The Opioid Spectrum: Promoting Health and Preventing Harm

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May 8th, 2017

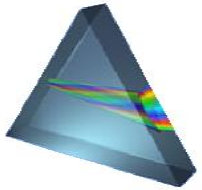
UNIVERSITY OF MANITOBA

COLLEGE OF PHARMACISTS OF MANITOBA

Disclosures

- The research elements of this presentation were funded from grants from the University of Manitoba, College of Pharmacists of Manitoba

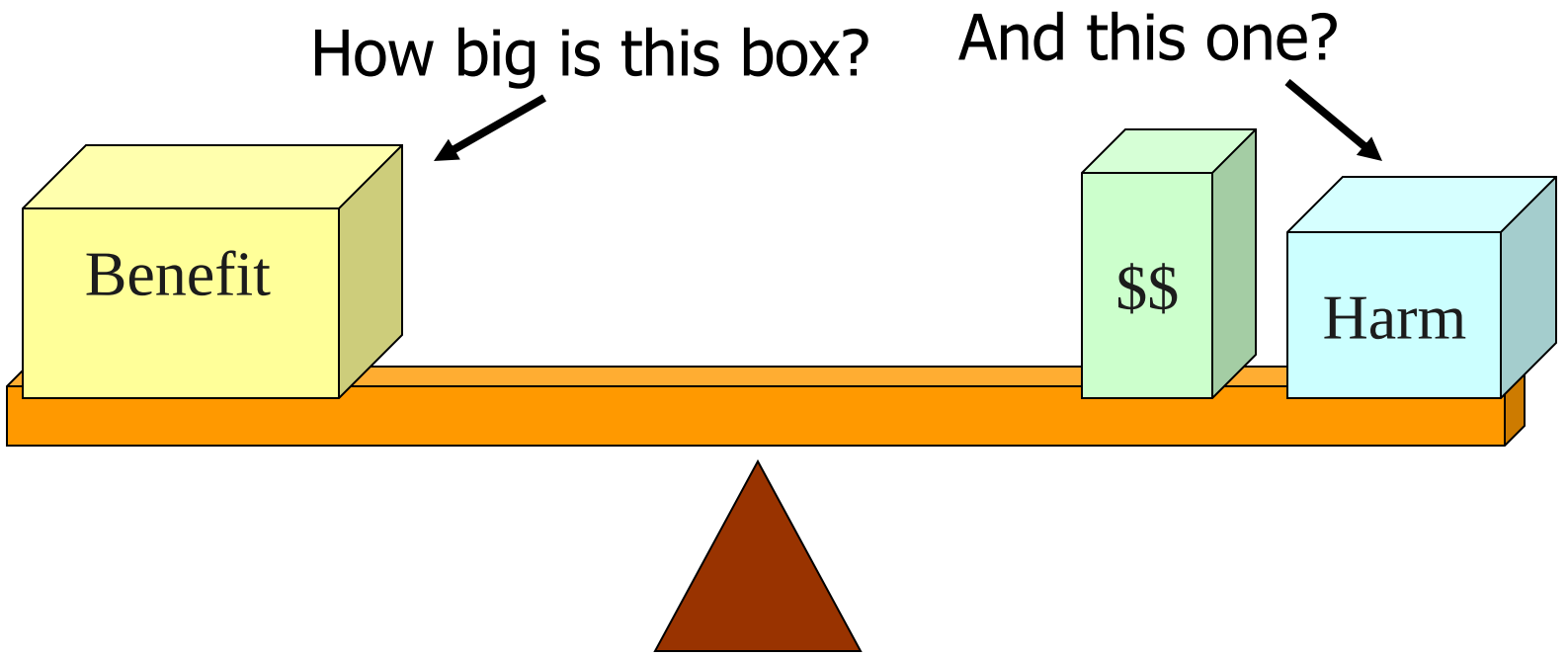
- No other relevant relationships to disclose

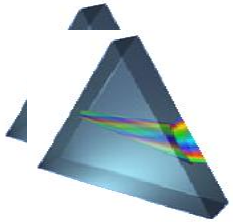


Learning Objectives

- Consider and review the evolution of current guidelines on the use of opioids in management of chronic non-cancer pain
- Evaluate the current utilization of opioids in Manitoba against guideline recommendations

How to Avoid a Mess





Hierarchy of Evidence

Meta-analysis of RCTs

Individual RCT

Observational Studies (Patient Important Outcomes)

Basic Research
(Test tube, animal/human physiology)

Clinical Experience
(Non-systematic clinical observation)

Dr Hershel Jick

- 1979
- Boston University
- Boston Collaborative Drug Surveillance Program
- How often do hospitalized patients given narcotic pain killers develop addiction

Porter and Jick

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

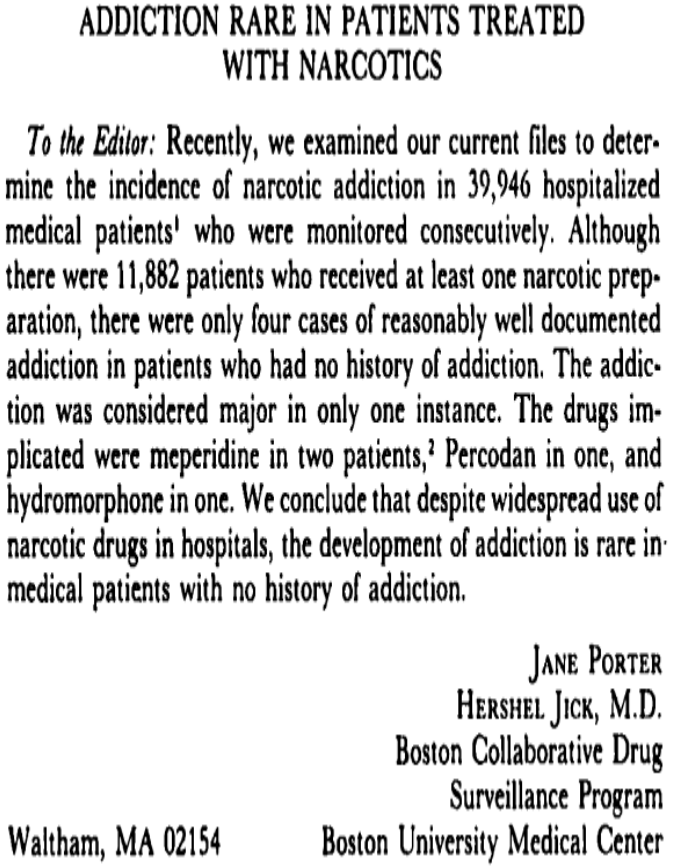
To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug
Surveillance Program
Boston University Medical Center
Waltham, MA 02154

Porter and Jick 1980;NEJM 302:123

Porter and Jick

- < 1% treated with opioids developed addition
- Educational seminars
- Only electronically archived in 2010
- Scientific American (1990) "an extensive study"
- Time (2001) "landmark study" "exaggerated fear that patients would become addicted" to opiates was "basically unwarranted."



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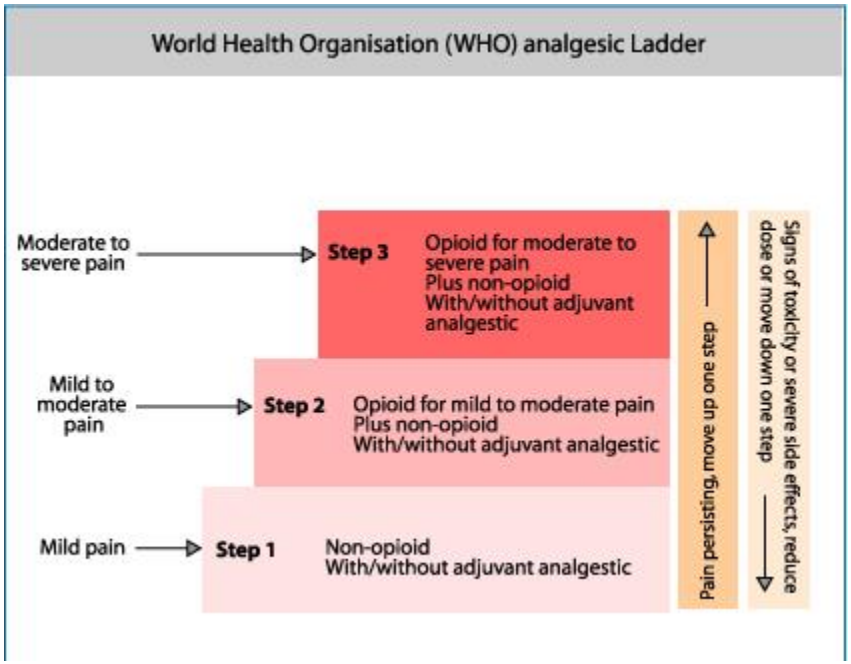
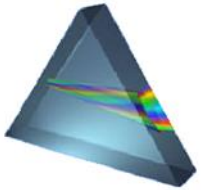
Porter and Jick 1980;NEJM 302:123

WHO Ladder
Pain Treatment as a Right



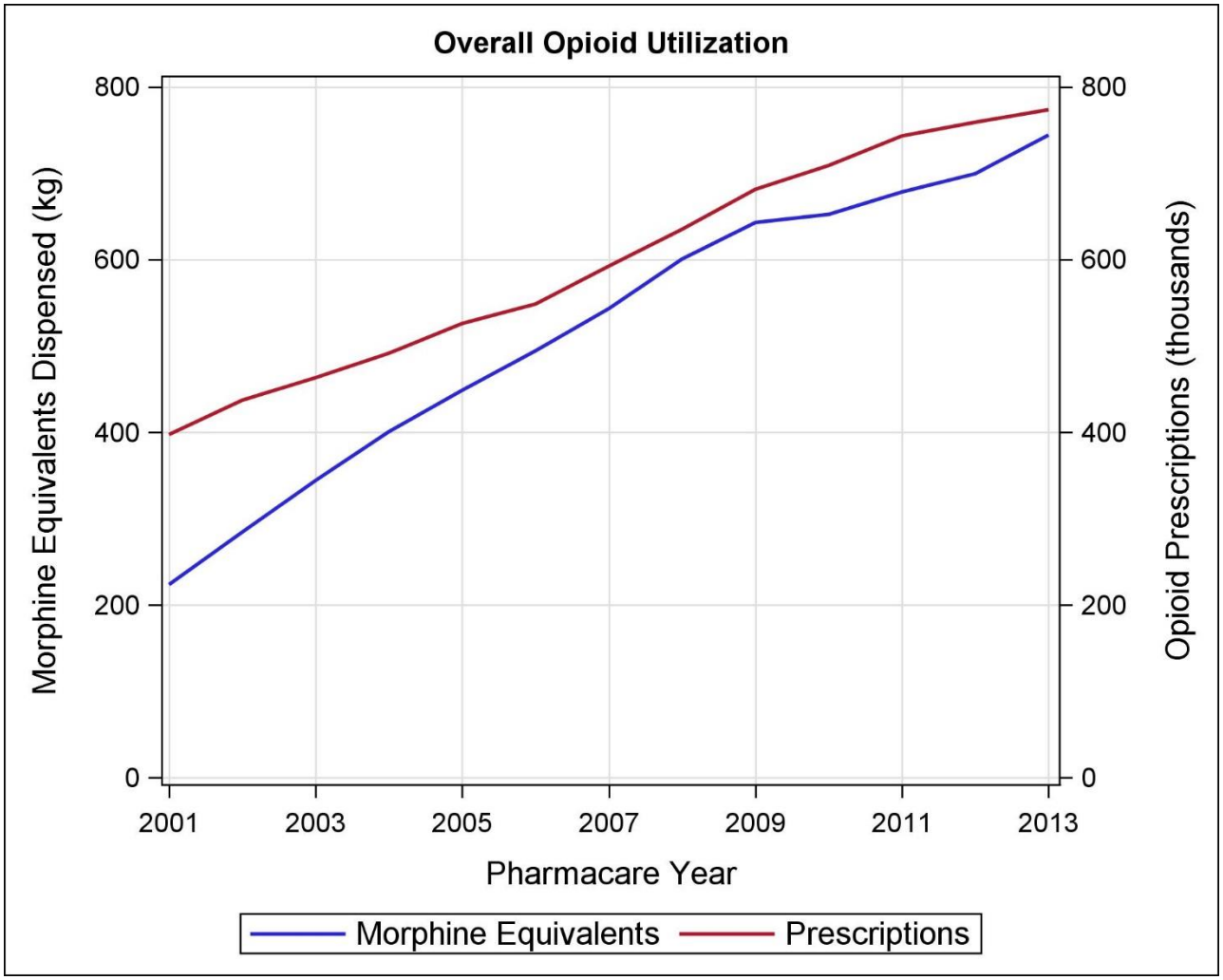
- Jan Stjensword – WHO Geneva 1980
- Vittario Ventafridda
- Cancer pain
- Morphine as an essential drug
- Freedom from pain as universal human right



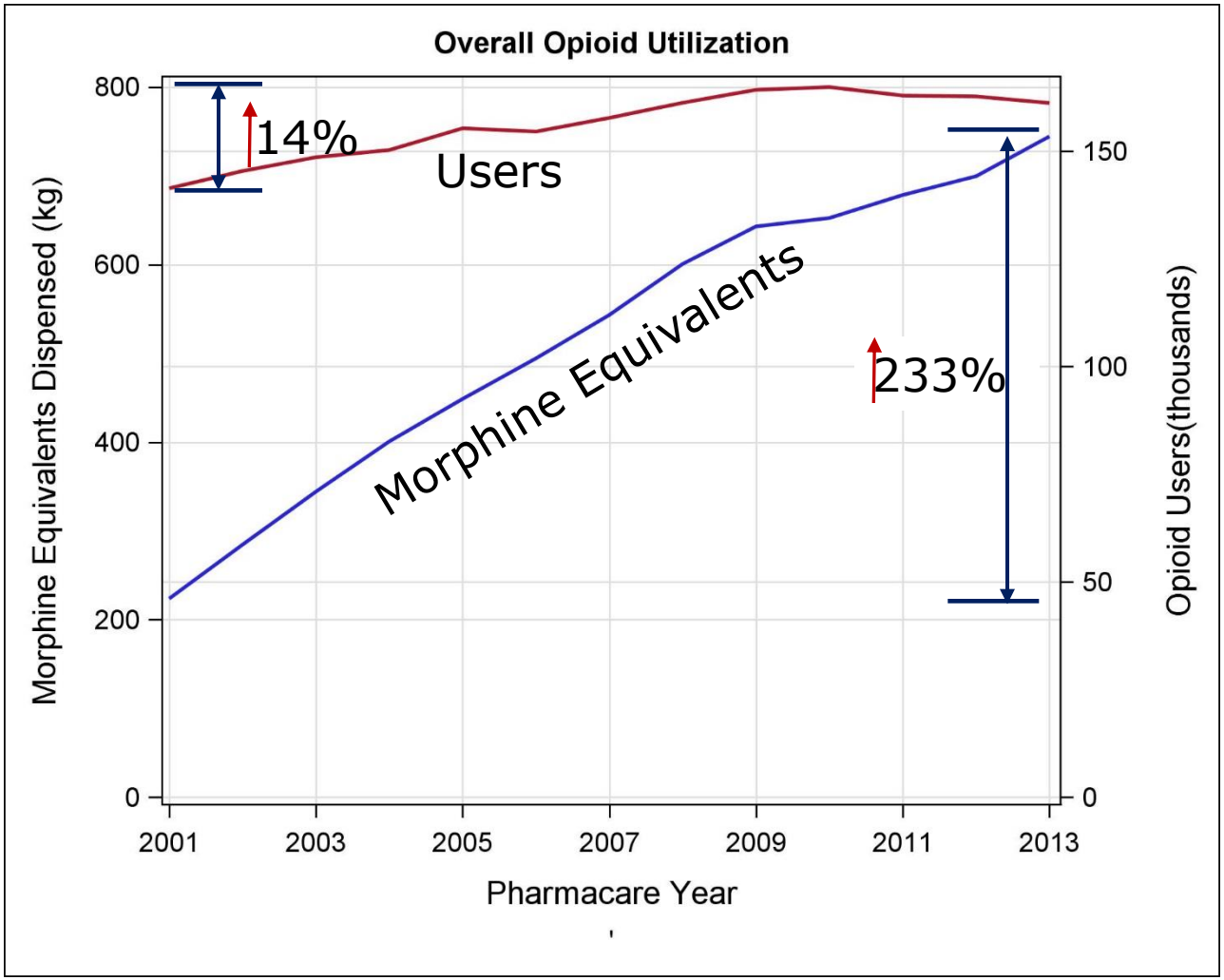
Response

- 1980 to 2011 30 fold increase in opioid use
- Not in developing world
- Fear and access issues opioids remain in developing world
- 20% of word consumes 90% of world's morphine

Opioid Utilization in Manitoba



Opioid Utilization in Manitoba



Non-Cancer Pain

Pain, 25 (1986) 171–186
Elsevier

PAI 00878

Chronic Use of Opioid Analgesics in Non-Malignant Pain: Report of 38 Cases

Russell K. Portenoy and Kathleen M. Foley

Pain Service, Department of Neurology, Memorial Sloan-Kettering Cancer Center, and Department of Neurology, Cornell University Medical College, New York, NY 10021 (U.S.A.)

(Received 10 June 1985, accepted 28 October 1985)

Non-Cancer Pain

- Risk of addiction was low when opiates used to treat patients in pain
- Pain as the "fifth vital sign"

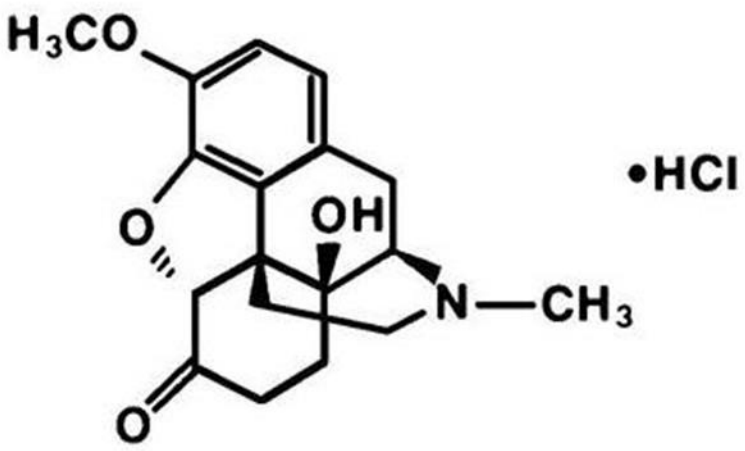
American Pain Society

Non-Cancer Pain

- 1998 Veterans Health Administration makes pain "5th vital sign"
- The Joint Commission for Accreditation of Healthcare Organizations (JCAHO) – pain as 5th vital sign

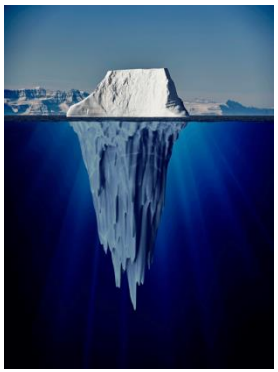
Non-Cancer Pain

- Oxycodone 1916



- OxyContin® 1996

- 30% adult population has acute or chronic pain



- Chronic pain prevalence of 40% in older adults

Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain

Part A: Executive Summary and Background
Part B: Recommendations for Practice

PART B

— Recommendations for Practice —

Published by the
National Opioid Use Guideline Group (NOUGG)
a collaboration of:

Federation of Medical Regulatory Authorities of Canada
College of Physicians & Surgeons of British Columbia
College of Physicians & Surgeons of Alberta
College of Physicians and Surgeons of Saskatchewan
College of Physicians & Surgeons of Manitoba
College of Physicians and Surgeons of Ontario
Collège des médecins du Québec
College of Physicians and Surgeons of New Brunswick
College of Physicians and Surgeons of Nova Scotia
College of Physicians and Surgeons of Prince Edward Island
College of Physicians and Surgeons of Newfoundland and Labrador
Government of Nunavut
Yukon Medical Council

April 30 2010 Version 5.6

http://nationalpaincentre.mcmaster.ca/opioid/

Canadian Guidelines 2010

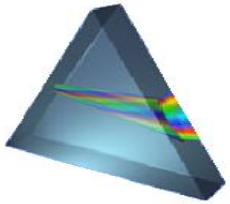
R04	Before initiating opioid therapy, consider the evidence related to effectiveness in patients with chronic non-cancer pain. (Grade A).	*Opioid efficacy*
R05	Before initiating opioid therapy, ensure informed consent by explaining potential benefits, adverse effects, complications and risks (Grade B). A treatment agreement may be helpful, particularly for patients not well known to the physician or at higher risk for opioid misuse. (Grade C).	*Risks, adverse effects, complications*
R10	Chronic non-cancer pain can be managed effectively in most patients with dosages at or below 200 mg/day of morphine or equivalent (Grade A). Consideration of a higher dosage requires careful reassessment of the pain and of risk for misuse, and frequent monitoring with evidence of improved patient outcomes. (Grade C).	*Watchful dose*

Do They Work?

Table 2: Duration of opioid therapy

Diagnosis	No. of studies	Duration of therapy (wk)		
		Average	Minimum	Maximum
Nociceptive pain	25	4.8	1	13
Neuropathic pain	12	4.4	1	6
Mixed pain	2	8.5	1	16
Fibromyalgia	2	8.8	6	11.5
Total	41	5.0	1	13

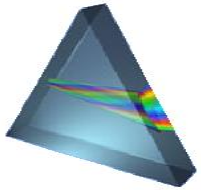
Furan et al 2006 CMAJ 174:1589



Do they Work?

Examples of CNCP conditions for which opioids *were shown to be effective* in placebo-controlled trials*		Examples of CNCP conditions that *have NOT been studied* in placebo-controlled trials
Tramadol only	**Weak or strong opioid**	
Fibromyalgia	• Diabetic neuropathy • Peripheral neuropathy • Postherpetic neuralgia • Phantom limb pain • Spinal cord injury with pain below the level of injury • Lumbar radiculopathy • Osteoarthritis • Rheumatoid arthritis • Low-back pain • Neck pain	• Headache • Irritable bowel syndrome • Pelvic pain • Temporomandibular joint dysfunction • Atypical facial pain • Non-cardiac chest pain • Lyme disease • Whiplash • Repetitive strain Injury

*A limitation of these trials was that the duration of opioid therapy was a maximum of three months.



Do They Work

Clinical Question/ PICO

Population: Patients with chronic non-cancer pain, without current or past substance use disorder and without other current serious psychiatric disorders, whose therapy is optimized with non-opioids with persistent problematic pain

Intervention: Trial of opioids.

Comparator: Continue established therapy without opioids.

Busse JW et al. 2017 CMAJ 189:E569

Do They Work?

Outcome Timeframe	Study results and measurements	Absolute effect estimates Continue established therapy without opioids.	 Trial of opioids.
Pain (difference in patients who achieve the MID or greater) 3-6 months	Relative risk 1.25 (CI 95% 1.21 - 1.29) Based on data from 13,876 patients in 27 studies. (Randomized controlled) Follow up 3-6 months	**448** per 1000	**560** per 1000
		Difference: **112 more** per 1000 (CI 95% 94 more - 130 more)	

Minimally important difference for pain on a 10-cm visual analogue scale (VAS) is a reduction of 1 cm.

Busse JW et al. 2017 CMAJ 189:E569

Do They Work?

Outcome Timeframe	Study results and measurements	Absolute effect estimates Continue established therapy without opioids.	 Trial of opioids.
Pain	Measured by: 10 cm VAS		
3-6 months	Scale: 0-10 Lower better Based on data from: 13,876 patients in 27 studies. (Randomized controlled) Follow up 3-6 months	Difference: **MD 0.64 fewer** (CI 95% 0.76 fewer - 0.53 fewer)	

Minimally important difference for pain on a 10-cm visual analogue scale (VAS) is a reduction of 1 cm.

Recognition of Side Effects

Adverse effect	Number of Studies	Incidence in Opioid Group	Incidence in Placebo Group	Difference (95% CI)
Nausea	38	28%	9%	17% (13% to 21%) P<0.00001
Constipation	37	26%	7%	20% (15% to 25%) P<0.00001
Somnolence/drowsiness	30	24%	7%	14% (10% to 18%) P<0.00001
Dizziness/vertigo	33	18%	5%	12% (9% to 16%) P<0.00001
Dry-skin/ itching/ pruritus	25	15%	2%	10% (5% to 15%) P<0.0001
Vomiting	23	15%	3%	11% (7% to 16%) P<0.00001

- Other concerns with long-term use
  - Sexual dysfunction
  - Sleep apnea
  - Opioid-Induced Hyperalgesia

Addiction

Outcome Timeframe	Study results and measurements	Absolute effect estimates Continue established therapy without opioids.	 Trial of opioids.
Addiction FU not reported	Based on data from 22,278 patients in 9 studies	Risk of opioid addiction is 5.5% (95% CI 3.91-7.03%)	

Busse JW et al. 2017 CMAJ 189:E569

Overdose

Outcome Timeframe	Study results and measurements	Absolute effect estimates Continue established therapy without opioids.	 Trial of opioids.
Fatal overdose median 2.6 years	Based on data from 285,520 patients in 1 studies	Estimated annual fatal overdose rates were 0.10%, 0.14%, 0.18% , and 0.23% in patients receiving <20 mg morphine equivalent per day, 20-49 mg/day, 50-99 mg/day, and >100 mg per day respectively.	

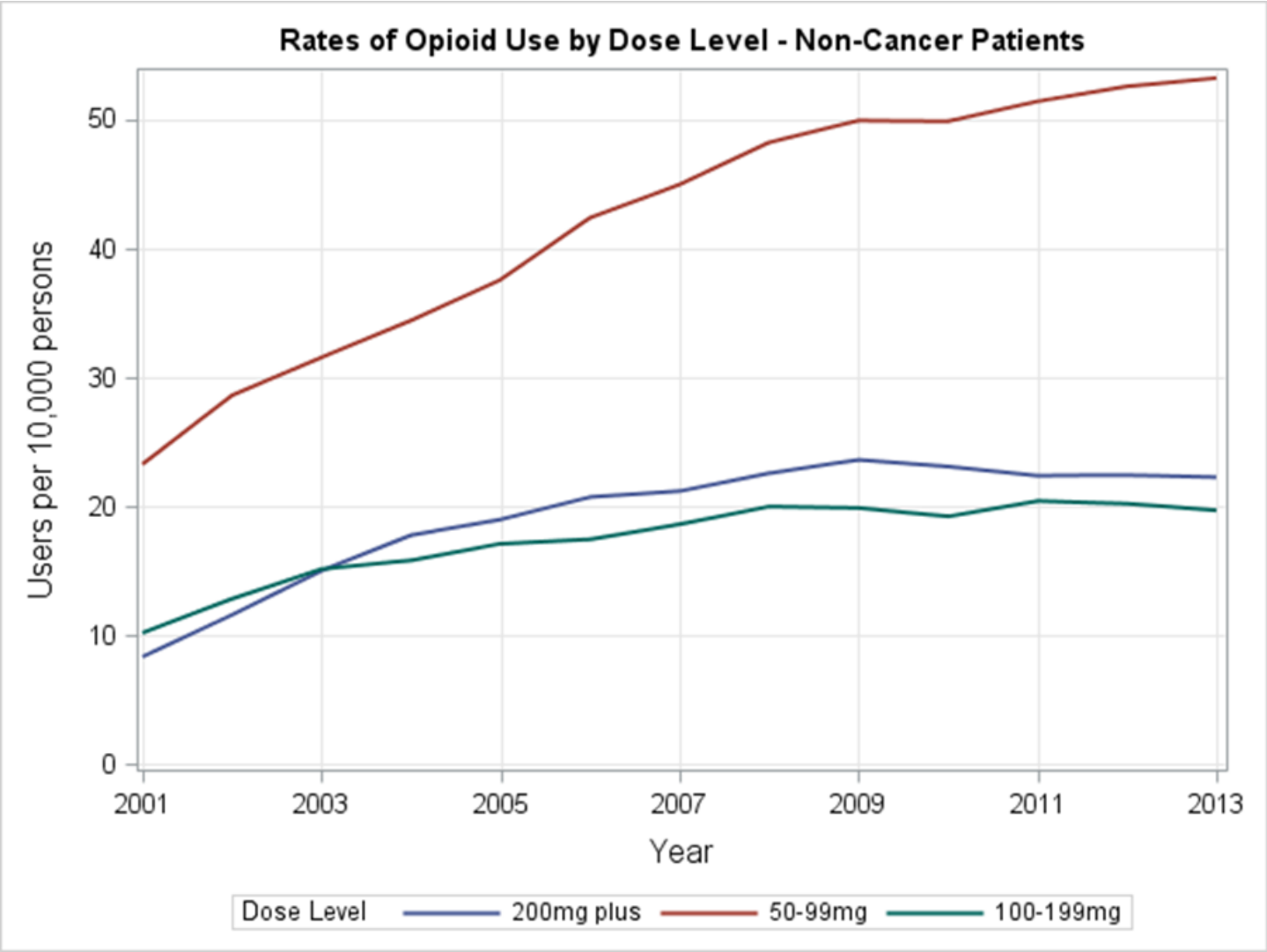
Busse JW et al. 2017 CMAJ 189:E569

Diversion

Outcome Timeframe	Study results and measurements	Absolute effect estimates Continue established therapy without opioids.	 Trial of opioids.
Diversion 1 year	Based on data from 472,200 patients in 1 studies	Among US adults, the prevalence of nonmedical use of prescription opioids was 4.9% (95% CI, 4.58%-5.22%) in 2013.	

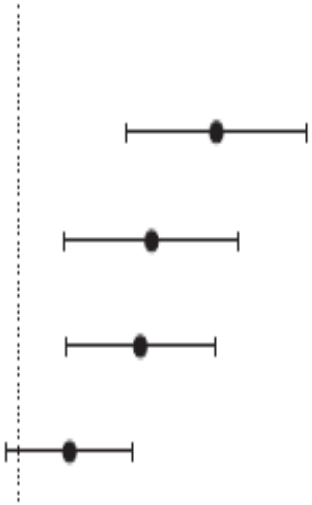
Busse JW et al. 2017 CMAJ 189:E569

Watchful Dose Analysis

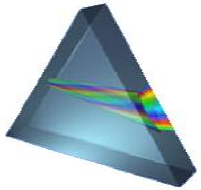


Watchful Dose Analysis

	Cases, n/N	Controls, n/N	Adjusted OR (95% CI)
Primary analysis: overlapping opioid prescriptions (Reference: 1-19 mg morphine equivalents)			
≥200 mg	116/498	223/1714	2.88 (1.79-4.63)
100-199 mg	82/498	181/1714	2.04 (1.28-3.24)
50-99 mg	97/498	273/1714	1.92 (1.30-2.85)
20-49 mg	118/498	514/1714	1.32 (0.94-1.84)



Gomes T et al. Arch Intern Med 2011;17197):686.



CDC

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 65 / No. 1
March 18, 2016

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

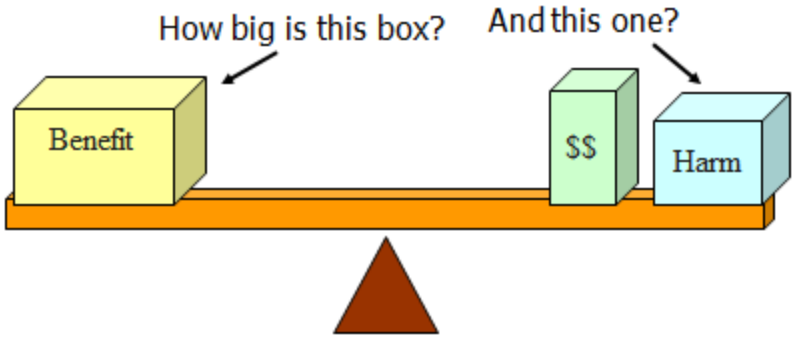
CDC

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.

3. 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.

How to Avoid a Mess



CDC

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.

Canadian Guidelines

The 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain

Main editor

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Canadian Guidelines

Recommendation 1: When considering therapy for patients with chronic non-cancer pain

Strong Recommendation

We recommend optimization of non-opioid pharmacotherapy and non-pharmacological therapy, rather than a trial of opioids

Recommendation 2: For patients with chronic noncancer pain, without current or past substance use disorder and without other active psychiatric disorders, who have persistent problematic pain despite optimized nonopioid therapy

Weak Recommendation

We suggest adding a trial of opioids rather than continued therapy without opioids.

Canadian Guidelines

Recommendations 6 and 7: For patients with chronic noncancer pain who are beginning long term opioid therapy

Strong Recommendation

Recommendation 6: We recommend restricting the prescribed dose to less 90mg morphine equivalents daily rather than no upper limit or a higher limit on dosing

Some patients may gain important benefit at a dose of more than 90mg morphine equivalents daily. Referral to a colleague for a second opinion regarding the possibility of increasing the dose to more than 90mg morphine equivalents daily may therefore be warranted in some individuals.

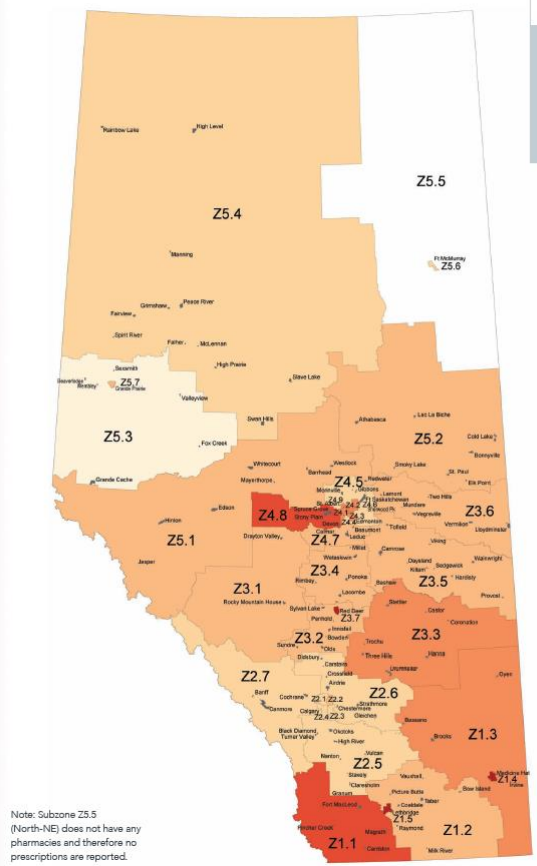
Weak Recommendation

Recommendation 7: For patients with chronic noncancer pain who are beginning opioid therapy, we suggest restricting the prescribed dose to less than 50mg morphine equivalents daily.

The weak recommendation to restrict the prescribed dose to less than 50mg morphine equivalents daily acknowledges that there are likely to be some patients who would be ready to accept the increased risks associated with a dose higher than 50mg in order to potentially achieve improved pain control.

Alberta

Figure 6a. Age and Sex Standardized, Patients Who Received Greater than 200 OME per Day per 1,000 Population by Subzone, 2014



Note: Subzone Z5.5 (North-NE) does not have any pharmacies and therefore no prescriptions are reported.

Figure 6b. Age and Sex Standardized, Patients Who Received Greater than 200 OME per Day per 1,000 Population by Urban Subzone, 2014

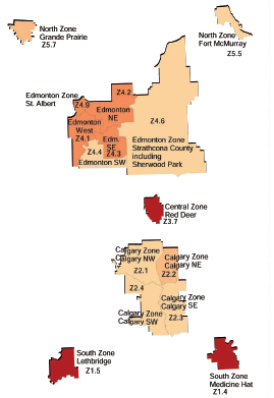
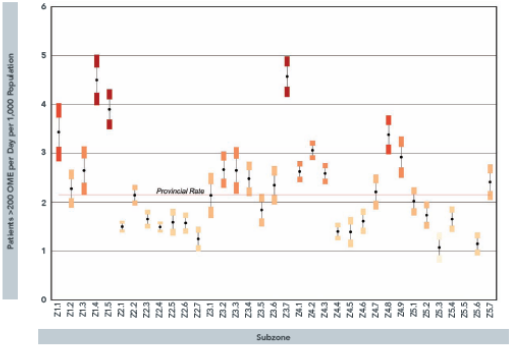
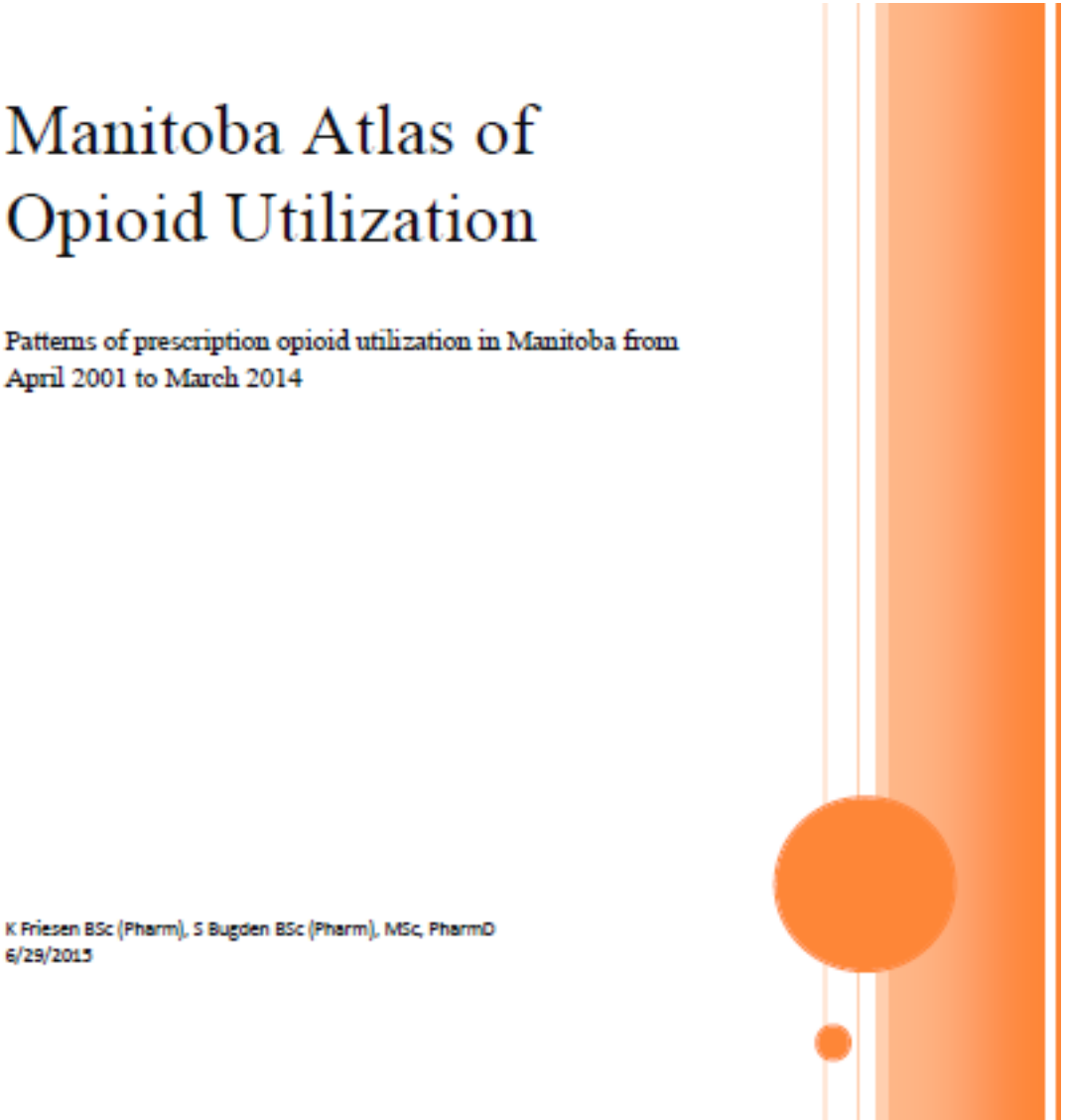
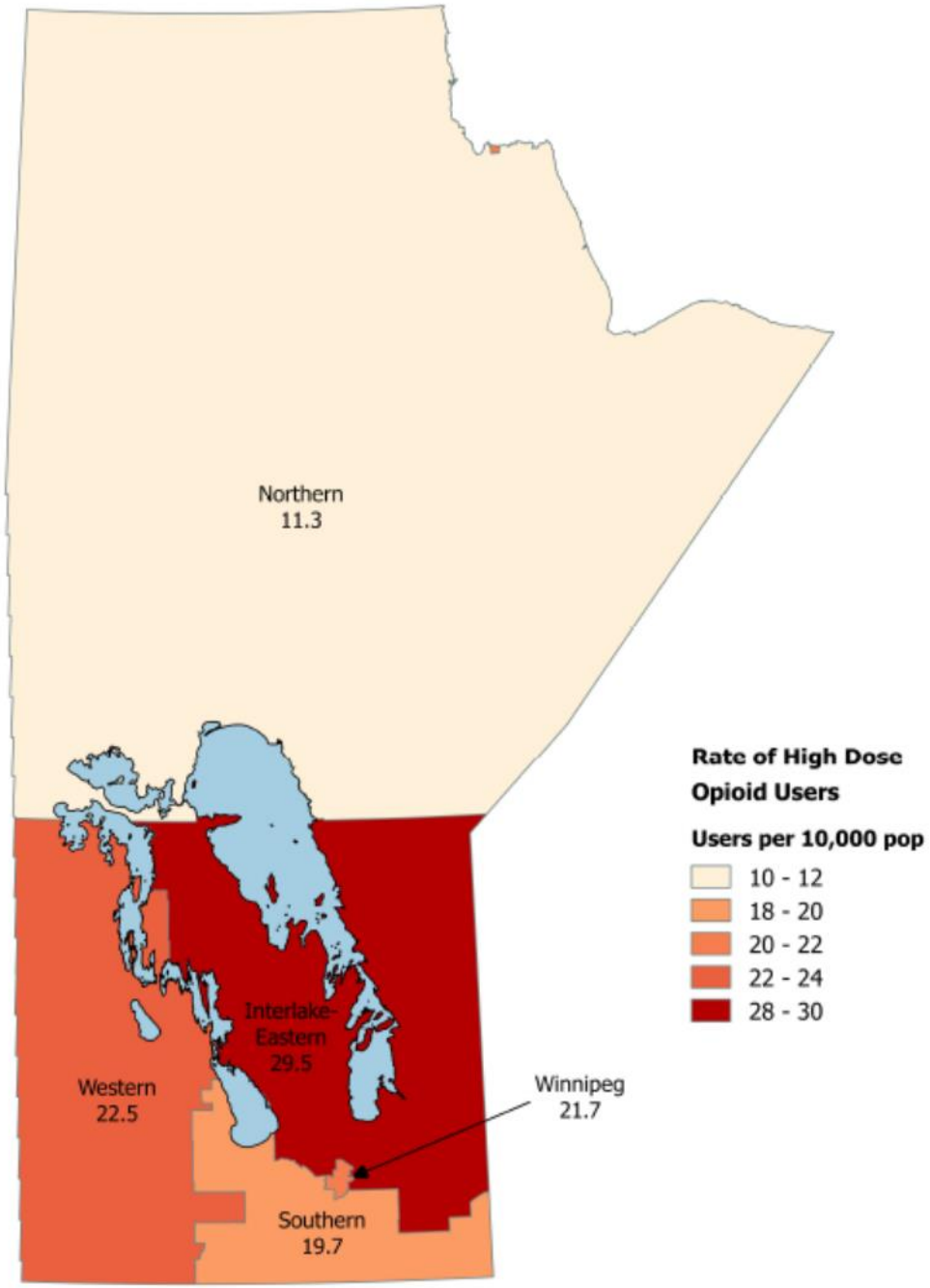


Figure 6c. Age and Sex Standardized, Patients Who Received Greater than 200 OME per Day per 1,000 Population by Subzone, 2014



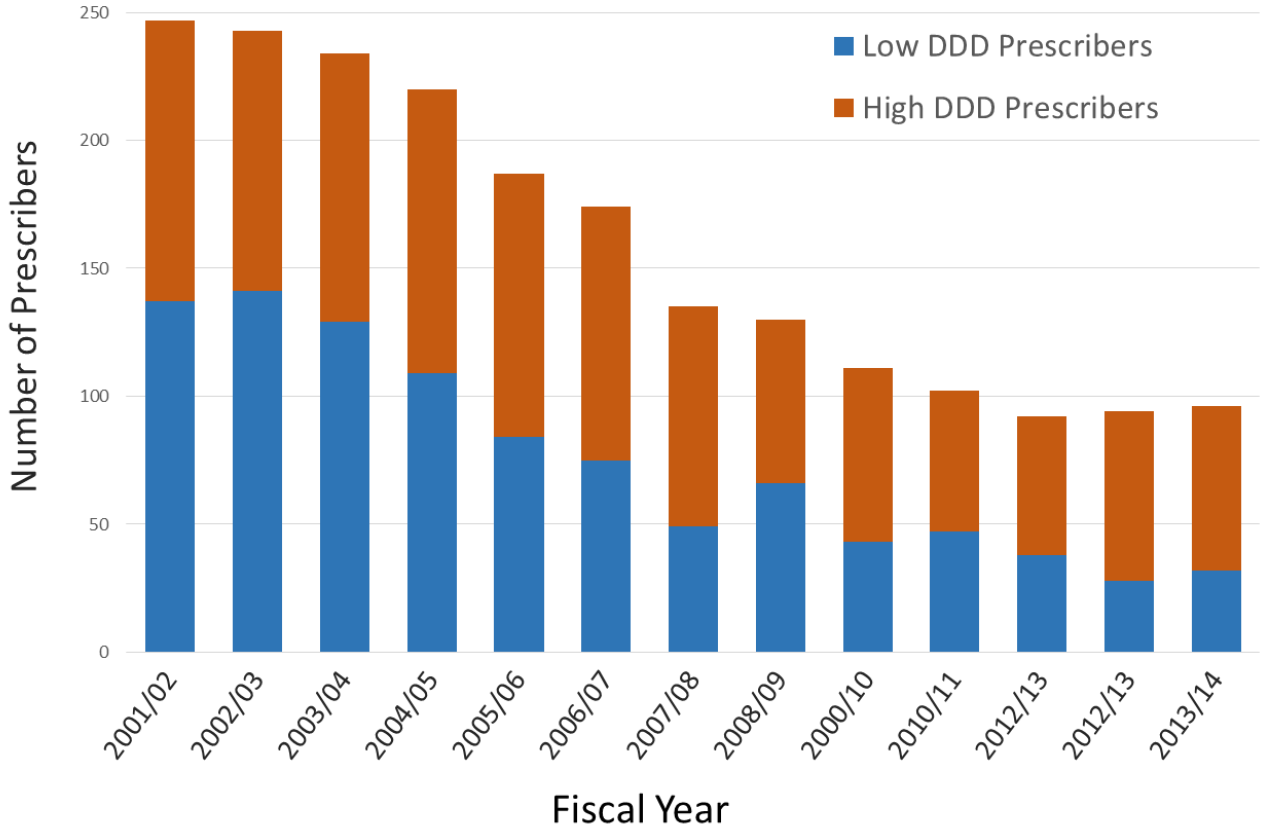
Manitoba Atlas of Opioid Utlization



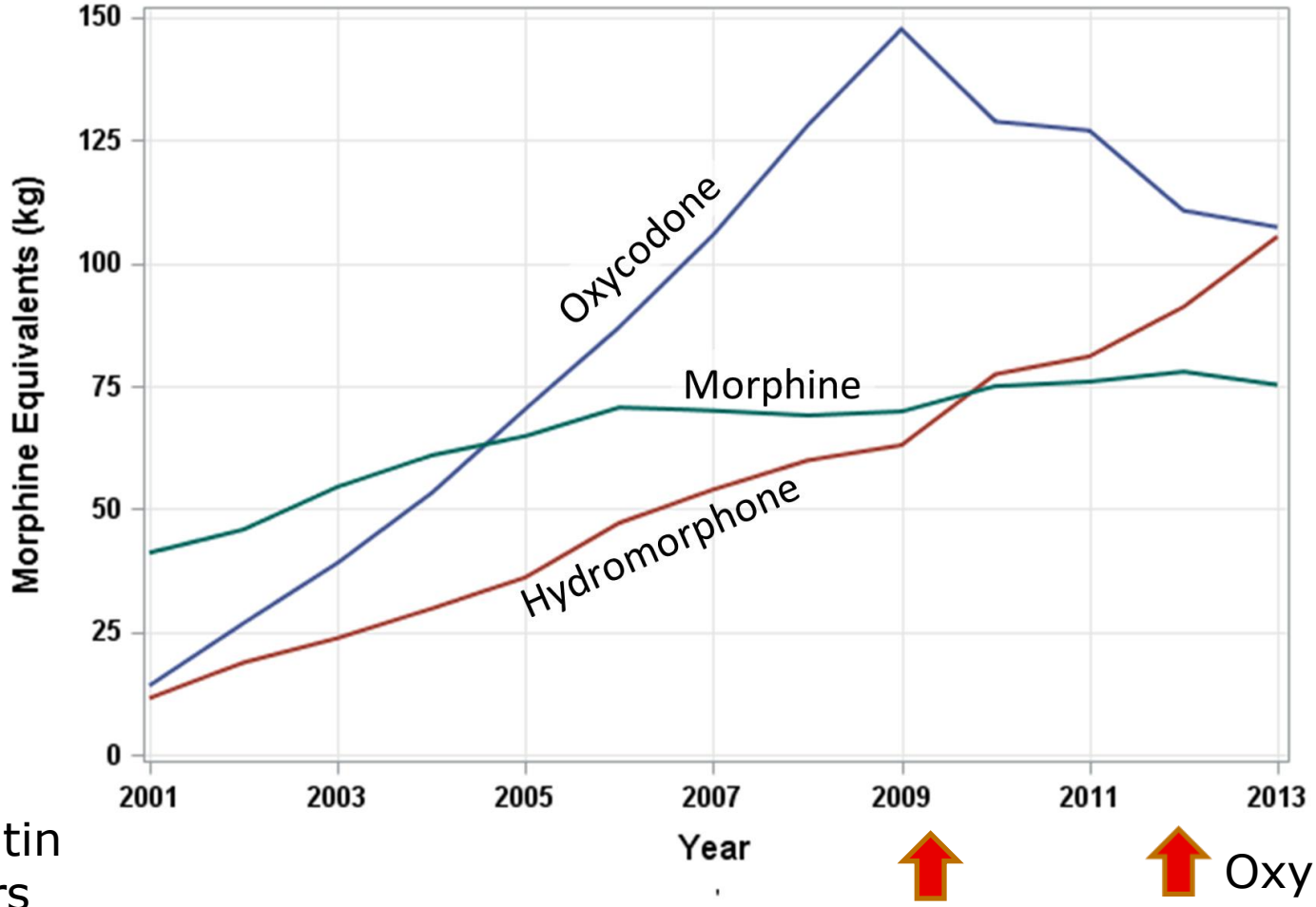

Northern
11.3
Interlake-
Eastern
29.5
Western
22.5
Winnipeg
21.7
Southern
19.7
Rate of High Dose
Opioid Users
Users per 10,000 pop
10 - 12
18 - 20
20 - 22
22 - 24
28 - 30

Meperidine

Figure 5: Trends Prescriber Patterns



Oxycodone – Long Acting

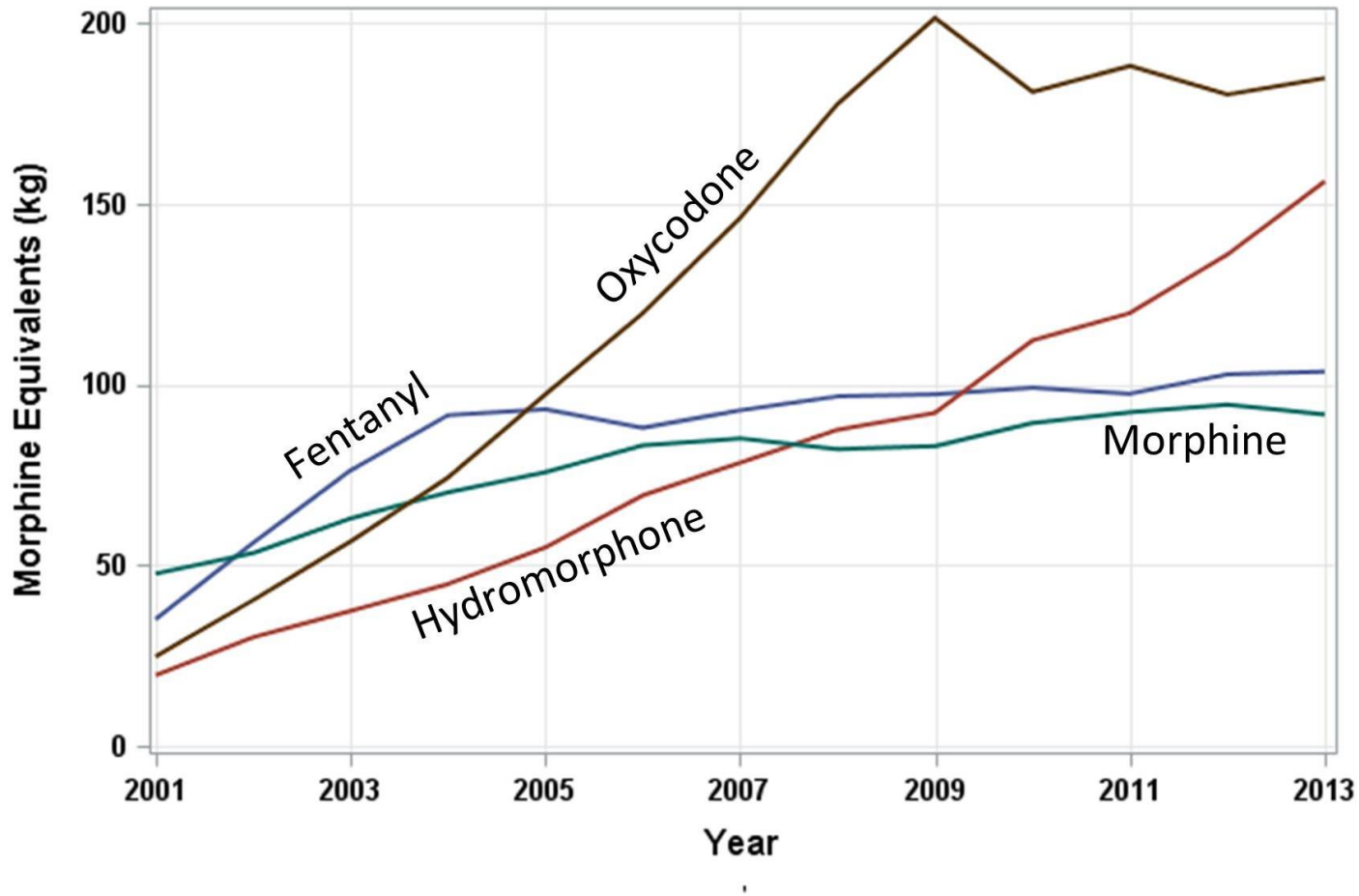


1999 OxyContin® enters market

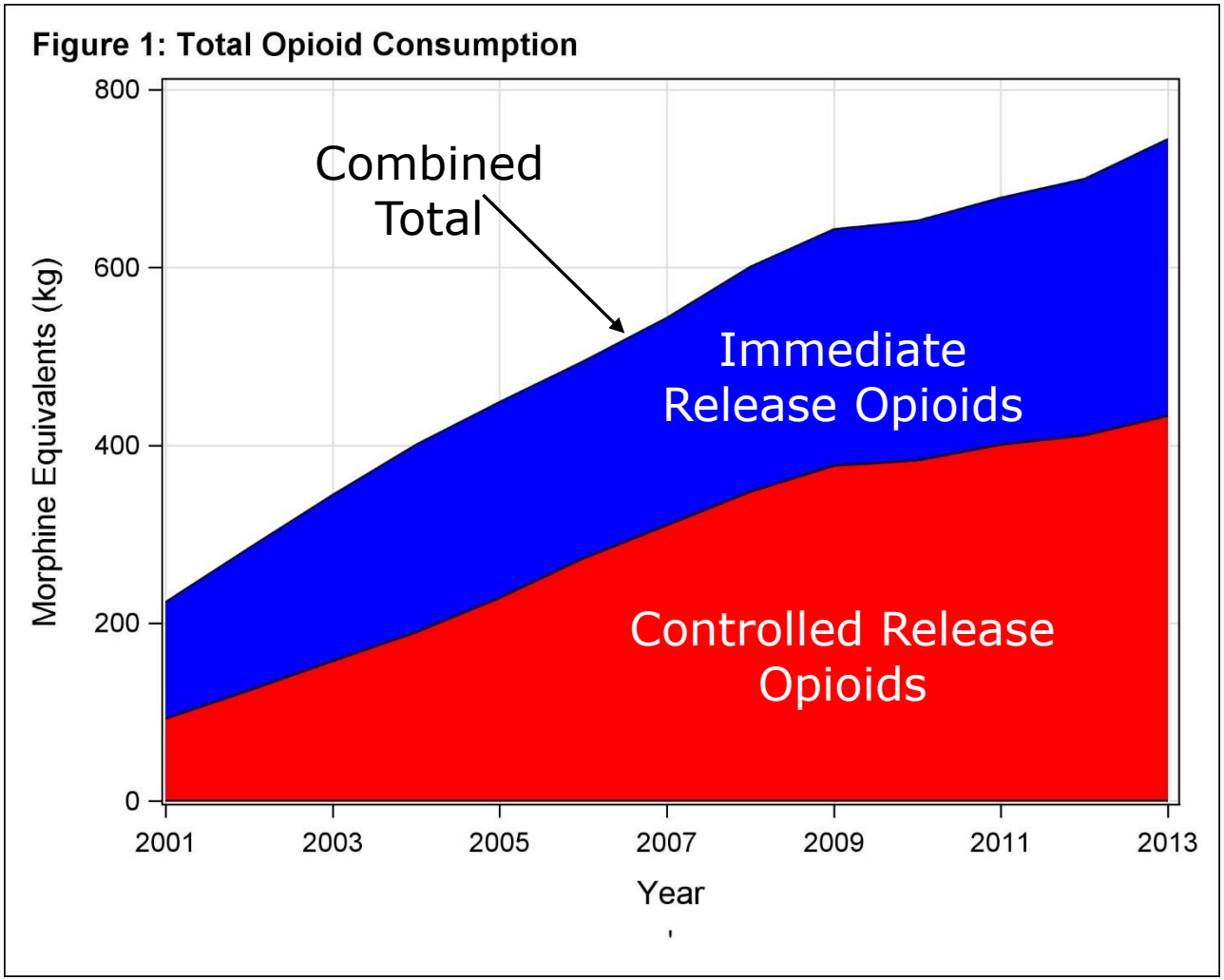
Pharmacare Change

OxyNeo® replaces Oxycontin®

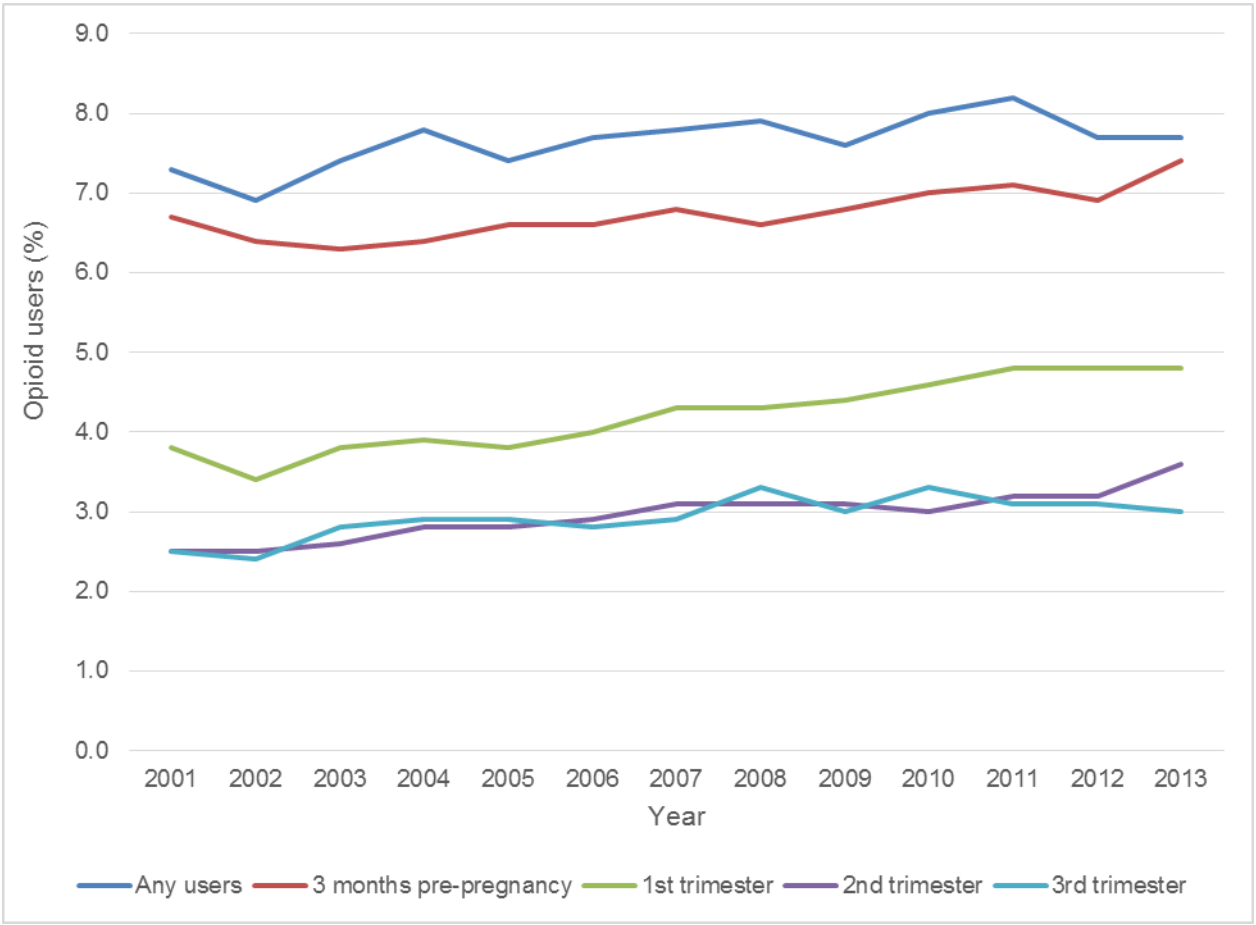
Oxycodone (Overall)



Opioid Utilization in Manitoba

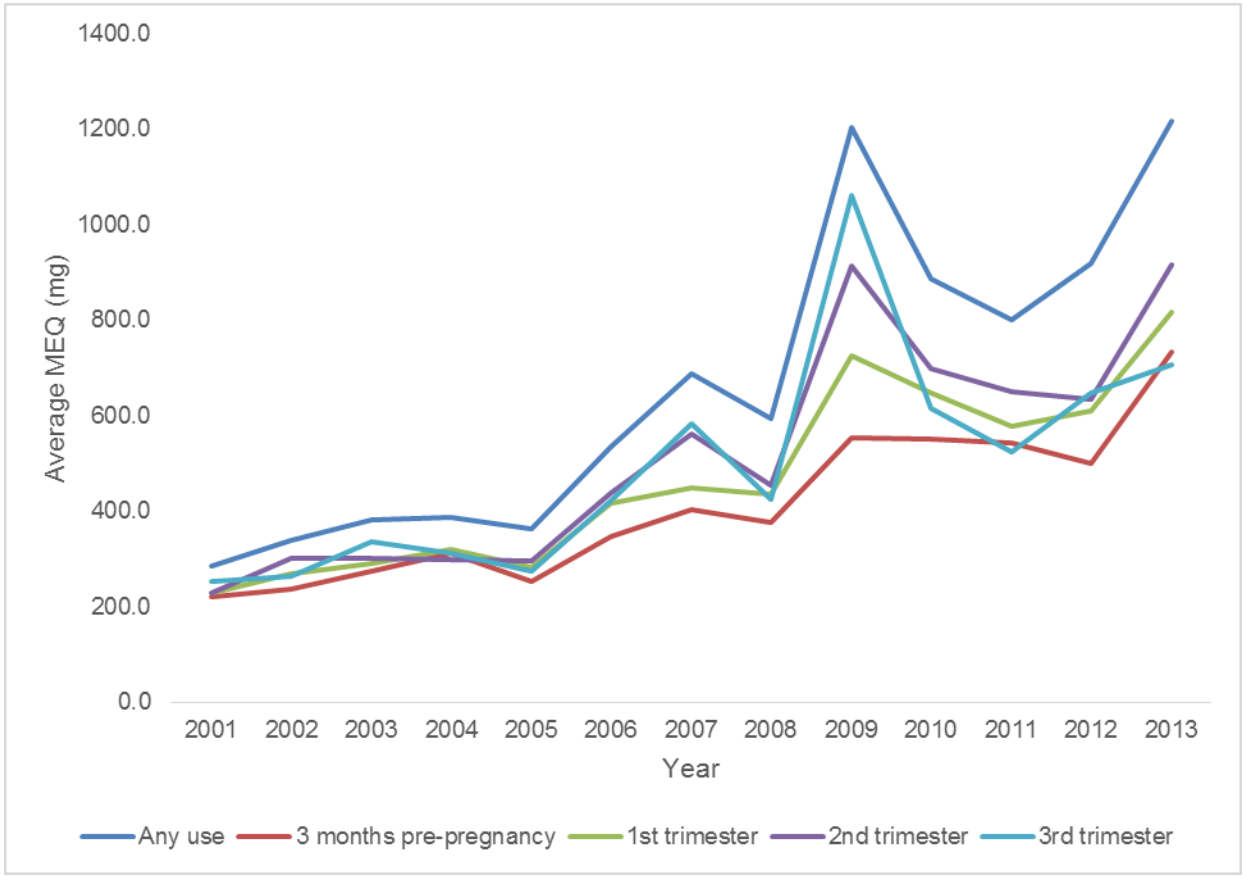


Pregnancy



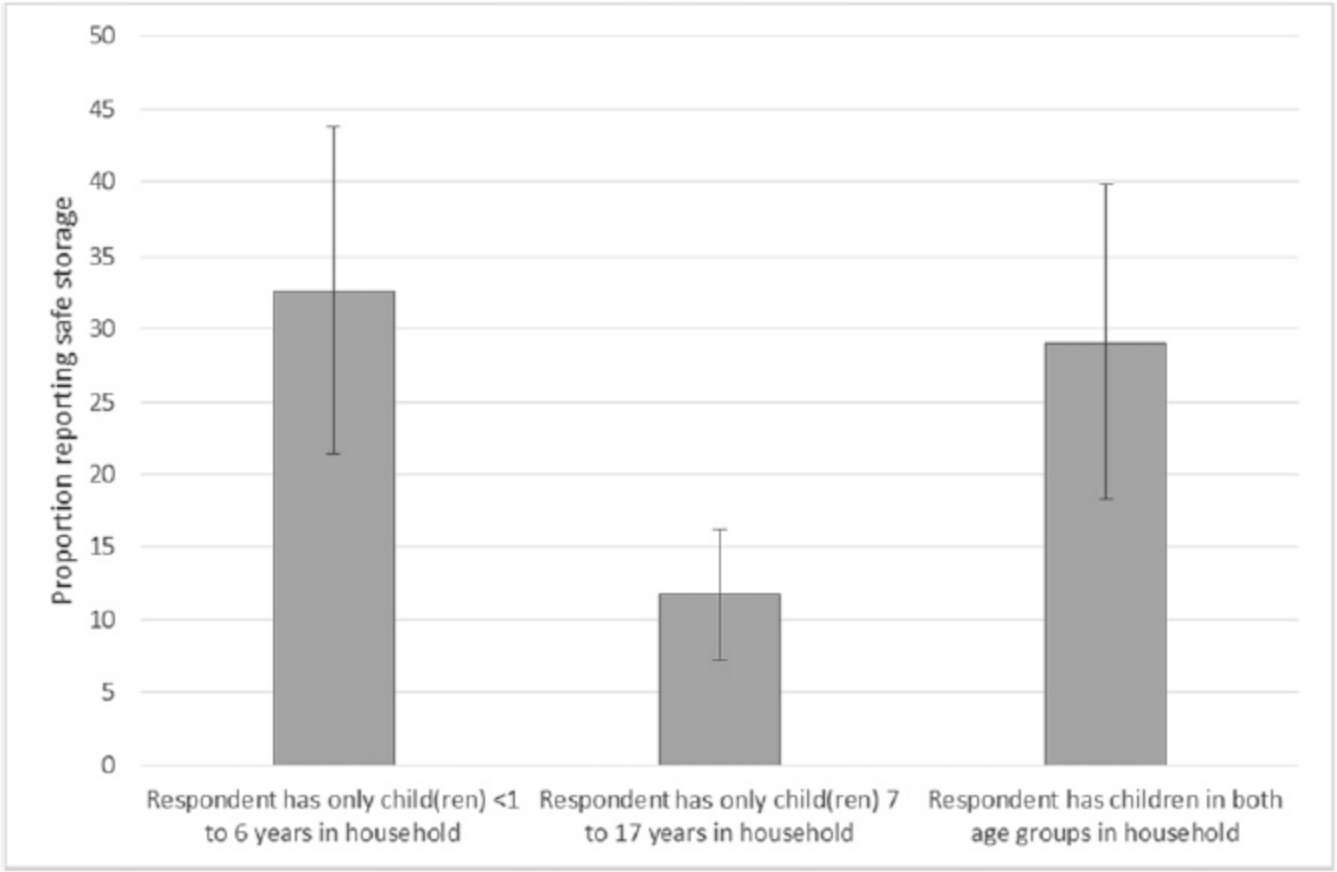
Falk et al. 2017 CMAJ Open *in press*

Pregnancy



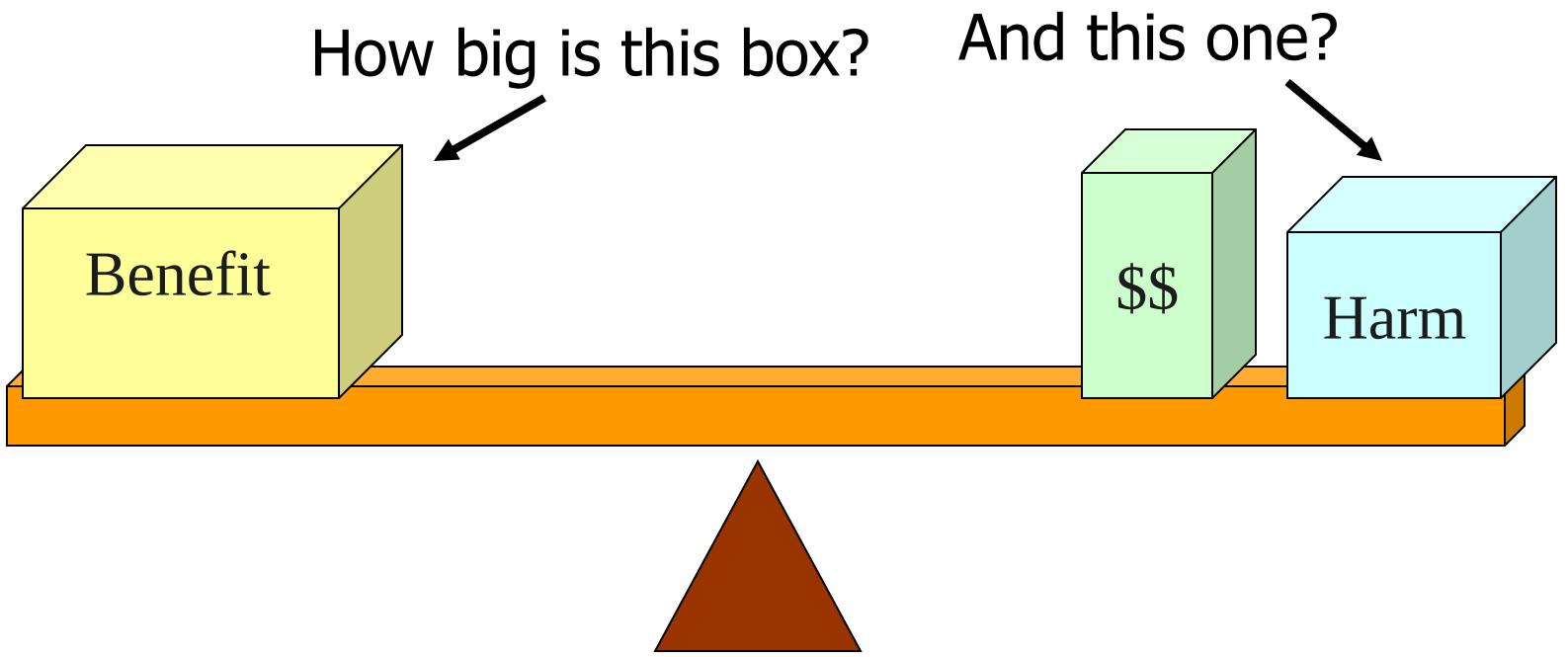
Falk et al. 2017 CMAJ Open *in press*

One Thing We Can Do ?



McDonald EM et al. 2017 Pediatrics 139:e20162161

Balance



Acknowledgements

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Manitoba Centre for Health Policy, University of Manitoba and were derived from data provided by Manitoba Health, Seniors and Active Living and the Manitoba Centre for Health Policy, University of Manitoba and were derived from data provided by Manitoba