WHAT ON EARTH (WTF)??

Cannabis, Cigarette Smoking and Lung Function – not all downhill?

Drug Delivery to the Lungs 2018
12th – 14th December 2018

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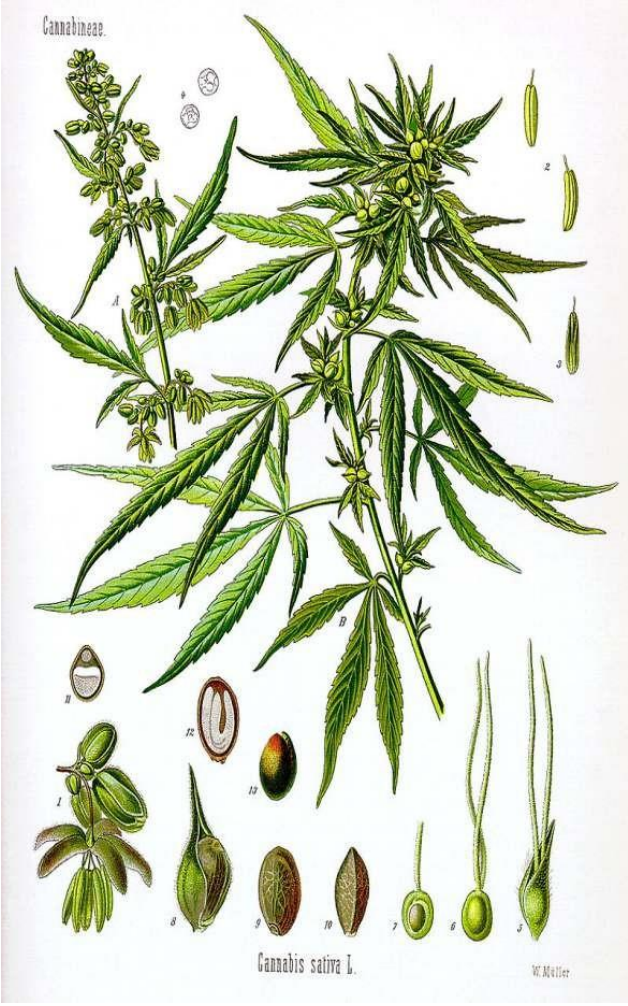
Why the interest?

- Cannabis most common illicit drug
- effects of tobacco smoking are well known
- common means of drug delivery to the lungs
- media attention
- new interest in licensing medical use
- complex cannabinoid pharmacology
- interesting respiratory effects

Cannabis (marijuana)



flowering plant native to central Asia + Indian sub-continent

genus includes 3 different species

-C. sativa, indica and ruderalis

contain >60 different cannabinoids

also metabolites + synthetic canabinols

~400 compounds in total

‘weed’, ‘dope’, ‘grass’, ‘hash’, ‘hemp’, ‘bud’, ‘resin’, ‘ganga’, ‘spliff’, ‘toke’

FE Köhler (1885)

Cannabis is in common widespread use

1st recorded use 3rd millennium BC

2013 128-232 m (2.7-4.9%) world's pop used cannabis

2016 51% US pop had ever used it 12% in past year

2016 2.1 m in UK

concern about increasing use with decriminalization

relatively little known about long-term effects generally, and on the respiratory system

note class B drug "It remains illegal for UK residents to possess cannabis in any form" 2014 cannabis possession -67% of UK recorded drug offences

Cannabis

Decriminalised possession	**Legal**
Argentina, Bolivia, Chile, Peru	Uruguay
Columbia, Ecuador, Paraguay	India West Bangal, Gujarat
Mexico, Costa Rica	Bihar, Odisha,
Cambodia	North East
Jamaica	South Africa
Austria, Belgium, Germany, Luxembourg, Malta, Netherlands Portugal, Spain, Switzerland, Czech rep, Russia, Ukraine, Georgia	North Korea
Slovenia Estonia, Moldova	US Alaska, California
Australia	Colorado, Nevada
	Washington, Oregon Maine, Mass, DC
	Canada

NO license in chronic pain, PTSD, depression, anxiety, glaucoma, IBD, Cancer etc

Licensed cannabinoid medication

name	drug	manufacturer	description	indication
Sativex Epidiolex	nabiximols	GW pharm	THC +CBD oromucosal Oral soln	MS pain + spasticity Dravets
Cesamet	nabilone	Meda Pharm	synthetic THC-like	chemo- induced
Canemes	nabilone	AOP Pharma AG		nausea + vomiting
Marinol	dronabinol	Abb Vie	synthetic	anorexia
Syndros	dronabinol	Insys Ther	Δ^9THC caps/soln	wt loss in AIDS

Cannabinoids

2 major active compounds delta-9-tetrahydrocannabinol (d-9-THC)
cannabidiol (CBD)

THC is the psychoactive compound, but is modulated by CBD

C. sativa-dominant strains have higher THC content

C. indica-dominant strains have higher CBD content

complex pharmacology effects on CB1, CB2, TRPV1 and 5HT1-A receptors + endocannabinoid system (eg anadamide)

THC -bronchodilator **Tetrault JM, et al. Arch Int Med 2007;167:221**

THC -various anti-inflammatory effects **Klein TW, et al. JI 2000;164**

CBD –multiple anti-inflammatory, anti-tumour, antihyperalgesia + neuroprotective + cardioprotective effects etc

British Thoracic Society

SMOKING STILL KILLS

- 10 million adults in Great Britain still smoke
- 100,000 deaths a year due to smoking
- Half of all smokers die from smoking-related diseases

Smoking causes 85% lung cancer(s) also mouth, pharynx, larynx, nasopharynx, oesophagus, stomach, pancreas, liver, bladder, renal pelvis, cervix, bowel, ovary, CML, ?breast

Better Lung Health For All

Image: ASH, 2015

other effects of cigarette smoking (tobacco)

~80-90% **COPD** (note smoking increasing in 3rd world)

causes ‘cough + spit’ ⩵ chronic bronchitis

alveolar damage ⩵ emphysema

progressive AW narrowing ⩵ small AW disease

in UK 4th commonest cause of death (30.000/y)

↑ to 3rd by 2020

commonest cause of hospital admission in winter

costs direct + indirect £1.91b/y (2014)

also

heart disease + strokes women>men ↑OR several fold

difficulties implicit in cannabis studies

- medico-legal considerations
- epidemiological >experimental studies
- difficulties of quantitation + standardization

  sinsemilla (skunk) >3x more potent

  (1 joint.year = 1 joint /day for 1 year)
- cannabis smokers usually concurrently smoke tobacco

  spliff = cannabis + tobacco
- variation in smoking/device

Cannabis smoking ↑respiratory symptoms

increased cough +

increased phlegm **'chronic bronchitis' ↑OR up to 2.98**

but

apparently reversible on quitting

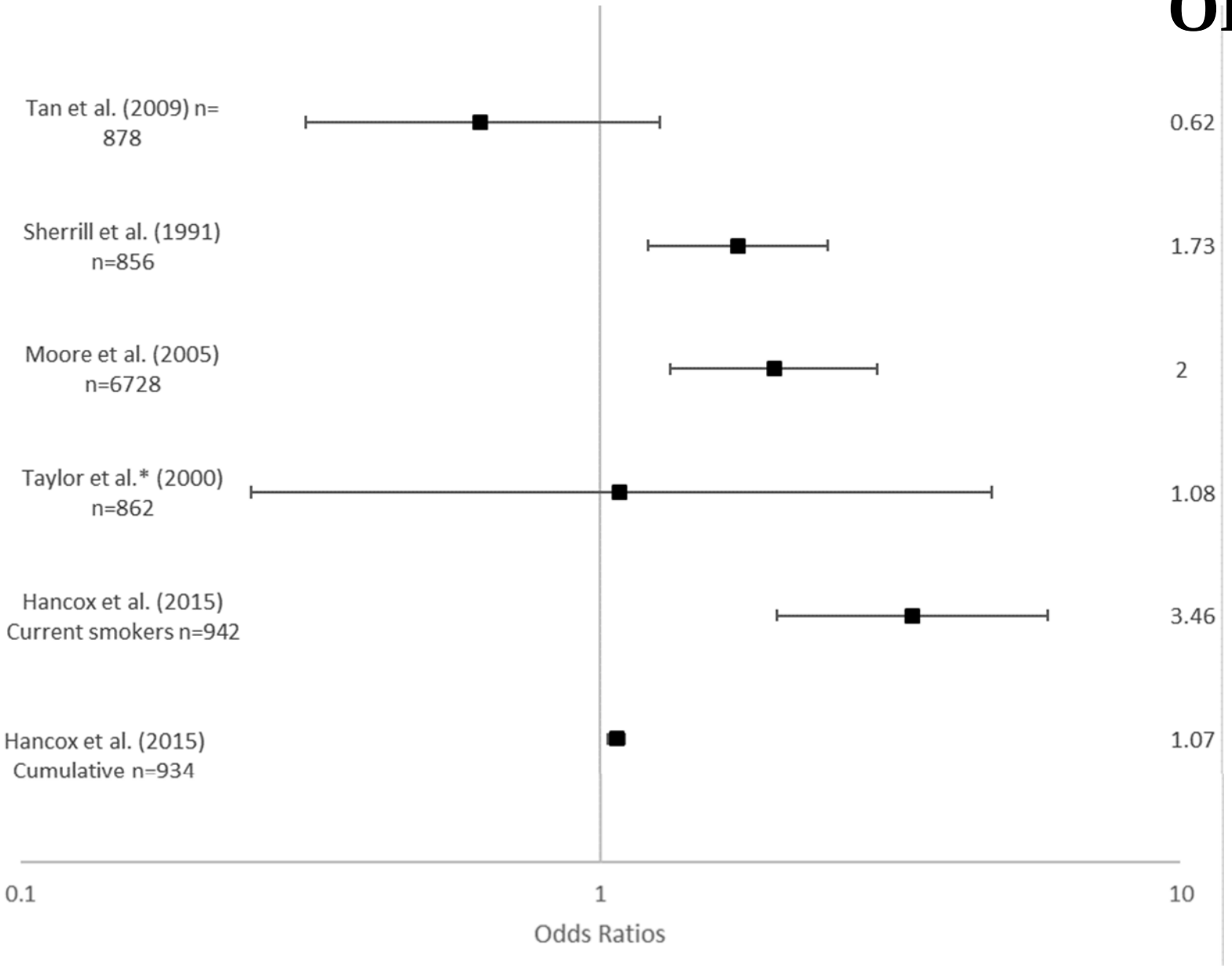
no increased SS cf 'never smokers' **Tashkin et al, 1987**

convenience sample n=34/299 75-100% quitters lost SS

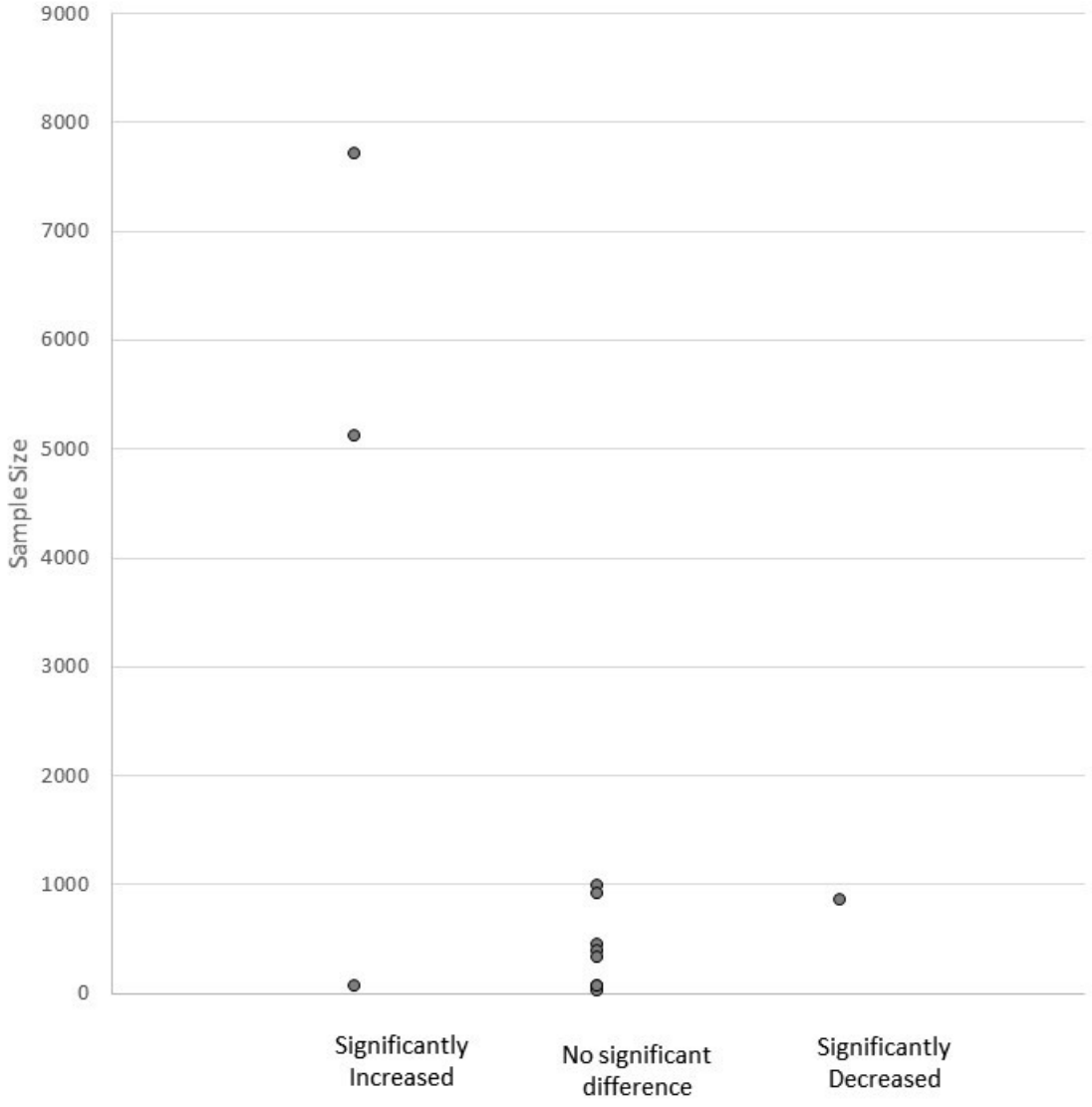
symptoms reduced to levels of 'never users' **Hancox et al, 2015**

birth cohort 0-38y quitters 50 frequent users 99

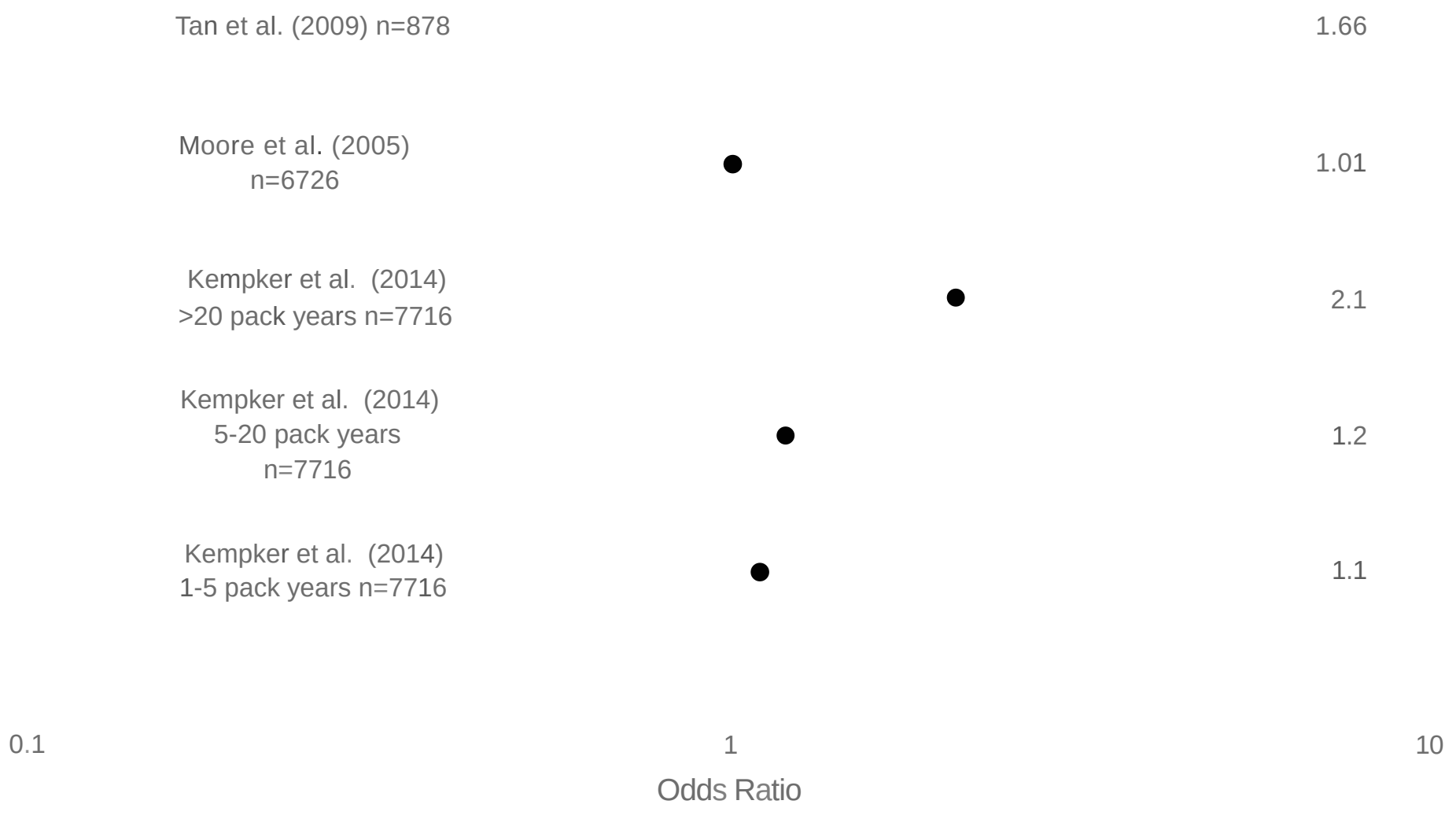
↑chronic cough in marijuana smokers



no change in FEV_1 in chronic marijuana smokers



airflow obstruction OR of FEV_1/FVC <0.7 in chronic marijuana smokers



effects of smoking cannabis

- marijuana causes chronic bronchitis cf tobacco smoking
- also produces similar large airway inflammation
  (inconsistent evidence that combination additive)

BUT does NOT cause chronic airflow obstruction

- **cannabis smoking produces ↑FVC** **Pletcher MJ, et al, 2012**
  (mechanism(s) unclear)
- also ↑TLC, ↑FRC, ↑RV **Hancox et al, 2010**
- consistent small ↑ in Raw (↓sGaw) **Tashkin 1980, 1987**
- no change in TLCO with cannabis alone

single HRCT cross-sectional study

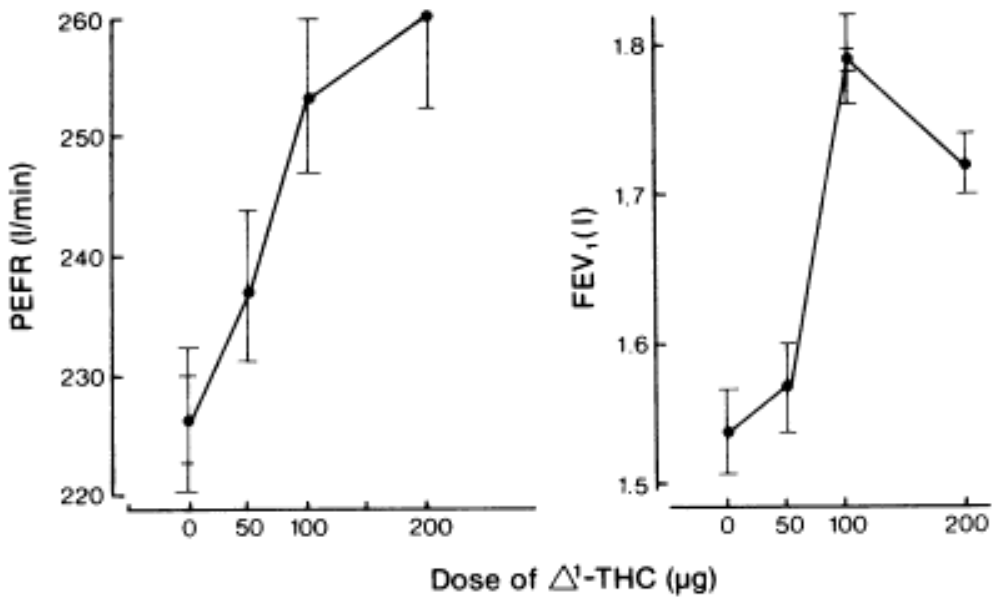
	mean age (y)	emphysema (macroscopic)	apical LD lung on HRCT (OR)
tobacco-only smokers	46.0	17/92	**-0.6** CI -2.0-0.8
tobacco + cannabis	41.3	15/91	
cannabis only	42.5	1/75	**2.4** CI 1.0-3.8
non-smokers	43.7	0	**1.0**

also showed small ↑TLC ↓sGaw

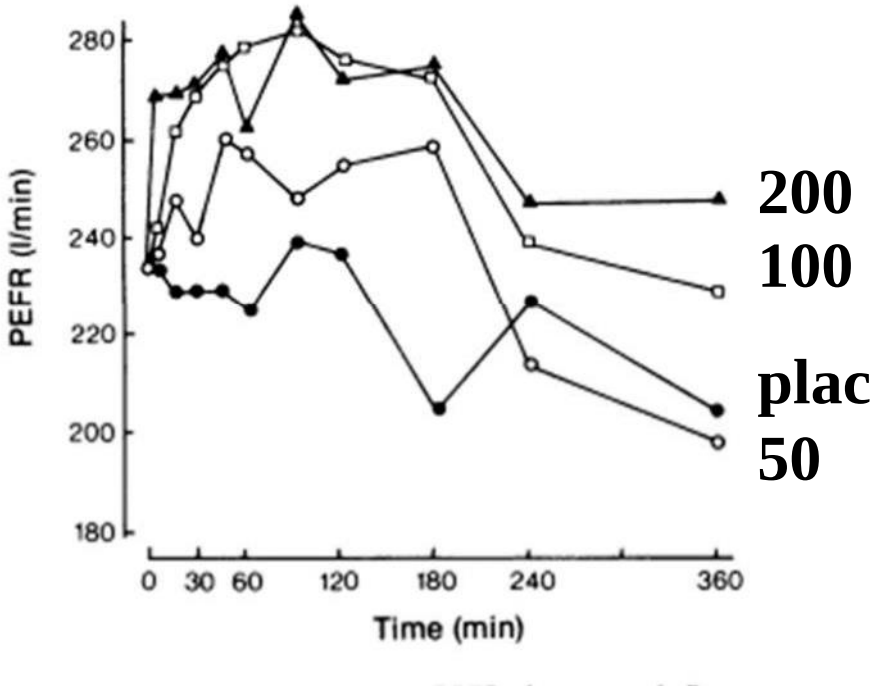
but nonsignif ↑ FRC ↑RV no change in TLCO

Aldington et al. Thorax 2007

d-r inhaled THC as bronchodilator



THC inhaled double blind
randomised order on 4 days
63mcL/puff by MDI



n=5 female patients aged 25-65y
recovering from acute asthma
on pred 10-15 mg/d

Hartley et al, Br J Clin Pharm 1978

Conclusions

cannabis most common illicit + 2nd most commonly smoked drug

usually smoked with tobacco

surprisingly different long-term effects cf tobacco

cannabis leads to ↑FVC not airflow obstruction

much research still needed

potential pharmacological roles (THC rather than CBD)?