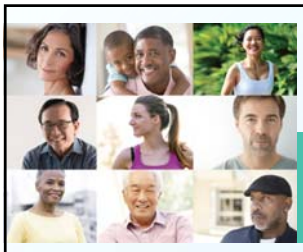


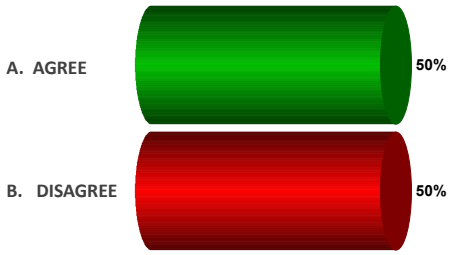
banyan
work health solutions

Medical Cannabis: a real medication or an excuse to get high?

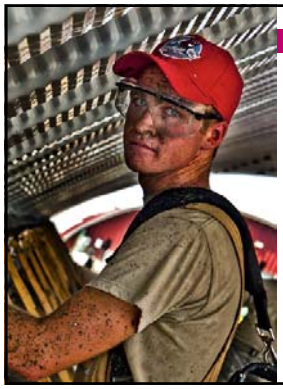
pillcheck DISCOVER PRECISION

60

I believe that medical cannabis is not a real medication. It's an excuse to get high.



Sometimes, drugs do not work the way they are supposed to



Frank

Works as
Field Technician

26 years old
Workplace injury

As a result of this accident:

- Chronic pain
- Took too much Tylenol 3
- Took too much Oxycodone
- Partial relief for only a short time.

Daily Mail .com health

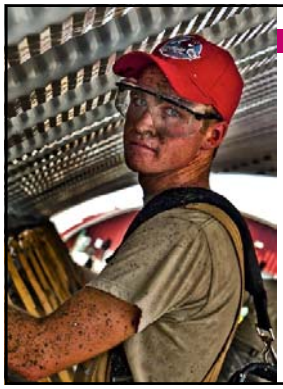
Why codeine painkillers don't work for millions - and may even harm your health

- Up to six million Britons do not produce enzyme CYP2D6
- It breaks down codeine into morphine to provide pain relief
- Pain killer codeine is the tenth most prescribed drug in the UK

By JO WATERS
PUBLISHED: 22:00 BST, 30 December 2013 | UPDATED: 09:13 BST, 31 December 2013

Frank

Pharmacogenetic report revealed that Frank is an "Rapid Metabolizer" of Codeine and Oxycodone



Frank

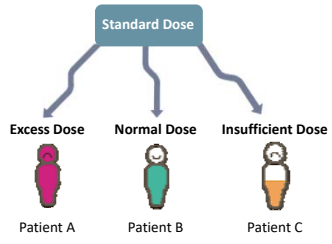
Based on report results, Frank was prescribed non-opioid medication in the 'green' category plus cannabis

PGx report = Better pain relief and shorter time off work

+

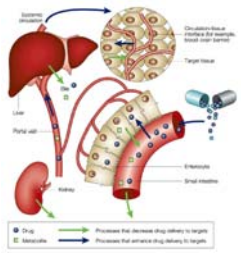
Ability to lead normal life

A medication and dose that works for one patient may not work for another



Why do drugs affect people differently?

What happens after we swallow that pill?



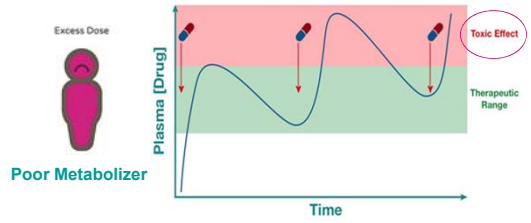
To be effective, the medication needs to be:

- **A**bsorbed
- **D**istributed
- **M**etabolized
- **E**xcreted

…at specific rates

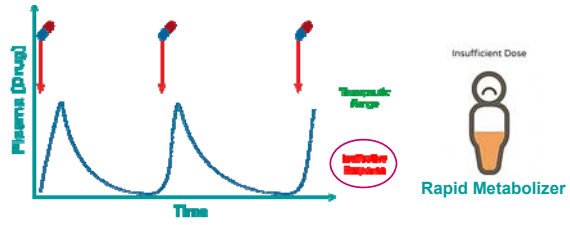
That is why medications are prescribed at regular dosing intervals

One person could be clearing a medication very slowly…



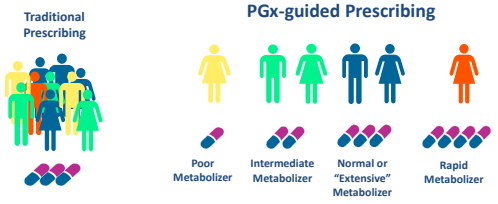
….leading to a build-up of the drug in the plasma, resulting in side effects

…while another could process the same medication too fast



…..and the standard dose is not effective

Pharmacogenetic-guided prescribing can optimize medications



Commonly used medications

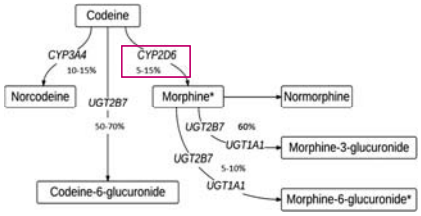
DRUG	GENE	ADR's
Codeine	*CYP2D6* Activation	Respiratory depression
Morphine	*OPRM1* Receptor interaction	**Response to ALL opioids**
Oxycodone	*CYP2D6* Activation	Adverse cardiovascular events
Celecoxib	*CYP2C9* Clearance	

...and Cannabis!

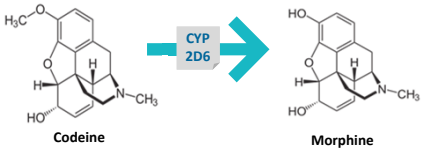
Opioids

Codeine

Indications: Relief of mild to moderate pain
Pro-drug: Metabolized to morphine



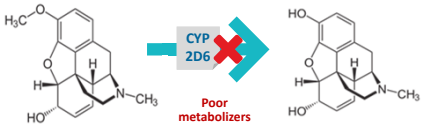
Codeine metabolism: CYP2D6



Codeine **Morphine**

Normal Dose

CYP2D6 and codeine metabolism



Codeine

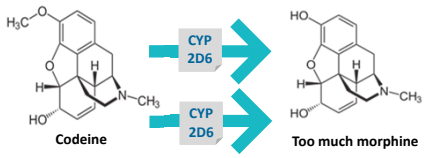
Poor metabolizers

No Morphine

Insufficient therapeutic effect
Pain

Insufficient Dose

CYP2D6 and codeine metabolism



Codeine

Too much morphine

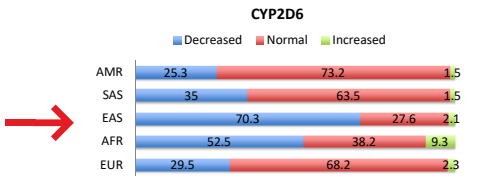
Excess Dose

Ultrarapid metabolizers

Intoxication:
Sedation, Respiratory depression

Pop Quiz! True or False?

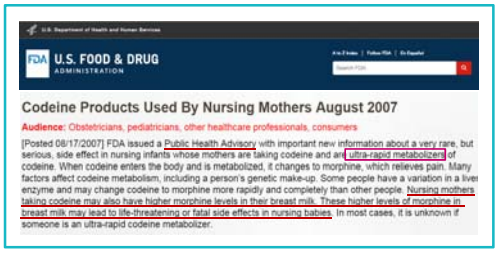
Based on the worldwide distribution of CYP2D6, East Asians have the highest chance of having **no response to codeine**.



AMR: Admixed Americans, SAS: South Asians, EAS: East Asians, AFR: Africans, EUR: Europeans

CLINICAL PHARMACOLOGY & THERAPEUTICS | VOLUME 102 NUMBER 4 | OCTOBER 2017

Codeine



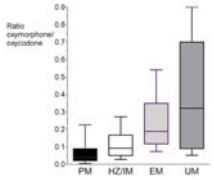
U.S. FOOD & DRUG ADMINISTRATION

Codeine Products Used By Nursing Mothers August 2007

Audience: Obstetricians, pediatricians, other healthcare professionals, consumers

[Posted 08/17/2007] FDA issued a Public Health Advisory with important new information about a very rare, but serious, side effect in nursing infants whose mothers are taking codeine and are ultra-rapid metabolizers of codeine. When codeine enters the body and is metabolized, it changes to morphine, which relieves pain. Many factors affect codeine metabolism, including a person's genetic make-up. Some people have a variation in a liver enzyme and may change codeine to morphine more rapidly and completely than other people. Nursing mothers taking codeine may also have higher morphine levels in their breast milk. These higher levels of morphine in breast milk may lead to life-threatening or fatal side effects in nursing babies. In most cases, it is unknown if someone is an ultra-rapid codeine metabolizer.

CYP2D6 Genotype Dependent Oxycodone Metabolism in Postoperative Patients



Plasma concentrations of oxycodone and oxymorphone dependent on CYP2D6 activity

Metabolite ratio oxymorphone : oxycodone
Lowest in Poor Metabolizer (PM) and highest in Ultrarapid Metabolizer (UM)

PLOS ONE | March 2013 | Volume 8 | Issue 3 | e60239

Morphine

Morphine (and fentanyl) exert their analgesic effect primarily via the μ-opioid receptor encoded by the *OPRM1* gene

The A118G variation in the *OPRM1* gene is present in 15% Caucasians and 40% Asians

Pain Physician 2015; 18:131-152 • ISSN 1533-3159

Systematic Review

The Impact of Genetic Variation on Sensitivity to Opioid Analgesics in Patients with Postoperative Pain: A Systematic Review and Meta-Analysis

PAIN MEDICINE

***OPRM1* A118G Gene Variant and Postoperative Opioid Requirement**

A Systematic Review and Meta-analysis

Anesthesiology 2014; 121:825-34

2 independent meta analyses on post-op pain and the variant A118G :

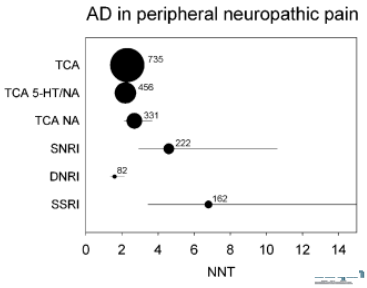
- Sample size 5902 and 4607 patients
- **Have higher opioid requirements**
- **Reported higher pain scores**

TCAs & SNRIs

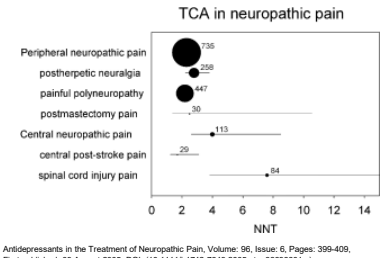
Antidepressants in the treatment of neuropathic pain

TCAs affect dopamine levels

SNRIs also affect dopamine



Antidepressants in the treatment of neuropathic pain



Antidepressants in the Treatment of Neuropathic Pain, Volume: 96, Issue: 6, Pages: 399-409, First published: 09 August 2005, DOI: (10.1111/j.1742-7843.2005.pto_96696601.x)

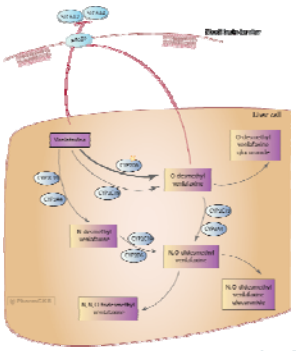
Venlafaxine

VEN> CYP2D6 > **ODV**

Poor and UM CYP2D6 metabolizers show reduced response

https://www.ncbi.nlm.nih.gov/books/NBK305561/

Desvenlafaxine is not dependent on CYP2D6



https://www.pharmgkb.org/pathway/PA166014758

NSAIDs

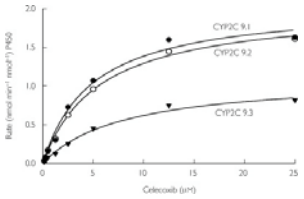
Pharmacogenetics of nonsteroidal anti-inflammatory drugs
The Pharmacogenomics Journal (2012), 462 – 467

Celecoxib

COX-2 selective inhibitor indicated for: acute pain, osteoarthritis, rheumatoid arthritis and ankylosing spondylitis

72-92% of celecoxib is metabolized by CYP2C9

Associated with a dose-related increase in cardiovascular events



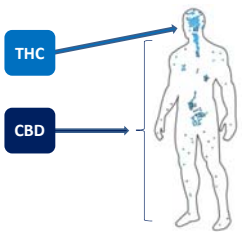
Other medications used in treatment of Pain

Gabapentin
An anticonvulsant that binds to voltage-gated calcium channels, leading to a reduction in the release of the neurotransmitters.
Demonstrated effectiveness in the treatment of diabetic neuropathy, post-herpetic neuralgia, trigeminal neuralgia, multiple sclerosis, migraine and chronic pain caused by malignancy. Gabapentin is not dependent on metabolism by the cytochrome P450 enzymes.

Cannabinoids
Delta-8-tetrahydrocannabinol (THC), the active component in cannabis, is responsible for its analgesic and psychoactive effects.
Effective in alleviating neuropathic pain associated with HIV, AIDS-related anorexia, central pain and spasticity associated with multiple sclerosis.

Cannabis & Cannabinoids

Cannabis and Cannabinoids



Clinical impact of cannabis metabolites

Metabolite/ reported effect	Δ8-THC	Δ8-THCV	CBD	CBN	CBC	CNDA	CBDV
Addiction	+						
Psychoactive	+						
Analgesia	+		+++		+		
Anti-inflammatory			+		+	+	
Antiemetic	+++						
Antipsychotic			+		+		
Antiepileptic		+	+				
Anxiety & sleep			+				
Bone stimulation		+			+		+
Hypothermia					+		

http://biochanvre.ch/info/en/IMG/pdf/Non-Psychoactive-Cannabinoids.pdf

Metabolism of Cannabinoids

	Δ^8THC	CBD	Nabilone*
CYP2C9	✔	✔	✔
CYP3A4	✔	✔	✔

***Poor CYP2C9 metabolizers show 3x increase in blood concentration of Nabilone**

https://link.springer.com/article/10.1007%2Fs13318-017-0416-z

Dosage challenges

- Dosing is highly individualized
- Relies on titration
- No precise dosage guidelines established
- Israel's medical marijuana program, 2011-2012 : **1.5 grams** of dried cannabis per day
- Dutch medical cannabis program, 2003-2010: average daily dose of dried cannabis used was **0.68** grams per day (range: 0.65 – 0.82 grams per day).

Health Canada recommendation:
maximum of 3 grams of dried cannabis/day

Source: https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-use-marijuana/information-medical-practitioners/information-health-care-professionals-cannabis-marihuana-marijuana-cannabinoids.html

Forms of consumption







Canadian Licensed Producers

https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-use-marijuana/licensed-producers/authorized-licensed-producers-medical-purposes.html

US situation

Summary: PGx influences therapeutic choices

	Morphine Hyrdomorphone Fentanyl Meperidine	Oxycodone Tramadol	TCAs	NSAIDs	Cannabis
CYP2D6-PM	✓	X	X	✓	✓
CYP2D6-UM	✓	X	X	✓	✓
ORPM1-PR	X	X	✓	✓	✓
CYP2C9-PM	✓	✓	✓	X	X

PM -poor metabolizer, UM -ultrarapid metabolizer, PR -poor responder

Jimmy

Chronic pain following motor bike accident

Prescribed upon intake:

Oxycodone Morphine + Nabilone THC = Uncontrolled pain & nausea

Jimmy

Does not convert Oxycodone to more active from
And resistant to opioid therapy

Oxycodone — CYP2D6 IM (X) — **Reduced activation Lower analgesic effect**

Oxycodone Morphine — **OPRM1 A118G** — **> Resistance to Opioids**

Jimmy

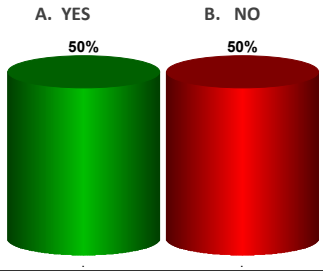
He was referred to multidisciplinary pain management program that included psychotherapy to learn how to cope with pain, along with physiotherapy, participate wood workshop.

Medications: cannabis vaporizer along with desvenlafaxine instead of using two opioids and THC

Case Management Considerations

60

Can someone taking medical cannabis return to work operating equipment?



Consumption considerations for RTW

Smoking is but 1 delivery method form of medical cannabis. Other options include:

- Low THC/high CBD strain
- THC at home/CBD at work
- Smoke at home/oil-spray-pill at work

If taking high THC dose, treat as with any other opiate – ensure safety:

- Do not drive or perform hazardous tasks 4-6 hours after taking THC
- What else can be done to ensure safety and accommodate the employee?

The facts

Medical accommodation does not override existing laws. It is illegal to:

- Smoke in the workplace, in restaurants, 9 meters from public doorways;
- Consume cannabis in public;
- Possess cannabis on your person.

The duty to accommodate extends to employees using medical cannabis.

Ensuring safety in the workplace

- Multidisciplinary pain management program
- Functional Abilities Evaluation

→

- Temporary accommodation in other role
- Long term work accommodation

- Medical Cannabis IME

→

- Evaluate dosage, form of consumption
- Identify red flags
- Ensure safety in the workplace

Red flags – work on visuals

- Patient is under age 25
- Uses > 3 grams/day
- Sudden increase in dosage (addiction?)
- No regular FU with prescribing physician
- No dosage decrease in other prescription drugs
- Orders from multiple providers
- Orders from unlicensed producer
- Lack of confirmation of LP verification card

Summary

- PGx can help guide prescribing in pain management
- Opioids should be administered with caution
- Consider patients response to a variety of therapeutic options including opioids, TCAs, SSRIs, SNRIs, NSAIDs and cannabinoids
- PGx–guided therapy can reduce utilization of opioids, improve pain management and reduce risk of addiction.
- Question :
  - Dosage & form of consumption
  - Source of product

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THANK YOU

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