Over the counter, down the hatch
OTC codeine use

Dr Matthew Frei
Clinical Director
OTC analgesics

• OTC codeine: a reflection
• Pharmaceutical opioids
• Over the counter...
• The special case of codeine
• Treatment of codeine dependence
2007: A REFLECTION
What’s going on?

- NSAID related presentations
- 24, 48 & 96 tablets a day
- Clinical “fingerprint”
Mr CT, 50-years old

• Presents to ED with 6 months pallor and fatigue

• Past history
  • Anaemia & GU on endoscopy
  • Chronic back pain initially oxycodone, OTC codeine when this was ceased
  • “NSAID related ulcer”, initially no referral to AOD
Mr CT, 50-years old: investigations

- K+ = 3.1
- Cr=0.05
- Hb=110
- Abnormal LFTs
Mr CT

- Taking 48 OTC ibuprofen-codeine tablets daily for 6 months
- Commenced treatment with buprenorphine-naloxone
- Good outcome to therapy
PHARMACEUTICAL OPIOID ADDICTION
21st Century Substance Use

- Polysubstance abuse
- Methamphetamine
- Hybrid & “medicinal” cannabis markets
- New devices
- “Novel psychoactive substances”
- Pharmaceutical drugs
  - benzodiazepines
  - opioids
Heroin-related deaths: Victoria, 2001-2014

Source: Victorian Department of Health, 2014
Hospital separations & AOD Tx

2 Indicators of harms associated with “other opioid”* and heroin use in Australia†

(A) Hospital separations for opioid poisoning

(B) Treatment episodes for problems related to morphine, oxycodone and heroin

*Morphine, oxycodone, and codeine. †Data obtained from the Australian Institute of Health and Welfare’s Alcohol and Other Drug Treatment Services National Minimum Dataset and National Hospital Morbidity Database.

Roxburgh et al. 2011 MJA

www.turningpoint.org.au
How effective is long term opioid therapy for non-malignant pain?

- Limited evidence for benefit of opioids, particularly at doses above 90mg morphine equivalent

- Growing evidence for risk:
  - Addiction (5-20%)
  - Toxic overdose
  - Cognitive problems
  - Opioid induced hyperalgesia (OIH)
There are few treatments with so little evidence of effectiveness that kill so many people

Tom Frieden
NEJM 2016
MISUSE OF OTC MEDICATIONS
OTC medication abuse

- Dextromethorphan abuse¹
- Codeine abuse and dependence²
  - Combination analgesic/cough medicine abuse
- Other OTC medication misuse³ & tampering⁴
  - Cold Water Extraction
  - Homebake morphine/heroin
  - Loperamide

4. Fleming et al Subs Use Misuse 2003; Cone Drug Alc Dep 2006
Australia’s love affair with OTC analgesia

- 1950s-70s: Australia leads in analgesic nephropathy with phenacetin combination products
  - Papillary necrosis
  - Chronic renal failure
  - Peptic ulcer
  - Chronic blood loss anaemia
  - Hypertension
  - Dialysis, renal transplant, death*

* 3,000 deaths reported in medical literature
NHDS 2016

- 4.8% pharmaceutical drug misuse
  - About two thirds of this is opioids
  - Most popular opioid: codeine (OTC and presc)
  - Then oxycodone, tramadol, morphine
- Pharmaceutical opioid use stable up to 2013
- Likely to change with codeine rescheduling
- Mean age mid 40s M=F
- OTC codeine analgesics=$145m per year
THE SPECIAL CASE OF CODEINE
Codeine (methylmorphine)

- WHO analgesic ladder: “mild opioid”
- Codeine 60mg/paracetamol 1g only marginally better than paracetamol alone (NNT for 50% improvement of pain=6)
- Simple analgesia equally effective as low dose codeine

Problems of codeine in some populations

• Poor metabolisers vs ultra-rapid metabolisers
• Breastfeeding mothers
• Children


Has the time come to phase out codeine?

Codeine is, second only to morphine, the most widely used narcotic analgesic.1 Health professionals and the public generally believe that codeine, used responsibly, is safe. However, the potential risk associated with codeine must be mitigated. Clearly, pretesting all patients for genetic variants before recommending codeine would be expensive and impractical. A

[ Further text not visible in the image ]
Published studies of harm of OTC codeine analgesics

- Around 20 published reports since 2003
- 4 countries: UK, Ireland, Australia and New Zealand
- 250 cases reported
Published reports of harm: OTC codeine-ibuprofen

- Addiction
- Hypokalaemia: profound weakness, quadriplegia, life-threatening condition - ICU
- Rhabdomyolysis
- Renal tubular acidosis – renal failure
- Duodenal ulcer
- Gastric ulcer – perforated
- Opioid dependence
- Pyloric stenosis
- Profound iron deficiency anaemia
- Small bowel NSAID enteropathy, diaphragm disease, ulceration, iron deficiency anaemia, hypolbuninaemia
Case series (Frei et al. 2010, MJA)

- Hospital & AOD clinic presentations
- 27 cases of ibuprofen-codeine (200mg/12.8mg product)

Serious morbidity associated with misuse of over-the-counter codeine–ibuprofen analgesics: a series of 27 cases

Matthew Y Frei, Suzanne Nielsen, Malcolm D H Dobbin and Claire L Tobin

While extensive overseas evidence is accumulating about the non-medical use of prescription opioids, there are currently few reports of otc codeine–ibuprofen analgesics.

**ABSTRACT**

**Objective:** To investigate morbidity related to misuse of over-the-counter (OTC) codeine–ibuprofen analgesics.
Frei et al. 2010

- Most self initiated for pain
- “Morbidity of thirds”
  - 1/3 renal
  - 1/3 GI
  - 1/3 addiction
- Good response to buprenorphine-naloxone
It’s all about the combination
Coroner

• A timely reminder that the abuse of readily available or over-the-counter medication can be just as harmful as the abuse of illicit substances, and potentially even fatal
TREATMENT OF CODEINE DEPENDENCE
OTC opioid users are different

- Older than typical opioid users
- More women
- Often no history of other drug use, minority inj opioid use
- Commenced treatment for painful condition
- Respond to buprenorphine Rx


Australian Pharmacist March 2012. Nielsen, Tobin, Dobbin
Treatment of codeine dependence

- Good response to Suboxone pharmacotherapy program in this group
  - Cost competitive
  - Inconvenience competitive
  - Well-tolerated
- Risks of reduction/tapering of OTC analgesics
Upscheduling again?

• 7 years after 2010 upscheduling still a steady stream of cases
• Anecdotal reports of little change to availability
• Amounts now multiples of 20 rather than 24
Opioid maintenance therapy: methadone & buprenorphine

- Cost of OMT
- Stigma
- Restrictive programs
- Access to prescribers in Victoria
The future

• New formulations
  • Tamper/misuse deterrent forms
  • Depot buprenorphine & depot naltrexone
• Regulation, prosecutions & rescheduling
• Real time prescription monitoring
THANK YOU