

SMOKE & MIRRORS

CANNABIS & E-CIGARETTES: APPROPRIATE FOR CARDIAC PATIENTS?

Canadian Cardiovascular Pharmacists Network
18th Annual Western Cardiovascular Fall Symposium
Saturday, October 5th, 2019
Lynette Kasar BSP, MSc

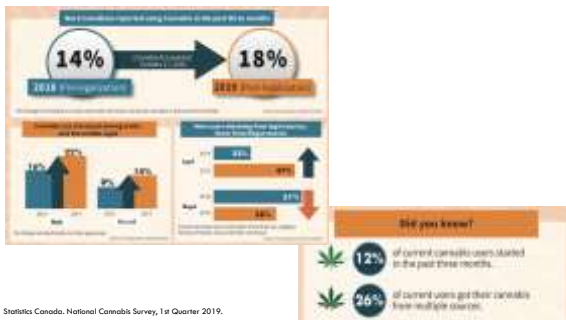
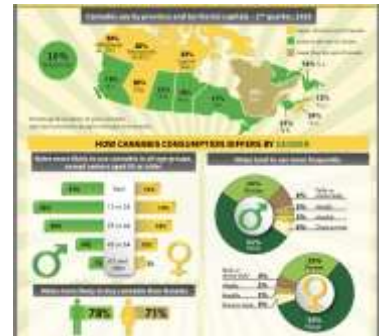
LEARNING OBJECTIVES

- To understand the types of cannabinoids & e-cigarettes.
- To review the cardiovascular data on cannabinoids & e-cigarettes.
- To share resources for discussing cannabinoids / e-cigarettes with patients.

CONFLICT OF INTEREST

None to declare

STATISTICS CANADA NATIONAL CANNABIS SURVEY 2ND QUARTER 2019



Statistics Canada, National Cannabis Survey, 1st Quarter 2019.



Statistics Canada, National Cannabis Survey, 4th Quarter 2018.

ENDOCANNABINOID SYSTEM

- **CB1 receptor:**
 - * predominately in the central nervous system
 - * peripheral organs & tissues, including the heart
- **CB2 receptor:**
 - * primarily in the immune system, but also in the heart & blood vessels

CANNABIS

contains over 100 cannabinoids

Delta-9-tetrahydrocannabinol (THC)

- CB1 and CB2
- Main "psychoactive" & cardioactive agent

Cannabidiol (CBD)

- Low affinity for CB1 and CB2
- Minimal "psychoactive" & cardioactive agent

You may have heard of...

PRESCRIPTION CANNABINOIDS (oral) THC and/or CBD as capsules, sprays or solutions available by prescription (e.g. solution, nabiximol)	VAPORIZED CANNABIS (inhaled) dried cannabis which is heated and inhaled
CANNABIS OIL (oral) cannabis extracts as oils that can be swallowed	SMOKED CANNABIS (inhaled) not usually recommended see page 6 for side effects specific to smoking cannabis

THC = delta-9-tetrahydrocannabinol, CBD = cannabidiol
<https://www.nrlf.ca/~/media/uploads/documents/Cannabis-Medical-Patient-Booklet.pdf>

PRODUCTS CONTAIN VARYING PROPORTIONS OF THC &/OR CBD

Prescription cannabinoids:

- Nabilone (Cesamet): THC analogue
- Nabiximol (Sativex): THC/CBD (2.7mg THC & 2.5mg CBD / spray)
- Cannabidiol (Epidiolex): almost 100% CBD, not available in Canada

Cannabis:

- Oral or dried (various ratios)

THC & CARDIOVASCULAR TOXICITY

Inhalation of combustion / vaporized products (e.g. smoking or vaping marijuana)

Direct CV effects of THC

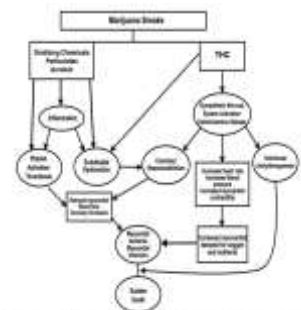
Indirect effects of THC related to acute anxiety, hallucinations, psychosis

INHALATION OF THC

Composition & toxicity of marijuana smoke is similar to cigarette smoke, except: THC vs nicotine greater exposure to ammonia & cyanide with THC

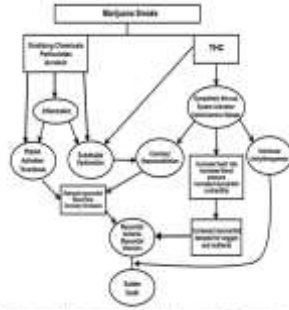
High levels of oxidants, particulates, toxic volatile organic chemicals, carbon monoxide

Bennett HL. Managing Cannabis Use in Patients With Cardiovascular Disease. *Can J Cardiol*. 2019 Feb;33(2):138-141.



DIRECT CV EFFECTS OF THC

Net effect is an increase in myocardial work & oxygen demand with an impaired compensatory increase in coronary blood flow

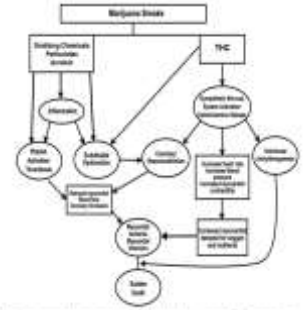


Bernards NL. Managing Cannabis Use in Patients With Cardiovascular Disease. *Can J Cardiol*. 2019 Feb;35(2):138-141.

DIRECT CV EFFECTS OF THC

THC can also cause orthostatic hypotension due to impaired venoconstriction → aggravate myocardial ischemia in the context of CAD or precipitate stroke

In elderly, orthostatic hypotension also increases the risks of syncope or falls



Bernards NL. Managing Cannabis Use in Patients With Cardiovascular Disease. *Can J Cardiol*. 2019 Feb;35(2):138-141.

INDIRECT CV EFFECTS OF THC

acute anxiety, hallucinations, psychosis



catecholamines



adverse acute CV effects

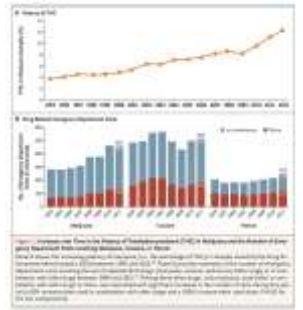
High doses of THC, synthetic cannabinoids, & small therapeutic doses in older patients

Allan GM et al. Simplified guideline for prescribing medical cannabinoids in primary care. *Can Fam Physician*. 2018 Feb;64(2):111-120.

Condition	THC	CB1	CB2
Chronic Pain	++	++	++
Acute Pain	+	+	+
Spasticity	++	++	++
Multiple Sclerosis	++	++	++
Chronic Obstructive Pulmonary Disease	+	+	+
Asthma	+	+	+
Chronic Kidney Disease	+	+	+
Chronic Liver Disease	+	+	+
Chronic Heart Disease	+	+	+
Chronic Lung Disease	+	+	+
Chronic Inflammation	+	+	+
Chronic Infection	+	+	+
Chronic Autoimmunity	+	+	+
Chronic Neurodegeneration	+	+	+
Chronic Mental Illness	+	+	+
Chronic Substance Use	+	+	+
Chronic Trauma	+	+	+
Chronic Injury	+	+	+
Chronic Illness	+	+	+
Chronic Disability	+	+	+
Chronic Death	+	+	+

OLDER STUDIES SUGGESTED CANNABIS WAS SAFE

- the THC content in marijuana has increased
- some studies which appeared neutral subsequently showed an increased risk in harm with longer follow-up



THC & CARDIOVASCULAR TOXICITY

Dose-related tachycardia:

- most consistent acute effect across a variety of patient populations
- HR increases 20-100%
- occasional & chronic users, but tolerance appears to develop

Blood pressure:

- reports of both hypertension & orthostatic hypotension

In patients with chronic stable angina, angina threshold was reduced by ~50% after smoking a single marijuana joint

Triggering Myocardial Infarction by Marijuana
 Minky A. Mittleman, MD, PhD; Rebecca A. Garsky, MSc; Michaela M. Kelly, PhD; S. Shadmehr, RM; James E. Muller, MD

Background—Marijuana use in the age group prone to coronary artery disease is higher than it was in the past. Smoking marijuana is known to have hemodynamic consequences, including a dose-dependent increase in heart rate, hypotension, and peripheral vasodilation, however, whether it can trigger the onset of myocardial infarction is unknown.

Methods and Results—In the Determinants of Myocardial Infarction Case Study, we interviewed 1000 patients 1200 (mean age 56) with acute myocardial infarction as a result of 8 days after admission onset. We used the case-control study design to compare the reported use of marijuana to the time preceding symptoms of myocardial infarction to the reported frequency of marijuana use in the 12 months prior to the myocardial infarction. The case-control study was conducted in 2007 and 2008. The study was conducted in 2007 and 2008. The study was conducted in 2007 and 2008.

Conclusion—Smoking marijuana was associated with a 25% increase in the risk of myocardial infarction in the 12 months prior to the myocardial infarction.

Case Report

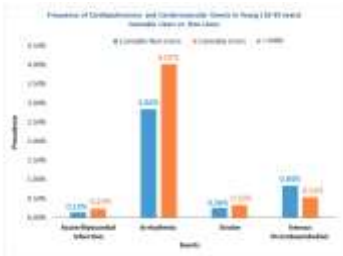
Marijuana Lollipop-Induced Myocardial Infarction
 Alexandra Saunders, MD, and Robert S. Secor, MD

Published Online First: February 1, 2019

See editorial by Bernards, pages 138–141 of this issue.

ABSTRACT
 A 45-year-old man with chronic coronary artery disease presented with chest pain, diaphoresis, and other symptoms of myocardial infarction. He was treated with 100 mg of aspirin, 80 mg of morphine, and 4 mg of nitroglycerin. He was then given 1 mg of atropine and 1 mg of metoprolol. He was then given 1 mg of aspirin and 1 mg of metoprolol. He was then given 1 mg of aspirin and 1 mg of metoprolol.

KEYWORDS
 Marijuana, lollipop, myocardial infarction, chest pain, diaphoresis, atropine, metoprolol, aspirin, nitroglycerin.



excluded concomitant substance abuse (alcohol, tobacco, cocaine, amphetamines)

Figure 1. Frequency of cardiovascular and cerebrovascular events in young (18-39 years) cannabis users vs. non-users.
Desai R et al. Rising Trends in Hospitalizations for Cardiovascular Events among Young Cannabis Users (18-39 Years) without Other Substance Abuse. *Medicina (Kaunas)*. 2019 Aug 5;55(8).

CONSIDERATIONS

- From a pharmacological view point... there is still a lot to learn, but there appears to be a biologically plausible dose-dependent effect for THC on surrogate outcomes
- From a clinical perspective... limited data suggests cardiovascular / cerebrovascular harm associated with THC
- Discourage recreational use
- Discourage smoking & vaping as methods of consumption
- If other therapeutic alternatives have failed to provide relief → use shared decision making and if cannabis is the next logical step, suggest an oral formulation with a high CBD, low THC ratio. There is no strong evidence to guide dosing.

RESOURCES

- RxFiles Newsletter. Cannabinoids / Medical Cannabis: A deep dive into shallow evidence, in the hunt for pearls. Fall / Winter 2018.
- RxFiles. Cannabis – Q&A Patient Booklet
- Allen GM et al. Simplified guideline for prescribing medical cannabinoids in primary care. CFP 2018.

Information Update - Health Canada warns of potential risk of pulmonary illness associated with vaping products

A 7th person has died in the U.S. from a vaping-related lung illness

Saskatoon

Sask. e-cigarette legislation expected in October

Trump calls for ban on flavoured e-cigarettes – what is Canada's stance on vaping?

HISTORY REPEATS ITSELF



Compared to non-smokers, smokers:

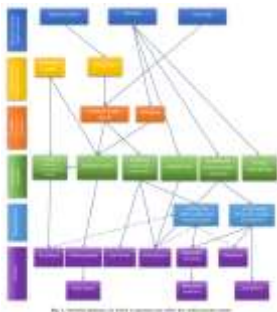
- live 10 fewer years
- are 3 times more likely to have a stroke
- are 2 to 4 times more likely to have a MI
- are up to four times more likely to experience sudden cardiac death

<https://cwhc.utoronto.ca/sites/default/files/images/infographics/cwhc-infographic-smoking.pdf>

Nicotine in one JUUL® pod = one pack of cigarettes

Mod-pods use nicotine salts → deliver higher levels of nicotine

<https://www.canada.ca/content/dam/health/publications/healthy-living/vaping-mechanics-infographic/vaping-mechanics-infographic.pdf>



Kennedy CD et al. The cardiovascular effects of electronic cigarettes: A systematic review of experimental studies. Prev Med. 2019 Jul 22;127:105770.

E-cigarettes have been on the market for a decade, making it challenging the long term effects



- 38 studies (24 human)
- 74.3% found potentially harmful effects:
- Increased sympathetic nervous system activity was found in all human studies (i.e. increased HR, BP, peripheral vasoconstriction)
 - Platelet activation, oxidative stress & endothelial dysfunction found across all studies
- Sensitivity analysis: when studies with conflicts of interest (e.g. funded by e-cigarette companies) or median-high risk of bias were excluded (n=8), 90% of included studies found potentially harmful effects

When used in total abstinence from combustible tobacco products, users may reduce – but not eliminate exposure to harmful chemical

65% of Canadians who use e-cigarettes also smoke tobacco cigarettes, i.e. “dual users”

Table 2. Association Between E-Cigarette Use and Cardiovascular Disease According to Combustible Cigarette Smoking Among U.S. Adults

	Cardiovascular Disease (Pooled NHANES 2011 & 2012)* 99 (94% CI)		Prestroke and Stroke-Free Status (Pooled NHANES 2011 & 2012)* 148 (94% CI)	
	Combustible Cigarette Smoking Status		Combustible Cigarette Smoking Status	
	Never Smoker (n = 392,501)	Current Smoker (n = 36,788)	Never Smoker (n = 218,653)	Current Smoker (n = 15,236)
E-Cigarette Use Status				
Never e-cigarette users	Ref	Ref	Ref	Ref
Current e-cigarette users	1.06 (0.43-1.72)	1.38 (1.18-1.58)	1.31 (0.58-1.81)	1.85 (1.28-2.74)
Occasional use	0.95	1.38	0.97	1.38
Daily use	0.90 (1.01)	1.11 (1.52)	0.97 (2.02)	1.11 (1.86)
Daily use	1.35 (1.11-1.64)	1.59 (1.20-2.08)	1.18 (0.58-2.41)	1.84 (1.57-2.36)

HRs = Hazard ratios that include 95% confidence intervals; **CI** = confidence interval; **Ref** = referent value.
 *Adjusted for age, sex, race, educational status, income, physical activity, health insurance, alcohol, and heavy drinking.

Osei A et al. Association Between E-Cigarette Use and Cardiovascular Disease Among Never and Current Combustible-Cigarette Smokers. Am J Med. 2019 Aug;132(8):949-954.e2.

Table 3. E-Cigarette Use and Cardiovascular Disease: What Clinicians and Researchers Need to Know

Key Points:

- E-cigarettes are not safe for cardiovascular health.
- E-cigarettes are not safe for pregnant women or children.
- E-cigarettes are not safe for people with chronic conditions.
- E-cigarettes are not safe for people with mental health conditions.
- E-cigarettes are not safe for people with respiratory conditions.
- E-cigarettes are not safe for people with cardiovascular disease.
- E-cigarettes are not safe for people with cancer.
- E-cigarettes are not safe for people with diabetes.
- E-cigarettes are not safe for people with kidney disease.
- E-cigarettes are not safe for people with liver disease.
- E-cigarettes are not safe for people with autoimmune diseases.
- E-cigarettes are not safe for people with chronic pain.
- E-cigarettes are not safe for people with chronic fatigue syndrome.
- E-cigarettes are not safe for people with chronic sinusitis.
- E-cigarettes are not safe for people with chronic urticaria.
- E-cigarettes are not safe for people with chronic hives.
- E-cigarettes are not safe for people with chronic itching.
- E-cigarettes are not safe for people with chronic dry eye.
- E-cigarettes are not safe for people with chronic dry mouth.
- E-cigarettes are not safe for people with chronic dry skin.
- E-cigarettes are not safe for people with chronic dry hair.
- E-cigarettes are not safe for people with chronic dry eyes.
- E-cigarettes are not safe for people with chronic dry mouth.
- E-cigarettes are not safe for people with chronic dry skin.
- E-cigarettes are not safe for people with chronic dry hair.

Non-smokers exposed to e-cigarette aerosol have serum cotinine levels similar to those exposed to secondhand smoke

Questions & Comments