

Epidemiology of Prescription Drug Misuse and The CPSBC Standards and Guidelines

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April 22, 2017

Disclosure

• Relationship with Commercial Interests: None

- Professional Roles:
 - Addictions physician Complex Pain & Addiction Service, VGH
 - Medical consultant CPSBC Prescription
 Review Program

Objectives

 Appreciate the individual and public health harms associated with increased prescription opioid use

• Describe the rationale for the College's Safe Prescribing Standards and Guidelines of Drugs with Potential for Misuse/Diversion

Scope of the Problem

Public Health Harms

'Too toxic to touch': Police struggle to deal with fentanyl

'We're simply not going to arrest our way out of this problem. It's too big an issue'

By Eric Rankin, CBC News Posted: Sep 15, 2016 2:00 AM PT | Last Updated: Sep 15, 2016 6:03 AM PT



Fentanyl deaths are a Canada-wide 'disaster'

Aysterious narcotic is hundreds of times more powerful than heroin

y Aleksandra Segan, CBC News Posted: Aug 10, 2015 5:00 AM ET | Last Updated: Aug 10, 2015 4:36 PM ET



POINT OF VIEW | The new face of fentanyl addiction:

'l just couldn't stop,' 22-year-old says

Vati Mather last December and new (Escobook & Oliff Chim/CDO)

By Eric Rankin, CBC News Posted: Sep 17, 2016 2:00 AM PT | Last Updated: Sep 17, 2016 8:55 AM PT





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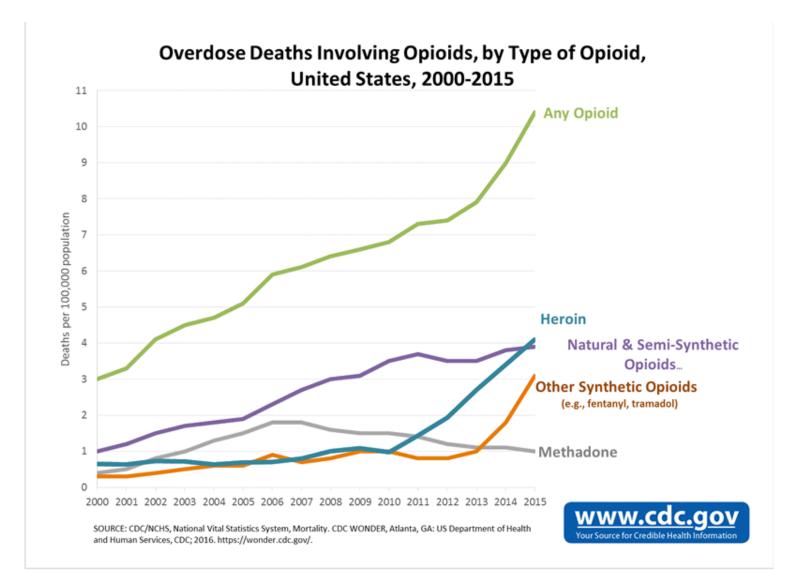
CBC INVESTIGATES | Fentanyl involved in at least 32 Maritime drug deaths

Experts warn that fentanyl crisis, which has killed hundreds in British Columbia, could be coming east. 8/ Kales Davis, Augus Harter (BC have Feater for 1, 2010 00 AM AT Land Upper Harter (BC 100 AM AT





Julie: Gould, pictured here with the france Jann Penry, died after taking fersary) in Nonctan in 2014. Theny wante people to know about the dargets at the drug. (Submitted)



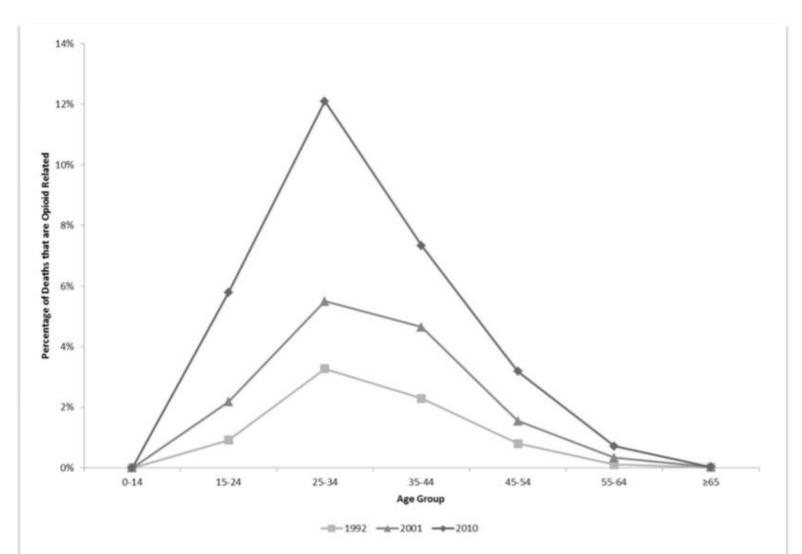


Figure 2 Proportion of all deaths that are opioid-related, by age group, 1992, 2001 and 2010. The proportion of deaths in each age group that involved an opioid was calculated using opioid-related death data abstracted from the Office of the Chief Coroner of Ontario and deaths from all causes identified using the Ontario Registered Persons Database. This analysis was performed at three time-points over our study period: 1992, 2001 and 2010

Prescription Opioid Analgesics (POA)

- Increase in opioid prescriptions has led to:
 - − ↑overdoses
 - 一 个ED visits for non-medical
 POA use

 - <u>900% 个 in individuals</u>
 <u>seeking addiction treatment</u>
 <u>for POA addiction (US data)</u>

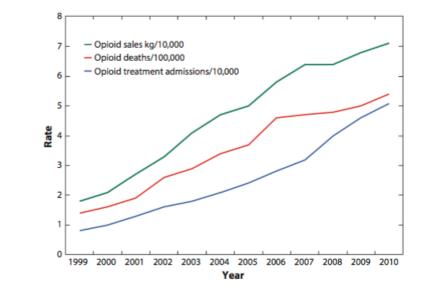


Figure 1

Rates of OPR sales, OPR-related unintentional overdose deaths, and OPR addiction treatment admissions, 1999–2010. Abbreviation: OPR, opioid pain reliever. Source: 10.

Kolodny A. et al. The Prescription Opioid and Heroin Crisis. Annu.Rev.Public Health 2015: 36; 559-574

80% of heroin users report their use began with POA

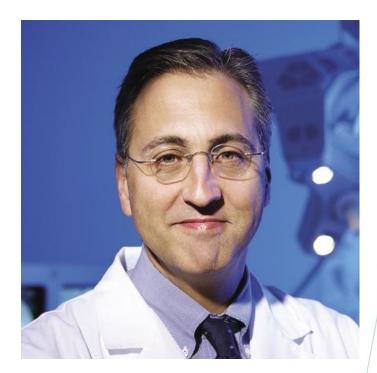
SAMHSA 2013

Scope of the Problem

Individual Harms

Management of chronic pain with opioids is "A perfect storm of controversy..."

-Dr. Scott Fishman

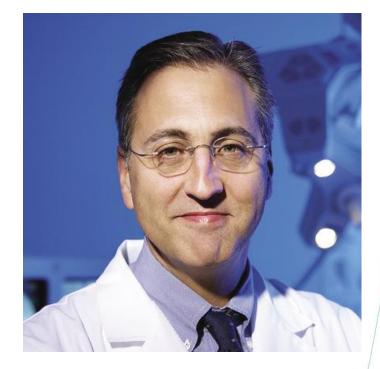


"A perfect storm of controversy..."

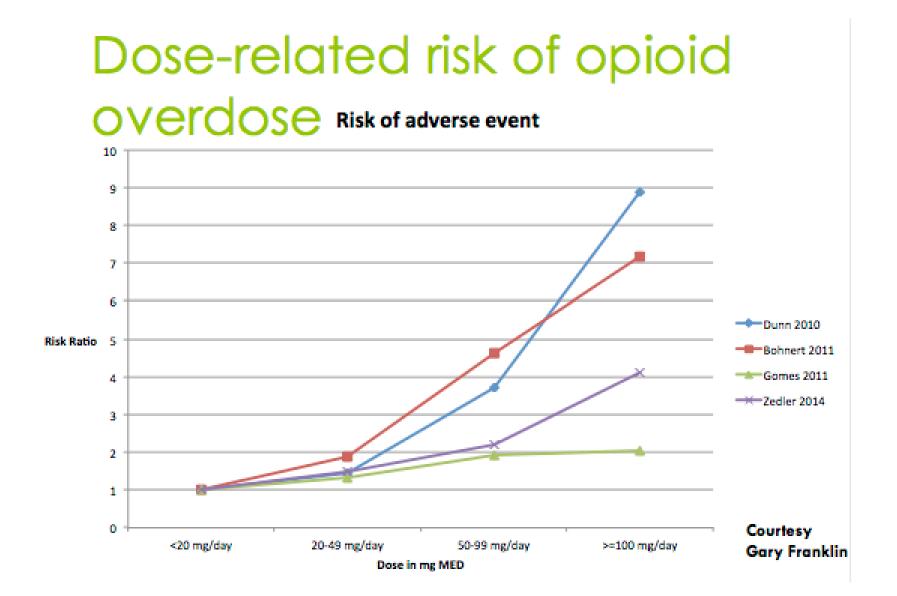
"... a War on Pain and a War on Drugs"

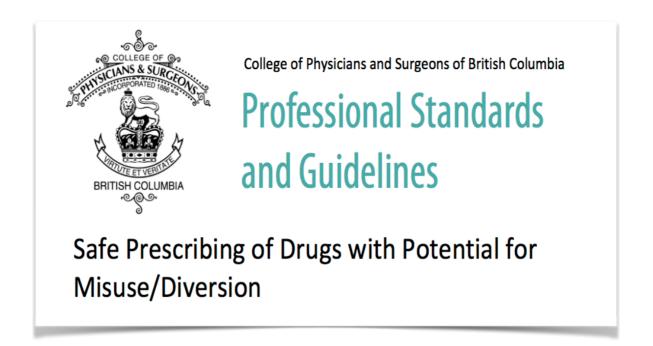
—Dr. Scott Fishman

- •Pain management
- latrogenesis
- Addiction
- Diversion



latrogenesis





 Always prescribe the lowest effective dosage of opioid medication. Doses >50 morphine milligram equivalents (MME) per day warrant careful reassessment and documentation. Doses >90 MME per day warrant substantive evidence of exceptional need and benefit. (This advice excludes treatment with methadone.)

Overvaluation of therapeutic effects?

"The explosive use of therapeutic opioids, however, is complicated by a lack of evidence regarding their effectiveness, long-term efficacy, and safety data in the treatment of **chronic non-cancer pain**, but *there is irrefutable evidence of adverse consequences* (46, 54-123)"

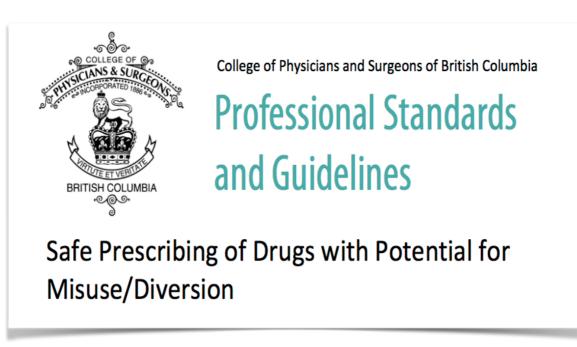
ASIPP - Opioid Guidelines 2012

American Society of Interventional Pain Physicians (ASIPP) Guidelines for Responsible Opioid Prescribing in Chronic Non-Cancer Pain: Part I – Evidence Assessment

Laxmaiah Manchikanti, MD¹, Salahadin Abdi, MD, PhD², Sairam Atluri, MD³, Carl C. Balog, MD⁴, Ramsin M. Benyamin, MD⁵, Mark V. Boswell, MD, PhD⁶, Keith R. Brown, PharmD³, Brian M. Bruel, MD¹, David A. Bryce, MD⁹, Patricia A. Burks, LPT¹⁹, Allen W. Burton, MD¹¹, Aaron K. Calodney, MD¹¹, David L. Caraway, MD¹¹, Kimberly A. Cash, RT¹⁴, Paul J. Christo, MD¹⁵, Kim S. Damron, RN¹⁶, Sukdeb Datta, MD¹⁰, Timothy R. Deer, MD¹¹, Sudhir Diwan, MD¹¹, Ike Eriator, MD²⁰, Fark J.E. Falco, MD²¹, Bert Fellows, MA²², Stephanie Geffert, MLIS²³, Christopher G. Gharibo, MD²⁴, Scott E. Glaser, MD²⁵, Jay S. Grider, DO, PhD²⁶, Haroon Hameed, MD²¹, Mariam Hameed, MD²¹, Hans Hansen, MD²⁰, Michael E. Harned, MD²⁰, Adam M. Kaye, PharmD²¹, Standiford Helm II, MD²⁰, Joavid A. Kloth, MD²⁰, Defrave M. Janata, PhD¹⁴, Adam M. Kaye, PharmD²¹, Alan D. Kaye, MD, PhD¹⁴, David S. Kloth, MD²⁰, Denalakshmi Koyalagunta, MD²⁰, Midyasgar Pampati, MS⁴⁰, Allan T. Parr, MD⁴⁰, Ramarao Pasupuleti, MD⁴⁰, Vikram B. Patel, MD⁴⁰, Nalini Sehal, MD⁴⁰, Sanford M. Silverman, MD⁴⁰, Vijay Singh, MD⁴⁰, Howard S. Smith, MD⁴⁰, Lee T. Snook, MD²¹, Baneshvari R. Solanki, MD²⁰, Deborah H. Tracy, MD⁴¹, Ricardo Vallejo, MD, PhD⁴², Bradley W. Wargo, DO⁴⁰

Evidence of LT effectiveness of POA for CNCP is lacking whilst evidence for risk of harm is plentiful

- Respiratory depression
- CNS depression
- Dysphoria and MDD
- + Falls
- H-P-G and H-P-A axis dysfunction
- Increased pain sensitivity (OIH)
- Gastroparesis
- Xerostomia
- Immunosuppression



6. Other concurrent medical conditions which should be carefully considered in the context of decisions to prescribe or continue LTOT include obesity, congestive heart failure, sleep apnea, chronic lung disease and renal or hepatic insufficiency. Elderly patients are more likely to suffer from these concurrent diagnoses and to be taking multiple medications and suffer from cognitive impairment all of which significantly increase risk.

Trends and sex differences in prescription opioid deaths in British Columbia, Canada

Emilie J Gladstone, Kate Smolina, Steven G Morgan

- Between 2004-2013 there were 3775 drug poisoningrelated deaths and prescription opioids were involved in 1674 of these
- The majority of prescription opioid deaths were secondary to opioids other than methadone (methadone was involved in 25% of deaths)
- Men experienced higher mortality rates than women
- The majority of prescription opioid deaths were <u>unintentional</u> (73% for women; 82% for men)

Gladstone EJ, et al. Inj Prev 2015;0:1–3. doi:10.1136/injuryprev-2015-041604

College of Physicians and Surgeons of British Columbia



College of Physicians and Surgeons of British Columbia

Professional Standards and Guidelines

Safe Prescribing of Drugs with Potential for Misuse/Diversion

Document the offer of a take-home naloxone prescription to all patients who are at risk of respiratory depression as a consequence of receiving opioid medications.

Combinations

Benzodiazepines: A Major Component in Unintentional Prescription Drug Overdoses With Opioid Analgesics

- During 2003-2009 the 2 prescription drugs with the highest increase in death rates were oxycodone (265%) and alprazolam (234%).
- Benzodiazepines involved in >5500 deaths in 2009 (5fold increase since 1999)
- ED visits in the US for nonmedical use of BZD between 2004-2010 increased by 139%
- The opioid and BZD combination had the highest predicted model for drug related fatality

Journal of Pharmacy Practice 27(1)

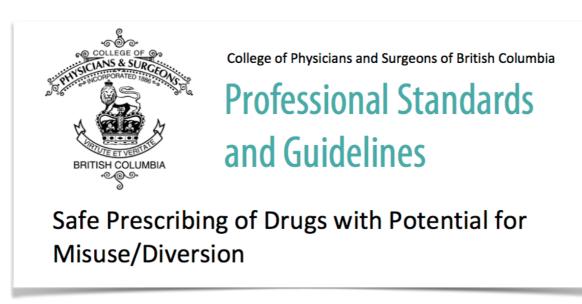
Opioids + BZD/sedatives = complications

- Respiratory depression \rightarrow overdose
- CNS depression
- Increased psychiatric comorbidity
- Increased risky behaviours
- Daytime somnolence \rightarrow Increased risk MVA, workplace injury
- Cognitive disturbance
- Balance disorder
- Addiction

BZD implicated in as many as 80% of unintentional overdoses involving opioids

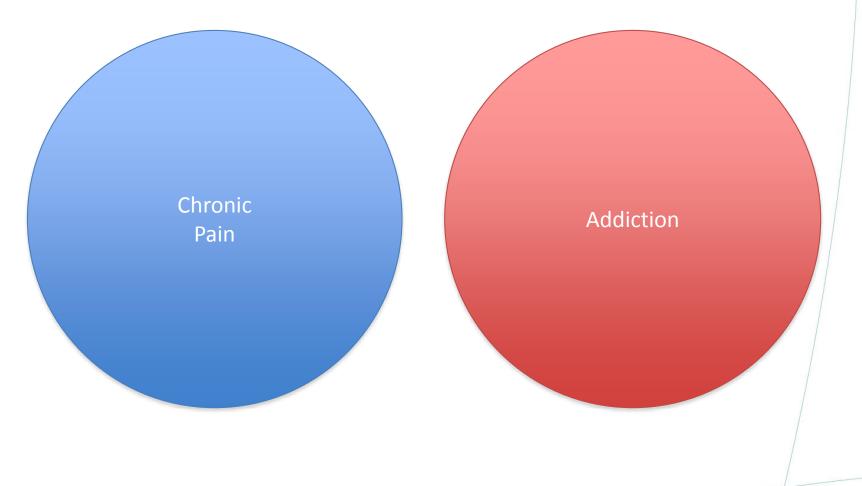
Opioids + BZD/sedatives + ETOH = complications

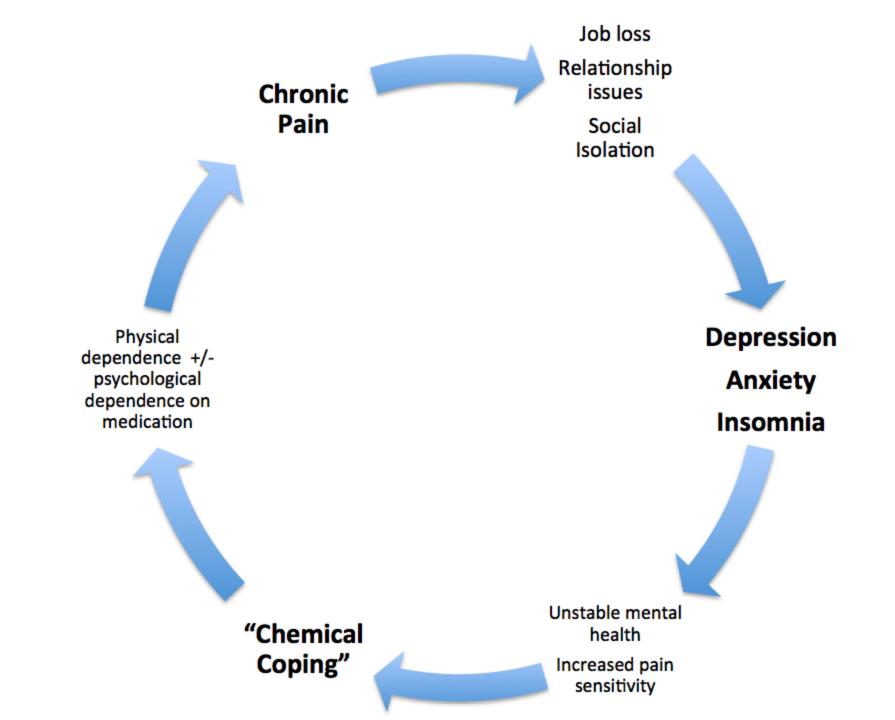
- Respiratory depression → overdose
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- Balance disorder
- Addiction



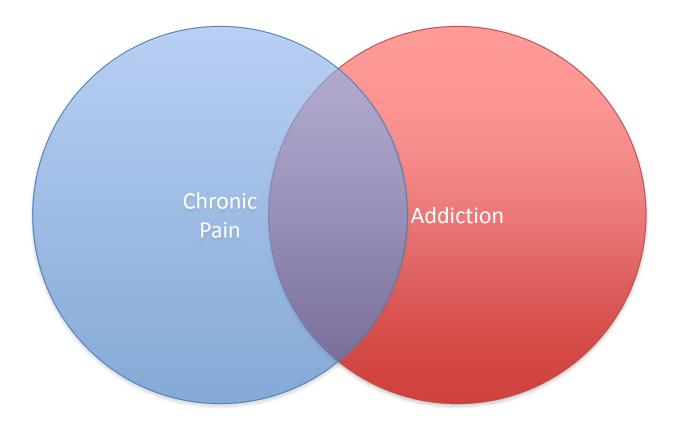
11. The advice to avoid concurrent prescribing of opioids and sedative hypnotics such as benzodiazepines is based on the significantly increased risk of overdose death in this patient population. However, physicians should be aware that other central nervous system (CNS) depressants (including muscle relaxants, anticonvulsants, sedating antidepressants, antipsychotics, some over-the-counter medications and alcohol) may also potentiate CNS and respiratory depression. If LTOT is clinically appropriate, benzodiazepines should be tapered and discontinued. Benzodiazepine tapering should be gradual because of the significant risks of benzodiazepine withdrawal.

Previous understanding: Separate silos





Current understanding: Intersection





Chronic Pain

85y spinal stenosis, No SUD/psychiatric hx Stable dose opioids 10 years

22y fibromyalgia; AUD as teen, Bipolar, FHx addiction, Escalating opioid doses, lost Rx



Chronic Pain

85y spinal stenosis, No SUD/psychiatric hx Stable dose opioids 10 years

22y fibromyalgia; AUD as teen, Bipolar, FHx addiction, Escalating opioid doses, lost Rx



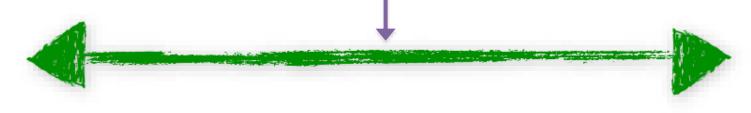
Chronic Pain

50y chronic abdo pain, chronic pancreatitis, AUD 25y remission, FHx depression, opioid doses 个 slowly



Chronic Pain

50y chronic abdo pain, chronic pancreatitis, AUD 25y remission, FHx depression, opioid doses 个 slowly

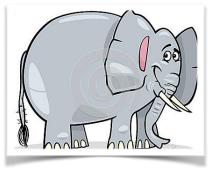


Chronic Pain

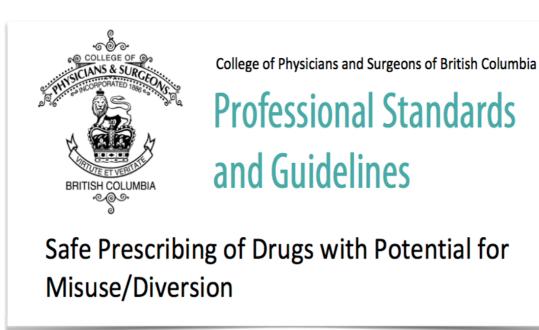
Prescription Medication Obtainment Methods and Misuse

Daniel Tyler Bouland, MD, Eric Fine, MD, David Withers, MD, and Margaret Jarvis, MD

- Small survey (n=36) Inpatient addiction program
- 75 % had contrived symptoms including fake MRIs to demonstrate pathology, fake prescription bottles
- 8.3 % physically harmed themselves to obtain Rx

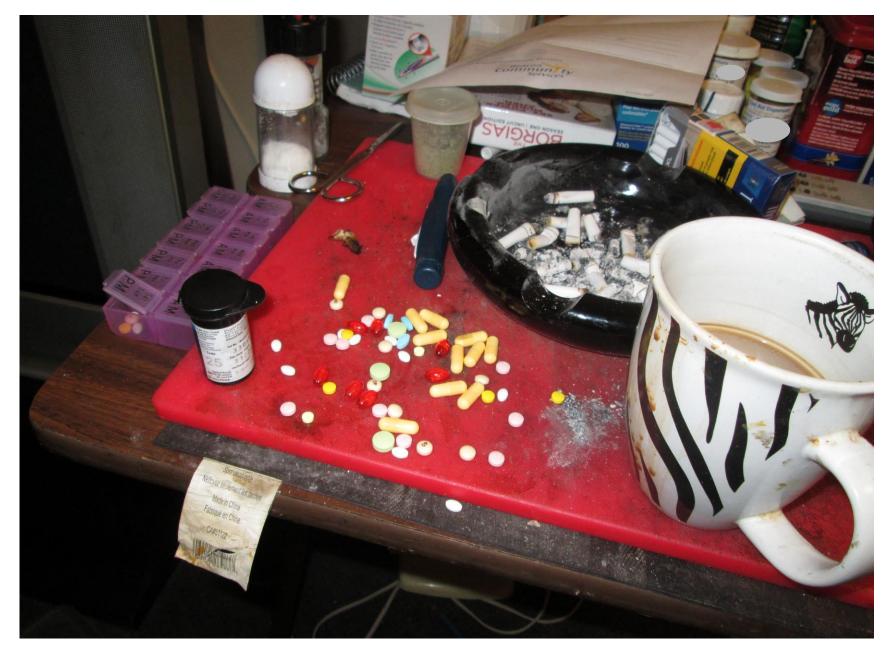


 66.7 % stated intervention may have changed their behaviours and 61.1% would have welcomed an empathetic intervention by their physician

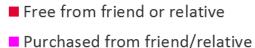


5. The prevalence of an opioid use disorder may be as high as 26% among primary care patients receiving opioids for CNCP. Patients with a diagnosis of an opioid use disorder should be offered treatment including medication assisted treatment with methadone or buprenorphine, as well as abstinence-based treatment where appropriate.

Diversion

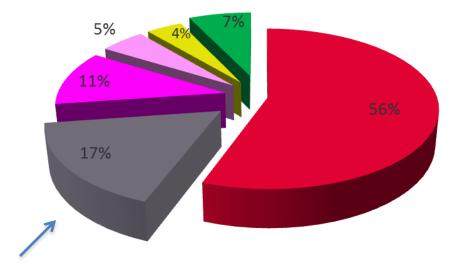


Sources of prescription opioids for those that abuse them (Adapted from SAMHSA 2010)



Drug dealer/stranger

- Prescribed by one doctor
- Taken from friend/relative without asking
- Other source



Sources of prescription opioids for those that abuse them (Adapted from SAMHSA 2010)

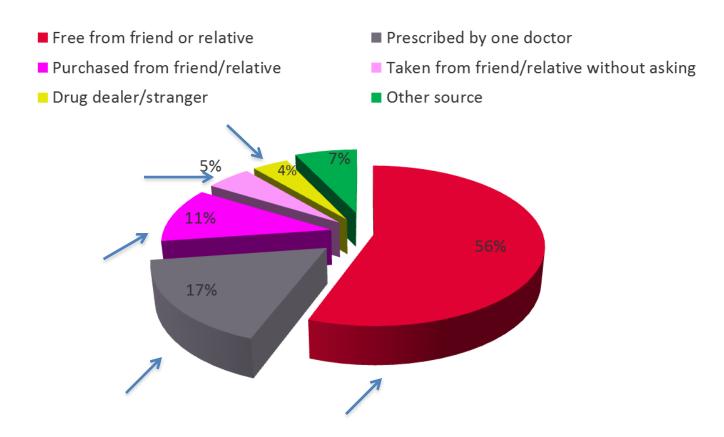


Table 1

Sources of pain relievers, stimulants, and tranquilizers, and when they were used.

	Pain relievers (%)	Stimulants (%)	Tranquilizers (%)
Source of drugs			
A friend gives them the drugs	59.6	78.6	60.5
Own prescription	32.7	21.4	13.2
Family member provides them	26.9	11.4	28.9
Purchases them from a friend	17.3	41.4	18.4
Purchases them from an acquaintance	9.6	14.3	7.9
Reason for use			
Studying for final exams	8.2	65.7	9.1
Studying for midterm exams	6.1	54.3	9.1
Studying for regular exams	6.1	48.6	9.1
Before attending class	2.0	31.4	12.1
Socializing and partying	69.4	47.1	48.5
Self-medication	24	N/A	97

Includes pain relievers used for self-medication of pain/sleep, and tranquilizers used for self-medication of anxiety and to aid in relaxation. Participants did not list any uses for stimulants that were for self-medication, rather, the principle reason for using stimulants was for studying purposes, as indicated above. A survey of nonmedication

A survey of nonmedical use of tranquilizers, stimulants, and pain relievers among college students: Patterns of use among users and factors related to abstinence in non-users

Sara A. Brandt^{a,1}, Elise C. Taverna^{b,1}, Robert M. Hallock^{b,*,1}



College of Physicians and Surgeons of British Columbia Professional Standards and Guidelines

Safe Prescribing of Drugs with Potential for Misuse/Diversion

8. Base decisions to prescribe long-term psychoactive medications, including LTOT, on well-documented, comprehensive initial assessments and frequent (at least every three months) reassessments. These assessments and reassessments must include documented history and physical examination of the patient. There must also be documentation that the patient has been screened regularly for the presence or emergence of mental health and substance use disorders and risk factors and advised about safety-sensitive occupational risks, child care responsibilities and driving.

 Provide prescriptions allowing dispenses of opioids, sedatives and stimulants, which exceed a three-month supply or 250 tablets, whichever is less.

The College mandate: Public protection



College of Physicians and Surgeons of British Columbia

Professional Standards and Guidelines

Safe Prescribing of Drugs with Potential for Misuse/Diversion

College's Position

The public health crisis of prescription drug misuse has developed in part due to the prescribing of physicians. The profession has a collective ethical responsibility to mitigate its contribution to the problem of prescription drug misuse, particularly the over-prescribing of opioids, sedatives and stimulants.



College of Physicians and Surgeons of British Columbia

Professional Standards and Guidelines

Safe Prescribing of Drugs with Potential for Misuse/Diversion

The public health crisis of prescription drug misuse has developed in part due to the prescribing of physicians. The profession has a collective ethical responsibility to mitigate its contribution to the problem of prescription drug misuse, particularly the over-prescribing of opioids, sedatives and stimulants.

The College acknowledges the appropriate role of pharmacotherapy in the context of active cancer, palliative, nursing home and end-of-life care. These standards may not apply to the treatment of patients in these situations.

Every physician is professionally responsible for the prescription that they provide to a patient.

Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain

Roger Chou,¹ Gilbert J. Fanciullo,² Perry G. Fine,³ Jeremy A. Adler,⁴ Jane C. Ballantyne,⁵ Pamela Davies,⁶ Marilee I. Donovan,⁷ David A. Fishbain,⁸ Kathy M. Foley,⁹ Jeffrey Fudin,¹⁰ Aaron M. Gilson,¹¹ Alexander Kelter,¹² Alexander Mauskop,¹³ Patrick G. O'Connor,¹⁴ Steven D. Passik,¹⁵ Gavril W. Pasternak,¹⁶ Russell K. Portenoy,¹⁷ Ben A. Rich,¹⁸ Richard G. Roberts,¹⁹ Knox H. Todd,²⁰ and Christine Miaskowski,²¹ FOR THE AMERICAN PAIN SOCIETY–AMERICAN ACADEMY OF PAIN MEDICINE OPIOIDS GUIDELINES PANEL

Perspective: Safe and effective chronic opioid therapy for chronic noncancer pain requires clinical skills and knowledge in both the principles of opioid prescribing and on the assessment and management of risks associated with opioid abuse, addiction, and diversion. Although evidence is limited in many areas related to use of opioids for chronic noncancer pain, this guideline provides recommendations developed by a multidisciplinary expert panel after a systematic review of the evidence.

Clinical Guidelines for the Use of Chronic Opioid Therapy

Part 2 - Guidance

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ASIPP - Opioid Guidelines 2012

Roger Chi Pamela Di Aaron M. Steven D. Richard G Society-Ai Perspective

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Laxmaiah Manchikanti, MD¹, Salahadin Abdi, MD, PhD², Sairam Atluri, MD³, Carl C. Balog, MD⁴, Ramsin M. Benyamin, MD⁵, Mark V. Boswell, MD, PhD⁶, Keith R. Brown, PharmD⁷, Brian M. Bruel, MD⁸, David A. Bryce, MD⁹, Patricia A. Burks, LPT¹⁰, Allen W. Burton, MD¹¹, Aaron K. Calodney, MD¹², David L. Caraway, MD¹³, Kimberly A. Cash, RT¹⁴, Paul J. Christo, MD¹⁵, Kim S. Damron, RN¹⁶, Sukdeb Datta, MD¹⁷, Timothy R. Deer, MD¹⁸, Sudhir Diwan, MD¹⁹, Ike Eriator, MD²⁰, Frank J.E. Falco, MD²¹, Bert Fellows, MA²², Stephanie Geffert, MLIS²³, Christopher G. Gharibo, MD²⁴, Scott E. Glaser, MD²⁵, Jay S. Grider, DO, PhD²⁶, Haroon Hameed, MD²⁷, Mariam Hameed, MD²⁸, Hans Hansen, MD²⁹, Michael E. Harned, MD³⁰, Salim M. Hayek, MD, PhD³¹, Standiford Helm II, MD³², Joshua A. Hirsch, MD³³, Jeffrey W. Janata, PhD³⁴, Adam M. Kaye, PharmD³⁵, Alan D. Kaye, MD, PhD³⁶, David S. Kloth, MD³⁷, Dhanalakshmi Koyyalagunta, MD³⁸, Marion Lee, MD³⁹, Yogesh Malla, MD⁴⁰, Kavita N. Manchikanti, MD⁴¹, Carla D. McManus, RN, BSN⁴², Vidyasagar Pampati, MSc⁴³, Allan T. Parr, MD⁴⁴, Ramarao Pasupuleti, MD⁴⁵, Vikram B. Patel, MD⁴⁶, Nalini Sehgal, MD⁴⁷, Sanford M. Silverman, MD⁴⁸, Vijay Singh, MD⁴⁹, Howard S. Smith, MD⁵⁰, Lee T. Snook, MD⁵¹, Daneshvari R.

Solanki, MD⁵², Deborah H. Tracy, MD⁵³, Ricardo Vallejo, MD, PhD⁵⁴, Bradley W. Wargo, DO⁵⁵

American Society of Interventional Pain

Physicians (ASIPP) Guidelines for Responsible

Opioid Prescribing in Chronic Non-Cancer Pain:

- 6. A robust agreement which is followed by all parties is essential in initiating and maintaining opioid therapy as such agreements reduce overuse, misuse, abuse, and diversion. (Evidence: fair)
- A) Once medical necessity is established, opioid therapy may be initiated with low doses and short-acting drugs with appropriate monitoring to provide effective relief and avoid side effects. (Evidence: fair for short-term effectiveness, limited for long-term effectiveness)
 - B) Up to 40 mg of morphine equivalent is considered as low dose, 41 to 90 mg of morphine equivalent as a moderate dose, and greater than 91 mg of morphine equivalence as high dose. (Evidence: fair)
 - C) In reference to long-acting opioids, titration must be carried out with caution and overdose and misuse must be avoided. (Evidence: good)

Laxmaia

Clinical Guidelines for the Use of Chronic Opioid Therapy

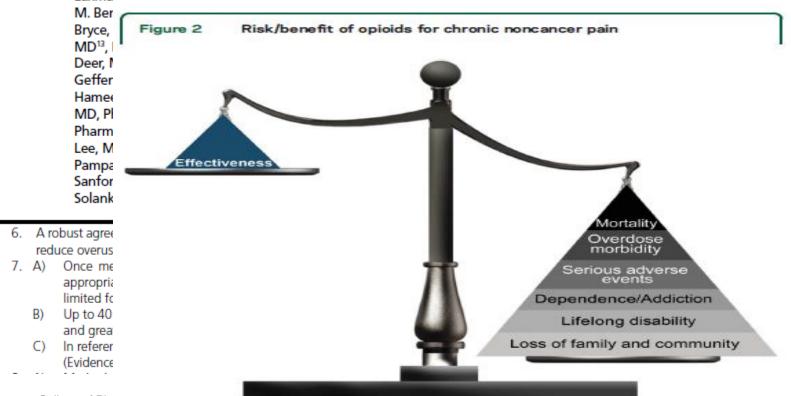
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ASIPP - Opioid Guidelines 2012

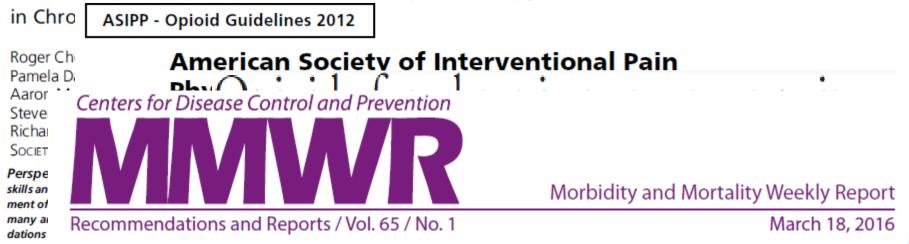
Roger Ch Pamela Di Aaron M. Steven D. Richard G Society-Ai Perspective skills and kno ment of risks many areas r

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American Society of Interventional Pain PhyOpioids for chronic noncancer pain Opi Par A position paper of the American Academy of Neurology



Clinical Guidelines for the Use of Chronic Opioid Therapy



CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

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Determining When to Initiate or Continue Opioids for Chronic Pain

- 1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
- 2. Before starting opioid therapy for chronic pain, clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
- Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

- When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
- 5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
- 6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.

7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

- 8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present.
- 9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
- 10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
- 11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
- 12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

Urine drug testing and checking PharmaNet: Objective tools as part of clinical assessment

Study to identify/quantify rate of aberrant drugtaking behaviours using objective data in a university-based, multidisciplinary pain centre

- Interview, questionnaire (prescription, illicit, OTC Rx), UDT
- Discrepancies between pt report, PDMP, referring physician records and UDT were reported to provide an overall Inconsistency Score (IS) (Max points 16)

Hamill-Ruth RJ et al. Pain Medicine 2013;14:1900-1907

 Addition of UDT or PDMP to patient questionnaire and referring physician records increased identification of inconsistencies by 400%

 Addition of UDT or PDMP to patient questionnaire and referring physician records increased identification of inconsistencies by 900%

Watch the Dr. Mike Evans video (and get your patients to watch it too!)

Currently at: https://www.youtube.com/watch?v=7Na2m7lx-hU

Opioids Videos

Posted by admin on Mar 19, 2013 in Videos | 1 comment

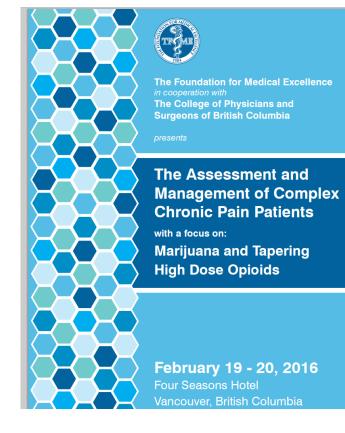
Here are our Opioid videos in English and French!



College of Physicians and Surgeons of British Columbia

Chronic Pain and Suffering Symposium

Come to our excellent annual CME event



Recommended Reading

- Lembke A. et al. Weighing the Risks and Benefits of Chronic Opioid Therapy. Am Family Physician 2016; 93 (12):982-990
 - How to talk to patients about the risks of chronic opioid therapy (COT)
 - Strategies for mitigating risk in patients receiving COT
 - Strategies for mitigating risk when discontinuing COT