Current Evidence: Cannabis and the Future

Through A Harm Reduction Lens

PRESENTERS:

- *Dr. Shelley Turner MD CCFP*

Disclosures

- *Speaker Engagements (Industry)*
- *McMaster University: Centre of Medicinal Cannabis Research*
  - DataCANN Study
- ***Speaking engagements sponsored by industry***
  - Travel expenses, educational grants
- ***Non profit funding for data analysis of database and resources***

Agenda

- Positionality
- Endocannabinoid Basics
- The Stats
- What we Do
- Medical vs. Recreational
- Research

Endocannabinoid System

Achieving balance

The Endocannabinoid System (ECS)

- A complex system within **every person.**
- Important functions in physiological and psychological changes to **maintain balance *(homeostasis)* in the body.**
- **Various functions include:**
  - Responds to injuries and inflammation, modulating the immune system
  - Protects against nerve damage, neurological diseases, and increases neuroplasticity
  - Regulates cell growth
  - Initiates pain control
  - Reproduction
  - Bone degradation/regeneration

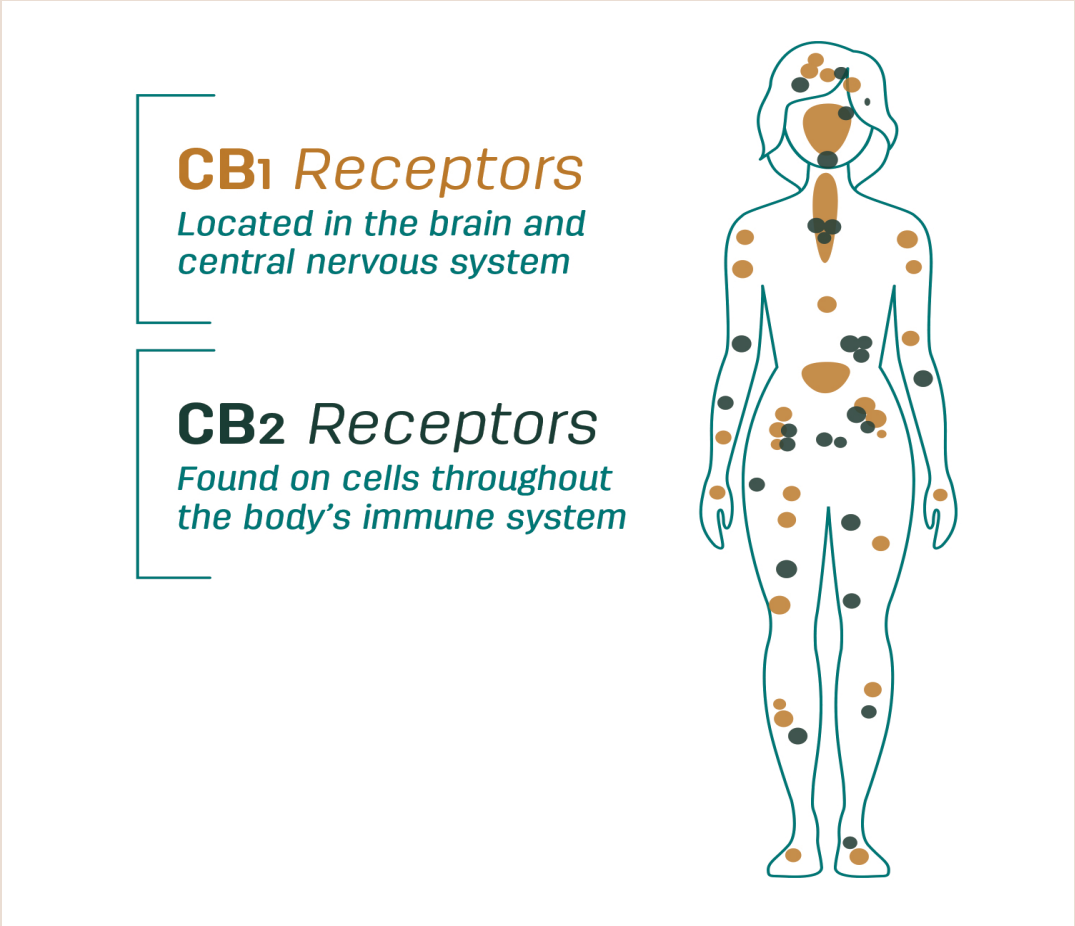
The Endocannabinoid System (ECS)

CB1 receptors are located in the nervous system (central & peripheral).

CB2 receptors are located in the immune system (tissues & cells).

Receptors can be activated by:

- *Endogenous Cannabinoids:* what the body makes itself
- *Exogenous Cannabinoids:*
- *Phytocannabinoids:* (E.g.: Cannabinoids like THC & CBD produced in the cannabis plant.)
- *Synthetic Cannabinoids:* (Dronabinol, Nabilone)

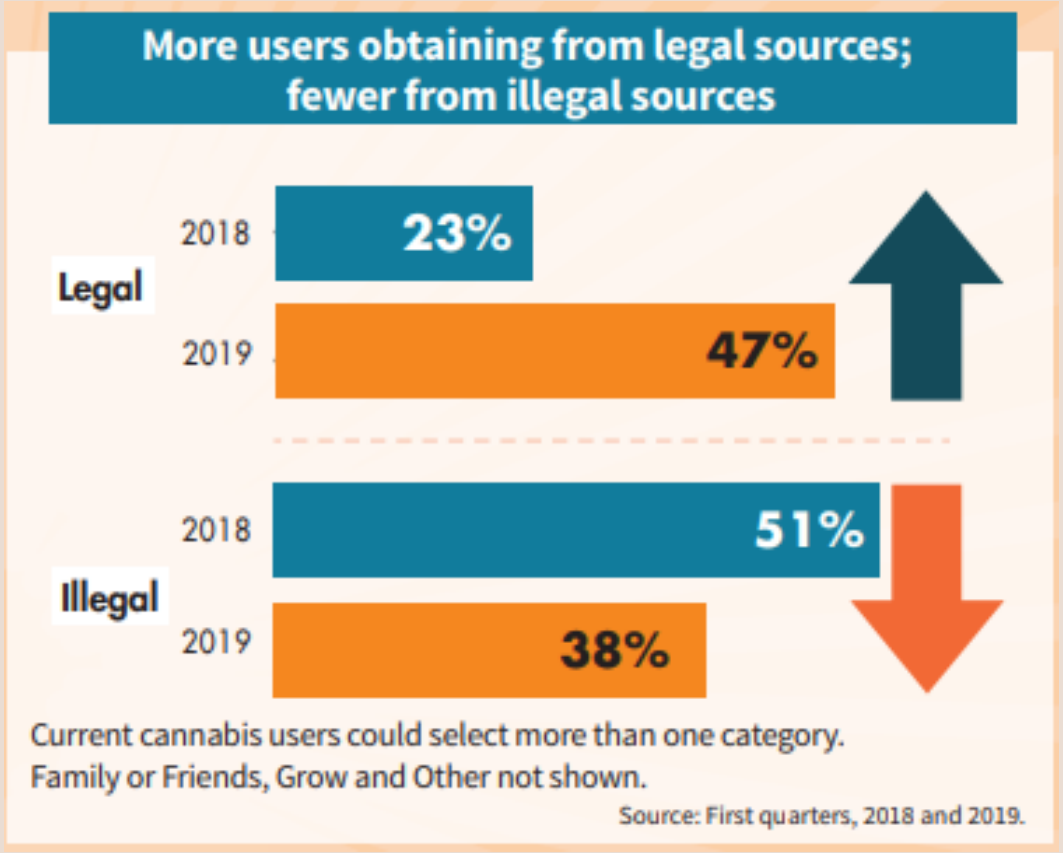


The Stats

What is happening out there?

National Cannabis Survey - Q1, 2019 Results

- 18% of Canadians (5.3 million people) 15 years or older reported using cannabis since 2019
  (increase from 14% since 2018)
- Increase in males & ages 45-64
  (half of new users >45 y/o)
- 15% of cannabis users reported driving within 2 hours of consuming cannabis
  (occurs more in frequent users than non-frequent users)
- 47% of users obtained from a legal source
  (compared to 23% in 2018)



Substances & Addiction

	Alcohol	Opioids	Cannabis	Tobacco
% Population Using	76.9% (2015)	13.1% (2015)	18% (2019)	15.1% (2017)
% Addiction Rate	20% heavy drinkers (leading to chronic illness'/AUD)	5-19%	9% (2019)	50+% (>15 y/o)
# of Death's	14,827 (2014)	3,286 (Jan – Sept 2018)	75 (2014) due to motor vehicle accidents	47,526 (2014)
Facts:	2015-2016 77,000 hospitalizations due to alcohol 75,000 hospitalization's due to heart attacks	17 Canadians were hospitalized every day due to opioid poisoning in 2017		75-80% of people trying to quit relapse Average of 8-11 attempts before quitting

*All rates are for the Canadian population

Opioid Related Deaths

Table 1. Summary of apparent opioid-related Total deaths by manner of death, 2016, 2017 and 2018. [1]

		2016	2017	2018
Number		3017	4100	4460
Rate per 100,000 population		8.4	11.2	12.0
Percent male [2]		71%	74%	74%
Percent by age group [3]	19 years and under	2%	2%	2%
	20 to 29 years	18%	19%	19%
	30 to 39 years	26%	27%	26%
	40 to 49 years	21%	21%	21%
	50 to 59 years	23%	20%	22%
	60 to 69 years	8%	8%	8%
	70 years and over	2%	1%	1%
Percent involving [4] fentanyl or fentanyl analogues		50%	67%	70%
Percent also involving non-opioid substances [5] (from January 2016 to December 2018)			76%	

Ontario's opioid-related death rates quadruple over the past 25 years

In 2015:

734 people died of an opioid-related cause, increasing 4-fold since 1991.

That's 2 people every day.

Who?

Typically male, middle aged, living in lower income, urban settings.

This number totals far more than the 481 people killed in motor vehicle collisions in 2014.

How?

4 in 5 of all opioid-related deaths were accidental.

60% of accidental deaths occurred among youth and younger adults (15-44 years),

while **80%** of suicide deaths occurred among older adults (45+ years).

Which drugs?

From 2006-2015:

Oxycodone involvement in opioid-related deaths peaked in 2010 before decreasing 24% by 2015.

Involvement of other opioids continued to increase:

Fentanyl by 548%,
Hydromorphone by 232%, and
Heroin by 975%.

What else?

Half of all opioid-related deaths also involved a benzodiazepine,

&

1 in 3 deaths involved cocaine.

Ontario Drug Policy Research Network. Emerging trends in opioid-related deaths in Ontario: 1991 to 2015. March 2017.

@ODPRN_Research
www.odprn.ca

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ICES

Accidental opioid overdose increases when opioids are co-prescribed with gabapentin

60% Increase in odds of accidental opioid-related death when opioids are co-prescribed with moderate and high dose gabapentin compared to opioid use alone.

2x The risk of accidental opioid overdose nearly doubled with a co-prescription of very high dose gabapentin and opioids.

46% Of all gabapentin users were co-prescribed an opioid in 2013, making the risk of overdose particularly concerning as these drugs are often used together.

ODPRN

Gomes et al. Gabapentin, opioids and the risk of opioid-related death: A population-based nested case-control study. PLoS Medicine, 2017.

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PROFILE:

Ontario

Canadian Substance Use Costs and Harms

More information can be found at **www.csuch.ca**

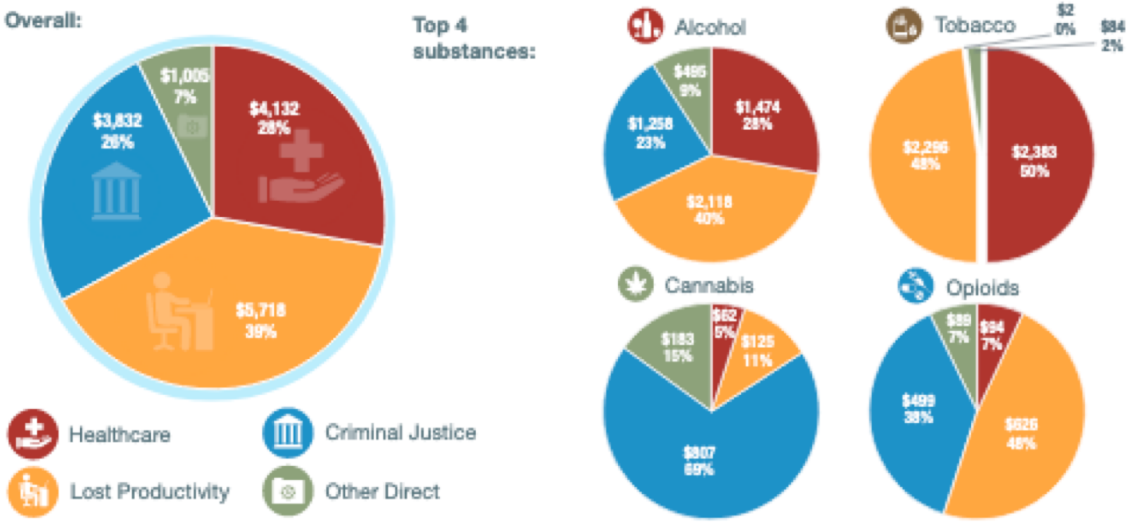
In 2014, substance use cost Ontario

$14.7 BILLION,

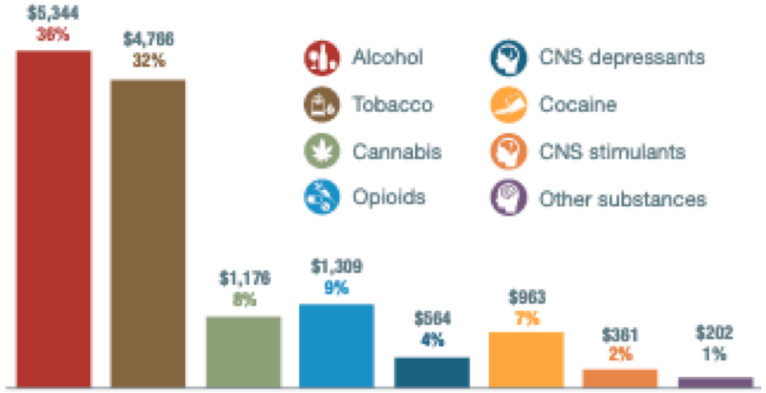
which amounts to $1,074 per person, regardless of age

Compared to $38.4 billion or $1,081 per person in Canada

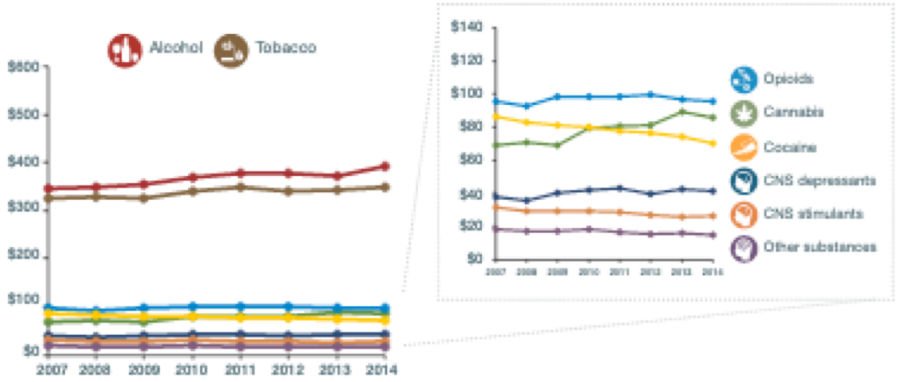
Costs of substance use by cost category in 2014 (in millions)



Overall costs by substance in 2014 (in millions)



Per person costs by substance over time



Canadian Centre on Substance Use and Addiction

University of Victoria | Canadian Institute for Substance Use Research

Suggested citation: Canadian Substance Use Costs and Harms Scientific Working Group. (2018). *Canadian substance use costs and harms in the provinces and territories (2007-2014)*. Prepared by the Canadian Institute for Substance Use Research and the Canadian Centre on Substance Use and Addiction. Ottawa, Ont.: Canadian Centre on Substance Use and Addiction.

Is Cannabis a Gateway Drug?

- The term “gateway drug” was popularized in 1984, during President Ronald Reagan’s renewed war on drugs
- Some studies have claimed that chronic cannabis use can lead to use of other illicit substances
- Recent studies have shown that *THC decreases cocaine-seeking behaviour/methamphetamine*, has no reinforcing effects on heroin use
- Animals studies have shown ***nicotine to be greater than THC in causing drug seeking behaviour***
- Too many factors (environment, genetic predisposition) to imply using cannabis will lead to using other substances
- Twin studies have shown that **approximately 50% of the vulnerability** for both beginning to use cannabis, and problematic cannabis use is genetically driven

“Simply stated, people who have used other drugs are more likely to have also used marijuana. Not the other way around” Drug Policy Alliance 2017

What We Do

Patient and Physician partnership in clinical research

Indications

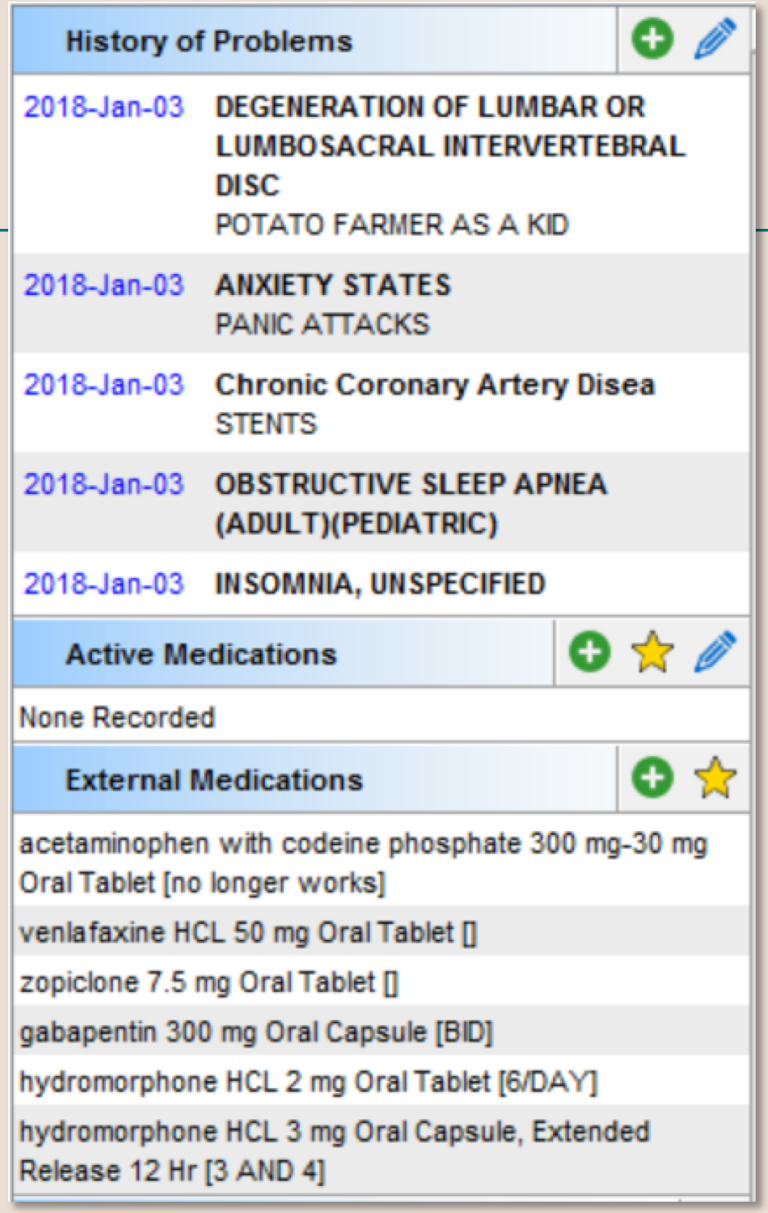
- Addiction
- Chronic Pain
- Anxiety
- Fibromyalgia
- Arthritis
- Autoimmune Disorders
- Insomnia
- Diabetes
- MS
- HIV
- Neuropathic Pain
- Alcoholism*
- Smoking Cessation*

Case

If we combine

pre-clinical, clinical, and patients' perspectives, medical cannabis can be applied to four broad categories:

1. Pain
2. Mood
3. Sleep
4. Autoimmune disorders



History of Problems

2018-Jan-03	**DEGENERATION OF LUMBAR OR LUMBOSACRAL INTERVERTEBRAL DISC** POTATO FARMER AS A KID
2018-Jan-03	**ANXIETY STATES** PANIC ATTACKS
2018-Jan-03	**Chronic Coronary Artery Disea** STENTS
2018-Jan-03	**OBSTRUCTIVE SLEEP APNEA (ADULT)(PEDIATRIC)**
2018-Jan-03	**INSOMNIA, UNSPECIFIED**

Active Medications

None Recorded

External Medications

- acetaminophen with codeine phosphate 300 mg-30 mg Oral Tablet [no longer works]
- venlafaxine HCL 50 mg Oral Tablet []
- zopiclone 7.5 mg Oral Tablet []
- gabapentin 300 mg Oral Capsule [BID]
- hydromorphone HCL 2 mg Oral Tablet [6/DAY]
- hydromorphone HCL 3 mg Oral Capsule, Extended Release 12 Hr [3 AND 4]

Harms of Cannabis

1. Lungs (if used by combustion)
2. Consuming THC and driving
3. Adverse reactions
4. Legal Harms
5. The greatest harm when using cannabis is misinformation and lack of education.

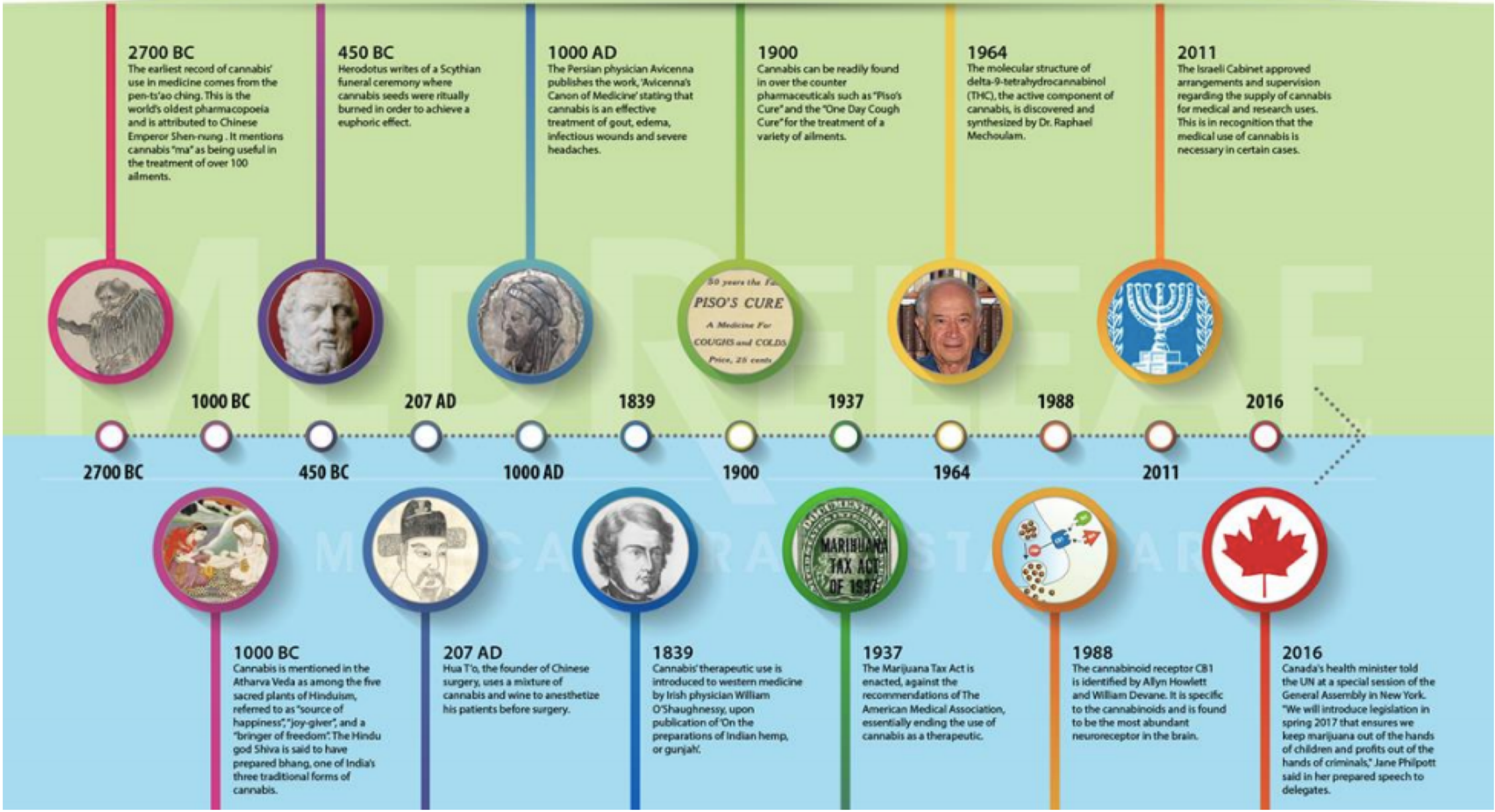
Table 4
Adverse events associated with cannabis-based medicines.

Side effect	Most common	Common	Rare
Drowsiness/fatigue	✓		
Dizziness	✓		
Dry mouth	✓		
Cough, phlegm, bronchitis (Smoking only)	✓		
Anxiety	✓		
Nausea	✓		
Cognitive effects	✓		
Euphoria		✓	
Blurred vision		✓	
Headache		✓	
Orthostatic hypotension			✓
Toxic psychosis/paranoia			✓
Depression			✓
Ataxia/dyscoordination			✓
Tachycardia (after titration)			✓
Cannabis hyperemesis			✓
Diarrhea			✓

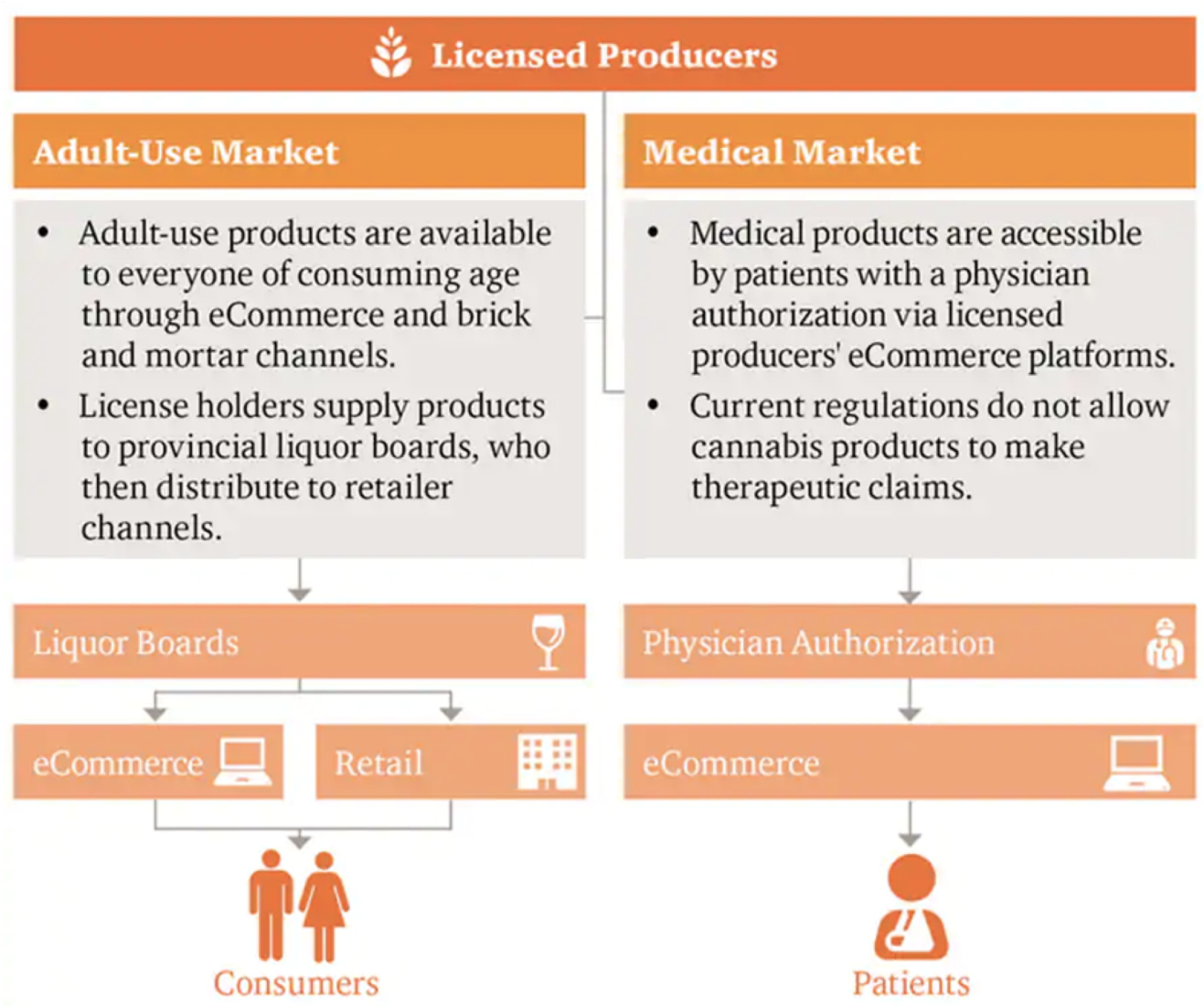
Medical & Recreational Cannabis

- *What is the Difference?*

TIMELINE OF MEDICAL CANNABIS



Recreational vs. Medical Overview



** Exception: Saskatchewan*

Medical vs. Recreational

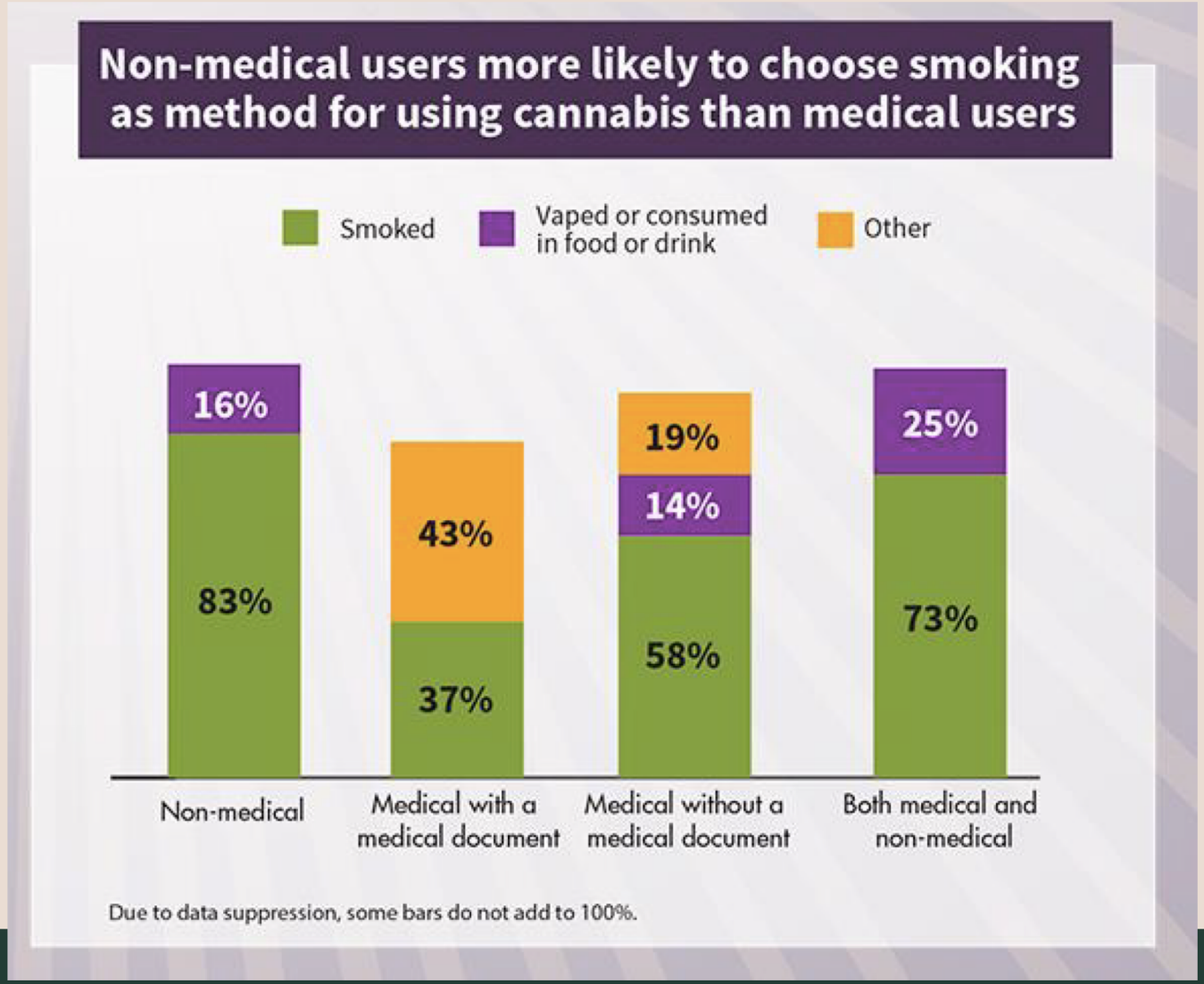
Medical Patients:

- Are educated on cannabis and follow authorization advice provided by their certified Health Care Provider to ensure safe and effective use.
- Consume cannabis to help reduce other harmful and addictive medications (opioids, benzodiazepines, etc).
- Ingestion is preferred method.
- Average age of Medical User >50 y/o.

Recreational Consumers:

- Receive limited information from retailers (by regulation).
- May use both medical (if authorized) and recreational cannabis.
- Not tracking how much recreational cannabis is consumed.
- Average age of Recreational User >19+.

“Smoke 2 doobies and call me in the morning?”



Vaping risks

- No incidents in Canada YET!
- As of Sept. 11, the CDC reported **380** confirmed and probable cases across 36 states and the U.S. Virgin Islands
- Up from 193 in 22 states nearly three weeks ago.
- Vitamin E acetate!!

Routes

FORM	METHOD	BENEFITS	ONSET OF ACTION	PEAK EFFECTS	DURATION OF ACTION
DRIED CANNABIS (Flower)	VAPORIZATION	*+ Safer alternative for those who wish to avoid smoking* *+ Fast acting, can help with symptoms such as break through pain quicker than any other method* *+ Less cannabis needed for desired effects making it cost effective*	**0 – 10 mins**	**15 – 30 mins**	**3 – 4 hrs**
CANNABIS OIL	INGESTED ORALLY	*+ Alternative method for people who are not comfortable with vaporizing (smoking) dried cannabis* *+ Long duration of action allowing for prolonged medicinal effects* *+ Can be discreet with no odor* *+ Dosing can be precise*	**30 – 90 mins**	**2 – 4 hrs**	**4 – 12 hrs**
CAPSULES / SOFTGEL (Cannabis Oil)	INGESTED ORALLY	*+ Alternative method for people who are not comfortable with vaporizing (smoking) dried cannabis* *+ Long duration of action allowing for prolonged medicinal effects* *+ Can be discreet with no odor* *+ Dosing can be precise* *+ East to understand dose (but less precise)*	**30 – 90 mins**	**2 – 4 hrs**	**4 – 12 hrs**
CANNABIS ORAL SPRAY (Cannabis Oil)	ORALLY OR SUBLINGUALLY (UNDER THE TONGUE)	*+ Faster onset than ingesting oils/capsules (with shorter duration)* *+ Discreet with no odor* *+ Easy to understand dose being used*	**5 – 30 mins**	**45 mins – 2 hrs**	**3 – 4 hrs**
TOPICALS (Cannabis infused lotions / creams / balms)	APPLIED TOPICALLY	*+ Provides localized symptom relief* *+ Discreet and easy to use*	**30 – 90 mins**	**2 – 4 hrs**	**4 – 12 hrs**

Research

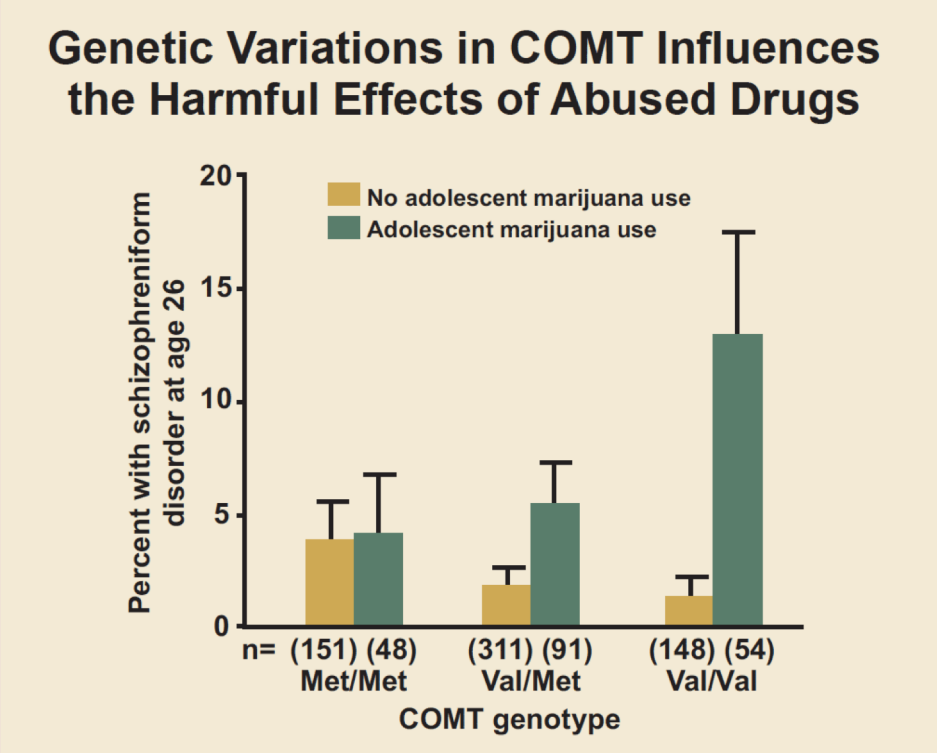
- *What Do We Know?*
- *What Don't We Know?*

Impact of Cannabis Use During Stabilization on MMT

- N=91 Men: 60, Female: 31
- Criteria > 18 yrs, (20-60 yrs) +UDS and >1 yr documented opiate use
- Cannabis and BZD use
- Objective ratings HIGH for cannabis use in induction and early stabilization
- Objective ratings of opiate withdrawal decreased in MMT patients using cannabis
- History of cannabis use correlated with cannabis use in MMT but did not natively impact induction

Schizophrenia

- Many studies published on an *association* between cannabis and schizophrenia
- The earlier & longer cannabis is used can increase chance of schizophrenia by 4-6x
- **Similar to addiction**, research is now **focused** on **genetics & environmental associations**
- Predisposition for schizophrenia, cannabis consumption can exacerbate symptoms and worsens the overall course of the illness
- Recent clinical trial (2018) using CBD with anti-psychotic medications showed decrease in positive symptoms, and increase in clinical well being (1000mg/day CBD) $$$$



Source: Caspi et al. *Biol Psychiatry*. 2005.

COMT gene - Catechol-O-methyltransferase
AKT1 gene
BDNF gene - brain-derived neurotrophic factor
CNR1 gene – may predispose people to schizophrenia & engage in cannabis use

Psychosis

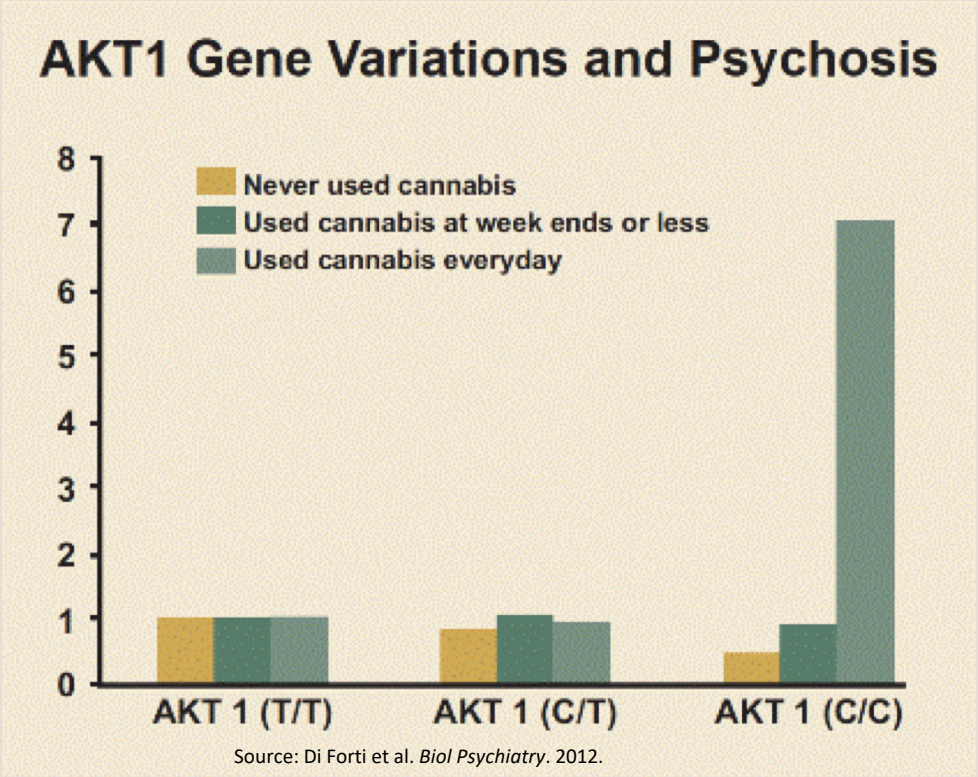
THC may cause *acute & transient effects* including suspiciousness, paranoid and grandiose delusions, conceptual disorganization, and illusions

- These effects can mimic short term psychosis
- Users vs non users have an increased chance of any psychotic episode (Odds ratio: 1.41)
- Users vs non users have an earlier onset of psychotic symptoms (average 3 years earlier)

Considerations:

- Studies factoring in behavioural, genetic and socio-economic factors show no correlation between cannabis use & psychosis
- Multifactorial causes of psychotic symptoms – cannot infer causation

CBD has been shown to reduced or prevent psychotic episodes



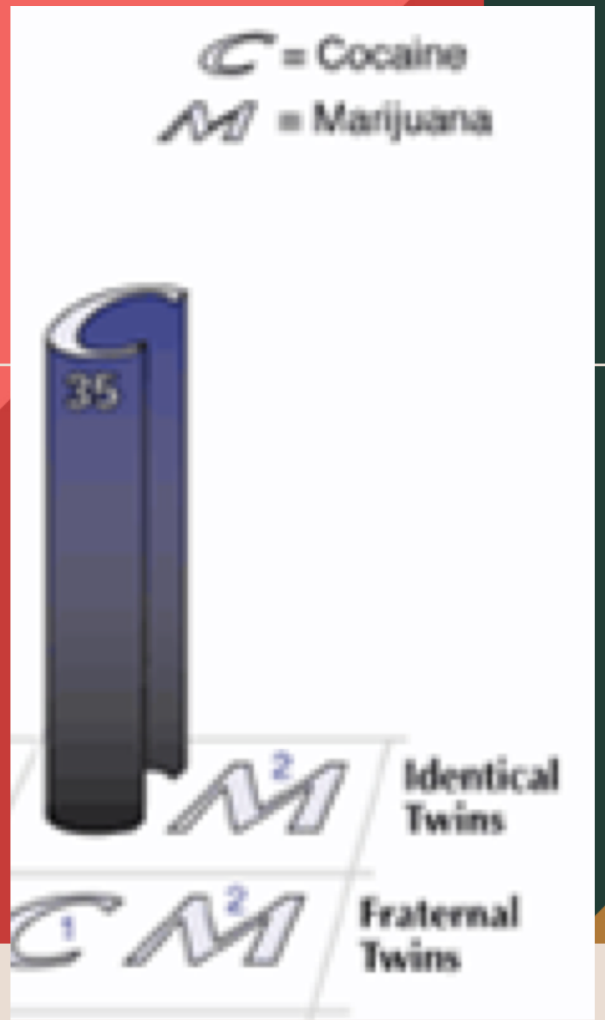
Source: Di Forti et al. *Biol Psychiatry*. 2012.

Metabolic effects of chronic cannabis smoking

- Chronic cannabis smoking was associated with visceral adiposity and adipose tissue insulin resistance

- NO hepatic steatosis insulin insensitivity
- NO impaired pancreatic b-cell function
- NO glucose intolerance.

The Cocaine/Cannabis study



- 1,934 twin sets studied
- 35% Identical twins (same DNA) - Dependence
- 1% Fraternal twins (different DNA) – Dependence

GENETICS ACCOUNT FOR 50-75% OF ADDICTION

Future research

Microdeletion in a FAAH pseudogene identified in a patient with high anandamide concentrations and pain insensitivity.

Abdella M. Habib[1,2], Andrei L. Okorokov[1], Matthew N. Hill[3], Jose T. Bras[4,5], Man-Cheung Lee[1,6,7], Shengnan Li[1], Samuel J. Gossage[1], Marie van Drimmelen[8], Maria Morena[3], Henry Houlden[5], Juan D. Ramirez[9], David L. H. Bennett[9], Devjit Srivastava[10],* and James J. Cox[1],*

Scientists find genetic mutation that makes woman feel no pain

Discovery in 71-year-old Jo Cameron may aid development of new pain relief treatments

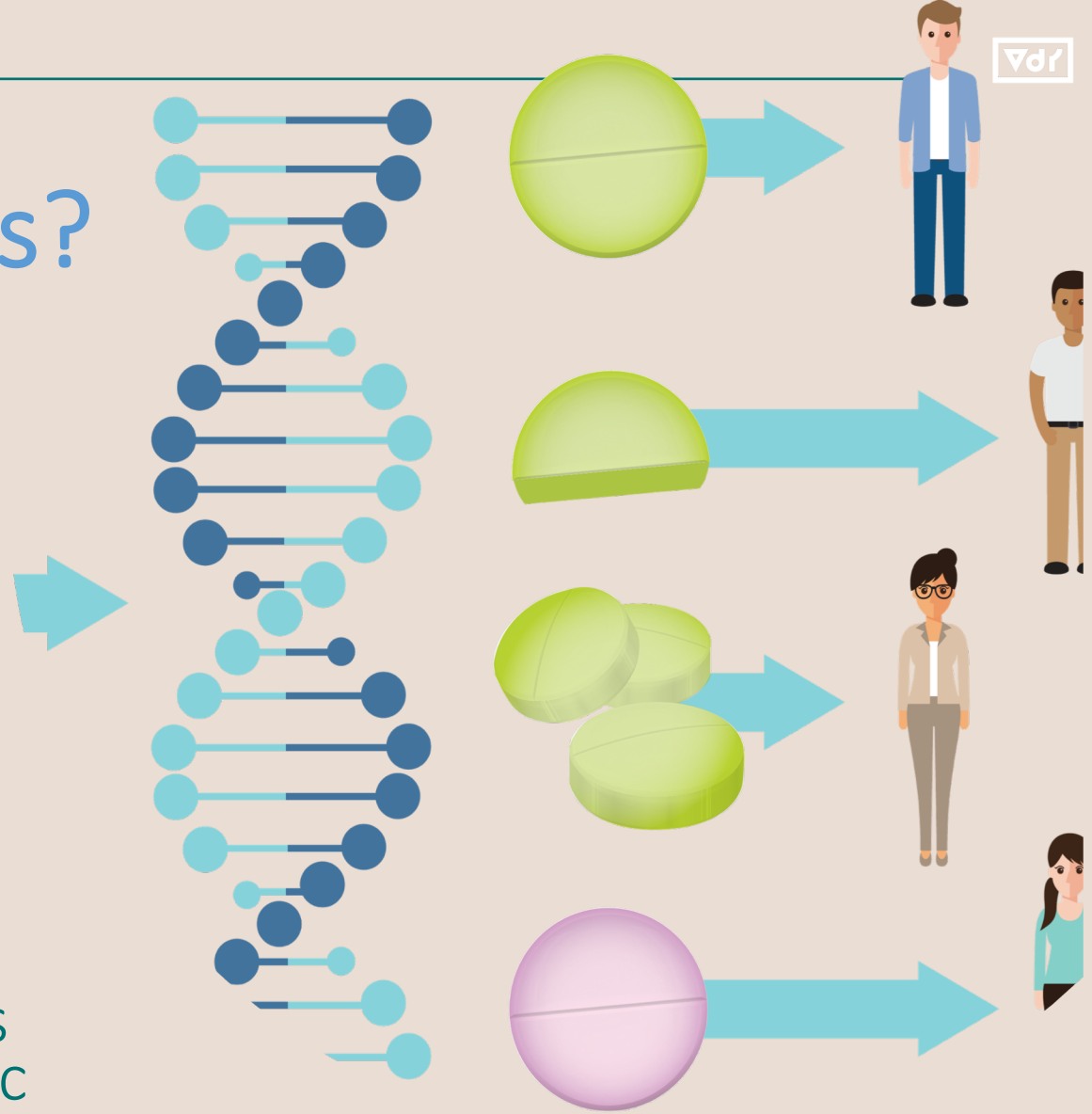
▲ Jo Cameron has experienced broken limbs, surgery and childbirth with little or no need for pain relief. Photograph: Mark Pinder/The Guardian

What is pharmacogenomics?

- The study of how genetic disposition affects a person's response to drugs.

- Pharmacology
- (the science of drugs)
+
- Genomics
- (the study of genes and their functions).

- Develop safe and effective medications and doses tailored to a person's genetic makeup.



Genes and Addiction

THE GENETICS OF ADDICTIONS: UNCOVERING THE GENES

David Goldman, Gabor Oroszi and Francesca Ducci

Impacts of *GRIN3A*, *GRM6* and *TPH2* genetic polymorphisms on quality of life in methadone maintenance therapy population

Ruey-Yun Wang[1,2☯], Hsiu-Ju Chen[3☯], Chieh-Liang Huang[2,4,5], Jiun-Yi Wang[6], Tsui-Er Lee[7], Hsiang-Yen Lee[8], Chin-Chuan Hung[3,9*]

Implication of *OPRM1* A118G Polymorphism in Opioids Addicts in Pakistan: In vitro and In silico Analysis

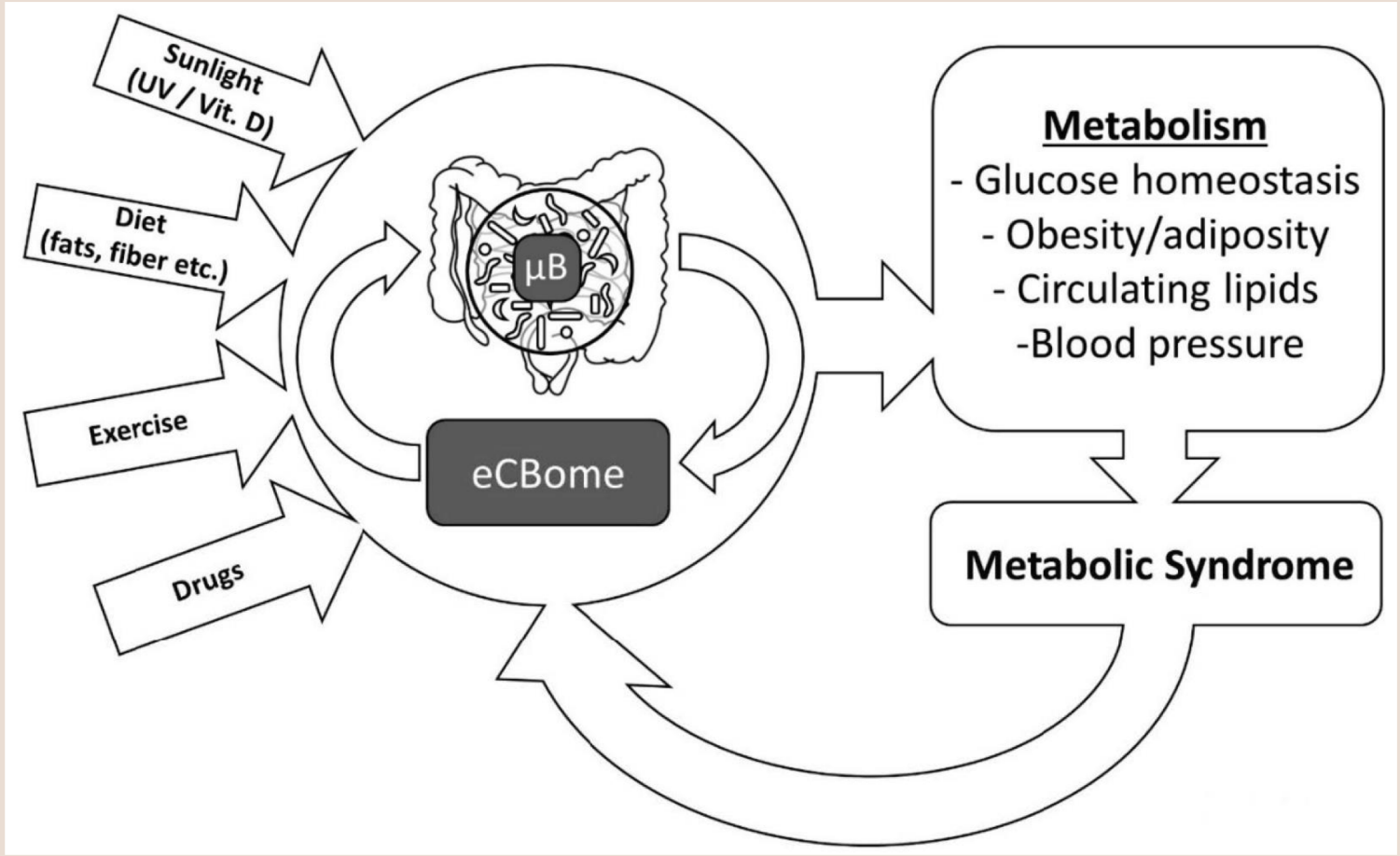
Madiha Ahmed[1] · Ihsan ul Haq[1] · Muhammad Faisal[2,3] · Durdana Waseem[1] · Malik Mumtaz Taqi[4]

Several clock genes polymorphisms are meaningful risk factors in the development and severity of cannabis addiction

Raphael Saffroy, Genevieve Lafaye, Christophe Desterke, Elisabeth Ortiz-Tudela, Ammar Amirouche, Pasquale Innominato, Patrick Pham, Amine Benyamina & Antoinette Lemoine

- Addiction has a **strong genetic** component and often ‘runs’ in the family.
- Understanding the prevalence of ‘addiction genes’ within patients will reveal better treatment strategies that may increase the chance of sobriety.

Diabetes


Sunlight
(UV / Vit. D)
Diet
(fats, fiber etc.)
Exercise
Drugs
µB
eCBome
Metabolism
- Glucose homeostasis
- Obesity/adiposity
- Circulating lipids
-Blood pressure
Metabolic Syndrome

The Future

Research Support on the Horizon!

- Canadian Institute of Health Research (Integrated Cannabis) Research Strategy)
- CIHR Neuroscience
- Mental Health and Addiction (INMHA)
- Institutes of Cancer Research (ICR)
- Circulatory and Respiratory Health (ICRH)
- Human Development, Child and Youth Health
- Indigenous Peoples health
- MSK Health and Arthritis

Moving Forward

- Research as it relates to an better understanding of the mechanism of action
- Pharmacogenomics
- Metabolomics
- Reducing harm
- Improving QOL
- Improving resiliency
- Patient experience

Questions?