## Canada's Lower-Risk Nicotine Use Guidelines - An Update

A Resource to Help Guide Decision-Making for People Living in Canada Who Use Nicotine

Published 2021 Updated March 31, 2025

# camh INTREPID Lab

#### **Funding Partner**

Production of the Lower-Risk Nicotine Use Guidelines has been made possible through funding from Health Canada's Substance Use and Addictions Program (SUAP). These materials herein do not necessarily represent the views of Health Canada.

#### About INTREPID Lab

The Innovation, Nicotine and Tobacco, Research, Education Programming, Implementation and Digital Health Lab (INTREPID Lab) at the Centre for Addiction and Mental Health (CAMH) is a leading hub for smoking and vaping treatment, research and education to create social change. INTREPID Lab addresses quality improvement and chronic disease prevention around tobacco use, health behaviour changes to improve quality of life, and improve access to knowledge and evidence-based research. To date, INTREPID Lab's STOP Program has collaborated with over 350 health settings across Ontario, helping over 400,000 patients with commercial tobacco addiction. The TEACH Project has provided continuing education in commercial tobacco cessation and ecigarette use to over 6,800 healthcare providers and allied professionals internationally.

For more information about INTREPID Lab, visit <u>intrepidlab.ca</u> or follow INTREPID Lab on X @PSQuitSmoking.

#### **Copyright and Disclaimer**

The Lower-Risk Nicotine Use Guidelines provide evidence-based recommendations but do not replace clinical judgment and individualized patient care. Compliance with these guidelines does not guarantee specific outcomes, and neither INTREPID Lab nor the contributors assume responsibility for their use. Clinicians should apply discretion and consult additional resources as needed.

Copying or distribution of these materials is permitted providing the following is noted on all electronic or print versions: © CAMH/INTREPID Lab. No modification of these materials can be made without prior written permission of CAMH/INTREPID Lab.

#### Contact

Centre for Addictions and Mental Health INTREPID Lab 1025 Queen Street West Toronto, Ontario, M6j 1h4 Email: Intrepid.Lab@camh.ca Tel: (416) 535-8501

#### **Suggested Citation**

Centre for Addiction and Mental Health (CAMH), INTREPID Lab. (2025). Lower-Risk Nicotine Use Guidelines (LRNUG) (Original work published 2021). Centre for Addiction and Mental Health. Retrieved from intrepidlab.ca/en/lower-risk-nicotine-userguidelin-es

## Foreword

The landscape of nicotine consumption in Canada has undergone a significant transformation with the introduction of nicotine pouches and e-cigarettes/vapes. These products have reshaped the way nicotine is consumed, presenting both opportunities and challenges for public health, policy development, and clinical practice.

In response to this evolving landscape, the Lower Risk Nicotine Use Guidelines (LRNUG) underwent significant updates in December 2024 to incorporate new evidence and improve usability. The e-cigarette section now integrates findings from INTREPID Lab's Project VECTOR Toolkit, summarizing and updating health outcomes while preserving existing recommendations related to e-cigarettes for smoking cessation. The guidelines also introduce nicotine pouches, drawing on evidence from a rapid review to provide recommendations on their risks, potential benefits, and place within the nicotine risk continuum. Further details on these updates are outlined in the following sections and appendices.

In addition to product-specific updates, the LRNUG now features a redesigned layout to improve readability and accessibility for clinicians and healthcare professionals. Updates include a modernized layout, accessible color-coding, streamlined graphics, and clearer language with concise formatting. Additionally, new resources have been added to support both clinicians and clients with providing guidance on nicotine use and harm reduction.

New and updated content is clearly marked throughout the Guidelines, with sections labeled (New) and (Updated) to indicate additions and revisions from the previous version. The archived version of the LRNUG remains available (see link below), with some sections greyed out to indicate outdated content. For the most current evidence and recommendations, please refer to this updated version. As new research emerges, the LRNUG will continue to evolve to reflect the latest scientific evidence and best practices.

We welcome feedback to improve these guidelines. To submit questions, report errors, or suggest updates, please email: <u>Intrepid.Lab@camh.ca.</u>

**Archived Version:** To view the 2021 LRNUG, visit: <u>intrepidlab.ca/en/lower-risk-nicotine-</u> <u>user-guidelin-es</u>

## **Table of Contents**

About INTREPID Lab	. i
Foreword	. ii
Evidence Brief	.5
Nicotine Risk Continuum	.7
Executive Summary	. 8
Methodology	.8
Recommendations and Clinical Considerations	. 11
Smokeless Tobacco, Heated Tobacco Products, and Water-Pipes	. 12
Nicotine Pouches	. 14
E-Cigarettes	16
Harm Reduction Tips	. 19
Resources	22
For Providers	22
For clients	23
Appendix A - Supporting Evidence for Guideline Development, By Product	24
Appendix B - Guideline Development Group (GDG) Members	28
Appendix C - Methodology for 2021 LRNUG Development	31
Notes	33

## **Evidence Brief (Updated)**

Replaces the Evidence Brief on Page 1 of the LRNUG Version 2021

#### What are the Lower-Risk Nicotine Use Guidelines?

Nicotine, when rapidly absorbed, is a highly addictive substance that can be difficult to quit. While no level of nicotine is considered safe for individuals who do not use tobacco, nicotine is approved for therapeutic use to support tobacco cessation, and recreational nicotine products remain commercially available in various forms. The Lower-Risk Nicotine Use Guidelines (LRNUG) present the current state of evidence and highlight modifiable behaviours that can help reduce the negative health outcomes associated with various forms of nicotine use from the most to the least dangerous for individual use.

*Note:* With evidence on novel nicotine products, including e-cigarettes and nicotine pouches, continuing to evolve, INTREPID Lab has updated the LRNUG in December 2024 to include the latest evidence on the harms and benefits associated with e-cigarette or nicotine pouch use.



#### Who Are the LRNUG For?

The LRNUG serves as a health education and prevention tool for:

- Individuals who currently use, or are considering using any type of nicotine product.
- Professionals, organizations or governments aiming to improve the health outcomes of individuals who use nicotine.

#### How Were the LRNUG Developed?

The LRNUG are based on comprehensive literature searches conducted up to June 2024, focusing on various nicotine products and their associated health outcomes. Guideline Development Groups (GDGs)—comprising of subject matter experts and people with lived and living experience—collaborated in-person or virtually to develop the recommendations outlined on *Page 11*. These groups rigorously assessed the quality of the evidence and collaboratively determined the language for the recommendations.



#### **Overview of Recommendations:**



<u>Smokeless Tobacco, Heat-not-Burn, and Waterpipes</u> The use of smokeless tobacco, heated tobacco products, and waterpipes are associated with significant health risks. While heated tobacco products may reduce some harmful exposures compared to conventional cigarettes, they still pose serious risks. Avoiding all forms of these tobacco products should be encouraged to protect both users and those exposed.



#### E-cigarettes (Updated)



E-cigarettes are not recommended for individuals who do not use tobacco products due to the risk of dependence and potential harms to health. While e-cigarettes are less harmful than combustible tobacco, they are not riskfree, and their long-term effects remain unknown. For individuals who currently smoke and are unable to quit using approved cessation methods, switching completely to e-cigarettes may reduce exposure to toxicants and carcinogens.

#### Nicotine Pouches (New)



Nicotine pouches (NPs) are not recommended for individuals who do not use nicotine due to the risk of dependence and potential health effects. Regulated and approved NPs are a lower-risk alternative for individuals looking to quit smoking combustible tobacco. In Canada, approved NPs containing 4mg or less of nicotine per pouch, are approved by Health Canada as short-acting nicotine replacement therapy (NRT), and are available behind the counter at pharmacies. A key ethical concern is that these approved pouches were developed and marketed by a subsidiary of a tobacco company. Additionally, nicotine per pouch, are illegal in Canada but remain readily accessible online.

#### Nicotine Replacement Therapy (Updated)



Nicotine replacement therapy (NRT), including patches, gum, lozenges, inhalers, oral sprays, and regulated and approved nicotine pouches are tools to help individuals quit smoking. Unlike tobacco, NRT delivers nicotine without the harmful chemicals found in tobacco smoke. It is generally safe when used as directed, but individuals should consult a healthcare provider before use.

## Nicotine Risk Continuum (Updated)

	Cigarettes	Waterpipe	Smokeless Tobacco	Heat- not- Burn	Nicotine Containing E-cigarettes	Unregulated Nicotine Pouches*	Short- Acting NRT**	Long- Acting NRT
How it enters the body:	Smoke	Smoke	Mouth	Aerosol	Aerosol	Mouth	Mouth	Skin
Does it contair	1:							
Tobacco	Y	Y	Y	Y	Ν	Ν	N	Ν
Nicotine	Y	Y	Y	Y	Y	Y	Y	Y

#### Does it increase risk of or risk factors for ...?

Dependence	Y	Y	Y	Y	Y	Y	N***	Ν
Respiratory Illness	Y	Y	Ν	?	Y	Ν	N	Ν
Cancer	Y	Y	Y	?	?	Ν	Ν	Ν
Cardiovascular Disease	Y	Y	?	?	Y	Ν	Ν	N
Fetal Health	Y	Y	?	?	?	?	?***	?***

*Note:* This table replaces the previous nicotine risk continuum found on Page XX of the LRNUG version 2021.

\*Refers to nicotine pouches (NPs) containing >4mg of nicotine per pouch and are sold online or illegally in Canadian convenience stores. \*\*Included in this category are nicotine replacement therapy (NRT) gum, lozenges, spray, inhaler, and nicotine pouches authorized for sale in Canadian pharmacies as a form of short-acting NRT and contain <4mg of nicotine per pouch. \*\*\*Long-acting NRT (i.e., nicotine patches) are not addictive. However, some patients might experience symptoms of dependence to short-acting NRT. \*\*\*\*Safer than smoking and use under the guidance of a healthcare professional.



## **Executive Summary (Updated)**

Replaces the Executive Summary on Page 3 of the LRNUG Version 2021

The Lower-Risk Nicotine Use Guidelines (LRNUG) present the current state of evidence on tobacco and nicotine products, outlining modifiable behaviours to reduce the negative health outcomes associated with tobacco and nicotine product use. They are designed to guide individuals who use, or are thinking about using nicotine, on how to lower the risk associated with various nicotine products. In response to new findings, the LRNUG is updated with revised e-cigarette recommendations from Project VECTOR, and introduces new recommendations on nicotine pouches to reflect the latest research on these products. The products covered in the Guidelines include heated tobacco products, smokeless tobacco (chew and snus), waterpipes, ecigarettes/vapes, and nicotine pouches.

### Methodology

The original LRNUG, developed in 2021, were based on a rigorous methodology to generate recommendations on ecigarettes, waterpipes, smokeless tobacco, and heat-not-burn products. The methodology included a literature review of peer reviewed articles from 2014-2021 and an expert panel review of evidence to develop recommendations and clinical considerations. Further details on this methodology are located in *Appendix C*.

However, in December 2024, the LRNUG underwent significant updates to include

recent evidence-based findings on nicotine pouches and e-cigarettes. The following sections outline the approach used to accomplish each update:

#### 1. Revised E-Cigarette Section (New)

On May 31, 2024, INTRPEID Lab released the Project VECTOR toolkit (funded by Health Canada's Substance Use and Addictions Program (SUAP)). This resource outlines the health impacts of e-cigarette use across four key areas: cancer, cardiovascular health, dependence, and respiratory health.



Based on the findings from Project VECTOR, the LRNUG e-cigarette section has been revised to reflect the key health outcome findings related to these four domains. *Note:* recommendations on the use of e-cigarettes for smoking cessation remains unchanged as The Canadian Task Force on Preventive Health Care plans to release updated national guidelines on this topic in 2025. For access to the full Project VECTOR toolkit, including details on the methodology, harm reduction strategies, frequently asked questions, and additional resources, visit <u>intrepidlab.ca/en/Pages/Project-</u> <u>VECTOR.aspx</u>

#### 2. Inclusion of Nicotine Pouches (New)

In April 2024, INTREPID Lab received funding to conduct a rapid review of nicotine pouches, a smokeless and tobacco-free nicotine delivery product gaining popularity. This review aimed to evaluate the potential harms and benefits of nicotine pouch use to inform evidencebased recommendations. The rapid review included:

- Peer-reviewed studies published between January 2021 and June 2024, covering a range of study designs, including randomized controlled trials, cohort studies, cross-sectional studies, and mixed-methods research. The full list of references reviewed is available in *Appendix A*.
- Literature searches conducted in the following databases: Ovid MEDLINE, Ovid EMBASE, Ovid PsycINFO, and the Cochrane Database of Systematic Reviews.
- An examination of key health outcomes, including cancer risk, cardiovascular health, respiratory illness, nicotine dependence potential, fetal health effects, and the effectiveness of nicotine pouches as a potential smoking cessation aid.
- A review of grey literature sources, such as public health reports, clinical guidelines, and expert consensus

expert consensus statements, to capture additional insights not available in peer-reviewed publications

 A risk-of-bias assessment using validated tools appropriate for each study design to ensure the quality and reliability of the evidence. Toxicological and chemical analyses were not included in the risk-of-bias assessment.



Following the completion of the evidence review, a Guideline Development Group (GDG) convened to evaluate the findings and develop recommendations regarding nicotine pouch use. The GDG consisted of four subject matter experts with expertise in nicotine and tobacco research, as well as one individual with lived experience. The group met virtually on October 17, 2024, and November 19, 2024, to review the evidence, formulate recommendations, and vote on the final guidance to be included in the updated LRNUG. As part of the update process, the GDG also determined where nicotine pouches belong within the nicotine risk continuum and developed practical recommendations for minimizing risks associated with nicotine pouch use.

*Note:* Due to the small size of the GDG, the strength of recommendations and evidence ratings were determined through verbal deliberation rather than formal consensus methods. For details on GDG membership, see *Appendix B*.





## Recommendations and Clinical Considerations (Updated)

Replaces the Recommendations on Page 9 of the LRNUG Version 2021

#### **Rating System (New)**

This section provides a comprehensive overview of recommendations and key considerations for each nicotine product, with a focus on their impact across a range of health outcomes.

#### Level of Evidence\*:



**High:** There is strong confidence in the evidence to predict actual outcomes.



**High-Moderate:** The guideline development group (GDG) designated the quality of the evidence as high or moderate, with a larger proportion rating the certainty of the evidence as high.



**Moderate-High:** The GDG designated the quality of the evidence as high or moderate, with a larger proportion rating the certainty of the evidence as moderate.



**Moderate:** There is strong confidence that the evidence is close to the actual outcomes.



**Low:** The predicted outcomes in the evidence may be markedly different from the actual effects.



**Very Low:** There is very little confidence in the evidence. The true effect is likely to be substantially different from the estimated effect.

#### Strength of Recommendation\*:



**Strong:** Implies that most or all individuals will be best served by the recommended course of action.



**Conditional:** Implies that not all individuals will be best served by the recommended course of action.



**No Consensus:** Among the GDG members, a consensus could not be reached regarding the strength of the recommendation.

\*Adapted from: Schünemann, H., Brożek, J., Guyatt, G., & Oxman, A. (2003). GRADE handbook for grading quality of evidence and strength of recommendations (Updated October 2013). The GRADE Working Group

## Smokeless Tobacco, Heated Tobacco Products, and Water-Pipes

**Recommendation #1:** Use of Smokeless Tobacco (SLT) should be discouraged.

#### Level of Evidence



#### **Strength of Recommendation**



#### **Clinical Considerations:**

- These products have been linked to a variety of adverse health outcomes. SLT (other than snus) is associated with an increased risk of oral, pharyngeal, and oesophageal cancer. Snus is associated with increased risk of pancreatic cancer.
- SLT is associated with an increased risk of fatal ischemic heart disease and stroke.
- SLT is associated with an increased risk of adverse health outcomes in newborns when used during pregnancy.

**Recommendation #2:** Use of Heated Tobacco Products (HTP) should be discouraged.



#### **Clinical Considerations:**

- There is moderate evidence from short-term studies that HTP reduce exposure to some, but not all, harmful/potentially harmful compounds (HPHCs) compared to conventional cigarettes. However, the impact of HTP on health outcomes is not known.
- There is strong evidence that HTP products produce side-stream exposure to HPHC for those exposed second-hand.
- The impact of HTP on conventional cigarette smoking behaviour is unclear.
- *Note:* The majority of research is largely industry-funded, but there is some independent corroboration.



**Recommendation #3 :** Water-pipe smoking should be discouraged.



**Strength of Recommendation** 



Strong

#### **Clinical Considerations:**

- Water-pipe smoking is associated with serious health risks (including various cancers and cardiovascular disease).
- Herbal water-pipe smoking is associated with serious health risks and is not a safe alternative to tobacco water-pipe smoking.
- Exposure to second-hand smoke from water-pipes poses serious health risks. Water-pipes should not be smoked indoors or in public places where others are exposed.
- Water-pipe smoking while pregnant is associated with low birth weight.

Recommendation #4: Use of SLT, HTP, and water-pipes should be discouraged in women who are pregnant.



### **Clinical Considerations:**

- There is evidence that smokeless tobacco use may be associated with adverse pregnancy outcomes, including an increased risk of low birth weight, preterm birth and stillbirth.
- Water-pipe smoking is associated with intrauterine growth restriction and low birth weight.
- Refer to the CAN-ADAPTT guidelines for smoking cessation for pregnant and breastfeeding/chestfeeding women.
- Women who are pregnant should be encouraged to switch to nicotine replacement treatment to reduce possible harms.

Note: the recommendation on e-cigarette use during pregnancy has been relocated from this section to the section dedicated to e-cigarettes. However, the recommendation, level of evidence, and strength of recommendation for SLT, HTP, and waterpipes remain the same from the LRNUG version 2021.

## **E-Cigarettes and Vaping**

#### **Dependence**

**Recommendation #1:** Those who do not smoke should not use nicotinecontaining e-cigarettes as it may lead to dependence.



#### **Clinical Considerations:**

- Several factors can influence the level of dependence among people who use nicotine-containing e-cigarettes, including prior use of nicotine products and duration of use. In general, the greater frequency and time spent using a substance, the higher the risk of dependence.
- Nicotine dependence can lead to cravings and withdrawal symptoms (e.g., irritability, headaches, inability to fall or stay asleep, etc.).

#### Health Outcomes



**Recommendation #2a:** People who do not smoke should not use e-cigarettes in order to avoid respiratory dysfunction and symptoms.



**Recommendation #2b:** People who do not smoke should not use e-cigarettes in order to avoid exposure to cancer-causing chemicals.

**Level of Evidence** 



**High-Moderate** 

#### **Strength of Recommendation**



**Recommendation #2c:** People who do not smoke should not use e-cigarettes in order to avoid exposure to adverse effects on the cardiovascular system.

#### **Level of Evidence**



Moderate-High

#### **Strength of Recommendation**





#### **Clinical Considerations:**

- E-cigarettes are less harmful than combustible tobacco, but are not completely harmless. The aerosol produced from e-cigarettes contains chemicals known to be toxic or cancer-causing. Some examples include formaldehyde and acetaldehyde, and metals like lead, aluminum, nickel, tin, and cadmium.
- Vaping can irritate the lungs and worsen symptoms of asthma, COPD, or other respiratory conditions, especially for adolescents and people who have never smoked.
- E-cigarettes are currently considered to be harm-reducing during pregnancy compared to combustible tobacco use, but any nicotine use increases the risk of negative effects to the fetus.
- At this time, additional research is needed to better understand the potential long-term health effects of e-cigarette use.

#### Cessation\*

**Recommendation #3:** E-cigarettes with nicotine may be an effective cessation aid for people who use combustible tobacco.



#### Strength of Recommendation



#### **Clinical Considerations:**

- Systematic reviews and randomized controlled trials (RCTs) provide some evidence of the effectiveness of e-cigarettes as a cessation aid.
- More frequent use (i.e. daily) of e-cigarettes is associated with an increase in cessation outcomes.
- People who use combustible nicotine products should try to quit using approved smoking cessation treatments first. If they are unable or unwilling to quit, e-cigarettes can be considered.
- E-cigarettes as a cessation aid may be most effective when combined with behavioural counselling.
- Continued use of e-cigarettes may reduce risk of relapse to combustible tobacco.
- People who smoke should be advised to switch completely from combustible tobacco to e-cigarettes and to use e-cigarettes when they would normally have smoked tobacco cigarettes.

- There is no evidence for a specific device type or amount of nicotine that is most effective for cessation.
- Switching completely to e-cigarettes will significantly reduce the harms associated with combustible tobacco. However, tobacco-users should be advised that harms associated with long-term e-cigarette use are currently unknown.

*Note: For more information on the health impacts of e-cigarette use, visit: <u>intrepidlab.ca/en/Pages/Project-</u> <u>VECTOR.aspx</u> to view INTREPID Lab's Project VECTOR toolkit.* 

\*The recommendation on using e-cigarettes for combustible tobacco remains unchanged from the LRNUG version 2021.

### **Nicotine Pouches**

#### **Dependence**

**Recommendation #1:** The use of nicotine pouches (NPs) should be discouraged among individuals who do not use nicotine due to the risk of dependence.



#### Strength of Recommendation



#### **Clinical Considerations:**

- 4mg nicotine pouches are the only approved NP products in Canada. Unregulated NP\* products may result in a higher risk of dependence.
- The abuse liability of NPs has not been empirically tested. However, the dependence potential is lower for NPs compared to traditional cigarettes.
- There are no studies to date comparing the dependence potential of NPs to ecigarettes. However, a small number of studies suggest that NPs deliver a similar amount and rate of nicotine as short-acting NRT (e.g., gum and lozenges).
- Nicotine pouches pose a potential risk to youth due to the risk of dependence.

#### <u>Fetal Health</u>



**Recommendation #2:** The use of NPs should be discouraged in pregnant women, as nicotine is associated with various pregnancy and neonatal complications.



#### **Clinical Considerations:**

- Nicotine has adverse effects on fetal health outcomes (including low birthweight), so complete abstinence from nicotine (including NPs) is recommended during pregnancy.
- For women who have not been able to stop smoking with existing support, including NRT, NPs can be considered.

#### Health Outcomes

**Recommendation #3:** For individuals who use combustible cigarettes and cannot quit by other means, switching to NPs will reduce their exposure to disease-causing chemicals found in tobacco and tobacco smoke.



Strength of Recommendation



#### **Clinical Considerations:**

- The long-term health effects of NP use on the oral cavity is unknown. Repeated use of high concentration NPs may lead to mouth and gum irritation.
- High concentration NPs may result in symptoms of nicotine toxicity. Additionally, potential health effects associated with various flavouring agents, as identified in a limited number of studies, should be considered.
- Nicotine can causes gastrointestinal distress (e.g., nausea, acid reflux) and acutely
  affects cardiovascular function (i.e., increases heart rate and blood pressure). It may
  contribute to impaired wound healing, heart palpitations and arrhythmias.
  Additionally, it has the potential for long-term effects, including insulin resistance
  and may increase mortality with those with pre-existing cardiovascular disease.
- Unregulated NP\* products should be avoided due to the potential of unknown chemicals, ingredients, and dosing.

#### **Cessation**



**Recommendation #4:** Due to the lack of relevant RCTs, a recommendation into the efficacy of NPs as a quit aid cannot be made at this time.



#### **Clinical Considerations:**

- Studies suggest that 2 and 4mg NPs have a similar nicotine bioequivalence to nicotine replacement therapy (gum and lozenge), and therefore 2 and 4mg NPs may be an effective quit aid among individuals looking to reduce or quit combustible tobacco use.
- There is a lack of evidence on NPs and quit outcomes, particularly across highly dependent combustible tobacco users. Other first line options, such as behavioural counselling and pharmacotherapy may be more suitable before trying NPs as a quit aid.
- For those looking to lower their risk from combustible tobacco products, individuals should consider NRT or regulated NPs\*.

*Note: The majority of research on nicotine pouches are largely industry-funded, but there is some independent corroboration.* 

\*Refers to nicotine pouches that are regulated for sale in Canada under current federal and provincial guidelines (i.e., sold behind the counter in Canadian pharmacies and contain <4mg of nicotine per pouch).



## Harm Reduction Tips (Updated)

Replaces the Quick Tips on Page 10 of the LRNUG Version 2021

Nicotine is a highly addictive substance. How dependent your client becomes determines how difficult it may be for them to reduce or quit nicotine. The type of nicotine product and usage pattern also influences the potential for dependence. For example, commercial tobacco cigarettes have the highest risk of dependence, while nicotine replacement therapy (NRT) – namely nicotine patches – has the least.

While avoiding nicotine is the only way to eliminate the associated health risks, harm reduction focuses on reducing the negative health impacts rather than completely eliminating use of the substance. The following harm reduction strategies can be shared with your clients:



#### Encourage your clients to cut back on their nicotine use.

Suggest limiting the number of time(s) they use any nicotine product. For example, if your client uses nicotine daily, encourage them to delay the interval between uses, ideally once every 3-4 hours or less.

Recommend your clients switch completely from commercial tobacco cigarettes to the least harmful form of nicotine they can use (i.e., NRT, nicotine pouches, e-cigarettes) to reduce their exposure to products of combustion.



Using both tobacco and e-cigarettes, (i.e., "dual use"), increases their exposure to harmful and cancer-causing chemicals. If your client is going to use nicotine products, advise them to switch completely from commercial tobacco cigarettes to NRT or e-cigarettes to reduce their exposure and increase their chances of staying cigarette-free.



## If your client is vaping, recommend e-cigarette cartridges with less nicotine.

Products with more nicotine may increase your client's risk of dependence.



#### Help your client learn to manage their cravings.

Cravings happen – but they will pass! Advise your clients to try taking a walk, chewing sugar-free gum, or doing breathing exercises. Work with your client to identify what works best for them.

#### Emphasize that NRT can be used to quit other nicotine products.



Explain to your client that NRT products, such as patches, gum, lozenges, oral mist, inhalers, and nicotine pouches authorized for sale in Canada are the safest way to use nicotine. These products can be used to manage your client's nicotine cravings without exposing them to the negative health effects such as cancers, lung or heart disease, caused by cigarettes and other forms of commercial tobacco.

#### If your client is vaping, advise that they use vaping devices that are authorized for sale in Canada, and suggest that they do not make changes to the product.



Remind clients to not buy or use products such as vaping devices, or e-cigarette cartridges, from illegal or unregulated sources. These are not subject to product safety controls or oversight. Further, clients should not modify vaping products or add any substances that are not intended by the manufacturer. For electronic devices, recommend that your client follow the manufacturer instructions for use and battery charging.

## Suggest switching to nicotine products that do not burn, or that do not contain tobacco.

Using tobacco in forms that don't burn, like smokeless tobacco or heat-not-burn products, will reduce your clients exposure to harmful combusted chemicals, including carbon monoxide. Your client can further reduce their risk by switching to products that don't have tobacco like NRT, e-cigarettes, or nicotine pouches.

#### If your client uses nicotine pouches, recommend pouches authorized for cessation (i.e., <4mg of nicotine per pouch and sold in Canadian pharmacies only) (New)



Unregulated products with more nicotine content increase the risk of poisoning and harm. Encourage your clients to choose nicotine pouches with lower nicotine levels and to purchase them from pharmacies only. If your client requires a higher nicotine concentration, suggest the 4mg of nicotine per pouch and/or combination with the nicotine patch.

For additional harm reduction tips specific to vaping, visit: <u>intrepidlab.ca/en/Pages/Project-VECTOR.aspx</u>



## Resources (New) For Providers

#### **Other Toolkits**

Project VECTOR: A resource providing healthcare providers and clients with recommendations, tips, and frequently asked questions about the health impacts of ecigarette use. Visit: intrepidlab.ca/en/Pages/Project-VECTOR.aspx to learn more.

Vaping Cessation Guidance Resource: A resource to help healthcare providers support their clients who want to quit vaping. Visit: <u>intrepidlab.ca/en/Pages/electronic-nicotine-</u> <u>delivery-systems-(ends).aspx</u> to learn more.



ITS TIME Toolkits: Culturally relevant commercial tobacco cessation resources that integrate evidence-based strategies with Indigenous ways of knowing. Visit: <u>intrepidlab.ca/en/teach/practitioner-resources</u> to learn more.

#### **Continuing Professional Development**

TEACH Courses: TEACH at INTREPID Lab offers a diverse mix of trainings related to tobacco and nicotine cessation. Visit: <u>intrepidlab.ca/en/teach/certificate-and-</u> <u>trainings</u> to learn more.

TEACH Educational Rounds: A monthly webinar series for healthcare providers across all disciplines to enhance knowledge and skills in offering tobacco cessation interventions. Visit: <u>intrepidlab.ca/en/teach</u> to learn more.

#### **Community of Practice**

INTREPID Lab Latest News: Interested in the latest updates from INTREPID Lab? Visit:

<u>intrepidlab.ca/en/latest-news</u> for the latest updates.

TEACH Listerv: A platform to exchange knowledge, discuss practice challenges, and share solutions with peers from various healthcare disciplines. Visit: <u>intrepidlab.ca/en/teach/connect-with-</u> <u>teach</u> to subscribe.

For additional resources for healthcare professionals, visit: intrepidlab.ca/en/resources-for-providers

### **For Clients**

#### Treatment Through INTREPID Lab

STOP Program: provides tobacco cessation treatment either through local Ontariobased healthcare providers, or online via the STOP on the Net program. Visit: <u>intrepidlab.ca/en/stop</u> to learn more.

Nicotine Dependence Clinic (NDC): provides treatment options for CAMH clients to quit smoking. Visit:

<u>intrepidlab.ca/en/Pages/NDC.aspx</u> to learn more.

#### **Self-Help Resources and Tools**

My Change Plan: A workbook clients can use to help put together a quit plan. Visit: <u>intrepidlab.ca/en/resources-for-providers</u> to download French and English versions.



#### How to Use NRT and FAQs: Visit: youtube.com/playlist?

<u>list=PLmLKlp1R6075RQGDKE8U4t7IXvsl3Ovs9</u> to watch videos on how to properly use nicotine replacement therapy (NRT), or visit:

<u>intrepidlab.ca/en/stop/Documents/SOTN%20NRT%20FAQ%20(10-week).pdf</u> to learn more about NRT

Resources to Help You Quit Vaping: Stories from individuals who have successfully quit or reduced their vaping, along with self-help tools and animated videos showcasing effective quitting strategies. Visit: <u>intrepidlab.ca/en/Pages/Resources-to-Help-You-Quit-Vaping.aspx</u> to learn more.

Mood Management Resource: a client resource for managing mood. Visit: <u>intrepidlab.ca/en/PublishingImages/Pages/Self-</u> <u>Help/Mood%20Management%20Resource.pdf</u> to learn more.

> For additional resources for clients, visit: <u>https://intrepidlab.ca/en/patients-and-caregivers</u>

## Appendix A- Supporting Evidence for Guideline Development, By Product (Updated)

Replaces the Executive Summary on Page 3 of the LRNUG Version 2021

#### **E-Cigarettes**

For more information on the resources used to develop the e-cigarette recommendations, please email <u>Intrepid.Lab@camh.ca</u>.

#### Smokeless Tobacco (Snus and Chewing Tobacco)

Burkey MD, Feirman S, Wang H, Choudhury SR, Grocer S, Johnston FM. The association between smokeless tobacco use and pancreatic adenocarcinoma: a systematic review. Cancer Epidemiol. 2014; 38(6):647-653.

Gupta B and Johnson NW. Systematic review and meta-analysis of association of smokeless tobacco and of betel quid without tobacco with incidence of oral cancer in South Asia and the Pacific. PLoS ONE. 2014; 9(11):e113385.

Gupta S, Gupta R, Sinha DN, Mehrotra R. Relationship between type of smokeless tobacco & risk of cancer: A systematic review. Indian J Med Res. 2018; 148(1):56-76.

Gupta R, Gupta S, Sharma S, Sinha DN, Mehrotra R. Risk of coronary heart disease among smokeless tobacco users: Results of systematic review and meta-analysis of global data. Nicotine & Tobacco Research. 2019; 21(1):25-31.

Inamdar AS, Croucher RE, Chokhandre MK, Mashyakhy MH, Marinho VC. Maternal Smokeless Tobacco Use in Pregnancy and Adverse Health Outcomes in Newborns: A Systematic Review. Nicotine Tob Res. 2015; 17(9):1058-1066.

Sinha DN, Abdulkader RS, Gupta PC. Smokeless tobacco-associated cancers: A systematic review and meta-analysis of Indian studies. Int J Cancer. 2016; 138(6): 1368-1379.

Sinha DN, Suliankatchi RA, Gupta PC, Thamarangsi T, Agarwal N, et al. Global burden of all-cause and cause-specific mortality due to smokeless tobacco use: systematic review and meta-analysis. Tob Control. 2018; 27(1):35-42.

Vidyasagaran AL, Siddiqi K, Kanaan M. Use of smokeless tobacco and risk of cardiovascular disease: A systematic review and meta-analysis. Eur J Prev Cardiol. 2016; 23(18):1970-1981.

#### Heat-not-burn

Jankowski M, Brozk GM, Lawson J, Skoczynski S, Majek P, Zejda JE. New ideas, old problems? Heated tobacco products - a systematic review. Int J Occup Med Environ Health. 2019; 32(5):595-634.

Khan Z, Khan S, Christianson L, Rehman S, Ekwunife O, Samkange-Zeeb F. Smokeless Tobacco and Oral Potentially Malignant Disorders in South Asia: A Systematic Review and Meta-analysis. Nicotine Tob Res. 2017; 20(1):12-21. McNeill A, Brose LS, Calder R, Bauld L, Robson D. Evidence review of e-cigarettes and heated tobacco products 2018. A report commissioned by Public Health England. 2018; London: Public Health England.

Simonavicius E, McNeill A, Shahab L, Brose LS. Heat-not-burn tobacco products: a systematic literature review. Tob Control. 2019; 28(5):582-594.

#### **Nicotine Pouches (New)**

Alizadehgharib, S., Lehrkinder, A., Alshabeeb, A., Östberg, A. K., & Lingström, P. (2022). The effect of a non-tobacco-based nicotine pouch on mucosal lesions caused by Swedish smokeless tobacco (snus). European Journal of Oral Sciences, 130(4). doi.org/10.1111/eos.12885

Avila, J. C., Maglalang, D. D., Nollen, N. L., Lee, S. C., Suh, R., Malone, M., Urvi Binjrajka, & Ahluwalia, J. S. (2024). Using pod based e-Cigarettes and nicotine pouches to reduce harm for adults with low socioeconomic status who smoke: A pilot randomized controlled trial. Nicotine and Tobacco Research, 26(9), 1150–1158. doi.org/10.1093/ntr/ntae047

Azzopardi, D., Ebajemito, J., McEwan, M., Camacho, O. M., Thissen, J., Hardie, G., Voisine, R., Mullard, G., Cohen, Z., & Murphy, J. (2022). A randomised study to assess the nicotine pharmacokinetics of an oral nicotine pouch and two nicotine replacement therapy products. Scientific Reports, 12(1). doi.org/10.1038/s41598-022-10544-x

Azzopardi, D., Haswell, L. E., Frosina, J., McEwan, M., Gale, N., Thissen, J., Filimon Meichanetzidis, & Hardie, G. (2023). Assessment of biomarkers of exposure and potential harm, and physiological and subjective health measures in exclusive users of nicotine pouches and current, former and never smokers. Biomarkers, 28(1), 118–129. doi.org/10.1080/1354750X.2022.2148747

Azzopardi, D., Liu, C., & Murphy, J. (2022a). Chemical characterization of tobacco-free "modern" oral nicotine pouches and their position on the toxicant and risk continuums. Drug and Chemical Toxicology, 45(5), 2246–2254. doi.org/10.1080/01480545.2021.1925691

Back, S., Masser, A. E., Rutqvist, L. E., & Lindholm, J. (2023). Harmful and potentially harmful constituents (HPHCs) in two novel nicotine pouch products in comparison with regular smokeless tobacco products and pharmaceutical nicotine replacement therapy products (NRTs). BMC Chemistry, 17(1). doi.org/10.1186/s13065-023-00918-1

Becker, E., McCaffrey, S., Lewis, J., Vansickel, A., Larson, E., & Sarkar, M. (2023). Characterization of ad libitum use behavior of on! Nicotine pouches. American Journal of Health Behavior, 47(3), 428–449. doi.org/10.5993/AJHB.47.3.1

Campbell, C., Feehan, M., Kanitscheider, C., Makena, P. S., Cai, J., & Baxter, S. A. (2022). Designing studies to inform tobacco harm reduction: Learnings from an oral nicotine pouch actual use pilot study. JMIR Formative Research, 6(8). doi.org/10.2196/37573

Chapman, F., McDermott, S., Rudd, K., Taverner, V., Stevenson, M., Chaudhary, N., Reichmann, K., Thompson, J., Nahde, T., & O'Connell, G. (2022). A randomised, openlabel, cross-over clinical study to evaluate the pharmacokinetic, pharmacodynamic and safety and tolerability profiles of tobacco-free oral nicotine pouches relative to cigarettes. Psychopharmacology, 239(9), 2931–2943. doi.org/10.1007/s00213-022-06178-6

Dowd, A. N., Johannes Thrul, Czaplicki, L., Kennedy, R. D., Moran, M. B., & Spindle, T. R. (2024). A cross- sectional survey on oral nicotine pouches: Characterizing use-motives, topography, dependence levels, and adverse events. Nicotine and Tobacco Research, 26(2), 245–249. doi.org/10.1093/ntr/ntad179

East, N., Bishop, E., Breheny, D., Gaca, M., & Thorne, D. (2021). A screening approach for the evaluation of tobacco-free "modern oral" nicotine products using Real Time Cell Analysis. Toxicology Reports, 8, 481–488. doi.org/10.1016/j.toxrep.2021.02.014

Jabba, S. V., Erythropel, H. C., Woodrow, J. G., Anastas, P. T., O'Malley, S., Suchitra Krishnan-Sarin, Zimmerman, J. B., & Jordt, S. E. (2023). Synthetic cooling agent in oral nicotine pouch products marketed as "Flavour-Ban Approved." Tobacco Control. doi.org/10.1136/tc-2023-058035

Keller-Hamilton, B., Alalwan, M. A., Curran, H., Hinton, A., Long, L., Chrzan, K., Wagener, T. L., Atkinson, L., Sriya Suraapaneni, & Mays, D. (2024a). Evaluating the effects of nicotine concentration on the appeal and nicotine delivery of oral nicotine pouches among rural and Appalachian adults who smoke cigarettes: A randomized cross-over study. Addiction, 119(3), 464–475. doi.org/10.1111/add.16355

Keller-Hamilton, B., Curran, H., Mahmood Alalwan, Hinton, A., Brinkman, M. C., El-Hellani, A., Wagener, T. L., Chrzan, K., Atkinson, L., Sriya Suraapaneni, & Mays, D. (2024b). Evaluating the role of nicotine stereoisomer on nicotine pouch abuse liability: A randomized crossover trial. Nicotine and Tobacco Research. doi.org/10.1093/ntr/ntae079

Liu, J., Rensch, J., Wang, J., Jin, X., Vansickel, A., Edmiston, J., & Sarkar, M. (2022). Nicotine pharmacokinetics and subjective responses after using nicotine pouches with different nicotine levels compared to combustible cigarettes and moist smokeless tobacco in adult tobacco users. Psychopharmacology, 239(9), 2863–2873. doi.org/10.1007/s00213-022-06172-y

Mallock-Ohnesorg, N., Schulz, T., Malke, S., Dreiack, N., Laux, P., & Luch, A. (2024a). Levels of nicotine and tobacco-specific nitrosamines in oral nicotine pouches. Tob Control, 33, 193–199. doi.org/10.1136/tobaccocontrol-2022-057280

Mallock-Ohnesorg, N., Rabenstein, A., Stoll, Y., Gertzen, M., Rieder, B., Malke, S., Burgmann, N., Laux, P., Pieper, E., Schulz, T., Franzen, K., Luch, A., & Rüther, T. (2024b). Small pouches, but high nicotine doses—nicotine delivery and acute effects after use of tobacco-free nicotine pouches. Frontiers in Pharmacology, 15. doi.org/10.3389/fphar.2024.1392027



McEwan, M., Azzopardi, D., Gale, N., Camacho, O. M., Hardie, G., Fearon, I. M., & Murphy, J. (2022). A randomised study to investigate the nicotine pharmacokinetics of oral nicotine pouches and a combustible cigarette. European Journal of Drug Metabolism and Pharmacokinetics, 47(2), 211–221. doi.org/10.1007/s13318-021-00742-9

Miller-Holt, J., Baskerville-Abraham, I., Masanori Sakimura, Fukushima, T., Puglisi, A., & Gafner, J. (2022). In vitro evaluation of mutagenic, cytotoxic, genotoxic and oral irritation potential of nicotine pouch products. Toxicology Reports, 9, 1316–1324. doi.org/10.1016/j.toxrep.2022.06.008

Rensch, J., Edmiston, J., Wang, J., Jin, X., & Sarkar, M. (2023). A randomized, controlled study to assess changes in biomarkers of exposures among adults who smoke that switch to oral nicotine pouch products relative to continuing smoking or stopping all tobacco use. Journal of Clinical Pharmacology, 63(10), 1108–1118. doi.org/10.1002/jcph.2293

Rensch, J., Liu, J., Wang, J., Vansickel, A., Edmiston, J., & Sarkar, M. (2021). Nicotine pharmacokinetics and subjective response among adult smokers using different flavors of on!® nicotine pouches compared to combustible cigarettes. Psychopharmacology, 238(11), 3325–3334. doi.org/10.1007/s00213-021-05948-y

Rinaldi, S., Pieper, E., Schulz, T., Zimmermann, R., Luch, A., Laux, P., & Mallock-Ohnesorg, N. (2023). Oral nicotine pouches with an aftertaste? Part 2: in vitro toxicity in human gingival fibroblasts. Archives of Toxicology, 97(9), 2343–2356. doi.org/10.1007/s00204-023-03554-9

Shaikh, S. B., Tung, W. C., Pang, C., Lucas, J., Li, D., & Rahman, I. (2022). Flavor Classification/Categorization and differential toxicity of oral nicotine pouches (ONPs) in oral gingival epithelial cells and bronchial epithelial cells. Toxics, 10(11). doi.org/10.3390/toxics10110660

Stanfill, S., Tran, H., Tyx, R., Fernandez, C., Zhu, W., Marynak, K., King, B., Valentín-Blasini, L., Blount, B. C., & Watson, C. (2021). Characterization of total and unprotonated (free) nicotine content of nicotine pouch products. Nicotine and Tobacco Research, 23(9), 1590–1596. doi.org/10.1093/ntr/ntab030

Yu, F., Bishop, E., Fabio Miazzi, Evans, R., Smart, D., Breheny, D., & Thorne, D. (2024). Multi-endpoint in vitro toxicological assessment of snus and tobacco-free nicotine pouch extracts. Mutation Research - Genetic Toxicology and Environmental Mutagenesis, 895. doi.org/10.1016/j.mrgentox.2024.503738

Yu, F., Rudd, K., Pour, S. J., Sticken, E. T., Dethloff, O., Wieczorek, R., Nahde, T., Simms, L., Chapman, F., Czekala, L., Stevenson, M., & O'Connell, G. (2022). Preclinical assessment of tobacco-free nicotine pouches demonstrates reduced in vitro toxicity compared with tobacco snus and combustible cigarette smoke. Applied in Vitro Toxicology, 8(1), 24–35. doi.org/10.1089/aivt.2021.0020

For a list of grey literature sources consulted, please email Intrepid.Lab@camh.ca

## Appendix B- Guideline Development Group (GDG) Members (Updated)

#### Replaces the Executive Summary on Page 3 of the LRNUG Version 2021

The following list details the GDG member' credentials, affiliations, and reported conflicts of interest within the past 5 years:

#### LRNUG Version 2021 GDG

Peter Selby, MBBS, CCFP(AM), FCFP, MHSc, dipABAM, DFASAM Centre for Addiction and Mental Health; University of Toronto Dr. Selby reports receipt of consulting fees from Johnson & Johnson, NVision Insight Group and Myelin and Associates; grant/research support from Pfizer, Bhasin Consulting Fund Inc., Canadian Institutes of Health Research, Health Canada, Canadian Cancer Society, Medical Psychiatry Alliance, Ontario Ministry of Health and Long-Term Care, Canadian Partnership Against Cancer, and the Public Health Agency of Canada; and has been a subject matter expert or chair on advisory boards for Pfizer Canada Inc., and Johnson & Johnson. Through an open tender process, Dr. Selby reports that Johnson & Johnson, Novartis and Pfizer Inc. are vendors of record for having provided free/discounted smoking cessation pharmacotherapy.

John Atkinson, MSW, BA, ONi Canadian Cancer Society Mr. Atkinson has no conflicts of interest to report.

Bruce Baskerville, MHA, PhD, CE Canadian Institutes of Health Research Dr. Baskerville reports receiving grant/research support from the Canadian Institutes of Health Research and Public Health Agency of Canada for research on tobacco and vaping cessation.

Mark Eisenberg, MD, IMHL, MPH Jewish General Hospital; McGill University Dr. Eisenberg reports pending and receiving grants/research support from Canadian Institutes of Health Research.

Brent Friesen, MD, FRCPC

Alberta Health Services

Dr. Friesen reports employment from Alberta Health Services Tobacco Reduction Program; consulting fees as the Acting Chief Medical Officer of Health for Alberta Health; expert testimony for the Alberta government for noncompliance with laws regarding tobacco; grants/research support from Alberta Cancer Prevention Legacy Fund; and acts as a surveyor with Accreditation Canada and Accreditation Canada International. Milan Khara, MBChB, CCFP, Dip. ABAM St. Paul's Hospital; University of British Columbia Dr. Khara has no conflicts of interest to report.

Jane Ling, R.Ph., BScPhm North Durham Family Health Team; Pharmacists for a Smoke Free Canada Ms. Ling reports receipt of honoraria from Johnson & Johnson and Pfizer.

Claudia Mariano, MSc, NP Nurse Practitioners Association of Ontario Ms. Mariano has no conflicts of interest to report.

Nadia Minian, PhD, MA CAMH Dr. Minian has no conflicts of interest to report.

Alice Ordean, MD St. Joseph's Health Centre; University of Toronto Dr. Ordean has no conflicts of interest to report.

Ron Pohar, BSc.Pharm, APA Consultant Pharmacist Mr. Pohar has no conflicts of interest to report.

Robert Reid, PhD, MBA

University of Ottawa Heart Institute Dr. Reid reports receiving honoraria from Pfizer Inc. and Johnson & Johnson for speaking engagements; stock ownership of Johnson & Johnson; and grant/research support received from Pfizer for clinical trial.

Robert Schwartz, PhD

Ontario Tobacco Research Unit; University of Toronto Dr. Schwartz reports receiving grant/research support from the Canadian Institutes of Health Research, Health Canada, and the National Institutes of Health

Laurie Zawertailo, PhD CAMH; University of Toronto Dr. Zawertailo has no conflicts of interest to report.

#### GDG Informing Nicotine Pouch Update (New)

Peter Selby, MBBS, CCFP(AM), FCFP, MHSc, dipABAM, DFASAM Principle Investigator, INTREPID Lab Senior Scientist, Addictions, CAMH Senior Medical Consultant; Senior Scientist – Addictions, CAMH Vice Chair, Research; Giblon Professor, DFCM, University of Toronto Professor: Psychiatry; and the Dalla Lana School of Public Health, University of Toronto Dr. Selby reports receiving grant/research support from Health Canada's Substance Use and Addictions Program.

Laurie Zawertailo, PhD Senior Scientist, INTREPID Lab Dr. Zawertailo has no conflicts of interest to report Laurie Zawertailo, PhD Senior Scientist, INTREPID Lab Dr. Zawertailo has no conflicts of interest to report

#### Neal Benowitz, MD

Professor of Medicine Emeritus, University of California San Francisco Dr. Benowitz reports receiving honoraria from various NIH-funded research programs as a Scientific Advisor; expert testimony as a witness in litigation against tobacco companies; grants/research support from NIH by the State of California; royalties from various book chapters; consulting fees from Achieve Life Sciences and Qnovia; and serves as an advisory board member for Achieve Life Sciences and Qnovia

Lion Shahab, MA (Oxon), MSc, MSc, PhD, QHP, CPsychol, AFHEA, FSRNT, FBPsS Professor of Health Psychology Head, Research Department of Behavioural Science and Health Director, MSc Health Psychology, University College London Co-Director, Tobacco and Alcohol Research Group, University College London Institute of Epidemiology and Health Care University College London Dr. Shahab has no conflicts of interest to report

#### **Connor Dorr**

Lived Experience Advisor Undergraduate Psychology Student Mr. Dorr has no conflicts of interest to report

#### GDG Informing E-Cigarette Update (New)

For Project VECTOR GDG member' credentials, affiliations, and reported conflicts of interest, please email <u>Intrepid.Lab@camh.ca</u>.

## Appendix C- Methodology for LRNUG Version 2021 (Updated)

#### Replaces the Executive Summary on Page 3 of the LRNUG Version 2021

Search strategy and execution were developed by the Centre for Addiction and Mental Health (CAMH) and the Centre for Effective Practice. A comprehensive literature search for systematic reviews published between January 2014 and October 2019 was performed in MEDLINE, PsycInfo, Cochrane Database of Systematic Reviews, and Embase, with a focus on nicotine products (e-cigarettes, waterpipe, smokeless tobacco, heat-not-burn) and selected health outcomes (cancer, cardiovascular disease and stroke, respiratory health, addiction, cessation, reproductive health). A supplemental search to identify additional Clinical Practice Guidelines (CPGs) published from 2014 to 2019 was also performed.

Quality assessment employed the AGREE II (Appraisal of Guidelines for Research and Evaluation) instrument for CPGs, and the AMSTAR instrument for systematic reviews. Due to the limited nature of e-cigarette study methodology, the use of the full AMSTAR instrument would have resulted in a prohibitively small pool of systematic reviews. Therefore, a rapid AMSTAR, using 2 key metrics (comprehensive literature search and assessment of scientific quality of included studies), was used to enable the inclusion of many well-done studies that nonetheless would not pass the high bar of the full AMSTAR AMSTAR criteria, while excluding less rigorously performed reviews.

The full list of references included in the Guideline development is available in Appendix A.

**Guideline Development Meeting:** The Guideline Development Group (GDG) consisted of nicotine experts from across Canada (see Appendix B for full list of GDG members), chosen for their expertise in the field and diversity of perspectives. All members of the GDG submitted GIN-inspired Conflicts of Interest declarations at two separate time points throughout the process

On November 18-9, 2019, the GDG convened for an in-person meeting in which fourteen voting members gathered to assess the quality of the literature; draft evidence-based recommendations on the use of the different products; and vote to confirm the final language to be used in the recommendations. Using a facilitated consensus-building approach, the group drafted and finalized ten evidence-based recommendations, supported by group consensus on the quality of the evidence base and the strength of each recommendation. Summary statements and additional considerations were drafted at this meeting and confirmed post- gathering via electronic communication.

Feedback from the GDG highlighted the fact that limiting the inclusion criteria to only systematic reviews resulted in an evidence gap for new e-cigarette literature. To address this gap, an updated literature search was conducted targeting high-quality randomized controlled trials (RCTs) on e-cigarettes published between 2015-2020. Quality of included RCTs was assessed using the Cochrane Risk of Bias Tool 2.0 (RoB tool) (Sterne et al., 2019).

Results from this supplemental search were mapped to determine support of, or opposition to, the recommendations developed by the GDG. A secondary 'up-to- the-moment' search was conducted in January 2021 to ensure that the recommendations were supported by available literature up to that date. A secure, anonymous electronic voting tool was used in March 2021 by the GDG to vote on necessary changes to the recommendations, including level of evidence and strength of the recommendation



Notes		

## Canada's Lower-Risk Nicotine Use Guidelines

intrepidlab.ca

camh INTREPID Lab