Mesa-redonda
O consumo de Cannabis é inofensivo à saúde humana?
Evidências científicas nas especialidades médicas

A visão da Pneumologia e da Clínica

28 / 03 / 2018 - Quinta-feira
14:30h às 14:50h

Dr. José Miguel Chatkin
Prof. Titular Med. Interna / Pneumologia Escola de Medicina PUC-RS
Presidente da Soc. Brasileira de Pneumologia e Tisiologia 2019-2020

CANNABIS: NOVOS TEMPOS?

Scientific Cannabis Science Conference
Baltimore Convention Center, April 8-10, 2019

THE MILBANK QUARTERLY
A MULTIDISCIPLINARY JOURNAL OF POPULATION HEALTH AND HEALTH POLICY

Original Investigation

Waiting for the Opportune Moment: The Tobacco Industry and Marijuana Legalization

RACHEL ANN BARRY,* HEIKKI HIILAMO,† and STANTON A. GLANTZ*

*Center for Tobacco Control Research and Education and Philip R. Lee Institute for Health Policy Studies, University of California, San Francisco;
†University of Helsinki*

INHALATION METHODS OF CANNABIS

blunt

Cannabis is rolled in cigar that is cut, removed of tobacco, and resealed.

bong

Combusted cannabis is bubbled through water, then resulting smoke is inhaled.

dabbing

Cannabis products are chemically dissolved in vapors of flammable solvent, such as butane or isopropyl alcohol, which is then inhaled.

g-pen

Cannabis is concentrated into wax,oil or hash and vaporized through an e-cigarette.

hookah

Cannabis is mixed with flavored tobacco, burned with charcoal. Smoke bubbles through water and is inhaled.

joint

Cannabis is rolled in paper and smoked like a cigarette.

pipe

Cannabis product is lit and smoked in a glass pipe.

vaporizer

Cannabis is heated to about 338F, below burning temperature, and vapors are inhaled..

Burnham, CHEST 2015

1. **Sintomas não estão limitados à via de exposição**
2. **Dermatite de contato e sintomas respiratórios são os mais prevalentes: a maioria dos usuários fumam a erva e preparam seus cigarros**
3. **Contato profissional indústria medicamentos com cannabis**
4. **Hiperresponsividade brônquica e sintomas respiratórios**

Maconha: dificuldades em avaliar ef. respiratórios

- diferenças folha de tabaco e maconha
  - diferen
- Técnica de uso:
  - Inalações mais prolongadas e mais profundas
  - Apneias mais longas: 4x mais alcatrão
  - Cigarro menos compacto
  - Sem filtros
- Aumento da pressão intratorácica:
  - pneumotórax, pneumomediastino,
  - bolhas de enfisema
- informações não confiáveis (culpa; medo)
- poucos pacientes em cada estudo (geralmente transversais)

Chem. Res. Toxicol. **2008,** *21,* 494–502

A Comparison of Mainstream and Sidestream
Tobacco Cigarette Smoke Produced und
Cond

David Moir,*,† Will
Reb

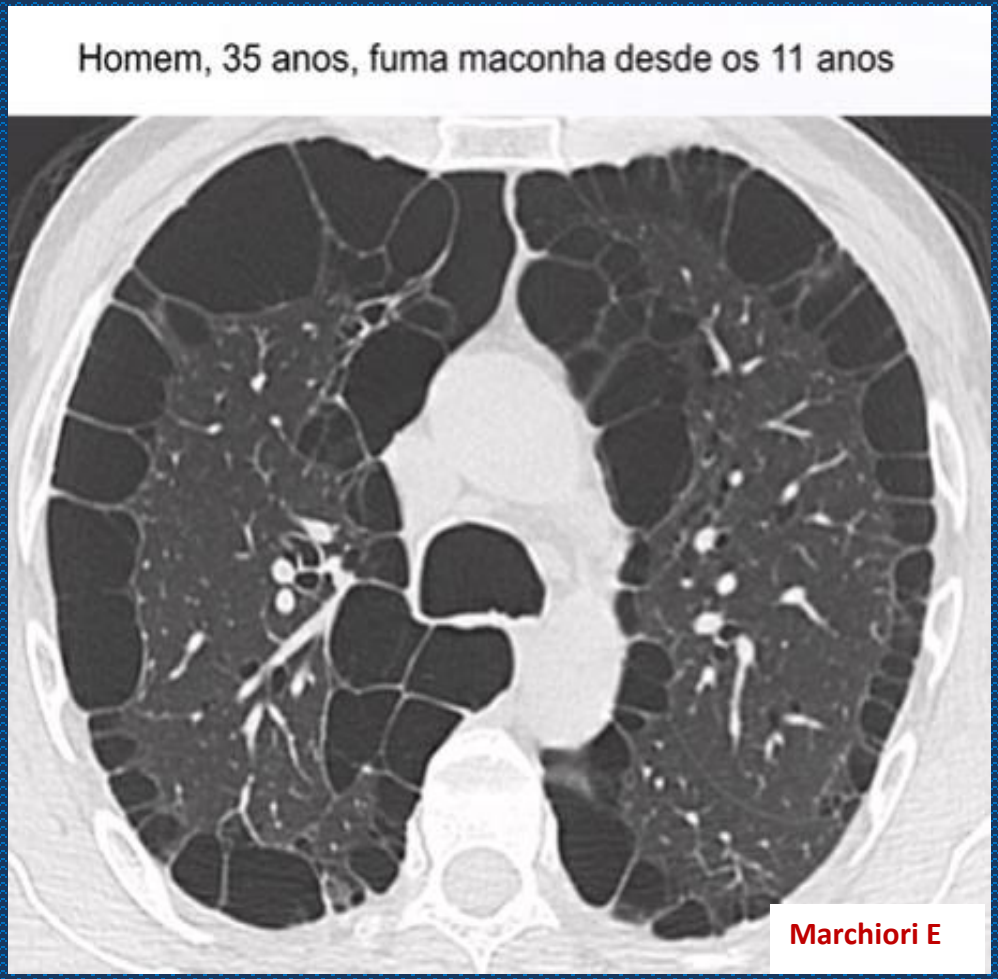
Além disso:

- **Altas concentrações de matéria particulada fina $PM_{2,5}$**
- **Quantidade significativas de mercúrio, cadmio, níquel, chumbo, cromo, cianeto de hidrogênio**

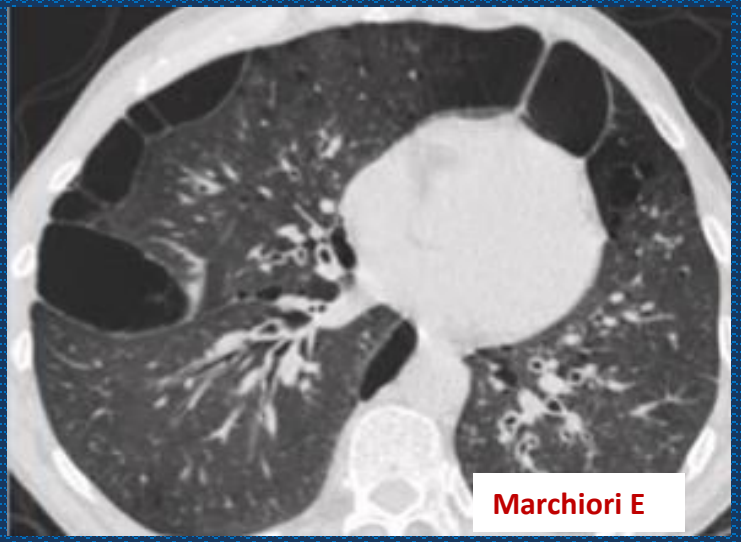
- **Fumaça cigarro e maconha composição similares**
- **Portanto, efeitos respiratórios crônicos seriam similares**
- **Estudos de resultados contraditórios e com limitações**

	400	2850
	190	—
	1200	—
...ic (µg)		
Acrolein (µg)		
Ammonia (µg)		
Acet...		
		22
		67
	2600	4100
	75	84
	532	498
	83	310
...ethylnitrosamine	27	30
m- and p-cresol (µg)	54.4	65
Naphthalene (µg)	3000	1200
o-Cresol (µg)	17,9	24
Phenol (µg)	76.8	39
Toluene (µg)	112	108

PULMÃO DO USUÁRIO DE CANNABIS



Usuários de maconha por muitos anos



REVIEW 2018

Annals of Internal Medicine

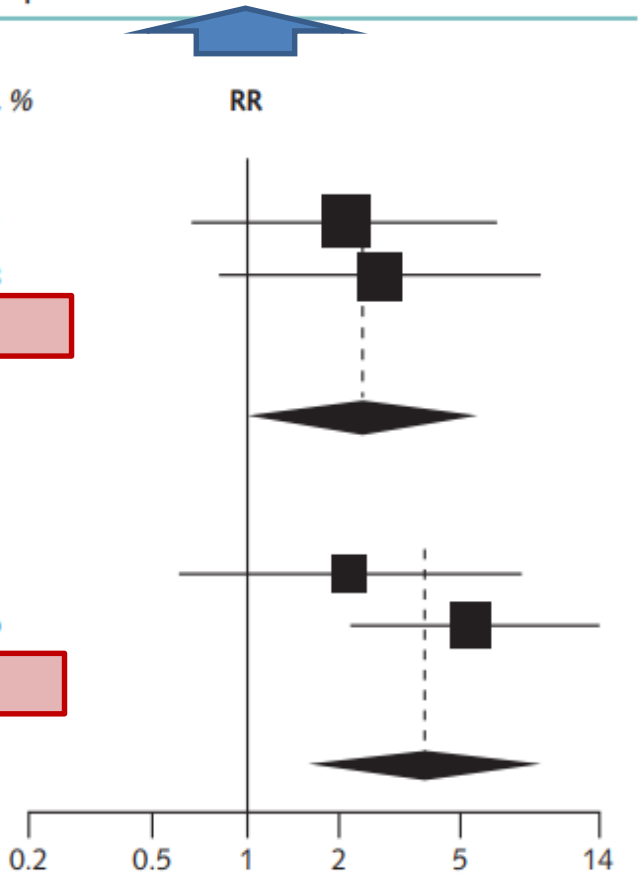
Marijuana Use, Respiratory Symptoms, and Pulmonary Function

A Systematic Review and Meta-analysis

Mehrnaz Ghasemiesfe, MD; Divya Ravi, MD, MPH; Marzieh Vali, MSc; Deborah Korenstein, MD; Mehrdad Arjomandi, MD; James Frank, MD; Peter C. Austin, PhD; and Salomeh Keyhani, MD, MPH

Figure 2. Association between marijuana use and cough and sputum production in prospective cohort studies.

Study, Year (Reference)	Events/Participants, *n/N*		RR (95% CI)	Weight, %
	Marijuana Smokers	Nonsmokers		
Cough				
Hancox et al, 2015 (16)	132/947	4/53	1.84 (0.71–4.77)	52.2
Tashkin et al, 2012 (17)	12/81	5/77	2.28 (0.84–6.17)	47.8
Overall (z = 2.03; P = 0.04)	144/1028	9/130	2.04 (1.02–4.06)	100
Heterogeneity: I^2 = 0%; τ^2 = 0; P = 0.76				
Sputum production				
Hancox et al, 2015 (16)	91/946	2/54	2.19 (0.62–7.73)	38.1
Tashkin et al, 2012 (17)	28/119	5/115	5.41 (2.16–13.53)	61.9
Overall (z = 3.06; P < 0.01)	119/1065	7/169	3.84 (1.62–9.07)	100
Heterogeneity: I^2 = 23%; τ^2 = 0.09; P = 0.26				



REVIEW 2018 Annals of Internal Medicine

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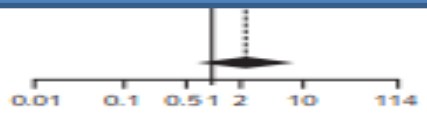
Figure 3. Association between marijuana use and cough, sputum production, wheezing, dyspnea, and chronic bronchitis in cross-sectional studies.

Conclusion: Low-strength evidence suggests that smoking marijuana is associated with cough, sputum production, and wheezing. Evidence on the association between marijuana use and obstructive lung disease and pulmonary function is insufficient.

Overall ($z = 1.33$; $P = 0.18$)	52/543	190/5234	2.28 (0.68–7.72)	100

Heterogeneity: $I^2 = 73\%$; $\tau^2 = 0.91$; $P = 0.02$



Effects of quitting cannabis on respiratory symptoms

Eur Respir J 2015;

Huang 2015

Robert J. Hancox[1], Hayden H. Shin[1], Andrew R. Gray[1], Richie Poulton[2] and Malcolm R. Sears[3]

TABLE 3 Associations between current cannabis use and respiratory symptoms across multiple assessments using generalised estimating equations

	Participants	Mean observations per participant	OR (95% CI)	p-value
Cough	1000	4.7	1.97 (1.57–2.48)	<0.001
Sputum	1000	4.7	2.31 (1.83–2.91)	<0.001
Wheeze	998	4.7	1.55 (1.23–1.94)	<0.001
Dyspnoea	1000	4.7	1.23 (0.97–1.56)	0.086

Analyses were adjusted for sex, age of assessment, and tobacco use and asthma at that age. Odds ratios represent the odds associated with current frequent cannabis use compared with non- or infrequent use.

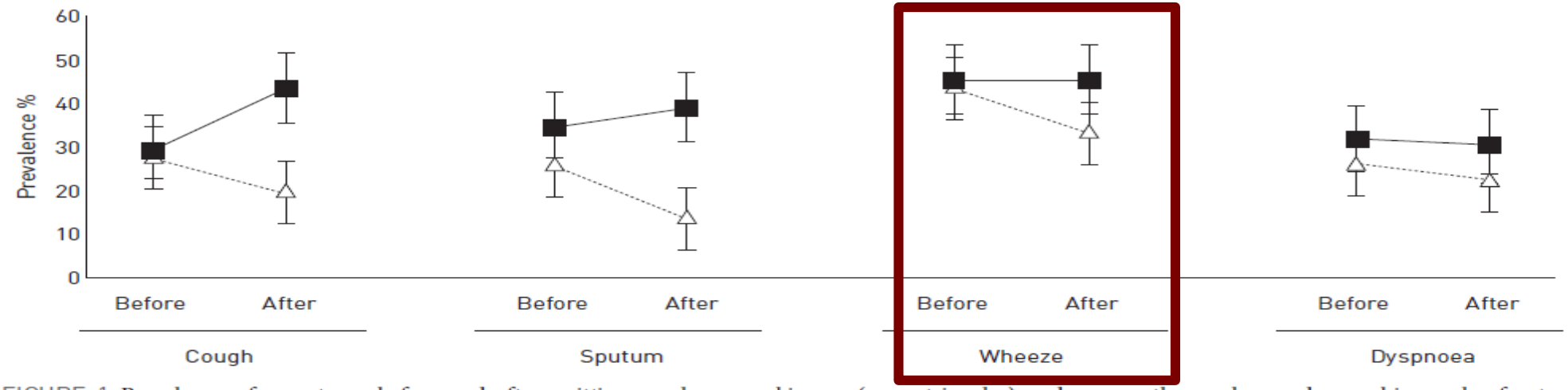


FIGURE 1 Prevalence of symptoms before and after quitting regular cannabis use (open triangles) and among those who used cannabis regular for two consecutive phases (solid squares). Vertical bars show 95% confidence intervals.

Doenças alérgicas associadas a *Cannabis sativa*

- Rinite alérgica
- Asma
- Conjuntivite alérgica
- Eczema
- Asma
- Urticária
- Anafilaxia
- Angioedema

Chatkin et al; Cannabis-Associated Asthma and Allergies, 2017
Clinical Reviews in Allergy & Immunology

Alérgenos associados a *Cannabis sativa*

- THC
- **Can s3 (nonspecific lipid transfer protein)**
- Thaumatin-like protein
- RuBisCO (ribulose 1,5- biphosphonate/oxygenase
- Oxygen-evolving enhancer protein 2

Ubiquidade da *nonspecific lipid transfer protein* (Can s3)

Fruits	Nuts	Beverages
Cherry	Hazelnut	Wine
Tangerine	Walnut	Beer
Orange	—	—
Peach	Others	—
Apple	Wheat	—
Tomato	Tobacco	—
Banana	Latex	—

Uso habitual de marijuana & asma

1. Efeito broncodilatador agudo inicial transitório
2. Aumento frequência e intensidade de sintomas da asma
3. Controle da asma mais frequentemente difícil, mesmo controlando idade, sexo, tabagismo, peso, outras alergias
4. Efeito positivo ao cessar uso

Bramness and von Soest *BMC Pulmonary Medicine* (2019) 19:52
https://doi.org/10.1186/s12890-019-0814-x

BMC Pulmonary Medicine

RESEARCH ARTICLE Open Access

A longitudinal study of cannabis use increasing the use of asthma medication in young Norwegian adults

2602 jovens por 13 anos; prescrição e retirada medicação para asma
ajuste: sexo, idade, escolaridade, IMC, auto relato atopias, tabagismo

OR 1.71 (95% CI: 1.06–2.77; p = 0.028)
Cannabis é fator risco para retirada de medicação para asma no sistema norueguês

Table 1. Challenge Studies That Reported Effects of Short-term Marijuana Inhalation

Tetrault, 2007

Source	No. of Subjects	
Vachon et al,[6] 1974	10	Marijuana smokin … aw 1 h after smoking (
Tashkin et al,[7] 1974	10	After smoking ma … immediately (*P* … placebo) in pati … d
Bernstein et a …		…subjects … tory
Laviolette and … Belanger,[9]		…mediate … arette …smokin … <.01)
Renaud and … 1986		…/₁ (*P*<.0 … …eased im … ng
Steadward ar … Singh,[11] 19		…nce in F … …seline o … npared
Tashkin et al, …		…king ma … …e in sGa … …g and re …
Tashkin et al, …		…methac … …ospasm … …correcti … uced ated
Tashkin et al, …		…hyperinf … …o 59 d o … …sed (*P*< … …01). Mod … …g capaci … …e quantit … n FEV₁ en ing the study and reduction of sGaw.
Tashkin et al,[15] 1977	11	FEV_1 and sGaw increased after smoked marijuana (*P*<.05)
Vachon et al,[16] 1973	17	Increase in sGaw after marijuana inhalation
Wu et al,[17] 1992	23	After smoking marijuana, airway resistance decreased significantly at all levels of marijuana compared with placebo (*P*<.05)

Síndrome cannabis-frutas/vegetais

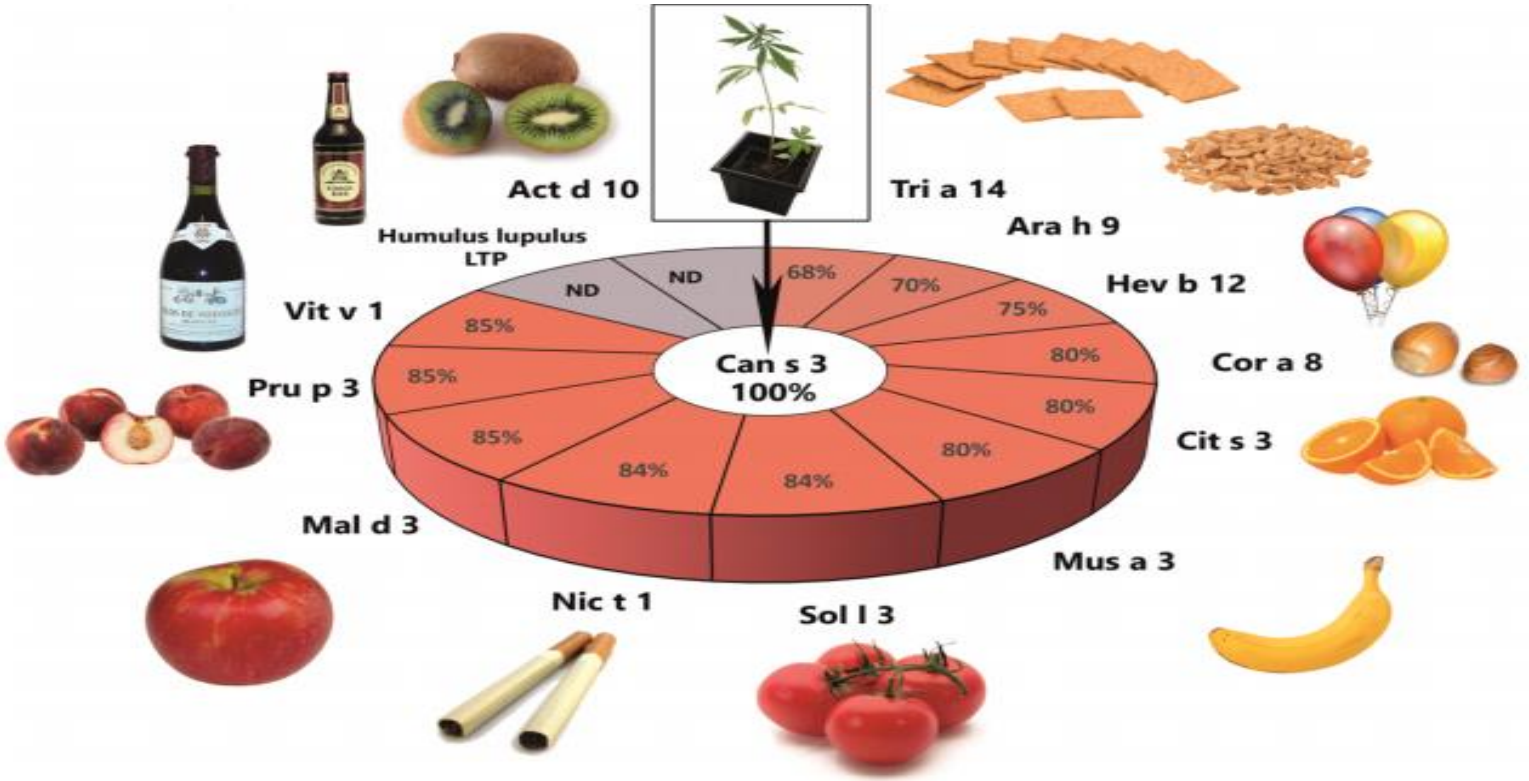


Fig. 1 The cannabis-fruit/vegetable syndrome and other cross-allergies. Non-specific lipid transfer proteins (ns-LTPs) are ubiquitously present in the plant kingdom. Consequently, sensitization to Can s 3, the ns-LTP from *Cannabis sativa*, could lead to a broad variety of cross-reactions. Cross-reactive substances displayed in the figure: cherry (*Prunus avium*), tangerine (*Citrus reticulata*), orange (*Citrus sinensis*), peach (*Prunus persica*), apple (*Malus domestica*), tomato (*Solanum Lycopersicum*), hazelnut (*Corylus avellana*), walnut (*Juglans regia*), banana (*Musa acuminate*), wheat (*Triticum aestivum*), latex (*Hevea brasiliensis*), tobacco (*Nicotiana tabacum*) and alcoholic beverages such as wine (grapes: *Vitis vinifera*) and beer (common hop: *Humulus lupulus*). Percentages represent sequence homology. *ND* no data (Boratyn et al. 2012)

Decuyper, 2015

Associação maconha-câncer pulmão: dados objetivos

1. THC ativa citocromo P450 $_{(1A1)}$: transforma PAHs em carcinógenos; +50% benzopireno; +75% benzantraceno

2

3

4 metaplasia escamosa e alterações pré-malignas

5. Imunohistoquímica mostra expressão aumentada de marcadores progressão pré-tumoral (EGRF e Ki67) e de outros com ação antimitogênica, proapotótica e antiangiogênica

California Office of Environmental Health Hazard Assessment, 2009

- **Fumaça de maconha incluída na lista de produtos com carcinógenos e toxinas nocivos à saúde humana e animal**

Marijuana use and risk of lung cancer: a 40-year cohort study

Cancer Causes Control (2013) 24:1811–1820

Table 4 Crude and adjusted hazard ratios (HRs) and 95 % CIs for lung cancer ($n = 179$) among 44,257 conscripts, in relation to lifetime frequency of cannabis-use categories

Cannabis smoking	Crude HR (95 % CI)	Tobacco-adjusted[a] HR (95 % CI)	Fully adjusted[b] HR (95 % CI)
Never (reference)	1.0	1.0	1.0
Once	2.07 (1.06–4.06)	1.48 (0.75–2.91)	1.52 (0.77–3.01)
2–4 times	0.95 (0.39–2.33)	0.65 (0.26–1.58)	0.66 (0.27–1.62)
5–10 times	1.02 (0.32–3.20)	0.66 (0.21–2.09)	0.68 (0.21–2.16)
11–50 times	2.69 (1.26–5.74)	1.68 (0.78–3.62)	1.68 (0.77–3.66)
More than 50 times	3.72 (1.96–7.06)	2.24 (1.17–4.29)	2.12 (1.08–4.14)

[a] Adjusted for tobacco smoking, using the following categories of tobacco use: do not smoke (reference category), daily smoking of 1–10 cigarettes per day, and daily smoking of more than 10 cigarettes per day

[b] Adjusted for tobacco smoking [do not smoke (reference category), daily smoking of 1–10 cigarettes per day, and daily smoking of more than 10 cigarettes per day]; level of alcohol consumption [abstainers (0 g 100 % alcohol/consumption per week; reference category), light (1–100 g/consumption per week), moderate (101–250 g/consumption per week), and high (more than 250 g/consumption per week)]; respiratory conditions [any of the following diagnosed at conscription, chronic bronchitis, emphysema, pneumonia, and asthma: no (reference category)/yes]; and conscripts' SES in 1970 [high/intermediate nonmanual (reference category), low nonmanual, manual skilled and unskilled, others (farmers, self-employed, and unclassified)]

Cannabis smoking and lung cancer risk: Pooled analysis in the International Lung Cancer Consortium *(Zhang, 2015)*

Há plausibilidade biológica, mas a relação maconha-neo de pulmão ainda não foi demonstrada em humanos

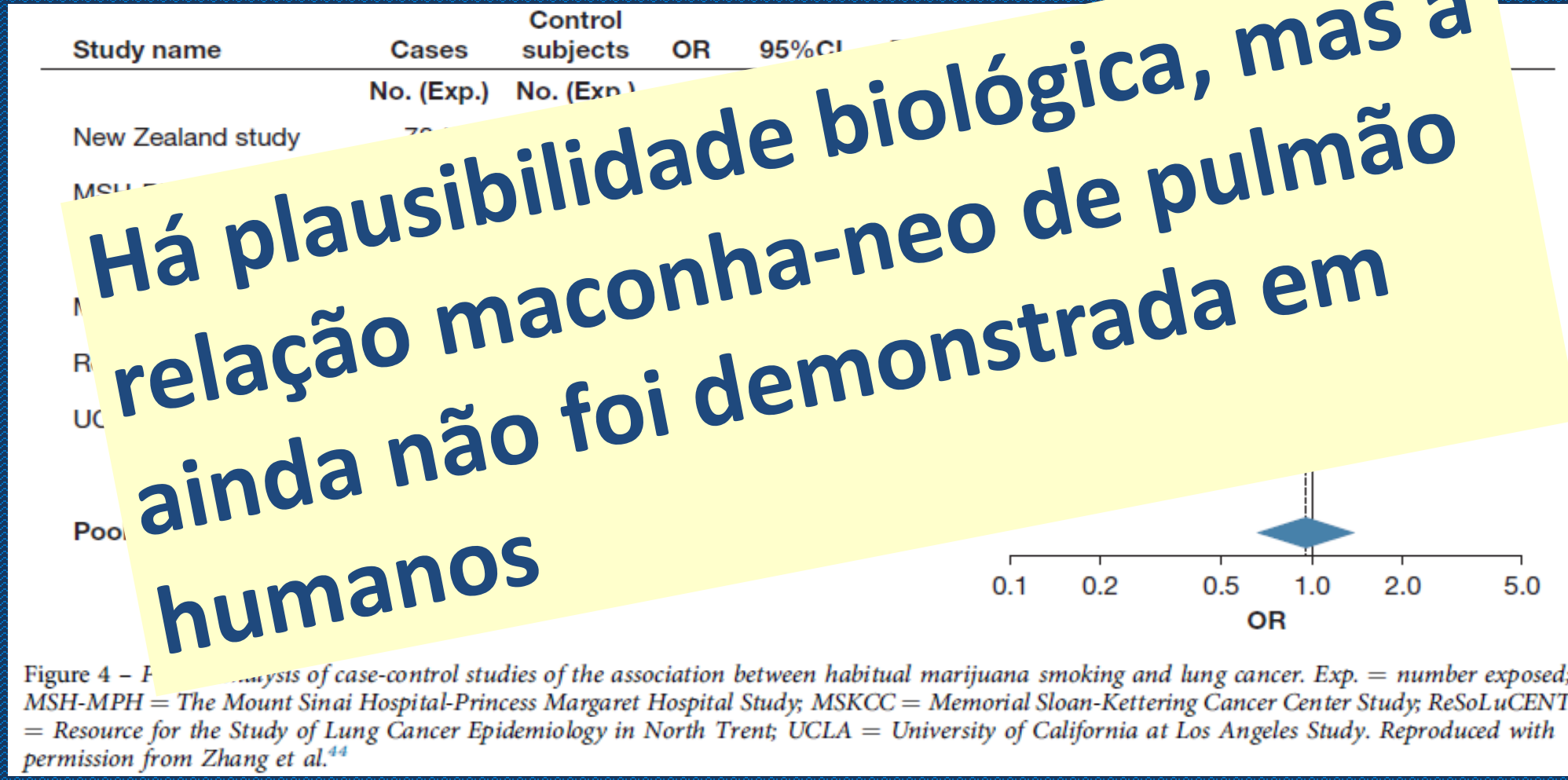


Figure 4 – F…ysis of case-control studies of the association between habitual marijuana smoking and lung cancer. Exp. = number exposed; MSH-MPH = The Mount Sinai Hospital-Princess Margaret Hospital Study; MSKCC = Memorial Sloan-Kettering Cancer Center Study; ReSoLuCENT = Resource for the Study of Lung Cancer Epidemiology in North Trent; UCLA = University of California at Los Angeles Study. Reproduced with permission from Zhang et al.[44]

Fig 2: Forest plot of the association between cannabis smoking (habitual vs. non-habitual) and lung cancer risk

Table 1 Cannabis use-related health effects: conclusions of the National Academies of Sciences, Engineering and Medicine's (NASEM) report compared with the World Health Organization (WHO) report. Cousijn, Addiction 2017

NASEM health outcome	*NASEM conclusions*	*WHO conclusion*
Cancer		
Non-seminoma-type testicular germ cell tumours	Limited evidence for increased risk in cannabis users	Suggestive evidence for increased risk in cannabis smokers
Lung cancer; Head and neck cancers	Moderate evidence for no association	Smoking mix of cannabis and tobacco may increase cancer risks; effect of cannabis alone is unknown
Acute leukaemia; rhabdo-myosarcoma; astrocytoma; neuro-blastoma in offspring	No or insufficient evidence to support or refute associations	
Other cancers	No or insufficient evidence to support or refute associations	
Cardiometabolic risk		
Ischaemic stroke; subarachnoid haemorrhage; pre-diabetes; acute myocardial infarction	Plausible theoretical link for triggering coronary events; limited evidence for a higher risk of suffering	Some evidence for intoxication triggered coronary events; long-term heavy use potentially triggers myocardial infarctions and strokes in young users
Diabetes; metabolic syndrome	Limited evidence for decreased risk of diabetes and metabolic syndrome; findings are counterintuitive, as THC tends to stimulate appetite, promote fat deposition, and promote adipogenesis	–

Cardiovascular effects of marijuana and synthetic cannabinoids: the good, the bad, and the ugly

Pal Pacher[1], Sabine Steffens[2], György Haskó[3], Thomas H. Schindler[4] and George Kunos[5]

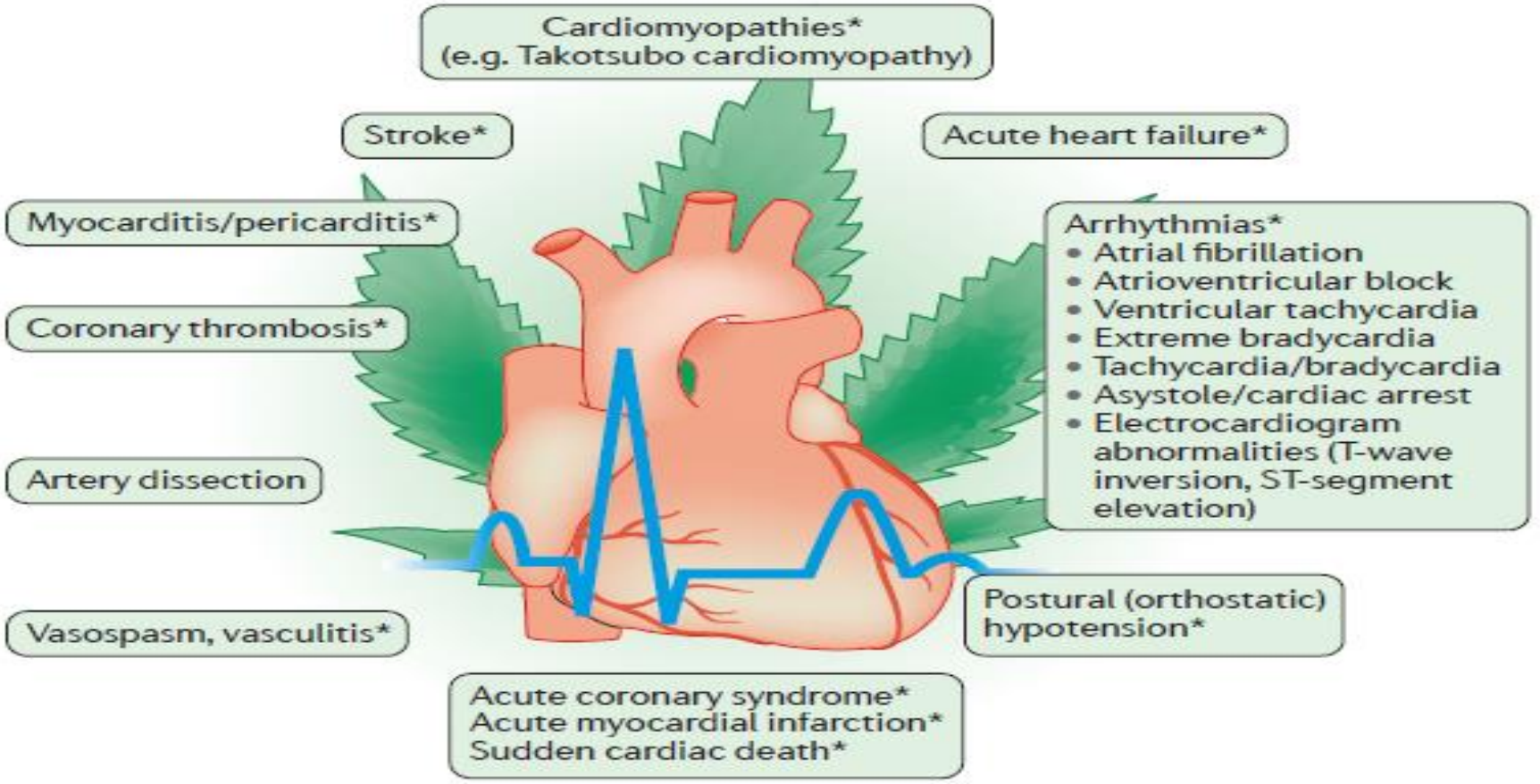


Figure 2 | **Reported cardiovascular adverse consequences of recreational marijuana and synthetic cannabinoid use.** *Adverse effects that were reported for synthetic cannabinoids; note almost complete overlap with the adverse effects of marijuana.

Cardiol Ther (2018)

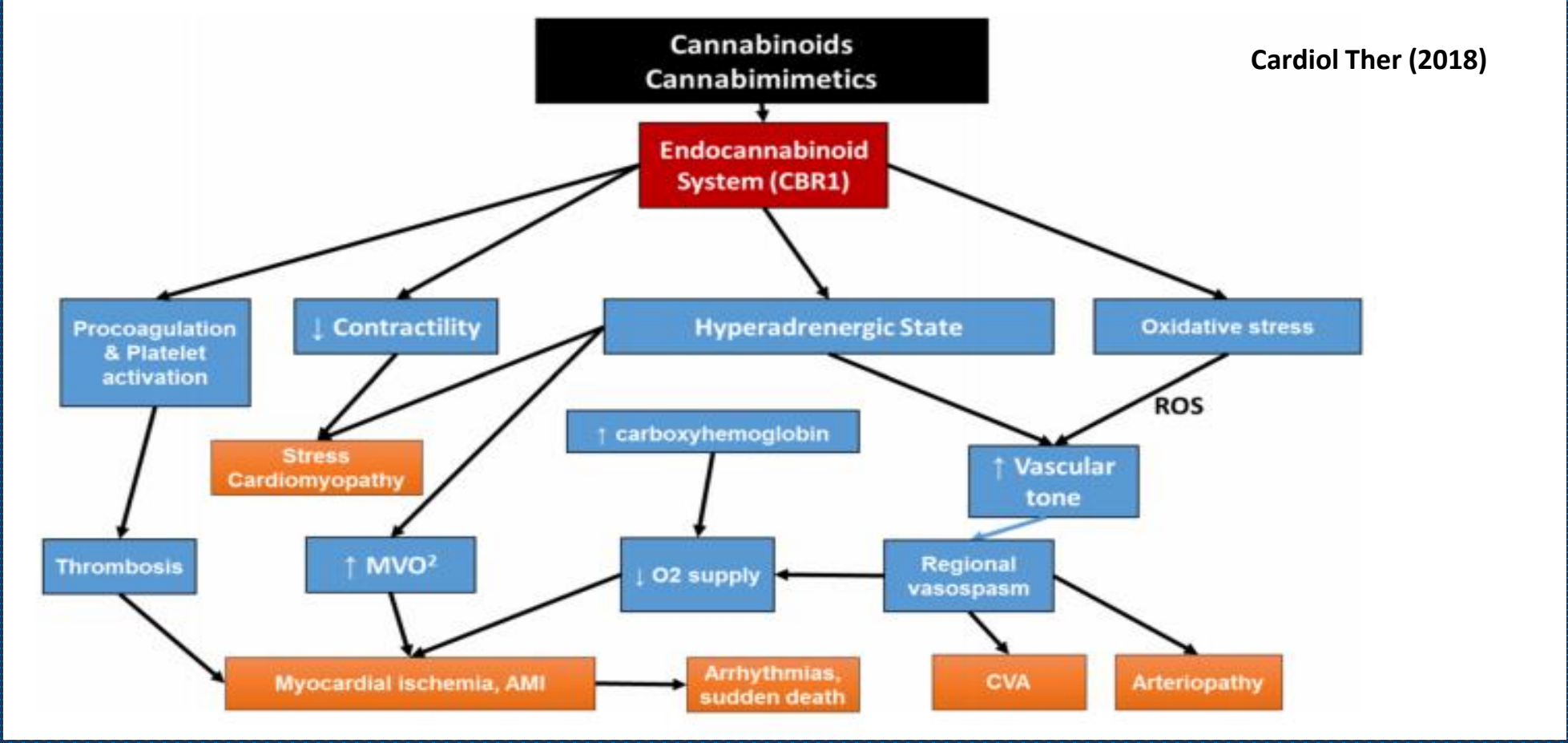


Fig. 1 Flow diagram demonstrating pathophysiologic pathways to common major adverse cardiovascular events reported in users of cannabis and related chemicals. Although non-receptor and non-endocannabinoid receptor-mediated pathways have been identified, most pathologic effects of cannabis are mediated through CBR1. Autonomic nervous system is a major contributor to the pathogenesis of most complications while oxidative stress, hypercoagulability and increased platelet aggregation potentiate such effects. CBR1 activation also has a direct negative inotropic effect on cardiomyocytes and together with catecholamine surge may precipitate stress cardiomyopathy. For those individuals who use cannabis by smoking, elevation of blood carboxyhemoglobin levels may contribute to reduction in oxygen supply to vital organs including the heart. AMI acute myocardial infarction; *CBR1* cannabinoid receptor 1, *CVA* cerebrovascular accident, MVO_2 myocardial oxygen consumption (demand), O_2 oxygen, *ROS* reactive oxygen species

Curr Diab Rep (2016) 16: 117
DOI 10.1007/s11892-016-0795-6

LIFESTYLE MANAGEMENT TO REDUCE DIABETES/CARDIOVASCULAR RISK (C SHAY AND B CONWAY, SECTION EDITORS)

Marijuana Use and Type 2 Diabetes Mellitus: a Review

Stephen Sidney[1]

Table 1 Studies of marijuana use and prediabetes/diabetes

Author (ref)	Dataset	Years	Endpoint	N	Diabetes	Odds ratio or hazard ratio
Bancks [24••]	CARDIA	2010–11 (cross-sectional)	Prediabetes	2,676	1,193	1.65 (1.15, 1.65) current v never use 1.49 (1.06, 2.11) lifetime use >100 times v never use
		1992–93 to 2010–11 (longitudinal)		2,758	1,410	1.40 (1.13, 1.72) hazard ratio life use >100 times v never use
Bancks [24••]	CARDIA	2010–11 (cross-sectional)	Diabetes	3,034	357	1.18 (0.67, 2.10) current v never use 1.42 (0.85, 2.16) lifetime use >100 times v never use
		1992–93 to 2010–11 (longitudinal)		3,151	351	1.10 (0.74, 1.64) hazard ratio life use >100 times v never use
Rajavashisth [25]	NHANES	1988–1994 (cross-sectional)	Diabetes	10,896	719	0.36 (0.24, 0.55) ever use v never use (analytic data set of 8,127 participants with laboratory data
Alshaarawy [26•]	NHANES and NSDUH	2005–2012 (cross-sectional)	Diabetes	12,666 242,252	1,120 9,553	0.7 (0.6, 0.8) recent v. never user (meta-analysis)

There is a plausible link between marijuana use and diabetes due to the known effects of cannabinoids on adipose tissue and glucose/insulin metabolism. However, the studies to date have shown that marijuana use is associated with either lower odds or no difference in the odds of diabetes than non-use.

Table 1 Cannabis use-related health effects: conclusions of the National Academies of Sciences, Engineering and Medicine's (NASEM) report compared with the World Health Organization (WHO) report. Cousijn, Addiction 2017

NASEM health outcome	*NASEM conclusions*	*WHO conclusion*
Immunity		
Immune competence; human immunodeficiency virus (HIV); oral human papilloma virus (HPV)	Animal models and cell cultures support immunosuppressive properties of cannabinoids but insufficient evidence to support or refute effects in healthy humans and humans with HIV and HPV; limited evidence for a decrease in production of several inflammatory cytokines in healthy individuals	–
Viral hepatitis C (VHC)	Limited evidence for no association	–
Injury and death		
Motor vehicle crashes	Substantial evidence for an increased risk	Acute use increases risk of traffic injuries
Cannabis overdose	Moderate evidence for a positive association of increased risk of overdose injuries; insufficient evidence to support or refute a death due to cannabis overdose	–
All-cause mortality; Occupational accidents	Insufficient evidence to support or refute associations	–
Prenatal, perinatal and neonatal exposure		
Maternal cannabis smoking	Substantial evidence for positive association with lower birth weight; limited evidence for association with pregnancy complications; insufficient evidence for negative association with later outcomes in offspring; attribution of outcomes to cannabis exposure is generally problematic	Understudied topic, but offspring demonstrate impaired attention, learning and memory, impulsivity and behavioural problems and a higher likelihood of using cannabis when they mature

Annals of Internal Medicine 2018 IDEAS AND OPINIONS

Brief Commentary: Consequences of Marijuana: Observations From the Emergency Department

Kennon Heard, MD, PhD; Andrew A. Monte, MD, PhD; and Christopher O. Hoyte, MD

Annals of Internal Medicine 2018 IDEAS AND OPINIONS

Brief Commentary: Marijuana Use During Gestation and Lactation—Harmful Until Proved Safe

Eli Y. Adashi, MD, MS

- **Crianças:** ingestão acidental, ingestão de doces, bolos com maconha; apresentação clínica *life-threatening*
- **Adultos:** SHC: sindrome hiperemese por cannabis: USA > 100 pacientes/ano; situação grave, diagnóstico difícil, desidratação grave, insuf. renal, acidose e morte.
- **Gestação:** interfere implantação do ovo, formação placenta, THC atravessa placenta e barreira sangue-cérebro feto; interage sistema endocanabinóide fetal e neonatal; diminuição cresc fetal, natimortos, nascimento prematuro, desenv neural postnatal

ORIGINAL RESEARCH

One Minute of Marijuana Secondhand Smoke Exposure Substantially Impairs Vascular Endothelial Function

Xiaoyin Wang, MD; Ronak Derakhshandeh, MS; Jiangtao Liu, MD; Shilpa Narayan, BS;* Pooneh Nabavizadeh, MD; Stephenie Le, BA;† Olivia M. Danforth, BS;‡ Kranthi Pinnamaneni, MD; Hilda J. Rodriguez, AS; Emmy Luu, BS; Richard E. Sievers, BS; Suzaynn F. Schick, PhD; Stanton A. Glantz, PhD; Matthew L. Springer, PhD

Background—Despite public awareness that tobacco secondhand smoke (SHS) is harmful, many people still assume that marijuana SHS is benign. Debates about whether smoke-free laws should include marijuana are becoming increasingly widespread as marijuana is legalized and the cannabis industry grows. Lack of evidence for marijuana SHS causing acute cardiovascular harm is frequently mistaken for evidence that it is harmless, despite chemical and physical similarity between marijuana and tobacco smoke. We investigated whether brief exposure to marijuana SHS causes acute vascular endothelial dysfunction.

Methods and Results—We measured endothelial function as femoral artery flow-mediated dilation (FMD) in rats before and after exposure to marijuana SHS at levels similar to real-world tobacco SHS conditions. One minute of exposure to marijuana SHS impaired FMD to a comparable extent as impairment from equal concentrations of tobacco SHS, but recovery was considerably slower for marijuana. Exposure to marijuana SHS directly caused cannabinoid-independent vasodilation that subsided within 25 minutes, whereas FMD remained impaired for at least 90 minutes. Impairment occurred even when marijuana lacked cannabinoids and rolling paper was omitted. Endothelium-independent vasodilation by nitroglycerin administration was not impaired. FMD was not impaired by exposure to chamber air.

Conclusions—One minute of exposure to marijuana SHS substantially impairs endothelial function in rats for at least 90 minutes, considerably longer than comparable impairment by tobacco SHS. Impairment of FMD does not require cannabinoids, nicotine, or rolling paper smoke. Our findings in rats suggest that SHS can exert similar adverse cardiovascular effects regardless of whether it is from tobacco or marijuana. **(*J Am Heart Assoc.* 2016;5:e003858 doi: 10.1161/JAHA.116.003858)**

MARIJUANA SMOKE

SECONDHAND MARIJUANA SMOKE IS NOT HEALTHY

SMOKE IS SMOKE

SECONDHAND MARIJUANA SMOKE CONTAINS HUNDREDS OF CHEMICALS

Just like secondhand tobacco smoke, many of the chemicals in secondhand marijuana smoke are toxic and contain hazardous fine particles that pose a significant health risk to nonsmokers.

MARIJUANA SMOKE IS A FORM OF INDOOR AIR POLLUTION

It is important to strengthen all smokefree laws — both existing and new — to include marijuana in the definitions of smoking and vaping. Clearly define smoking as "inhaling, exhaling, burning, or carrying any lighted or heated cigar, cigarette, or pipe, or any other lighted or heated tobacco or plant product intended for inhalation, including hookahs and marijuana, whether natural or synthetic, in any manner or in any form."

Increasing cannabis use: what we still need to know about its effects on the lung

- "Estamos entrando em um experimento social massivo, em diferentes níveis de legalidade entre vários países em relação ao uso de cannabis.
- Somente a implantação de farmacovigilância consciente poderá avaliar o significado do uso desta droga em saúde pública em médio e longo prazo.
- O impacto do uso de cannabis poderá ser estudado de modo amplo e objetivo se houver planejamento adequado"

Tashkin, Respirology, 2014