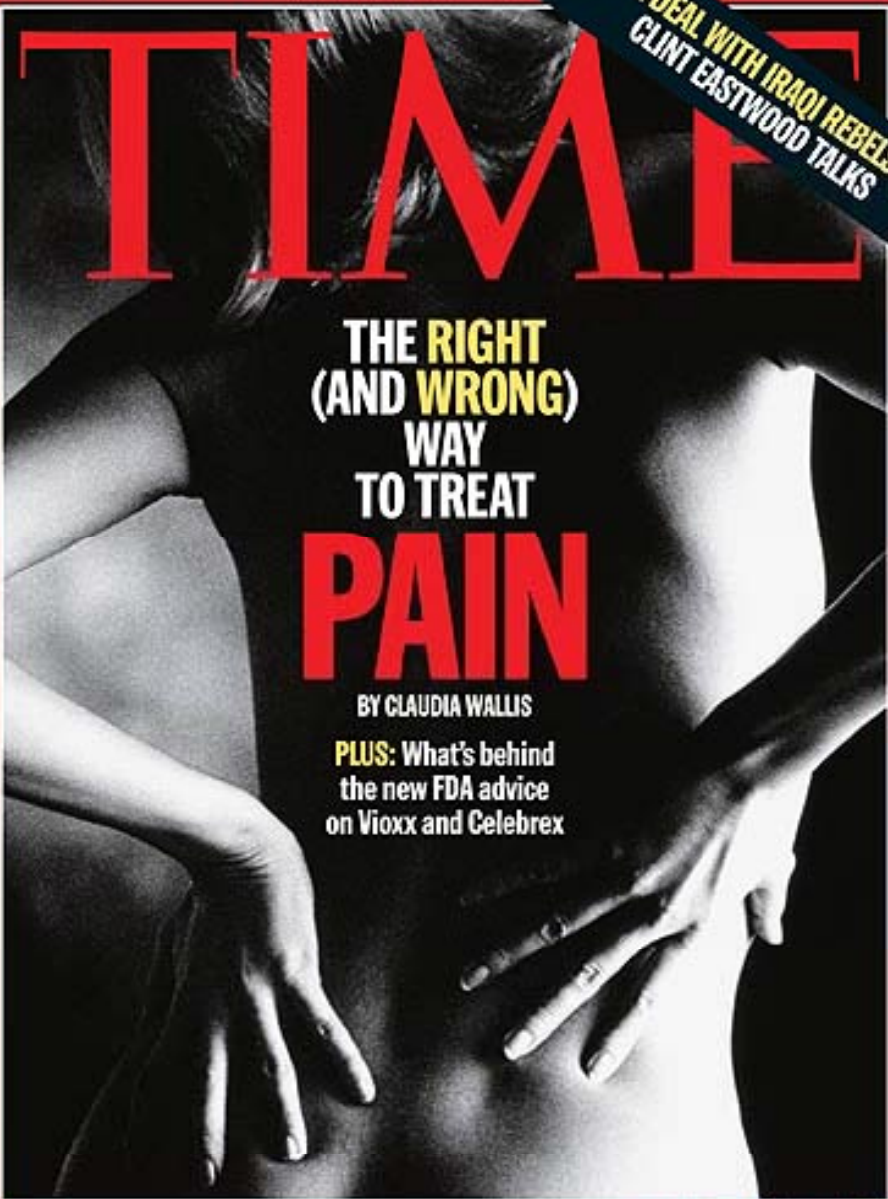


FEBRUARY 28, 2005



TIME

A DEAL WITH IRAQI REBELS?
CLINT EASTWOOD TALKS

THE RIGHT
(AND WRONG)
WAY
TO TREAT
PAIN

BY CLAUDIA WALLIS

PLUS: What's behind
the new FDA advice
on Vioxx and Celebrex

www.time.com AOL Keyword: TIME

Opioids for Chronic Pain - Problem or Progress?

Dr. Roman D. Jovey

Program Director, CPM Centres for Pain Management,
Physician Director, ACDC, Credit Valley Hospital,
Mississauga, Ontario

Dr. Jovey: Conflict of Interest Disclosure Speakers' Bureau / Advisory Boards

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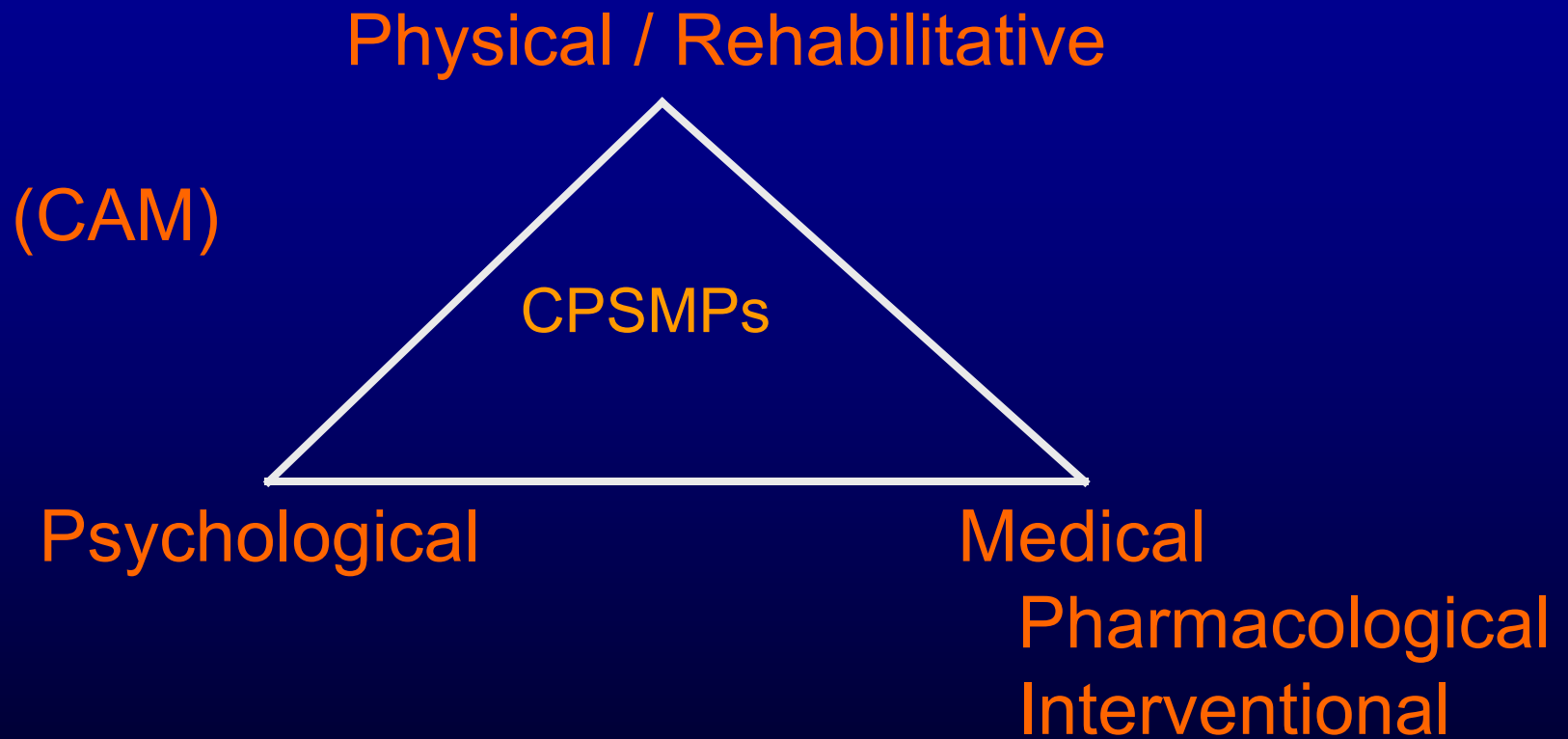
Learning Objectives

- ✔ Discuss/debate the evidence for opioids in chronic pain
- ✔ Discuss/debate the impact of long-term opioid side effects
- ✔ Discuss/debate the issue of misuse, abuse and addiction to prescribed opioids

My Position:

Opioids are an evidence-based treatment with a favourable risk-benefit ratio for the treatment of chronic pain.

The Ideal Treatment of CNCP



Pharmacotherapy will be a part of most chronic pain treatment plans

Evidence for Opioids in CNCP

- ✓ *“There is now strong consistent evidence that opioids relieve chronic neuropathic and nociceptive pains and improve function in placebo-controlled trials with patients who suffer chronic non-cancer pain”.*

Furlan A et al. CMAJ 2006

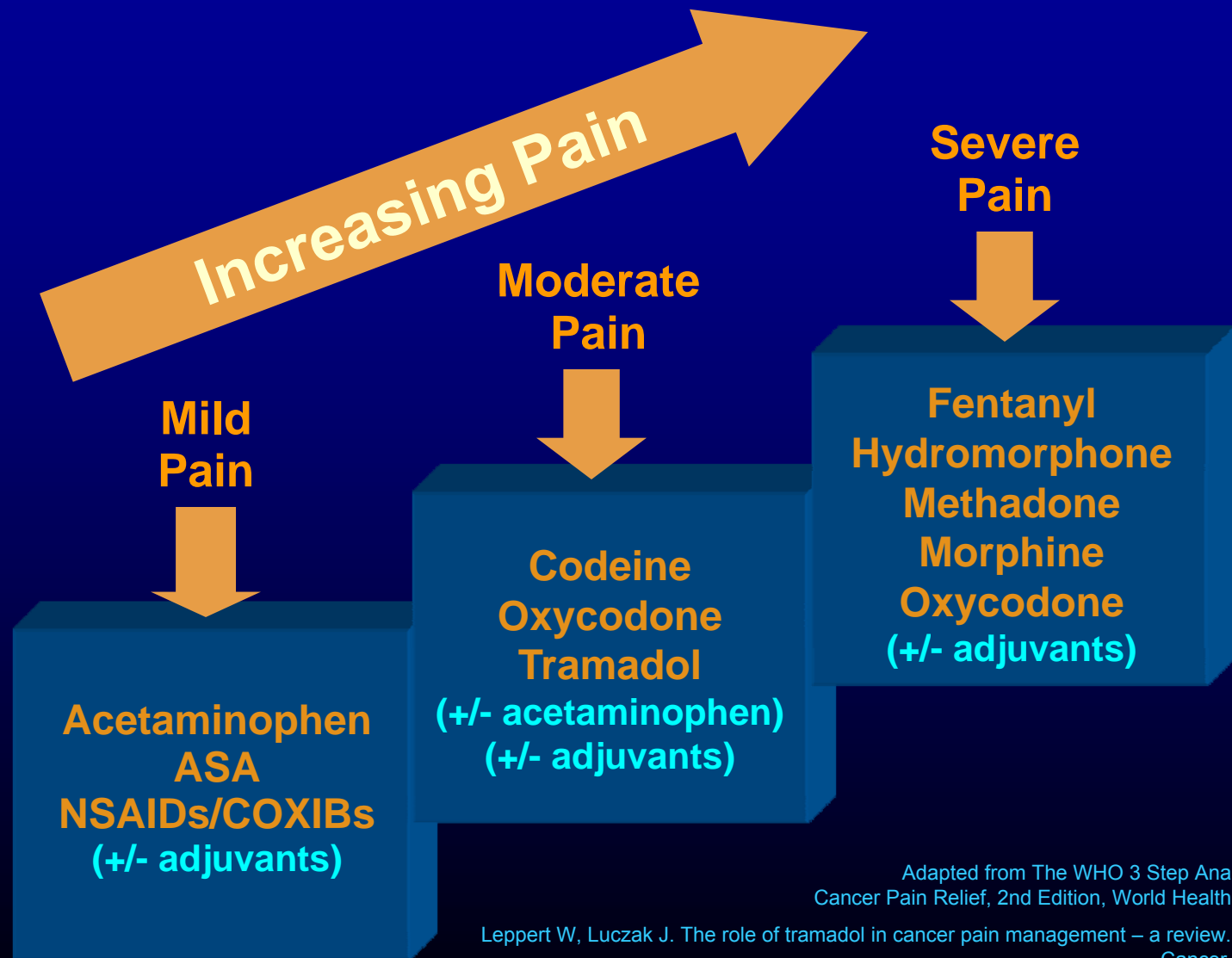
Evidence for the Pharmacotherapy of Neuropathic Pain

▼ Tricyclics	NNT 1.5-2.0
▼ *Opioids	NNT 2-3
▼ Gabapentin / Pregabalin	NNT: 3-5
▼ Tramadol	NNT: 3-6
▼ Venlafaxine / Duloxetine	NNT: 4.5-5
▼ SSRI	NNT : 6-7

(NNT= # of patients treated to get 1 with a 50% pain reduction)

*Average pain reduction across studies ~ 30% (Kalso Pain, 2004)

Modified “WHO Analgesic Ladder”



Adapted from The WHO 3 Step Analgesic Ladder, Cancer Pain Relief, 2nd Edition, World Health Organization.

Leppert W, Luczak J. The role of tramadol in cancer pain management – a review. Support Care Cancer 2005;13:5-17.

Acetaminophen for Osteoarthritis

Cochrane Systematic Review

- ✓ 7 RCTs of Acet. vs. placebo
- ✓ 5/7 Acet. trials positive
 - "statistically significant reduction in pain (5%) which is of questionable clinical significance"

Towheed TE et al 2006

Acetaminophen for Pain

- Concern over risks of chronic use:
 - Hepatotoxicity
 - Renal toxicity
 - Hypertension may develop or worsen
 - Increased risk CV events
 - Increased risk of UGI toxicity

FDA

Forman JP. Hypertension, 2005;Curhan GC, Arch Int Med, 2004;Chan AT. Circulation 2006;Garcia Rodriguez, Arthritis Res 2001;Zimmerman, 1995, 2000; Bromer, 2003; FDA Sept. 2002; Health Canada Feb. 2003; Dedier J, Hypertension, 2002.

Analgesia: Opioids vs. NSAIDs

Opioids

NSAIDs

Titratable	Yes	No
Ceiling Dose	Not in pure agonists	Yes
Allergic reactions	Rare Pruritis: Histamine	Common (Resp & Derm)
Acute Adverse Effects	Nausea, Drowsiness, Constipation	GI, Renal, Hepatic, CVS, BP, Resp
Addiction Risk	Potential	None
Long Term Adverse Effects	Sweats, Reflux, Hormonal, Hyperalgesia, Central Sleep Apnea	GI, Renal, Hepatic, CVS, BP, GU
Drug Interactions	Few	Many
Reported Organ Damage: Medical Use	None	GI, Renal, Hepatic, CVS

**Approximately 1900 Canadians die
annually due to NSAID-related adverse
effects ***

Canadian Arthritis Society

* more than the total number of deaths due to MVCs, fires and
gunshot wounds combined

“The Management of Persistent Pain in Older Persons”

American Geriatrics Society Clinical Practice Guidelines

- Opioids are effective
- Addictive behaviour less common among older patients
- Opioids have fewer long-term risks than other analgesic drugs
- Careful monitoring for adverse side effects is important

AGS Clinical Practice Guidelines, 2002.
http://www.americangeriatrics.org/products/positionpapers/persistent_pain_guide.shtml

Chronic Opioid Side Effects

- ✓ Constipation
- ✓ Sedation during titration (driving, work)
- ✓ Pruritis/sweats
- ✓ Dry mouth
- ✓ Hyperalgesia / myoclonus
- ✓ GE Reflux symptoms
- ✓ Hormonal effects
- ✓ Sleep apnea
- ✓ (Immune dysfunction ???)

Stable dose, scheduled, titrated, long-term opioid therapy does not cause clinically significant cognitive impairment

- ✓ Hendler N. et al. Amer J Psychiatr 1980
- ✓ Zacny JP. Exp Clin Psychopharmacol 1995
- ✓ Vainio A. et al. Lancet 1996
- ✓ Zacny JP. Addiction 1996
- ✓ Lorenz J. et. al. Pain 1997
- ✓ Haythornthwaite JA, et al. JPSM 1998
- ✓ Sjogren P, et al. Pain; 2000
- ✓ Galski T, et al. JPSM 2000
- ✓ Chapman S. Clin J Pain 2002
- ✓ Sabatowski R. et al. JPSM 2003
- ✓ Tassain V. et al. Pain; 2003
- ✓ Fishbain DA. et al. JPSM 2003
- ✓ Menefee, Pain Med 2004

Opioids and Endocrine Function

- ✓ Opioid receptors in hypothalamus, pituitary, testes, ovaries
- ✓ Opioids seem to have a central effect to decrease GnRH, LH, FSH and peripheral effects on the adrenals, testes, ovaries
 - Secondary (Hypogonaotropic) hypogonadism
 - Reduced testosterone, estradiol, progesterone
- ✓ **Long-term concerns:**
 - Sexual function, energy, mood, osteoporosis
 - ?? Effect on pain sensitivity ??

Katz N, Mazer NA. Clin J Pain 2009; 25(2):170-175

Benyamin R. Pain Physician 2008; 11: s105-s120

Practical considerations

- ✓ Education and informed consent
- ✓ Monitor testosterone, LH, (FSH) estradiol, DHEAS + R/O other causes
- ✓ Discuss options with patients
- ✓ Reduce dosage, try other therapies
- ✓ Switch opioids:
 - Tramadol , buprenorphine may have less effect
- ✓ Replace testosterone in men (?women)
- ✓ Calcium and Vit D and wt-bearing exercise
- ✓ The effect reverses when opioids stopped

Opioids and Sleep Apnea

- ✔ Sleep apnea has impact on energy, mood cardiovascular risk and pain
- ✔ ~ 30-70% of people on long-term opioids have central sleep apnea
- ✔ 7 studies; No prospective studies
- ✔ Lots of other meds affect sleep and may increase the risk of sleep apnea (BNZ)
- ✔ Higher risk with methadone?

Teichtal H. Expert Opin Drug Saf. 2007; 6(6): 641-49

Webster L. Pain Medicine 2007;

Opioid Induced Hyperalgesia

- ✓ Robust phenomenon in animal models of acute pain
- ✓ No animal studies looking at OIH in chronic pain models
- ✓ Human data is anecdotal thus far – mostly acute, cancer, post-op, experimental pain
- ✓ Cancer literature – aggressive opioid dosing may cause hyperalgesia
- ✓ No systematic data on hyperalgesia exacerbating clinical pain states in CNCP

Angst MS Anesthesiology, 2006

Chu LF. Clin J Pain, 2008

Immune Effects of Opioids

- ✓ **Lots of things affect immune function!**
 - Nutrition, stress, surgery, other drugs, pain
- ✓ **Animal data and scant human data that acute opioid Tx may reduce the activity of certain parts of the immune system**
 - may develop tolerance
- ✓ **Certain opioids have more effect**
 - Morphine, fentanyl
- ✓ **Certain opioids may have little effect (Bup) and others may actually enhance immunity (Tramadol) and for others – no data**

Immune Effects of Opioids

- ✓ In 2009, this is not a major concern for long-term opioid therapy

“The use of narcotics in terminal cancer is to be condemned if it can possibly be avoided...because of undesirable side effects. Dominant in the list of these unfortunate effects is addiction.”

Lee Jr LE. JAMA 1941;116:216-9

OTTAWA CITIZEN

SUNDAY, JULY 27, 2003

When the damage is done


THE KINGSTON WHIG-STANDARD
SATURDAY, JANUARY 25, 2003

Scam artists make doctors wary

CALGARY HERALD
TUESDAY, DECEMBER 17, 2002

Methadone clinic 'may be a lifesaver'

NATIONAL POST
WEDNESDAY, JANUARY 22, 2003

New Brunswick: Police seize prescription drugs and \$84,000 in cash

THE PROVINCE

SUNDAY, MAY 11, 2003

Illegal B.C. prescription drugs flood across border to reserve

The Gazette

MONDAY, MAY 12, 2003

Doctors arrested for prescribing OxyContin to addicts: Crackdown in Appalachia began after cancer painkiller showed up on black market

THE HAMILTON SPECTATOR
SATURDAY, DECEMBER 14, 2002

'Hillbilly heroin' hits Hamilton area

CAPE BRETON POST

Our Island's Tradition since 1901

FRIDAY, JUNE 13, 2003

Regional police say drugs causing increase in crime

GUELPH MERCURY
Serving Guelph & Wellington County, Ontario, Canada

TUESDAY, NOVEMBER 5, 2002

Thousands of painkillers taken from store

L SATURDAY
11 FEB.
2006.>

GTA Weekend

NARCOTIC PAINKILLERS: A huge markup and a readily available supply are making opioids ever more popular among dealers, users

Prescription for trouble

STAR INVESTIGATION

Health plan funds killer drug

Publicly paid prescriptions for potent, often-abused painkiller skyrocket – and so does the death rate

Jan 31, 2009 04:30 AM

[Comments on this story](#) (61)

KEVIN DONOVAN
STAFF REPORTER

Public dollars are funding a dramatic rise in the use of narcotic pain pills that are killing more and more people in Ontario every year, a *Star* investigation shows.



STEVE RUSSELL/TORONTO STAR

OxyContin, a potent painkiller, is being doled out under the Ontario's Drug Benefit plan at alarming rates in Toronto.

MD faked billings, got pills for drug ring

Admits cheating OHIP of \$750,000 while supplying OxyContin to black market dealers

Aug 30, 2007 04:30 AM

[Be the first to comment on this article...](#)

MICHELE HENRY
STAFF REPORTER

A Toronto family doctor admitted yesterday to pumping more than 130,000 prescription sedatives into the black market and defrauding Ontario's health care system of more than \$750,000.



AP FILE PHOTO

OxyContin painkillers are seen in this 2001 file photo.

Definitions & Diagnosis

It matters!

Rx Opioid Misuse

- ▼ Any use of a prescribed opioid for a reason not intended

Rx Opioid Abuse

- ✓ Any intentional use of opioids outside of a physician's prescription for a bona fide medical condition (excluding accidental misuse.) (Compton & Volkow 2005)

DSM-IV Opioid Dependence 1994

1. Tolerance
2. Physical dependence/withdrawal
3. Used in greater amounts or longer than intended
4. Unsuccessful attempts to cut down or discontinue
5. Much time spent pursuing or recovering from use
6. Important activities reduced or given up
7. Continued use despite knowledge of persistent physical or psychological harm

3/7 required for diagnosis

~~DSM-IV Opioid Dependence~~ Addiction

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6. Important activities reduced or given up
7. Continued use despite knowledge of persistent physical or psychological harm

3/7 required for diagnosis

4/7 common in non-addicted pain patients

**Physical
Dependence** \neq **Addiction**

Changing patterns in opioid addiction

Characterizing users of oxycodone and other opioids

Beth Sproule PharmD Bruna Brands PhD Selina Li MSW Laura Catz-Biro MD

ABSTRACT

OBJECTIVE To evaluate the clinical observation that the number of individuals seeking opioid detoxification from oxycodone was increasing at the Centre for Addiction and Mental Health (CAMH) in Toronto, Ont; and to identify the characteristics of individuals seeking opioid detoxification at CAMH.

DESIGN Retrospective analysis of patient health records.

SETTING Medical Withdrawal Management Service at CAMH.

PARTICIPANTS All patients admitted for opioid detoxification between January 2000 and December 2004.

MAIN OUTCOME MEASURES Number of opioid detoxification admissions each year; type, dose, and source of opioids; comorbid problems and symptoms.

The 4 C's of Addiction

- ✓ Loss of Control
- ✓ Compulsive Use
- ✓ Craving
- ✓ Consequences (Use Despite Harm)

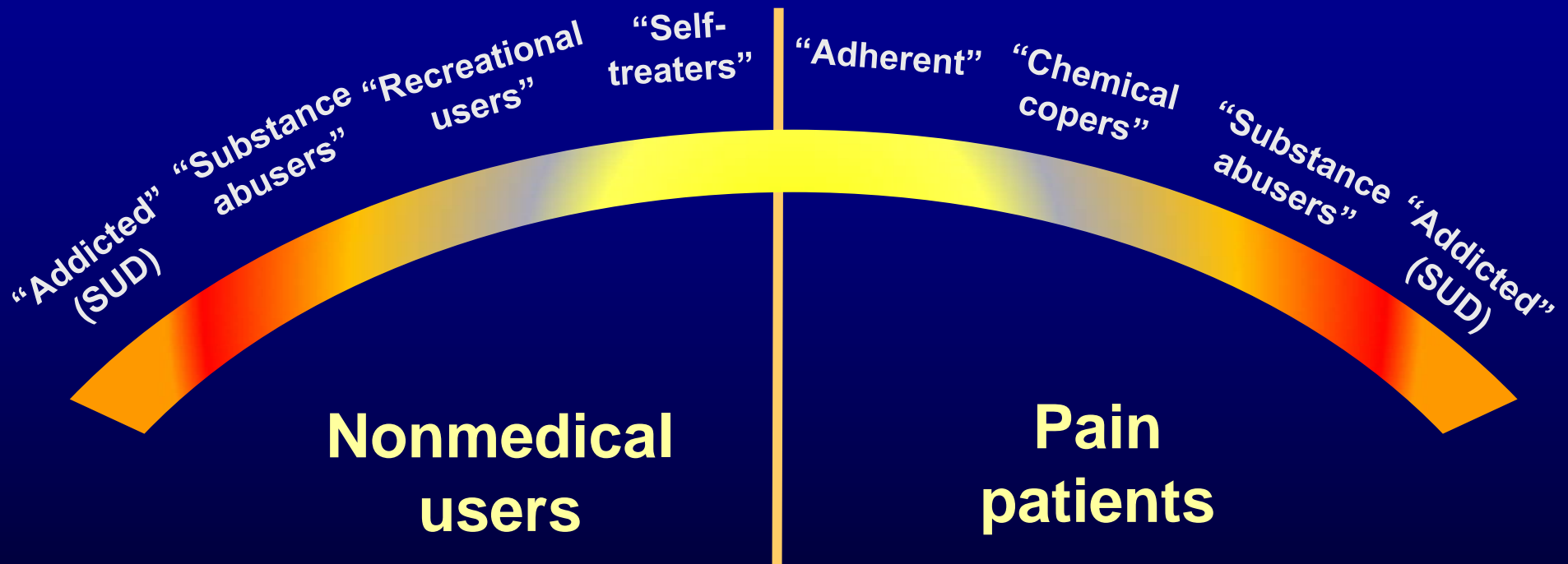
Consensus Statement on Pain and Opioids ASAM, APS, AAPM, April 2001

<http://www.painmed.org/productpub/statements/pdfs/definition.pdf>

**Opioids are not a panacea for all
pains in all patients**

**There is always an individual
risk / benefit ratio**

Population of Rx Opioid Users Is Heterogeneous



SUD=substance use disorder

Passik 2008

What percentage of patients COAT develop a SUD or ADR behaviours

- ✔ **Structured evidence-based review**
- ✔ **24 studies, 2507 CPPs → SUD rate 3.27%**
 - No prev. Hx SUD → SUD rate 0.19%
- ✔ **17 studies, 2466 CPPs → ADRBs 11.5%**
 - No prev. Hx SUD → 0.59%
- ✔ **5 studies, 15,422 CPPs → +ve UDTs 14-20%**

What percentage of patients COAT develop a SUD or ADR behaviours

“COAT exposure will lead to abuse / addiction in a small percentage of CPPs...

...but a larger percentage will demonstrate ADRBs and illicit drug use.”

- ▼ These percentages appear to be much less if CPPs are pre-selected for the absence of a current or previous history of SUD.

It means that if we can identify those at higher risk, we may be able to reduce opioid misuse by more careful prescribing and monitoring

Screening for Opioid Misuse Risk

Initial Screening Questions:

- Ask in a routine, straightforward manner
- (CAGE, SOAPP, DIRE,)
- Ask older patients about amount and frequency of ETOH
- Opioid Risk Tool

Hierarchy of Risk for Therapeutic Opioids

Higher Risk



Personal history opioid addiction

Personal history non-opioid addictions

Family history of addiction

No personal or family history

Lower Risk

Savage, 2004

Risk-Based Pain Management

Group III – Management with tertiary specialist

Written agreement, random UDTs 1-2x per month, pill counts
Exhaust all other options before considering step 3 opioids
Dispensing daily → weekly, less “abusable” meds

Group II – Primary Care with consultation

More assessment and focus on functional goals
Written agreement, UDT 3-4x per year, collateral information
Follow-up monthly, dispense q 2 wks, choose opioids carefully

Group I – Treatment by Primary Care

Utilize all Tx options, including opioids, focus on S/E
Verbal or written agreement, UDT 1-2x per year
F/U q 2-3 months, meds dispensed q 4 weeks

Minimizing the Risks of Opioid Misuse – Universal Precautions

- ✔ Set boundaries around medication use (Rx agreement)
- ✔ Use random urine drug screening
- ✔ Identify drug misuse behaviors early and intervene
- ✔ Introduce opioids as a “trial of therapy” with agreed upon goals
- ✔ Taper opioids when goals not achieved

Does Adherence Monitoring Reduce Controlled Substance Abuse in Chronic Pain Patients?

- ✔ **500 consecutive patients followed prospectively compared to historic controls**
- ✔ **Risk assessment, written agreements, UDTs, pill counts, collateral info**
- ✔ **50% reduction in ADRBs from controls**

Pain Management Goals

- ▼ **Decrease pain**
- ▼ **Improve function**
 - Physical
 - Psychological
 - Social
- ▼ **Minimize risk**
 - Patient
 - Physician
 - Society

Treatments for Pain

Risk

Benefit



Summary

- ✔ Opioids are an evidence-based treatment for CNCP
- ✔ Opioids have side effects which can be identified and managed
- ✔ The risks of prescribing opioids can be reduced by screening, risk stratification and the use of Universal Precautions

“Doctors have to be risk managers in any medical condition. In treating pain, there is no risk-free treatment option – including doing nothing.”

S. Fishman

ICPCD New York, 2007

Canada's Weekly Newsmagazine

Maclean's

August 16, 1999

SPECIAL REPORT

What's **RIGHT**—and
WRONG—with Canada

BANKING

Canada Trust Goes Gre

**COPING
WITH**

PAIN