

Opioid/Opiate & Chronic Pain

Misuse & Addiction...

Pain and Sleep Interaction

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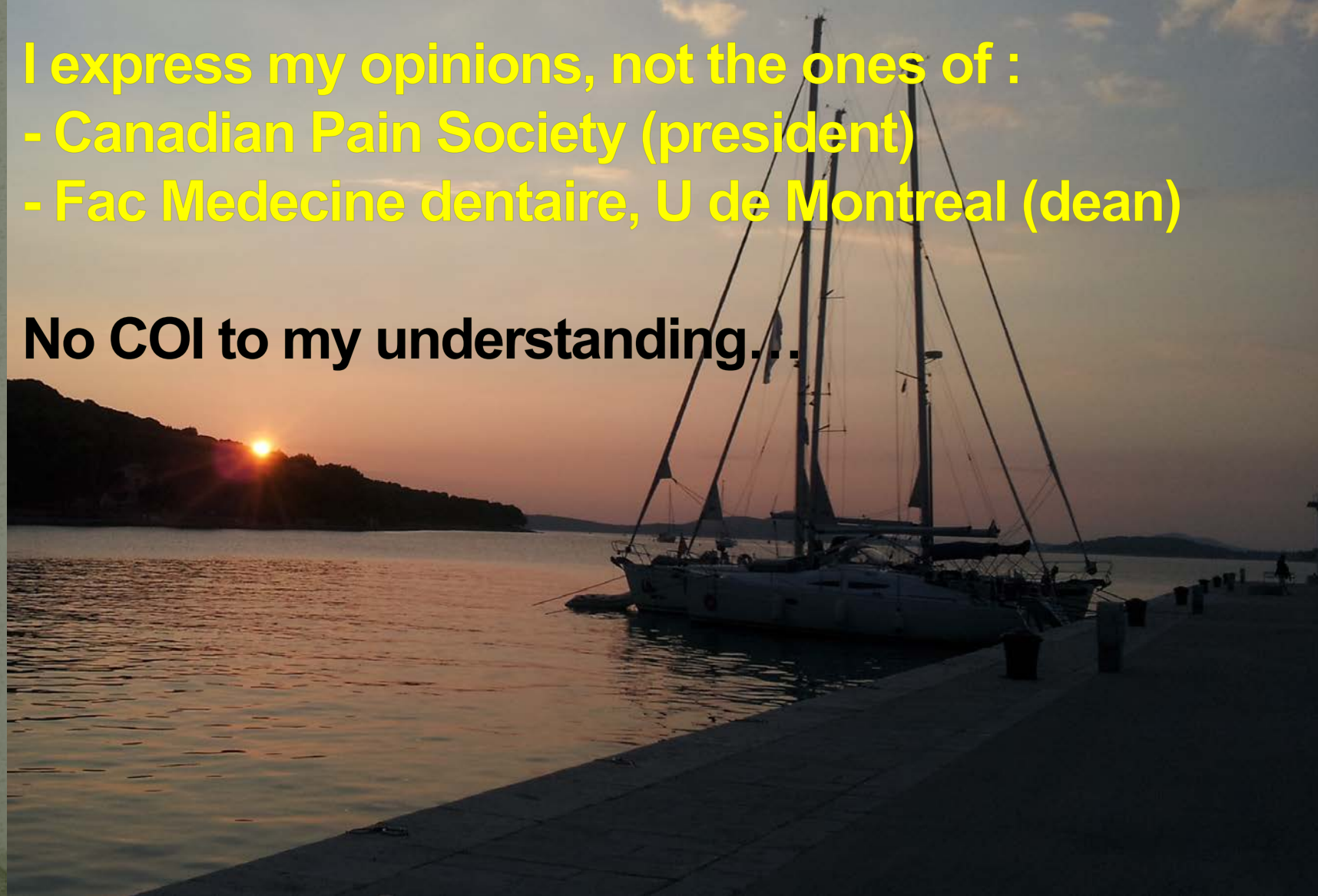
IMHA- Vancouver 2014

Gilles Lavigne

I express my opinions, not the ones of :

- Canadian Pain Society (president)**
- Fac Medecine dentaire, U de Montreal (dean)**

No COI to my understanding...



Key Points: 20 % & 5% to remember

- 20 % population in Canada have CHRONIC pain (Boulanger et al 2007; Reitsma et al 2011) // female = risk is greater (Velly et al 2003; Reitsma et al 2013)
- 1/5 of chronic pain patients use OPIOIDS (Percocet, Percodan, Tylenol 3, Dilaudid, Oxycontin, codeine...)
- 4.5% = Addiction prevalence in non cancer chronic pain population (Minozziet al 2013)
- 5%= Misuse of medication in Canada & USA

Definitions

Medication misuse: use of a medication (prescribed for a medical purpose) other than as directed or as indicated... (Denisco et al, J Am Dent Ass 2011)

Misuse may involve a patient taking **more pain medicine than prescribed up to diversion** (selling or giving own pills).

It may lead to abusive behaviors and ultimately to abuse and addiction.

ABUSE: use of illegal drug or intentional self administration of medication for non medical purpose (get a high)

ADDICTION: neurobiological disease...genetic, psychosocial & environmental factors...

Behaviour / compulsive use (reward system)

We know a little about these

Physical dependence: state of adaptation..... Withdrawal syndrome risk...

**Canadian Research Initiative in
Substance Misuse / **CRISM***
from **CIHR** and **INMHA**
(with other institutes) =
NODES (3-4)
and eventually **Network (1-2)****

*** 2014-5 grant to our PAIN & Opioid group and now
in process**

Morphine is a family of major analgesic- *pain killer* prescribed in post-operative, emergency & chronic pain medicine

Street / (pharmacy) names

M, morph (for morphine)

meth (for methadone)

percs (for Percodan, Percocet)

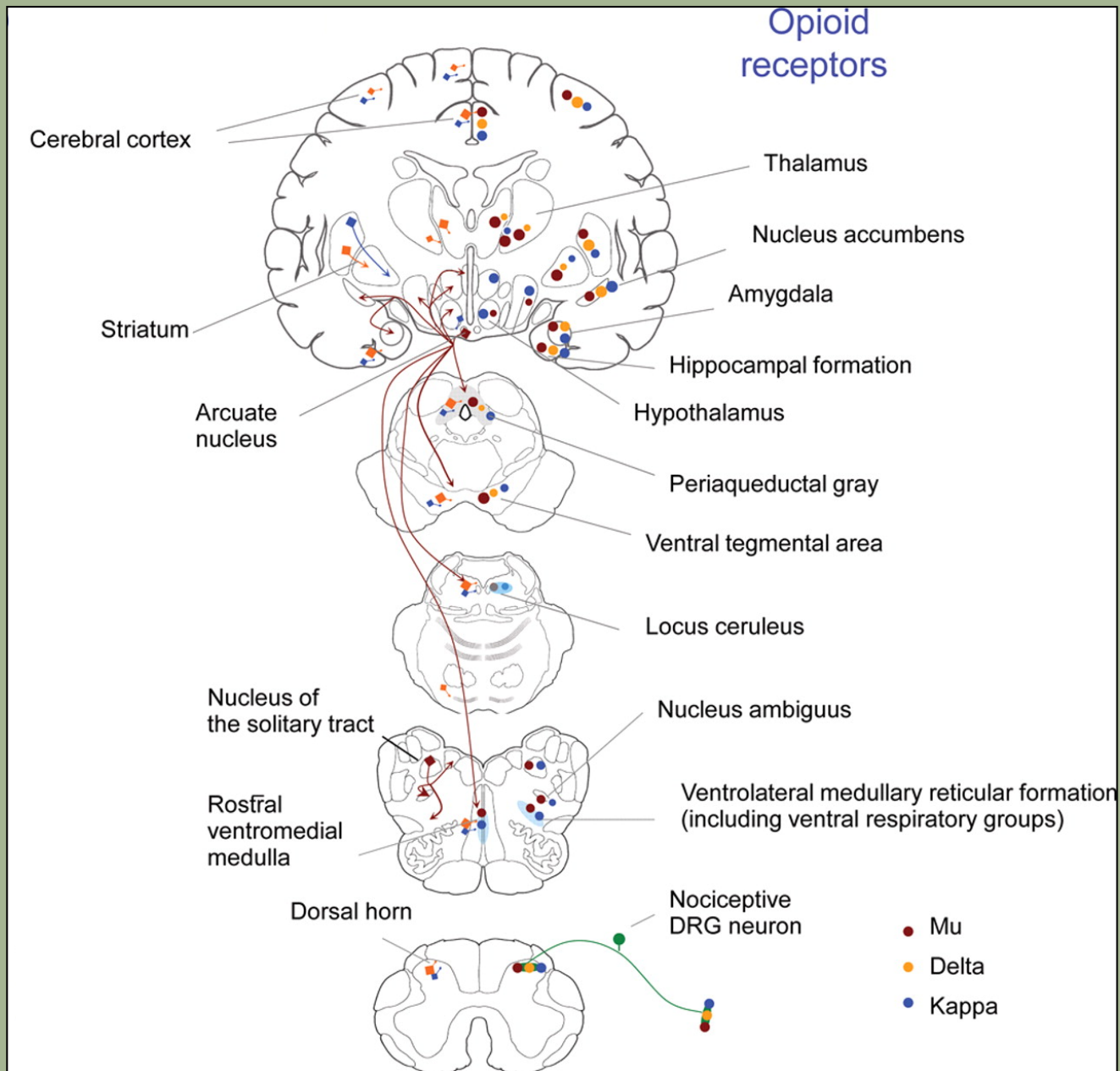
juice (for Dilaudid)

oxy, OC,

hillbilly heroin (for OxyContin)



Figure 2 – Distribution of the opioid receptors



The mesocorticolimbic system: *Probably not overactive, lack of ABS brakes...* P Schweinhardt

Reward evaluation

Attention
Judgement

Prefrontal
cortex

Nucleus
accumbens

Cingulate gyrus

Striatum

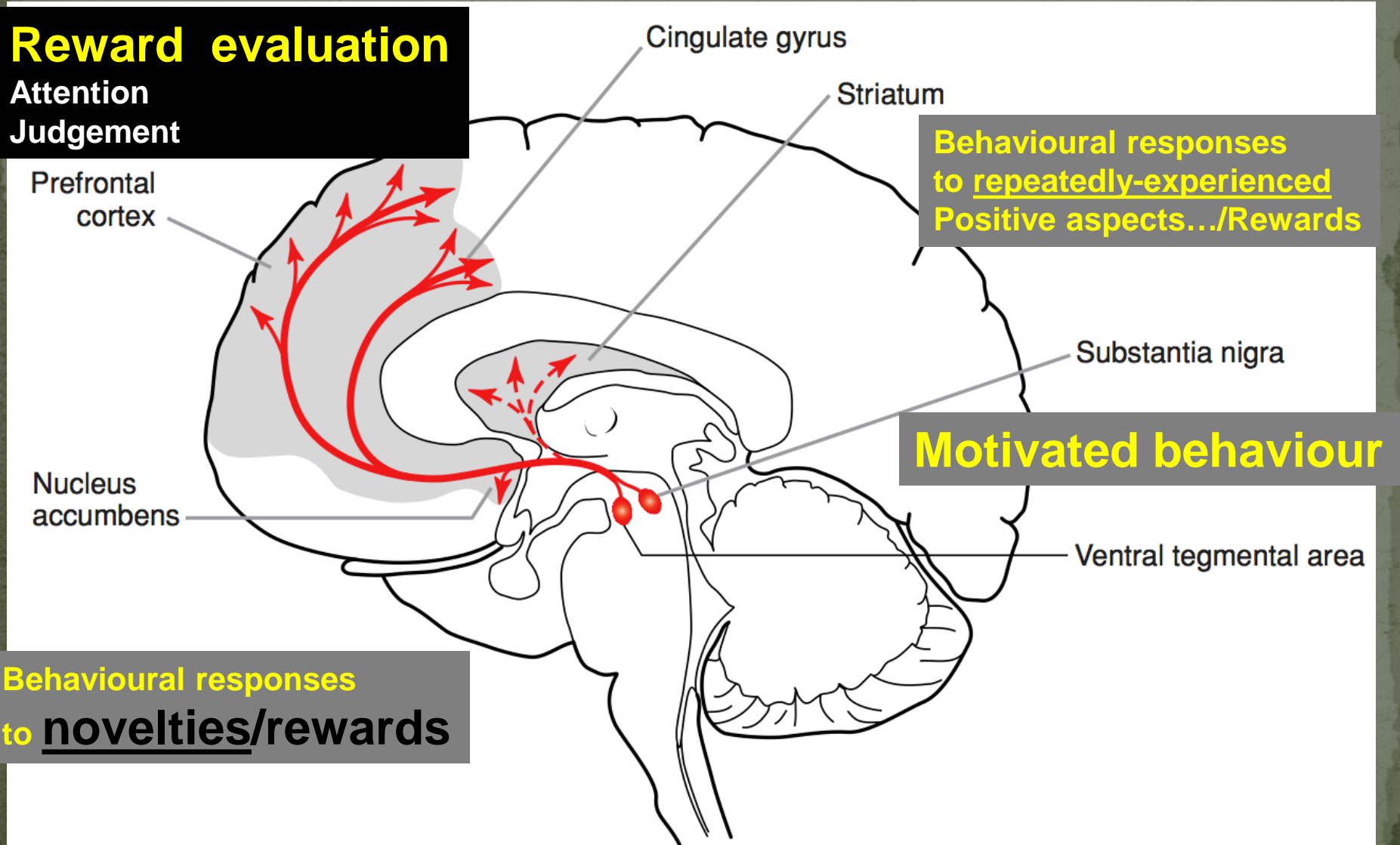
Behavioural responses
to repeatedly-experienced
Positive aspects.../Rewards

Substantia nigra

Motivated behaviour

Ventral tegmental area

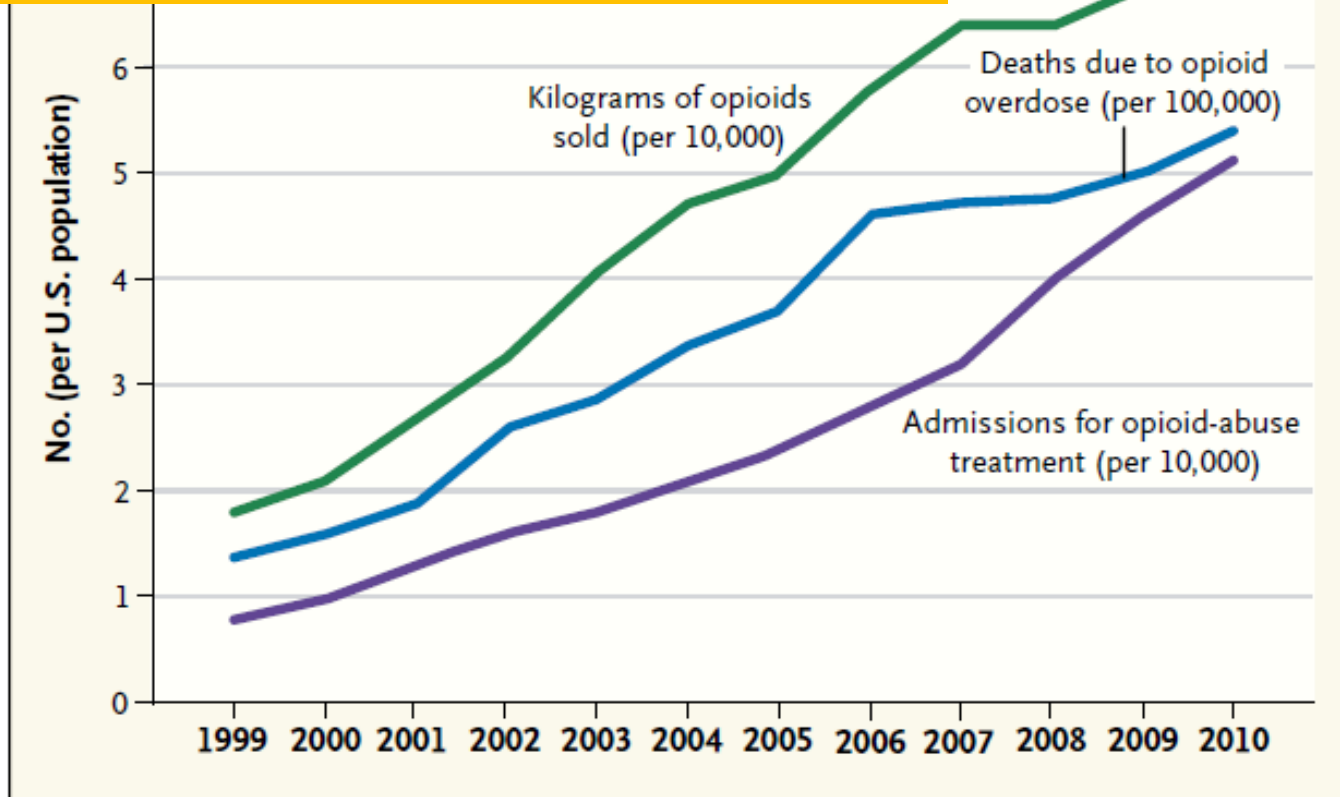
Behavioural responses
to novelties/rewards



Adapted from Hyman et al., 2006 by Dr A Samaha, Uni Montreal

YES Opiate use is growing, pain and aging also...

Tackling the Opioid-Overdose Epidemic
Volkow, ND, NEJM 2014



Opioid Sales, Admissions for Opioid-Abuse Treatment, and Deaths Due to Opioid Overdose in the United States, 1999–2010.

Data are from the National Vital Statistics System of the Centers for Disease Control and Prevention, the Treatment Episode Data Set of the Substance Abuse and Mental Health Services Administration, and the Automation of Reports and Consolidated Orders System of the Drug Enforcement Administration.

In Canada: Ongoing Law Project

Canada Gazette, June 28, 2014

CONTROLLED DRUG AND SUBSTANCE ACT

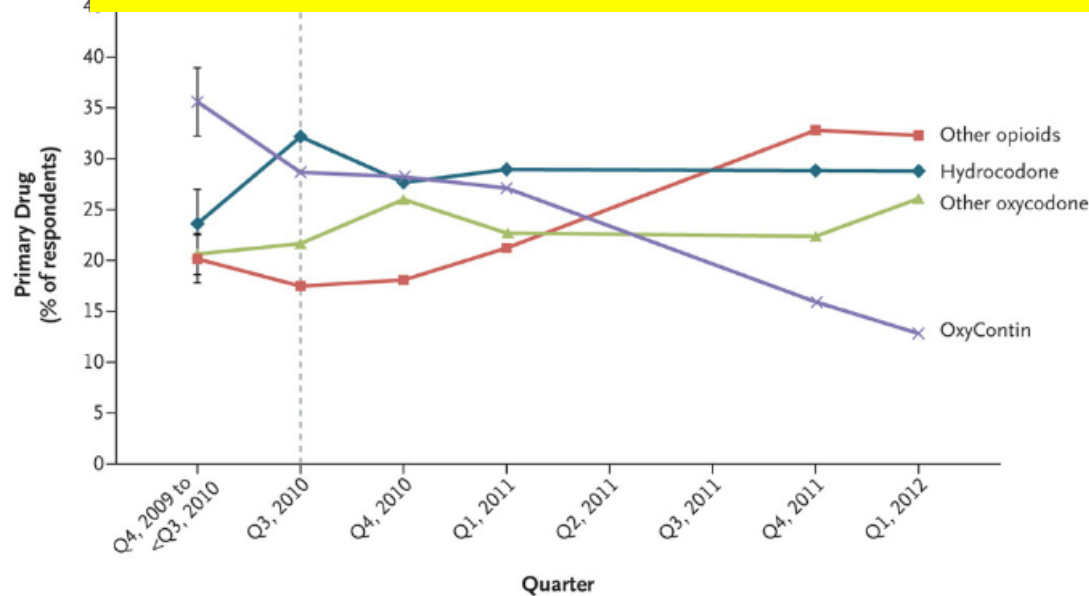
Proposal on **Tamper Resistance Properties** ++

BUT:

- Do they have the same EFFICACY as usual Pain Medication?
- Heroin use may rise if no EFFECTIVENESS?

Addiction Medicine should not drive but collaborate with Pain Medicine based on EVIDENCES

Reduction of 1st choice from 36 to 13% when Oxy is Tampered – Cicero TJ, NEJM, 2012

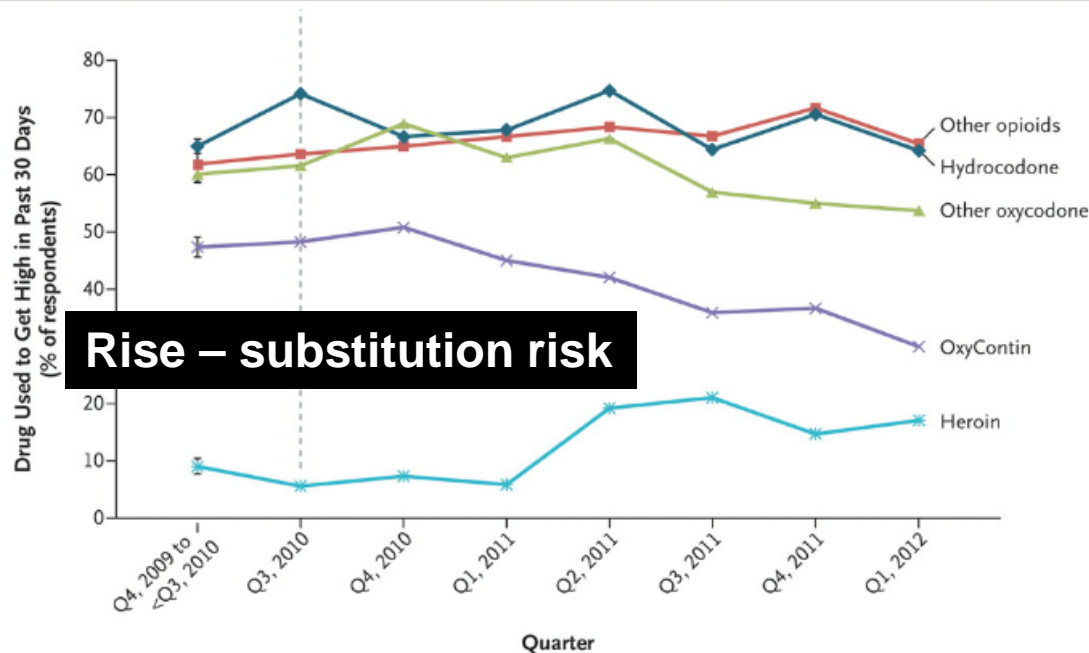


OxyContin.

Panel A shows the percentage of respondents in each quarter who selected a specific prescription opioid as their primary drug (used most often and preferred over all others).

Respondents could make only one choice. Heroin was not included as a primary drug to limit the population to those who primarily used prescription opiates. Panel B shows the use of opioids to get high at least once in the past 30 days from July 1, 2009, through March 31, 2012.

Respondents could select as many drugs as were applicable, and hence the percentages sum to more than 100. In both panels, the dashed vertical line represents the quarter in which the abuse-deterrent formulation of OxyContin was introduced, and the first point the mean (\pm SE) for the four quarters before the introduction of the abuse-deterrent formulation.



Rise – substitution risk

First exposure to Misuse Risk: our healthy teenagers... Oral surgeries, trauma...

- Oral surgeries (3rd molar) in USA: **1st choice Ibuprofen**
but 80% also Rx opioids in parallel (**64%= hydrocodone + acetaminophen**)
- 3.5 millions (Oral Surgeons only) tooth extractions in **20 years old patients = 1st exposure to opioids**


Main source of MISUSE is
family members & friends
(55%) or Rx (17%) / 2009 Nat Survey
on Drug Use and Health, USA...

Over prescription =

- Risk of Rx opioids Left Over in over 72%
cases (Utah data, 2010)
and Left Over in dentistry 41% (10-20 pills per
Rx) = risk Misuse

Research Agenda: Collaborative work needed

**(Extracted from IMHA Network for Canadian Oral Health Research /
Workshop on Chronic Orofacial Pain and literature)**

- 
- Survey the situation in Canada / ongoing
 - Team work (medicine, dental, pharmacy, nurses, etc)
 - Stimulate collaboration between Addiction and Pain Medicines
 - Education to trainees and practicing doctors and follow trend / (Health Canada grant summer 2014)

Research Agenda: Collaborative work needed

- Research on reward – addiction mechanism
AND Pain Relief EXPECTATION /
- Research on drug delivery system: (Tamper Resistant) / Pharma driven – our role?
- Research on role anxiety to pain, risk
chronicisation, sleep/insomnia as a risk factors, etc
- Implement prevention/friendly protocol for clinicians

Chronic pain = Non Restorative Sleep or sleep restriction (shorter duration)?

- About **2/3 of patients** with chronic pain also complain of poor sleep quality and/or un-refreshing sleep sensation
- This is reported by about 50% of orofacial patients and up to 70% OA & 60-90% of *fibromyalgia (FM)*- chronic widespread pain (CWP) patients

Chronic pain & FATIGUE

Deprivation of sleep or Non Restorative Sleep ?

- Non restorative sleep (NRS)

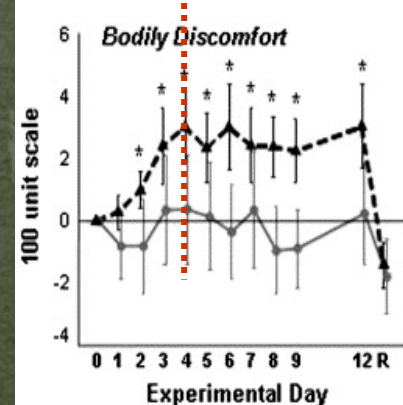
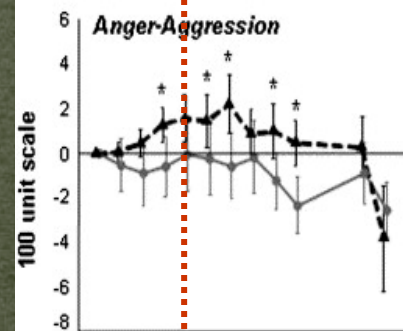
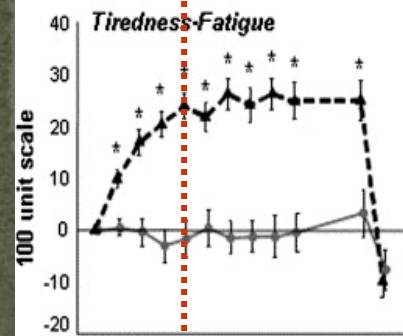
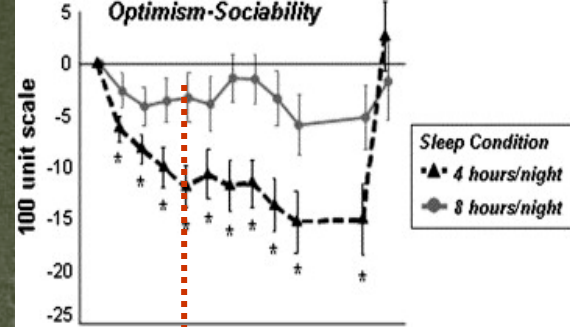
10% pop (Ohayon 2005) =

Sleep is restless, light or of poor quality.

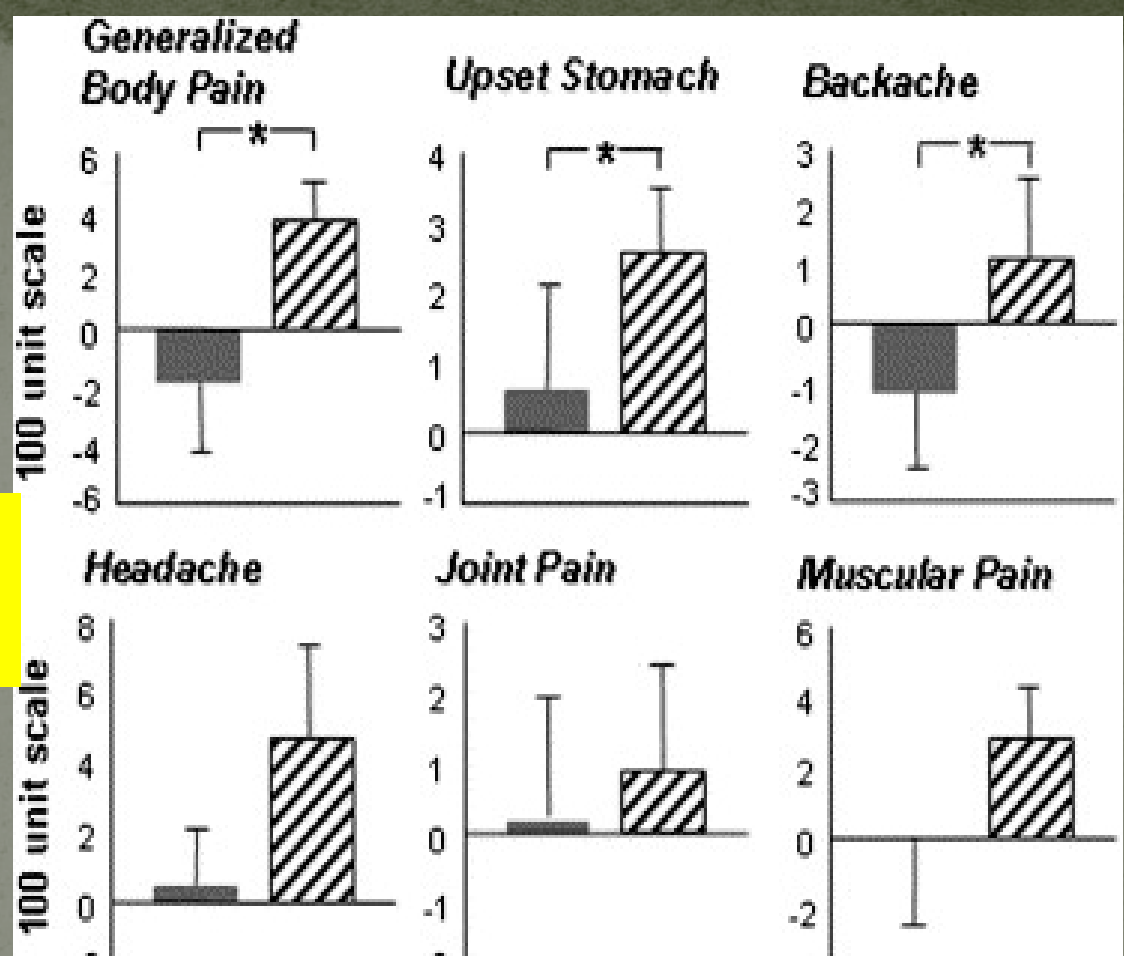
Link to sleep duration and disorders in many cases!

NRS is further define as (Stone 2008) =

Persistent feeling of un-refreshing sleep upon awakening not due to lack of sleep



**4 vs. 8 h
Normal
subjects**



**THRESHOLD of 3 to 4 nights
of Sleep Restriction (4 hr instead of 8 hr) =
MOOD influences & somatic *Pain* complaints**

Haack and Mullington, Pain 2005

PAIN & SLEEP: linear or circular interaction?

When pain is chronic, a **circular relationship** seem to dominates BUT...

INSOMNIA impact on such outcomes

(Prevalence: 10% general pop; up to 30% in chronic pain patients)

Present in 56% of Substance Abuser
Subjects (Mafoud Y et al, 2009 /Pilot study)

- **Initial insomnia induce significant rise in pain over time** (explain 16% of the variance;
Temporomandibular pain, n=53; Quartana et al, PAIN 2010)

Opiates improve sleep but LESS DEEP SLEEP and LESS REM sleep plus RISK Central Sleep Apnea (2.8/hr/100 mg Morphine; Threshold at 200 mg)
Shaw-Raymond, Sleep, 2006; Mistakidou, Pain Pract 2010; Jungquist CR 2012, Pain Manag Nursing; Rose, J Clin Sleep Med 2014)

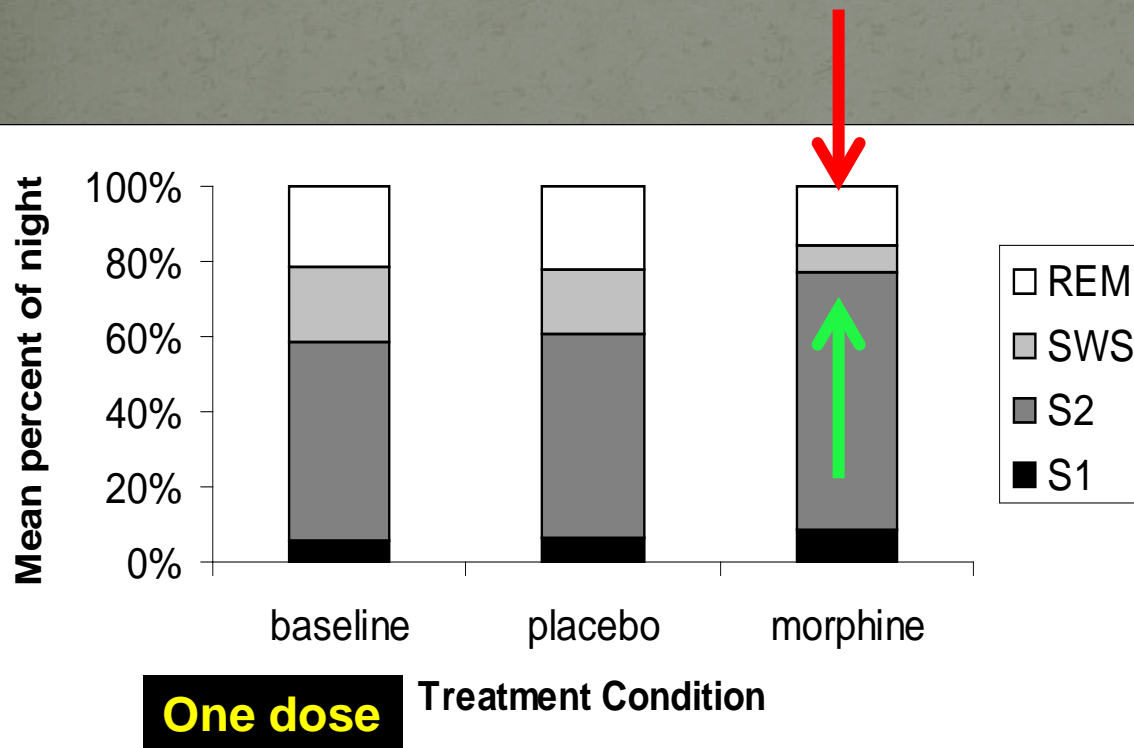
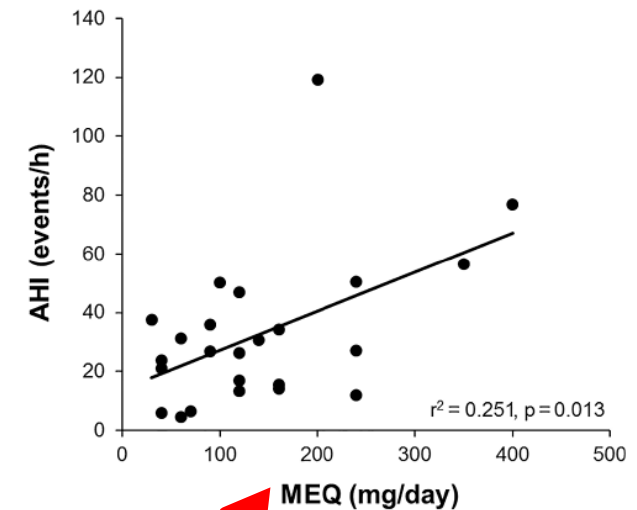


Figure 1—Relationship between morphine equivalent dose (MEQ) and apnea hypopnea index (AHI), N = 24.



Other issues in opioid use for chronic pain

Oligoanalgesia (lack of pain relief according to patient) reported by **40%** of patients in post-op or emergency medicine
(Tood KH 2007; same in our group in Montreal)

Most opioids efficacy/effectiveness
tested only for short term

(Kissin, J Pain Res 2013)...

Merci / Thank you to:

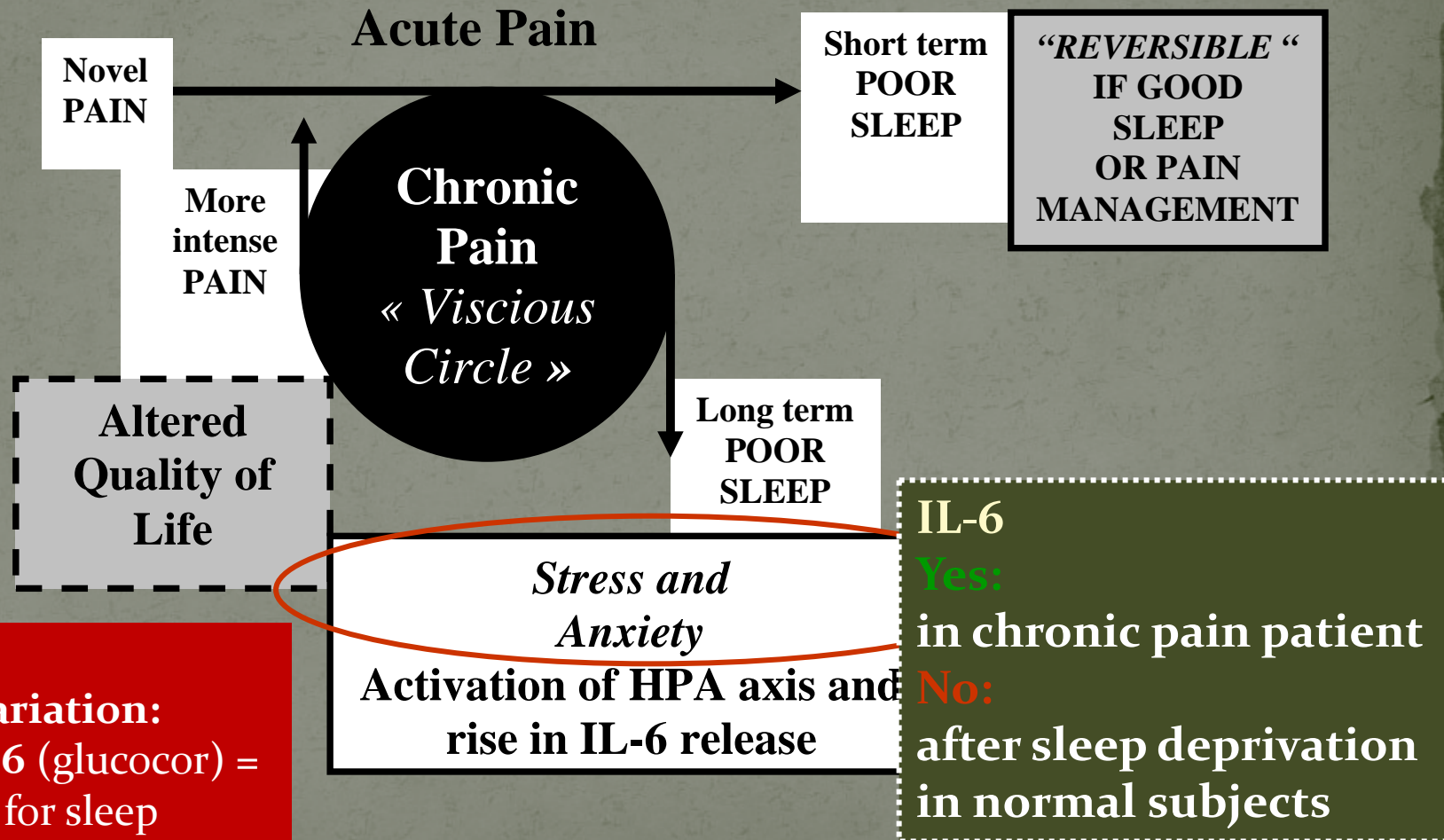
IMHA/Network for Canadian Oral Health Research

INMHA/CRISM

CIHR & CRC



Linear and Circular effects of pain on sleep (do not explain everything!)



HPA axis:
genetic variation:
SERPINA 6 (glucocor) =
protective for sleep

Opioid receptors are a group of G protein-coupled receptors with opioids as ligands.

The endogenous opioids are: dynorphins, enkephalins, endorphins, endomorphins and nociceptin.

4 Opioid receptors & Functions

delta (δ) DOR, OP₁ & **mu (μ)** MOR, OP₃ =
Analgesia, Physical Dependence,
Depression, Euphoria (mu 2), delta:
Respiratory mu 2 receptor Depression

kappa (κ) KOR, OP₂ = Analgesia,
Sedation, Stress...

Nociceptin receptor NOP, OP₄ = Anxiety,
Depression, Tolerance to mu opioid

Morphine: effet ??? en usage prolongé

Dogme = RISQUE DÉPRESSION RESPIRATOIRE lors sommeil

Débat = respiration irrégulière (Biot's) et effort plus grand

MAIS **pas plus hypoxie ou Apnées** (AHI et Centrales) si compare les cas OSAS + opiacé & OSAS sans opiacé / témoins (Guilleminault 2010 Lung; morphine, fentanyl, oxycodone, methadone)

TOUTEFOIS **plus Apnées centrales selon dose: 2.8/h par 100 mg morphine** – SEUIL à 200 mg pour troubles de la respiration

(Jungquist CR 2012, Pain Manag Nursing)

TX Ventilation en pression positive continue

MAIS... BiPAP... CPAP...

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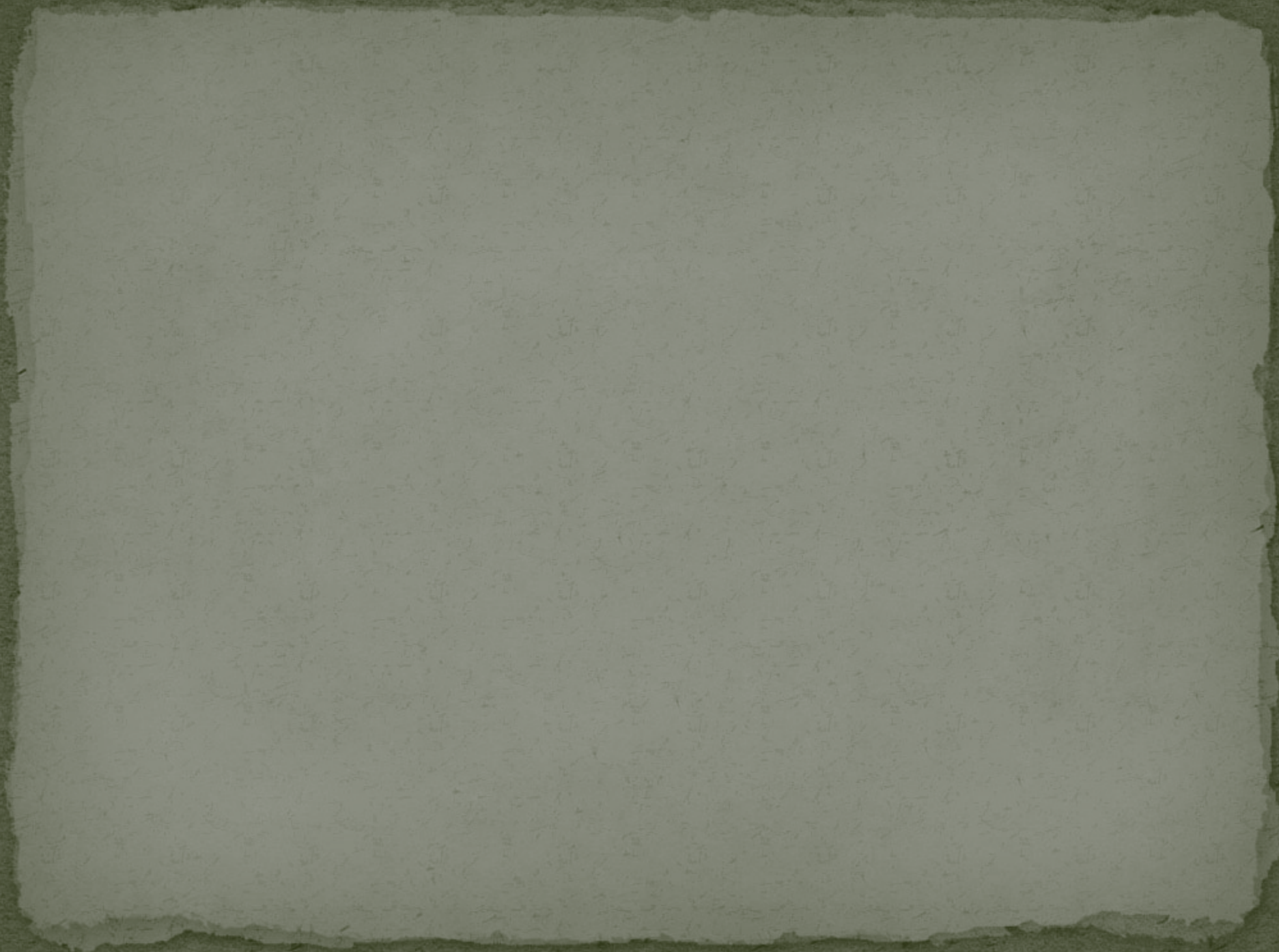
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Missing the Route with Misuse...

Drug deaths in Ontario: 58 % due to opioids, 1/3 oxycodone

Oxycodone crisis is REAL but diminished: crush pills behaviours in teenagers & rise in death with opioids (16% increase in Ontario, 2X in some area...)

Now ERO formula/Tamper medication= 36-38% reduction -- **But RISE on other Oxy 20% & Heroin 42%** (Coplan PM 2013; Severtson SG 2013)

Missing the Route with Misuse...

Users reduced OXY misuse from 96% to 33% (19.5 to 1.9 day/month): Still methods to use, less in injection, etc... (Havens JR 2014)

- Improvements since removed from reimbursement list, better education, public awareness/media, change in Rx of analgesic... (B Fischer; BMC Health Services Res, 2014)



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Canadian Alcohol and Drug Use Monitoring Survey (CADUMS)

Nonmedical prescription opioid use:

- Individuals who acknowledge using their own pain relievers more than they were supposed to
- Obtaining a pain reliever from family or friend
- Obtaining medication from the internet
- Obtaining the medication from any source without a prescription
- Using a pain reliever to get high

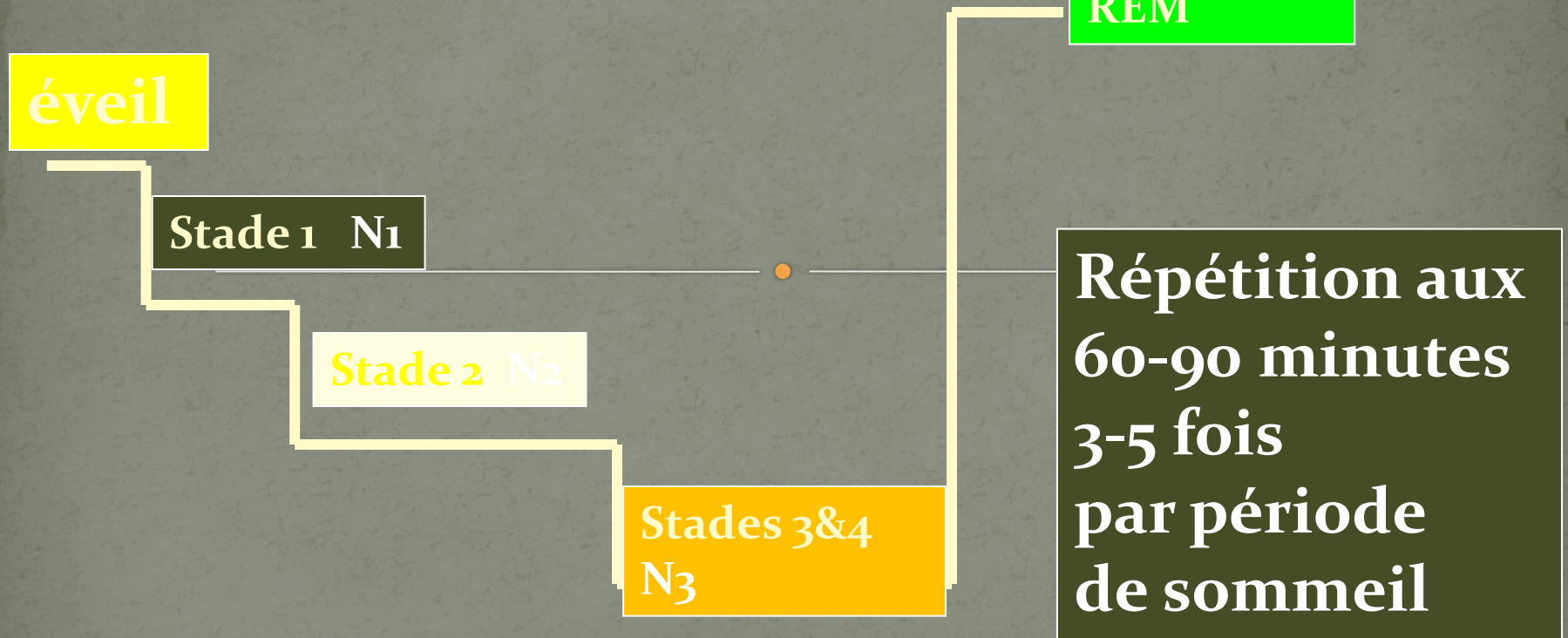
CADUMS one of the few surveys distinguishing between using an opioid for pain relief vs for a recreational purpose “to get high”

Slide from M Lynch, Dal Uni

Rythme ULTRADIAN

Sommeil léger, profond = non-REM

Paradoxal = REM



Health Association
Ontario

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MENTAL HEALTH **TEENAGERS** LIVED

HOME ► NEWS AND EVENTS ► ONTARIO STUDENT DRUG USE AND HEALTH SURVEY (OSDUH) RELEASES FINDINGS THROUGH WEBINAR

News

+ **Mental Health Notes**

Events

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Media

Ontario Student Drug Use and Health Survey (OSDUH) releases findings through webinar

MAY 17, 2012

The 2011 Ontario Student Drug Use and Health Survey (OSDUHS) recently highlighted its findings using a two-hour webinar on April 27, 2012. The OSDUHS began in 1977 and is the longest running



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The Alberta Youth Experience Survey (TAYES)

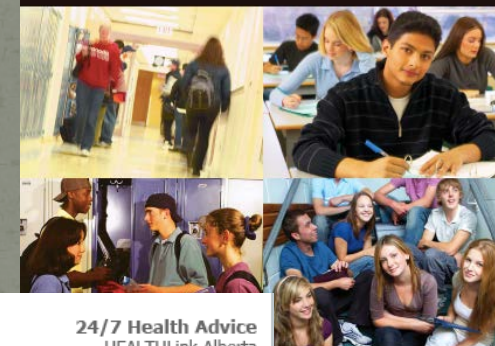
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The Alberta Youth Experience Survey (TAYES)

Slide from M Lynch, Dal Uni

Student Drug Use Survey
in the Atlantic Provinces 2007

ATLANTIC TECHNICAL REPORT



24/7 Health Advice
HEALTHLink Alberta
1-866-408-5465



Percentage of students Grade 7-12 reporting use of an opioid without a prescription in the past year

- 18% in Ontario, 15.5% in Alberta, 20% in NS, 18% NB, 17% Nfld&L, 19% PEI
- “question tapped into use of opiates for pain and does not have face validity as an item on opiate use for recreational purposes (SDUSAP)

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In USA:

82 % of **overdose deaths** due to Opioids

Only 1/3 had used Medication Assisted Tx (MAT's):
methadone, buprenorphine, naltroxone

Doctors should:

- Reduce number pills Rx to minimum needed
 - Sequence Rx
- and improve collaboration with Pharmacist
to monitor and control renewal
- Close monitoring if suspicion Addiction, Abuse...
 - Use Medication Assisted Tx/ MAT's