Opioids for Chronic Pain Problem or Solution?

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Conflict of Interest Disclosure
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King Pharmaceuticals	Valeant
Levopharm	Wyeth

Questions:

1. How big is the chronic pain problem?
2. How big is the prescription opioid misuse problem?
3. Who is at risk for misusing prescription opioids?
4. Why the shift to prescription drugs?
5. How can we optimize the use of opioids to treat pain while reducing the harms of misuse?

How big is the problem of chronic pain?

Nanos Canadian Pain Survey 2007-2008

18% Canadians complain of moderate – severe pain dailyor most days of the week

~ 6 million people

Schopflocher et al, PR&M 2011 (in press)

Epidemiology of chronic pain from three large, high quality surveys of adult general populations

✓Blyth et al PAIN (2001): N = 17 543 Australia
pain most days for 3 months: 18.5%

✓Eriksen et al PAIN (2003): N = 20 000 Denmark
pain lasting more than 6 months: 19 %

✓Breivik et all EJP (2004): N = 30 701 in 12 European countries
pain >6 months > 5/ 0-10 pain scale = 18%

Chronic Pain: Workplace Costs

Among those Canadians with moderate or severe pain:

- → 33% - lost a job because
- → 47% - reduced job responsibilities
- → on average lost $12,558 dollars in income over a one-year period because of their pain.

Schopflocher, 2011

Chronic Pain: Societal Costs

Work losses:	**$42 Billion / yr**
Health Care:	**$11 Billion / yr**
Total:	**$53 Billion / yr**

Schopflocher, 2011

INSTITUTE OF MEDICINE
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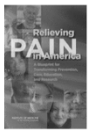


Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research

Released: June 29, 2011
Type: Consensus Report
Topics: Education, Public Health, Select Populations and Health Disparities
Activity: Advancing Pain Research, Care, and Education
Board: Board on Health Sciences Policy

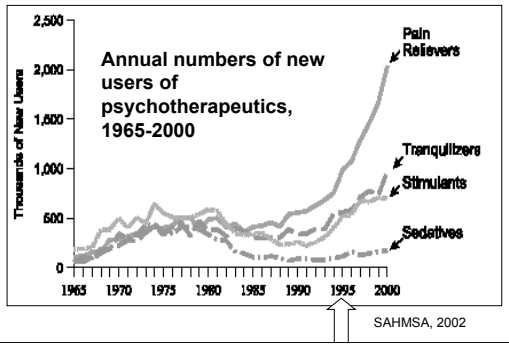
"Chronic pain affects an estimated 116 million American adults – more than the total affected by heart disease, cancer and diabetes combined. Pain also costs the nation up to $635 billion each year in medical treatment and lost productivity"

Chronic Pain Is a Major Public Health Problem

- ranks among the top reasons for health care visits and health-related work absences
- negatively affects <u>all</u> aspects of a person's biopsychosocial life
- high cost to society
- both patients and physicians are not satisfied with current care

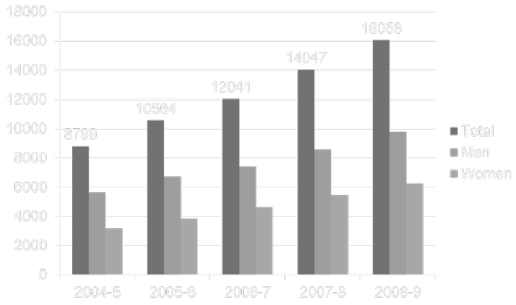
How big is the prescription opioid misuse problem?

Misuse of Psychotherapeutic Agents



SAHMSA, 2002

Ontario DATIS Data – Rx Opioid Tx



Fischer B. Drug Alcohol Depend 2010; 109 (1-3): 257-60

Ontario DATIS Data – Rx Opioid Tx

- **Total of ~ 102,000 visits to Tx programs / yr**
- **Not including MMT programs**
- **Rx opioids made up ~ 16% in 2008-9**
  - → 75% were also abusing other substance
  - → 50% abusing crack / cocaine
- **Rx opioid abusers were younger, low education, unemployed, legal problems**

Fischer B. Drug Alcohol Depend 2010; 109 (1-3): 257-60

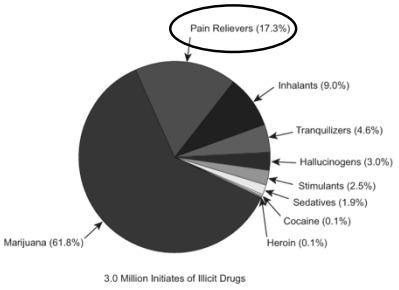
Are we expanding the total pool of "addicts" by prescribing opioids for pain?

U.S. National Household Survey on Drug Use and Health - 2010

- **8.7% of U.S. population 12yrs or older met criteria for DSM IV substance abuse or dependence in the past year**
  - → 68% alcohol; 19% illicit drugs, 13% both
  - → No change since 2002

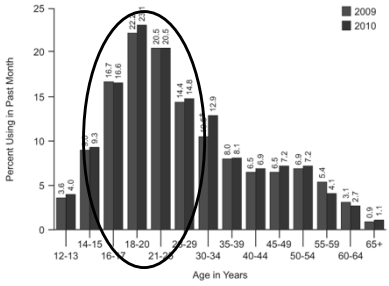
U.S. NSDUH 2010

New Illicit Drug Users in the Past Year – USA 2008



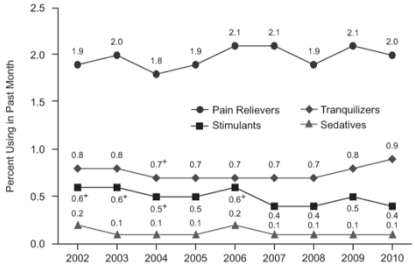
U.S. NSDUH 2010

Past Month Illicit Drug Use by Age USA 2010



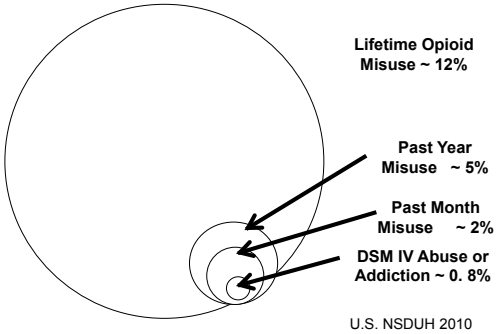
U.S. NSDUH 2010

Past-Month Non-Medical Use: 2002-2010



U.S. NSDUH 2010

Rx Opioid Misuse, Abuse, Addiction in the Total Population



U.S. NSDUH 2010

Sources of Pain Relievers for Students in Ontario grades 7-12

- 72.4% from home
- 6.0% from a friend
- 2.9% from someone I know
- <0.5% from the street
- 18.5% don't remember/don't know

OSDUHS, 2007

Why the shift to Rx drugs?

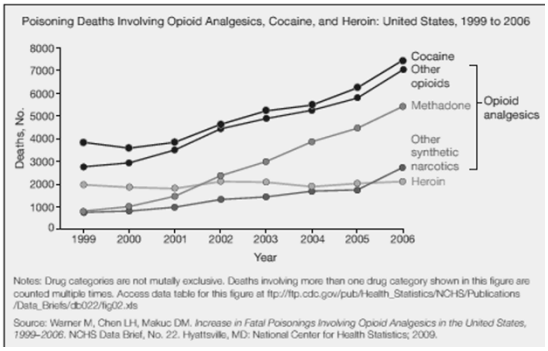
- Purity and dosage more predictable
  - → ? "safer"
- More socially acceptable then illicit drugs
- Easier to obtain in rural or suburban areas
  - → family medicine cabinets
  - → ? easy to obtain prescriptions (and free in some cases!)
- Law enforcement limited ability to prosecute Rx diversion due to current laws

Problem or a Symptom?

Social Pain and Opioid Use

- As more people lose their jobs or fear losing them, as more young people despair of any meaningful future, as life becomes harder and social supports disappear, human pain increases and so does the need for relief. I have found that distressed individuals and families request less pharmacological analgesia when they get more social support. Unfortunately, social policy is going in the opposite direction.

Rosenthal SM. CMAJ 2009; 181(11):827



JAMA Feb 10, 2010

CMAJ RESEARCH

Prescribing of opioid analgesics and related mortality before and after the introduction of long-acting oxycodone

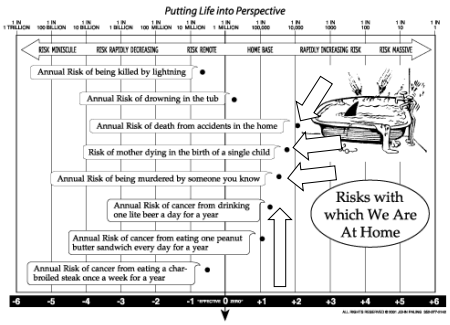
Irfan A. Dhalla MD MSc, Muhammad M. Mamdani PharmD MPH, Marco L.A. Sivilotti MD MSc, Alex Kopp BA, Omar Qureshi MD, David N. Juurlink MD PhD

Results: From 1991 to 2007, annual prescriptions for opioids increased from 458 to 591 per 1000 individuals. Opioid-related deaths doubled, from 13.7 per million in 1991 to 27.2 per million in 2004. Prescriptions of oxycodone increased by 850% between 1991 and 2007. The addition of long-acting oxycodone to the drug formulary was associated with a 5-fold increase in oxycodone-related mortality ($p < 0.01$) and a 41% increase in overall opioid-related mortality ($p = 0.02$). The manner of death was deemed unintentional by the coroner in 54.2% and undetermined in 21.9% of cases. Use of health care services in the month before death was common: for example, of the 3066 patients for whom data on physician visits were available, 66.4% had visited a physician in the month before death; of the 1095 patients for whom individual-level prescribing data were available, 56.1% had filled a prescription for an opioid in the month before death.

CMAJ Dec 8, 2009

Comments on Dhalla et al, 2009

- Death rate went from 13.7 per million to 27.2 per million population from 1991-2004
- = 1.37 per 100,000 to 2.72 per 100,000
- ~1/73,000 to 1/36,000 in the overall population of Ontario



Paling J. Helping People Understand Risk. 2006

Comments on Dhalla et al, 2009

- Death rate went from 13.7 per million to 27.2 per million population from 1991-2004
- = 1.37 per 100,000 to 2.72 per 100,000

Compared to:

15.3 deaths per 100,000 NSAID users
(Lanas A, et al. Am J Gastro 2005;100:1685-93)

5.3 deaths per 100,000 dying in a MVC

2.2 deaths per 100,000 dying in a pedestrian accident

The vast majority of people dying are misusing opioids. If opioids are used appropriately to treat pain, then the risk of dying becomes much, much less.

What about the denominator?

- **Ontario population 2006 ~ 12 million**
- **19% ~ 2.3 million with CNCP (Nanos)**
  - → If 30% on opioids ~ 690,000
    - – Then 500 deaths ~ 60/100,000 deaths on opioids
  - → If 50% on opioids ~ 1 million
    - – Then 500 deaths ~ 50/100,000 deaths on opioids
- **Canadian suicide rate ~ 15/100,000**
  - → In patients with CNCP it is about double

Coroner: "Deaths related to opioids"

- **Definitions are important (2-fold difference)**
- **Large overlap between therapeutic levels and post-mortem levels**
- **What about the role of other drugs found?**
- **Motivation?**
  - → Suicide (double in CNCP)
  - → Abuse/Addiction (90% in Hall - West Virginia study)
  - → Therapeutic misadenture ?

Jauncey 2005,Wallage 2006, Thompson 2008, Ferner 2008, Tennant 2007

Methadone deaths in Ontario

"There is solid evidence that Ontario's methadone-related death rate has risen, despite introduction of the college's methadone program in 1996. Contrary to what's claimed on the college's website – that this death rate fell from 4.2 fatalities per 1,000 patients to 1.7 by 2000 – a more rigorous examination of the data shows that under the college's watch, the rate actually rose, from 1.4 deaths per 1,000 to 1.7."

(140-170 / 100,000)

Dr. Philip Berger, 2009
http://www.healthzone.ca/health/articlePrint/728844

Risks of Other Drugs for CNCP

- **TCAs – 35% increased risk of CVD**

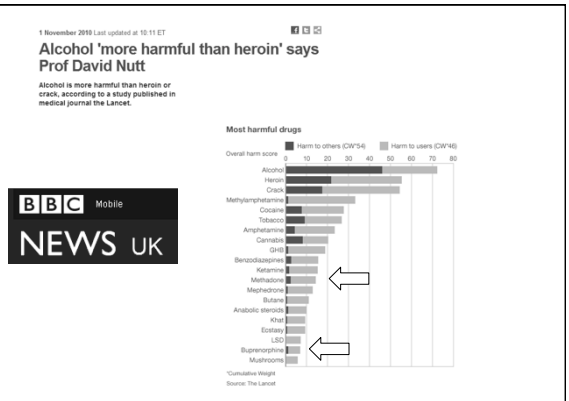
  Hamer M. Eur Heart J. 2011

- **Ibuprofen or diclofenac → 3 x increase CVAs**
  Diclofenac → 4 x increase CV deaths

  Trelle S. BMJ 2011

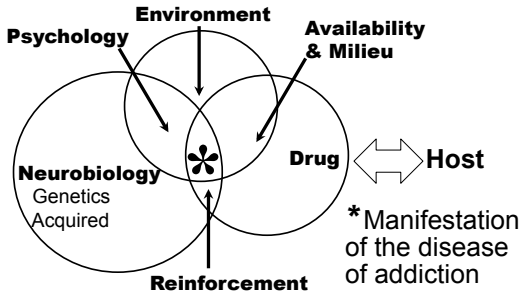
- ~4% of people on NSAIDs will have UGI bleed/yr
  - → 7-20% of those with an UGI bleed will die
  - → 2007 – 4 million Rx's written in Canada ~ 1 million people on NSAIDs
    - – 40,000 UGI bleeds → 2800-8000 deaths

  Straube S. BMC Gastroenterol. 2009



Nutt D. Lancet 2010

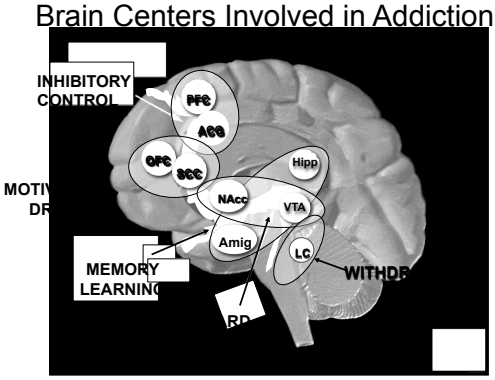
Addiction: A Biopsychosocial Illness



*Manifestation of the disease of addiction

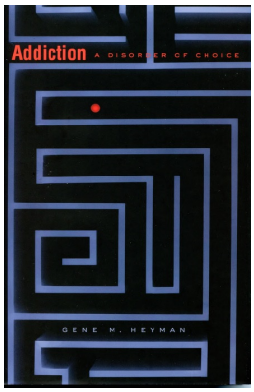
Adapted from JD Haddox, DDS, MD.

Brain Centers Involved in Addiction



After Nora Volkow, Director NIDA, 2004

Locus Ceruleus added, after Koob



CHOICE

In biogenetically vulnerable people, the drug hijacks the brain's natural motivational control circuits that evolved to ensure survival

CHOICE

Proper definitions are important!

In a Patient With Pain on Opioids…

Physical Dependence ≠ Addiction

Tolerance ≠ Addiction

High dose ≠ Addiction

DSM-IV Opioid Dependence

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

Sees and Clark, J Pafter, Savage, 2004

DSM-IV Opioid ~~Dependence~~ Addiction

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
4/7 common in non-addicted pain patients

Sees and Clark, J Pafter, Savage, 2004

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

DSM V: Substance Use Disorder
(Draft Definition Feb 2010)

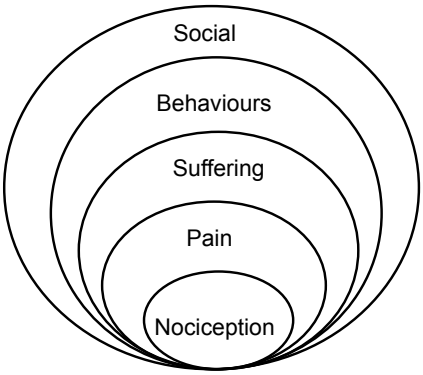
Tolerance:

(Note: Tolerance is not counted for those taking medications under medical supervision such as analgesics, antidepressants, ant-anxiety medications or beta-blockers.)

Withdrawal:

- ***(Note: Withdrawal is not counted for those taking medications under medical supervision such as analgesics, antidepressants, anti-anxiety medications or beta-blockers.)***

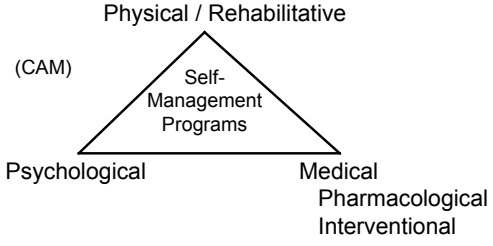
www.dsm5.org



Treatment Options for Pain

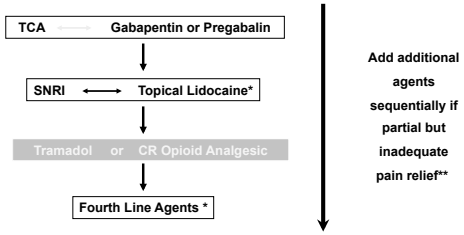
PHYSICAL	PSYCHOLOGIC	PHARMACOLOGIC	INTERVENTIONAL
Normal activities	Hypnosis	OTC medication	I.A. steroids
Splinting / Taping	Stress	Alternative therapies	I.A. hyaluronan
Aquafitness	Management	Topical medications	Trigger pt. therapy
Physio	Cognitive-	NSAIDs / COXIBs	IntraMuscular stim.
• Passive	Behavioural	DMARDs	Prolotherapy
• Active	Family therapy	Immune modulators	Nerve blocks
Stretching	Psychotherapy	Tricyclics	Epidurals
Conditioning	Mindfulness-	Anti-epileptic drugs	Orthopedic surgery
Weight training	Based Stress	Opioids	Radio frequency
Massage	Reduction	Local anesthetic	facet neurotomy
TENS	Mirror Visual	congeners	Neurectomy
Transcranial	Reprogramming	Muscle relaxants	Implantable
Magnetic Stimulation		Sympathetic agents	stimulators
Chiropractic		NMDA blockers	Implantable pain
Acupuncture		CGRP blockers	pumps

The Best Treatment for Chronic Pain



Pharmacotherapy will be a part of most chronic pain treatment plans

Pharmacologic Treatment of Neuropathic Pain



* e.g., carbamazepine, cannabinoids, methadone, lamotrigine, topiramate
** In using multiple agents, be aware of synergistic or additive adverse effects

Moulin DE *et al. Pain Res Manag* 2007;12(1):13-21.

Evidence for the Pharmacotherapy of Neuropathic Pain

	NNT	NNH
Tricyclics	2.1-2.8	15.9
*Opioids	2.1-5.1	17.1
Gabapentin	4.3-6.4	32.5
Pregabalin	3.8-5.6	10.6
Tramadol	4.8-4.9	13.3
Venlafaxine / Duloxetine	5.0	13.1
SSRI	6.8	
Cannabinoids	3.4-8.3	
BOTOX-A	2.3-3.0	

(NNT= # of patients treated to get 1 with a 50% pain reduction)
(NNH = # patients treated for 1 to drop out of the study)

Finnerup N.B. et al. Pain 2010; 150: 573-581

Opioids are effective pain relievers for some types of chronic pain in some people…

…in whom?
…for how long?
…with what side effects?

What percentage of patients on 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% ⇦

COAT = Chronic Opioid Analgesic Therapy
SUD = Substance Use Disorder
ADR = Aberrant Drug Related

Fishbain et al. 2008

What percentage of patients on 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.

Fishbain et al. 2008

Long-term opioid therapy for chronic non-cancer pain. Review

The findings of this systematic review suggest that proper management of a type of strong painkiller (opioids) in well-selected patients with no history of substance addiction or abuse can lead to long-term pain relief for some patients with a very small (though not zero) risk of developing addiction, abuse, or other serious side effects.

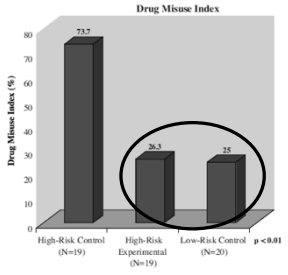
Noble M, et al. Cochrane Collaboration, Jan 2010

Long-term opioid therapy for chronic non-cancer pain. Review

However, the evidence supporting these conclusions is weak, and longer-term studies are needed to identify the patients who are most likely to benefit from treatment.

Noble M, et al. Cochrane Collaboration, Jan 2010

Does that mean that people with both pain and addiction should never be treated with opioids?



High risk patients provided with structure and monitoring can benefit from opioid therapy

Jamison RN, et al. Pain 2010

How can we balance the good with the potential harm?

Solutions

For every complex problem there is a simple solution…

…and it is usually wrong.

H.L. Mencken

A Survey of Pain Curricula in Health Science Faculties in Canada – CPS 2007

	Total Hours (mean)	Range
Dentistry	15	0 - 24
Medicine	16	0-38
Nursing	31	0-109
Occupational Therapy	28	0-48
Pharmacy	13	2-33
Physical Therapy	41	18-69
Veterinary Medicine	87	27-200

Watt-Watson J, et al. Pain Research Manage 2009; 14(6): 439-444

Ontario
MINISTRY OF HEALTH AND LONG-TERM CARE

Public Information

Ontario Drug Benefit Program

Ontario's Narcotics Strategy

- Proposed monitoring database and proposed legislation.
- Partnering with the health care sector to educate on appropriate prescribing
- Partnering with the health care sector to educate on appropriate dispensing.
- Education to prevent excessive use of prescription narcotics.
- Treatment of addictions.

People with pain are becoming the collateral damage in the war against drug misuse.

Any strategy aimed at reducing opioid misuse should not penalize people with pain

Elements of a Good Pain Assessment:

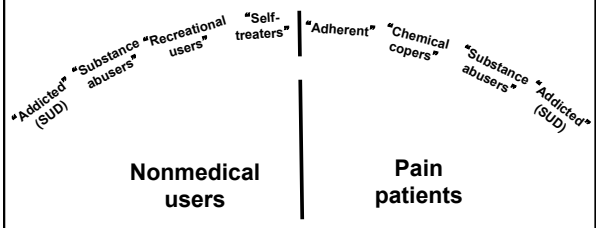
1. Current pain descriptions (including pain scoring)
2. Previous pain history (including treatments and results)
3. Current treatments, effectiveness and adverse effects
4. Other concurrent medical / psych problems
5. Social history (family, work, income, relationships)
6. Addiction screening
7. Physical examination +/- investigations
8. Current functioning and future goals

Reducing the Risks of Opioid Misuse – Universal Precautions

- Screen and risk stratify all patients with pain
- Set boundaries around medication use (Opioid Prescribing 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

Gourlay D.L. Pain Med. 2005 Mar;6(2):107-12.

Population of Rx Opioid Users Is Heterogeneous



SUD=substance use disorder

Passik 2008

The best tool we currently have to screen for addiction risk is to ask questions.

ORIGINAL INVESTIGATION

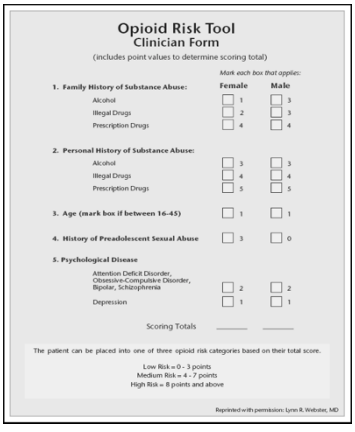
A Single-Question Screening Test for Drug Use in Primary Care

Peter C. Smith, MD, MSc; Susan M. Schmidt, BA; Donald Allensworth-Davies, MSc; Richard Saitz, MD, MPH

"How many times in the past year have you used an illegal drug or used a prescription medication for non-medical reasons?"

"Once" = Sensitivity: 100% Specificity: 73.5%

Smith P.C. et al Arch Int Med 2010; 170(13): 1155-60



Opioid Risk Tool
Clinician Form

(includes point values to determine scoring total)

	Mark each box that applies: Female	Male
1. Family History of Substance Abuse:		
Alcohol	☐ 1	☐ 3
Illegal Drugs	☐ 2	☐ 3
Prescription Drugs	☐ 4	☐ 4
2. Personal History of Substance Abuse:		
Alcohol	☐ 3	☐ 3
Illegal Drugs	☐ 4	☐ 4
Prescription Drugs	☐ 5	☐ 5
3. Age (mark box if between 16-45)	☐ 1	☐ 1
4. History of Preadolescent Sexual Abuse	☐ 3	☐ 0
5. Psychological Disease		
Attention Deficit Disorder, Obsessive-Compulsive Disorder, Bipolar, Schizophrenia	☐ 2	☐ 2
Depression	☐ 1	☐ 1
Scoring Totals	_____	_____

The patient can be placed into one of three opioid risk categories based on their total score.

Low Risk = 0 - 3 points
Medium Risk = 4 - 7 points
High Risk = 8 points and above

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Reducing Prescription Diversion

- Ask about the home mileau
- Limit the amounts dispensed
- Discuss security of meds (lock them up!)

Opioids are not a panacea for all pains in all patients

There is always an individual risk / benefit ratio

Part of using opioids effectively in chronic pain is knowing how to discontinue them when they are doing more harm than good

FPs/GPs need some back-up

ONTARIO COLLEGE OF FAMILY PHYSICIANS

Promoting the Quality of Family Medicine in Ontario through Leadership, Research, Education and Advocacy

Medical Mentoring for Addictions and Pain (MMAP)

Avoiding Abuse, Achieving Balance

1. Better training for all doctors
2. Pain and addiction working together
3. Network of specialized pain clinics in Ontario
4. Fair remuneration for pain management
5. Online drug information system
6. Improved communication among doctors, pharmacists, regulators and law enforcement

www.canadianpainsummit2012.ca/

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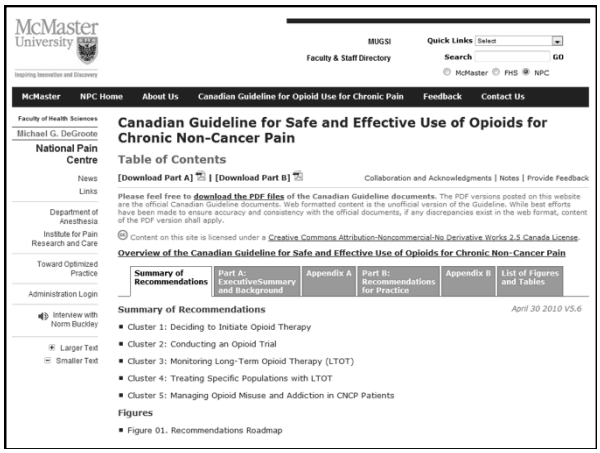


Pain Management Goals

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

Take Home Messages:

1. **Opioids are an evidence-based treatment that can be very helpful in some people for some pain problems…**
2. **…but they can do harm when used by the wrong person for the wrong reason**
3. **Keep things in perspective (denominator!)**
4. **Huge educational gap that must be filled**

Take Home Messages:

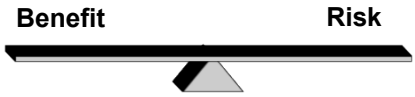
5. **Screen and risk stratify patients**
   Including their home environment
6. **Pain Tx requires a biopsychosocial approach – and adequate Tx resources**
7. **We need to prescribe opioids with Universal Precautions**
8. **Addiction medicine and pain medicine have to work together!**

"People in pain have a right to fully adequate pain relief treatment. Indeed, for the healthcare professional to act unreasonably in leaving a person in pain is a breach of a fundamental human right.

Physicians should not fear that giving adequate pain relief treatment is unethical or illegal; in fact, they should fear the ethical and legal consequences of not doing so."

Dr. Margaret Somerville, Director of the McGill Centre for Medicine Ethics and Law; Samuel Gale Professor of Law. July 2010

The Pain Management Challenge



Questions?

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