



A World Top 200 university, Times Higher Education 2018

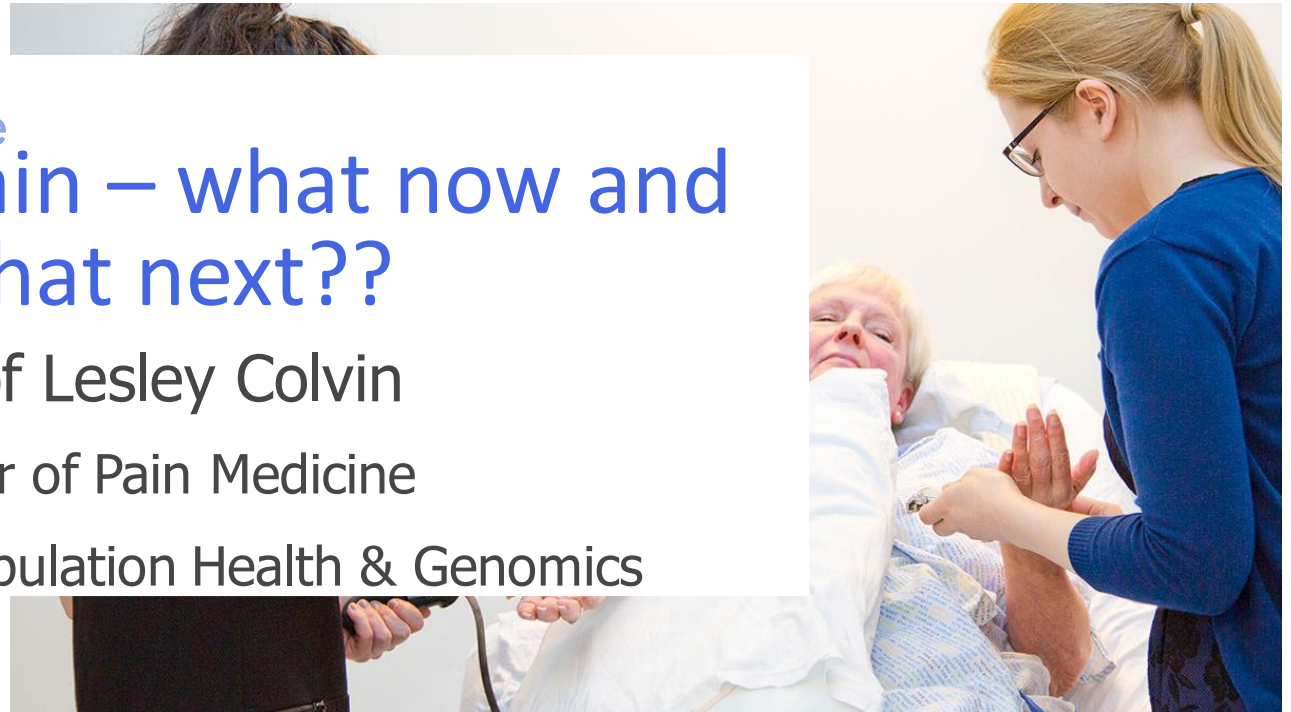
School of Medicine  
University of Dundee

# Treating pain – what now and what next??

Prof Lesley Colvin

Chair of Pain Medicine

Division of Population Health & Genomics



# Declaration of interests



- Editor, British Journal of Anaesthesia



- Chair of Scottish Pain Research Community (SPaRC)/  
NRS Pain Network



- Member of SIGN Council



- Member of National Advisory Committee for  
Chronic Pain





“Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” (IASP, 1986)



Acute ↔ Chronic

“Physiological” ↔ “pathological”

Chronic (>3 months):

~18% of Scottish population

# Is chronic pain a problem?



## Top causes of disability (global)

Leading causes 2016

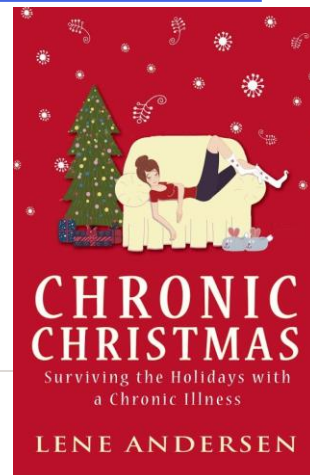
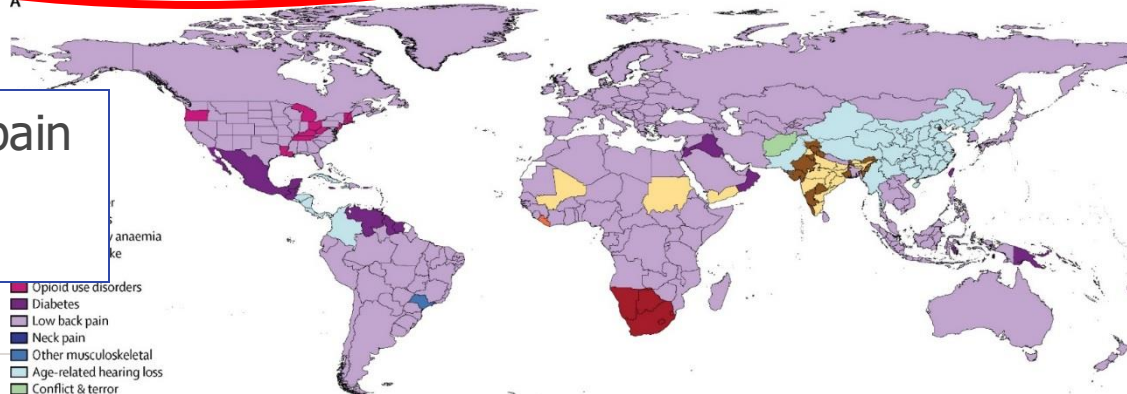
Mean % change in number of YLDs (2006-16)  
 Mean % change in all-age YLD rate (2006-16)  
 Mean % change in age-standardised YLD rate (2006-16)

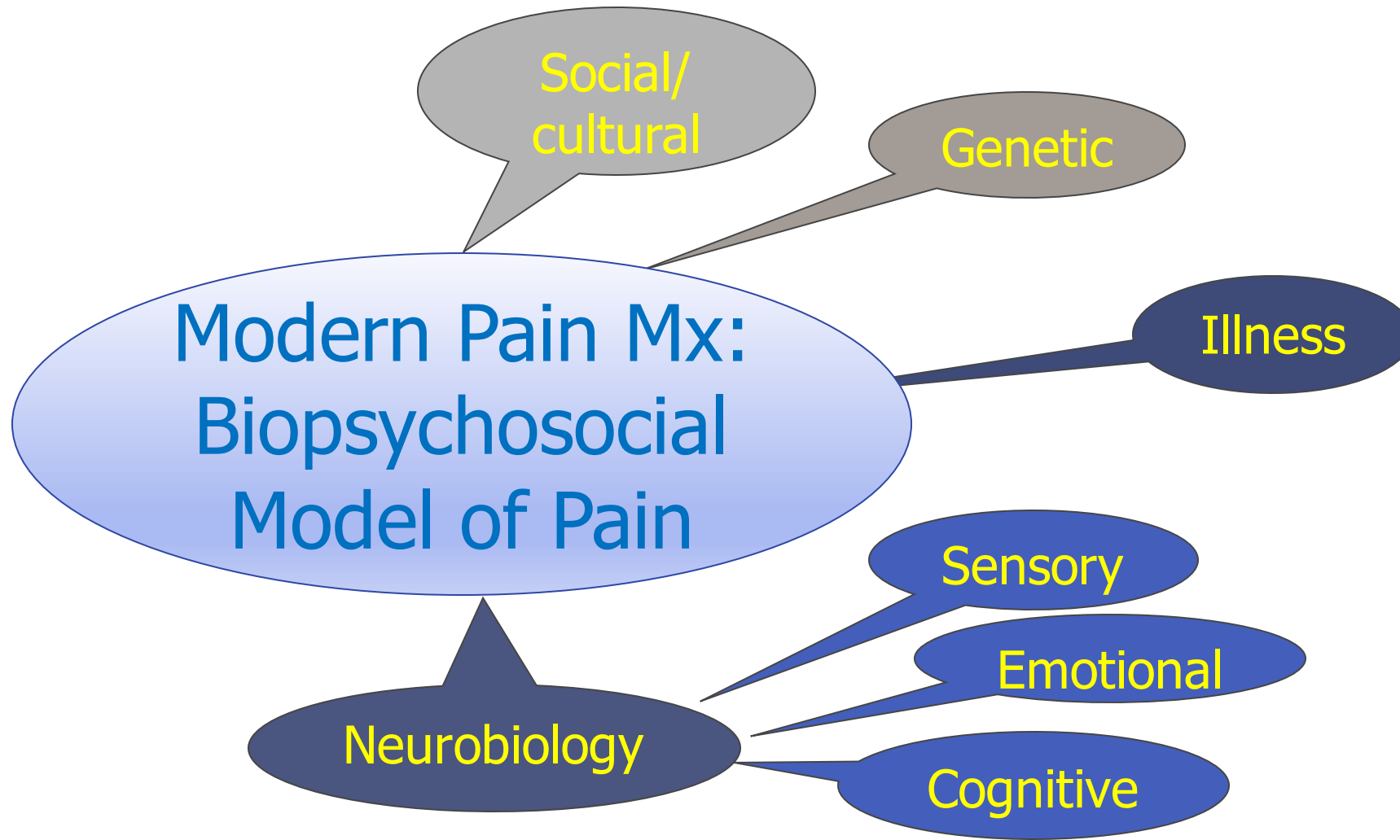
Rank	Leading cause	Mean % change in number of YLDs (2006-16)	Mean % change in all-age YLD rate (2006-16)	Mean % change in age-standardised YLD rate (2006-16)
1	Low back pain	18.0	5.0	-2.0
2	Migraine	14.3	1.6	0.1
3	Age-related hearing loss	22.3	8.8	-1.7
4	Iron-deficiency anaemia	7.5	-4.4	-1.8
5	Major depression	11.2	-1.1	-4.9
6	Neck pain	21.9	8.4	0.1
7	Other musculoskeletal disorders	14.4	1.7	-3.5

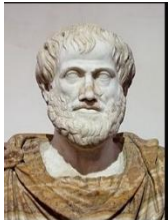
## UK prevalence

- 35 to 51% Pain more than 3 months
- 10 to 14% Moderate to severely disabling
- F > M, increasing age
- ~ 28 million adults affected

<http://dx.doi.org/10.1136/bmjopen-2015-010364>







The aim of the wise is not to secure pleasure, but to avoid pain.  
(Aristotle)



Healthcare Improvement Scotland | SIGN

**Clinical Challenges**

**Pain assessment**

**Long term opioid use**

**Neuropathic pain**

SIGN 136 • Management of chronic pain

A national clinical guideline

First published December 2013  
Revised edition published August 2019

Evidence

**Pain assessment**

**Clinical Challenges**

**Long term opioid use**

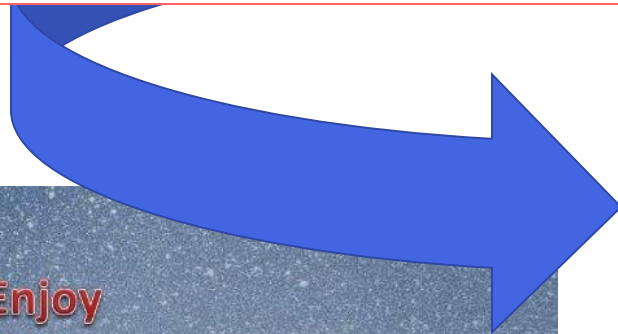
**Neuropathic pain**



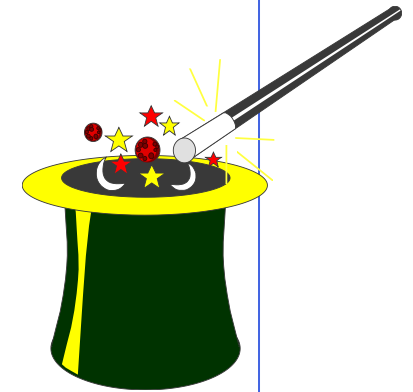
# Pain Management



Starts with  
comprehensive  
assessment



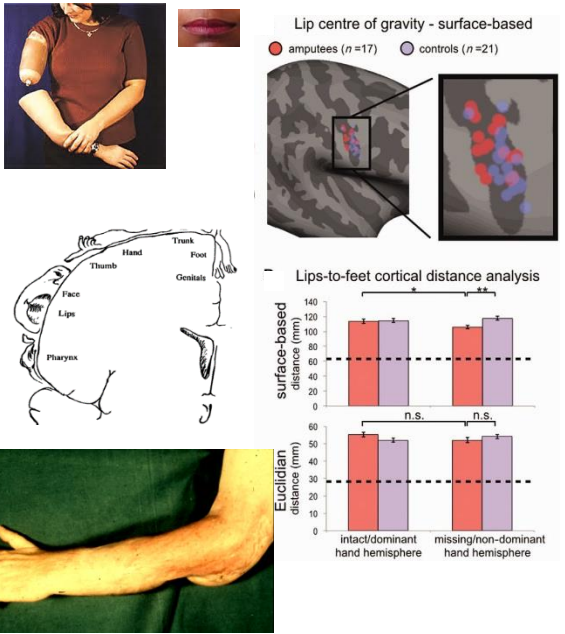
- Psychological
- Physical
- Pharmacological
- Stimulation therapies
  - TENS
  - Acupuncture
- Injection / ablation



Tips to Enjoy  
Christmas  
in spite of  
Chronic Pain  
and Illness



# Assessment



## Detailed phenotyping

- Link signs and symptoms with mechanisms
- QST, PROMs, neuroimaging, genetic

## Individualize treatment

## Understand risk





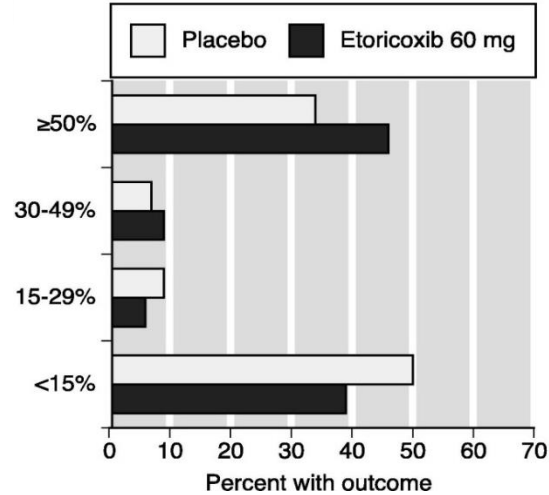
# Neuropathic pain



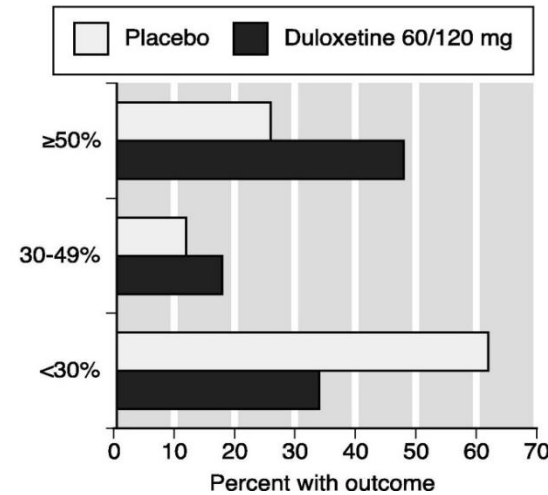
- ❖ Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system: IASP, 2008
- ❖ Affects ~7-10% of the population
- ❖ Number of causes
  - **Chemotherapy (CIPN)**
  - Surgery/ trauma
  - Infection (eg after shingles)
  - Diabetes
- ❖ Limited treatment options
- ❖ Miserable



# Variation in treatment response



Low back pain



Diabetic neuropathy

- Limits of the evidence: case definition, trial design and analysis ([www.immpact.org](http://www.immpact.org))
- Individual variation – most patients will respond to something, but there is nothing that everyone will respond to

# Understanding mechanisms to direct treatment



PAIN® 155 (2014) 2263–2273

PAIN®

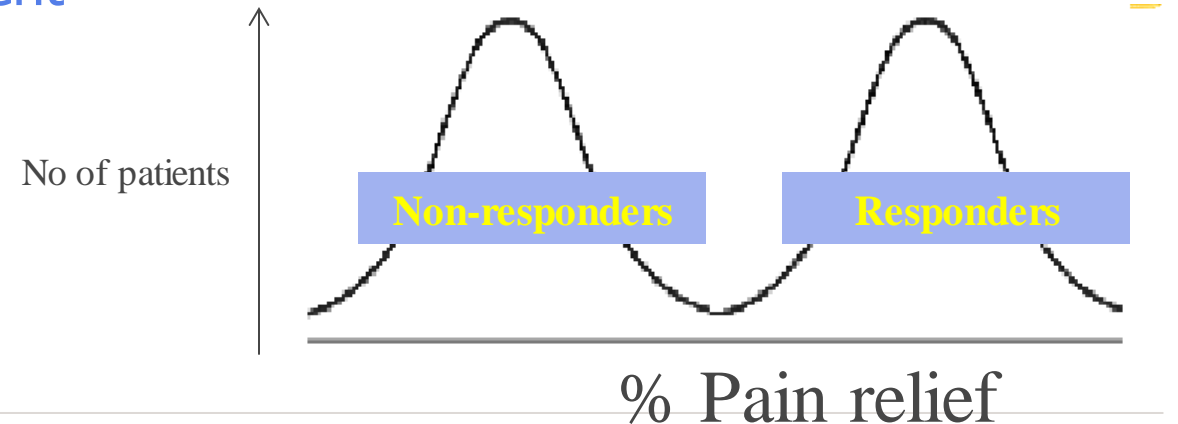
www.elsevier.com/locate/pain

The effect of oxcarbazepine in peripheral neuropathic pain depends on pain phenotype: A randomised, double-blind, placebo-controlled phenotype-stratified study

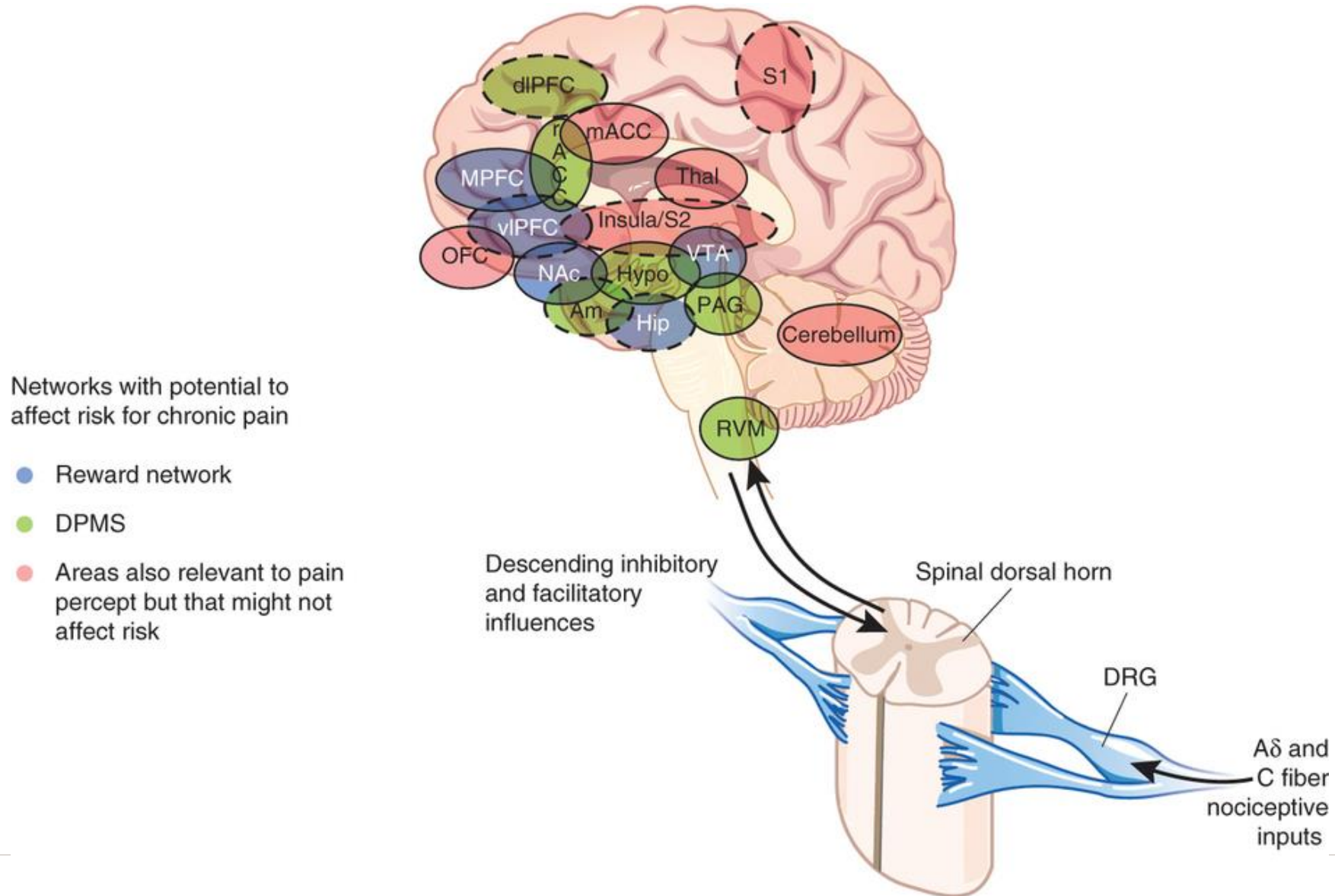


Dyveke T. Demant<sup>a</sup>, Karen Lund<sup>b</sup>, Jan Vollert<sup>c</sup>, Christoph Maier<sup>c</sup>, Märtha Segerdahl<sup>d,e</sup>, Nanna B. Finnerup<sup>b</sup>, Troels S. Jensen<sup>b</sup>, Søren H. Sindrup<sup>a,\*</sup>

- ❑ Hypothesis: Na<sup>+</sup> channel blockers should work where irritable nociceptors predominate
- ❑ Precise sensory profiling to stratify treatment
- ❑ NNT overall: 6.9
  - ❑ Irritable nociceptor group: 3.9
  - ❑ Non-irritable group: 13



# Pain vulnerability - endogenous systems





## Modifiable risk factors

- Choice of chemotherapy (type & dose)
- Obesity
- Smoking
- Alcohol
- Opioid use
- Beta-blockers

## Potentially modifiable

- Neurobiology
  - Peripheral
  - Central (eg placebo)
- Comorbid disease
  - Diabetes
  - Renal impairment

## Identifiable, not easily modifiable

- Genetic (*ARHGEF10* rs9657362; *CYP2C8* rs11572080/rs10509681; *FGD4* rs10771973)
- Age

CIPN

# Pre-existing vulnerability to CIPN



## *Central mechanisms:*

- Structural and functional differences demonstrated for subacute CIPN
- Functional differences for chronic CIPN (9 months)
- Preliminary data shows that there are pre-existing supraspinal differences

## *Peripheral mechanisms:*

- Intraepidermal nerve fibre density
- Understanding vulnerability:
  - allows informed choice about chemotherapy
  - modification of chemotherapy used (dose/ type)
  - Move towards individualised Rx





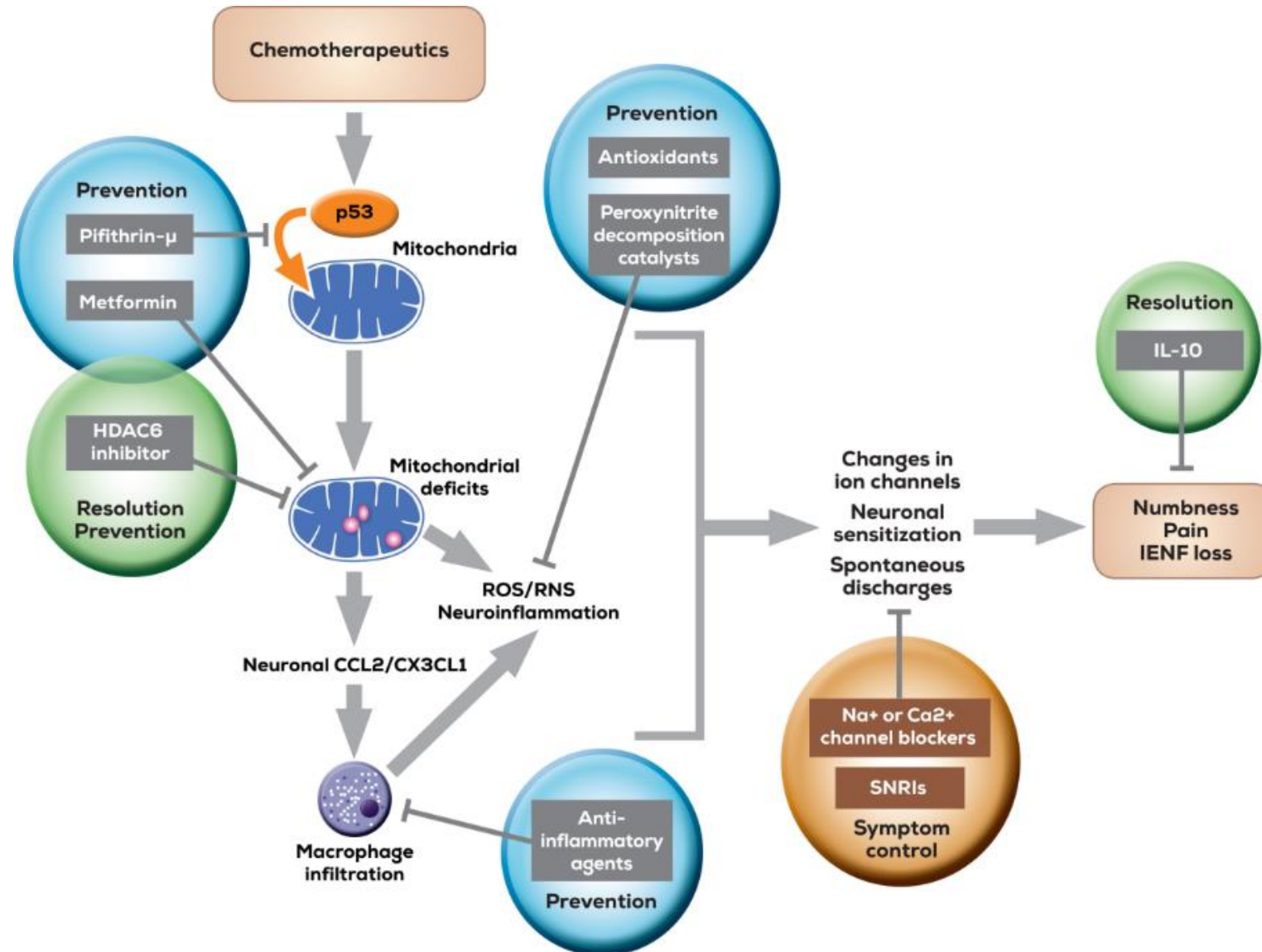
# CIPN Treatment (ASCO Guidelines)

Duloxetine: moderate evidence for CIPN

Evidence mainly extrapolated from other NeuP syndromes:

- Tricyclic antidepressants
- Gabapentin: 1 –ve RCT in CIPN, but established efficacy in other neuropathic pain
- A topical gel treatment containing baclofen (10 mg), amitriptyline HCL (40 mg), and ketamine (20 mg), 1 single +ve trial

# CIPN mechanisms and sites for intervention



From: Beyond symptomatic relief for chemotherapy-induced peripheral neuropathy: Targeting the source, Ma et al

Cancer, Volume: 124, Issue: 11, Pages: 2289-2298, First published: 20 February 2018, DOI: (10.1002/cncr.31248)

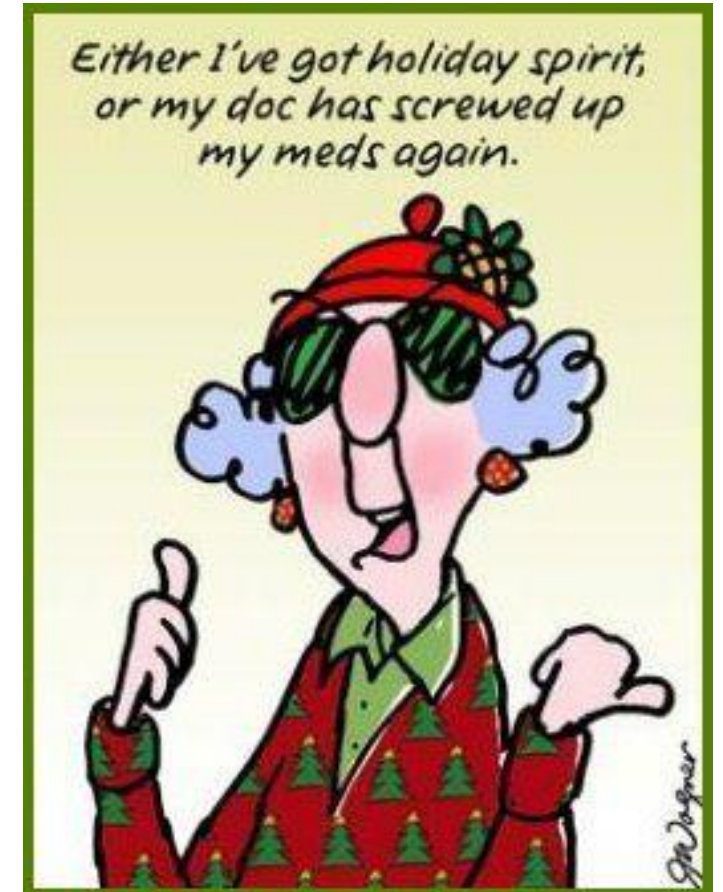




Clinical challenges



Opioid Use





# Medication: Opioids (e.g.morphine)



Acute Pain

Work well  
Long term  
problems?

Cancer pain

Usually  
work well

Chronic pain

Should  
opioids be  
used at all???



# So...opioids for chronic pain? The balance of evidence:



JAMA | Original Investigation

Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain  
The SPACE Randomized Clinical Trial

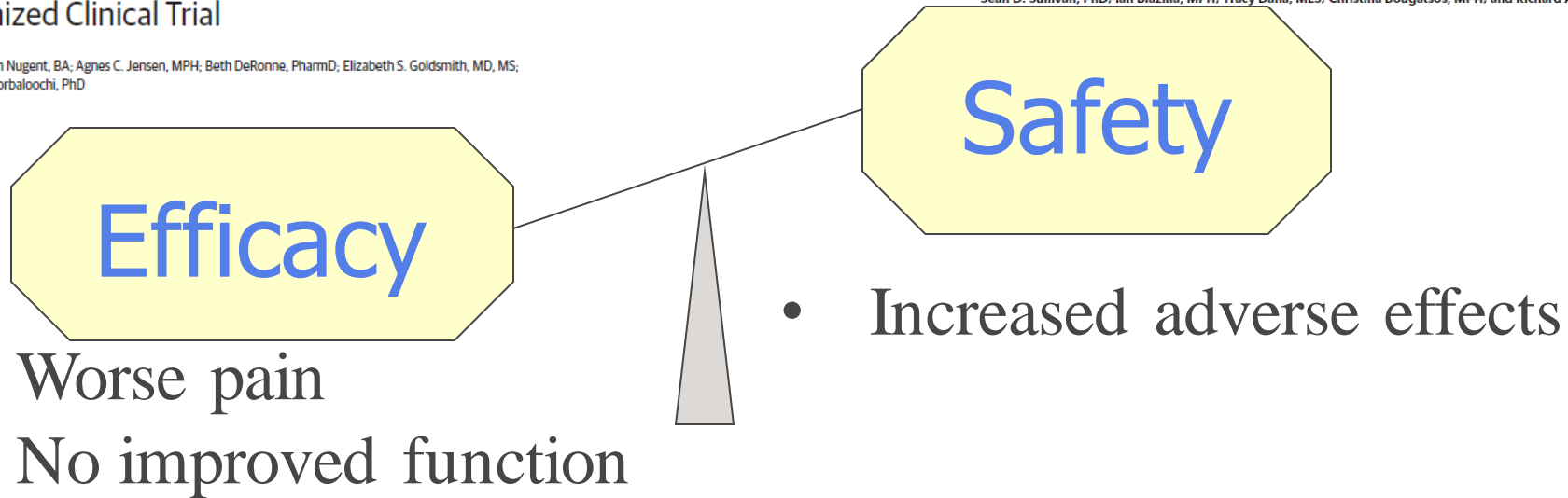
Erin E. Krebs, MD, MPH; Amy Gravely, MA; Sean Nugent, BA; Agnes C. Jensen, MPH; Beth DeRonne, PharmD; Elizabeth S. Goldsmith, MD, MS; Kurt Kroenke, MD; Matthew J. Bair; Siamak Noorbaloochi, PhD

Annals of Internal Medicine

REVIEW

The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop

Roger Chou, MD; Judith A. Turner, PhD; Emily B. Devine, PharmD, PhD, MBA; Ryan N. Hansen, PharmD, PhD; Sean D. Sullivan, PhD; Ian Blazina, MPH; Tracy Dana, MLS; Christina Bougatsos, MPH; and Richard A. Deyo, MD, MPH



- IASP: “There may be a **role for medium-term, low-dose opioid therapy** in **carefully selected patients** with chronic pain who can be managed in a **monitored setting**. However, with continuous longer-term use, tolerance, dependence, and other neuroadaptations compromise both efficacy and safety.” <https://www.iasp-pain.org/Advocacy/Content.aspx?ItemNumber=7194>
- Update of SIGN 136 [www.sign.ac.uk](http://www.sign.ac.uk)



# Do opioids make pain worse?



Opioid induced hyperalgesia (OIH)

Opioid withdrawal

Tolerance

[Neuropathic pain]

**Pain**

**Stop  
opioids**





# The Opioid Epidemic in the U.S.

USA:  
**5%** of the world's population;  
**80%** of the world's opioid  
use



In 2015...



12.5 million

People misused prescription opioids<sup>1</sup>

## Opioid crisis continues

The Surgeon General has issued a national advisory urging more Americans to carry naloxone, the life-saving opioid overdose antidote.

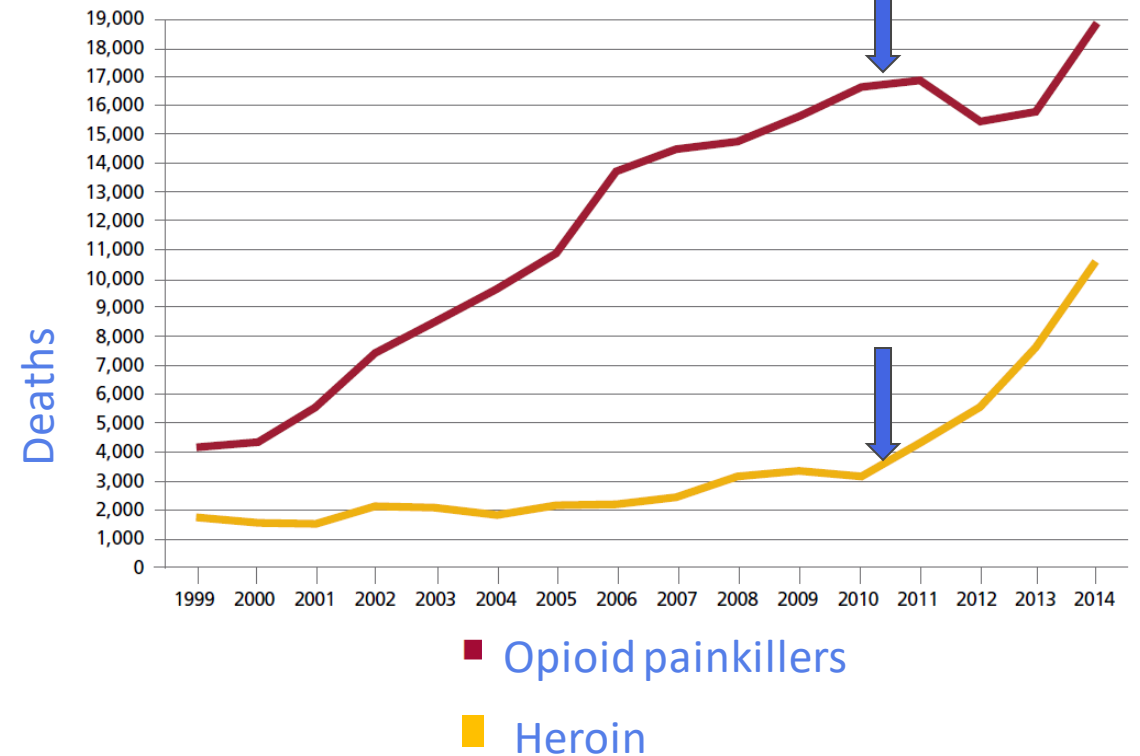


**115** Americans die every day  
from opioid overdoses

...1 death every 12 minutes

1997 – 2007:  
*402% increase* in therapeutic use  
of opioids among Americans

## U.S. Deaths from Opioids & Heroin: 1999-2014



- 3.7 million opioid prescriptions: 2003
- Increase to 5.9M opioid prescriptions in 2012
- Strong opioids: 470K to >1 million
- **18% of the Scottish population had opioid script in 2012**

❖ Deprivation level

❖ Pain severity

- Severe pain: 47% prescribed an opioid

❖ Co-prescribing with benzodiazepines

- Female; Age 25-40: 40%

ition/scotland/opioid-crisis-fears-as-fifth-of-scots-given-powerful-painkillers-njgwk298

THE TIMES

Read the full article  
Just register a few details [Get access](#)

## Opioid crisis fears as fifth of Scots given powerful painkillers

Marc Horne  
August 30 2018, 12:01am,  
The Times

Celebrity



More than a million Scots were prescribed strong opioid painkillers in one year  
ALAMY

Alarming research revealing that at least one in five Scots has been given opioid drugs has prompted a review of powerful painkillers being handed out.

Torrance et al, BJA June 2011

# Opioid prescribing in Scotland Dec 2015 – June 2019



isdscotland.org/Health-Topics/Prescribing-and-Medicines/Publications/2019-10-15/visualisation.asp

NHS BOARD DATA

HSCP DATA

PRACTICE DATA

Select indicator:

Analgesics (opioid DDDs)

Select time period:

Dec 2015

Jun 2019

Highlight NHS Board:

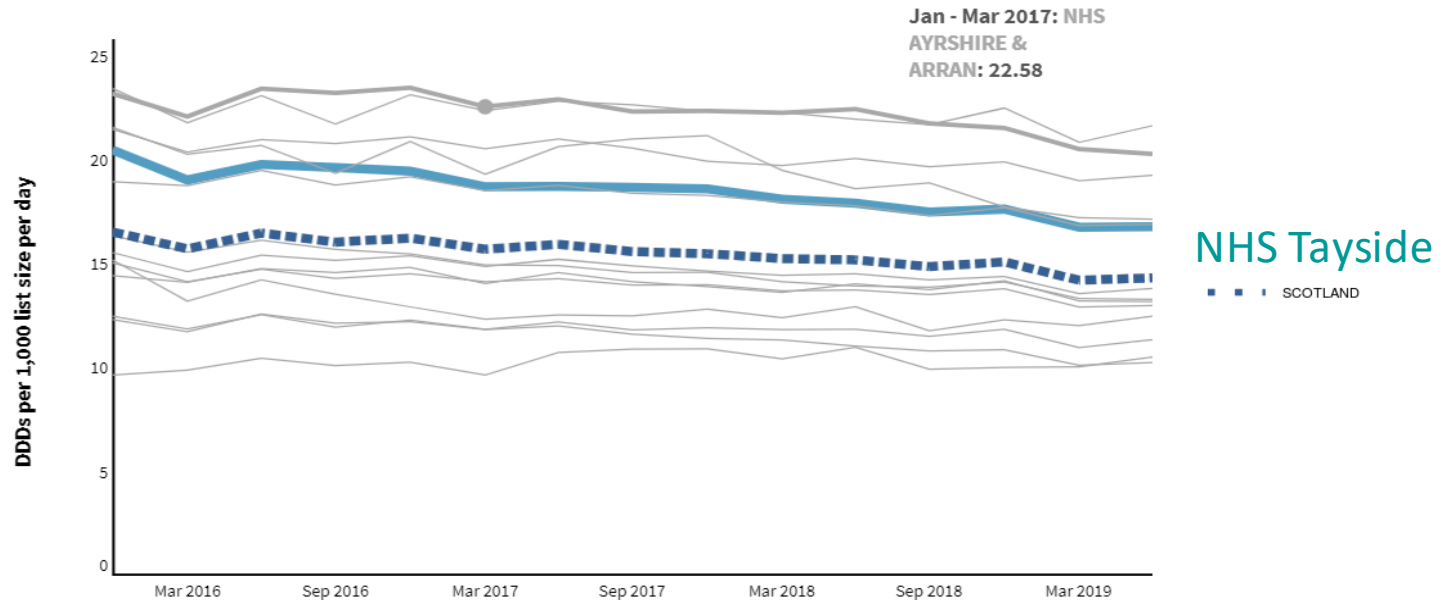
NHS TAYSIDE

Select colour scheme for highlighted NHS Boards:

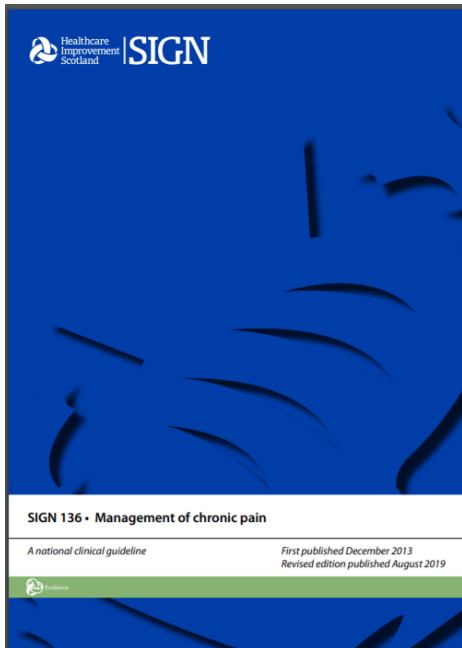
Blues

SHOW INDICATOR DETAIL

Opioid analgesics: strong opioids (including tramadol preparations) DDDs per 1,000 list size per day



DDDs refer to Daily Defined Doses. Find out more information on DDDs in Metadata.



# Updated SIGN 136: Opioids (Aug 2019)



**B** Opioids should be considered for short- to medium-term treatment of carefully selected patients with chronic non-malignant pain, for whom other therapies have been insufficient, and the benefits may outweigh the risks of serious harms such as addiction, overdose and death.

✓ At initiation of treatment, ensure there is agreement between prescriber and patient about expected outcomes (*see Annex 4*). If these are not attained, then there should be a plan agreed in advance to reduce and stop opioids.

✓ All patients on opioids should be assessed early after initiation, with planned reviews thereafter. These should be reviewed annually, at a minimum, but more frequently if required. The aim is to achieve the minimum effective dose and avoid harm. Treatment goals may include improvements in pain relief, function and quality of life. Consideration should be given to a gradual early reduction to the lowest effective dose or complete cessation.

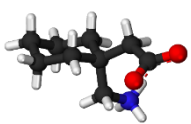
**B** Currently available screening tools should not be relied upon to obtain an accurate prediction of patients at risk of developing problem opioid use, but may have some utility as part of careful assessment either before or during treatment.

**C** Signs of abuse, addiction and/or other harms should be sought at reassessment of patients using strong opioids.

**D** All patients receiving opioid doses of  $>50$  mg/day morphine equivalent should be reviewed regularly (at least annually) to detect emerging harms and consider ongoing effectiveness. Pain specialist advice or review should be sought at doses  $>90$  mg/day morphine equivalent.





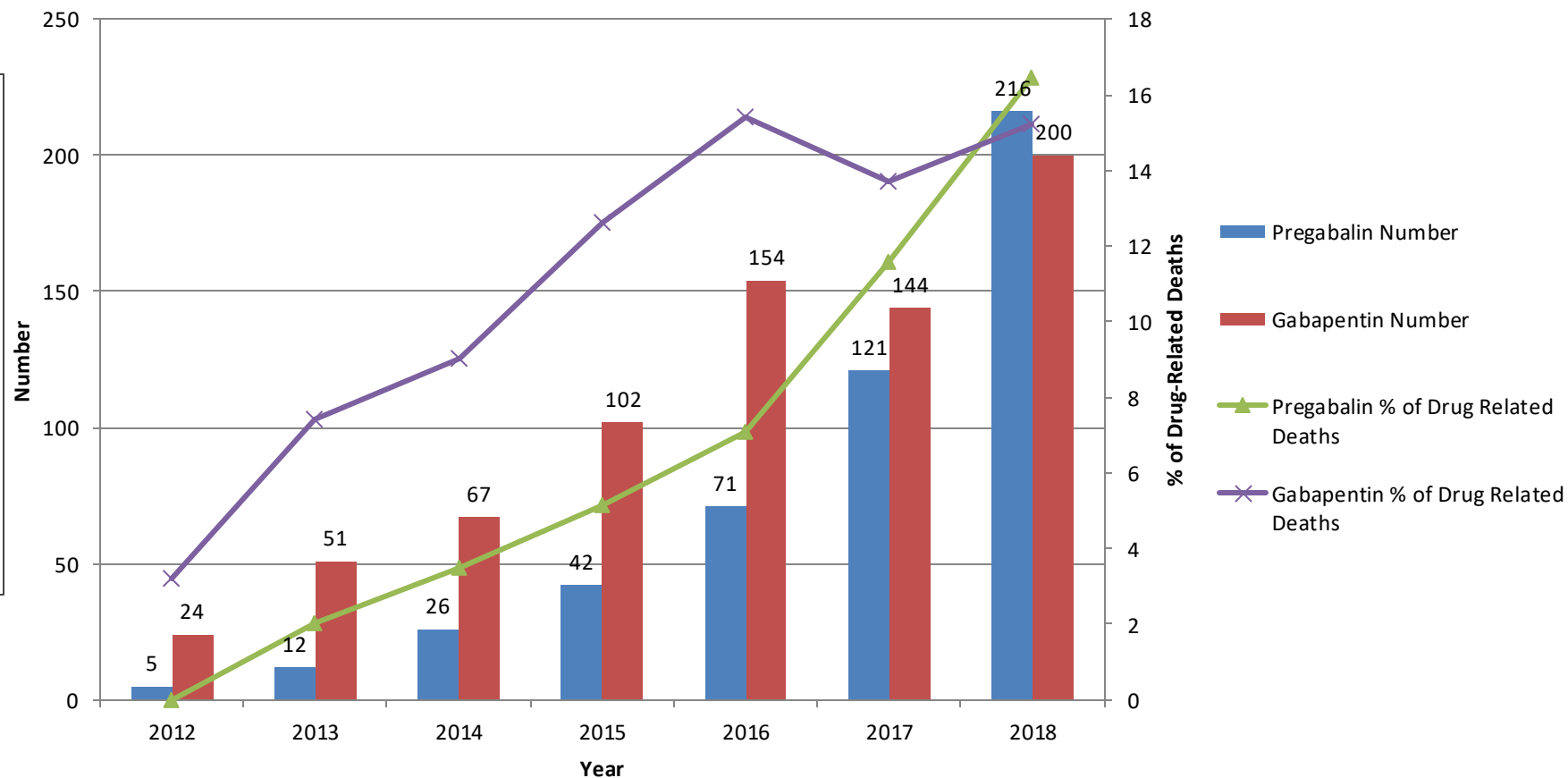
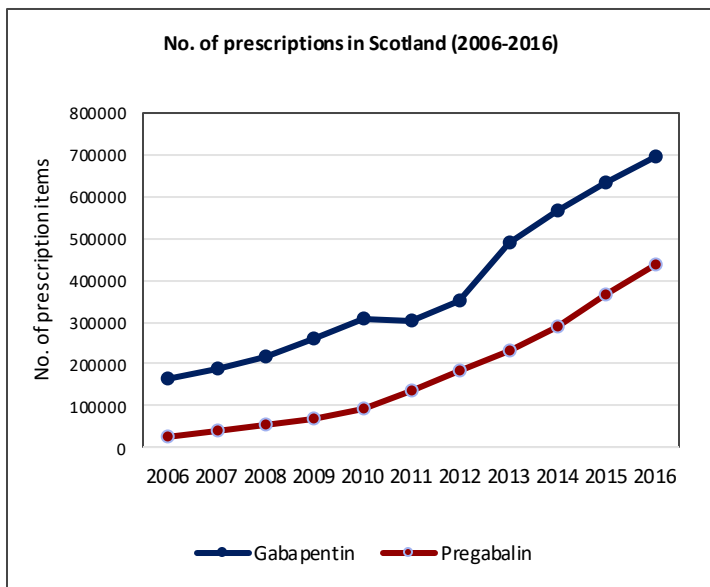


# It's not just opioids...



## Gabapentinoid prescribing

## Gabapentinoid drug deaths





# Pain management

➤ Medication



➤ **Non-drug approaches**

- **Physical activity – good evidence**
- **Psychological techniques**



## Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews (Review)

Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH

Geneen LJ, Moore RA, Clarke C, Martin D, Colvin LA, Smith BH.

Physical activity and exercise for chronic pain in adults: an overview of Cochrane Reviews.

*Cochrane Database of Systematic Reviews* 2017, Issue 1. Art. No.: CD011279.

DOI: 10.1002/14651858.CD011279.pub2.

[www.cochranelibrary.com](http://www.cochranelibrary.com)



- Exercise – good for chronic pain
- Type/ intensity – not clear
- Assessment – no clear standard

# Where next?



Perth and Kinross Health and Social Care Partnership

Supporting healthy and independent lives

**Give**  
Take Notice **Connect**  
**Be Active**  
**Keep Learning**

**Social Prescribing**

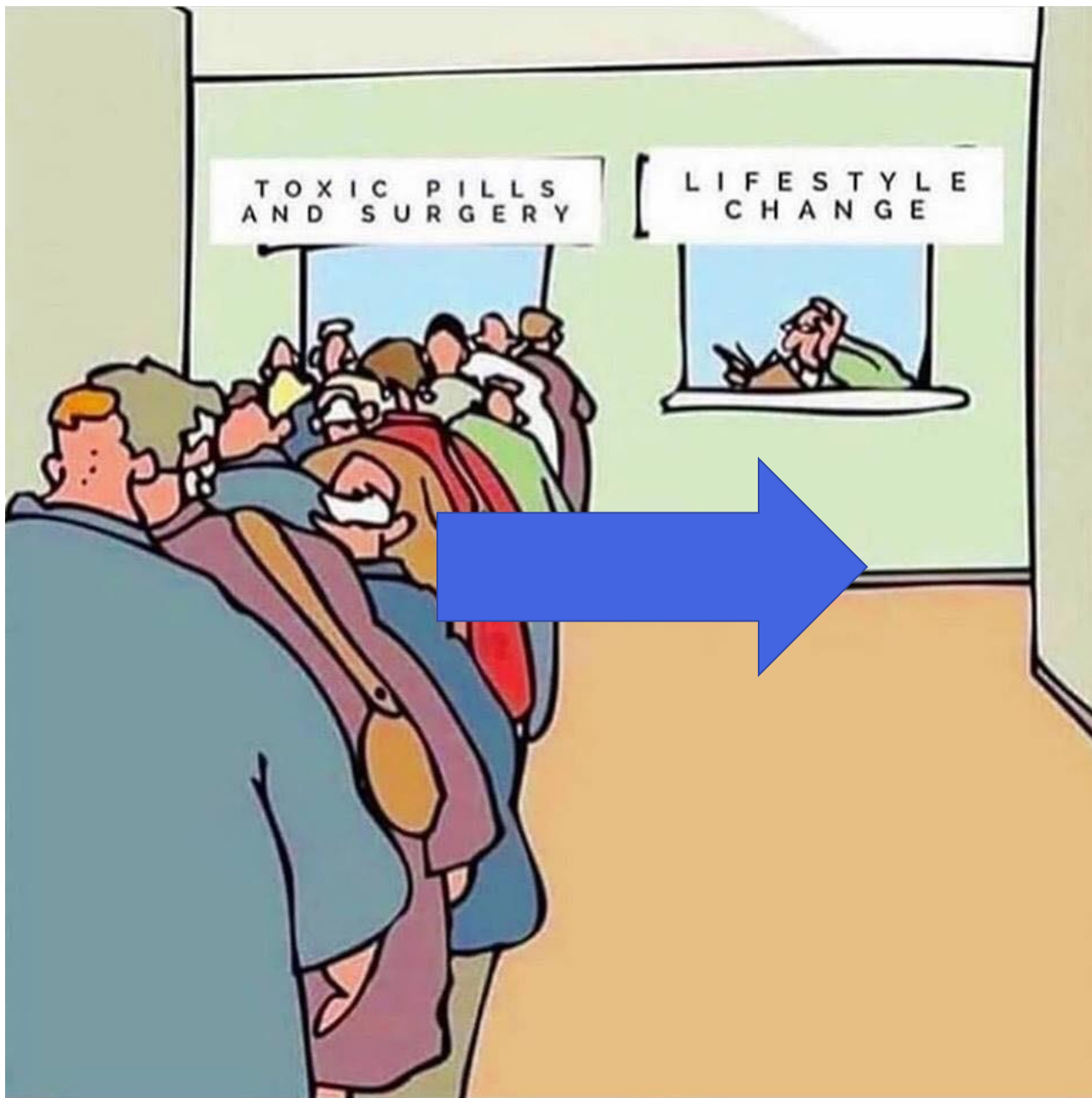
The graphic features a blue header with a group of colorful silhouettes of people. Below this is a green speech bubble containing the text 'Give Take Notice Connect Be Active Keep Learning'. The central part of the graphic shows a collection of colorful hands of various colors (green, yellow, pink, blue, orange, red, purple) raised in the air. At the bottom, a blue banner contains the text 'Social Prescribing'.



Dundee  
Green Health  
Partnership



Understanding barriers to increasing physical activity in chronic pain: an exploratory study to develop the SUsustainable Self Effective Exercise Development (SUSSED) intervention



[l.a.colvin@dundee.ac.uk](mailto:l.a.colvin@dundee.ac.uk)



**Clinical practice:  
informed by  
current research**

**NHS**  
SCOTLAND  
NHS RESEARCH SCOTLAND

PAIN

**Pain research:  
relevant to  
clinical challenges**

## Students, clinical colleagues and patients

John Wilson  
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Gillian Currie  
Ada Delaney  
Sabrina Ramnarine  
Magda Laskawska  
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PAIN



