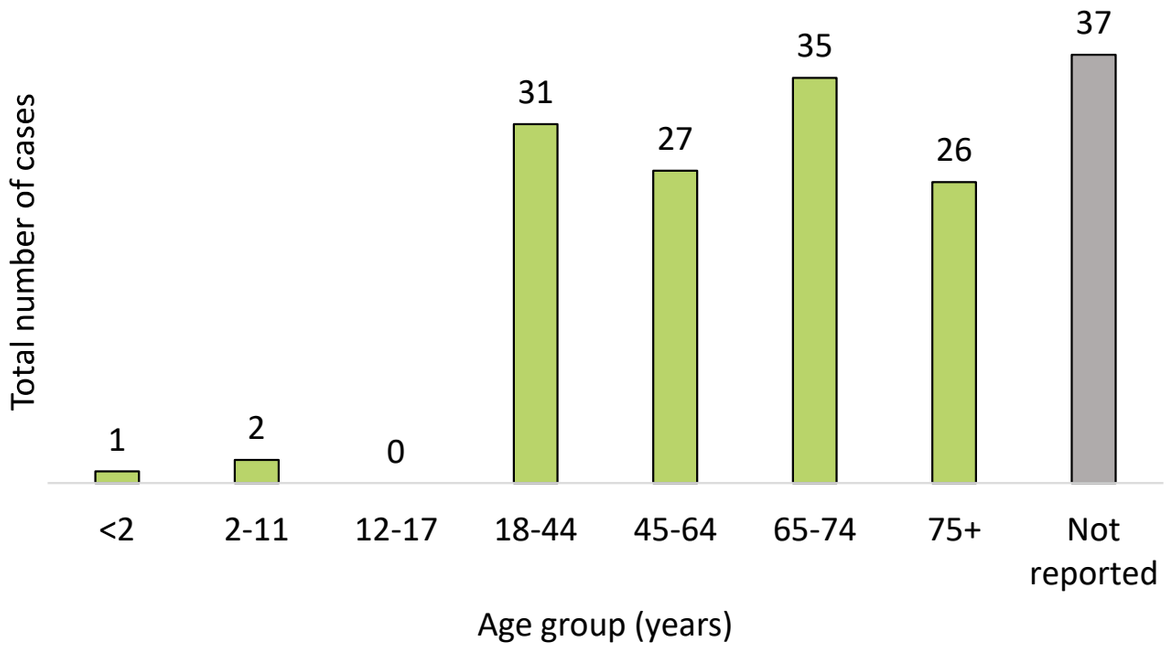
Adverse reaction reports by initial reporter and source

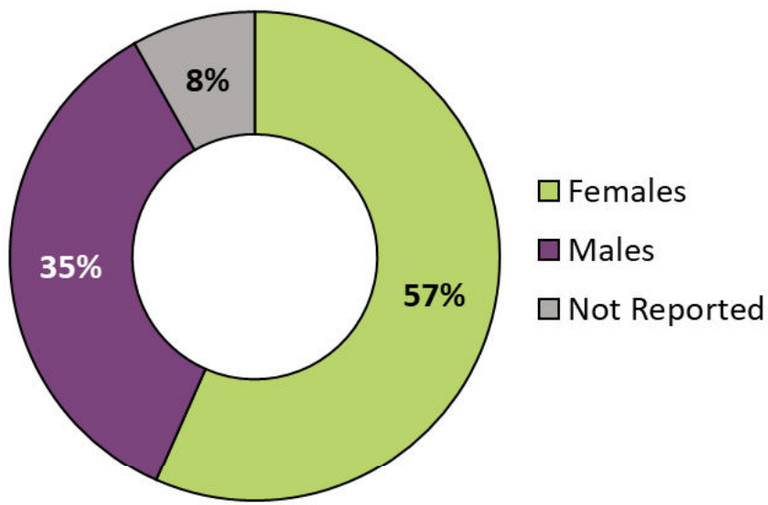
- The majority of adverse reaction reports were initially reported by patients or consumers (88%, n=141), and were submitted to Health Canada by cannabis licence holders (86%).



Adverse reaction cases by age and sex

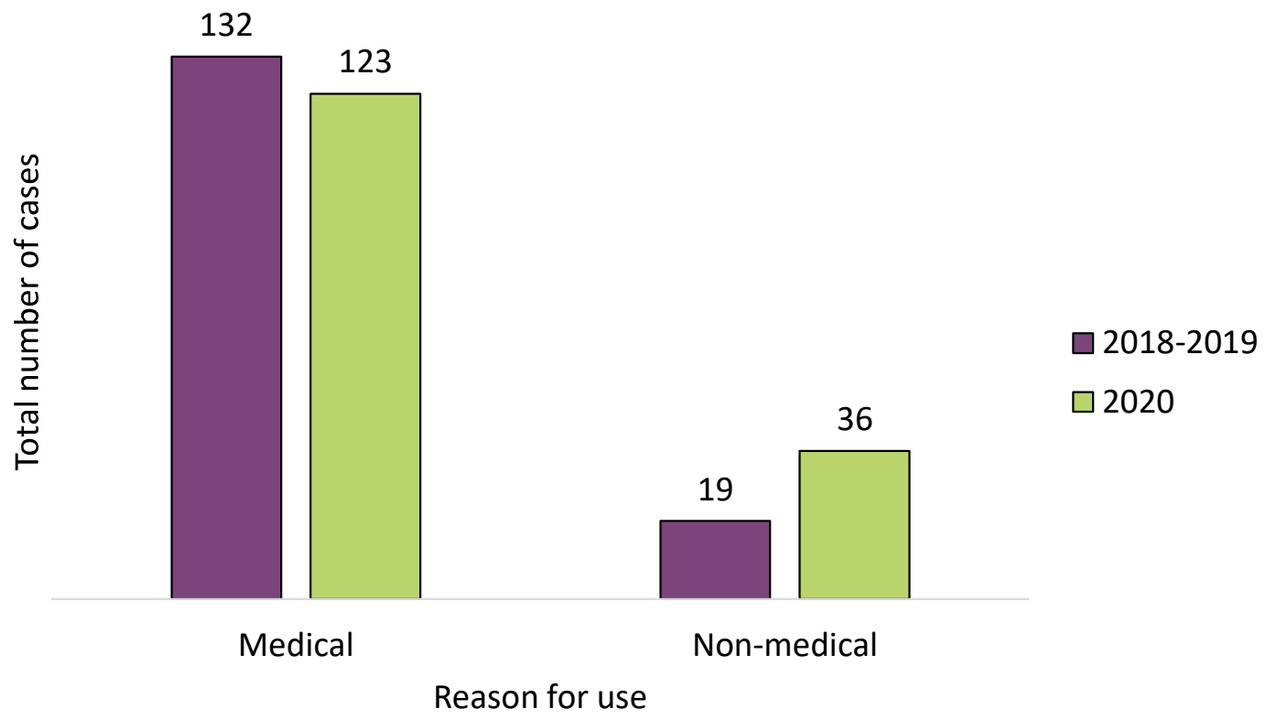
- Adverse reaction cases were most frequently reported in older adults aged 65-74 years (n=35), followed by adults aged 18-44 years (n=31)
  - In the previous reporting period, cases most frequently involved young to middle aged adults (18-44 years, n=37; 45-64 years, n=36)
- Overall, cases more frequently involved females than males
  - Consistent with the previous reporting period





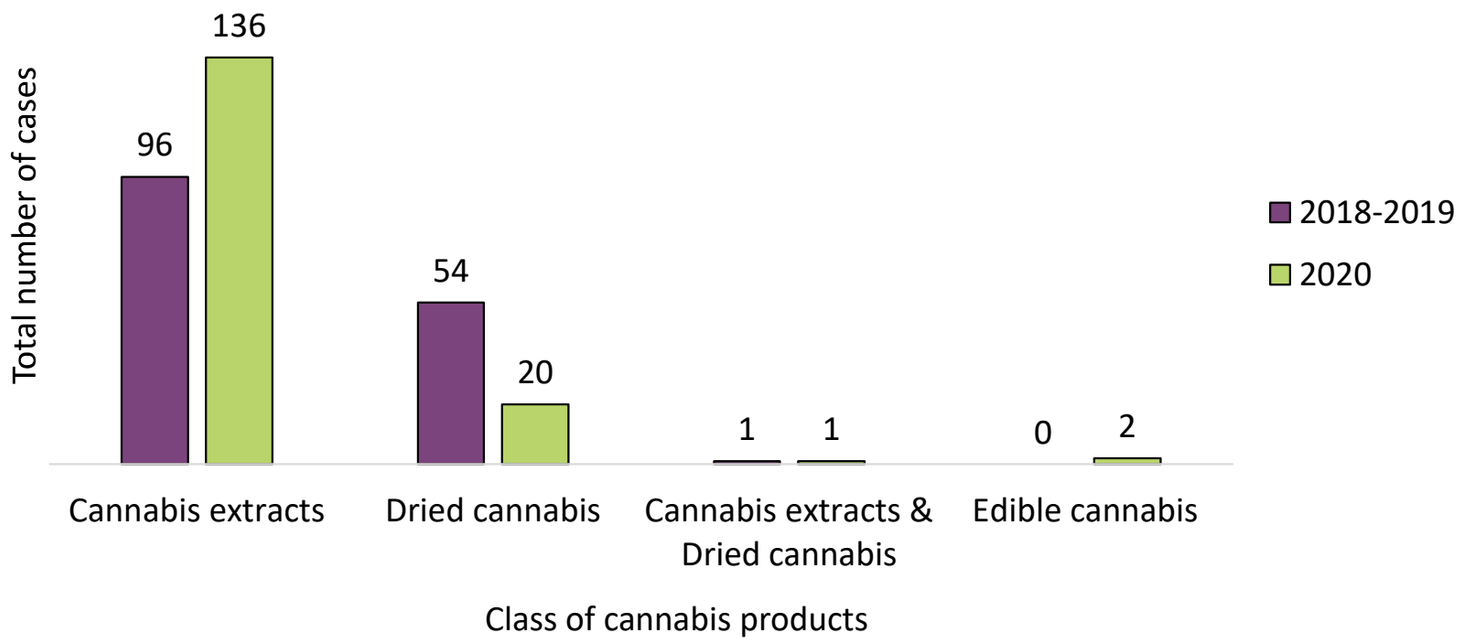
Adverse reaction cases by reason for use

- The majority of adverse reaction cases involved suspect cannabis products for self-reported medical purposes (77%)
  - A decrease from the previous reporting period (87%)



Adverse reaction cases by product class and route of administration

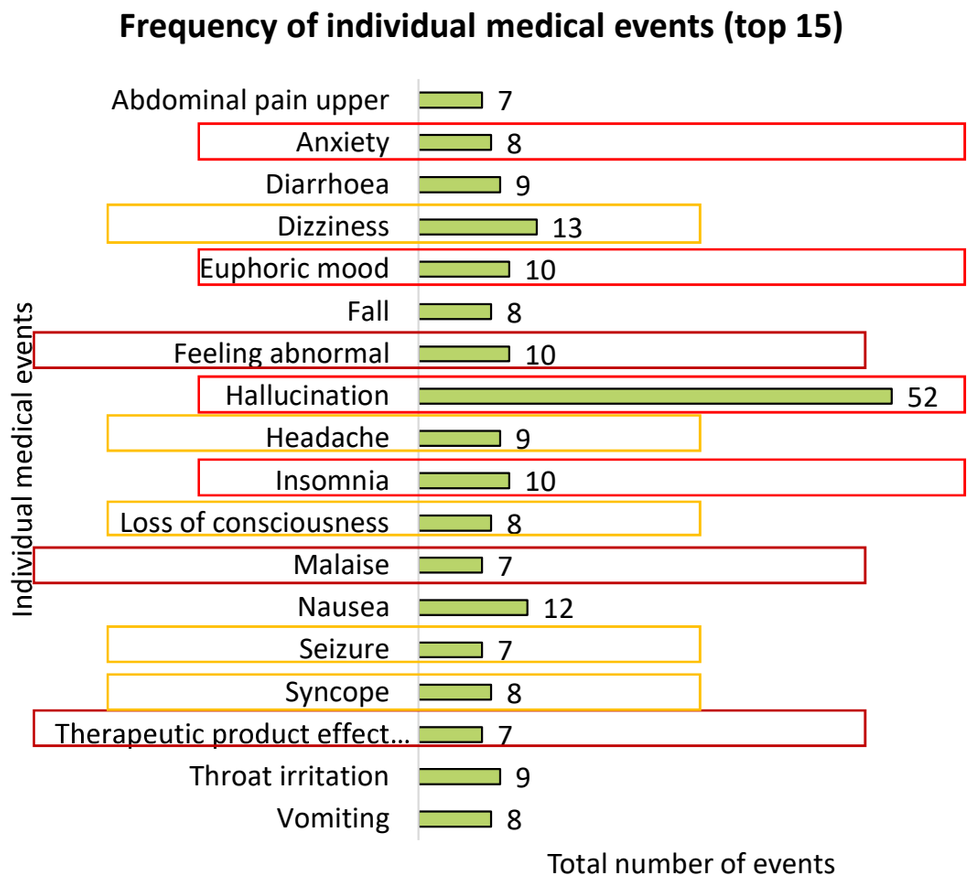
- Most adverse reaction cases were associated with cannabis extract products (86%) versus other product classes (dried cannabis: 13%, edible cannabis: 1%).
  - Most cannabis extracts were ingestible oils (92%).
  - Cannabis oils were also the most frequently associated type of suspect cannabis product during the previous reporting period (dried, fresh cannabis and cannabis oils only).



Adverse reaction cases by adverse event type

- Various individual adverse events were reported across the adverse reaction cases in 2020;
- Psychiatric, general and neurologic events were the most frequently reported:
  - Psychiatric events: hallucination**, insomnia, euphoric mood, anxiety
  - General events: feeling abnormal, malaise, therapeutic product ineffective/incomplete
  - Nervous system events: dizziness, headache, loss of consciousness, seizure, syncope
- A small number of suspected drug interaction cases and product quality issues were also reported.

Note: The inclusion of a particular report in the database does not necessarily mean that the suspected product(s) caused the listed adverse events. Additional scientific investigations are required to establish a cause-and-effect relationship between a cannabis product and an adverse event.



** includes visual, auditory, mixed, hypnagogic and pseudohallucination

Important potential risks identified during 2020

- Risk of high intraocular pressure (IOP)/aggravation of glaucoma associated with the use of CBD-dominant cannabis products:
  - New and unexpected signal (i.e., not previously well characterised) resulting in an in-depth assessment (case series), which revealed a potential association between consumption of CBD-dominant cannabis products and a limited number of cases of increased IOP in humans.
  - This risk has been disseminated in various public education materials and continues to be monitored.
- Risk of cannabis – drug interactions:
  - Medically confirmed pediatric case of a suspected interaction between an equilibrated cannabis oil and metronidazole.
  - Non-medically confirmed suspected interaction between a CBD-leaning cannabis softgel product and lorazepam.
- Risk of hallucination involving CBD products:
  - Several cases of hallucination following the use of CBD-dominant or leaning products were submitted to Health Canada during the reporting period (n=34); hallucination with CBD products is considered to be new and unexpected.

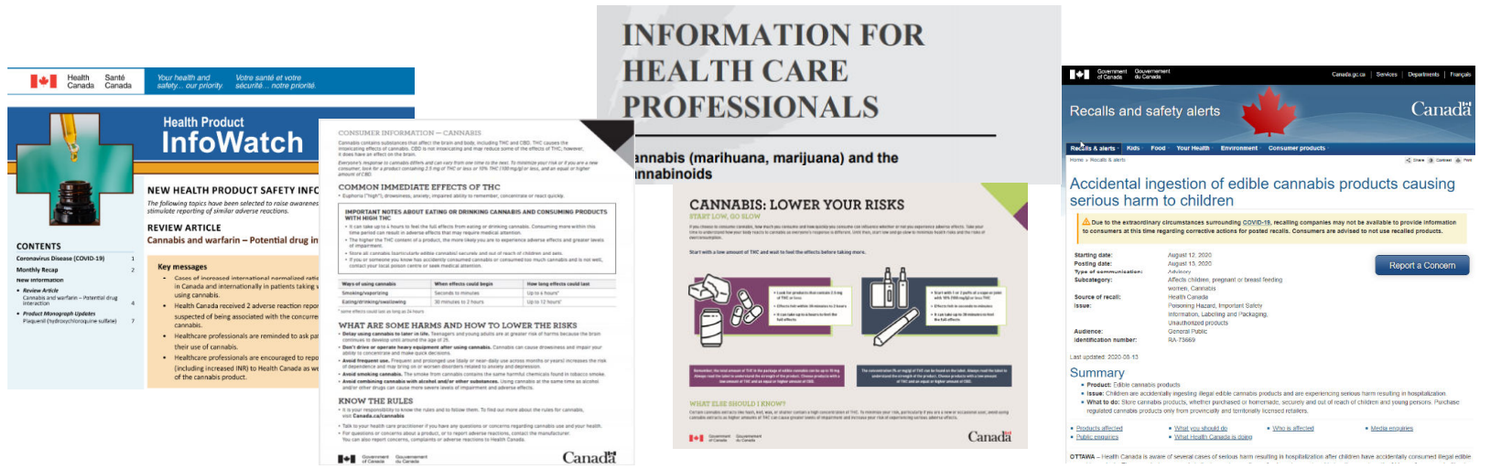
Summary and next steps

Summary

- Adverse reaction cases reported to Health Canada in 2020 were predominantly serious and largely involved cannabis for medical purposes, in particular, ingestible oils.
- Some findings have changed while others have remain consistent between the first and second years of legalization.
- Conclusions are only preliminary at this time and further years of data are required to conduct proper trend analysis and to assess any long-term changes in findings.

Next steps

- The first and second annual report of cannabis ARs have been published online;
- Ongoing monitoring and assessment of adverse reactions to help inform evidence-based information on health and safety risks with cannabis, including risk communications and educational resources;
- Exploration of new sources of adverse reactions to cannabis products (e.g. real world evidence studies and data).



Thank you

For further inquiries, please contact the Office of Cannabis Science and Surveillance

cannabis_oss-cannabis_bss@hc-sc.gc.ca

Annex 1

Data considerations

Data Considerations

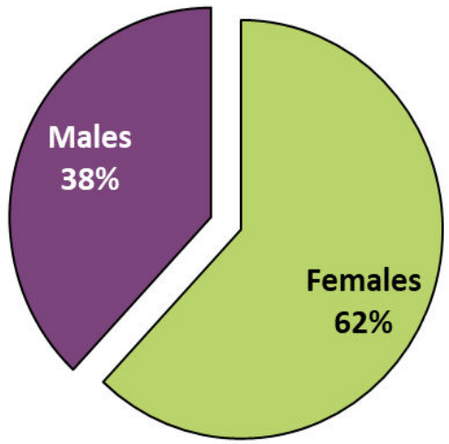
- Most adverse reactions are spontaneously reported to Health Canada and should not be used to determine the incidence or prevalence of adverse reactions to cannabis in the general population.
  - Some solicited reports from organised data collection systems exist in the adverse reaction dataset.
- Serious adverse reactions have a greater representation in this dataset as licence holders have a regulatory obligation to report these under the *Cannabis Regulations*.
  - The submission of non-serious adverse reactions by license holders to Health Canada is voluntary; therefore, it is likely that there are additional non-serious adverse reaction cases that have not been reported to Health Canada.
  - Non-serious cases are required to be included in the license holder's summary report of all adverse reactions that must be prepared and maintained on an annual basis as per S.248 of the *Cannabis Regulations*.
- Reporting of adverse reactions by consumers, healthcare professionals and retailers is voluntary, therefore, both serious and non-serious cases from these reporters are likely underreported.
- Individuals experiencing serious outcomes or using cannabis products for medical purposes may be more motivated to report or seek out medical attention.
- The inclusion of a particular report in the database does not necessarily mean that the suspected product(s) caused the listed adverse events. Additional scientific investigations are required to establish a cause-and-effect relationship between a cannabis product and an adverse event.

Annex 2

Sex-based gender analysis (SGBA+)

A SGBA+ Perspective

- Of the cases with a designation for sex, 62% (n=90) involved females.
  - Females represented 66% of all serious cases.
- Females reporting adverse reactions to cannabis products were older than males.
  - The average age of females was 64.2 years vs. 51.2 years for males.
- Adverse reaction cases involving inhaled dried cannabis (whole flower) and vaping liquids more frequently involved males than females.
  - Ingestible cannabis oils in liquid form (bottles or sprays) and softgel capsules more frequently involved females than males.



Top three events reported, by sex:

	Females	Males
1	Hallucination (n=37)	Hallucination (n=14)
2	Dizziness (n=12)	Fall (n=5)
3	Nausea (n=9)	Psychotic disorder (n=5)