Managing Pain in Residential Care while being aware of the implications of the “opioid crisis”

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Faculty/Presenter Disclosure

Faculty: Romayne Gallagher

Relationships with commercial interests:
  ◦ **Speakers Bureau/Honoraria**: Purdue Pharma prior to 2018

Mitigating potential bias
  ◦ **Generic names only**
Cost of substance use in Canada

Overall cost in 2014: $38.4B

70% of costs due to Tobacco and Alcohol

Health care costs are Aprox 29% of the costs.

Other costs are lost productivity, criminal justice and other direct costs.

Canadian Centre on Substance Use 2018
Figure 1: Trends in Opioid-Related Deaths by Year and Age Groups in Ontario, 1991 to 2015

BC Data and Rates

Illicit Drug Overdose Deaths and Death Rate per 100,000 Population

All prescription related deaths

3.9 pharmaceutical opioid-associated deaths per 100,000 population in BC from 2004 to 2013, with no significant change over this time period

This rate includes all pharmaceutical opioid deaths, intentional and unintentional, as well as those involving pharmaceutical opioids taken with and without a prescription.

- Gladstone et al. Injury Prevention 2015
Illicit drugs includes illegal drugs and opioids taken without a prescription (diversion)

Other pharmaceutical drugs includes antidepressants, benzodiazepines, anticonvulsants, antihistamines, antipsychotics

97% of the cases included other substances than the prescribed opioid

BC Coroners Service 2017
BC Coroner’s findings – Sept 27, 2018

Fig. 12. Illicit drug overdose deaths by pattern of illicit drug use

- Regular/chronic: 77%
- Occasional/infr: 19%
- Unknown: 4%

Fig. 10. Illicit drug overdose deaths and pain among decedents with contact with health services in year preceding death

- Sought assistance for pain: 44%
- Did not seek assistance for pain: 56%

Fig. 11. Illicit drug overdose deaths and reported mental health disorders

- Reported clinical diagnosis or anecdotal mental health disorder: 8%
- No reported clinical diagnosis or anecdotal mental health disorder: 40%
- Unknown: 52%
Opioid use disorder in chronic pain population

- Lack of high quality evidence or consistent prevalence evidence
  - Voon P et al. Subst Abuse Treat Prev Policy 2017

- Systematic review of 38 studies opioid-treated patients with chronic pain
  - misuse averaged between 21% and 29%
  - addiction averaged between 8% and 12%

- Chronic pain prevalence in Canada: 19-25%
  - Schopflocher et al. Pain Research & Management 2011
Figure 3  Proportion (%) of people starting opioid therapy, by age group, * 2013 to 2018

Note
* Includes data from Ontario, Saskatchewan and British Columbia. Manitoba is excluded from trends because data prior to March 2015 is unavailable.
Big Data Studies

**PRO**

- Large sample size
- Actual practice as opposed to “sterile” research setting
- Easily available data/ much cheaper than RCT
- Decision-makers love data
- Compare across settings and societies
- Good accuracy of the Null hypothesis – no diff between groups
Big Data Studies

**CON**

Observational studies are not causal

Quality of data input: 4.3 – 86% incompleteness of records (Balas et al. MedInfo 2015)

Selection bias of data bases: may not include everyone (Docherty et al. Curr Opin Crit Care 2015)

Medical billing/Hospital data not collected for research reasons (compliance, reimbursement etc..) (Patel et al. J Am Acad Ortho Surg 2016)


Pharmacy data: What is dispensed is not always taken as directed

Assumptions are made: On Opioids = No Pain; All opioids are the same
Effect of Opioid vs Non-opioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain JAMA 2018

Interpretation: Results do not support initiation of opioid therapy for moderate to severe chronic back pain or hip or knee osteoarthritis pain.

Mean age 58. Range 21 – 80. Only 13% were women.

Moderate depression (PHQ-9 ≥ 10) 21-23% in both groups.

The mean pain score was 5. Not severe Pain.

Non-Opioid group was able to be treated with Tramadol. 10% used it.

Does not distinguish between mechanical back pain and neuropathic pain

Populations were different: 42% of opioid group employed, 26% non-opioid employed
What appears in the media....

Medscape: More data confirm that opioids no better than non-opioids....

WebMD: Opioids Not Best Option for Back Pain, Arthritis....

CBC: Prescription opioids no better than over-the-counter drugs for chronic pain, study shows

Vox Media: Finally, proof: opioids are no better than other medications for some chronic pain
Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study  BMJ Open 2017

- 1 015 116 “opioid naïve” patients undergoing surgery
- Only had access to their pharmaceutical records and hospital records
- 568 612 (56.0%) patients received postoperative opioids
- 5906 patients had opioid misuse event
  - 0.6%, 183 per 100 000 person years
Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study  BMJ Open 2017

- Analysis of 5906 patients: each refill, additional week of opioid use associated with an adjusted increase in the rate of misuse of 44.0% (95% P<0.001), and 19.9% increase in hazard (P<0.001)

- Error in design of the study:
  - did not analyze opioid events in those who did not get a post-operative prescription
Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study BMJ Open 2017

WHAT IS ALREADY KNOWN ON THIS TOPIC
Opioid misuse is increasing rapidly in the US and internationally
Surgical patients are four times more likely to get opioids at discharge than their non-surgical counterparts
It is unknown how opioid prescribing habits by clinicians are related to rates of misuse

WHAT THIS STUDY ADDS
Each refill and additional week of opioid prescription is associated with a large increase in opioid misuse among opioid naive patients
The duration of a prescription rather than opioid dosage was more strongly associated with ultimate misuse in the early postsurgical period

the bmj | BMJ 2018;360:j5790 | doi: 10.1136/bmj.j5790
Association Between Opioid Use and Survival Time in Patients With Unresectable Pancreatic Cancer: 10 Years of Clinical Experience

- 10 year retrospective of patients seen for surgical diagnosis of pancreatic cancer
- 40% of data was incomplete so not used
- 566 patients with stage III or IV pancreatic cancer
- Data available: mortality info, diagnosis and stage, comorbidities, age, BMI, time to initiation of opioids, opioid dose prescribed initially, rate of increase of opioid dose and final opioid dose
- Data not measured: pain, physical function, psychological function, prn doses of opioids
### TABLE 3

**Association Between Opioid Use and Survival Time in Patients With Unresectable Pancreatic Cancer: 10 Years of Clinical Experience.**

Oh, Tak; Do, Sang-Hwan; MD, PhD; Yoon, Yoo-Suk; MD, PhD; Song, In-Ae; MD, PhD

_Pancreas. 47(7):837-842, August 2018._

DOI: 10.1097/MPA.0000000000001094

<table>
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<th>Variables</th>
<th>≤90</th>
<th>91–180</th>
<th>181–365</th>
<th>≥366</th>
<th>P</th>
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<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>75.90 (10.04)</td>
<td>74.96 (10.44)</td>
<td>70.77 (11.52)</td>
<td>69.68 (11.36)</td>
<td>&lt;0.001</td>
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<td>BMI, mean (SD), kg/m²</td>
<td>22.45 (3.16)</td>
<td>22.33 (3.26)</td>
<td>22.22 (3.08)</td>
<td>22.02 (3.24)</td>
<td>0.800</td>
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<tr>
<td>Last opioid dosage, MEED, mean (SD), mg</td>
<td>129.65 (91.96)</td>
<td>172.04 (146.95)</td>
<td>163.06 (124.88)</td>
<td>184.52 (148.38)</td>
<td>&lt;0.001</td>
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<tr>
<td>Initial opioid dosage, MEED, mean (SD), mg</td>
<td>81.61 (66.03)</td>
<td>59.50 (56.87)</td>
<td>46.80 (46.77)</td>
<td>37.90 (30.26)</td>
<td>&lt;0.001</td>
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<tr>
<td>Duration from diagnosis of pancreatic cancer to the time of initial opioids use, mean (SD), d</td>
<td>8.33 (13.02)</td>
<td>26.08 (35.18)</td>
<td>64.68 (84.61)</td>
<td>300.38 (411.75)</td>
<td>&lt;0.001</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Variables</th>
<th>Male, n (%)</th>
<th>Female, n (%)</th>
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<tbody>
<tr>
<td>Sex, female, n (%)</td>
<td>65 (25.7%)</td>
<td>62 (24.5%)</td>
<td>75 (29.6%)</td>
<td>51 (20.2%)</td>
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<tr>
<td>History of tuberculosis, n (%)</td>
<td>6 (18.8%)</td>
<td>7 (21.9%)</td>
<td>5 (15.6%)</td>
<td>14 (43.8%)</td>
<td>0.043</td>
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<td>History of hypertension, n (%)</td>
<td>38 (16.6%)</td>
<td>38 (26.4%)</td>
<td>66 (28.8%)</td>
<td>60 (26.2%)</td>
<td>0.043</td>
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<td>History of diabetes mellitus, n (%)</td>
<td>37 (18.4%)</td>
<td>55 (27.4%)</td>
<td>60 (29.9%)</td>
<td>49 (24.4%)</td>
<td>0.325</td>
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<td>History of ischemic heart disease, n (%)</td>
<td>2 (33.3%)</td>
<td>1 (16.7%)</td>
<td>0 (0%)</td>
<td>3 (50.0%)</td>
<td>0.262</td>
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<td>History of chronic hepatitis, n (%)</td>
<td>6 (15.8%)</td>
<td>9 (23.7%)</td>
<td>13 (34.2%)</td>
<td>10 (26.3%)</td>
<td>0.634</td>
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<tr>
<td>Radiotherapy, n (%)</td>
<td>11 (52.4%)</td>
<td>7 (33.3%)</td>
<td>4 (8.8%)</td>
<td>9 (5.5%)</td>
<td>0.007</td>
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<tr>
<td>Celiac plexus neurolysis, n (%)</td>
<td>4 (100%)</td>
<td>4 (100%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.003</td>
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<tr>
<td>Chemotherapy, n (%)</td>
<td>10 (18.2%)</td>
<td>2 (3.6%)</td>
<td>7 (12.7%)</td>
<td>36 (65.5%)</td>
<td>&lt;0.001</td>
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BMI indicates body mass index.
### TABLE 4

Multivariate Logistic Regression Analysis for Death Within 180 Days After Diagnosis of Unresectable Pancreatic Cancer

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>1.019 (0.997–1.041)</td>
<td>0.094</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>0.963 (0.580–1.598)</td>
<td>0.883</td>
</tr>
<tr>
<td>History of tuberculosis</td>
<td>0.909 (0.396–2.085)</td>
<td>0.822</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>0.693 (0.448–1.071)</td>
<td>0.099</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>1.187 (0.781–1.804)</td>
<td>0.421</td>
</tr>
<tr>
<td>History of ischemic heart disease</td>
<td>2.576 (0.366–18.110)</td>
<td>0.342</td>
</tr>
<tr>
<td>History of chronic hepatitis</td>
<td>1.262 (0.579–2.748)</td>
<td>0.558</td>
</tr>
<tr>
<td>Radiotherapy after diagnosis</td>
<td>0.915 (0.328–2.553)</td>
<td>0.866</td>
</tr>
<tr>
<td>Chemotherapy after diagnosis</td>
<td>0.760 (0.368–1.567)</td>
<td>0.457</td>
</tr>
<tr>
<td>Stage IV (reference: stage III)</td>
<td>1.447 (0.902–2.321)</td>
<td>0.126</td>
</tr>
<tr>
<td>Initial opioid dosage (MEDD)</td>
<td>1.008 (1.002–1.013)</td>
<td>0.005</td>
</tr>
<tr>
<td>Rate of increasing opioid dose (MEED/mo)</td>
<td>1.006 (1.002–1.010)</td>
<td>0.004</td>
</tr>
<tr>
<td>Last opioid dosage (MEDD)</td>
<td>0.997 (0.995–0.999)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**TABLE 4** Multivariate Logistic Regression Analysis for Death Within 180 Days After Diagnosis of Unresectable Pancreatic Cancer
There was a significant positive correlation between the final opioid dose prescribed and survival time after starting opioids (correlation coefficient 0.189, \( P < 0.01 \)) but not with survival time after diagnosis.

Increases in MEDD to 1.154 mg per day and 36.948 mg per month were associated with a 50% probability of death in \( \leq 180 \) days.

Abstract conclusion: There was a correlation between patient survival and the initial opioid doses, the rates of increase in these doses, and the final opioid doses prescribed.

Paper limitations: “not possible to assess patient satisfaction with pain control in a consistent manner” “previous study reported that approximately 40% to 50% of patients with cancer were not satisfied with their pain management”
Pain and Mortality

English Longitudinal Study of Aging followed 6324 adults >50 years for 10 years.

Pain, function were measured and tracked (among other variables)

People who were “often troubled with pain” or who had “quite a bit” or “extreme” pain interference with daily life had significant increase of all cause mortality

Only pain that interferes with daily life affects mortality
  ◦ Smith et al. Arthritis Care Res 2018

Further analysis of data showed strongest mediating factors between pain interference and mortality:
  ◦ functional limitation (hazard ratio 1.31; 95% confidence interval 1.20-1.39),
  ◦ symptoms preventing walking quarter of a mile (1.45 [1.35-1.58]),
  ◦ physical inactivity (1.14 [1.10-1.20]),
  ◦ poor self-rated health (1.32 [1.23-1.41])
  ◦ Smith et al Pain 2018
Pain and Opioids - evidence

- Subject to cultural and political bias

- Big data studies:
  - correlation not causative
  - where does the data come from – does it represent the people you see?
  - seek local/provincial data if available
  - often key variables not collected – i.e. pain, function

- Consider reading more than the headline and abstract
  - particularly if results of study are different from your training and experience
What’s new in our understanding of pain in older adults?

- Pain and depression often occur together in older adults
- Depression in chronic pain patients 19-28%
- Is neuroinflammation a common pathway for both disorders?
- Peripheral nerve damage and previous injury result in activation of microglia
- Activated microglia respond vigorously – release cytokines – increase central sensitization
- Depression may heighten pain perception and central sensitization
Figure 1 The differences between normal and “primed” microglia consist of an increased sensibility of the latter to any kind of stimulation. The consequence is an increased production of cytokines.

Figure 1: The HPA microbiota–gut–brain–endocrine pathway and intersecting organs demonstrating a known afferent and efferent cross-talk, which is yet to be well characterized and is very complex.

Note: Movement of metabolites, anterograde, retrograde, or both, from the gut and the brain to distal organs constitutes co-metabolism in a metabolic interactome.

Abbreviations: ACTH, adrenocorticotropic hormone; CRH, corticotropin releasing hormone; HPA hypothalamus pituitary adrenal; SCFA, short chain fatty acid; NE, norepinephrine; HPA, hypothalamic–pituitary–adrenal; 5-HT, 5-hydroxytryptamine.
Pain Assessment
Pain reports and cognitive impairment

ePAT pain assessment tool

Figure 3
Automated facial recognition and extraction of facial action units (step 2) using active appearance model and facial landmarking.

Figure 4
Detection of facial actions using AU descriptors of FACS (step 3).

Abbreviation: AU, action unit; FACS, Facial Action Coding System.

Atee et al Clin Interv Aging 2018
ePAT

10 second video to look at Facial Action Coding System = Face domain

User scores other domains:
- Voice (moaning, groaning, calling out etc...)
- Movement (guarding, freezing, pacing etc...)
- Behaviour (aggressive, verbally abusive, extreme dislike of touch...)
- Activity (resisting care, prolonged resting, etc...)
- Body (signs of acute pain, known painful conditions...)

353 paired assessments of people with dementia +/- pain the tool scored well.
- Atlee et al J Alzheimer’s Disease 2017
Pain Assessment in Verbally Responsive Dementia Patients

Focus on present pain “do you hurt right now?”
Use verbal reports by staff and family
  ◦ What was their pre-dementia behavior when in pain?
What behavior do staff and family identify as distress?
Observations during care, mobilizing or other pain-inducing activities
Medical Problems - Previous and Current

Other mobidities: CHF, COPD, CRF, CVA, Cancer

Past painful conditions
- previous traumatic injuries, medication history

Past medical history
- 35% of post stroke patients will have a central post-stroke neuropathic pain
  - Siniscalchia et al. Pharmachol Research 2012
- Vascular dementia patients likely have similar central neuropathic pain
  - Scherder et al. Drugs Aging 2012
- 20-24% of diabetics experience painful DPN
- 25-50% of patients >50 years with herpes zoster develop PHN
  - Schmader Clin J Pain. 2002
Hierarchy of Data Sources

“Most reliable”

- Resident report \textit{(if possible)}
- Family/caregiver report
- Prior pain history
- Painful comorbidities
- Behavioral indicators
- Observer assessment

“Least reliable”
Empirical trials of analgesics

Behaviours suggest it could be pain

Trial of analgesics

Behaviours decrease

It probably is pain!
Evidence for empirical trials of analgesics

352 residents in facility care

Moderate to severe dementia with agitation

Randomized: step wise protocol vs regular care

Intervention was daily pain care using step-wise protocol

Protocol used acetaminophen – morphine or buprenorphine patch + pregabalin

◦ Husebo et al BMJ 2011
Using step-wise pain management in agitated residents

ADLs and cognition unchanged

Husebo et al BMJ 2011
Pain Management

Non-pharmacologic
Pharmacologic
Interventional
Non-invasive non-pharmacological therapies in chronic pain – Agency Health Research & Quality 2018

Interventions that improved function and/or pain for at least 1 month when used for—

Chronic low back pain: Exercise, psychological therapies (primarily cognitive behavioral therapy [CBT]), spinal manipulation, low-level laser therapy, massage, mindfulness-based stress reduction, yoga, acupuncture, multidisciplinary rehabilitation (MDR).

Chronic neck pain: Exercise, low-level laser, Alexander Technique, acupuncture.

Knee osteoarthritis: Exercise, ultrasound.

Hip osteoarthritis: Exercise, manual therapies.

Fibromyalgia: Exercise, CBT, myofascial release massage, tai chi, qigong, acupuncture, MDR.

Chronic tension headache: Spinal manipulation.

Most effects were small. Long-term evidence was sparse.

There was no evidence suggesting serious harms from any of the interventions studied; data on harms were limited.
Evidence for analgesics in older adults

The efficacy studies for opioids have no patients over 73 years of age
  ◦ Papaleontiou A et al JAGS 2010

Guidelines for management of pain in older adults focus primarily on analgesic efficacy

The efficacy of analgesics must be balanced with adverse drug events (ADE) since the risk of ADE are much higher in older adults
Acetaminophen
Systematic Review/Meta analysis of RCT

10 trials of 3521 patients for OA hip and knee
3 trials of 1825 patients for low back pain

Acetaminophen is ineffective:
• for reducing pain, disability or improving quality of life in low back pain

Acetaminophen detectable but not clinically important:
• for reducing pain and disability in knee and hip osteoarthritis

Acetaminophen users have almost 4 times likelihood of abnormal liver function tests – effect uncertain
• Machado et al. BMJ 2015;350:h1225 | doi: 10.1136/bmj.h1225
NSAIDS in older adults

NSAIDS significantly higher all cause mortality (OR 1.76) than those not receiving NSAID

Risk of acute renal failure significantly higher in all NSAIDS and significant progression of CKD

Composite cardiovascular outcome (MI, stroke, CHF, cardiac death) higher in all NSAIDS
  ◦ Solomon et al Arch Int Med 2010
Efficacy of Opioids in Older Adults

Systematic review and meta-analysis

43 studies, 8690 patients, age 60-73, mean age 64 years

Mean duration of treatment: 4 weeks (12% of studies > 12 weeks)

Osteoarthritis (70%), neuropathic pain (13%) and other conditions (17%)

Significant pain reduction (p<0.001), physical disability reduction (p<0.001)

Sleep improvement (p=0.31)

Adverse events: constipation (30%), nausea (28%), dizziness (22%)

Adverse events caused 25% to stop opioid

- Papaleontiou et al J Am Geriatr Soc 2010
Pharmacologic Treatment Options: Stepped Approach to Opioid Selection

Mild-to-moderate pain

First-line for mild-to-moderate pain:
- Codeine** or tramadol**

Second-line for mild-to-moderate pain:
- Morphine*, oxycodone* or hydromorphone*

Severe pain

First-line for severe pain:
- Morphine, oxycodone, hydromorphone

Second-line for severe pain:
- Fentanyl transdermal

Third-line for severe pain:
- Methadone

*Not indicated for mild pain
*Please refer to product monographs for specific indication and complete prescribing information.

**±acetaminophen
NRS, numerical rating scale. NSAID, non-steroidal anti-inflammatory drug.

Effectiveness of opioids

• Selection criteria: adults, ≥10 subjects per arm, any chronic pain condition, double-blind treatment period lasting ≥12 weeks, and all μ-agonist opioids approved in the USA

• Enrolled enrichment design trials only – individual titration to optimum dosing before start of analysis.

• 15 studies met criteria

• Opioid efficacy was statistically significant ($p<0.001$) versus placebo: for pain intensity, ≥30% and ≥50% improvement in pain, patient global impression of change, and patient global assessment of study medication.

• There were minor benefits on physical function and no effect on mental function.
  • Meske et al. J Pain Research 2018
Effectiveness of Opioids

Meske et al J Pain Research 2018

Figure 2. Change in PI from randomization baseline to week 12 with active study opioid drug versus placebo.

Notes: The standardized mean difference effect size was −0.416 and p<0.001, with a lower bound estimate of −0.521 and an upper bound −0.312.

Abbreviation: PI, pain intensity.
Opioid classes

Are all opioids the same?
- Opioids bind to three opioid receptors with differing effects
- There are at least two distinct classes of opioids based on structure
- Methadone also targets NMDA receptors
- There are two pathways of metabolism for opioids
- Two opioids are lipophilic and the rest are more hydrophilic

- They are NOT the same, beware of studies that compare all opioids
Variability of Response to Strong Opioids

- four-arm multicenter, randomized, comparative, of superiority, phase IV trial
- 520 patients randomized to receive morphine, oxycodone, buprenorphine or fentanyl for 1 month to manage cancer pain
- Mean age = 67 (12 SD)
- Started on morphine 30mg/day (opioid naïve) or 60mg/day (already on opioid) OR morphine equivalents
- Assessed non-responder or poor responder, prevalence of adverse effects, changes to therapy to maintain pain control
- Aprox. 25% were poor to non-responders
## Variability of Response to Strong Opioids

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<tr>
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<th>Morphine</th>
<th>Oxycodone</th>
<th>Buprenorphine</th>
<th>Fentanyl</th>
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<td>% Increase in daily dose</td>
<td>32.7</td>
<td>70.9</td>
<td>56.4</td>
<td>121.2</td>
<td>Significant</td>
</tr>
<tr>
<td>% requiring increase dose</td>
<td>29.5</td>
<td>26.4</td>
<td>37.8</td>
<td>37.1</td>
<td>Not sig.</td>
</tr>
<tr>
<td>Rotation</td>
<td>22.1</td>
<td>12</td>
<td>16.5</td>
<td>12.9</td>
<td>Significant</td>
</tr>
<tr>
<td>Stopped due to toxicity/pain</td>
<td>27</td>
<td>15.2</td>
<td>20.5</td>
<td>14.5</td>
<td>Significant</td>
</tr>
<tr>
<td>Severe confusion</td>
<td>15.5</td>
<td>9.3</td>
<td>9.2</td>
<td>6.3</td>
<td>Significant</td>
</tr>
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Opioid genomics

Molecules associated with the action of opioids:

- Metabolism
- Transportation
- Opioid receptors
- Ca & K channels
- Gene expression - CREB
Opioids of choice in frail elderly and renal failure

Hydromorphone is better than morphine and codeine

Oxycodone
Fentanyl
Methadone
Buprenorphine
Tramadol

Dual Action
  ◦ Opioid agonist
  ◦ Inhibits reuptake of Serotonin and Norepinephrine

Metabolism: like codeine requires metabolism to become active

View as a weak opioid – i.e. for moderate pain

Available dosage strengths (CR tramadol, q24h)
  ◦ 150mg q24h is the usual adult starting dose for opioid naïve patients
  ◦ Not to exceed 400 mg total daily dose

Recent report of increased risk of hypoglycemia and hyponatremia

Recent report of 29% nausea and vomiting in palliative patients
  ◦ Husic et al. Mater Sociomed 2015
Fentanyl patch

Fentanyl is highly lipophilic and poorly absorbed orally

A 25mcg fentanyl patch = 100mg morphine/day = 20 Tylenol #3 per day

Takes 12 hours for onset of analgesia

Need adequate subcutaneous tissue for absorption

Takes 24 hours to reach maximum effect

Change patch every 72 hours

Dosage change after six days on patch
Sufentanil for incident pain

Well absorbed through buccal, sublingual and nasal mucosa
- Onset is 5-10 minutes
- Cleared in 30 minutes
- 12.5mcg- 25mcg starting dose
- Up to 100mcg per dose
- For sublingual use must be able to follow directions

If unable to follow directions may use intranasally
Oxycodone/Naloxone CR tablets

Oxycodone with core of naloxone

Lower incidence of constipation

Naloxone not absorbed from the gut – no effect on analgesia

Comes in 5, 10, 20, 40mg oxycodone size

Not covered by Pharmacare but may have other coverage
Buprenorphine

Partial agonist of mu receptor
Requires metabolism to become analgesic
Slow onset, highly bound to receptor
Can be started in opioid naïve patients
Ceiling effect – consider as a weak opioid
Comes in patch that lasts 7 days
Useful for moderate pain
Buprenorphine patch currently not reimbursed by Pharmacare – may have other coverage
Methadone in older adults

Well tolerated and effective

Starting dose 1mg q12hr

Well absorbed orally and bucally

Titrate once weekly only

Use other short acting opioid for breakthrough pain while titrating methadone

Use methadone for breakthrough dose bid-tid once on stable dose

- Gallagher Pain Med. 2009
Long acting opioids

- Increase dose by 15-20% each time if symptom not controlled

- Starting with long acting opioids?
  - Officially NO but in reality.....
  - In residential care inadequate staff to do q4hr opioids
  - Oxycodone SR 5mg = 1.5 Tylenol #3
  - Methadone 1mg q12 hrs = 2 Tylenol #3
  - ½ 12mcg patch = 5 Tylenol #3

- Buprenorphine patch is safe in opioid naive
Cannabis for neuropathic pain

Very low to moderate quality of evidence
- Small study numbers
- High rate of patients drop out or lost to follow up
- Multiple products used (including nabilone)

Many adverse events

Conclusion: risk of adverse events may outweigh small benefits that were seen
- Mucke et al Cochrane Database Syst Rev 2018

If you are going to try it: use CBD only
Neuropathic Pain Adjuvants

NNT gabapentin 7.7, NNT pregabalin 7.2
NNT for strong opioids 4.3
  ◦ Finnerup et al. Lancet Neurology 2015

▪ systematic review of gabapentinoids
  ▪ Non-specific back pain and lumbar radicular pain
  ▪ 9 trials, 859 patients
  ▪ Gabapentinoids: high-quality evidence that gabapentinoids did not reduce pain or disability compared to placebo
  ◦ Adverse events were common: drowsiness, dizziness, nausea
  ▪ Enke et al CMAJ 2018
Neuropathic Pain Adjuvants

NNT TCA = 3.6    NNT SNRI = 6.4
  ◦ Finnerup et al. Lancet Neurology 2015

TCAs have intolerable side effects
  ◦ In a trial of TCA vs opioids for neuropathic pain both were effective but patients preferred opioids (54%) to TCAs (30%) to placebo (10%) p=0.02
     ◦ Raja et al Neurology 2003

SNRIs are likely the best option for older adults with neuropathic pain
  ◦ Study of >80 years old found it safe and efficacious for depression
     ◦ Baca et al Int J Geriatr Psychiatry 2006
Figure. Trial of analgesics for older adults with advanced dementia exhibiting distress behavior.

Adapted from the World Health Organization’s “Three-step analgesic ladder” for cancer pain relief.
Pain and depression

▪ If pain and depression coexist – treat both at the same time

▪ Use non-pharmacological therapies that target both pain and depression
  ▪ CBT, hypnotherapy, acceptance therapy

▪ Use antidepressants that work for pain and depression
  ▪ SNRI, mirtazapine
  ▪ May need higher doses than typical for depression alone
iPal

Essential information for palliative care
Web-based app works on any smart phone

http://ipalapp.com

Developed by Providence Health Care Palliative Care Program
WHAT IS IPAI?