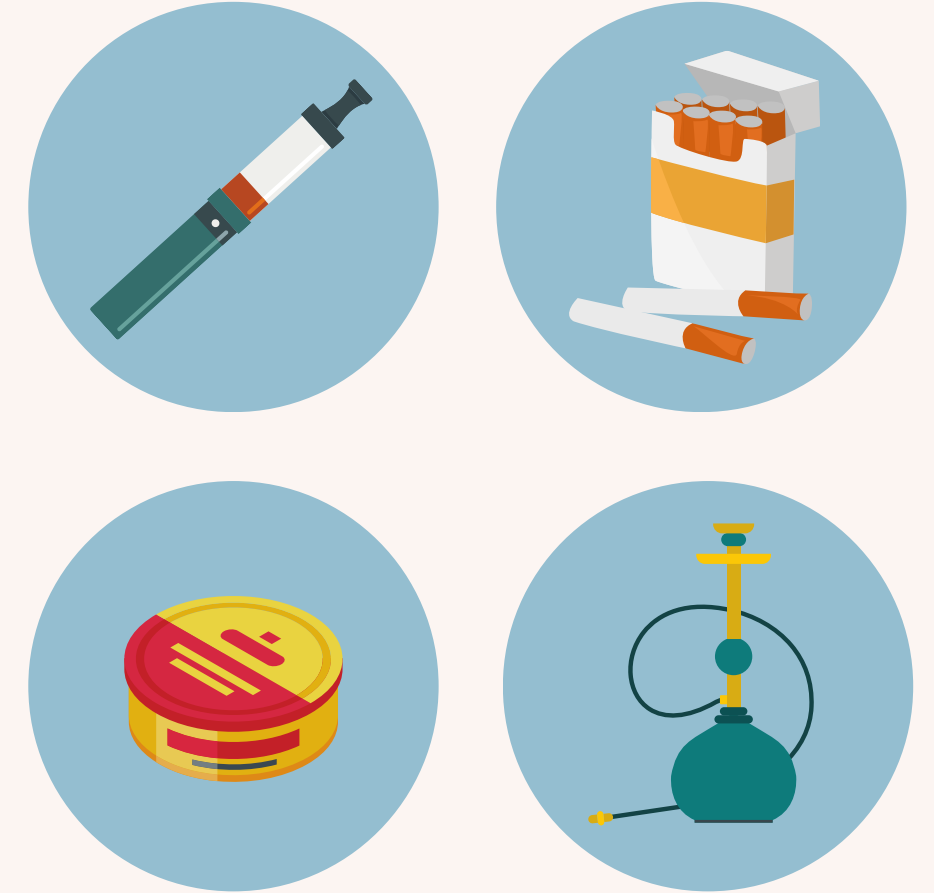


EVIDENCE BRIEF

THIS VERSION HAS BEEN ARCHIVED. TO VIEW THE LATEST VERSION, **VISIT:** [INTREPIDLAB.CA/EN/LOWER-RISK-NICOTINE-USER-GUIDELINES](https://intrepidlab.ca/en/lower-risk-nicotine-user-guidelines)

Nicotine is an addictive substance that can be difficult to quit. No nicotine use is considered completely safe and the use of nicotine is discouraged. However, nicotine use is a personal choice. 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 nicotine use.



Who are the LRNUG for?

The LRNUG are a health education and prevention tool for:

- Anyone who currently uses, or who is considering using any type of nicotine product(s).
- Any professional, organization or government aiming to improve the health of Canadians who use nicotine.

How were the LRNUG developed?

A comprehensive literature search with a focus on nicotine products and selected health outcomes was completed up to January 2021. The full table of included references is available [here](#). The Guideline Development Group (GDG), made up of 14 experts in the nicotine field from across Canada convened for an in-person meeting to develop the Recommendations found on page 2 of this document. The GDG was responsible for assessing the quality of the literature, and voting on the language used to create the Recommendations.

The LRNUG have been endorsed by the following organizations:



Pharmacists *for* a Smoke-Free Canada
Pharmaciens *pour un* Canada Sans Fumée



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TOBACCO
RESEARCH
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Generating knowledge for public health

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DE RECHERCHE
SUR LE TABAC
DE L'ONTARIO

CEP

Centre
for Effective
Practice

Production of the Lower-Risk Nicotine Use Guidelines has been made possible through Health Canada's Substance Use and Addictions Program. These materials do not necessarily reflect the views of Health Canada.

If you choose to use nicotine, learn how to reduce risks to your health, [here](#).

E-CIGARETTES

People who do not use any tobacco products should not use **e-cigarettes** because of the high risk of addiction and potential physical health harms. E-cigarettes are less harmful than combustible tobacco, but are not completely harmless. In addition to the known effects of nicotine, most e-cigarette products contain and emit substances with unknown harms when inhaled.

People who switch from combustible tobacco to e-cigarettes will **reduce their exposure to numerous toxicants and carcinogens**. Switching completely to e-cigarettes will significantly reduce exposure to numerous toxins and cancer causing chemicals and thus the harms associated with smoking tobacco.

People who are currently using e-cigarettes should **stop or switch to safer forms of nicotine such as NRT**. The long-term health effects of e-cigarette use are unknown. There is some evidence that e-cigarettes can cause negative health effects such as cough and mouth and throat irritation, as well as potential negative pulmonary, cardiovascular, and respiratory effects.

For people who use combustible tobacco products and cannot quit by other means, **e-cigarettes may be a lower risk alternative**. When choosing a vaping product, consider the following:

- Do not purchase illicit/black market e-liquids, pods, or devices;
- Do not adulterate your products (with THC, vitamin E/other oils, etc.) or modify the device;
- Follow instructions on use, charging, cleaning and disposal of the device

CESSATION

People should try and quit using approved smoking cessation treatments first, but if they are unable or unwilling to quit, **e-cigarettes with nicotine may be an effective cessation aid for people who use combustible tobacco**. Smokers should be advised to switch completely from combustible tobacco to e-cigarettes and to use e-cigarettes when they would normally have smoked.



ADDICTION

There is substantial evidence that e-cigarettes with nicotine are addictive. Use of high-dose nicotine salts may increase risk of addiction. **Use of e-cigarettes with nicotine should be discouraged among non-smokers due to risk of addiction.**

OTHER NICOTINE PRODUCTS

Use of Smokeless Tobacco (SLT) is associated with serious health risks including increased risk of oral, pharyngeal, and esophageal cancers, and increased instance of fatal ischemic heart disease and stroke. **Use of SLT should be discouraged.**

Heated Tobacco Products (HTP) may reduce exposure to some but not all harmful and potentially harmful compounds when compared to conventional cigarettes. However, these products still pose serious health risks, and harm to those exposed second-hand. **Use of HTP should be discouraged.**

Water-pipe smoking is associated with various cancers and cardiovascular disease. There is strong evidence that water-pipes also pose serious health risks to those exposed to second-hand smoke. **Water-pipe smoking should be discouraged.** Water-pipes should be smoked outdoors away from public spaces where others are exposed.

REPRODUCTIVE HEALTH

Use of SLT, HTP, water-pipes, and e-cigarettes should be **discouraged in women who are pregnant**. They should be encouraged to switch to NRT to reduce possible harms. If unable or unwilling to quit, pregnant women should be advised to reduce the frequency of use and the concentration of nicotine. Despite lack of evidence, e-cigarettes may reduce some risk for women who are pregnant.



The Guidelines are intended as an evidence-based decision making tool, and are subject to change as scientific knowledge evolves. They are not intended to be a substitute for clinical judgment or medical advice. Adherence to these recommendations will not necessarily produce successful outcomes in every case.

EXECUTIVE SUMMARY

The Lower-Risk Nicotine Use Guidelines (LRNUG) present the current state of evidence on tobacco/nicotine products, highlighting modifiable behaviours that can help reduce the negative health outcomes associated with tobacco/nicotine product use. They have been designed to guide people who use, or are thinking about using nicotine, on how to lower the risk associated with various nicotine products. The products covered in the Guidelines include heated tobacco products, smokeless tobacco (chew and snus), waterpipes, and e-cigarettes/vapes.

METHODOLOGY: Search strategy and execution were developed by the Centre for Addiction and Mental Health 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, CVD 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 criteria, while excluding less rigorously performed reviews. The full list of references included in Guideline development is available below in Table 1.

GUIDELINE DEVELOPMENT MEETING: The Guideline Development Group (GDG) consisted of nicotine experts from across Canada, chosen for their expertise in the field and diversity of perspectives (see below for full list of GDG members). 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 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.

GUIDELINE DEVELOPMENT GROUP (GDG) MEMBERS:

The following list details the Guideline Development Group members’ credentials, affiliations, and reported conflicts of interest within the past 5 years:

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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.

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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.

Table 1. Supporting evidence for guideline development, by product

E-cigarettes	Article Type
Boulay M-È, Henry C, Bossé Y, Boulet L-P, Morissette MC. Acute effects of nicotine-free and flavour-free electronic cigarette use on lung functions in healthy and asthmatic individuals. <i>Respir Res.</i> 2017; 10;18(1):33.	Randomized Control Trial (RCT)
Callahan-Lyon, P. Electronic cigarettes: human health effects. <i>Tob Control.</i> 2014; 23 Suppl 2: ii36–40.	Systematic Review (SR)
Campagna D, Cibella F, Caponnetto P, Amaradio MD, Caruso M, Morjaria JB, et al. Changes in breathomics from a 1-year randomized smoking cessation trial of electronic cigarettes. <i>Eur J Clin Invest.</i> 2016; 46(8):698–706.	RCT
Cardenas VM, Fishbach LA, Chowdhury P. The use of electronic nicotine delivery systems during pregnancy and the reproductive outcomes: A systematic review of the literature. <i>Tob Induc Dis.</i> 2019; 17:52.	SR
Chatterjee K, Alzghoul B, Innabi A, Meena N. Is vaping a gateway to smoking: a review of the longitudinal studies. <i>Int J Adolesc Med Health.</i> 2016; 30(3).	Review (R)
Chaumont M, Bernard A, Pochet S, Mélot C, El Khattabi C, Reye F, et al. High-Wattage E-Cigarettes Induce Tissue Hypoxia and Lower Airway Injury: A Randomized Clinical Trial. <i>Am J Respir Crit Care Med.</i> 2018; 198(1):123–126.	RCT
Chaumont M, de Becker B, Zaher W, Culie A, Deprez G, Melot C, et al. Differential Effects of E-Cigarette on Microvascular Endothelial Function, Arterial Stiffness and Oxidative Stress: A Randomized Crossover Trial. <i>Sci rep.</i> 2018; 8(1):10378.	RCT
Chaumont M, Tagliatti V, Channan EM, Colet J-M, Bernard A, Morra S, et al. Short halt in vaping modifies cardiorespiratory parameters and urine metabolome: a randomized trial. <i>Am J Physiol Lung Cell Mol Physiol.</i> 2020; 318(2):L331–344.	RCT
Chaumont M, van de Borne P, Bernard A, Van Muylem A, Deprez G, Ullmo J, et al. Fourth generation e-cigarette vaping induces transient lung inflammation and gas exchange disturbances: results from two randomized clinical trials. <i>Am J Physiol Lung Cell Mol Physiol.</i> 2019; 316(5):L705–19.	RCT
Cibella F, Campagna D, Caponnetto P, Amaradio MD, Caruso M, Russo C, et al. Lung function and respiratory symptoms in a randomized smoking cessation trial of electronic cigarettes. <i>Clin Sci.</i> 2016; 130(21):1929–1937.	RCT
Copp SR, Collins JL, Dar R, Barrett SP. The effects of nicotine stimulus and response expectancies on male and female smokers’ responses to nicotine-free electronic cigarettes. <i>Addictive Behaviors.</i> 2015; 40:144–147.	RCT
Czoli CD, Fong GT, Goniewicz ML, Hammond D. Biomarkers of Exposure Among “Dual Users” of Tobacco Cigarettes and Electronic Cigarettes in Canada. <i>Nicotine Tob Res.</i> 2019; 21(9):1259–1266.	RCT
De La Garza R, Shuman SL, Yammine L, Yoon JH, Salas R, Holst M. A Pilot Study of E-Cigarette Naïve Cigarette Smokers and the Effects on Craving After Acute Exposure to E-Cigarettes in the Laboratory. <i>Am J Addict.</i> 2019; 28(5):361–366.	RCT
D’Ruiz CD, Graff DW, Yan XS. Nicotine delivery, tolerability and reduction of smoking urge in smokers following short-term use of one brand of electronic cigarettes. <i>BMC Public Health.</i> 2015; 15:991.	RCT
De La Garza R, Shuman SL, Yammine L, Yoon JH, Salas R, Holst M. A Pilot Study of E-Cigarette Naïve Cigarette Smokers and the Effects on Craving After Acute Exposure to E-Cigarettes in the Laboratory. <i>Am J Addict.</i> 2019; 28(5):361–366.	RCT
D’Ruiz CD, Graff DW, Robinson E. Reductions in biomarkers of exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes. <i>BMC Public Health.</i> 2016; 16:543.	RCT
Eisenberg MJ, Hébert-Losier A, Windle SB, Greenspoon T, Brandys T, Fülöp T, et al. Effect of e-Cigarettes Plus Counseling vs Counseling Alone on Smoking Cessation: A Randomized Clinical Trial. <i>JAMA.</i> 2020; 324(18):1844–1854.	RCT
Fearon IM, Eldridge A, Gale N, Shepperd CJ, McEwan M, Camacho OM, et al. E-cigarette Nicotine Delivery: Data and Learnings from Pharmacokinetic Studies. <i>American Journal of Health Behavior.</i> 2017; 41(1):16–32.	RCT
Ferrari M, Zanasi A, Nardi E, Morselli Labate AM, Ceriana P, Balestrino A, et al. Short-term effects of a nicotine-free e-cigarette compared to a traditional cigarette in smokers and non-smokers. <i>BMC Pulm Med.</i> 2015; 15:120.	RCT
El Dib R, Suzumura EA, Akl EA, Gomaa H, Agarwal A, et al. Electronic nicotine delivery systems and/or electronic non-nicotine delivery systems for tobacco smoking cessation or reduction: a systematic review and meta-analysis. <i>BMJ Open.</i> 2017; 7(2):e012680.	Systematic Review and Meta-analysis (SR & MA)
Flach S, Maniam P, Manickavasagam J. E-cigarettes and head and neck cancers: A systematic review of the current literature. <i>Clin Otolaryngol.</i> 2019; 44(5):749–756.	SR

Gualano MR, Passi S, Bert F, La Torre G, Scaioli G, Siliquini R. Electronic cigarettes: assessing the efficacy and the adverse effects through a systematic review of published studies. J Public Health (Oxf). 2015; 37(3):488–497.	SR
Hajek P, Etter JF, Benowitz N, Eissenberg T, McRobbie H. Electronic cigarettes: review of use, content, safety, effects on smokers and potential for harm and benefit. Addiction. 2014; 109(11):1801–1810.	R
Hartmann–Boyce J, McRobbie H, Bullen C, Begh R, Stead L, Hajek P. (2016). Electronic cigarettes for smoking cessation. Cochrane Database Syst Rev. 2016; 9:CD010216.	SR
Hatsukami DK, Meier E, Lindgren BR, Anderson A, Reisinger SA, Norton KJ, et al. A Randomized Clinical Trial Examining the Effects of Instructions for Electronic Cigarette Use on Smoking–Related Behaviors and Biomarkers of Exposure. Nicotine Tob Res. 2020; 22(9):1524–1532.	RCT
Jay J, Pfaunmiller EL, Huang NJ, Cohen G, Graff DW. Five–Day Changes in Biomarkers of Exposure Among Adult Smokers After Completely Switching From Combustible Cigarettes to a Nicotine–Salt Pod System. Nicotine Tob Res. 2020; 22(8):1285–1293.	RCT
Kalkhoran S and Glantz SA. E–cigarettes and smoking cessation in real–world and clinical settings: a systematic review and meta–analysis. Lancet Respir Med. 2016; 4(2):116–128.	SR & MA
Kennedy CD, van Schalkwyk MC, McKee M, Pisinger C. The cardiovascular effects of electronic cigarettes: A systematic review of experimental studies. Prev Med. 2019; 127:105770.	SR
Khoudigian S, Devji T, Lytvyn L, Campbell K, Hopkins R, O'Reilly D. The efficacy and short–term effects of electronic cigarettes as a method for smoking cessation: a systematic review and a meta–analysis. Int J Public Health. 2016; 61(2):257–267.	SR & MA
Liu, X., Lu W, Liao S, Deng Z, Zhang Z, Liu Y, Lu W. Efficiency and adverse events of electronic cigarettes: A systematic review and meta–analysis (PRISMA–compliant article). Medicine (Baltimore). 2018; 97(19):e0324.	SR & MA
Maglia M, Caponnetto P, Di Piazza J, La Torre D, Polosa R. Dual use of electronic cigarettes and classic cigarettes: a systematic review. Addiction Research & Theory. 2018; 26(4):330–338.	SR
Malas M, van der Tempel J, Schwartz R, Minichiello A, Lightfoot C, et al. Electronic Cigarettes for Smoking Cessation: A Systematic Review. Nicotine Tob Res. 2016; 18(10):1926–1936.	SR
Masiero M, Lucchiari C, Mazzocco K, Veronesi G, Maisonneuve P, Jemos C, et al. E–cigarettes May Support Smokers With High Smoking–Related Risk Awareness to Stop Smoking in the Short Run: Preliminary Results by Randomized Controlled Trial. Nicotine Tob Res. 2019; 21(1):119–126.	RCT
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.	R
McRobbie H, Bullen C, Hartmann–Boyce J, Hajek P. Electronic cigarettes for smoking cessation and reduction. Cochrane Database Syst Rev. 2014; 12:CD010216.	SR & MA
National Academies of Sciences, Engineering, and Medicine 2018. Public Health Consequences of E–Cigarettes: Consensus Study Report. Washington, DC: The National Academies Press. https://doi.org/10.17226/24952 .	Clinical Practice Guideline (CPG)
O'Connell G, Graff DW, D'Ruiz CD. Reductions in biomarkers of exposure (BoE) to harmful or potentially harmful constituents (HPHCs) following partial or complete substitution of cigarettes with electronic cigarettes in adult smokers. Toxicol Mech Methods. 2016; 26(6):443–454.	RCT
O'Connell G, Pritchard JD, Prue C, Thompson J, Verron T, Graff D, et al. A randomised, open-label, cross-over clinical study to evaluate the pharmacokinetic profiles of cigarettes and e–cigarettes with nicotine salt formulations in US adult smokers. Intern Emerg Med. 2019; 14(6):853–861.	RCT
Palmer AM, Brandon TH. How do electronic cigarettes affect cravings to smoke or vape? Parsing the influences of nicotine and expectancies using the balanced–placebo design. J Consult Clin Psychol. 2018; 86(5):486–491.	RCT
Poulianiti K, Karatzaferi C, Flouris AD, Fatouros IG, Koutedakis Y, Jamurtas AZ. Antioxidant responses following active and passive smoking of tobacco and electronic cigarettes. Toxicol Mech Methods. 2016; 26(6):455–461.	RCT
Pulvers K, Nollen NL, Rice M, Schmid CH, Qu K, Benowitz NL, et al. Effect of Pod e–Cigarettes vs Cigarettes on Carcinogen Exposure Among African American and Latinx Smokers: A Randomized Clinical Trial. JAMA Network Open. 2020; 3(11): e2026324–e2026324.	RCT
Rahman MA, Hann N, Wilson A, Mnatzaganian, Worrall–Carter L. E–cigarettes and smoking cessation: evidence from a systematic review and meta–analysis. PLoS One. 2015; 10(3):e0122544.	SR & MA
Riley HE, Berry–Bibee E, England LJ, Jamieson DJ, Marchbanks PA, Curtis KM. Hormonal contraception among electronic cigarette users and cardiovascular risk: a systematic review. Contraception. 2016; 93(3):190–208.	SR
Round EK, Chen P, Taylor AK, Schmidt E. Biomarkers of Tobacco Exposure Decrease After Smokers Switch to an E–Cigarette or Nicotine Gum. Nicotine Tob Res. 2019; 21(9):1239–1247.	RCT

Siu AL and USPST Force. Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2015; 163(8):622–634.	CPG
Soneji S, Barrington–Trimis JL, Wills T, Leventhal AM, Unger JB, Gibson LA, et al. Association Between Initial Use of e–Cigarettes and Subsequent Cigarette Smoking Among Adolescents and Young Adults: A Systematic Review and Meta–analysis. JAMA Pediatr. 2017; 171(8):788–797.	SR & MA
Tseng T–Y, Ostroff JS, Campo A, Gerard M, Kirchner T, Rotrosen J, et al. A Randomized Trial Comparing the Effect of Nicotine Versus Placebo Electronic Cigarettes on Smoking Reduction Among Young Adult Smokers. Nicotine Tob Res. 2016; 18(10):1937–1943.	RCT
Valentine GW, Jatlow PI, Coffman M, Nadim H, Gueorguieva R, Sofuoglu M. The effects of alcohol-containing e–cigarettes on young adult smokers. Drug Alcohol Depend. 2016; 159:272–276.	RCT
Wang M, Wang JW, Cao SS, Wang HQ, Hu RY. Cigarette Smoking and Electronic Cigarettes Use: A Meta–Analysis. Int J Environ Res Public Health. 2016; 13(1).	SR & MA
Whittington JR, Simmons PM, Phillips AM, Gammill SK, Cen R, Magann EF, Cardenas VM. The Use of Electronic Cigarettes in Pregnancy: A Review of the Literature. Obstet Gynecol Surv. 2018; 73(9):544–549.	SR
Yuki D, Takeshige Y, Nakaya K, Futamura Y. Assessment of the exposure to harmful and potentially harmful constituents in healthy Japanese smokers using a novel tobacco vapor product compared with conventional cigarettes and smoking abstinence. Regul Toxicol Pharmacol. 2018; 96:127–134.	RCT
Zucchet A and Schmaltz G. Electronic cigarettes—A review of the physiological health effects. FACETS. 2017; 2(1):575–609.	R

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.	SR
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.	SR & MA
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.	SR
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.	SR & MA
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.	SR
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.	SR & MA
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.	SR & MA
Vidyasagan 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.	SR & MA

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

Reproductive Health	
Cardenas VM, Fischbach LA, Chowdhury P. The use of electronic nicotine delivery systems during pregnancy and the reproductive outcomes: A systematic review of the literature." Tob Induc Dis. 2019; 17:52	SR
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.	SR
National Academies of Sciences, Engineering, and Medicine 2018. Public Health Consequences of E-Cigarettes: Consensus Study Report. Washington, DC: The National Academies Press. https://doi.org/10.17226/24952 .	CPG
Riley HE, Berry–Bibee E, England LJ, Jamieson DJ, Marchbanks PA, Curtis KM. Hormonal contraception among electronic cigarette users and cardiovascular risk: a systematic review. Contraception. 2016; 93(3):190–208.	SR
Siu AL and USPST Force. Behavioral and Pharmacotherapy Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Women: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2015; 163(8):622–634.	CPG
Waziry R, Jawad M, Ballout RA, Al Akel M, Akl A E. The effects of waterpipe tobacco smoking on health outcomes: an updated systematic review and meta-analysis. Int J Epidemiol. 2017; 46(1):32–43.	SR & MA
Whittington JR, Simmons PM, Phillips AM, Gammill SK, Cen R, Magann EF, Cardenas VM. The Use of Electronic Cigarettes in Pregnancy: A Review of the Literature. Obstet Gynecol Surv. 2018; 73(9):544–549.	SR

Lower-Risk Nicotine Use Guidelines

PRODUCTS AND RECCOMENDATIONS	LEVEL OF EVIDENCE	STRENGTH OF RECOMMENDATION	SUMMARY STATEMENTS AND CONSIDERATIONS
Recommendation #1: Use of Smokeless Tobacco (SLT) should be discouraged.	Low	Strong	1. 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. 2. SLT is associated with an increased risk of fatal IHD and stroke. 3. SLT is associated with an increased risk of adverse health outcomes in newborns when used in pregnancy.
Recommendation #2: Use of Heated Tobacco Products (HTP) should be discouraged.	Moderate	Strong	1. 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. 2. There is strong evidence that HTP products produce side-stream exposure to HPHC for those exposed second-hand. 3. The impact of HTP on conventional cigarette smoking behaviour is unclear. 4. Majority of research is largely industry-funded, but there is some independent corroboration.
Recommendation #3. Water-pipe smoking should be discouraged.	High	Strong	1. Water-pipe smoking is associated with serious health risks (including various cancers and cardiovascular disease). 2. Herbal water-pipe smoking is associated with serious health risks and is not a safe alternative to tobacco water-pipe smoking. 3. 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. 4. Water-pipe smoking while pregnant is associated with low birth weight.

<p>Reproductive Health</p> <p>Recommendation #4: Use of SLT, HTP, water-pipes, and e-cigarettes should be discouraged in women who are pregnant</p>	<p>Very Low</p>	<p>Strong</p>	<ol style="list-style-type: none"> 1. 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. 2. Water-pipe smoking is associated with intrauterine growth restriction and low birth weight. 3. There is no evidence from human studies to conclude that it is safe for pregnant women to use e-cigarettes. 4. There are no human studies on pregnancy and fetal outcomes associated with the use of e-cigarettes during pregnancy. 5. There is no evidence to support the use of e-cigarettes as a smoking cessation strategy for pregnant women. 6. There is some evidence from animal studies that e-cigarettes can adversely affect fetal development, including changes in DNA and fetal anomalies. 7. There is insufficient evidence on the effects of e-cigarettes on reproductive health. <div> <p>Considerations</p> <ul style="list-style-type: none"> • Refer to the CAN-ADAPTT guidelines for smoking cessation for pregnant and breastfeeding women. • Despite the lack of evidence, e-cigarettes may reduce some risk for women who are pregnant. Refer to considerations under e-cigarettes if using. • The risks of e-cigarettes may be estimated by the risk of exposure to nicotine during pregnancy. Women who are pregnant should be advised to reduce the frequency of use and the concentration of nicotine in e-cigarettes. • Women who are pregnant should be encouraged to switch to nicotine replacement treatment to reduce possible harms. </div>
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<p>E-cigarettes: Addiction</p> <p>Recommendation #5a: Use of E-cigarettes with nicotine should be discouraged among non-smokers due to the risk of addiction.</p>	Moderate	Strong	<p>1. There is substantial evidence that e-cigarettes with nicotine are addictive, and that their use results in symptoms of dependence on e-cigarettes.</p> <p>2. There is substantial evidence that e-cigarette use increases the risk of ever using combustible tobacco cigarettes among youth and young adults. However, transition to regular use of tobacco cigarettes is unclear at this time.</p> <p>Considerations</p> <ul style="list-style-type: none"> • Use of high-dose nicotine salts may increase risk of addiction. • Youth and young adults should be advised that e-cigarettes are addictive and that nicotine addiction may increase the risk of using combustible tobacco cigarettes. • Restrict the use of e-cigarettes to protect non-users from airborne particulate matter.
<p>E-cigarettes: Cessation</p> <p>Recommendation #5b: E-cigarettes with nicotine may be an effective cessation aid for people who use combustible tobacco.</p>	Moderate	Conditional	<p>1. Systematic reviews and RCTs provide some evidence of the effectiveness of e-cigarettes as a cessation aid.</p> <p>2. More frequent use (i.e.: daily) of e-cigarettes is associated with an increase in cessation outcomes.</p> <p>3. 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.</p> <p>Considerations</p> <ul style="list-style-type: none"> • E-cigarettes as a cessation aid may be most effective when combined with behavioural counselling. • Smokers should be advised to switch completely from combusted 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 combusted tobacco. However, smokers should be advised that harms associated with long-term e-cigarette use are currently unknown. • Continued use of e-cigarettes may reduce risk of relapse to combustible tobacco.
<p>E-cigarettes: Health Outcomes</p> <p>Recommendation #5c: People who do not use any tobacco products should not use e-cigarettes</p> <p>Recommendation #5d: People who are currently using e-cigarettes should stop or switch to safer forms of nicotine such as NRT.</p> <p>Recommendation #5e: People who switch from combustible tobacco to e-cigarettes will reduce their exposure to numerous toxicants and carcinogens.</p> <p>Recommendation #5f: For people who use combustible tobacco products and cannot quit by other means, e-cigarettes may be a lower risk alternative.</p>	Low - Moderate	Conditional	<p>1. The long-term health effects of e-cigarette use are unknown.</p> <p>2. In addition to the known effects of nicotine, there is some evidence that e-cigarettes can cause negative health outcomes such as cough and mouth and throat irritation as well as potential negative pulmonary and cardiovascular effects.</p> <p>Considerations</p> <ul style="list-style-type: none"> • E-cigarettes are less harmful than combustible tobacco, but are not completely harmless. In addition to nicotine, most e-cigarette products contain and emit substances with unknown harms when inhaled. • If you use these products, you should consider the following : <ul style="list-style-type: none"> ◦ Do not purchase unsafe illicit/black market e-liquids, pods or devices. ◦ Don't adulterate your products (THC, vitamin E, other oils, etc.) or modify the device. ◦ Keep the products away from children. ◦ It is unclear what risks are associated with using e-cigarettes and combustible tobacco concurrently. ◦ Receive instruction on the use of the device given the variability in device types, etc.

*For more information on the creation of this document and the scientific literature it's based on, visit the **Executive Summary**.*

7 tips to lower your risk when using nicotine

Nicotine is addictive. How addicted you become determines how difficult it will be for you to stop. The products you use and the way you use them make a difference. Cigarettes are the most addictive while Nicotine Replacement Therapy is the least. The only way to completely avoid health risks is by not using nicotine at all. We always recommend that you try to fully quit any nicotine product. If you do decide to use nicotine, follow the tips below to help lower the risks to your health. You can also speak with a knowledgeable health care provider about your options.

Cut back on your nicotine use.

Limit the number of time(s) you use any nicotine product. Try to use less than daily. If using daily, try not to use more than once every 3 – 4 hours.



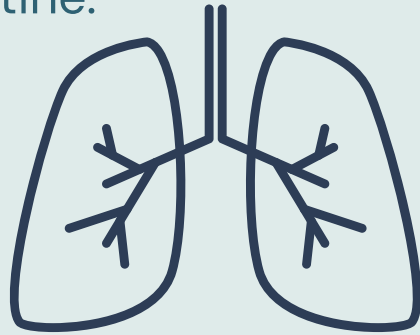
Learn to manage your cravings.

Cravings happen – but they will pass! Try things like taking a walk, chewing sugar-free gum, or doing breathing exercises until you find what works best for you.



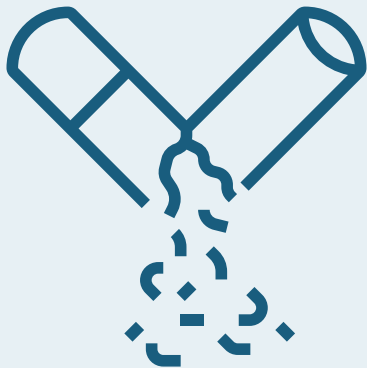
Use Nicotine Replacement Therapy (NRT) to help you stop using other nicotine products.

NRT products are the safest way to use nicotine. They can help you manage your nicotine cravings while you are trying to quit other nicotine products. NRT products include the patch, gum, lozenge, oral mist, and inhaler. These are not associated with the negative health effects such as cancers, lung or heart disease, which are caused by cigarettes and other forms of tobacco.



Make the switch 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 exposure to harmful combusted chemicals, including carbon monoxide. Further reduce your risk by switching to products that don't have tobacco like NRT or e-cigarettes.



Switch completely from smoking to e-cigarettes.

Using both tobacco and e-cigarettes, i.e. "dual use", increases your exposure to harmful chemicals. If you are going to use nicotine, switch completely from cigarettes to e-cigarettes to reduce your exposure and increase your chances of staying cigarette-free.



If you are vaping, choose e-cigarette cartridges with less nicotine.




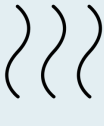
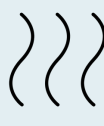

Choose products that have lower levels of nicotine. Products with more nicotine increase your risk of addiction. Purchase cartridges with the lowest amount of nicotine available.



If you are vaping, only use vaping devices that have been authorized for sale in Canada, and do not make changes to the product.

Do 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 oversights. Do not modify vaping products or add any substances that are not intended by the manufacturer, particularly THC oil, which can cause serious lung damage. For electronic devices, follow the manufacturer instructions for use and battery charging.



	Cigarettes	Waterpipe	Smokeless tobacco	Heat-not-burn (HNB)	E-cigarettes/vaping	Nicotine Replacement Therapy
How it enters the body:	 Smoke	 Smoke	 Chew or snuff	 Aerosol	 Aerosol	 Mouth or skin
What's in it:						
Tobacco	Y	Y	Y	Y	N	N
Nicotine	Y	Y	Y	Y	Y	Y
Does it increase risk or risk factors for...?						
Addiction	Y	Y	Y	Y	Y	N*
Respiratory illness	Y	Y	N	?	Y	N
Cancer	Y	Y	Y	?	?	N
Cardiovascular disease	Y	Y	?	?	Y	N
Reproductive health	Y	Y	?	?	?	?**

*NRT patches are not addictive. However, some patients might experience symptoms of addiction to short acting NRT.

**Safer than smoking and use under the guidance of a healthcare professional.

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