The trouble with opioids

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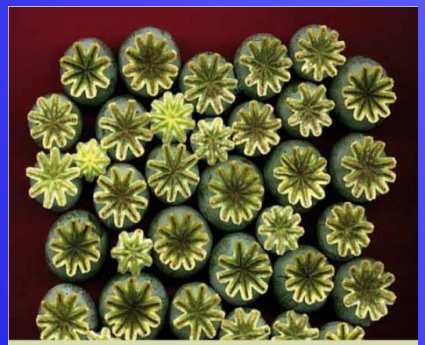
Aim of Session

- Use opioids in chronic non-cancer pain
  - Efficacy, Trends, Costs
  - Long term effects
- The elderly population
  - Specific problems
  - Specific opioids

“Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium.”

Thomas Sydenham (1624-1689)



The British Pain Society's

Opioids for persistent pain:
Good practice

A consensus statement prepared on behalf of the British Pain Society, the Faculty of Pain Medicine of the Royal College of Anaesthetists, the Royal College of General Practitioners and the Faculty of Addictions of the Royal College of Psychiatrists

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Elsevier

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

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SPECIAL ARTICLE

Opioids for the Treatment of Chronic Pain: Mistakes Made, Lessons Learned, and Future Directions

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An overreliance on opioids has impacted all types of pain management, making it undoubtedly a root cause of the "epidemic" of prescription opioid abuse in the United States. Yet, an examination of the statistics that led the US Centers for Disease Control and Prevention to declare that prescription opioid abuse had reached epidemic levels shows that the abuse occurrences and deaths are arising outside the hospital or hospice setting, which strongly implicates the outpatient use of opioids to treat chronic pain. Such abuse and related deaths are occurring in chronic pain patients themselves and also through diversion. Overprescribing to outpatients has afforded distressed and vulnerable individuals access to these highly addictive drugs. The focus of this article is on what we have learned since opioid treatment of chronic pain was first popularized at the end of the 20th century and how this new information can guide chronic pain management in the future. (Anesth Analg 2017;125:1769–78)

What is the efficacy for opioids in chronic non-cancer pain?

Efficacy in Chronic Non-Cancer Pain (CNCP)

PAIN

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www.elsevier.com/locate/pain

Opioids in chronic non-cancer pain: systematic review of efficacy and safety

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Abstract

Opioids are used increasingly for chronic non-cancer pain. Controversy exists about their effectiveness and safety with long-term use. We analysed available randomised, placebo-controlled trials of WHO step 3 opioids for efficacy and safety in chronic non-cancer pain. The Oxford Pain Relief Database (1950–1994) and Medline, EMBASE and the Cochrane Library were searched until September 2003. Inclusion criteria were randomised comparisons of WHO step 3 opioids with placebo in chronic non-cancer pain. Double-blind studies reporting on pain intensity outcomes using validated pain scales were included. Fifteen randomised placebo-controlled trials were included. Four investigations with 120 patients studied intravenous opioid testing. Eleven studies (1025 patients) compared oral opioids with placebo for four days to eight weeks. Six of the 15 included trials had an open label follow-up of 6–24 months. The mean decrease in pain intensity in most studies was at least 30% with opioids and was comparable in neuropathic and musculoskeletal pain. About 80% of patients experienced at least one adverse event, with constipation (41%), nausea (32%) and somnolence (29%) being most common. Only 44% of 388 patients on open label treatments were still on opioids after therapy for between 7 and 24 months. The short-term efficacy of opioids was good in both neuropathic and musculoskeletal pain conditions. However, only a minority of patients in these studies went on to long-term management with opioids. The small number of selected patients and the short follow-ups do not allow conclusions concerning problems such as tolerance and addiction.

Keywords: Opioid; Pain; Chronic; Non-malignant; Randomised controlled trial; Systematic review

Efficacy of opioids in CNCP

- Cochrane low back pain (Chaparro 2013)
  - <12 weeks low to moderate evidence
  - >12 weeks, no better than placebo
- Cochrane neuropathic pain (McNichol,2013)
  - Efficacy subject to considerable uncertainty
- Cochrane rheumatoid arthritis (Whittle 2011)
  - Low evidence for weak opioids short duration
  - No evidence over 12 weeks or for strong opioid

Do opioids work in CNCP?

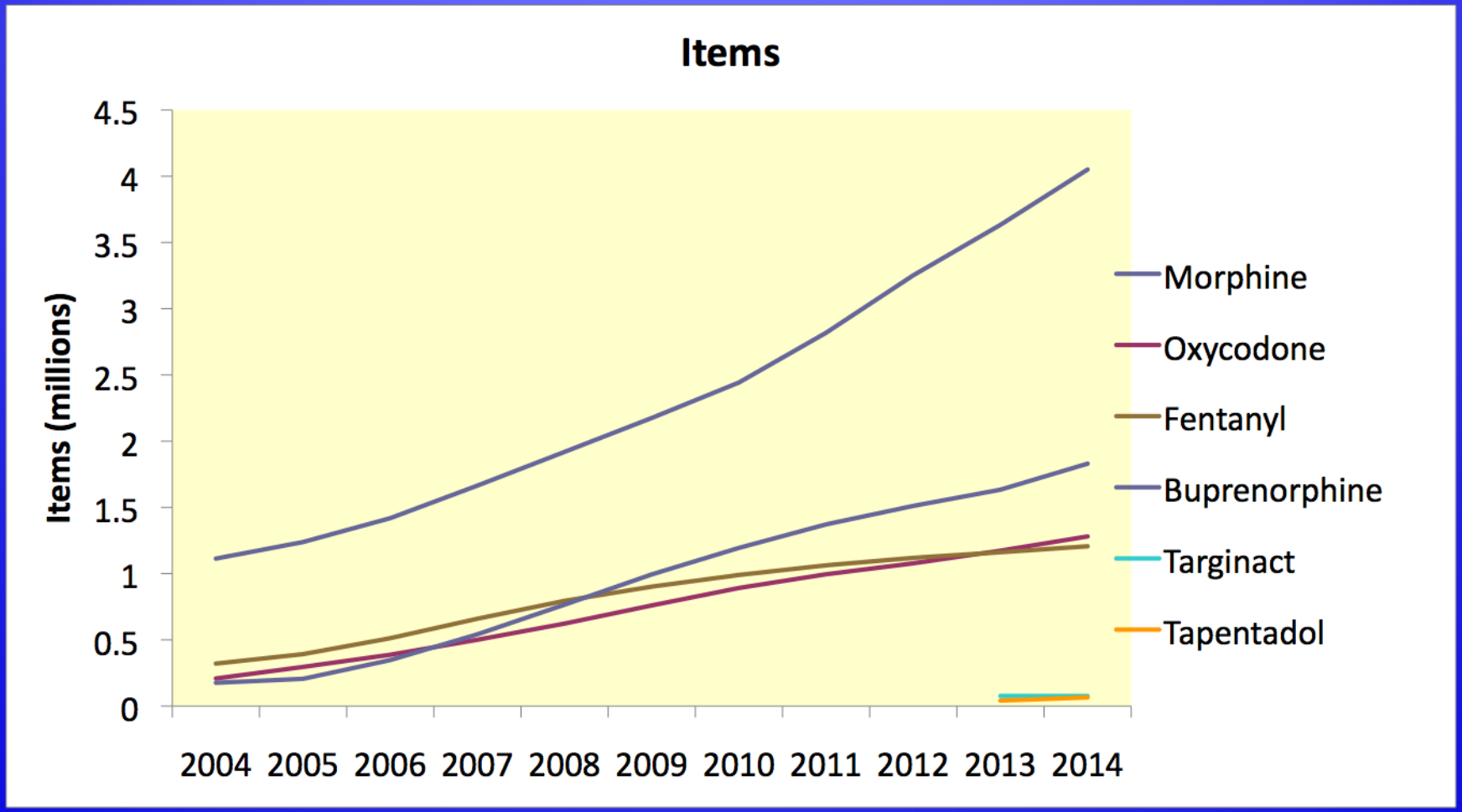
- Pain only reduced in 5-10% patients
- 80% suffer at least one side-effect
- 20% stop taking them
- Cause harm
- They stop people returning to work, higher doses less likely (USA)
- Doses greater than 50 mg/morphine/day in over 60 year olds, doubles the risk of fracture (USA)

Not working – why are we prescribing?

Opioid Trends in UK

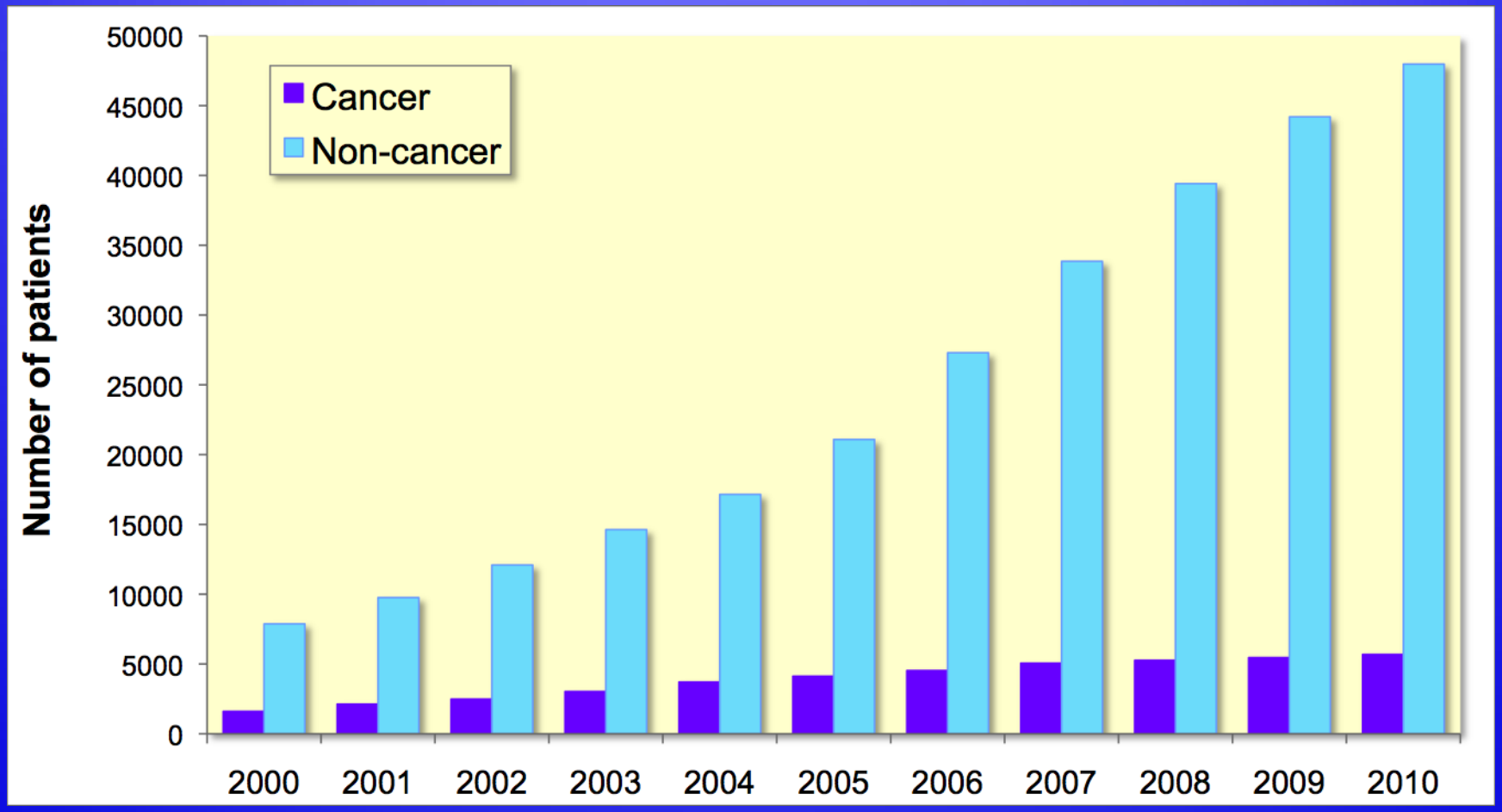
- Increase in prescriptions in UK until 2016
- Costs primary care £300 million
- Significant risk of harm

Opioid Prescribing



Health and Social Care Information Centre. Prescription Cost Analysis

Number of patients prescribed opioids



Zin C et al. Eur J Pain 2014.

Opioids for chronic pain

Published Sept 2019

- 5.6 million taking opioids
  - Excluding cancer
- 13% adult population
- 540,000 taking for 3 years
- Deprivation

What are the costs?

Cost

Butrans 5mcg £17.60/month
Fentanyl 12mcg £25/month
Oxycodone (MR)
    5mg - £25.04 for 56 tabs
Tapentadol (MR)
    100 mg - £50 for 56
    200 mg - £100 for 56
Morphine (MR)
    10 mg - £3.29 for 60

Costs

- Falls
- Unplanned admissions
- Managing side-effects
- Delayed discharge
- Impairment of function:
  - Physical
  - Psychological
  - Social

What are the harms?

Side-effects of opioids

- Respiratory depression
- Feeling sleepy
- Nausea and vomiting
- Pruritus (itching)
- Hallucinations
- Nightmares
- Cough suppression
- Hypotension
- Urine retention
- Constipation
- Biliary spasm
- Double vision

Long-term side effects

- Impairment cognitive function
  - Memory & concentration
- Sweating
- Dry Mouth
- Falls
- Opioid induced bowel disorder
- Suppression of immune system
- Opioid induced hyperalgesia

Long-term side effects

- Suppression hypothalamic-pituitary axis
  - Hypogonadism,
  - Low oestrogen and testosterone levels
  - Suppression adrenal glands
  - Low muscle mass
  - Low bone mass
  - Fatigue
  - Depression
  - Weight gain

Patients taking long-term opioids

Monitoring – every 6 months

- Fasting blood cortisol, DHEA, ACTH, GH
- Oestrogen or testosterone levels
- Bone density in at risk groups

Seyfried & Hester, 2012

Opioids Aware

1. Opioids are very good analgesics for acute pain and for pain at the end of life but there is little evidence that they are helpful for long term pain.

2. A small proportion of people may obtain good pain relief with opioids in the long-term if the dose can be kept low and especially if their use is intermittent (however it is difficult to identify these people at the point of opioid initiation).

3. The risk of harm increases substantially at doses above an oral morphine equivalent of 120mg/day, but there is no increased benefit.

4. If a patient is using opioids but is still in pain, the opioids are not effective and should be discontinued, even if no other treatment is available.

5. Chronic pain is very complex and if patients have refractory and disabling symptoms, particularly if they are on high opioid doses, a very detailed assessment of the many emotional influences on their pain experience is essential.

Specific problems in the elderly population

Elderly population

- Drug metabolism less efficient
- Renal function declined by 50% age 75
  - Reduced rate of elimination of drugs
  - Creatinine normal, reduced muscle mass
- Body composition changes
  - Fat ↑, distribution differs
- Potential for drug interactions increased

Elderly population

- Increase risk of side-effects
- Increased sensitivity to drugs
- Multiple comorbidities
- Oral / Topical administration
- Only change one drug at a time
- Combination therapy

Opioid use in the elderly

- Caution!
- Don’t try first line
- Avoid in patients with:
  - Drug dependence (alcohol), psychiatric illness
- Smallest dose for the shortest time
- Intermittent
- If not effective – taper and discontinue!

Opioid trial

- No longer than 6 weeks

- Set three specific agreed goals
  - Reduction in pain (50 to 70%)
  - Improved sleep (BPI)
  - Functional goal

- Keep a diary – pain, sleep, activity, dose
- Frequent review
- Patient information

Which opioid?

- Buprenorphine
  - Most studied in elderly
  - Excreted in the bile
  - Greater potential of constipation
  - Less costly than fentanyl/tramadol
  - Potential to give small doses of opioid
    - 5mcg patch = 10mg oral morphine per 24 hours

Which opioid?

- Fentanyl – extremely potent
  - 12mcg patch = 30-45mg oral morphine
  - Metabolised by liver
- Oxycodone
  - 5mg = 10mg oral morphine
  - Able to give smaller doses of elixir
  - Few metabolites, renal excretion
- Morphine – best avoided

Summary

Chronic pain – "Opioids are neither effective nor safe enough to warrant their widespread use. We should begin to think of opioid treatment for chronic pain as the exception rather than the rule.

Jane Ballantyne, 2017