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

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Faculty/Presenter Disclosure

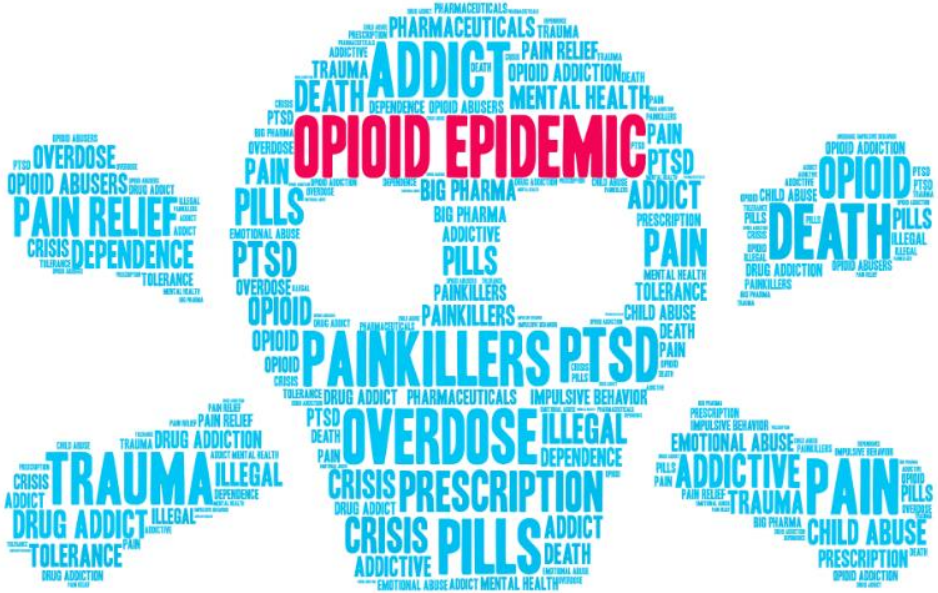
Faculty: Romayne Gallagher

Relationships with commercial interests:

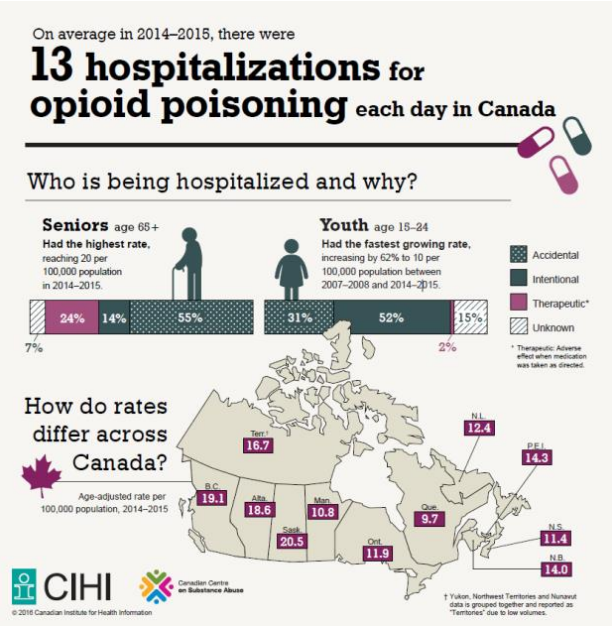
- **Speakers Bureau/Honoraria:** Purdue Pharma prior to 2018

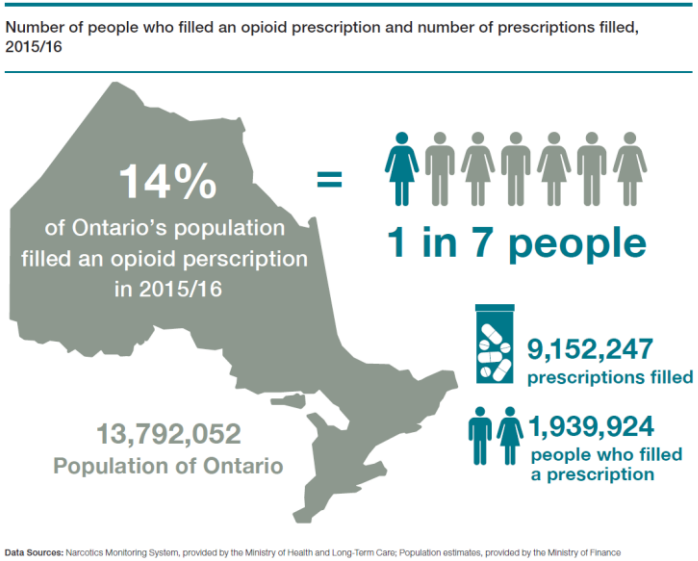
Mitigating potential bias

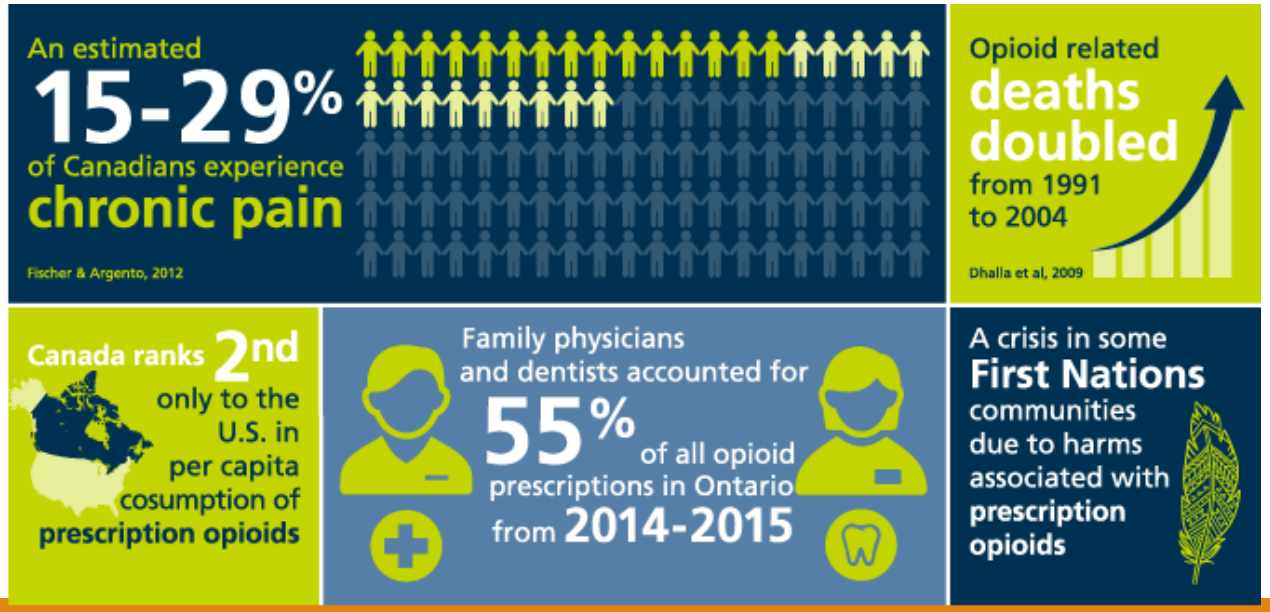
- **Generic names only**


OPIOID EPIDEMIC
ADDICT
PAINKILLERS
PTSD
OVERDOSE
PRESCRIPTION
CRISIS
PILLS
TRAUMA
PAIN RELIEF
DEPENDENCE
OVERDOSE
OPIOID ABUSERS
DEATH
ADDICTIVE
CHILD ABUSE
TOLERANCE
ILLEGAL
MENTAL HEALTH
BIG PHARMA


SPONSORED BY
DRUG
LIKE

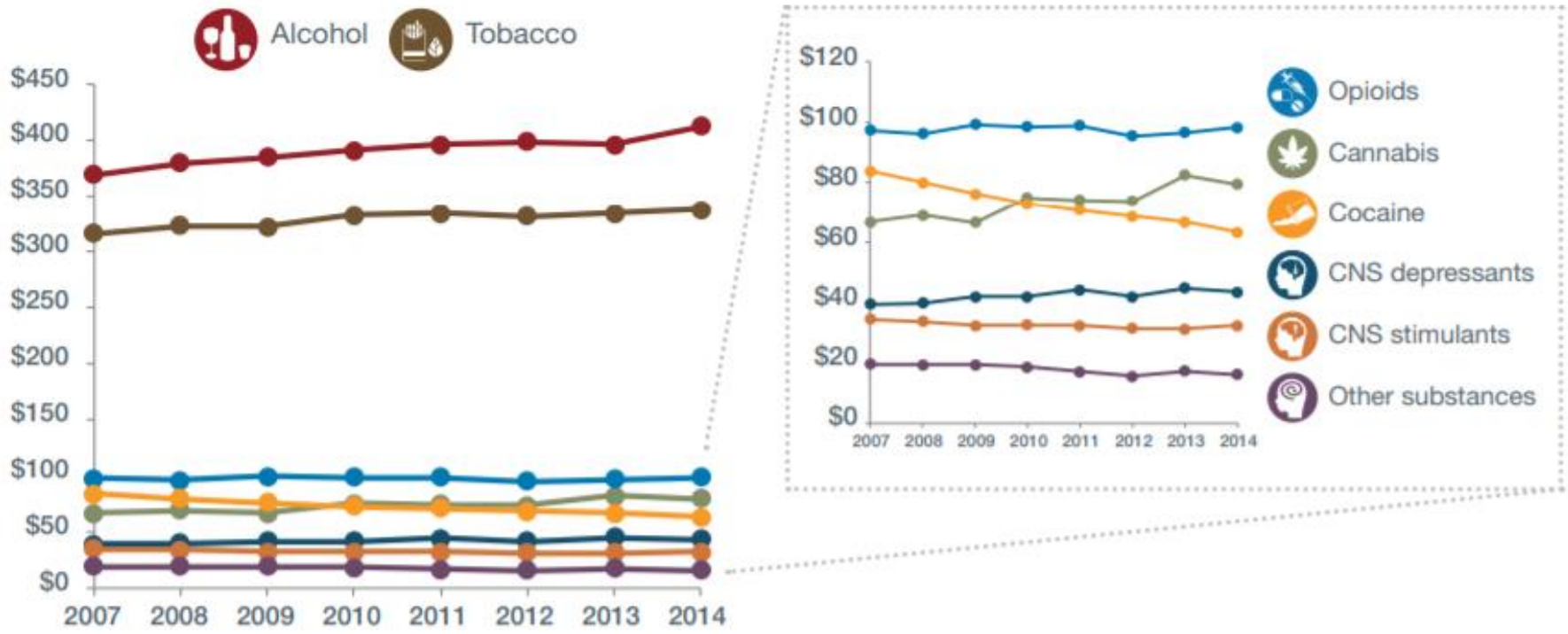

On average in 2014–2015, there were
13 hospitalizations for opioid poisoning each day in Canada
Who is being hospitalized and why?
Seniors age 65+
Had the highest rate, reaching 20 per 100,000 population in 2014–2015.
Youth age 15–24
Had the fastest growing rate, increasing by 62% to 10 per 100,000 population between 2007–2008 and 2014–2015.
24%
14%
55%
7%
31%
52%
15%
2%
Accidental
Intentional
Therapeutic*
Unknown
How do rates differ across Canada?
Age-adjusted rate per 100,000 population, 2014–2015
Ter.†
16.7
B.C.
19.1
Alta.
18.6
Sask.
20.5
Man.
10.8
Ont.
11.9
Que.
9.7
N.L.
12.4
P.E.I.
14.3
N.S.
11.4
N.B.
14.0
CIHI
Canadian Centre on Substance Abuse


Number of people who filled an opioid prescription and number of prescriptions filled, 2015/16
14%
of Ontario's population filled an opioid perscription in 2015/16
=
1 in 7 people
9,152,247
prescriptions filled
1,939,924
people who filled a prescription
13,792,052
Population of Ontario
Data Sources: Narcotics Monitoring System, provided by the Ministry of Health and Long-Term Care; Population estimates, provided by the Ministry of Finance


An estimated
15-29%
of Canadians experience
chronic pain
Fischer & Argento, 2012
Opioid related
deaths
doubled
from 1991
to 2004
Dhalla et al, 2009
Canada ranks 2nd
only to the U.S. in per capita cosumption of prescription opioids
Family physicians and dentists accounted for
55%
of all opioid prescriptions in Ontario
from 2014-2015
A crisis in some
First Nations
communities
due to harms
associated with
prescription
opioids

Cost of substance use in Canada

Figure 4. Overall per person costs (2014 CAD) attributable to substance use in Canada by substance, 2007-2014



Note: Due to missing Quebec data, costs are likely 1% to 2% higher than what is reported here.

Overall cost in 2014 $38.4B

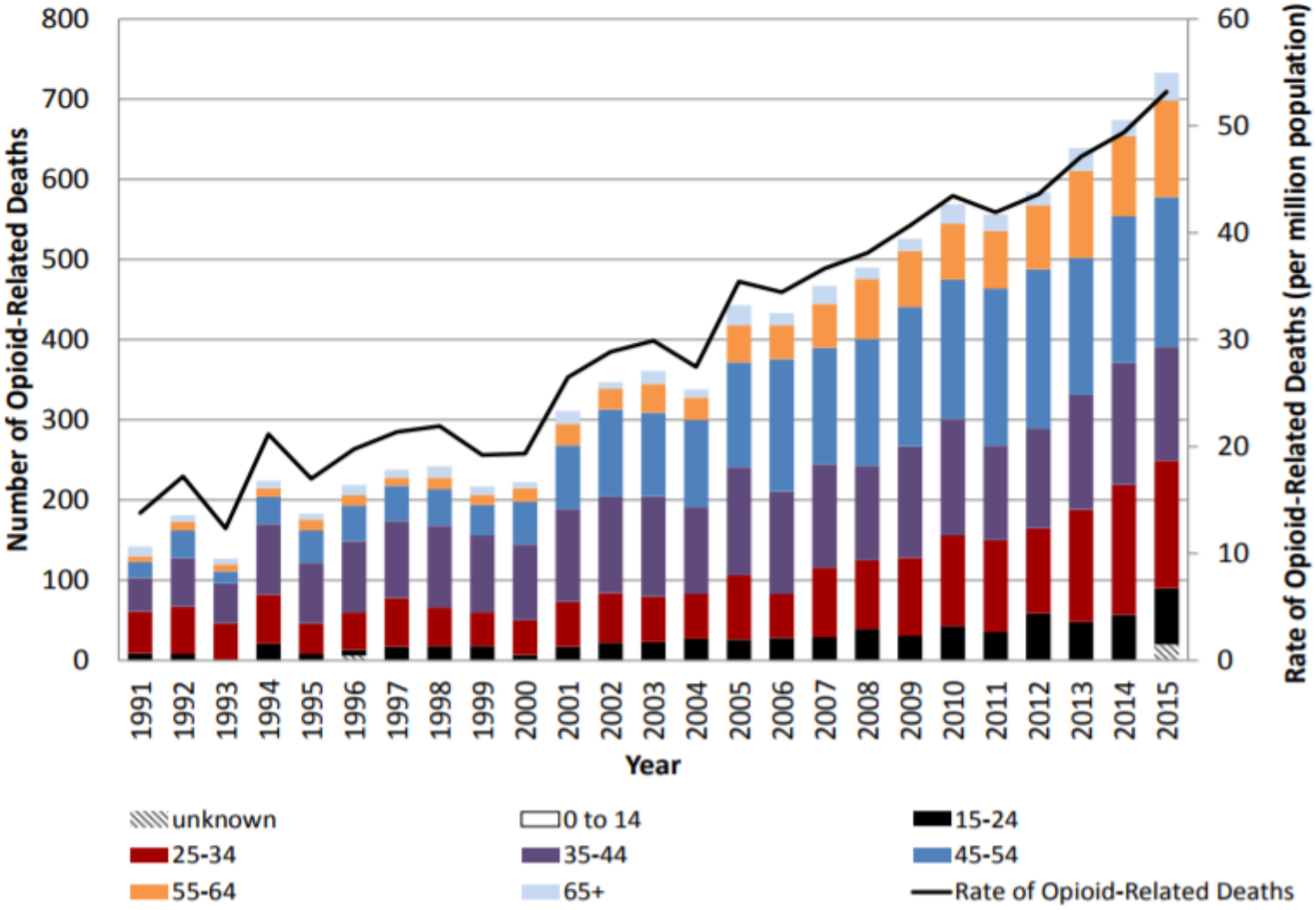
70% of costs due to Tobacco and Alcohol

Health care costs are Aprox 29% of the costs.

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

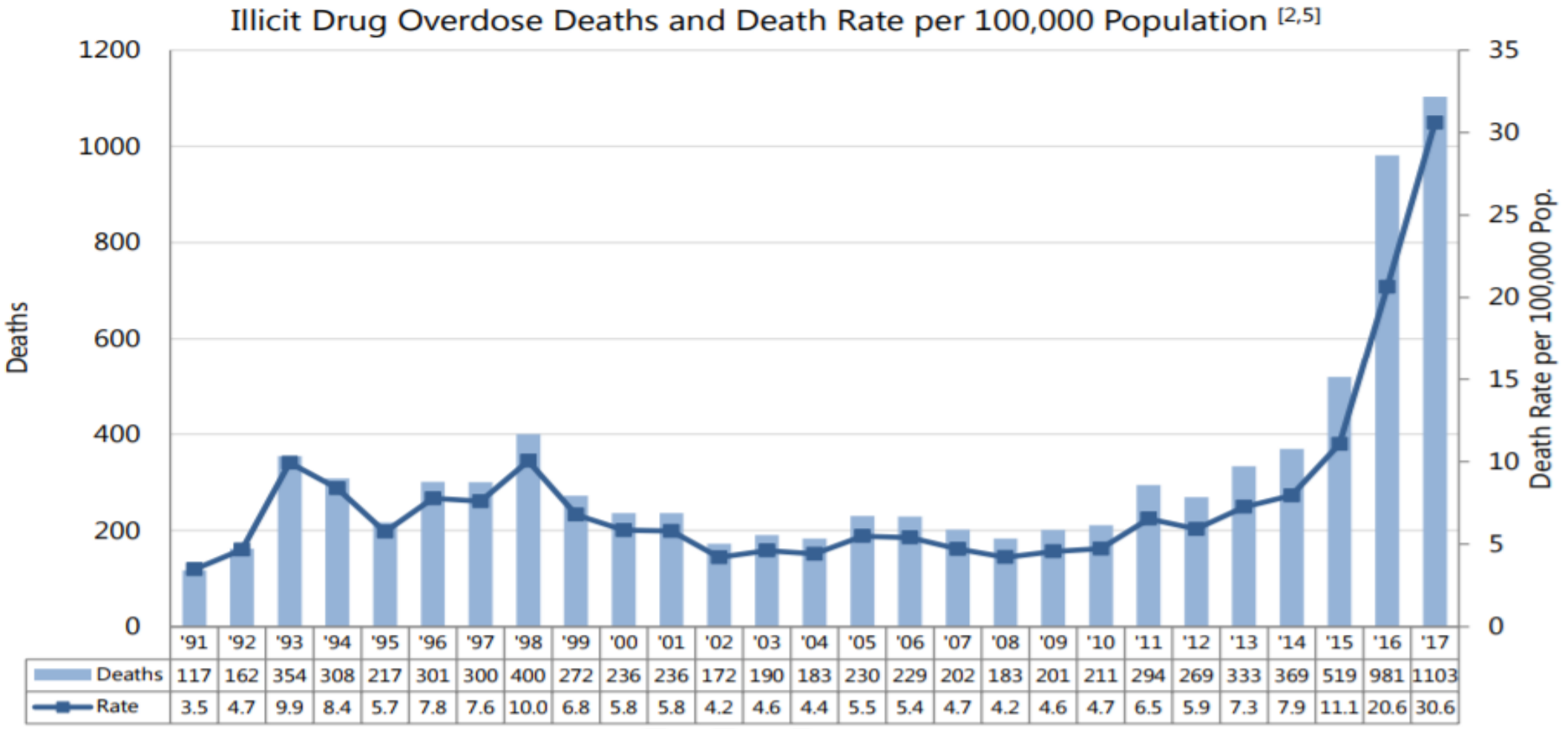
Canadian Centre on Substance Use 2018

Figure 1: Trends in Opioid-Related Deaths by Year and Age Groups in Ontario, 1991 to 2015



The Ontario Drug Policy Research Network April 2017: http://odprn.ca

BC Data and Rates



	'91	'92	'93	'94	'95	'96	'97	'98	'99	'00	'01	'02	'03	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14	'15	'16	'17
Deaths	117	162	354	308	217	301	300	400	272	236	236	172	190	183	230	229	202	183	201	211	294	269	333	369	519	981	1103
Rate	3.5	4.7	9.9	8.4	5.7	7.8	7.6	10.0	6.8	5.8	5.8	4.2	4.6	4.4	5.5	5.4	4.7	4.2	4.6	4.7	6.5	5.9	7.3	7.9	11.1	20.6	30.6

https://www2.gov.bc.ca/assets/gov/public-safety-and-emergency-services/death-investigation/statistical/illicit-drug.pdf

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

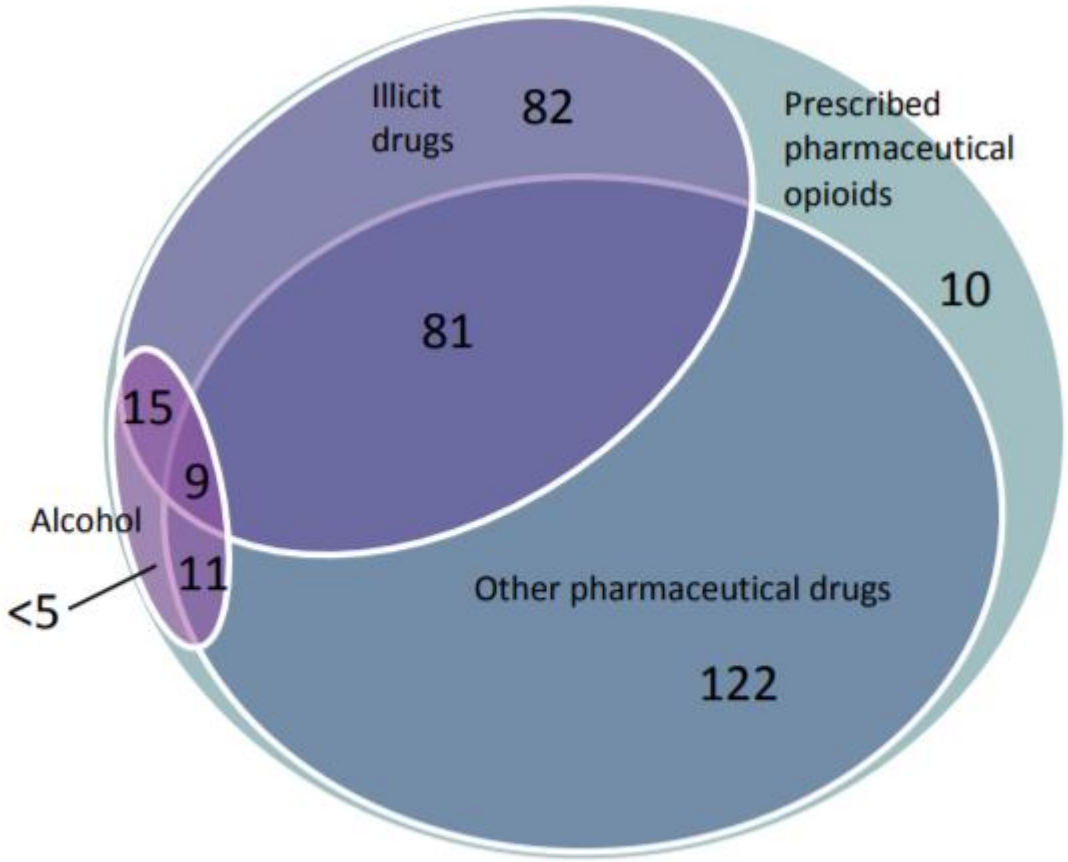


Figure 8. Number of prescribed pharmaceutical opioid-associated deaths in BC from 2009 to 2013 involving prescribed pharmaceutical opioids alone and in combination with other substances. Illicit drugs include illegal drugs as well as pharmaceutical opioids taken without an active prescription. Other pharmaceutical drugs include medications other than opioids detected through toxicology testing. The diagram is for illustrative purposes and is not to scale.

Illicit drugs includes illegal drugs and opioids taken without a prescription (diversion)

Other pharmaceutical drugs incudes 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

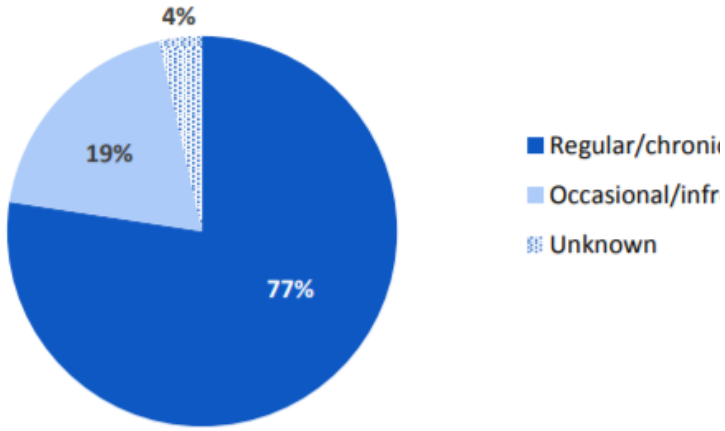


Fig. 10. Illicit drug overdose deaths and pain among decedents with contact with health services in year preceding death

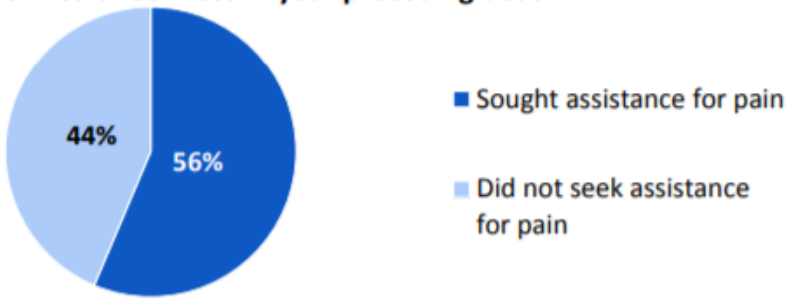
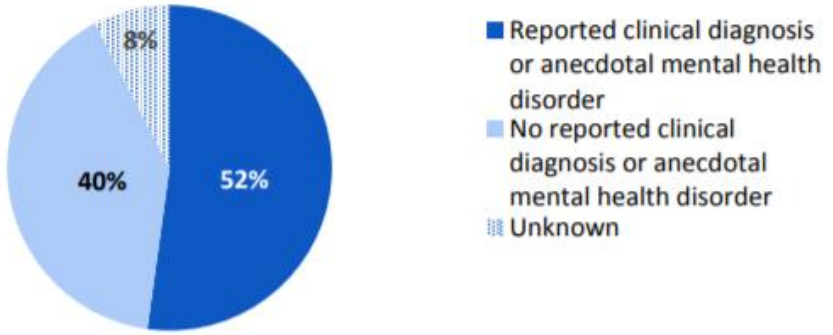


Fig. 11. Illicit drug overdose deaths and reported mental health disorders

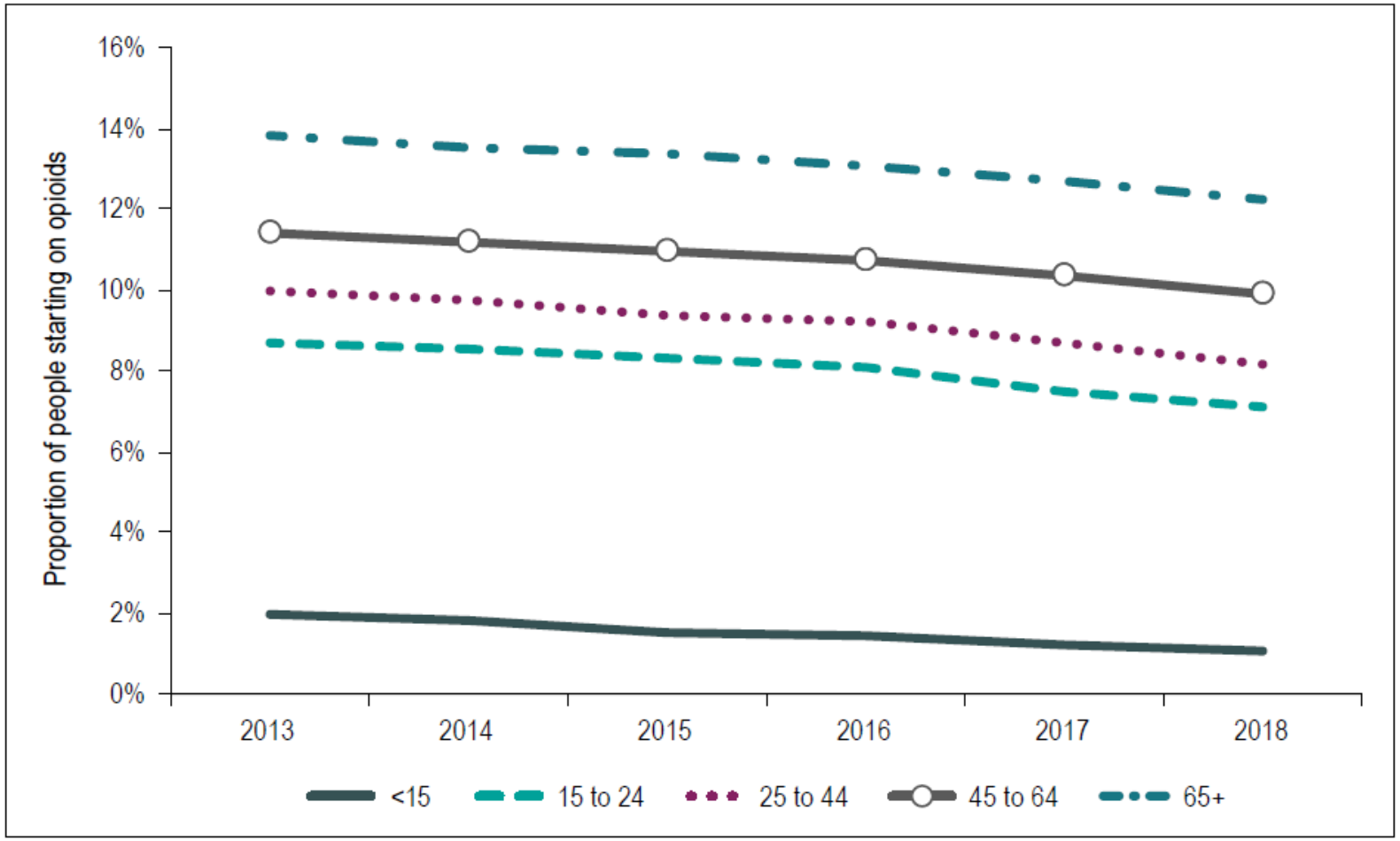


Opioid use disorder in chronic pain population

- 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%
  - Vowles et al. *Pain*. 2015
- 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.

CIHI data on opioid prescribing 2019

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)

Lack of Patient Related Outcome Measures – functional status, pain, patient satisfaction, test results, imaging, cognitive impairment (EHrenstein et al. Clin Epid 2017)

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

Variables	Survival Time After Diagnosis of Pancreatic Cancer, d				*P*
	≤90	91–180	181–365	≥366	
Age, mean (SD), y	75.90 (10.04)	74.96 (10.44)	70.77 (11.52)	69.68 (11.36)	<0.001
BMI, mean (SD), kg/m^2	22.45 (3.16)	22.33 (3.26)	22.22 (3.08)	22.02 (3.24)	0.800
Last opioid dosage, MEDD, mean (SD), mg	129.65 (91.96)	172.04 (146.95)	163.06 (124.88)	184.52 (148.38)	<0.001
Initial opioid dosage, MEDD, mean (SD), mg	81.61 (66.03)	59.50 (56.87)	46.80 (46.77)	37.90 (30.26)	<0.001
Duration from diagnosis of pancreatic cancer to the time of initial opioids use, mean (SD), d	8.33 (13.02)	26.08 (35.18)	64.68 (84.61)	300.38 (411.75)	<0.001
Sex, female, n (%)	65 (25.7)	62 (24.5)	75 (29.6)	51 (20.2)	0.184
History of tuberculosis, n (%)	6 (18.8)	7 (21.9)	5 (15.6)	14 (43.8)	0.043
History of hypertension, n (%)	38 (16.6)	65 (28.4)	66 (28.8)	60 (26.2)	0.034
History of diabetes mellitus, n (%)	37 (18.4)	55 (27.4)	60 (29.9)	49 (24.4)	0.325
History of ischemic heart disease, n (%)	2 (33.3)	1 (16.7)	0 (0)	3 (50.0)	0.262
History of chronic hepatitis, n (%)	6 (15.8)	9 (23.7)	13 (34.2)	10 (26.3)	0.634
Radiotherapy, n (%)	11 (52.4)	7 (33.3)	1 (4.8)	2 (9.5)	0.002
Celiac plexus neurolysis, n (%)	4 (100)	0 (0)	0 (0)	0 (0)	0.003
Chemotherapy, n (%)	10 (18.2)	2 (3.6)	7 (12.7)	36 (65.5)	<0.001

BMI indicates body mass index.

TABLE 3 Patients' Characteristics According to Survival Time After Diagnosis of Pancreatic Cancer

TABLE 4

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

Variables	OR (95% CI)	*P*
Age, y	1.019 (0.997–1.041)	0.094
Body mass index, kg/m^2	0.963 (0.580–1.598)	0.883
History of tuberculosis	0.909 (0.396–2.085)	0.822
History of hypertension	0.693 (0.448–1.071)	0.099
History of diabetes mellitus	1.187 (0.781–1.804)	0.421
History of ischemic heart disease	2.576 (0.366–18.110)	0.342
History of chronic hepatitis	1.262 (0.579–2.748)	0.558
Radiotherapy after diagnosis	0.915 (0.328–2.553)	0.866
Chemotherapy after diagnosis	0.760 (0.368–1.567)	0.457
Stage IV (reference: stage III)	1.447 (0.902–2.321)	0.126
Initial opioid dosage (MEDD)	1.008 (1.002–1.013)	0.005
Rate of increasing opioid dose (MEDD/mo)	1.006 (1.002–1.010)	0.004
Last opioid dosage (MEDD)	0.997 (0.995–0.999)	<0.001

TABLE 4 Multivariate Logistic Regression Analysis for Death Within 180 Days After Diagnosis of Unresectable Pancreatic Cancer

Abstract v.s. paper

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 ≤ 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 interfers 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:

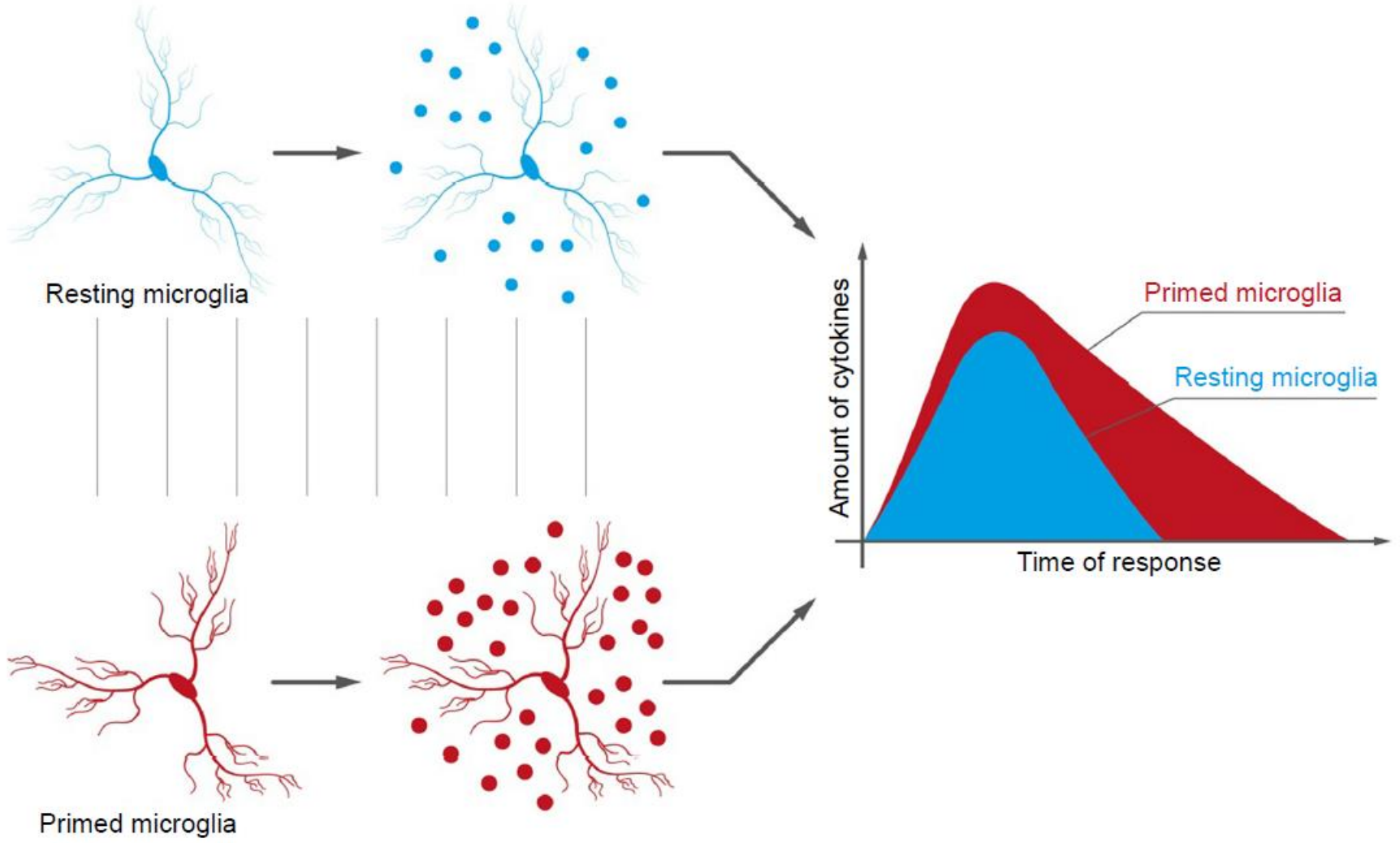
- functional limitation (hazard ratio 1.31; 95% confidence interval 1.20-1.39),
- symptoms preventing walking quarter of a mile (1.45 [1.35-1.58]),
- physical inactivity (1.14 [1.10-1.20]),
- poor self-rated health (1.32 [1.23-1.41])
  - Smith et al Pain 2018

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 vigourously – release cytokines – increase central sensitization
- Depression may heighten pain perception and central sensitization



Zis et al. Clinical Interventions in Aging 2017

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.

Note: Copyright, with permission from Pain Nursing Magazine, Fusco M, Paladini A, Skaper SD, Varrassi G. Chronic and neuropathic pain syndrome in the elderly: Pathophysiological basis and perspectives for a rational therapy. *Pain Nursing Magazine*. 2014;3:94–104.[156]

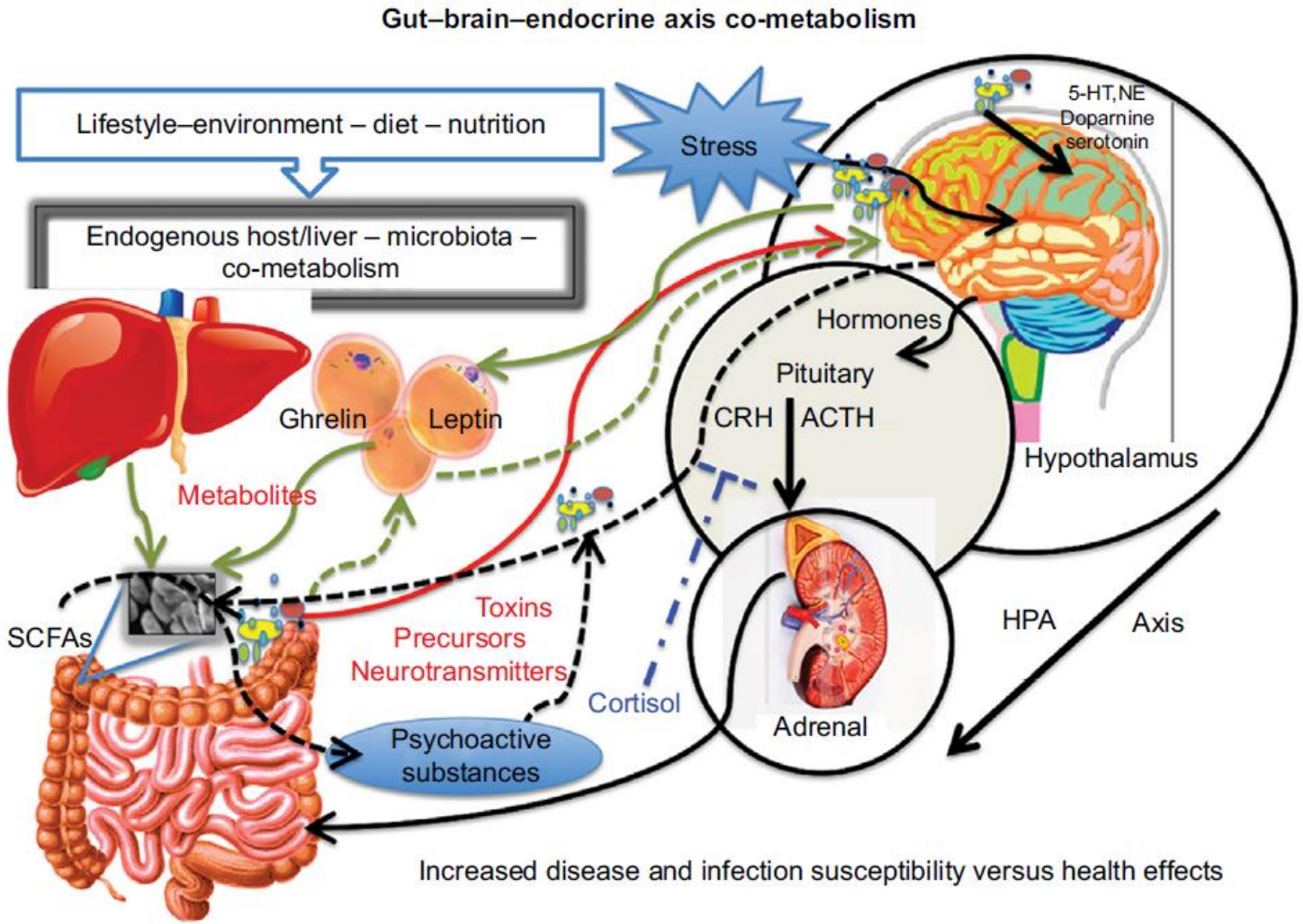


Figure 1 The HPA microbiota–gut–brain–endocrine pathway and intersecting organs demonstrating a known afferent and efferent cross-talk, which is yet to be well characterized and is very complex.

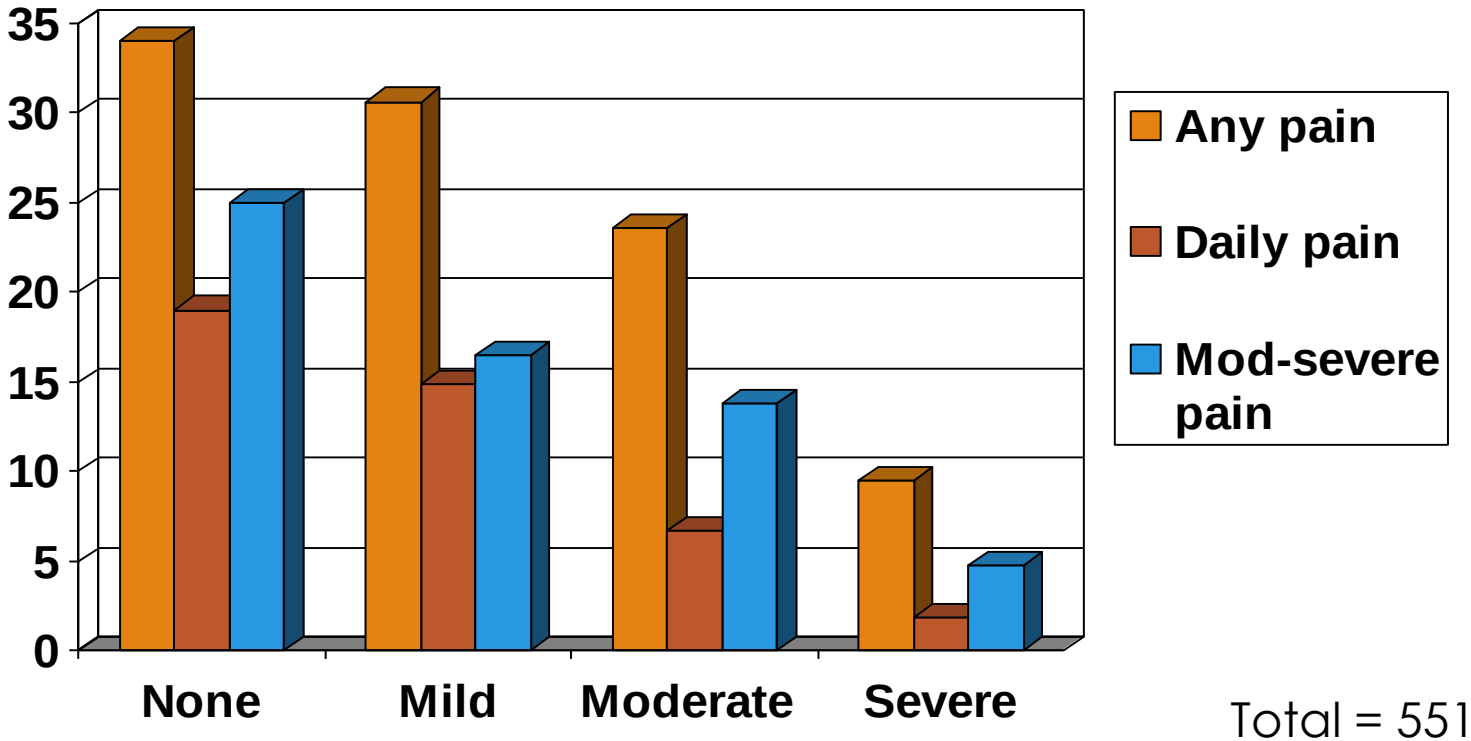
Note: Movement of metabolites, anterograde, retrograde, or both, from the gut and the brain to distal organs constitutes co-metabolism in a metabolic interactome.

Abbreviations: ACTH, adrenocorticotropic hormone; CRH, corticotropin releasing hormone; HPA hypothalmus pituitary adrenal; SCFA, short chain fatty acid; NE, norepinephrinegiven; HPA, hypothalamic–pituitary–adrenal; 5-HT, 5-hydroxytryptamine.

Obrenovich et al. Pathology and Laboratory Medicine International 2017

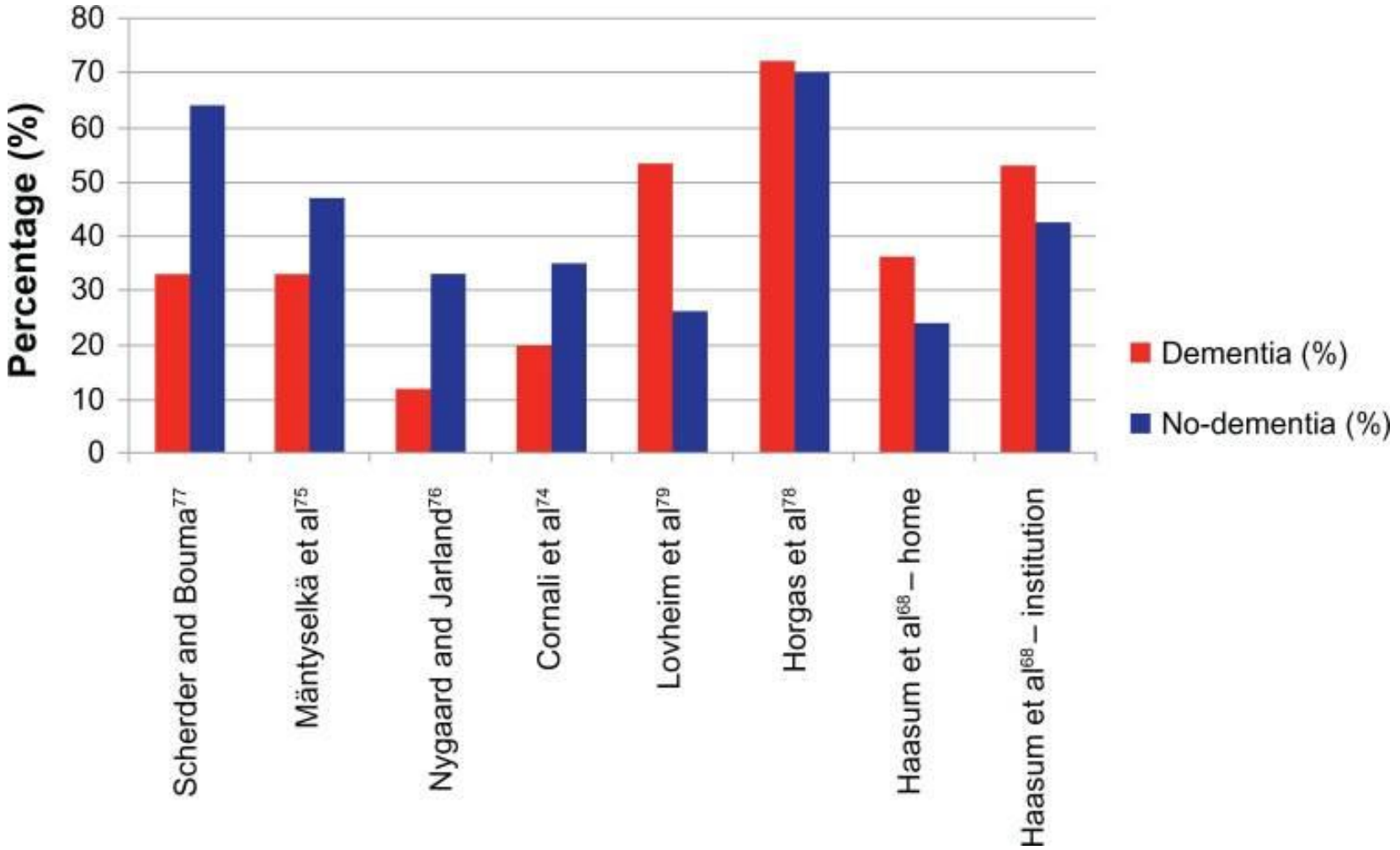
Pain Assessment

Pain reports and cognitive impairment



Total = 551

Reynolds et al. J Pain & Symptom Management 2008



Studies on the prevalence of analgesic use in patients with dementia vs no dementia. Achterberg et al Clin Intervent Aging 2013

ePAT pain assessment tool

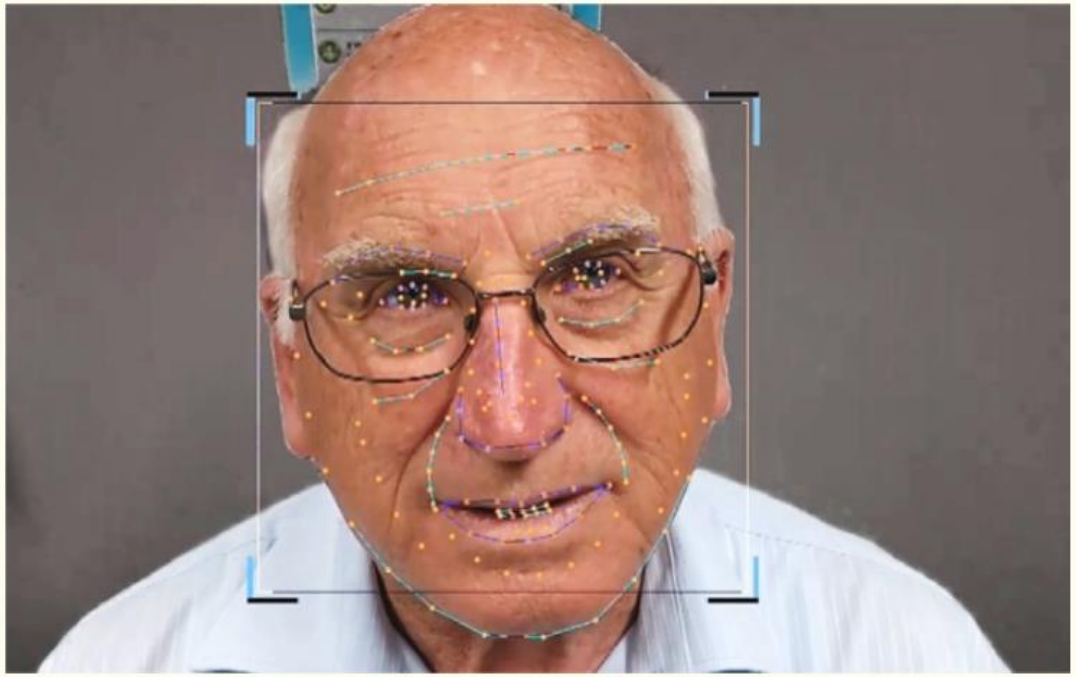


Figure 3

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

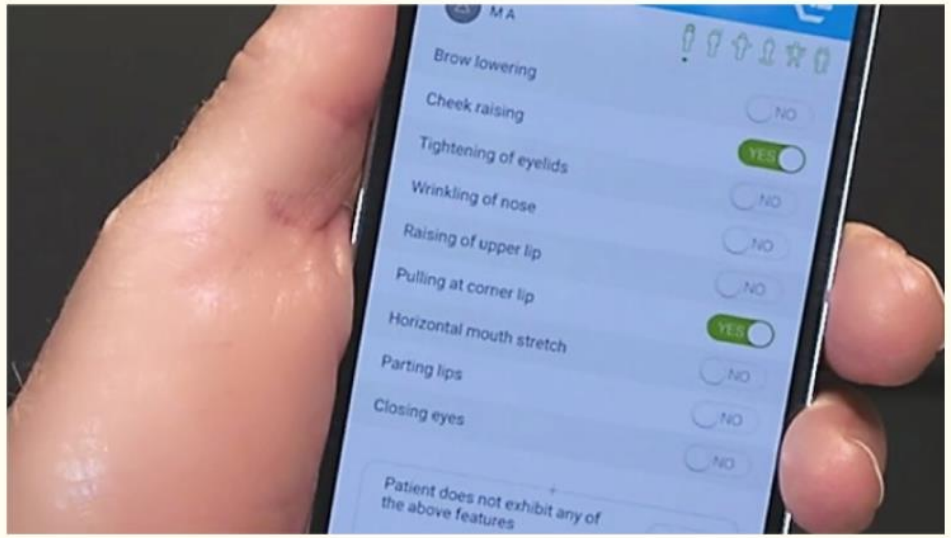


Figure 4

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

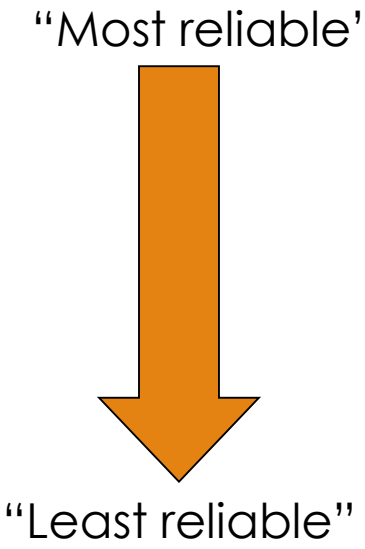
Medical Problems - Previous and Current

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



Resident report *(if possible)*

Family/caregiver report

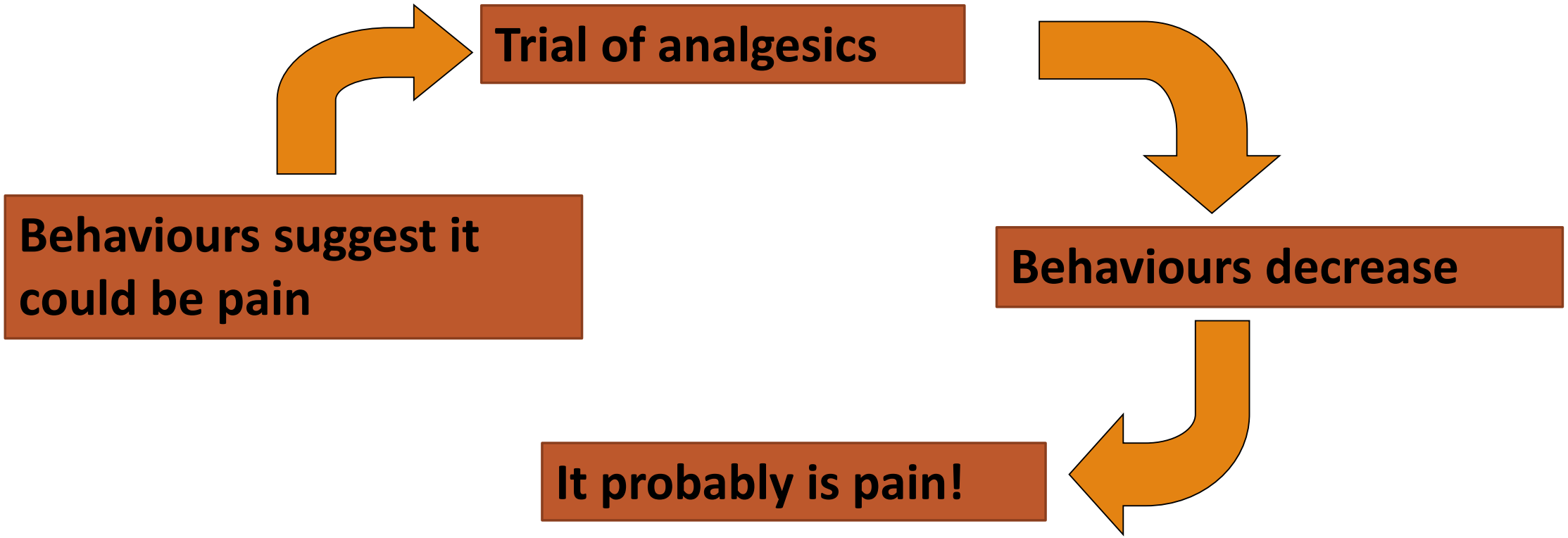
Prior pain history

Painful comorbidities

Behavioral indicators

Observer assessment

Empirical trials of analgesics



Evidence for empirical trials of analgesics

352 residents in facility care

Moderate to severe dementia with agitation

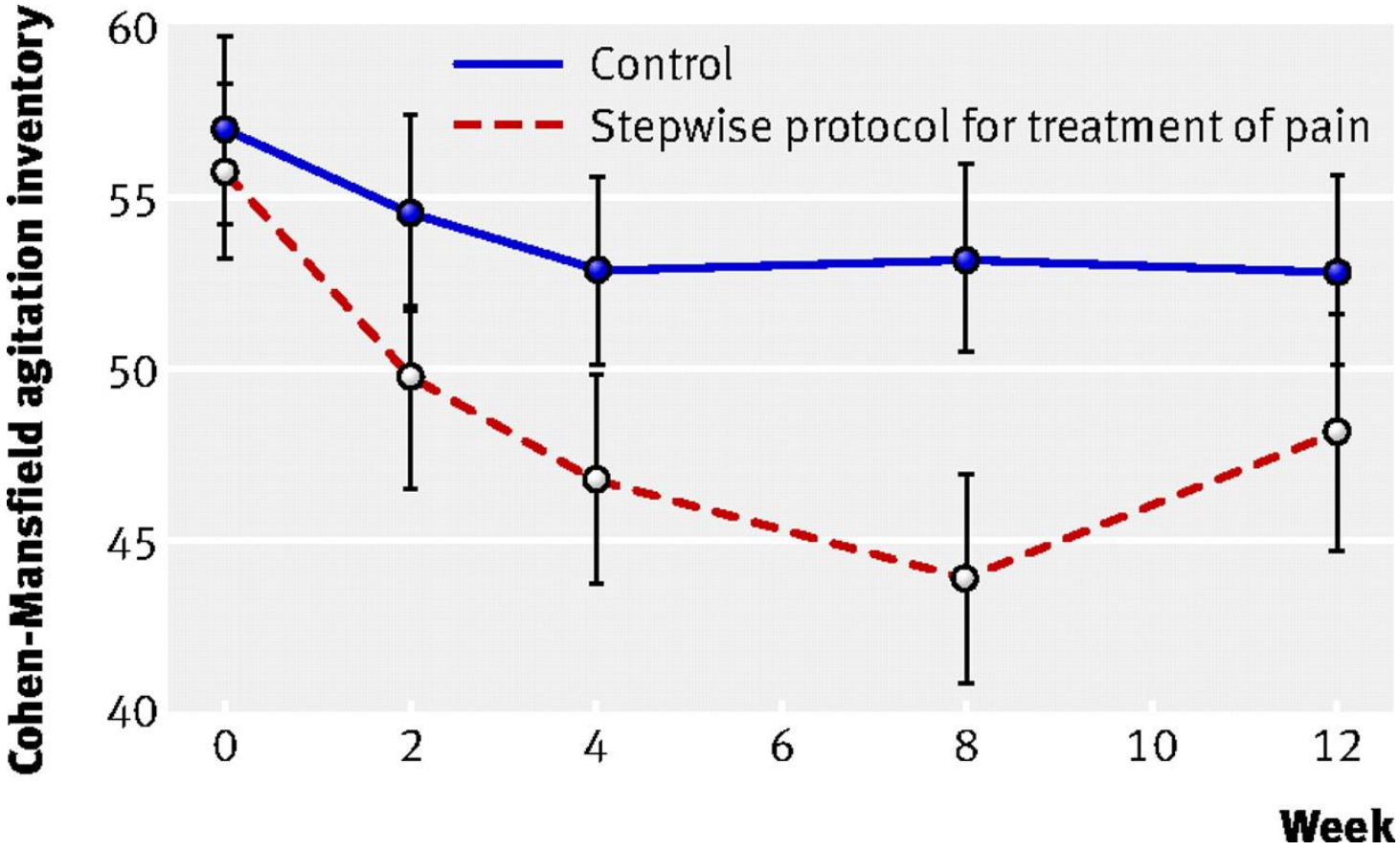
Randomized: step wise protocol vs regular care

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

- O'Neil C et al Am J Geriatr Pharmacother. 2012

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

- Kerr et al. Clin Pharmacol 2011

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

- Schneider V et al. Am J Epid. 2006

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 ($p<0.001$)

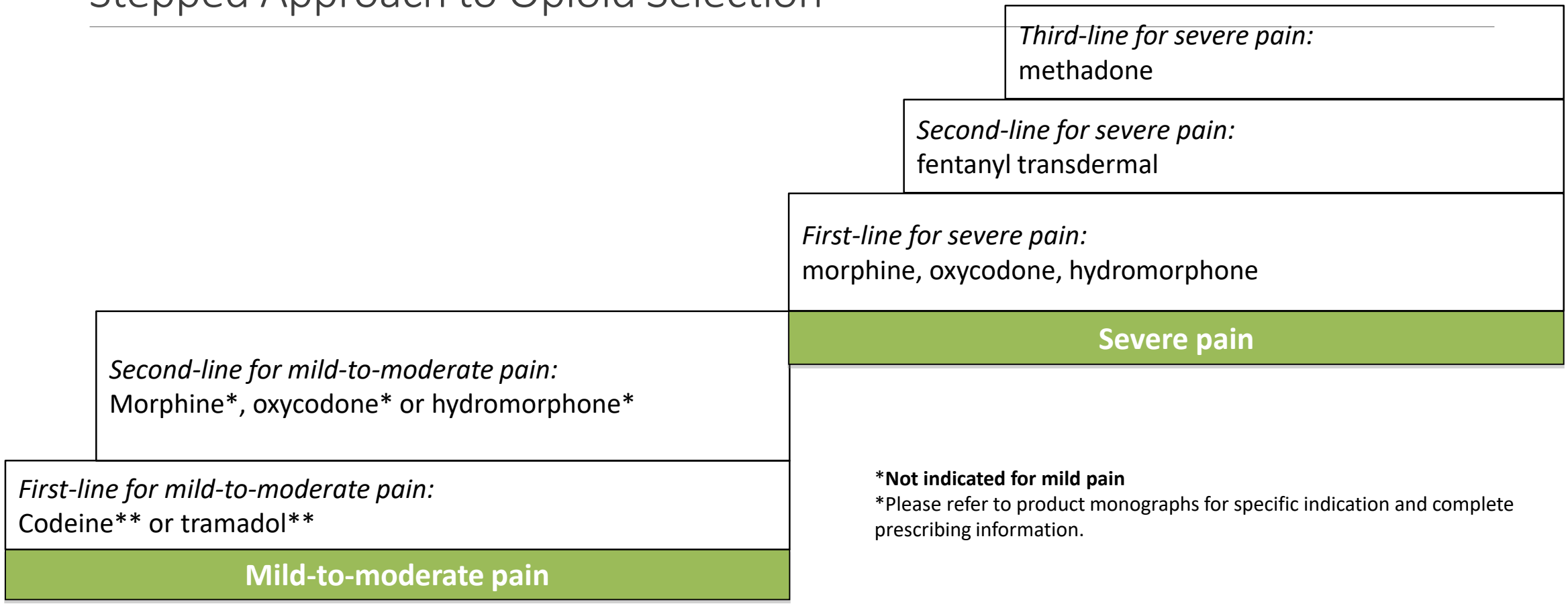
Sleep improvement ($p=0.31$)

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



***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.

National Opioid Use Guideline Group (NOUGG), 2010.

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

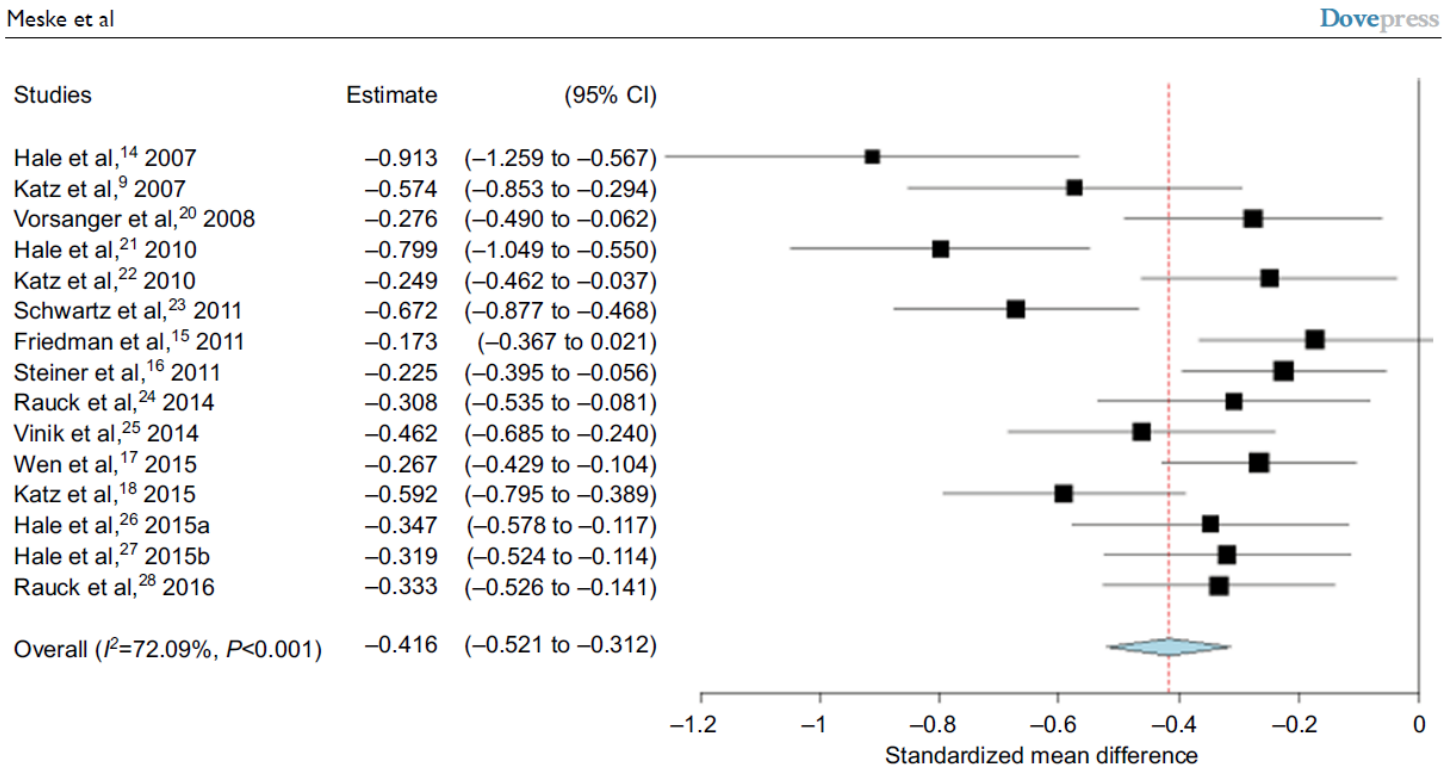


Figure 2 Change in PI from randomization baseline to week 12 with active study opioid drug versus placebo.
Notes: The standardized mean difference effect size was −0.416 and p<0.001, with a lower bound estimate of −0.521 and an upper bound −0.312.
Abbreviation: PI, pain intensity.

Meske et al J Pain Research 2018

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

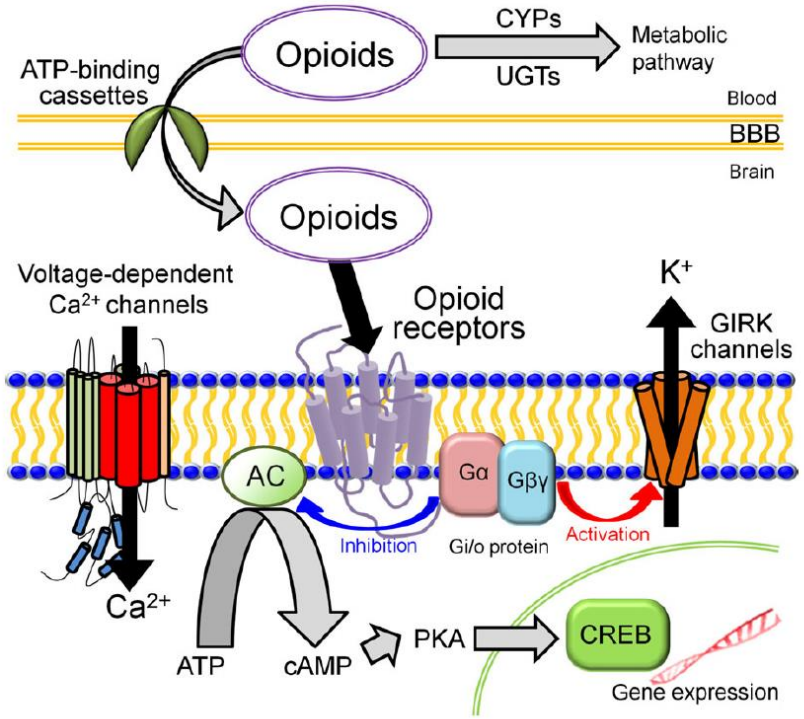
- Corli et al. Annals of Oncology 2016

Variability of Response to Strong Opioids

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

Corli et al. Annals of Oncology 2016

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

- Fournier et al. JAMA Internal Medicine 2015; Fournier et al Am J Med 2015

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

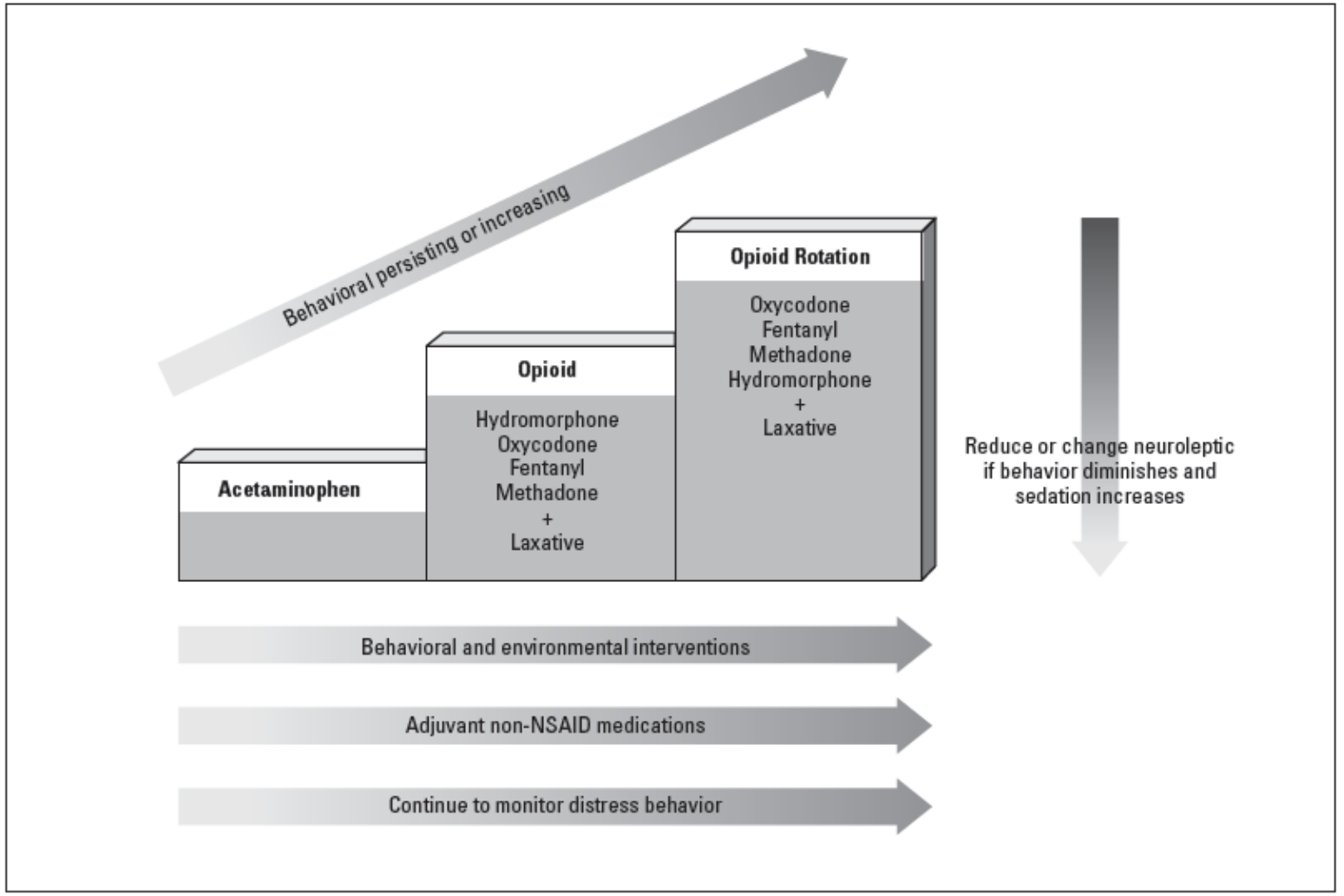


Figure. Trial of analgesics for older adults with advanced dementia exhibiting distress behavior.

Adapted from the World Health Organization's "Three-step analgesic ladder" for cancer pain relief[17]

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

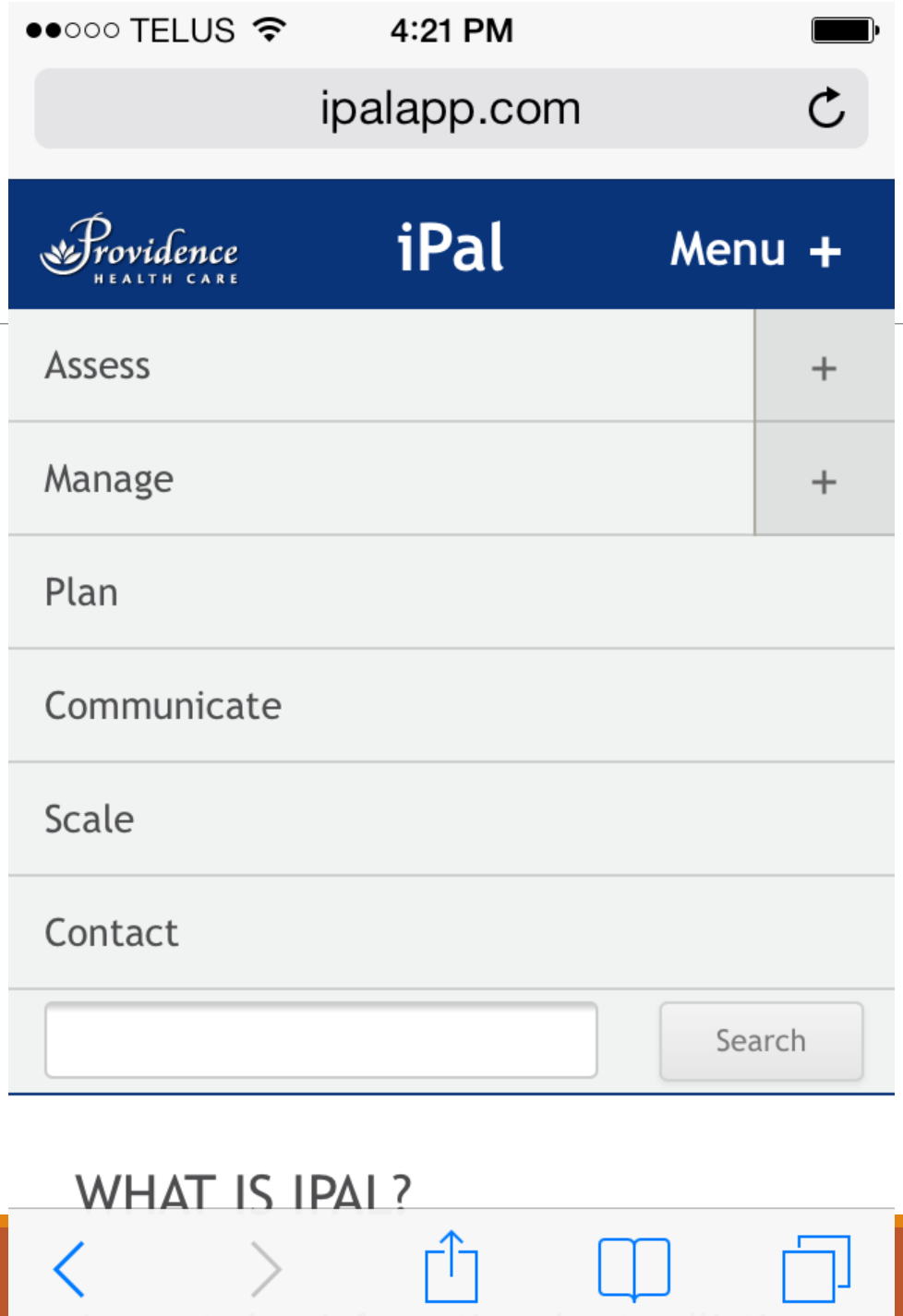
iPal

Essential information for palliative care

Web-based app works on any smart phone

http://ipalapp.com

Developed by Providence Health Care Palliative Care Program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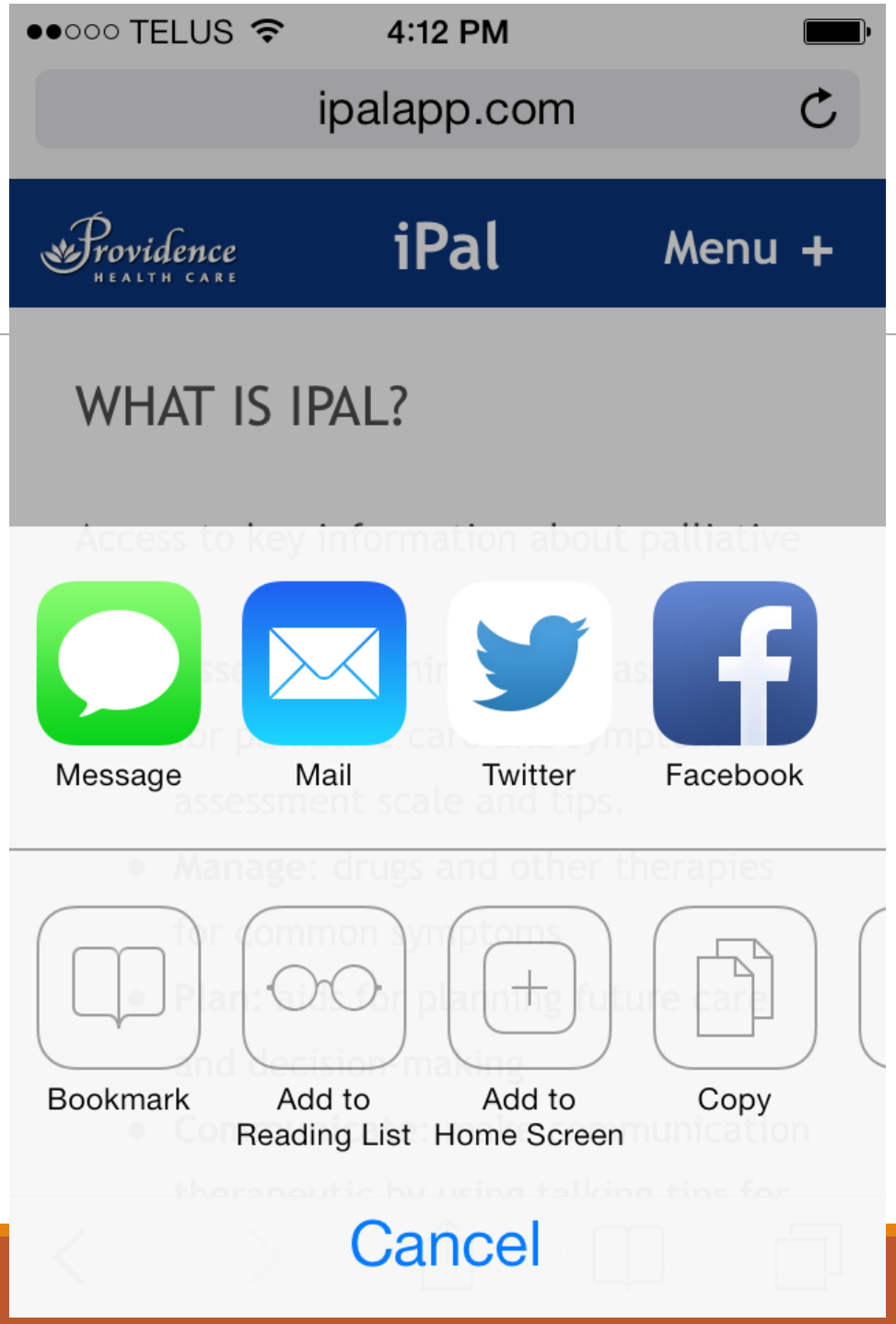
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