

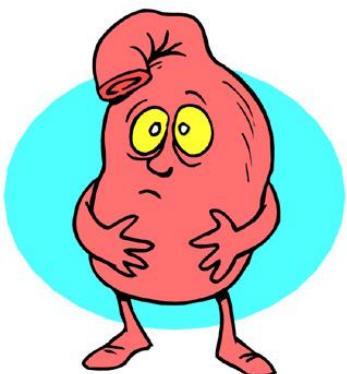


Functional Abdominal Pain - Inpatient management

Dr Peter Paine

Salford Royal Foundation Trust

2016





“I’m afraid that your irritable bowel syndrome has progressed. You now have furious and vindictive bowel syndrome.”

Definitions:

Rome or “real life”?

D1. Diagnostic Criteria^a for Centrally Mediated Abdominal Pain Syndrome^b

Must include all of the following:

- Continuous or nearly continuous abdominal pain
- No or only occasional relationship of pain with physiological events (eg, eating, defecation, or menses)^c
- Pain limits some aspect of daily functioning^d
- The pain is not feigned
- Pain is not explained by another structural or functional gastrointestinal disorder or other medical condition

^aCriteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

^bCAPS is typically associated with psychiatric comorbidity, but there is no specific profile that can be used for diagnosis.

^cSome degree of gastrointestinal dysfunction may be present.

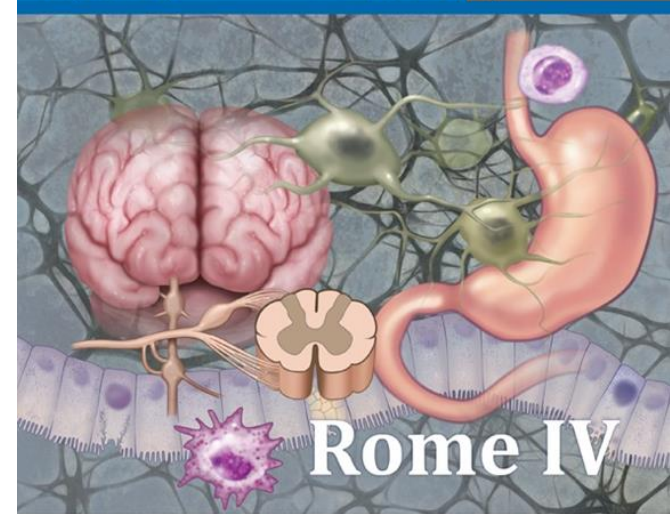
^dDaily function could include impairments in work, intimacy, social/leisure, family life, and caregiving for self or others.

Special Issue

Gastroenterology

www.gastrojournal.org

Volume 150 Number 6 May 2016



Functional Gastrointestinal Disorders:
Disorders of Gut-Brain Interaction



OFFICIAL JOURNAL OF THE ACG



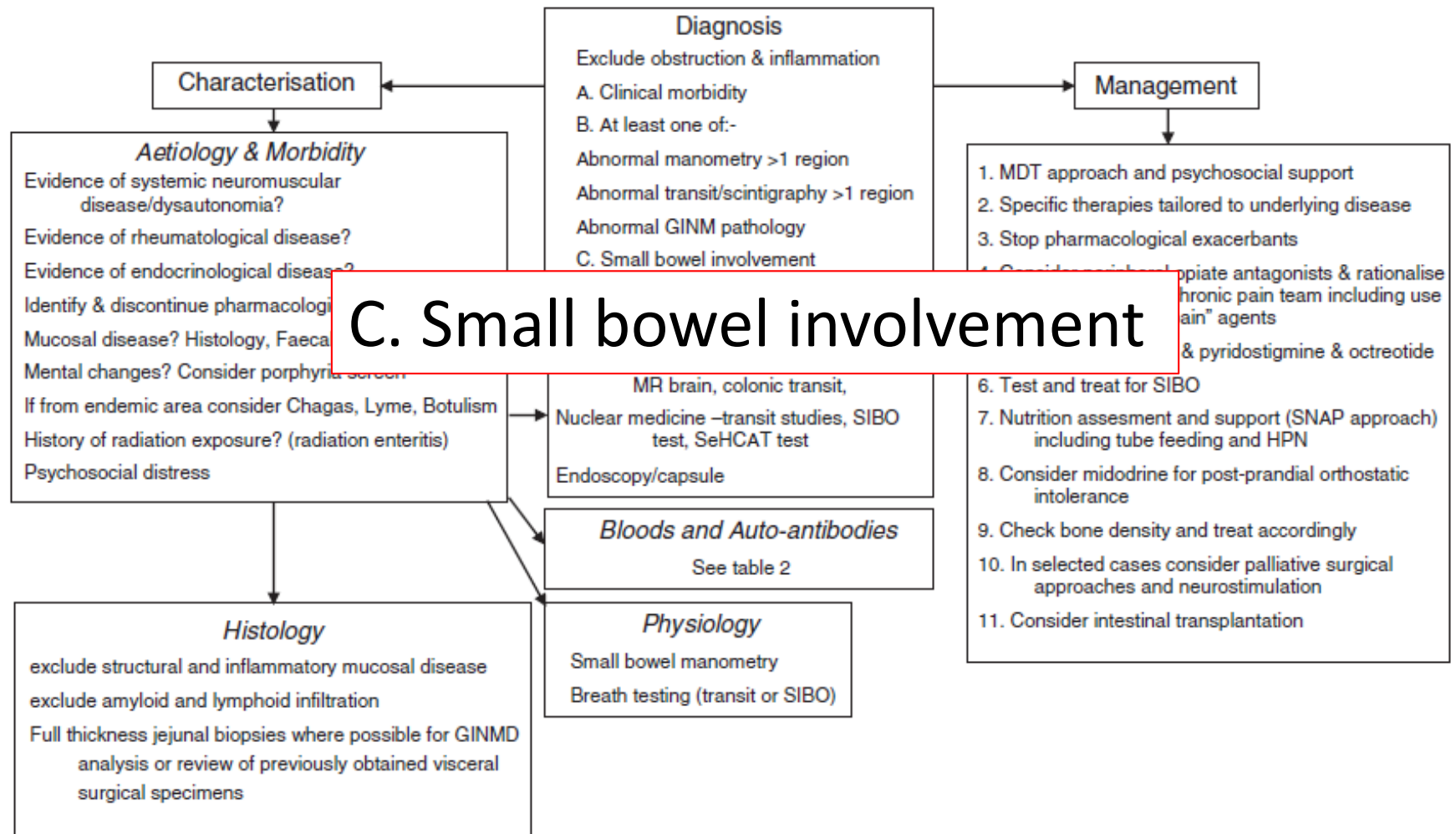
CAPS or “severe IBS” or?

- Overlapping symptoms
 - Bloating
 - Constipation
 - Nutrition (Nausea/vomiting)
 - Dysmotility
- Overlapping nosology
 - Chronic (burnt out?) pancreatitis
 - Previous IBD/surgery/gastroenteritis
 - Overlap with other functional syndromes and psychiatric disorders
 - Confounding pharmacology (NBS)
- Obscure pathophysiology
 - Neuropathic abdominal pain?

Review article: the assessment and management of chronic severe gastrointestinal dysmotility in adults

P. Paine^{*,†}, J. McLaughlin^{*,†} & S. Lal^{*,†,‡}

Aug 2013

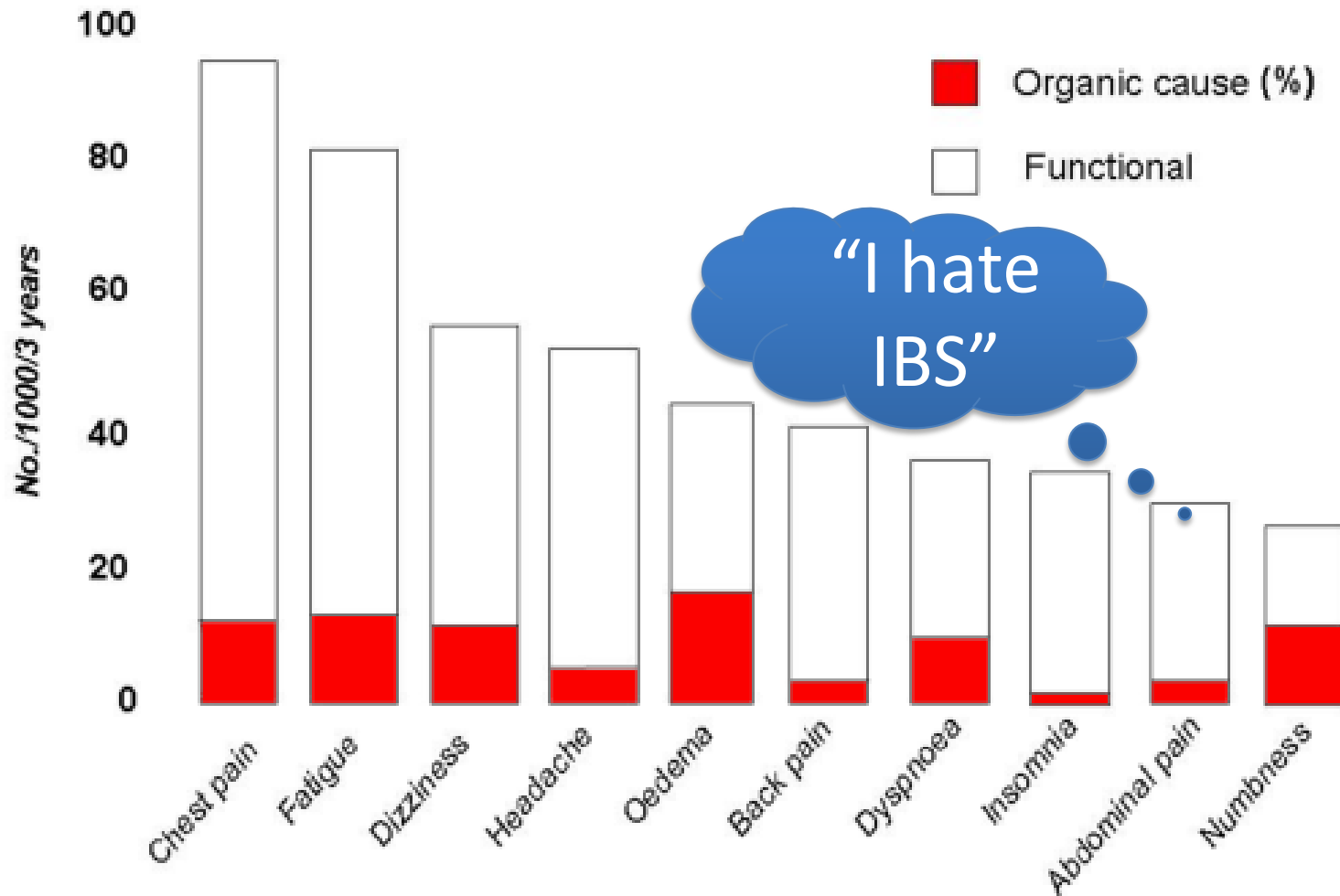


Scylla or Charibdis?



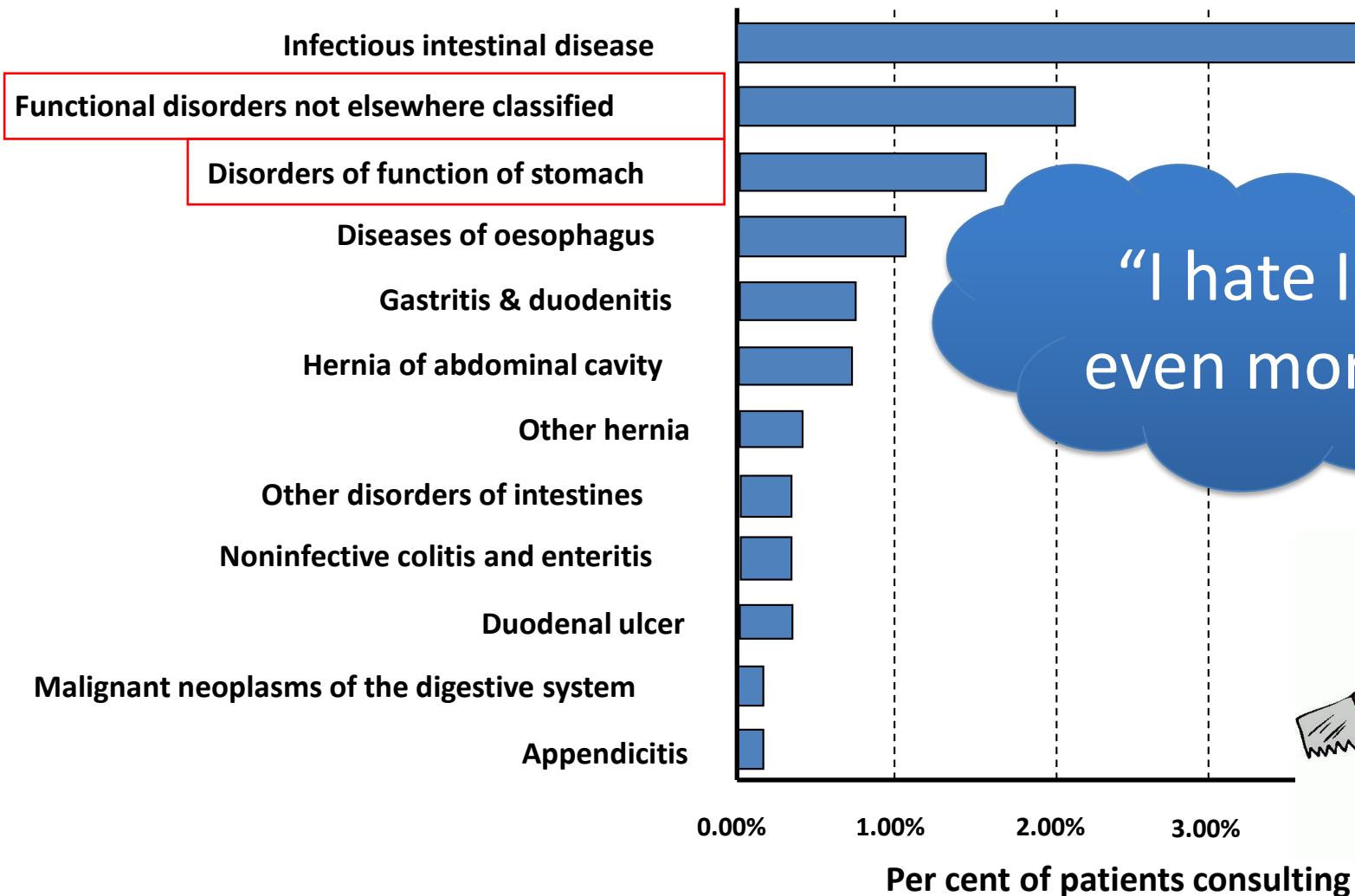
How big is the problem?

3 year incidence and cause of common symptoms in 1000 medical outpatients



Adapted from Kroenke and Mangelsdorff 1989

Gastrointestinal disease (*not liver*)

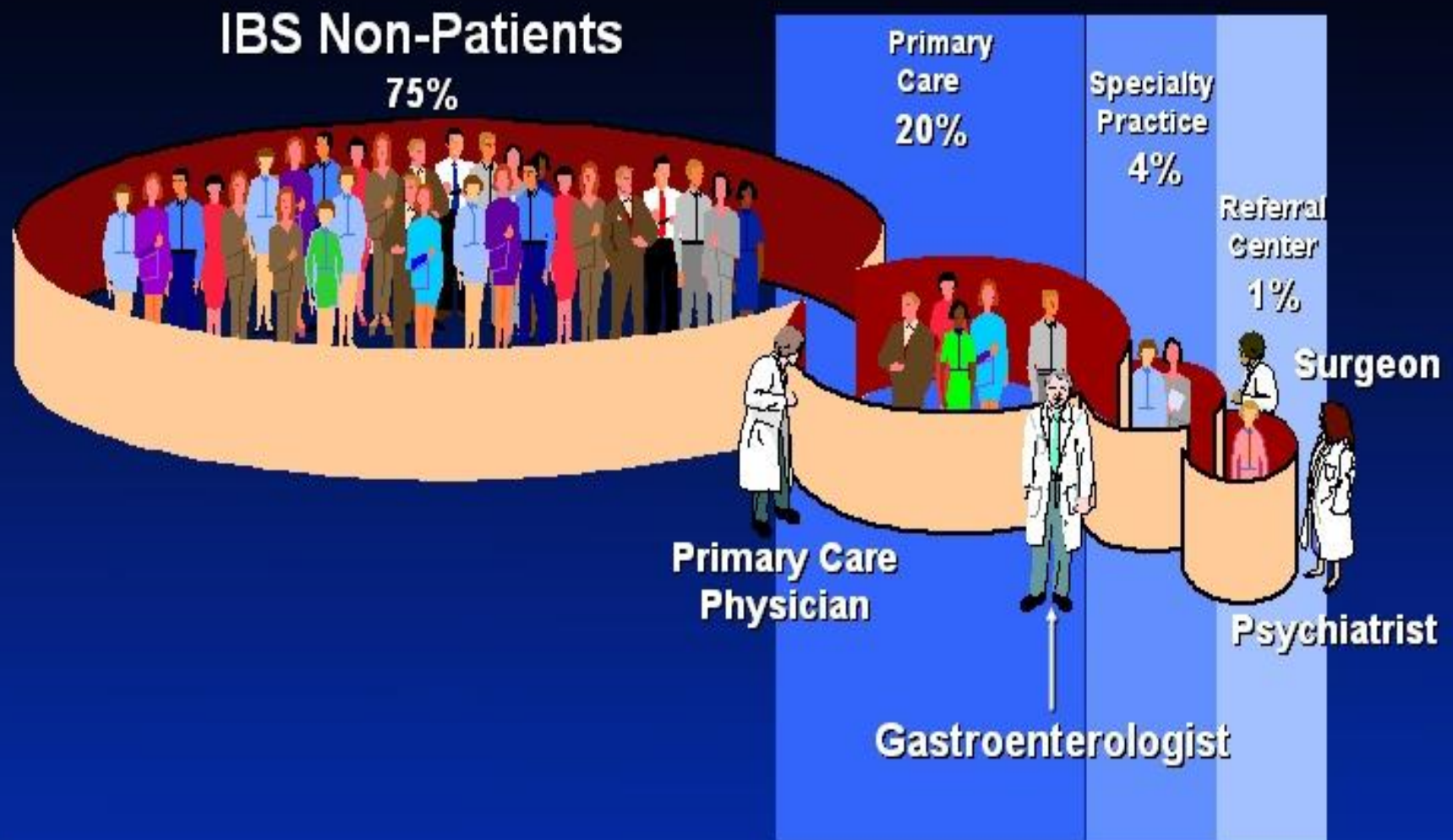


Percentage hospital admissions for major ICD-10 disease groupings in England, 1998/99-2001/2002: based on number of finished consultant episodes (FCEs)

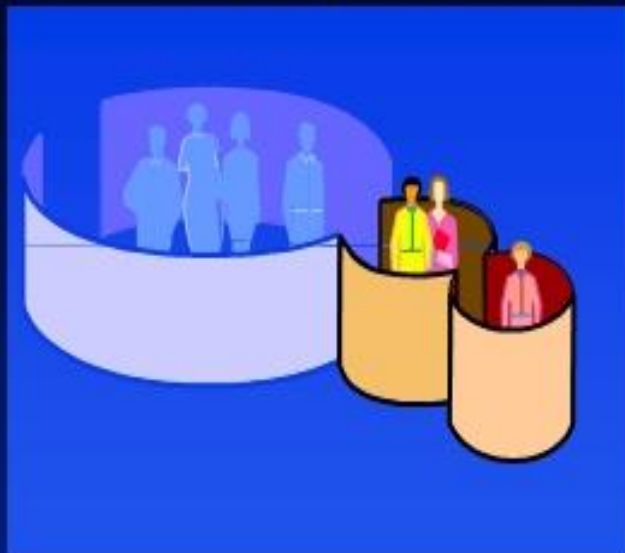
Source: Department of Health, 2004.

Excludes hepatic/pancreaticobiliary

Self Selection Into Clinical Practice



Referral practices



**Up to 60% have
psychologic
disturbances**

- **Depression and anxiety**
- **Somatoform disorders**
- **Personality difficulties**
- **Life stress**
- **Chronic pain behavior**

Common CAPS pitfalls

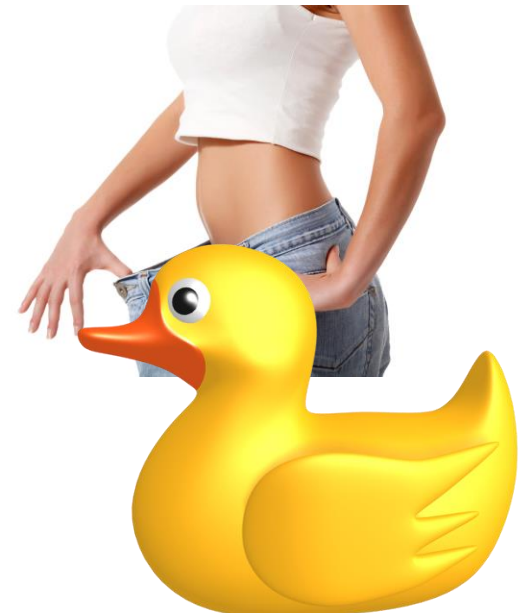
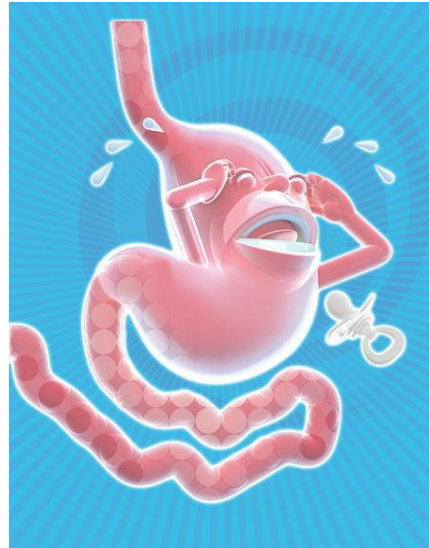
Mixed up with surgeons

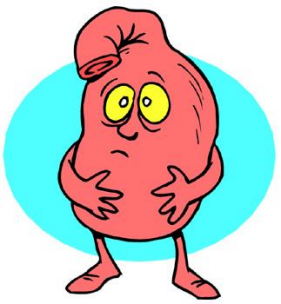
Mixed up with opiates

Malnutrition (disordered eating)

Psychological distress – maladaptive coping/beliefs

Symptom severity

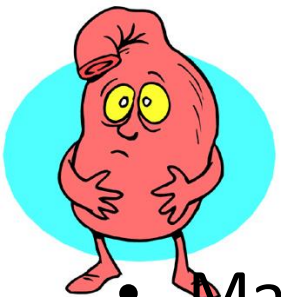




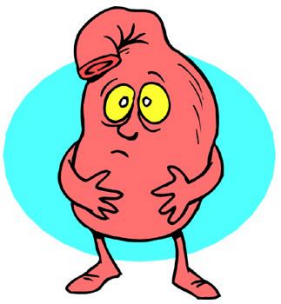
Case 1



- H 35yo ♀ - tertiary referral Yorkshire surgeon to IFU
- Teenager in social care: abdominal pains and bowel disturbance “IBS” – self managed, settling
- Miscarriage mid-20s. Recurrent severe lower abdominal pains. Gynae: “blocked tubes” → TAH and BSO.
- Post-surgery → progressively worsening abdo pains → recurrent lap adhesiolysis
- Increasing doses of opiates:- fentanyl patch and lozenges for breakthrough. Doses escalating.
- Severe constipation → digitates intermittently. One episode severe impaction → anal tear and manual evac under GA (York)



- Main pain = RIF. Barium → small bowel “fixed” but no obstruction/strictures.
- Bloated & distended “like 6/12 pregnant”
- Eating worsened pains → PEG.
- Drip feeding by PEG also worsened pains and some peri-PEG discomfort.
- Avoiding food but at other times “binge eats”.
- “Wants TPN” → IFU
- Normal “nutrition bloods” high normal BMI. AXR left sided faecal loading +++.
- O/E Mildly tender peri-PEG but rest of abdomen non-tender except RIF.
- RIF exquisitely tender to light touch → feels deep pain, nauseous.



Assessment



I think she exhibits several problems:

1. hypersensitivity in the right iliac fossa

- allodynia
- hyperalgesia



"neuropathic pain"

2. sitophobia

3. severe constipation

- element longstanding
- exacerbated by opioid bowel dysfunction

4. possible element of "narcotic bowel syndrome"

5. Mechanical element SB adhesional matting but also abdominophrenic dysinergia

Diagnosing postoperative neuropathic pain: a Delphi survey

R. D. Searle^{1*}, S. J. Howell² and M. I. Bennett³ *British Journal of Anaesthesia* **109** (2): 240–4 (2012)

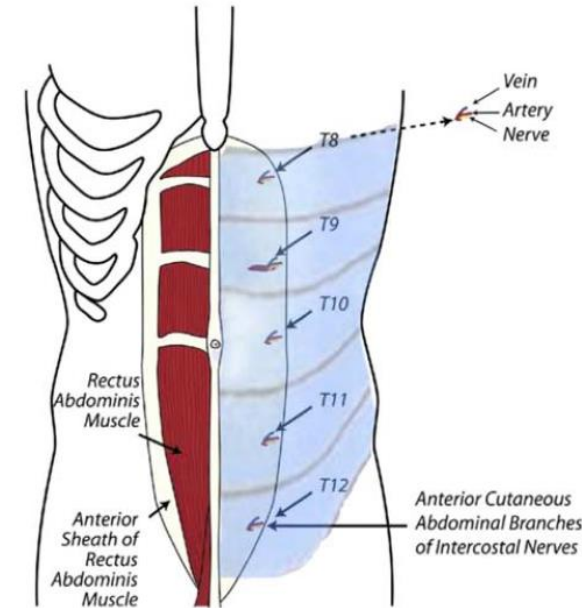
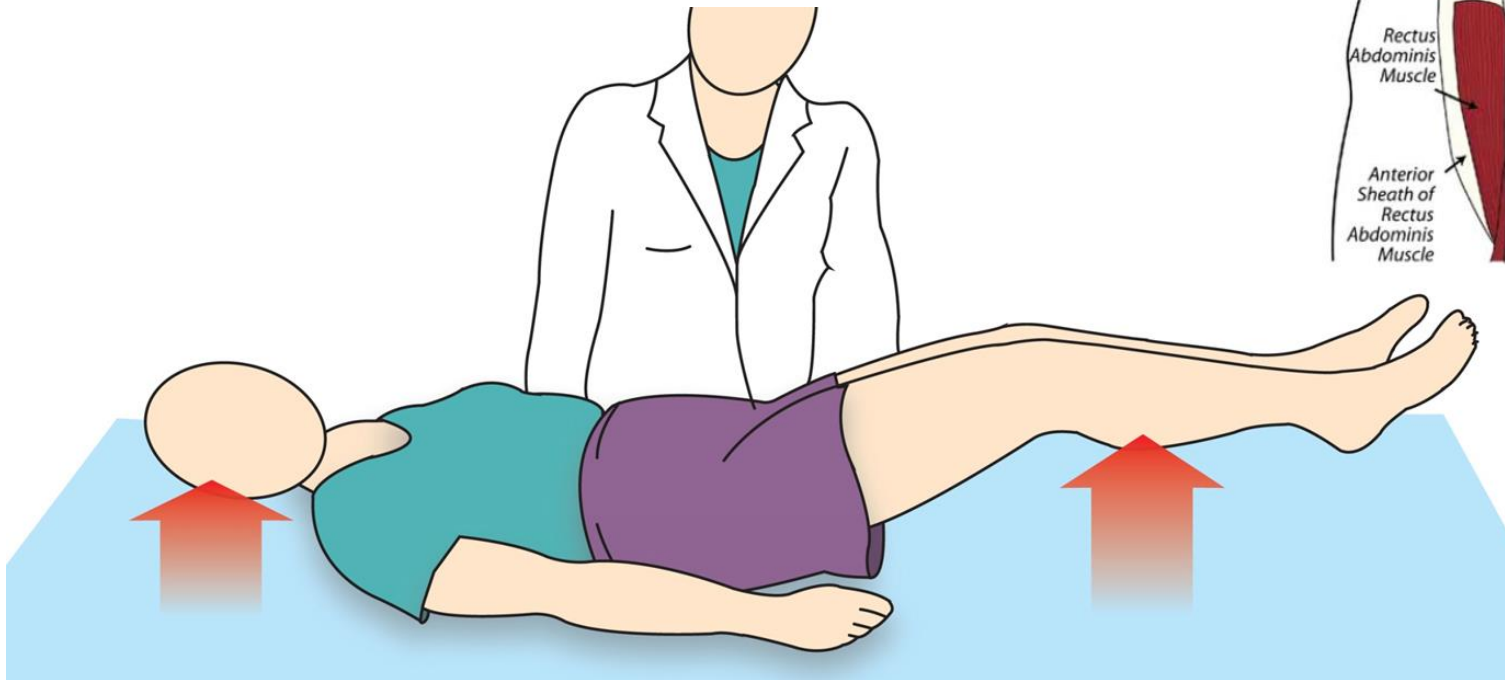
Table 2 Items achieving consensus after survey round 3

Important	Not important
Spontaneous	Paroxysmal
Shooting	Pulsing
Burning	Radiology
Dysaesthesia	Nerve conduction
Allodynia	
Hyperalgesia	
Difficult to manage pain	
Poor response to opioids	
Good response to anti-neuropathics	

How does NP differ from ACNES?

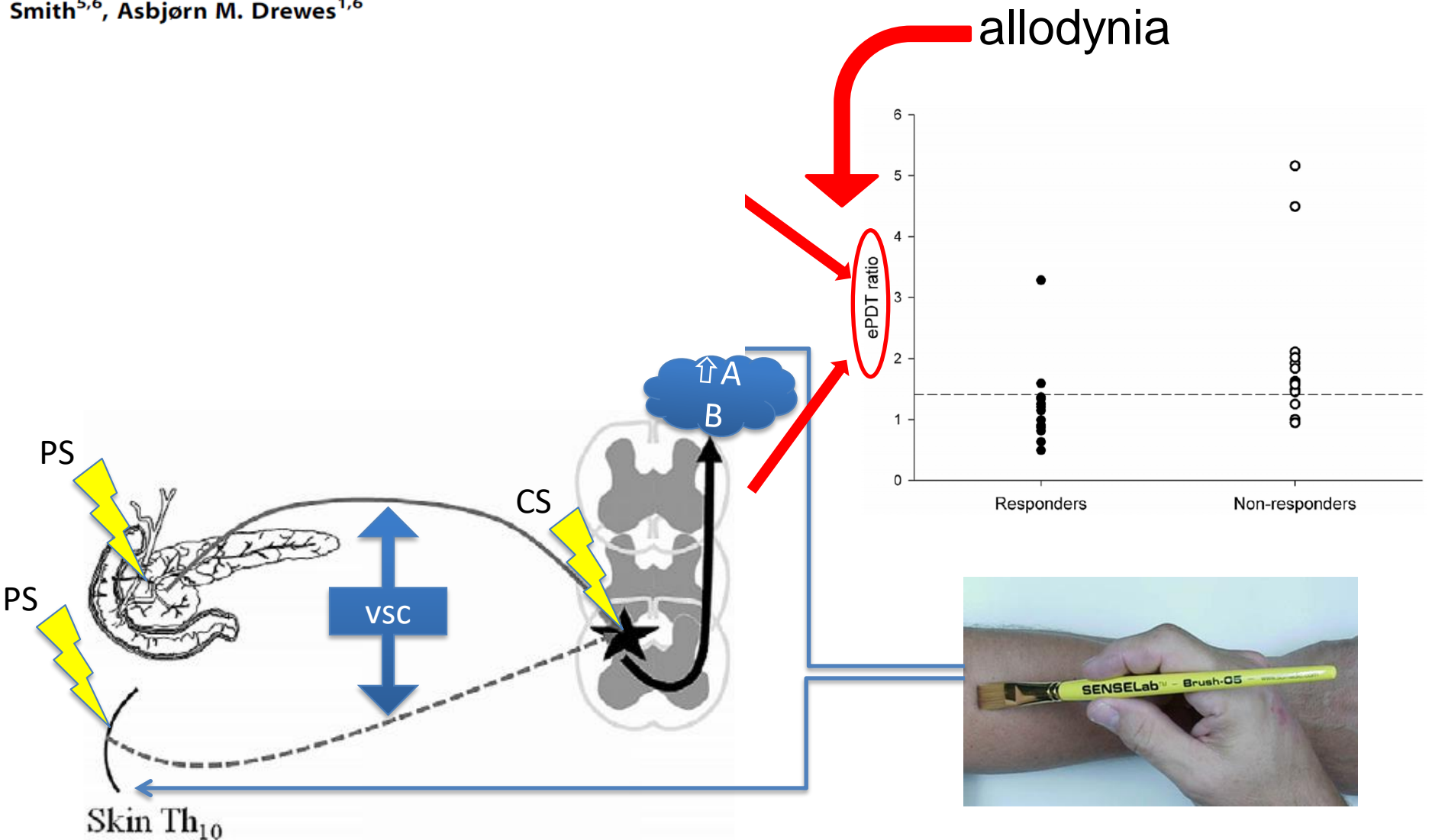
Diffuse vs focal

Carnett's sign – rectus sheath pain on tensing



Quantitative Sensory Testing Predicts Pregabalin Efficacy in Painful Chronic Pancreatitis

Søren S. Olesen^{1*}, Carina Graversen^{1,2,3}, Stefan A. W. Bouwense⁴, Harry van Goor⁴, Oliver H. G. Wilder-Smith^{5,6}, Asbjørn M. Drewes^{1,6}



Surgeons: friend or foe?

- *“all the operations were necessary - except the first”*

Sir Miles Irving
Prof of surgery
IFU, Hope Hospital



POST-SURGICAL NEUROPATHIC PAIN

ANZ J. Surg. 2008; **78**: 548–555

EDWARD SHIPTON

- Neuropathic pain prevalence post-op
 - Post-thoracotomy 35%
 - Post-inguinal hernia 7-20%
 - C-Section 10%
- Laparotomy 18%
 - Re-ops → increased pain intensity
 - Mostly moderate-severe neuropathic pain
 - Lap adhesiolysis → 5% serious complications, 1% mortality
 - Most studies → adhesion & pain recurrence



Avoiding unnecessary surgery in irritable bowel syndrome

George F Longstreth Gut 2007

Protecting patients with IBS from the risks and costs of unnecessary surgery

- 3x cholecystectomy rate
- 2x hysterectomy rate
- 2x appendicectomy rate
 - (IBS OR 2.17 for negative appendicectomy)
- Increased colon resection
- Increased back surgery

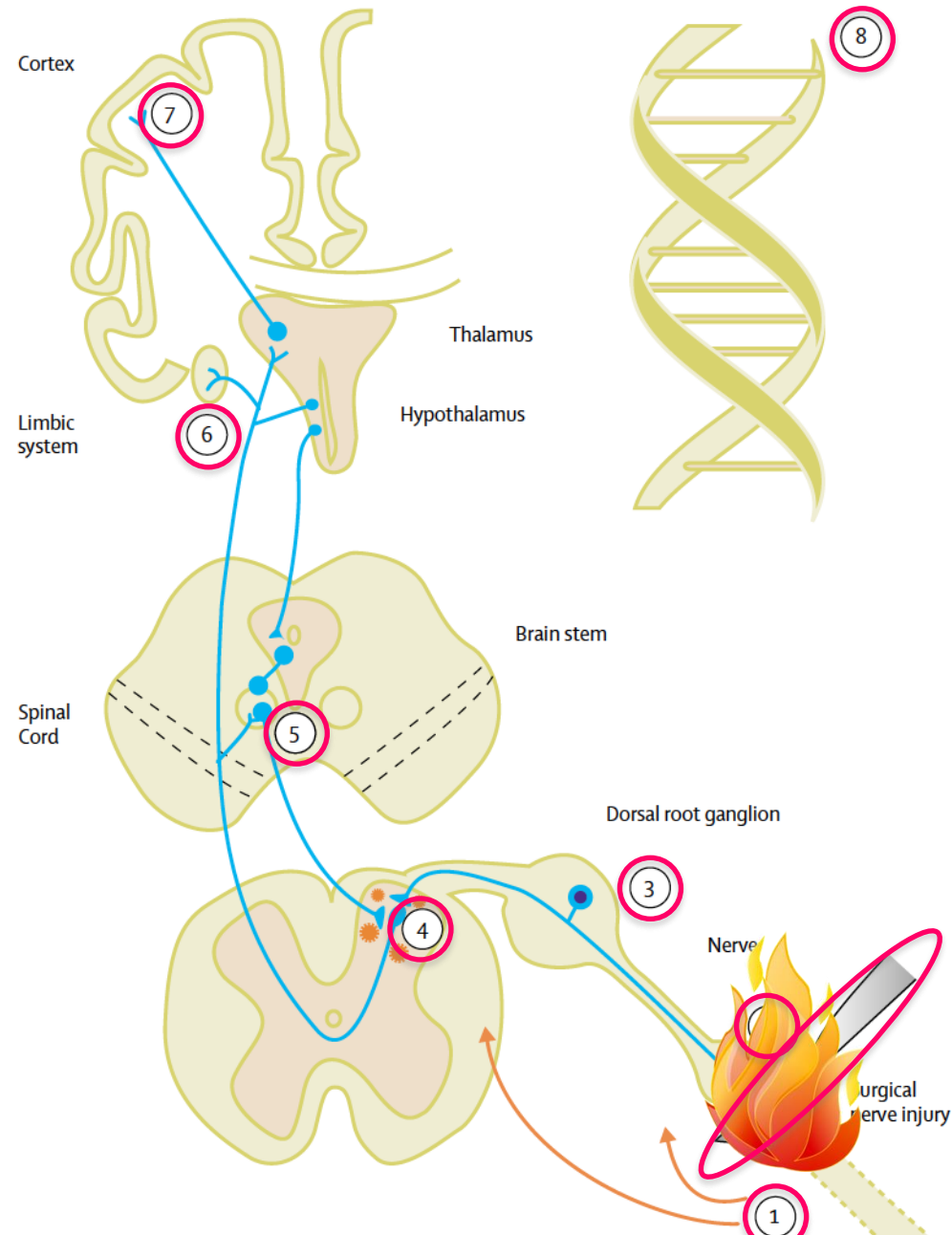


Persistent postsurgical pain: risk factors and prevention *Lancet 2006; 367: 1618-25*

Henrik Kehlet, Troels S Jensen, Clifford J Woolf

Sites & mechanisms of chronic post-surgical neuropathic pain

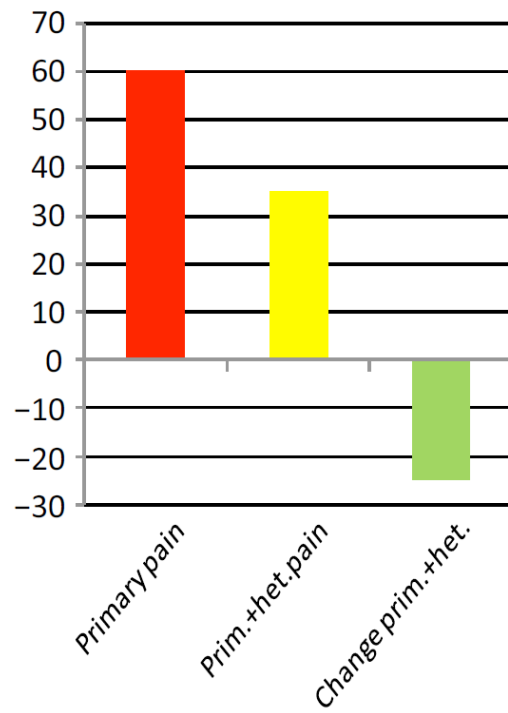
1. Peripheral sensitisation (distal chemicals)
2. Neuroma at injury site (ectopic excitability)
3. DRG gene expression (excitability)
4. Central sensitisation (dorsal horn gene expression, inhibitory interneurone loss, microglia activation)
5. reduced DNIC (brainstem)
6. Limbic & hypothalamus (emotion, behaviour, ANS)
7. Cortex (cognitive-evaluative)
8. Genomic DNA predisposition & Rx responsiveness?



'Heterotopic pain'



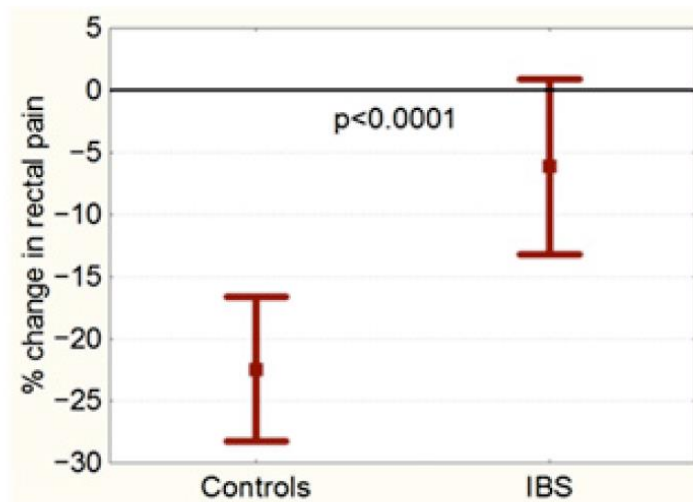
'Primary pain'



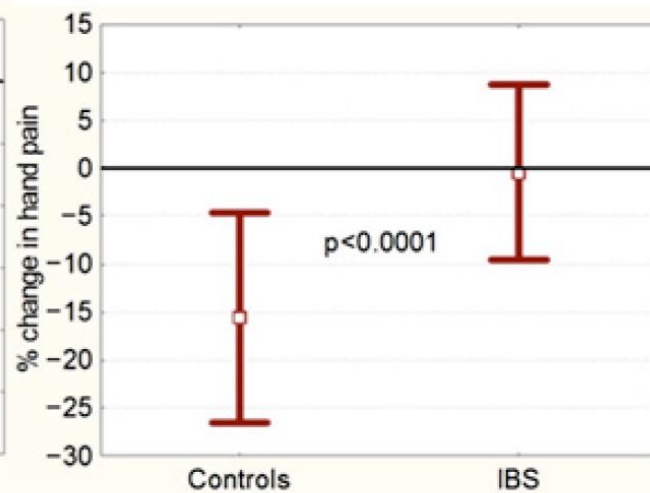
Diffuse Noxious
Inhibitory Controls
(DNIC)

Wilder-Smith, Gut
2011

A

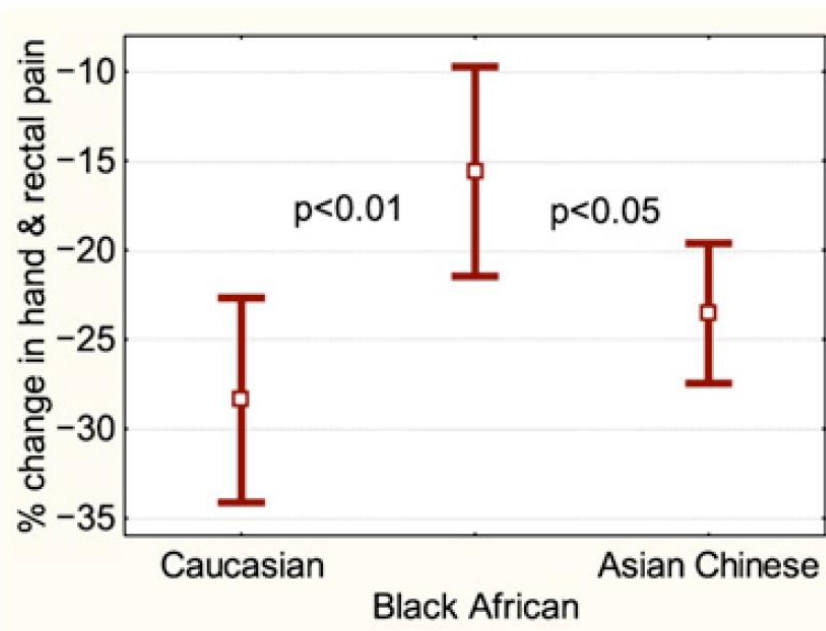


B



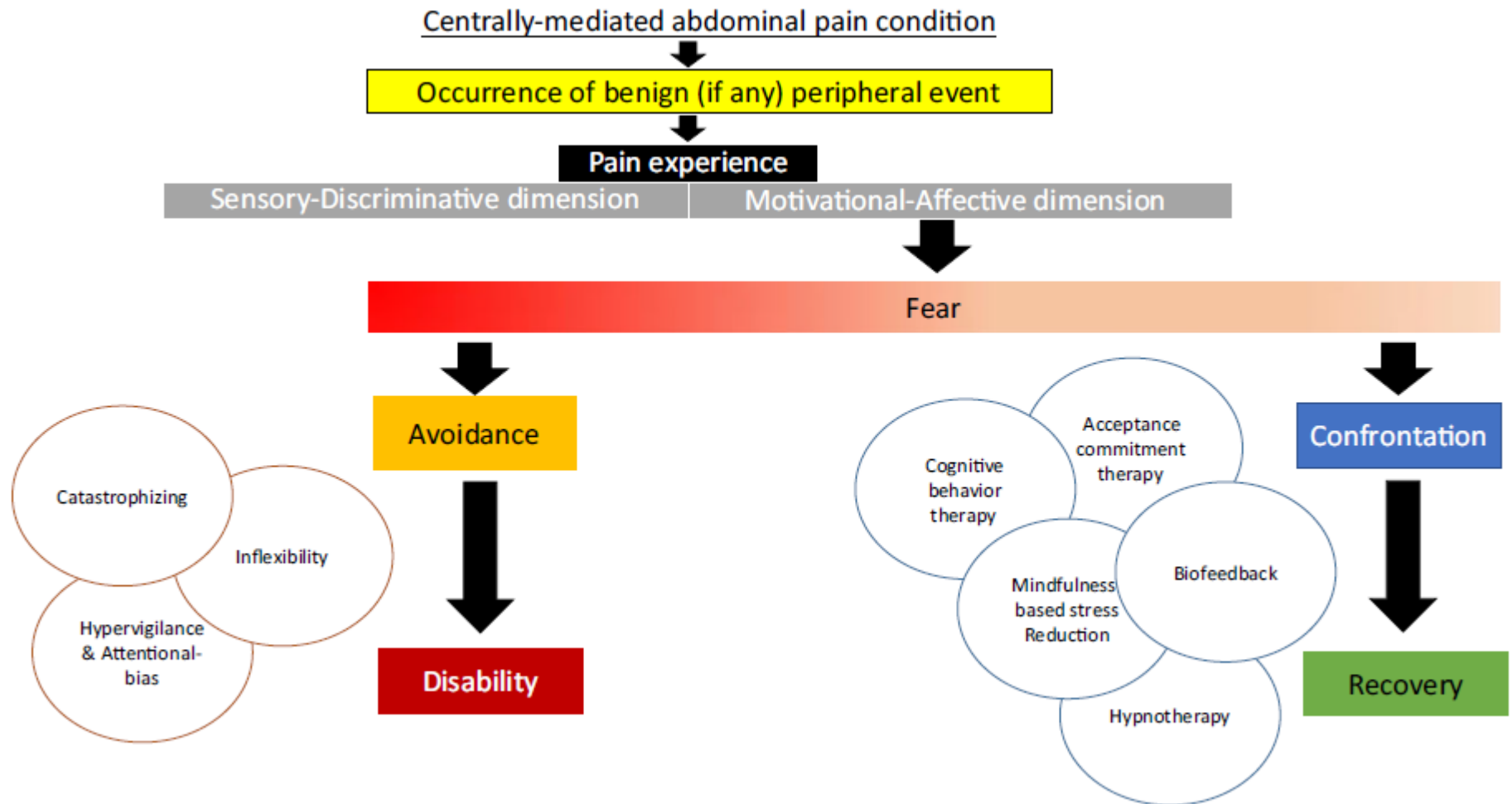
Facilitation ↑
Inhibition ↓

C



Wilder-Smith, 2011

Fear Avoidance Model in chronic abdominal pain



Top-down sensitizers

- Hypervigilance
- Catastrophising
- Depression
- Poor coping
- Abuse
- Anxiety
- Stress
- Genetics

“brakes” Inhibition



Facilitation “accelerator”

Bottom-up sensitizers

- Immune activation
- Subclinical inflammation
- Dysmotility
- Distension
- Chemical, bacterial luminal factors
- Genetics

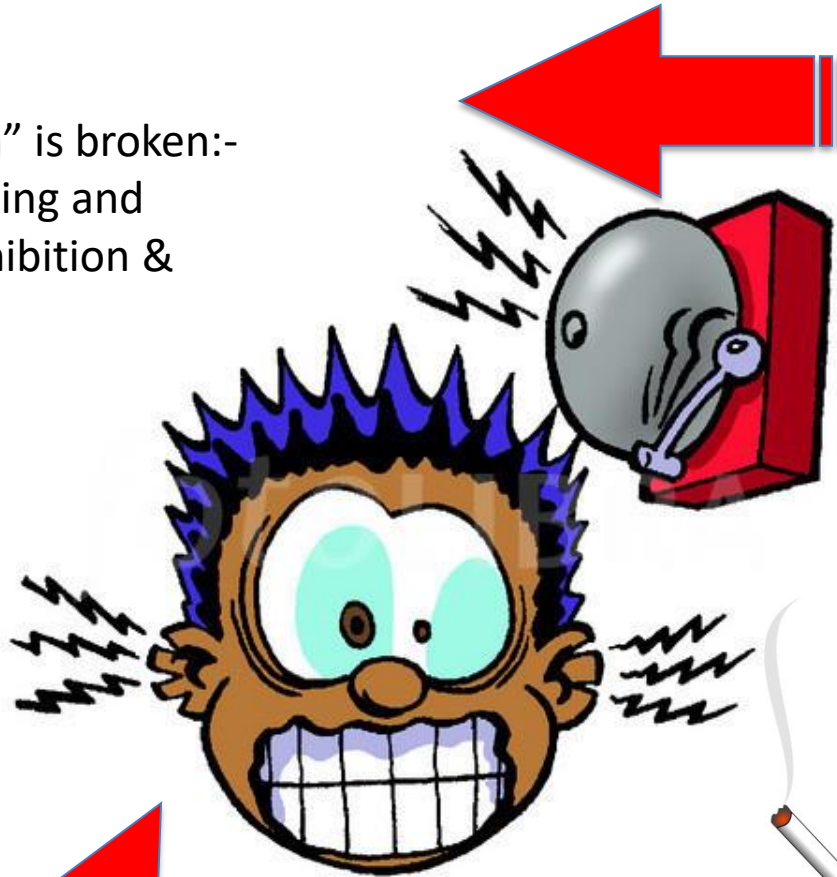
Shifting the balance in endogenous pain modulation

Wilder-Smith; 2011 Gut

The broken fire alarm: a wiring problem

The “off switch” is broken:-
Faulty CNS gating and
descending inhibition &
Continuous

The volume is turned
right up/amplified:-
Central sensitisation &
Hyperalgesia

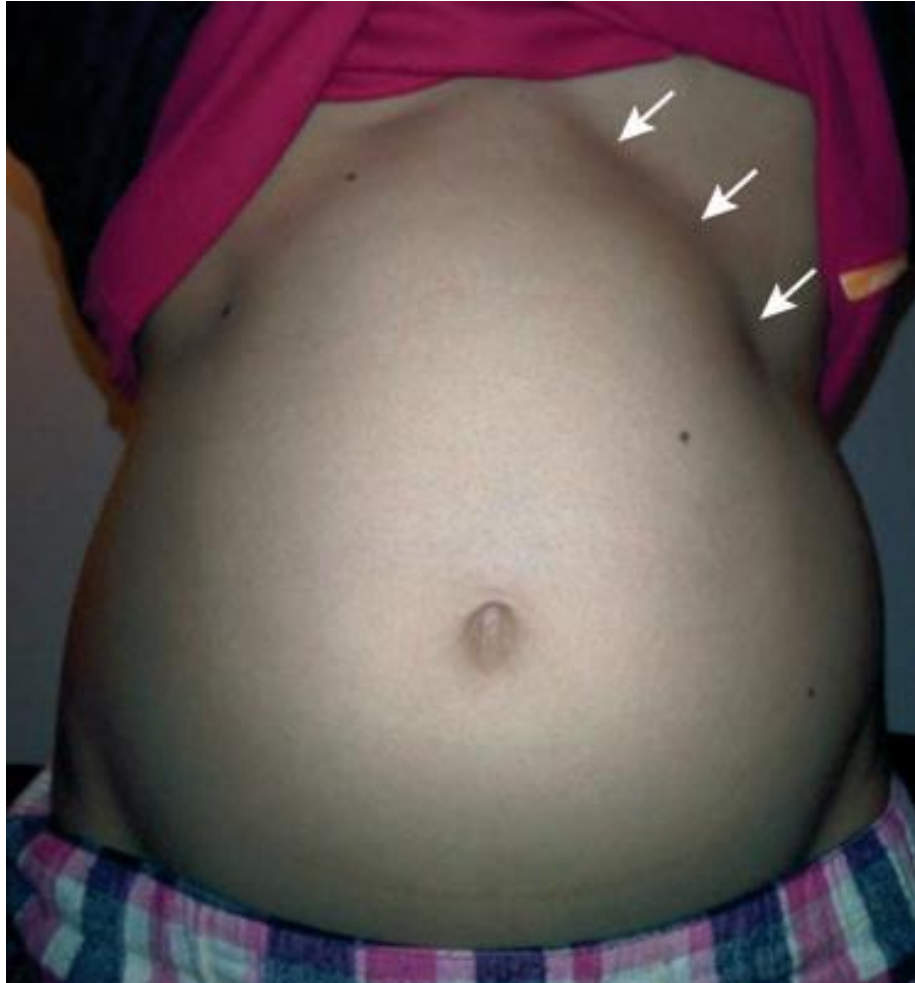


It's driving me
mad!:-
Coping strategies
over-whelmed –
for any sane
person

NP agents: Cushions up a step-
ladder
dimmer switches not off switches
Opiates turn up the dial
May deaden/burn out over years

It's on a “hair
trigger”:-
Peripheral
sensitisation &
allodynia

APD “guttering”

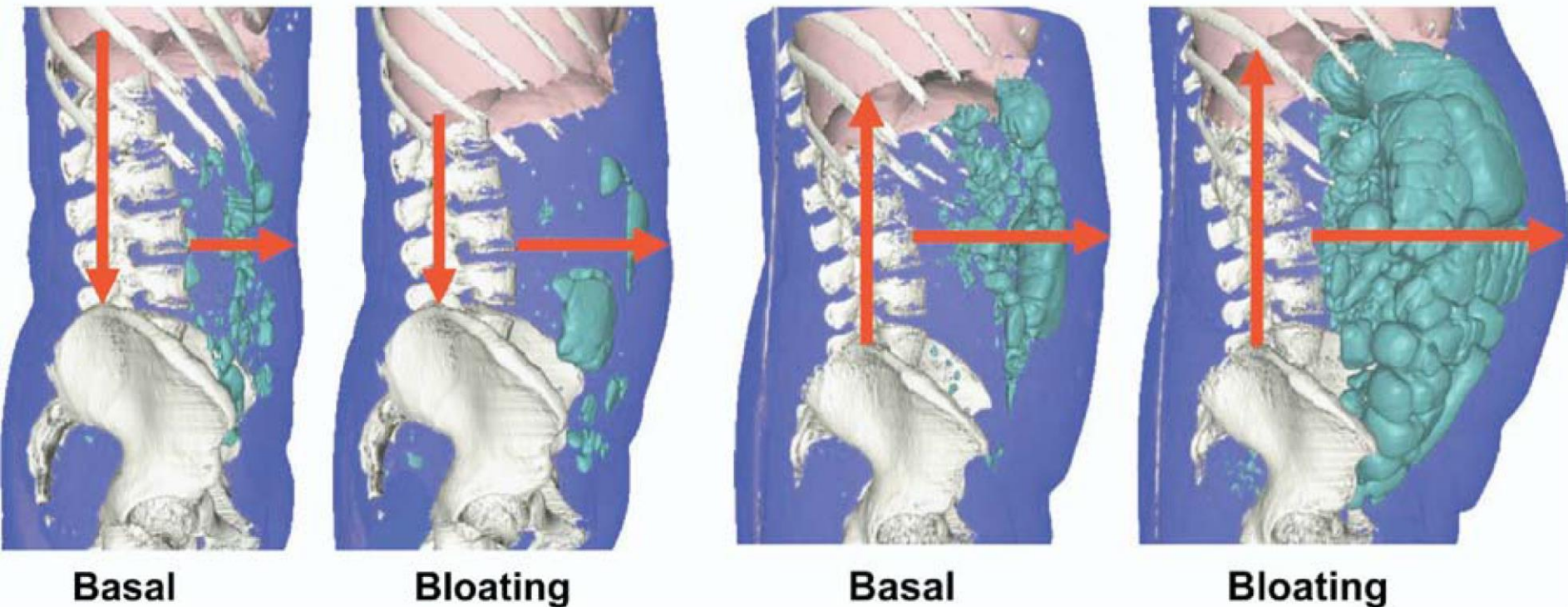


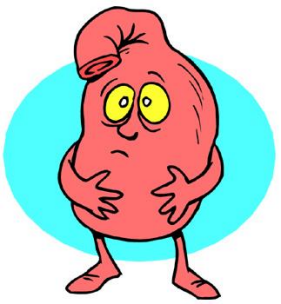
Is it mechanical, CIPO or enteric dysmotility or APD?

Accarino et al
Gastro, 2009

Functional
bloaters

CIPO

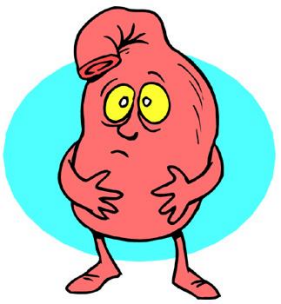




Management



- Explained: problems =
 - “wiring” nerve & muscle > “plumbing” pipes (CNS element/opioid exacerbated-driven). (*broken fire-alarm*)
 - Pain on eating but not true “nutritional” problem.
 - TPN will *not* help and could be dangerous.
 - I do not think further surgery will help either.
 - Unrealistic to expect complete/quick resolution.
 - She would benefit additionally from psychological support in coping with her chronic refractory symptoms
- Commenced duloxetine: may help neuropathic pain less constipation than tricyclics.
- Plan to commence: Methylnaltrexone s/c to help opioid bowel dysfunction
- Explained: “Rehabilitative” chronic pain team approach & possible controlled opiate reduction



Outcome

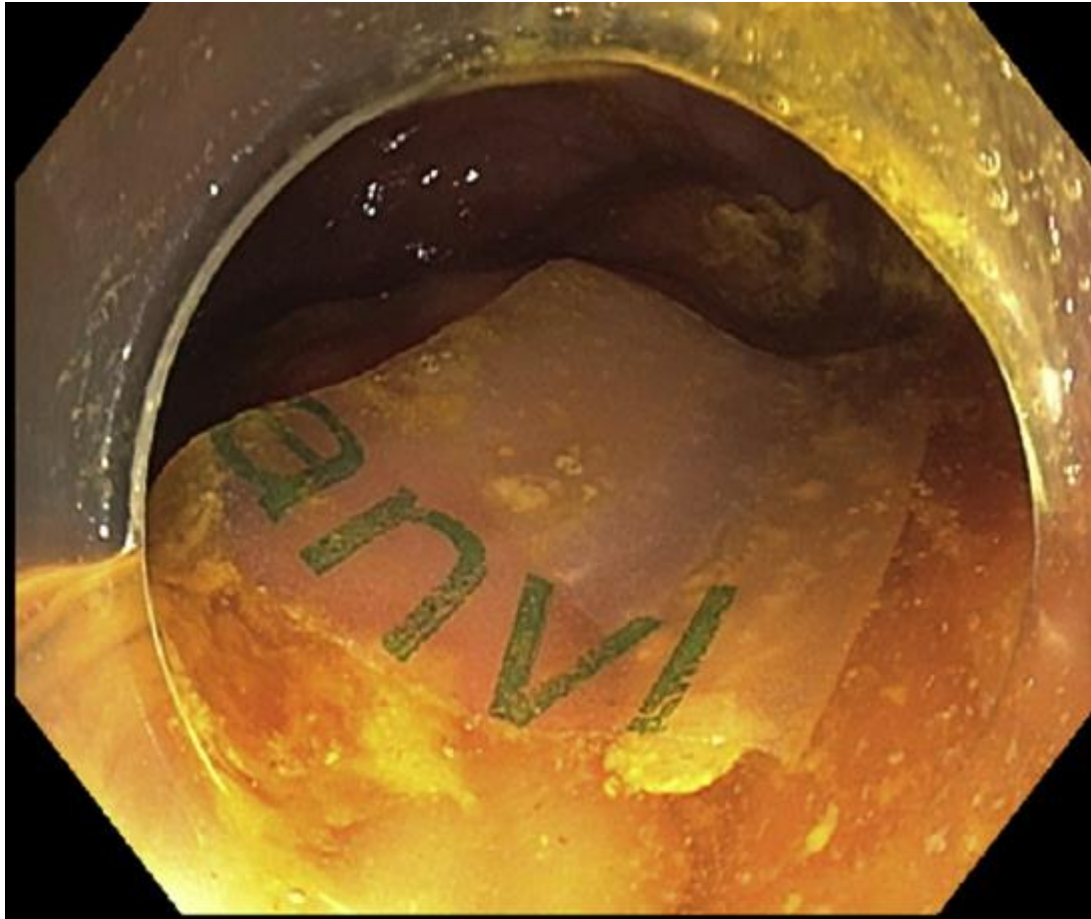


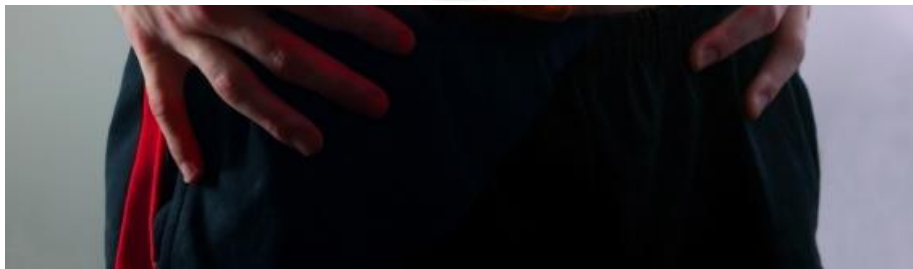
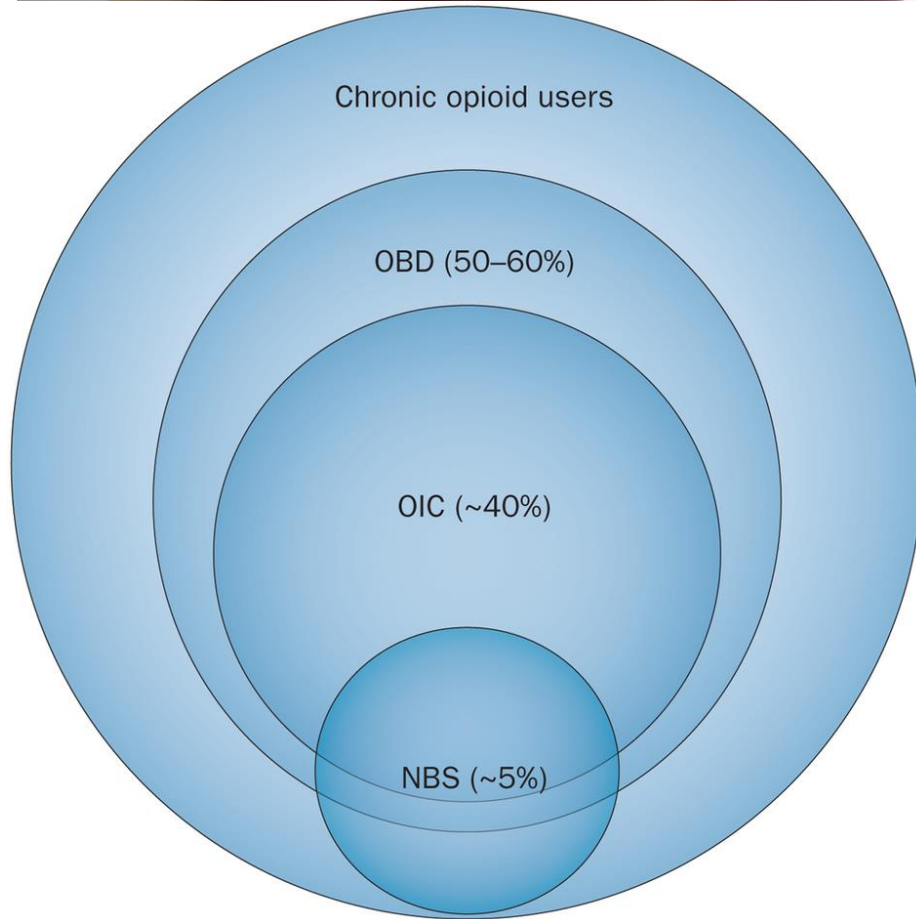
- Discharged + clinic f/u 6/52
- 2/52 post-discharge: Went cold turkey!
- BO <q 4days, Weight increasing, PEG out
- Chronic pain team shared care
- 6months later on targinact → improved bowel function than previously
- Not engaging initially with psychological approaches but 1 year later “significant help”
- 3 year follow up – remained out of hospital and back into work. Discharged.

Colonoscopy Enables the Diagnosis of Opiate Abuse

Andrew P. Copland,^{*} Jonathan P. Gaspar,[‡] and Andrew Y. Wang^{*}

CGH 2016

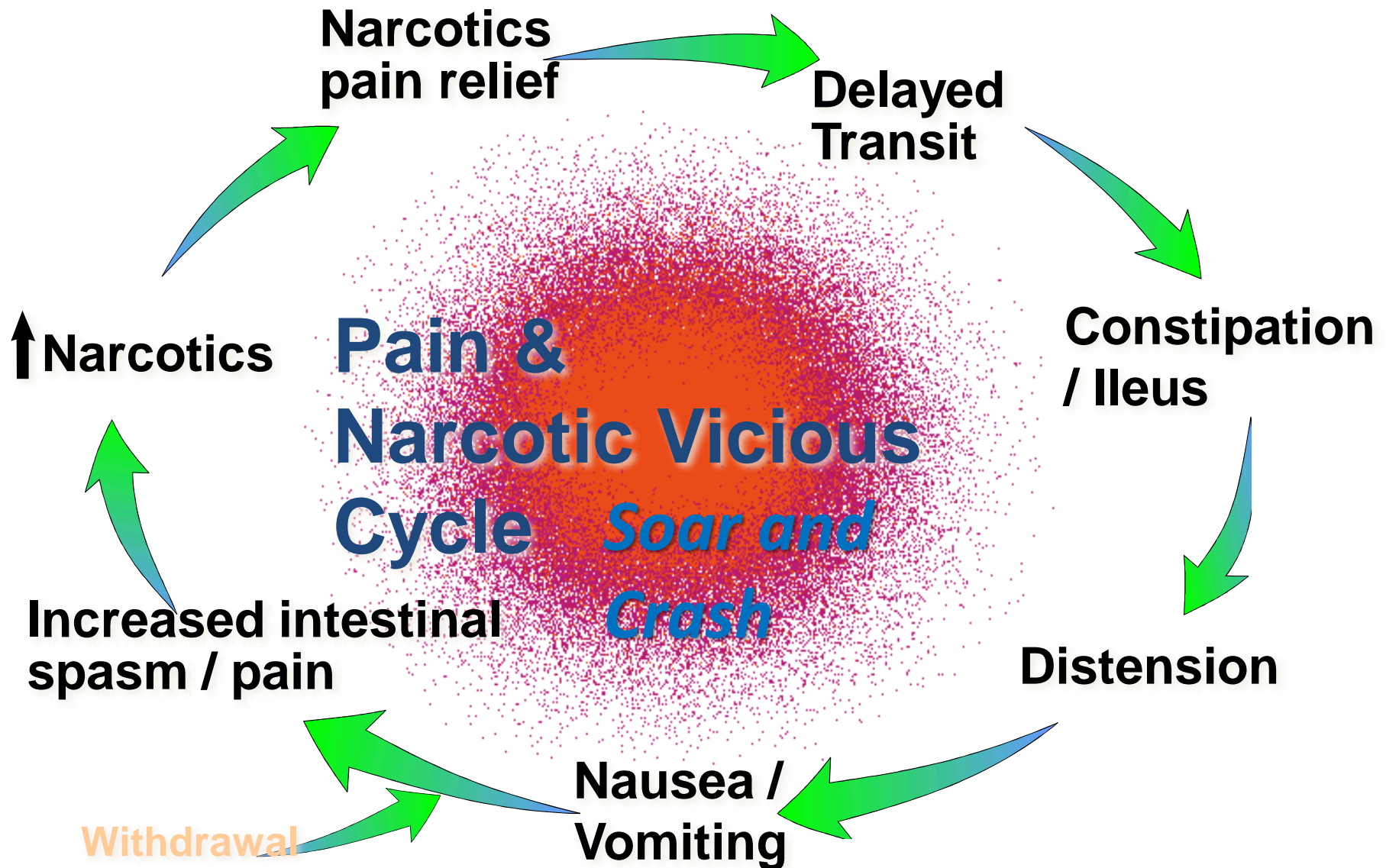




Opiates: friend or foe?

- Opiates and the gut:— clinical scenarios
 - Opioid bowel dysfunction
 - Narcotic bowel syndrome
 - Opiate dependency/addiction
 - Opiophobia
 - PN deaths (?immune paresis)
- Is it the opiates (pseudo-obstruction) or is it pseudo-pseudo-obstruction?
- Are some opiates better?
 - Methadone (NMDA antag)
 - Tapentadol (NA reuptake inhibition)
 - Tramadol
 - Long acting transdermal (reduce soar and crash)

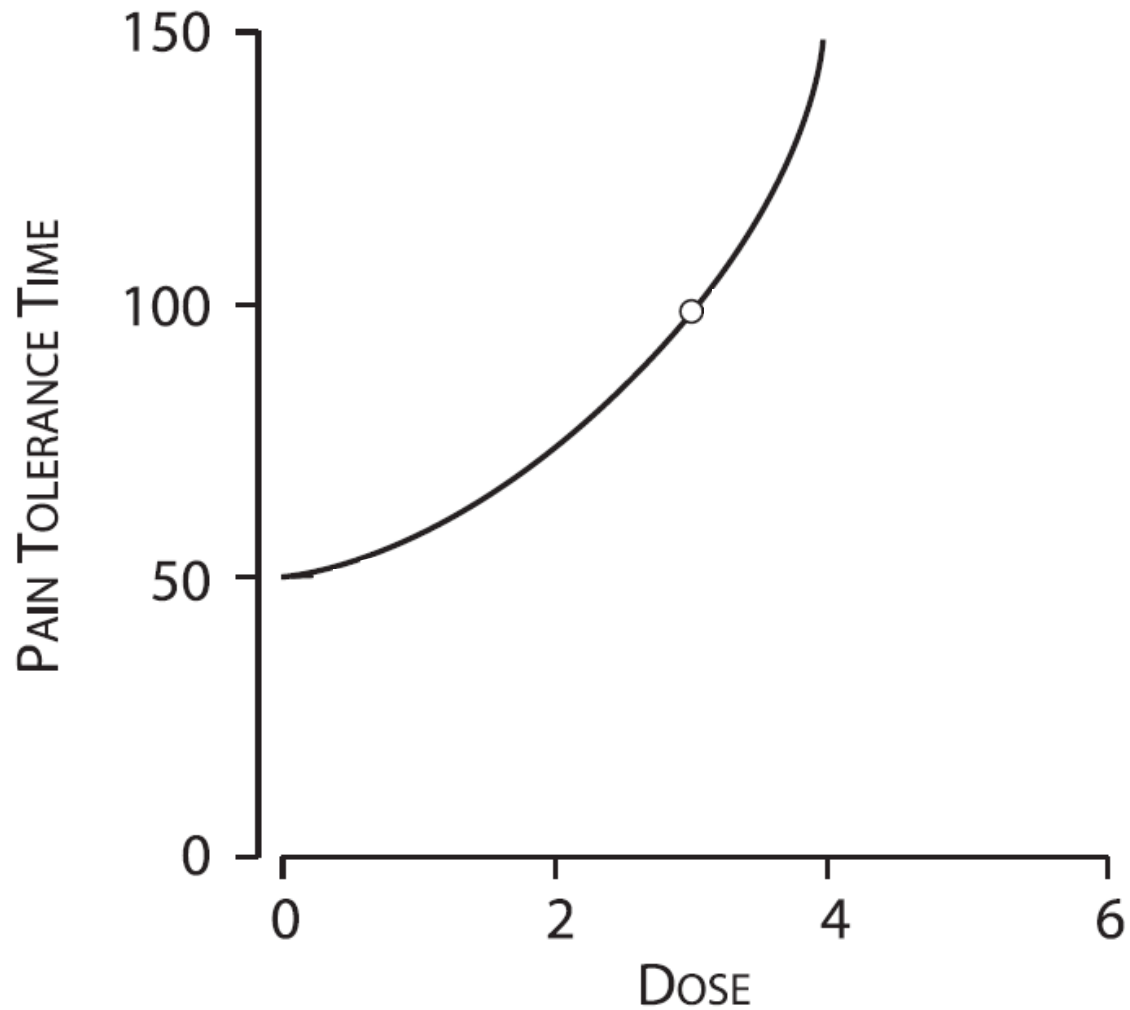
IBS - Narcotic Bowel Syndrome



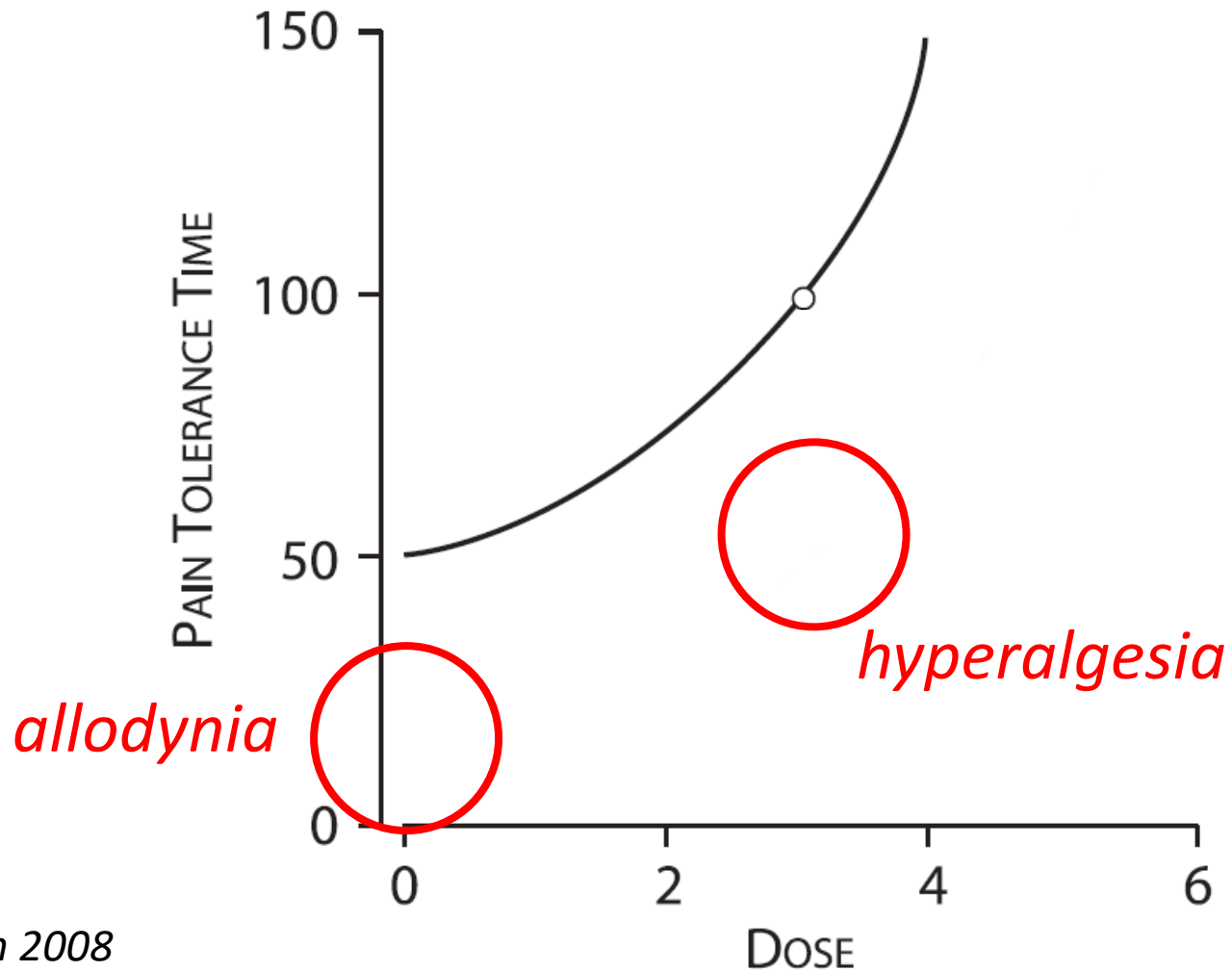
Pain

**Vicious Cycle of
Patient - Physician
Interactions**

Opioid tolerance



Opioid induced Hyperalgesia



Salford data 2009-2016

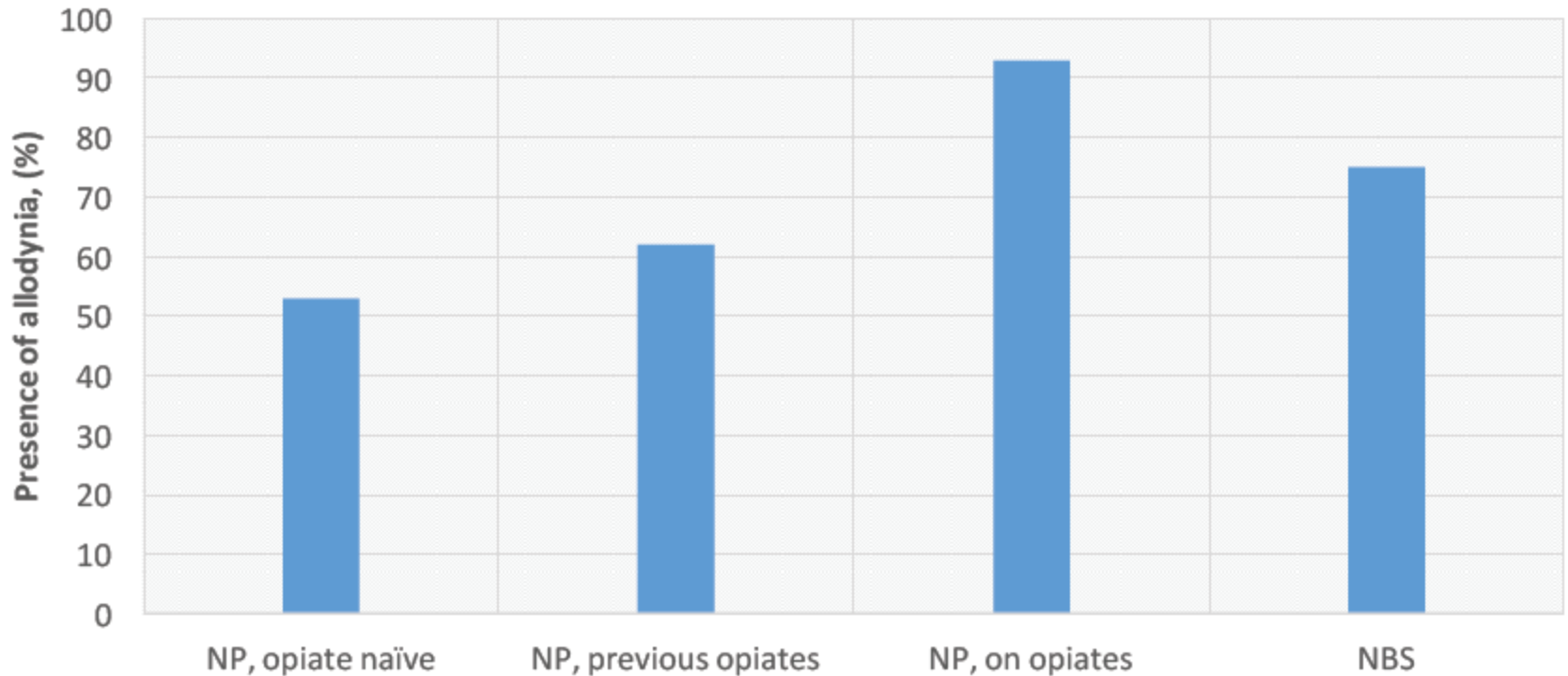
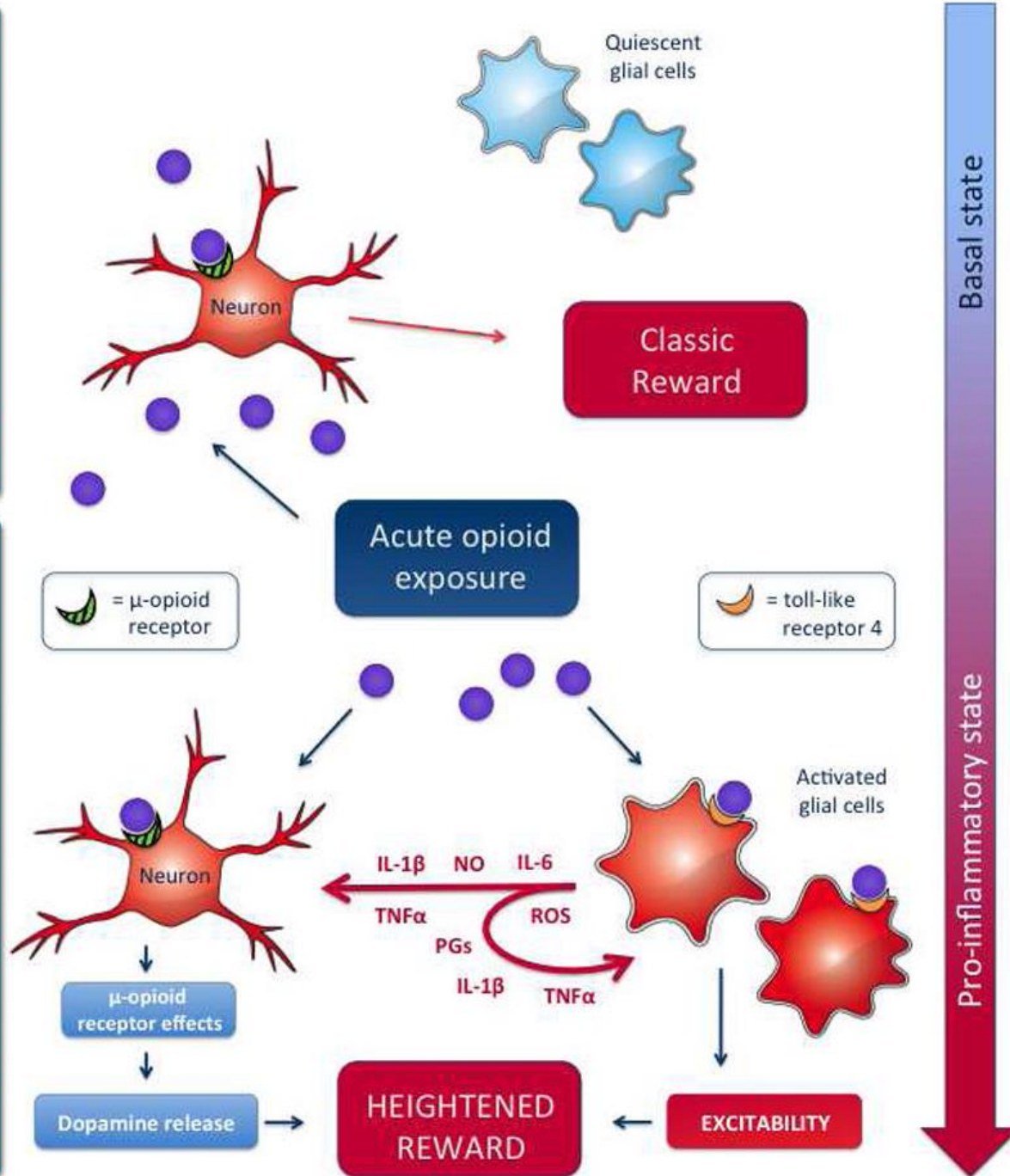


Figure 3 – Association between allodynia and opiate use ($p=.0002$). NBS, narcotic bowel syndrome; NP, neuropathic pain.

(a) Classic Opioid Reward

(b) Novel Neuroimmune Reward

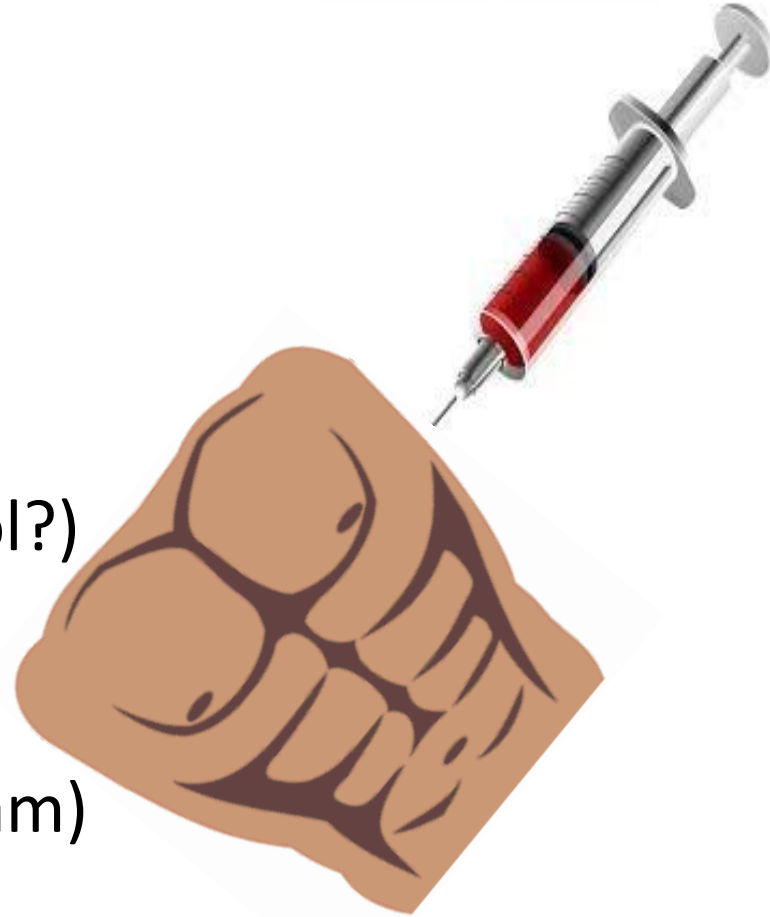


Hutchinson and
Watkins, 2014
Neuropharmacology

TLR4 mediated
pain
intensification
AND activation of
the mesolimbic
dopaminergic
reward circuits \rightarrow
drug-seeking
behaviour

Treatment of NBS

- Recognition
- Relationship
- Replacement
 - TCA, α_2 ligands, NSRI (SSRI)
 - Linaclootide?
 - μ -opioid antagonists (naloxegol?)
 - Psychological therapies
- Reduction
 - Rapid? (GA, drug & alcohol team)
 - Slow controlled patient driven
- Prevention? TLR4 antagonists



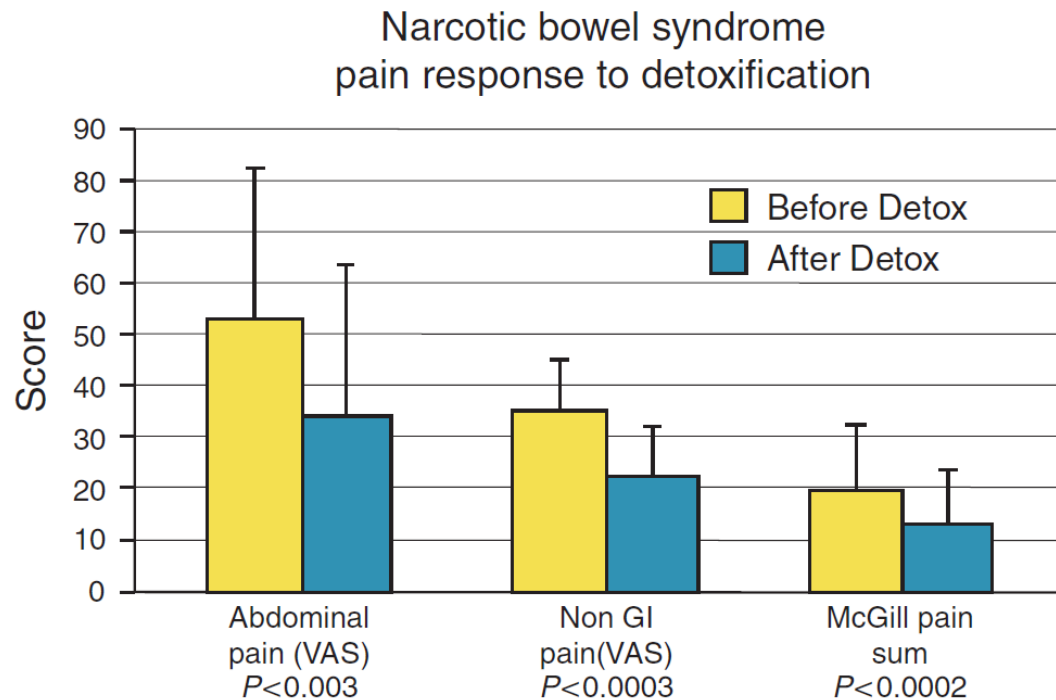


Figure 1. Pain response due to detoxification. The before and after detoxification levels of pain using a visual analog scale (VAS; 0–100) and the McGill Pain Questionnaire are shown. There is a statistically significant reduction in abdominal and non-gastrointestinal (non-GI)-related pain. This is also significant if one can define clinically meaningful response as >30% reduction (VAS abdominal pain 35%, VAS non-abdominal pain 42%, and McGill abdominal pain 31%).

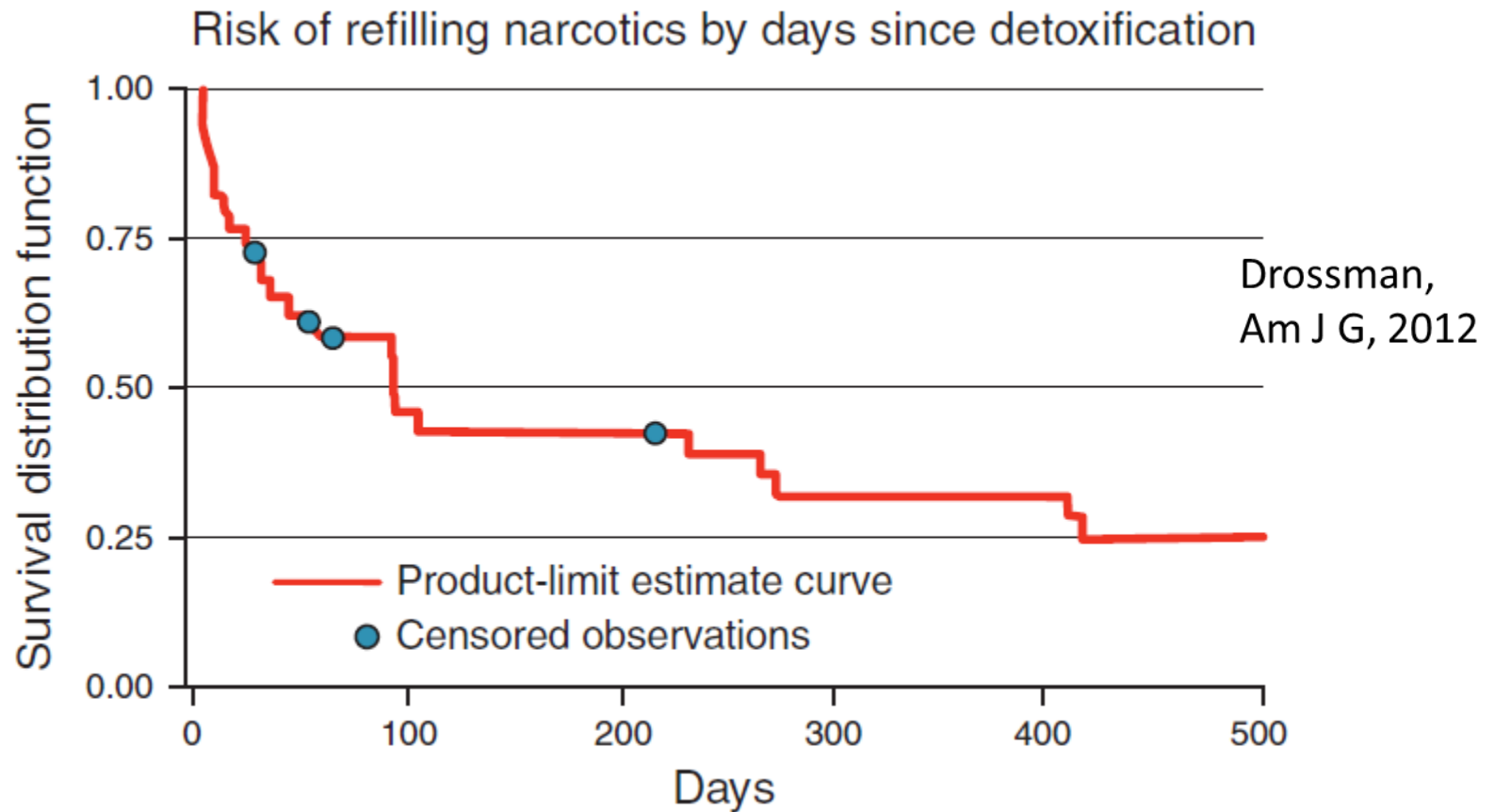
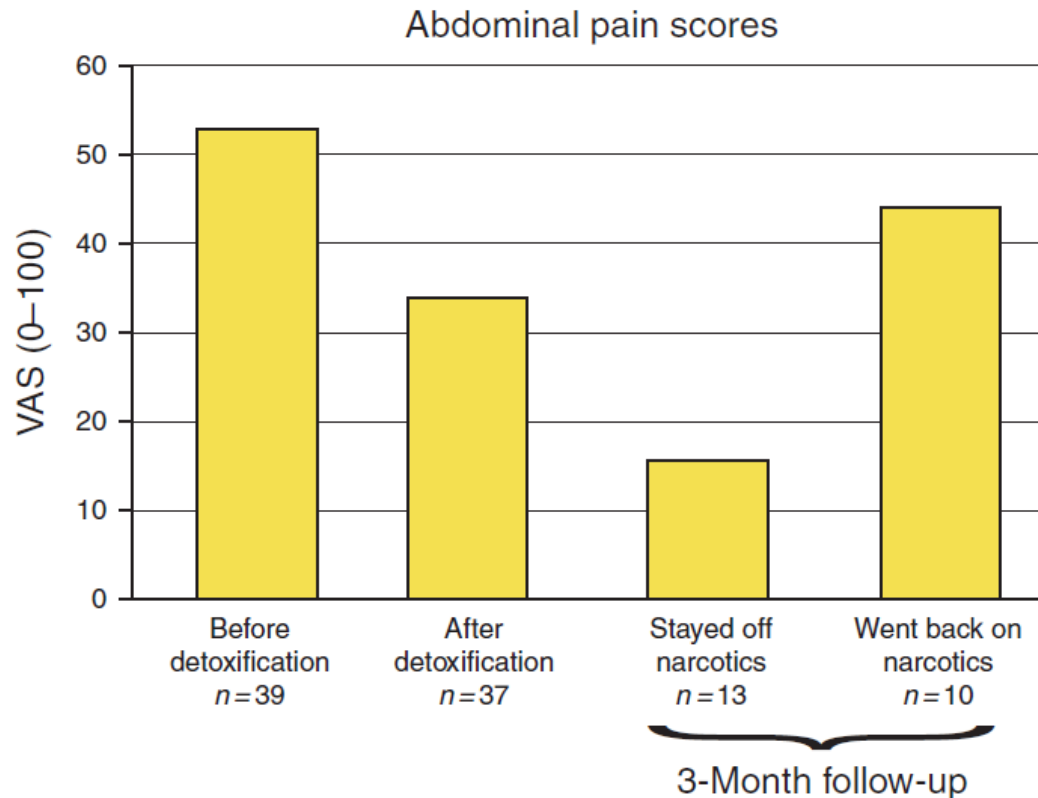


Figure 3. Survival graph for returning back on narcotics. A survival probability graph for the 24 patients who went back on narcotics and the 12 who did not is shown. Of note, almost 1/5 of this group (17%) went back at 1 week, 50% at 3 months (93 days), 61% at 9 months, and 66.7%, after 1 year (416 days).



Drossman,
Am J G, 2012

“Buy in”
Boundaries
“Opioid aware”

Figure 4. Visual analog scale (VAS) abdominal and non-gastrointestinal (non-GI) pain before and after detoxification and at 3 months. Abdominal pain reporting using a VAS before and after detoxification and at 3 months is shown. Notably, there continues to be a reduction in scores from before to after detoxification and at 3-month follow-up for patients who stay off narcotics. However, for those who go back on narcotics, the pain score reverts almost to predetoxification values.

Salford data 2009-2016

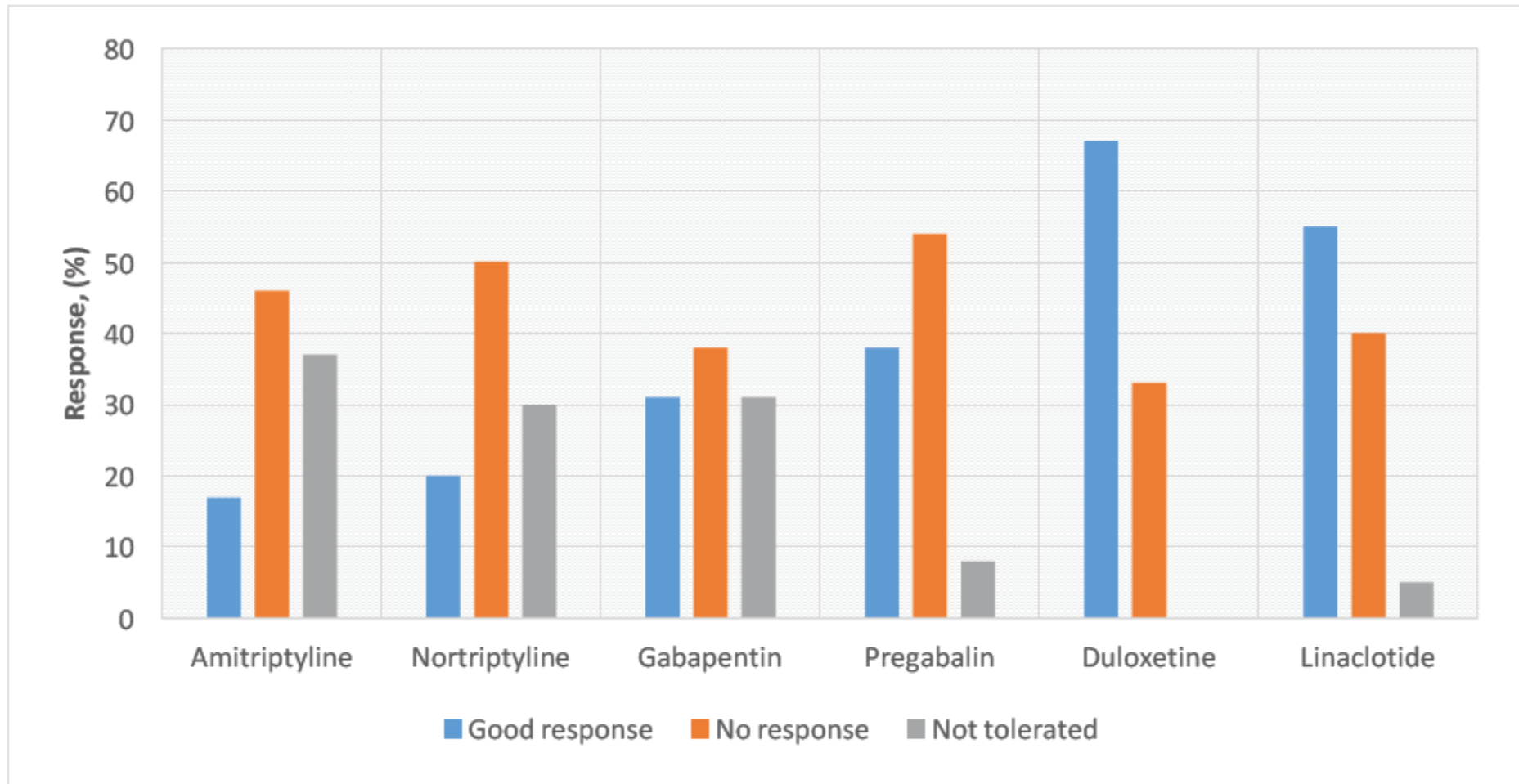
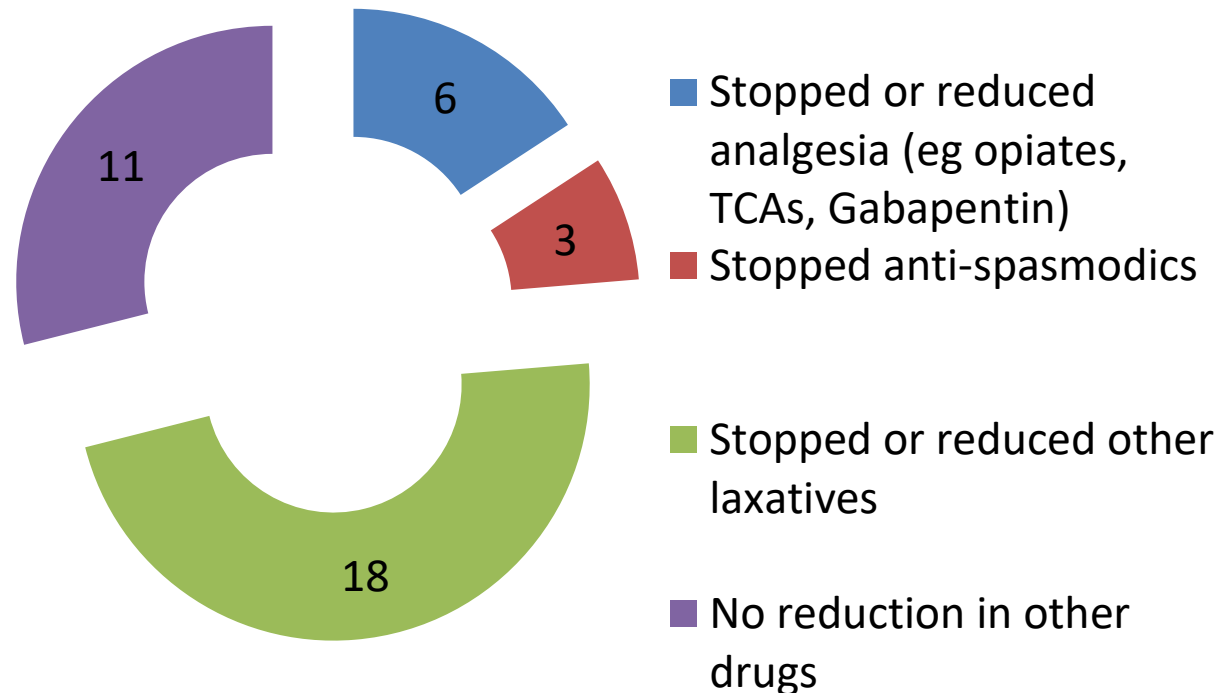


Figure 8 – Response rates of patients to specific anti-neuropathic pain drugs for whom data was available.

Linaclootide audit SRFT to Jan 2015

Reductions in other drug usage (4 stopped/ reduced drugs in 2 categories)



- Responder (34/79 = 43%) IBS SSS baseline = 390/500
- Equivocal response (4/79) = 5%
 - Average score reduction at 4 weeks = 165
 - Average score reduction at 12 weeks = 201 (n=25)
- non-responders (41/79 = 52%) IBS SSS baseline = 404/500

Salford data 2009-2016

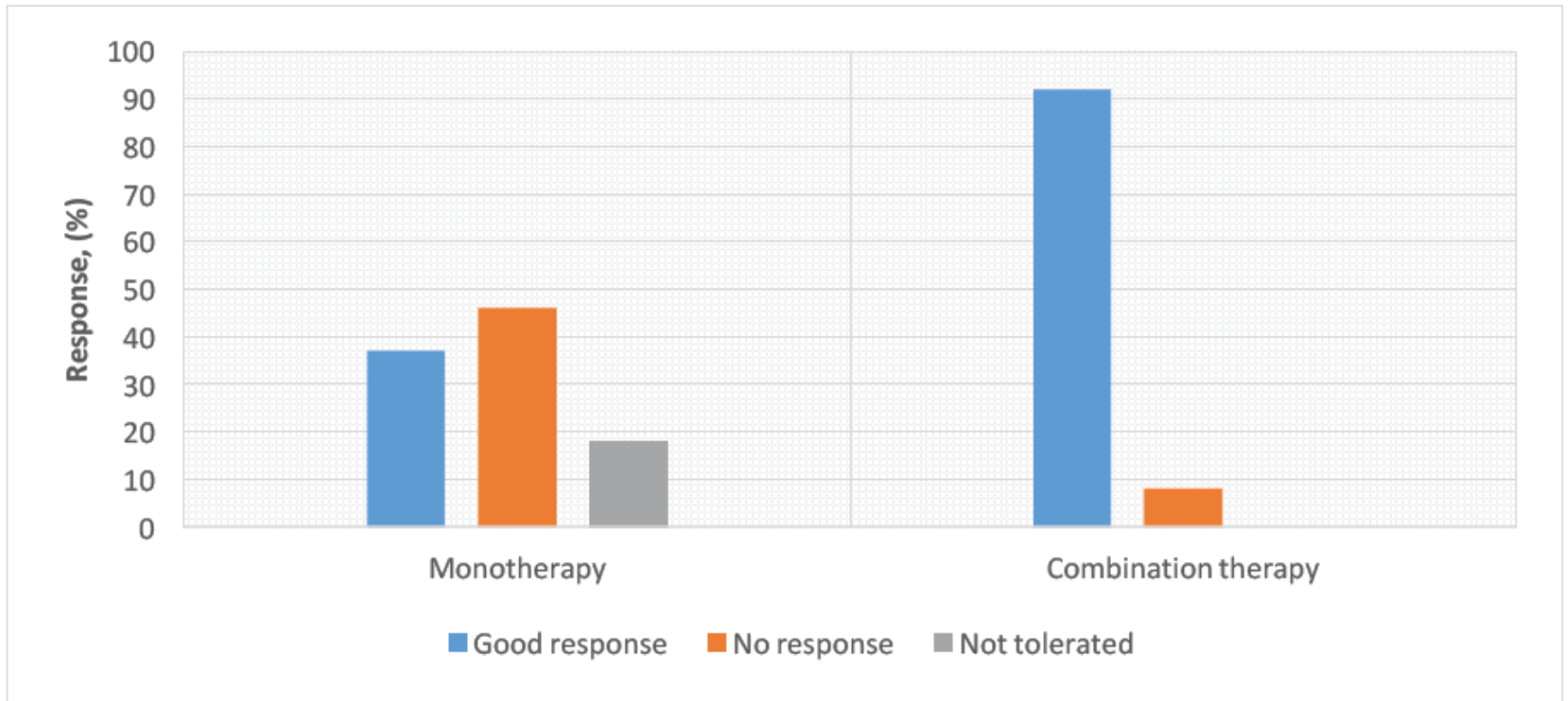


Figure 9 – Response rates of patients to monotherapy and combination therapy with anti-neuropathic pain drugs for whom data was known.



Naloxegol for treating opioid-induced constipation

Issued: July 2015

NICE technology appraisal guidance 345

guidance.nice.org.uk/ta345

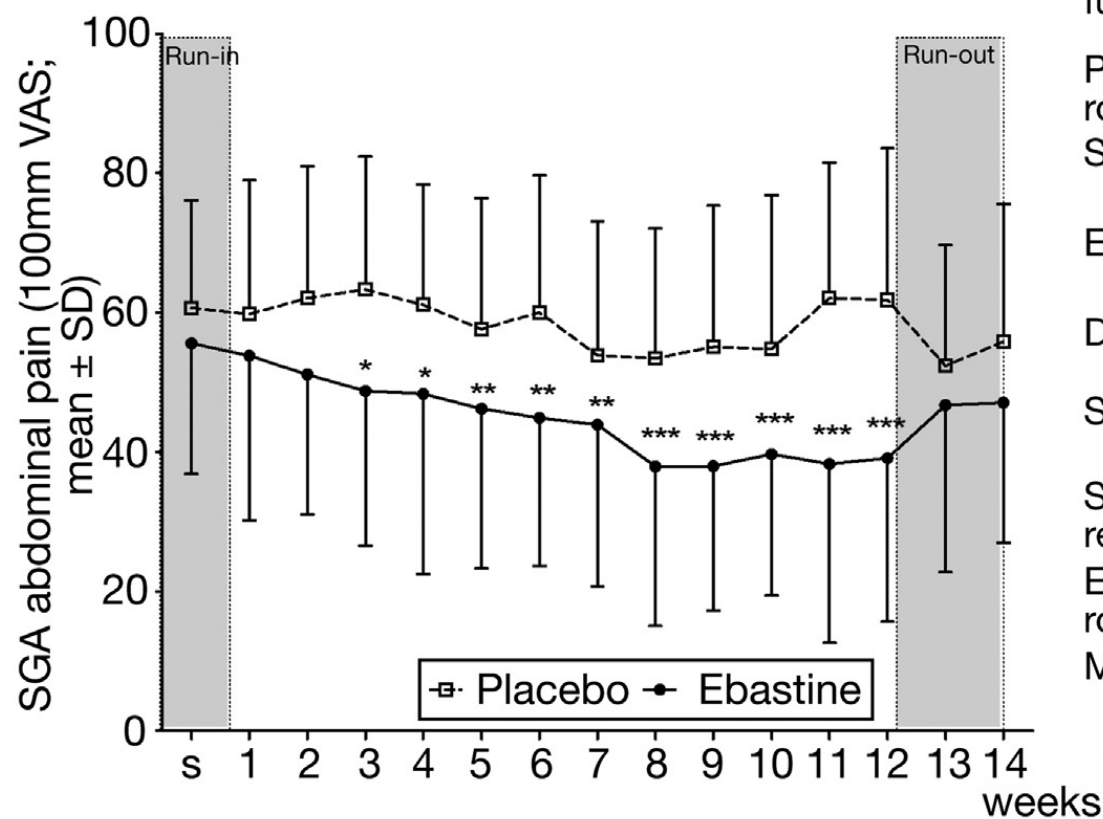
- KODIAC: laxative inadequate responders
- Not injected
- Not combined with opiate
- Pegylation should prevent crossing BBB and withdrawal
- May help motility BUT will it help opiate induced hyperalgesia?

Histamine Receptor H1-Mediated Sensitization of TRPV1 Mediates Visceral Hypersensitivity and Symptoms in Patients With Irritable Bowel Syndrome

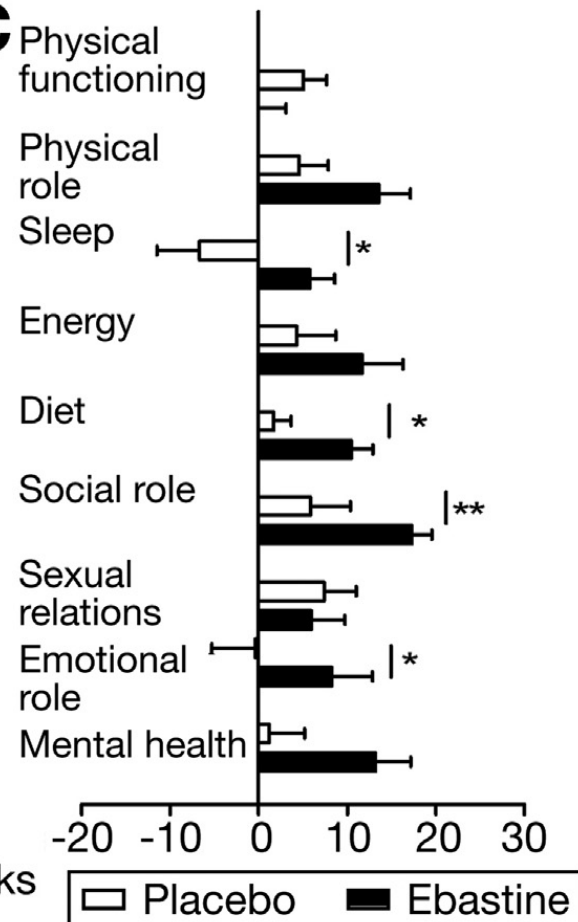
Gastroenterology 2016;150:875–887

Mira M. Wouters

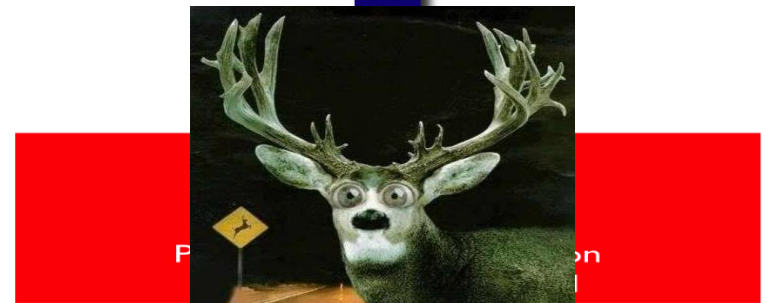
B



C



Overall Pain Phenotypes in Health & Disease



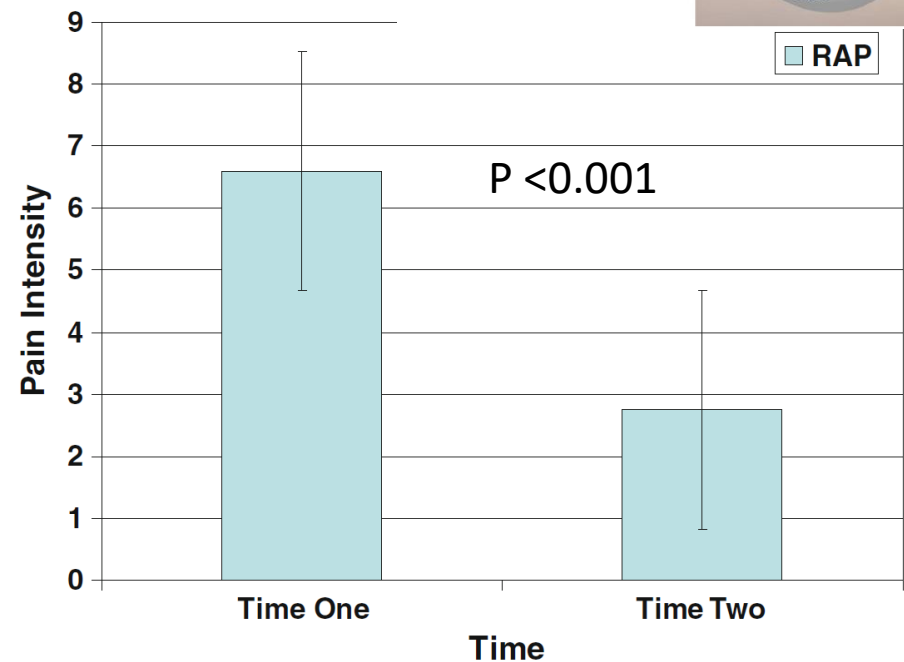
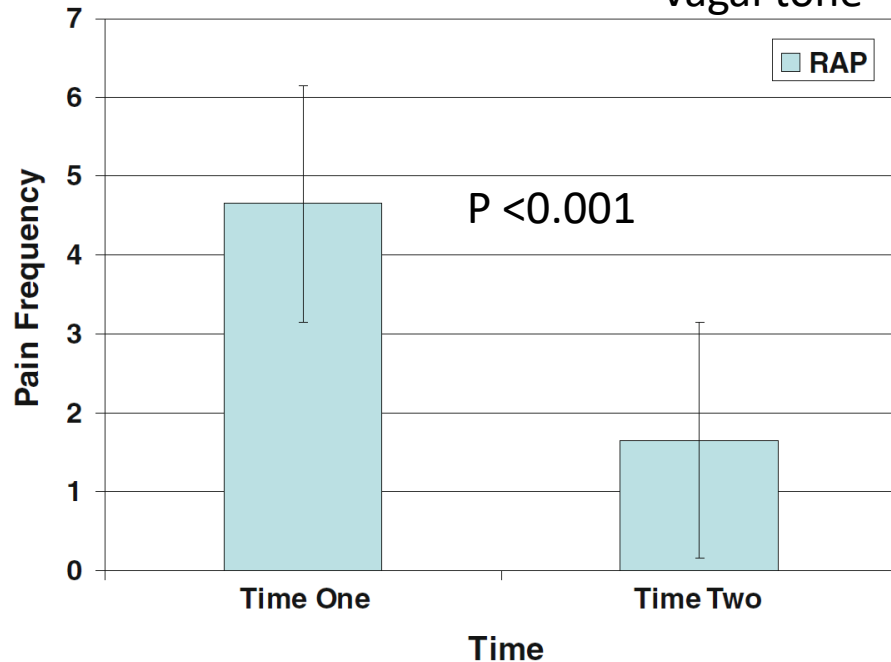
Modulating vagal tone

Appl Psychophysiol Biofeedback (2010) 35:199–206
DOI 10.1007/s10484-010-9128-8

Restoration of Vagal Tone: A Possible Mechanism for Functional Abdominal Pain

Erik Sowder · Richard Gevirtz · Warren Shapiro · Crystal Ebert

$r = 0.54$ $p < 0.018$
for increased
vagal tone



Also, Zautra et al Pain 2010, Bonaz NGM, 2016

Prevention is better than cure?.....

Case 2

- 26 male STC for pancolitis (ileostomy, mucus fistula)
- developed neuropathic pain syndrome on lots of opiates almost immediately → protracted readmission (slow penny drop!)
- Settled well with opiate reduction and gabapentin and TCA over next several months
- Weaned off all analgesics but now wants pouch!

REVIEW ARTICLE

Gabapentin: a multimodal perioperative drug?

Beyond Neuropathic Pain

Gabapentin Use in Cancer Pain and Perioperative Pain

Clin J Pain • Volume 30, Number 7, July 2014

*Peter Z. Yan, MD, Paul M. Butler, MD, PhD, Donna Kurowski, MD,
and Michael D. Perloff, MD, PhD*

- Option 1 To minimise the chances most -Do not have the operation
- Or if he does he has to accept there is a risk that he will have on going pain which may not settle second time around
- Option 2 600mg gabapentin as a premed higher doses have greater side effects (and so if admitted DOS then this can be a problem).
- Chose option 2 and successful pouch with no post-op pain



I SURVIVED

**A TUMMY
ACHE**

