

Pain, Older People, Opioids and OTC Drugs

Dr Tim Semple

Grey Matters

clinical scenario

Request - to provide inpatient pain review for female, 92yrs with severe nonsurgical abdo pain, unresponsive to oxycodone, agitated+++

Background – nursing home resident with moderate dementia, widespread musculoskeletal pains on fentanyl patch 150mcg/hr (!)

Further background - had been on Panadeine Forte 6/day for 2 yrs, changed to fentanyl patch 25mcg/hr 6 months earlier

Initial benefit but dose escalation after 2 months, then monthly

Outcome....

No major pathology found

Presumed opioid-induced agitation/pain

Settled with rapid reduction/cessation of fentanyl dose

Conversion to buprenorphine patch 10mg weekly

Nursing home prescriber surprised when informed of daily oral morphine equivalence of 500mg causing severe pain state

Pain Medicine 2015; 16: 217–218
Wiley Periodicals, Inc.

EDITORIAL

Optimal Pharmacologic Pain Management in the Older Adult: An Ongoing Quagmire

So how did we get here?

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"I think the dosage needs adjusting. I'm not nearly as happy as the people in the ads."

Unrealistic prescriber and patient expectations of benefit from opioids

Current thinking on efficacy and role of opioids for chronic pain

4 systematic reviews and meta-analyses 2004-2008

NNT > 2.5only 2 out of 5 patients with CNCP benefit

- not “painkillers”
- usual analgesic benefit 20 - 30%, if component of multimodal approach
- encourage weaning after 3 – 6 months

What has changed with the pain medicine viewpoint of opioids for CNCP?

- Evidence for benefit less than expected
- Evidence for harm greater than expected

The “big picture” behind the clinical scenario

- Prevalence of pain in elderly - undertreated
- Rapid escalation of opioid use in elderly over past decade
- Adverse events associated with opioids
- Impact of prior longterm codeine intake initiating tolerance
- Shortfalls in knowledge of and access to non-pharmacological pain management options



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SA - ABS Australian Health Survey: First Results, 2011-12

- [Australian Health Survey Data -SA \(Excel 53 KB\)](#)

Latest health survey results for chronic conditions

South Australia

ABS Catalogue 4364.0.55.001

Selected Health Characteristics (Estimate)	2007-08	2011-12
High/Very high psychological distress(b)(c)	154,600	142,900
Selected current long-term conditions(d)		
Arthritis(e)	272,400	271,900
Asthma	154,400	174,200
Back pain/problem, disc disorder(f)	232,900	240,900
Chronic obstructive pulmonary disease(g)	37,200	38,100
Deafness(h)	180,100	178,600
Diabetes mellitus(i)	73,200	76,200
Hayfever and allergic rhinitis	269,900	318,700
Heart, stroke and vascular disease(j)	93,700	83,300
Hypertensive disease	176,500	183,000
Kidney disease(k)	**1000	11,700
Long sightedness	434,000	507,600
Malignant neoplasm (cancer)	26,000	20,300
Mental and behavioural problems(l)	190,800	238,800
Osteoporosis	49,300	63,800
Short sightedness	305,500	352,100

“I have back pain” - 240,900

“I have arthritis” – 271,900

Severity of chronic pain in an elderly population in Sweden—impact on costs and quality of life

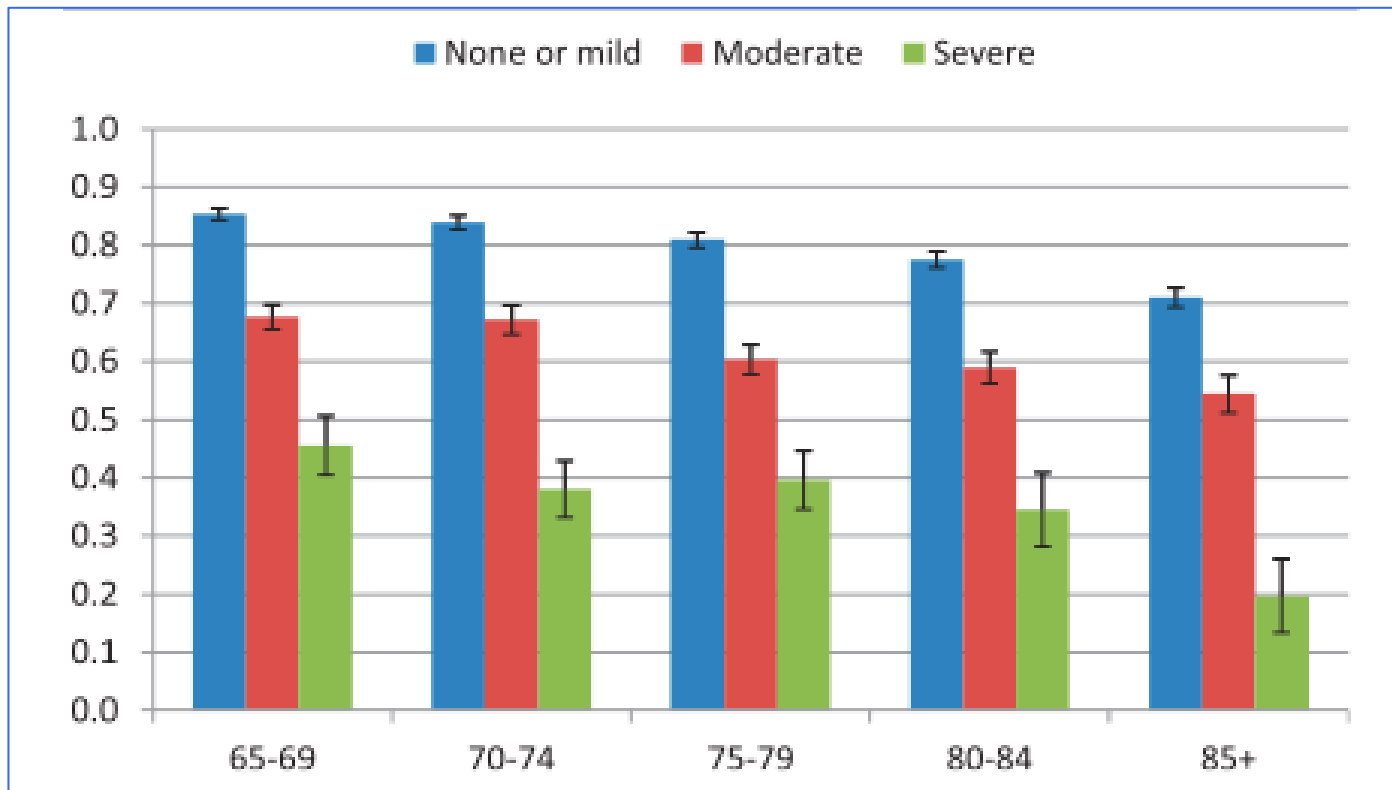
Lars Bernfort^{a,*}, Björn Gerdle^{b,c}, Mikael Rahmqvist^a, Magnus Husberg^a, Lars-Åke Levin^a

Survey of 6700 elderly Swedes

None or mild chronic pain – 77%

Moderate chronic pain – 19%

Severe chronic pain – 4 %



EQ -5D index measures 5 dimensions of health-related quality of life (HRQoL)

- HRQoL severely impacted by chronic pain

*Pain Medicine 2013; *: **-***
Wiley Periodicals, Inc.*

Prevalence, Causes, Severity, Impact, and Management of Chronic Pain in Australian General Practice Patients

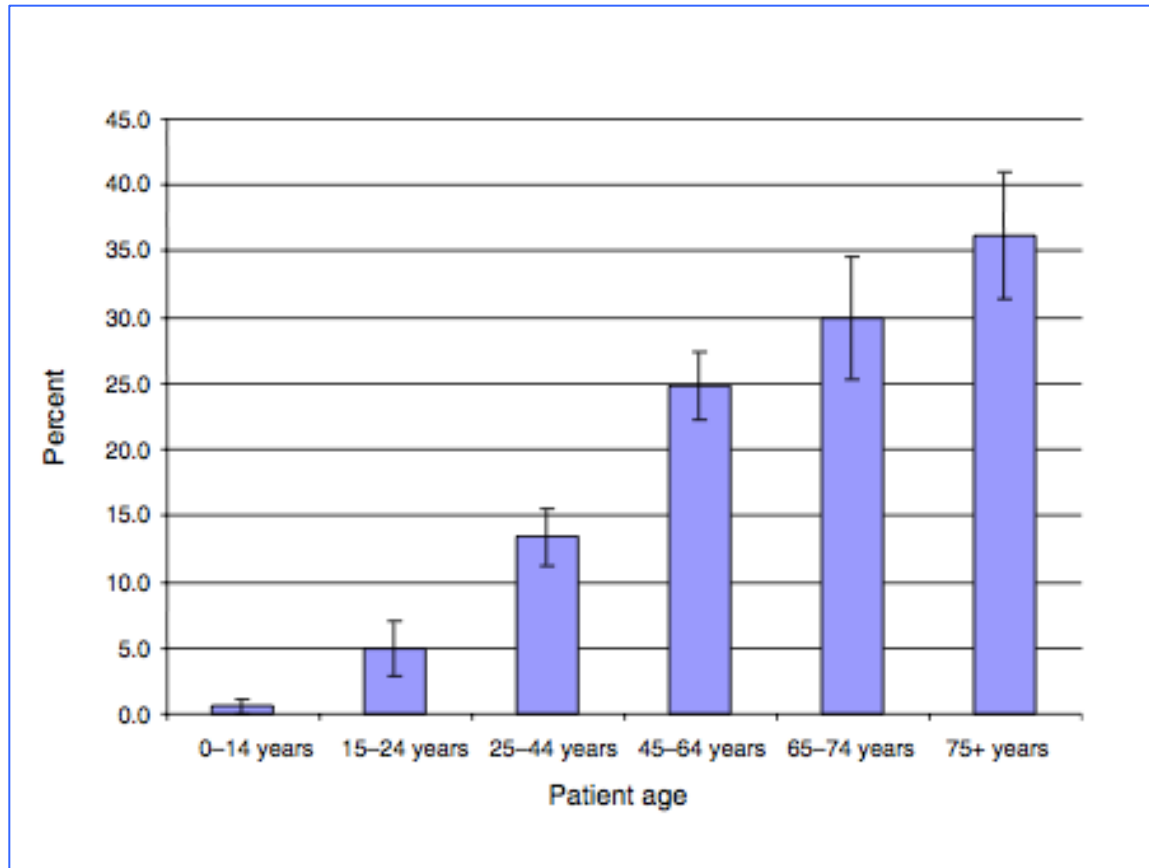
Henderson et al, BEACH program 2013

192 GPs, 5800 patients

20% of patients report chronic pain

osteoarthritis - 50%

back pain - 30%

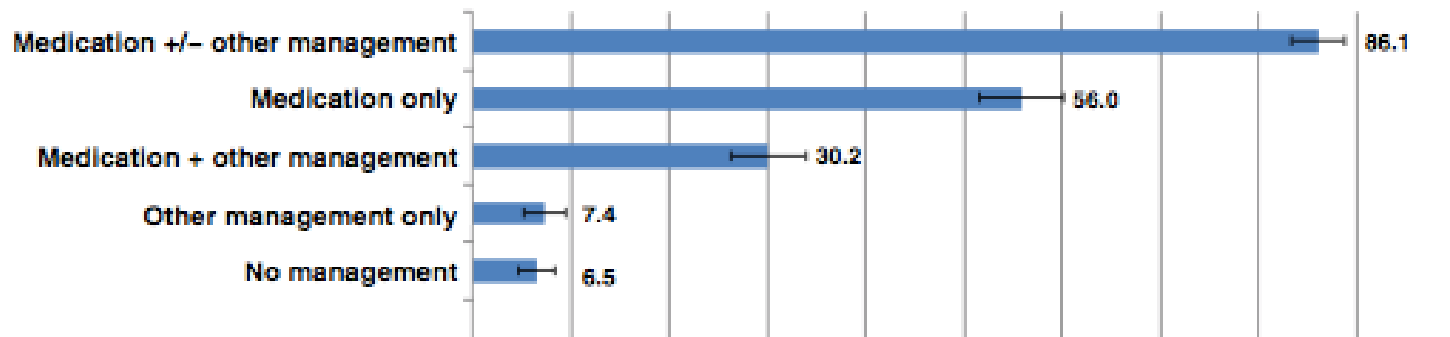


66% of GP pain workload in patients > 65yrs

Chronic Pain in Australian General Practice

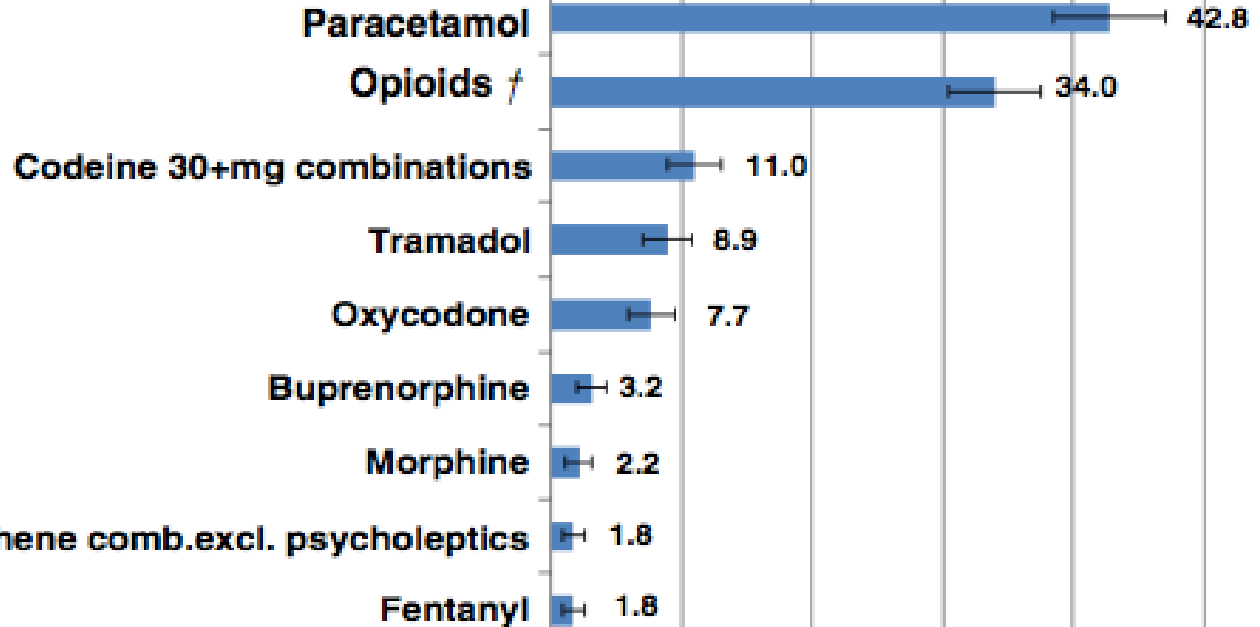
Pain management*

Total respondents with chronic pain - N = 1,113*



“Medication only “ in 56% reflects unrealistic expectations of benefit of medication

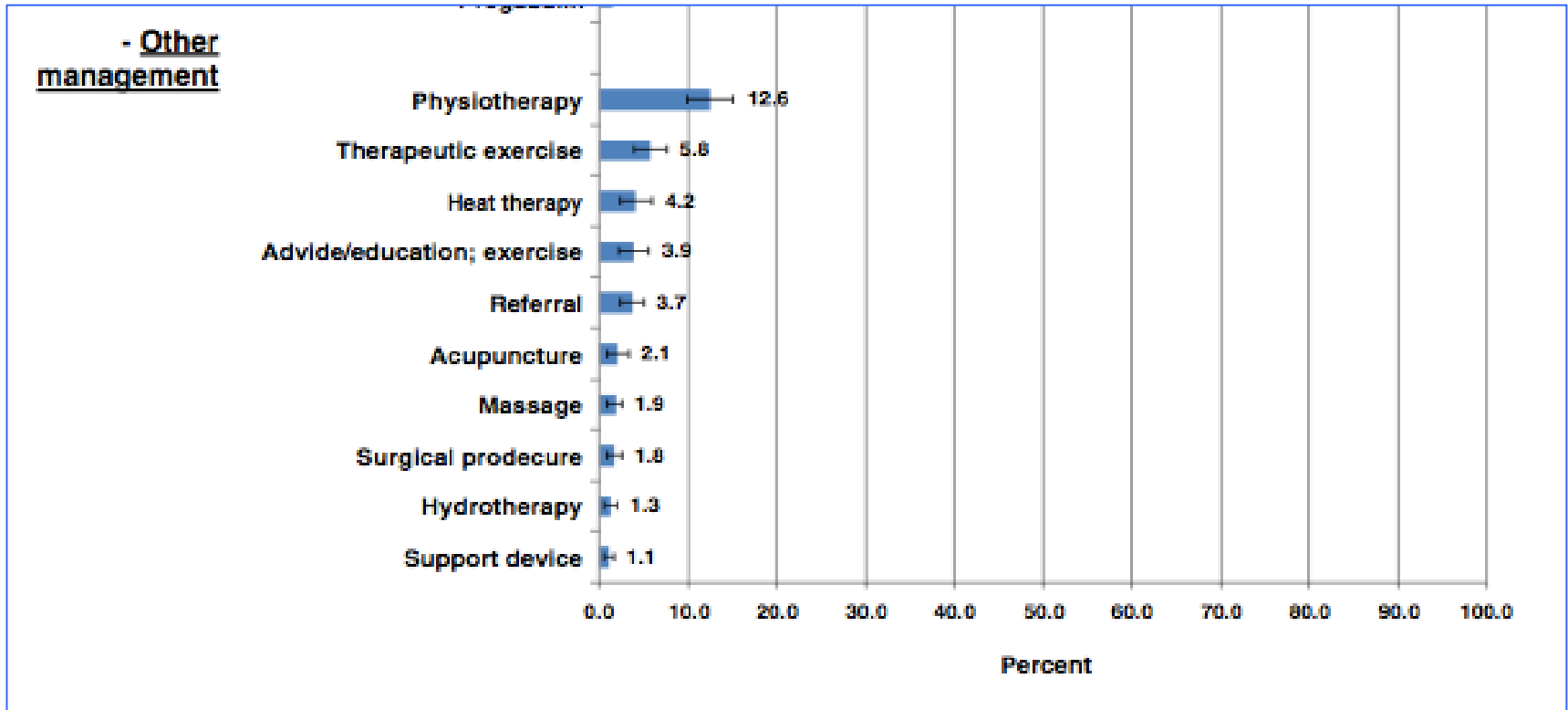
- Medication



Underutilisation of paracetomal

Panadeine Forte 1st place (2.2 % of adult NSW population)

High popularity of oxycodone (1.2% of adult NSW population!)



Apparent under-utilisation of nonpharmacological options

Referral only “3.7%”

PAIN & AGING SECTION

Original Research Article

Use of Opioids and Other Analgesics by Older Adults in the United States, 1999–2010

Between 1999 – 2000 and 2009 – 2010, opioid prescribing for older adults doubled.

Difficult to distinguish between “quality prescribing” or not

Drugs Aging (2013) 30:921–926
DOI 10.1007/s40266-013-0115-7

SHORT COMMUNICATION

What Analgesics Do Older People Use Prior to Initiating Oxycodone for Non-Cancer Pain? A Retrospective Database Study

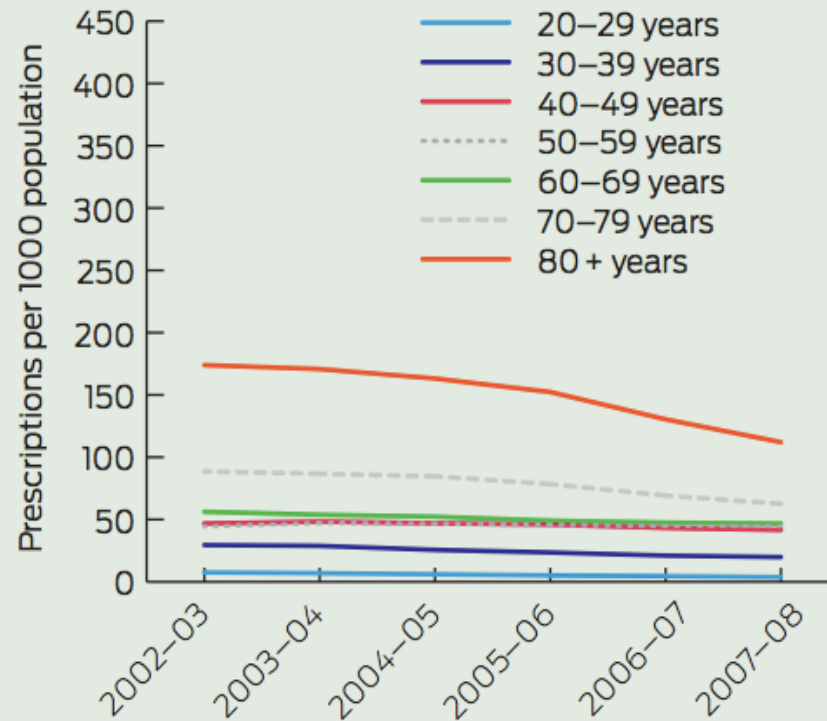
**Svetla Gadzhanova · J. Simon Bell ·
Elizabeth E. Roughead**

11,000 DVA clients dispensed oxycodone in 2010

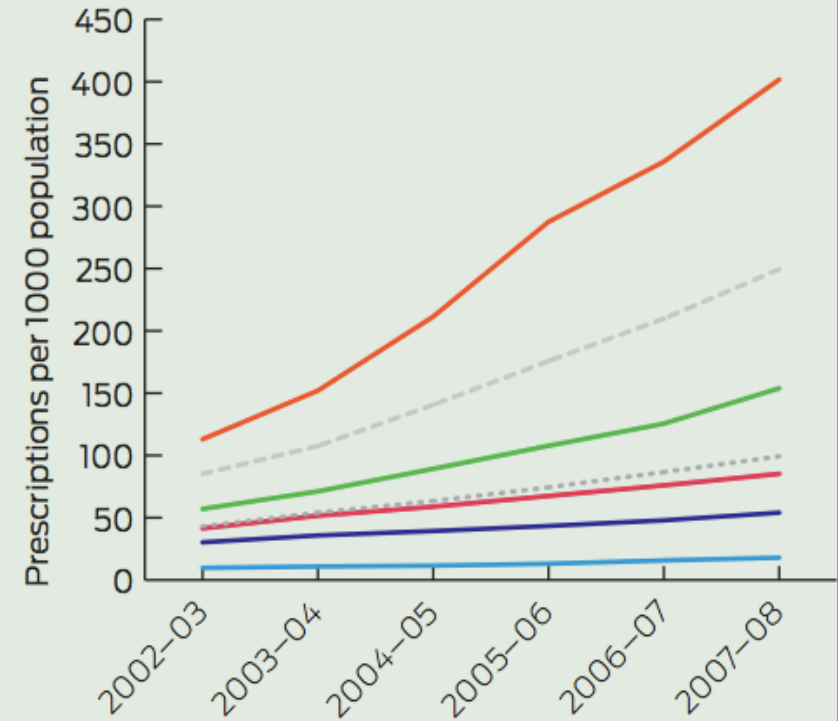
Initiation of a strong opioid (oxycodone) occurred in over 1/3 community-living DVA clients without prior simple analgesics or weak opioids

1 Prescriptions for morphine* and oxycodone[†] dispensed on the Pharmaceutical Benefits Scheme in Australia from 2002 to 2008, per thousand population, by 10-year age group[‡]

(A) Morphine



(B) Oxycodone



morphine Vs oxycodone 2002 – 2008

- **oxycodone becomes preferred strong opioid – why ?**
- **greatest increases in 80+ age group**

The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy

| Art Van Zee, MD

American J Public Health Feb 2009

- Labelled as “PHARMAGEDDON” of successful marketing in the USA
- Commercial triumph despite \$670 million fine for “false marketing” in USA
- Amphetamine-like effects in some = increased likeability

Oxy ban puts crunch on crime 67

BY DANIELLE BELL, OTTAWA SUN

FIRST POSTED: WEDNESDAY, JULY 18, 2012 05:38 PM EDT | UPDATED: WEDNESDAY, JULY 18, 2012 11:14 PM EDT



Canada bans Oxycontin – May 1, 2012

Trends in fentanyl prescriptions and fentanyl-related mortality in Australia

AMANDA ROXBURGH¹, LUCY BURNS¹, OLAF H. DRUMMER^{3,4}, JENNIFER PILGRIM⁴,
MICHAEL FARRELL¹ & LOUISA DEGENHARDT^{1,2}

¹National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia, ²Centre for Health Policy, Programs and Economics, School of Population Health, University of Melbourne, Melbourne, Australia, ³Victorian Institute of Forensic Medicine, Melbourne, Australia, and ⁴Department of Forensic Medicine, Monash University, Melbourne, Australia

Highlights increases in fentanyl-related deaths in younger IVDU population

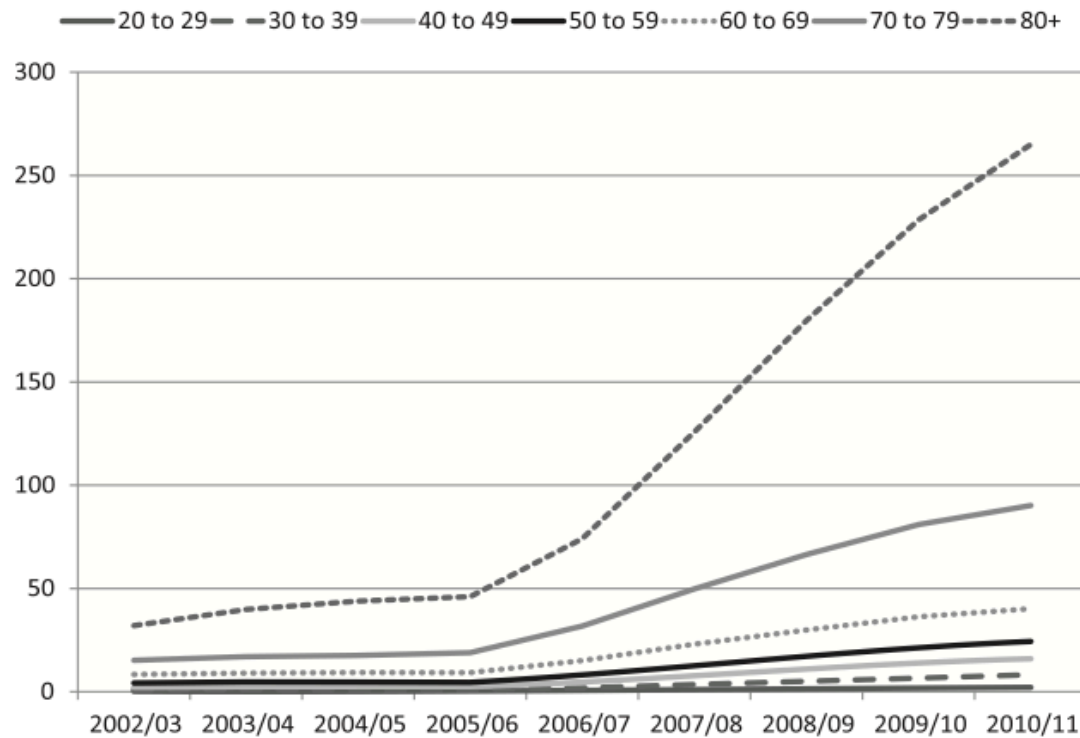


Figure 1. *Fentanyl prescriptions per 1000 population in Australia. Includes 12, 25, 50, 75 and 100 $\mu\text{g h}^{-1}$ transdermal patches. Source: Drug Utilisation Sub-Committee of the Pharmaceutical Benefits Advisory Committee.*

Rapid escalation of fentanyl patch use in 80yrs + population – appropriate or not ?

Clinician concerns re rapid tolerance to fentanyl

Association between mental health disorders, problem drug use and regular prescription opioid use

Sullivan et al. Arch Int Med 2006

- Common mental health disorders increase likelihood by 3 X of later initiation of prescription opioids for pain
- Problem drug use increases likelihood to a significantly lesser extent of prescription opioids for pain

“Undertreated mental health disorder patients prescribed opioids in response to high levels of distress”

Adverse Selection? A Multi-Dimensional Profile of People Dispensed Opioid Analgesics for Persistent Non-Cancer Pain

Kris D. Rogers^{1,2*}, Anna Kemp³, Andrew J. McLachlan^{4,5}, Fiona Blyth^{1,2,5}

1 The Sax Institute, Sydney, New South Wales, Australia, **2** Sydney Medical School, University of Sydney, Sydney, New South Wales, Australia, **3** School of Population Health, The University of Western Australia, Perth, Western Australia, Australia, **4** Faculty of Pharmacy, University of Sydney, Sydney, New South Wales, Australia, **5** Centre for Education and Research on Ageing, Concord Hospital, Sydney, New South Wales, Australia

PBS Prescription review 2006 – 2009 of 100,000 patients “45 and Up” cohort

50% over 70yrs

5% on longterm opioids

5% on intermittent opioids

Adverse selection in opioid dispensing

Opioid dispensing associated with

- younger age group (45-49yrs)
- treatment of osteoarthritis
- smoking / obesity / lower levels of physical activity
- lower income / reduced private health insurance rates
- living outside major city
- psychological distress

The Pain and Opioids IN Treatment study: characteristics of a cohort using opioids to manage chronic non-cancer pain

Gabrielle Campbell^{a,*}, Suzanne Nielsen^{a,b}, Raimondo Bruno^{a,c}, Nicholas Lintzeris^{b,d}, Milton Cohen^e,
Wayne Hall^f, Briony Larance^a, Richard P. Mattick^a, Louisa Degenhardt^{a,g,h,i}

Prospective cohort study of 1500 patients dispensed opioids

- **strong association with psychological distress, poor health and lower income**
- **social and psychological factors more significant in younger patients**

Opioid use in community dwelling elderly in Australia



Veal F, Bereznicki L, Peterson G, Thompson, A

Unit for Medication Outcomes Research and Education, School of Pharmacy, University of Tasmania

- **Home Medicines Review data analysed 2010-2012**
- **10,444 reviews of > 60yrs**
- **2711 taking opioids**
- **1816 taking regular dose opioids**

Poster presentation ASEAPS 2013

Patient characteristics based on daily MEQ dose

	≤120mg PO MEQ	>120mg PO MEQ
N	1659 (91.4%)	157 (8.6%)
Mean age*	76.3 (±8.6)	74.0 (±8.7)
MEQ PO dose (mg)**		
Mean (±SD)	33.5 (±25.4)	238.9 (±121.5)
Median	27mg	180mg
Anxiolytic and/or hypnotic**	39.3%	56.1%
Antidepressants and/or antipsychotics**	44.2%	64.3%

- **Nearly 10% taking > 120mg oral morphine equivalents daily**
- **Over 50% on additional anxiolytics/hypnotics**
- **Optimised paracetamol in only 50%**

Opioid use in Australian nursing home residents



Veal F, Bereznicki L, Peterson G, Thompson, A

Unit for Medication Outcomes Research and Education, School of Pharmacy, University of Tasmania

Medicine Review of nursing home residents

7177 assessed

11% taking > 120mg MEQ/day

Proportion of all RACF residents and analgesic use

	N (%)
Analgesic therapy	6526 (90.5%)
Analgesic use in patients who have at least 1 pain condition	6513 (90.7%)
Analgesic use in RACF residents who have at least 1 pain condition	6513 (90.7%)
NSAID	426 (5.9%)
Adjunct agents	
Tricyclic antidepressant (TCAs)	391 (5.4%)
Pregabalin/gabapentin	33 (0.5%)
Serotonin-noradrenalin reuptake inhibitors	439 (6.1%)
Optimised paracetamol	2867 (39.9%)
Opioids (RD and/or PRN)	2796 (39.0%)
RD opioids	28% (56.5mg MEQ/D)
RD opioids and optimised paracetamol	56%
RD opioids and anxiolytics/hypnotics	978 (48.3%)

90% with analgesic therapy – 28% on opioids

Mean MEQ/day 56.5mg

Relationship of Opioid Use and Dosage Levels to Fractures in Older Chronic Pain Patients

*Kathleen W. Saunders, JD¹, Kate M. Dunn, Ph. D², Joseph O. Merrill, M.D, M.P.H.³,
Mark Sullivan, M.D., Ph.D.⁴, Constance Weisner, DrPH, M.S.W.^{6,6},
Jennifer Brennan Braden, M.D., M.P.H.⁴, Bruce M. Psaty, M.D., Ph.D.^{1,7},
and Michael Von Korff, Sc.D.¹*

2-fold increase in fracture risk if MEQ/day > 50mg

One in ten of individuals on > 50mg will have a fracture each year



PAIN® 152 (2011) 1803–1810

PAIN®

www.elsevier.com/locate/pain

Prescription opioid analgesics rapidly change the human brain

Jarred W. Younger^{a,*}, Larry F. Chu^a, Nicole T. D'Arcy^a, Kiley E. Trott^b, Laura E. Jastrzab^a, Sean C. Mackey^a

^a Department of Anesthesia, School of Medicine, Stanford University, Palo Alto, CA, USA

^b Department of Human Biology, School of Arts & Sciences, Stanford University, Palo Alto, CA, USA

10 chronic LBP patients given oral morphine (< 100mg) for 4 weeks then ceased

Functional MRI at baseline, one month, four months

Control group – no opioids

Gray matter brain changes after 4 weeks

- Dose-related volume decrease in amygdala
- Dose-related volume increase in hypothalamus, frontal gyrus, pons
- Structural and functional changes in reward- and affect-processing circuitry

Most changes sustained at 4 months



PAIN® 155 (2014) 843–844

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Commentary

Will data destroy our faith in long-acting opioids?



Longstanding belief - slow-release long-acting opioids are preferable to intermittent short-acting opioids for CNCP

Challenged by failure to prove improvements in -

- safety
- efficacy
- QOL
- pain stability
- sleep

M Sullivan Pain 2014

For three days use only. Can cause addiction.

NUROFEN[®]
PLUS

Ibuprofen,
Codeine

DUAL ACTION
PAIN RELIEF

12 TABLETS

PHARMACY ONLY ⊕

THE NEW ZEALAND MEDICAL JOURNAL

Journal of the New Zealand Medical Association



Combination NSAID-codeine preparations and gastrointestinal toxicity

Claire Evans, Teresa A Chalmers-Watson, Richard B Gearry

OPEN

Citation: *Transl Psychiatry* (2014) **4**, e482; doi:10.1038/tp.2014.121

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www.nature.com/tp

ORIGINAL ARTICLE

Codeine-induced hyperalgesia and allodynia: investigating the role of glial activation

JL Johnson¹, PE Rolan^{1,2,3}, ME Johnson⁴, L Bobrovskaya⁴, DB Williams⁴, K Johnson⁵, J Tuke⁶ and MR Hutchinson⁷

codeine mg : mg activates glia as much as morphine

glial activation initiates tolerance and hyperalgesia

Regular use of codeine for milder pain conditions may lead to as much tolerance and increased pain sensitivity as larger doses of strong opioids

So, what to think about codeine?

- Unpredictable pro-drug with no effect in 5-10% and high effect in 5-10%
- Little evidence of benefit – would not get to market now
- Associated with initiating dependency, especially in combination with NSAID as OTC analgesic
- May induce tolerance rapidly and prevent stronger opioids working when needed

Research papers

Different profiles of buprenorphine-induced analgesia and antihyperalgesia in a human pain model

Wolfgang Koppert^{a,*}, Harald Ihmsen^a, Nicole Körber^a, Andreas Wehrfritz^a,
Reinhard Sittl^a, Martin Schmelz^b, Jürgen Schüttler^a

^a*Department of Anaesthesiology, University Hospital Erlangen, Krankenhausstrasse 12, D-91054 Erlangen, Germany*

^b*Department of Anaesthesiology Mannheim, University of Heidelberg, Theodor-Kutzer Ufer 1-3, D-61087 Mannheim, Germany*

Received 7 February 2005; received in revised form 17 May 2005; accepted 20 June 2005

Buprenorphine – quite different from other opioids

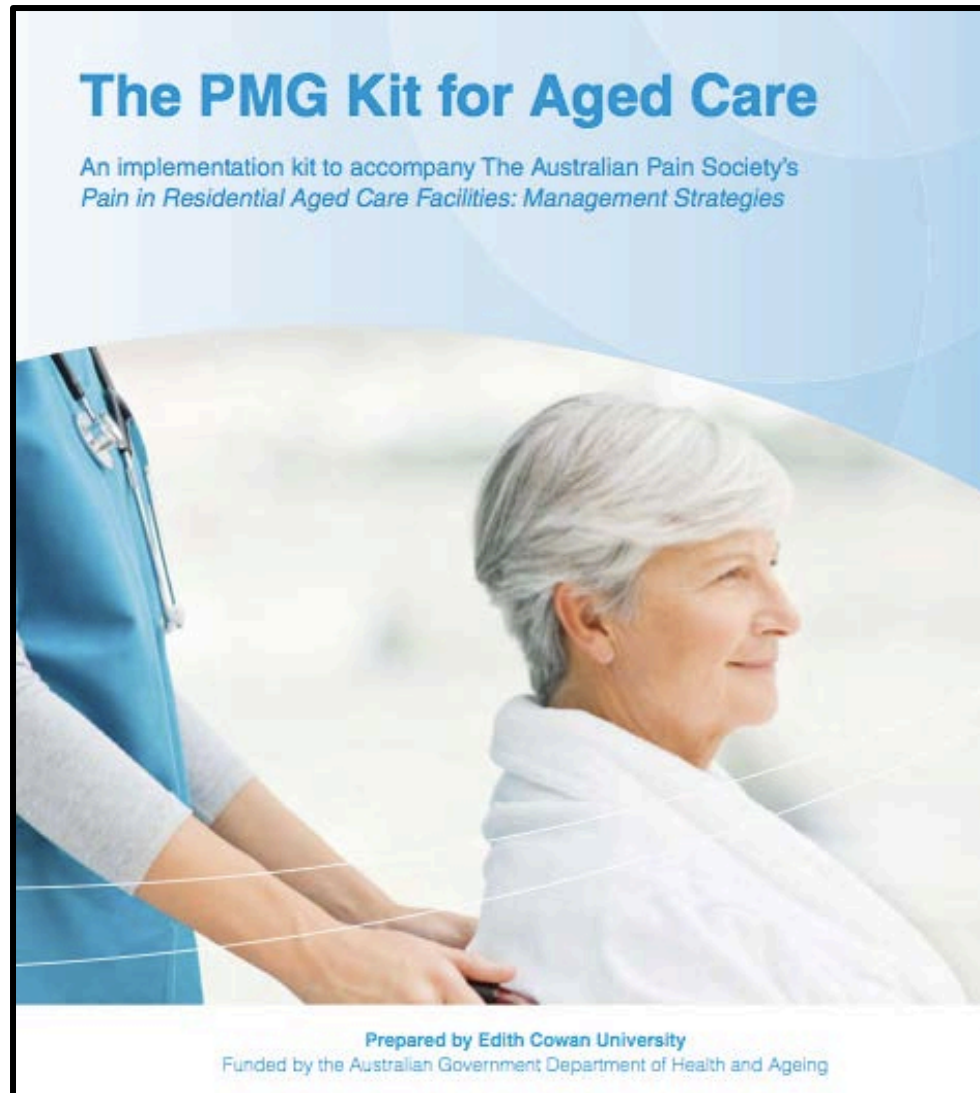
potential lower association with tolerance and hyperalgesia

may be a preferable choice if tolerated.....

PAIN 2005

Options for managing pain

APS Pain in RACF – Management Strategies





PAIN[®] 154 (2013) 824–835

PAIN[®]

www.elsevier.com/locate/pain

Self-management intervention for chronic pain in older adults: A randomised controlled trial

Michael K. Nicholas^{a,*}, Ali Asghari^{a,b}, Fiona M. Blyth^{a,c,d}, Bradley M. Wood^a, Robin Murray^a,
Rebecca McCabe^a, Alan Brnabic^e, Lee Beeston^a, Mandy Corbett^a, Catherine Sherrington^f, Sarah Overton^a

Eight 2 hour sessions – significant improvements in pain disability and distress



PAIN[®] 154 (2013) 942–950

PAIN[®]

www.elsevier.com/locate/pain

The *Pain Course*: A randomised controlled trial of a clinician-guided Internet-delivered cognitive behaviour therapy program for managing chronic pain and emotional well-being

Blake F. Dear^{a,*}, Nick Titov^a, Kathryn Nicholson Perry^b, Luke Johnston^a, Bethany M. Wootton^a, Matthew D. Terides^a, Ron M. Rapee^a, Jennifer L. Hudson^a

^aThe Centre for Emotional Health, Department of Psychology, Macquarie University, Sydney, Australia

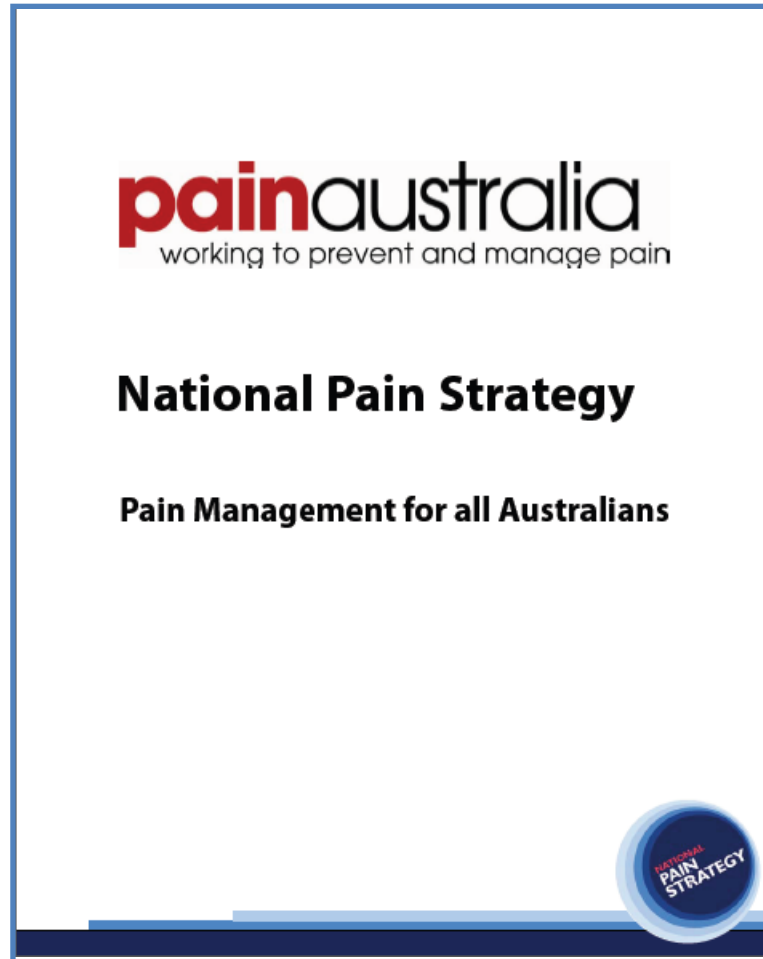
^bSchool of Social Sciences and Psychology, Centre for Health Research, University of Western Sydney, Australia

Cost-effective, accessible and no side-effects

In an ideal world

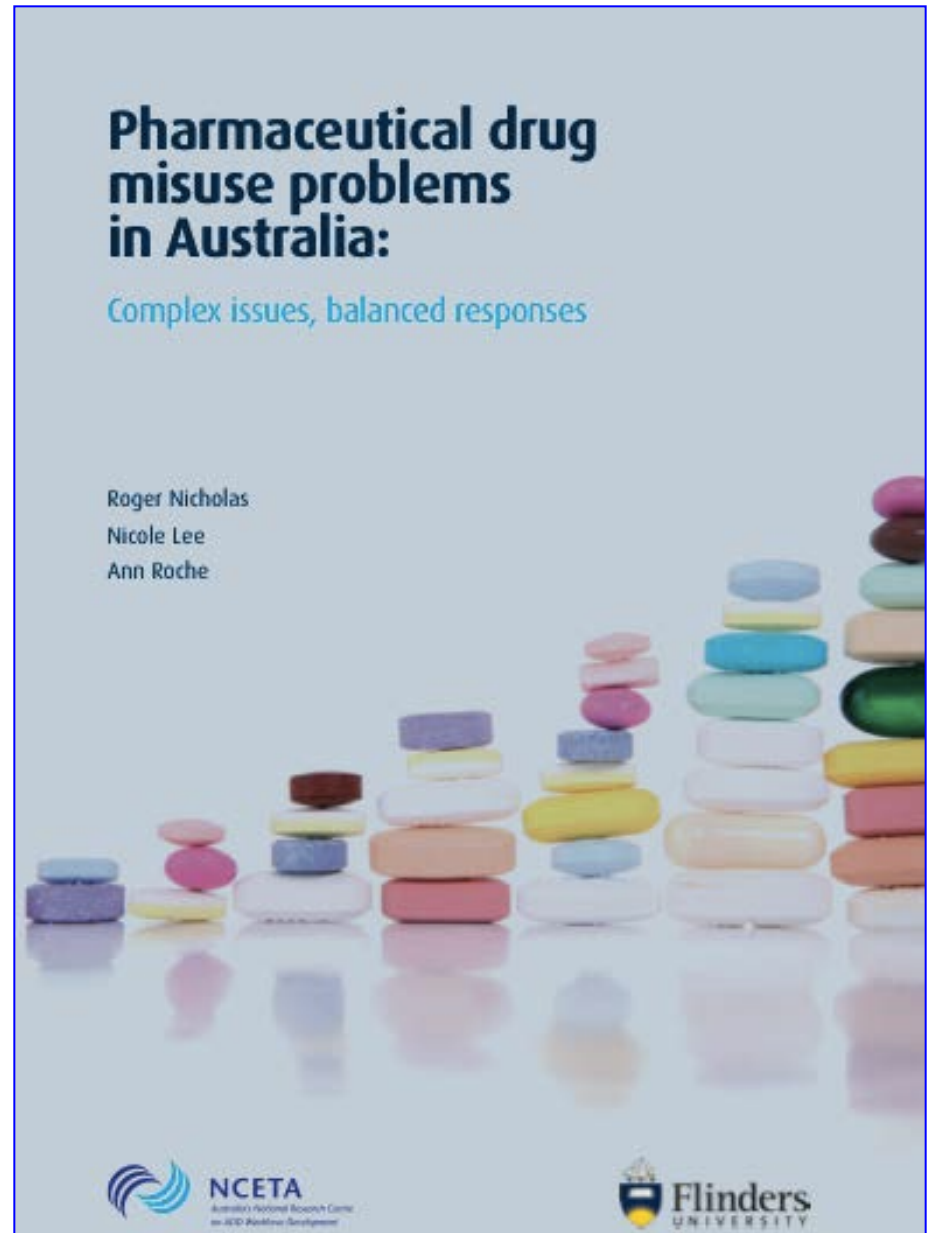
- **GP confident with pain management skill-base and time available**
- **Repeated doses of medical consistency – same positive message reinforced about CNCP and prognosis**
- **Ready access to self-management tools – practice and RACF nurse coaching and consumer support**
- **Community chronic pain-orientated allied health for pacing / exercise / coping**
- **Appropriate safe and sustainable analgesic drug management**

New national body to lobby government



Australian government review

Pharmaceutical drug misuse
strategy March 2012



Tasmanian review
July 2012

