Neuropathic Pain
Where Guidelines Fail

Dr Andrew J Souter MB ChB FRCA FFPMRCA
Consultant in Anaesthesia and Pain Medicine
Bath UK

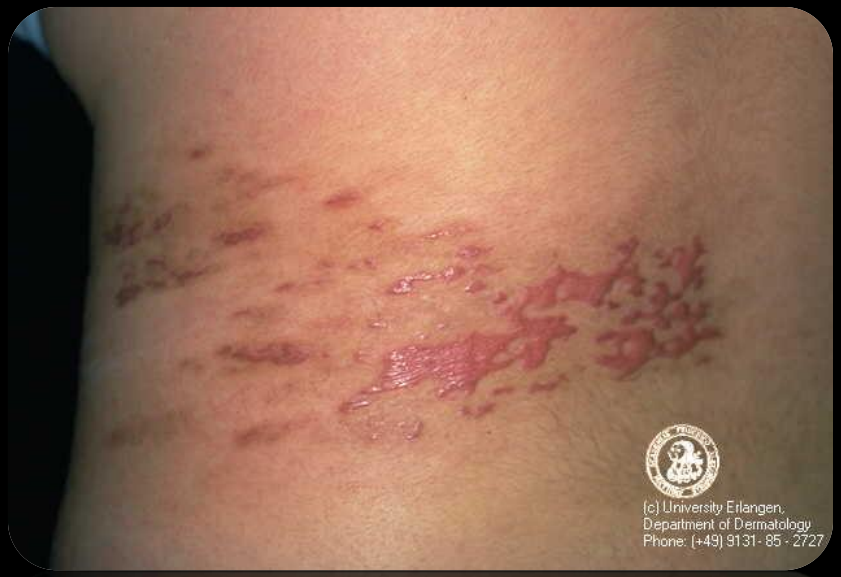
Neuropathic pain; definition

"pain due to an abnormal function of a neuron in the peripheral or central nervous system in the absence of a noxious stimulus"

What is neuropathic pain?

- Pain initiated or caused by a primary lesion or dysfunction in the peripheral or central nervous system[1]
- The painful region may not necessarily be the same as the site of injury – pain occurs in the neurological territory of the affected structure (nerve, root, spinal cord, brain)
- Almost always a chronic condition (e.g. postherpetic neuralgia [PHN], central post stroke pain [CPSP])[2]
- Responds poorly to conventional analgesics[3]

1. Merskey H, Bogduk N (Eds). Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms (2nd Ed). Seattle: IASP Press, 1994
2. Dworkin RH, Backonja M, Rowbotham MC *et al*. Arch Neurol 2003; 60(11): 1524–1534
3. Serpell M. Neuropathic pain. In: Peripheral Neuropathy & Neuropathic Pain Under the Spotlight. Nantwich: The Neuropathy Trust, 2004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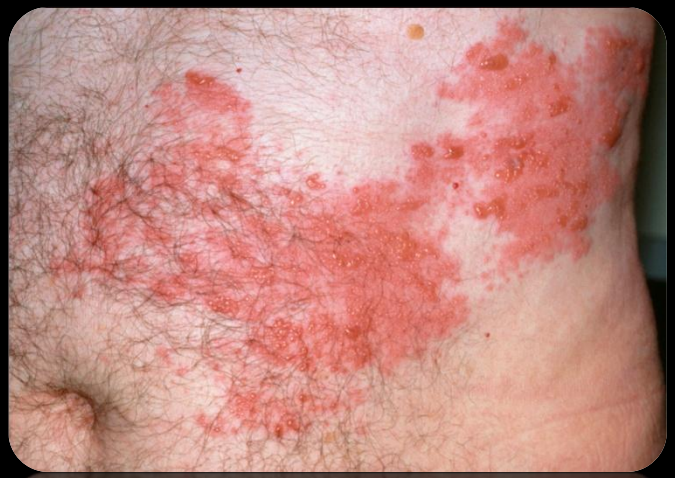
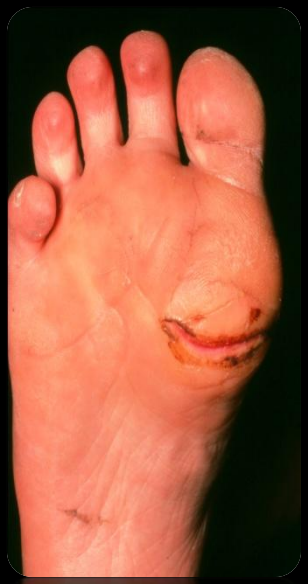
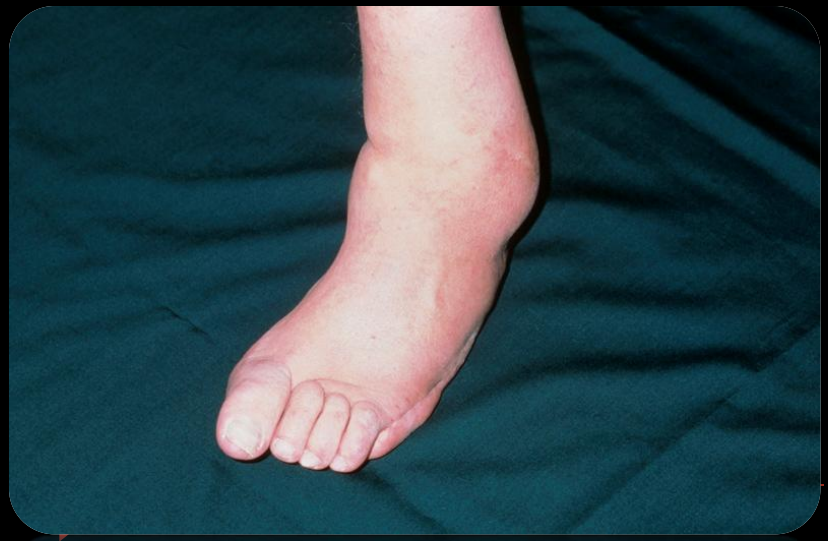
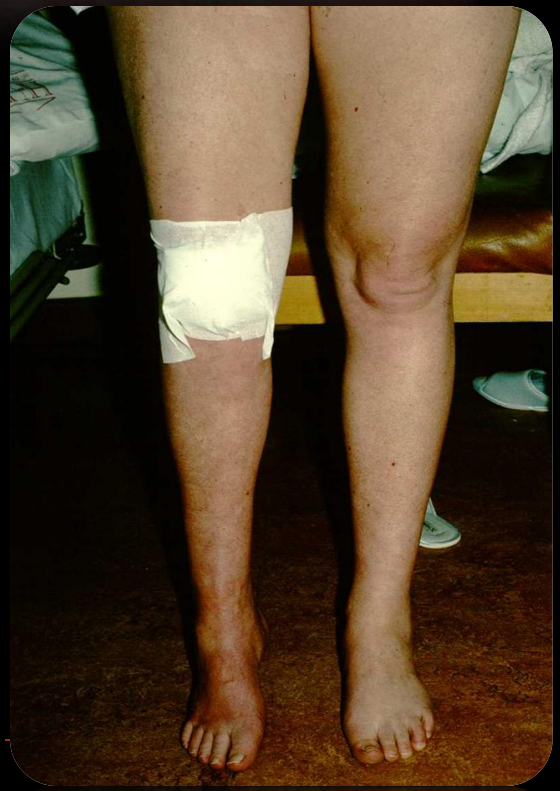
Phone: (+49) 9131 - 85 - 2727









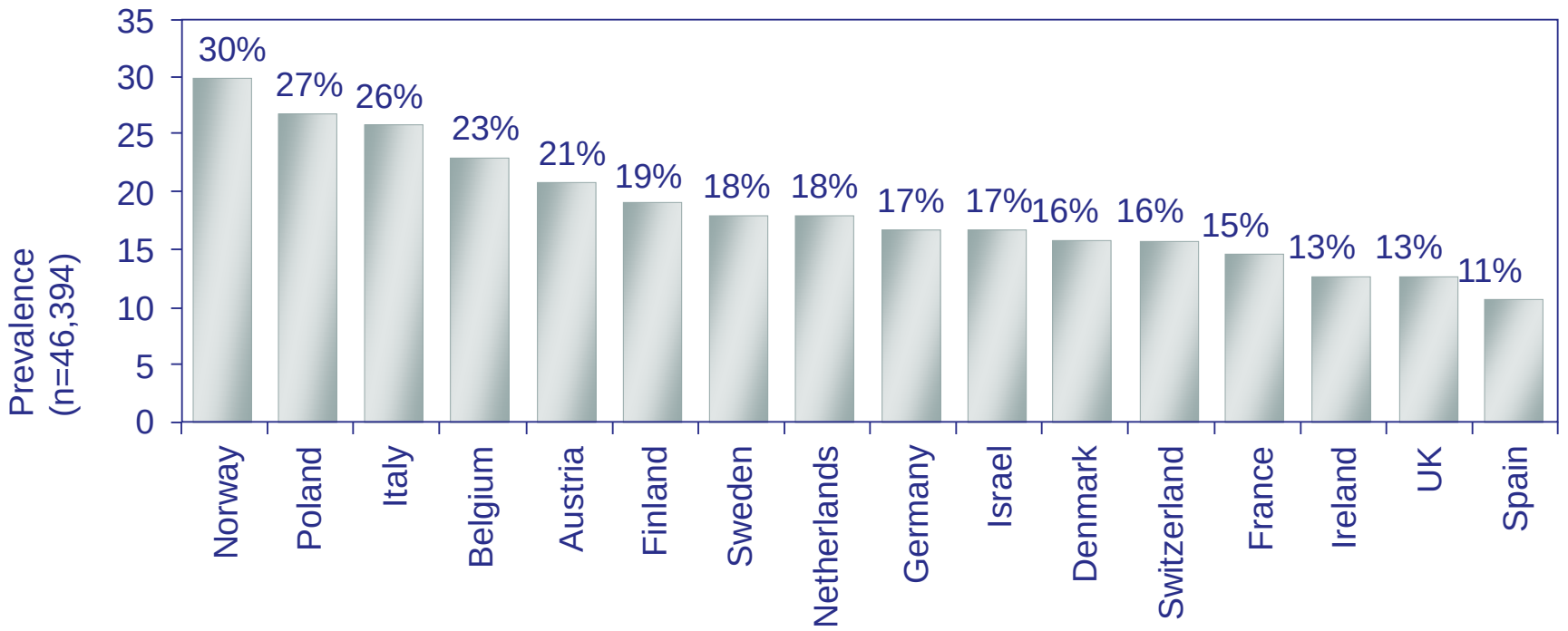
Problems in the treatment of neuropathic pain

- Failure to diagnose neuropathic pain
  - Undertreatment
- Efficacy
- Pain associated symptoms
  - Sleep, mood, social aspects
- Side effects
- Reliance on ineffective drugs
- Reliance on monotherapy
- Expense of non-pharmacological treatment

Diagnosis

- Underdiagnosis
- Undertreatment

Prevalence of chronic pain across Europe



1. Pain In Europe – A Report – Janet Fricker in association with Mundipharma International Ltd.

UK survey of pain of predominantly neuropathic origin

- 6000 questionnaires were mailed
  - 3002 questionnaires were completed (52.4%)
  - 2957 questionnaires could be assessed for presence or absence of chronic pain
- 241 had a positive S-LANSS score (8.2%; 95% CI: 7.2–9.2)

1. Torrance N, Smith BH, Bennett MI *et al*. J Pain 2006; 7(4): 281–289

Diagnosis of neuropathic pain

- History
  - Burning lancinating dysaesthetic pain
  - Paraesthesia, hyperaesthesia, anaesthesia
- Examination
  - Hyperalgesia, allodynia
  - Anaesthesia, hypoaesthesia
- Validated scoring systems
  - LANSS
  - Paindetect

painDETECT

PAIN QUESTIONNAIRE

Date: _____ Patient: Last name: _____ First name: _____

How would you assess your pain **now**, at this moment?

0 1 2 3 4 5 6 7 8 9 10

none max.

How strong was the **strongest** pain during the past 4 weeks?

0 1 2 3 4 5 6 7 8 9 10

none max.

How strong was the pain during the past 4 weeks **on average**?

0 1 2 3 4 5 6 7 8 9 10

none max.

Mark the picture that best describes the course of your pain:

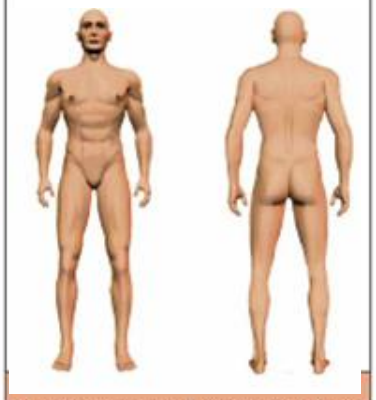
Persistent pain with slight fluctuations ☐

Persistent pain with pain attacks ☐

Pain attacks without pain between them ☐

Pain attacks with pain between them ☐

Please mark your main area of pain



Does your pain radiate to other regions of your body? yes ☐ no ☐

If yes, please draw the direction in which the pain radiates.

Do you suffer from a burning sensation (e.g., stinging nettles) in the marked areas?

never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Do you have a tingling or prickling sensation in the area of your pain (like crawling ants or electrical tingling)?

never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Is light touching (clothing, a blanket) in this area painful?

never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Do you have sudden pain attacks in the area of your pain, like electric shocks?

never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Is cold or heat (bath water) in this area occasionally painful?

never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Do you suffer from a sensation of numbness in the areas that you marked?

never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

Does slight pressure in this area, e.g., with a finger, trigger pain?

never ☐ hardly noticed ☐ slightly ☐ moderately ☐ strongly ☐ very strongly ☐

(To be filled out by the physician)

never	hardly noticed	slightly	moderately	strongly	very strongly
x 0 = 0	x 1 =	x 2 =	x 3 =	x 4 =	x 5 =

Total score ☐☐ **out of 35**

painDETECT

SCORING OF PAIN QUESTIONNAIRE

e: _____ Patient: Last name: _____ First name: _____

Please transfer the total score from the pain questionnaire:

Total score ☐☐

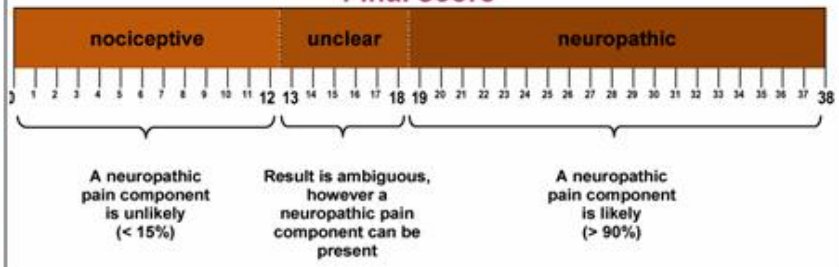
ease add up the following numbers, depending on the marked pain behavior pattern and the pain diation. Then total up the final score:

 Persistent pain with slight fluctuations	0	
 Persistent pain with pain attacks	- 1	if marked, or
 Pain attacks without pain between them	+ 1	if marked, or
 Pain attacks with pain between them	+ 1	if marked
 Radiating pains?	+ 2	if yes

Final score ☐☐

Screening Result

Final score



This sheet does not replace medical diagnostics.
It is used for screening the presence of a neuropathic pain component.

Development/Reference: R. Freynhagen, T.R. Tölle, U. Gockel, R. Baron / DGN 2005

Neuropathic pain: Clinical assessment

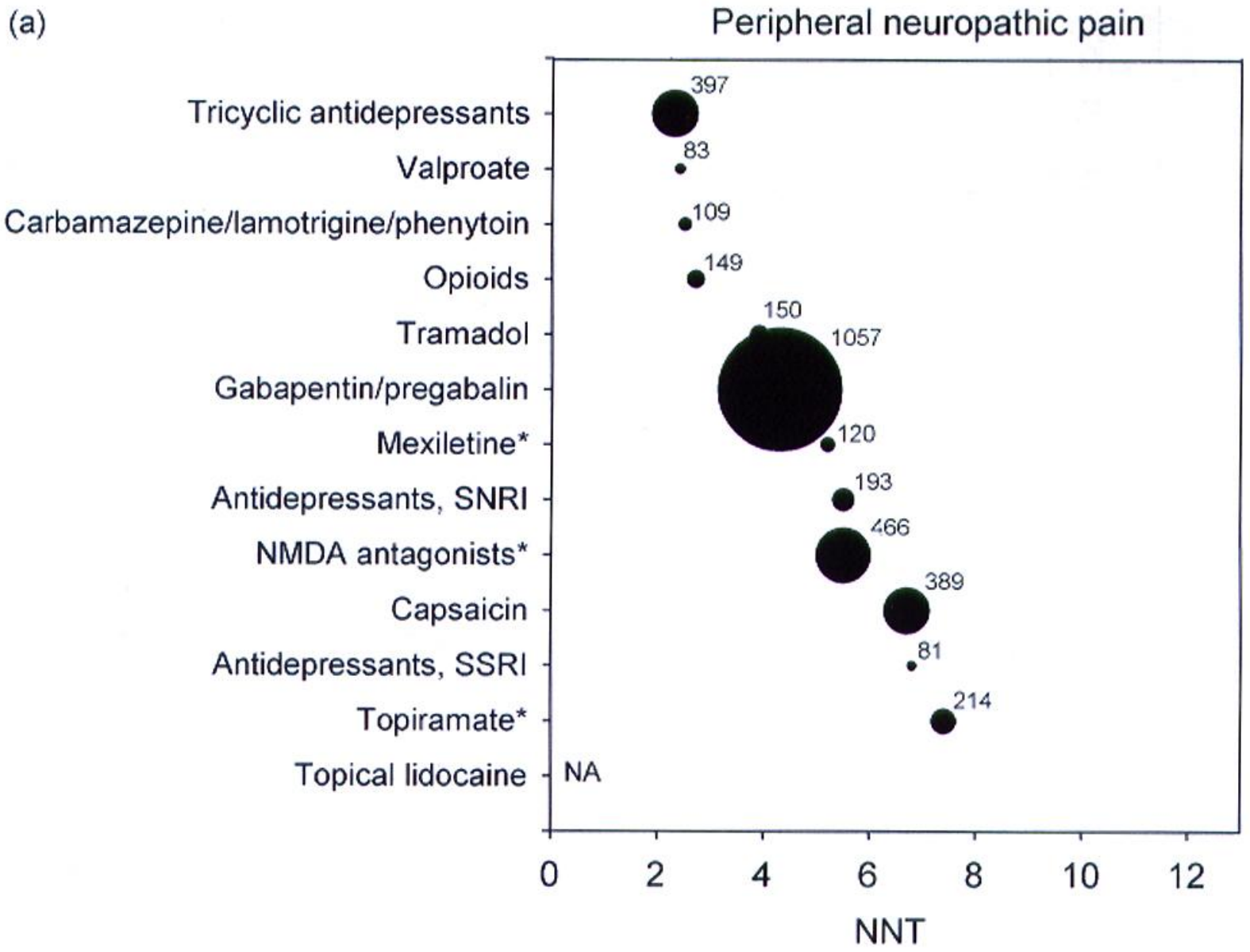
- THE S-LANSS PAIN SCORE (Leeds Assessment of Neuropathic Symptoms and Signs)
- Five symptom items and two examination items.
  - 1. In the area where you have pain, do you also have 'pins and needles', tingling or prickling sensations?
  - 2. Does the painful area change colour
  - 3. Does your pain make the affected skin abnormally sensitive to touch?

- 4. Does your pain come on suddenly and in bursts for no apparent reason when you are completely still?
- 5. In the area where you have pain, does your skin feel unusually hot like a burning pain?
- 6. Gently rub the painful area with your index finger. How does this rubbing feel in the painful area?
- 7. Gently press on the painful area with your finger tip. How does this feel in the painful area?

Whatever the definition it's difficult to treat

however

Pharmacotherapy for neuropathic pain is highly evidence based



Finnerup NB et al 2005 Pain 118

Conventional drugs

- Tricyclic antidepressants
  - Amitriptyline
  - Nortryptiline
  - Dosulepin
- Antiepileptic drugs
  - Carbemazepine
  - Oxcarbazepine
  - Na Valproate

Gabapentin and Pregabalin

- Bind to $\alpha 2$ subunit of Ca^{++} channel
- Reduce pain, allodynia, hyperalgesia

- Pregabalin: 11 RCTs n=2887 NNT 4

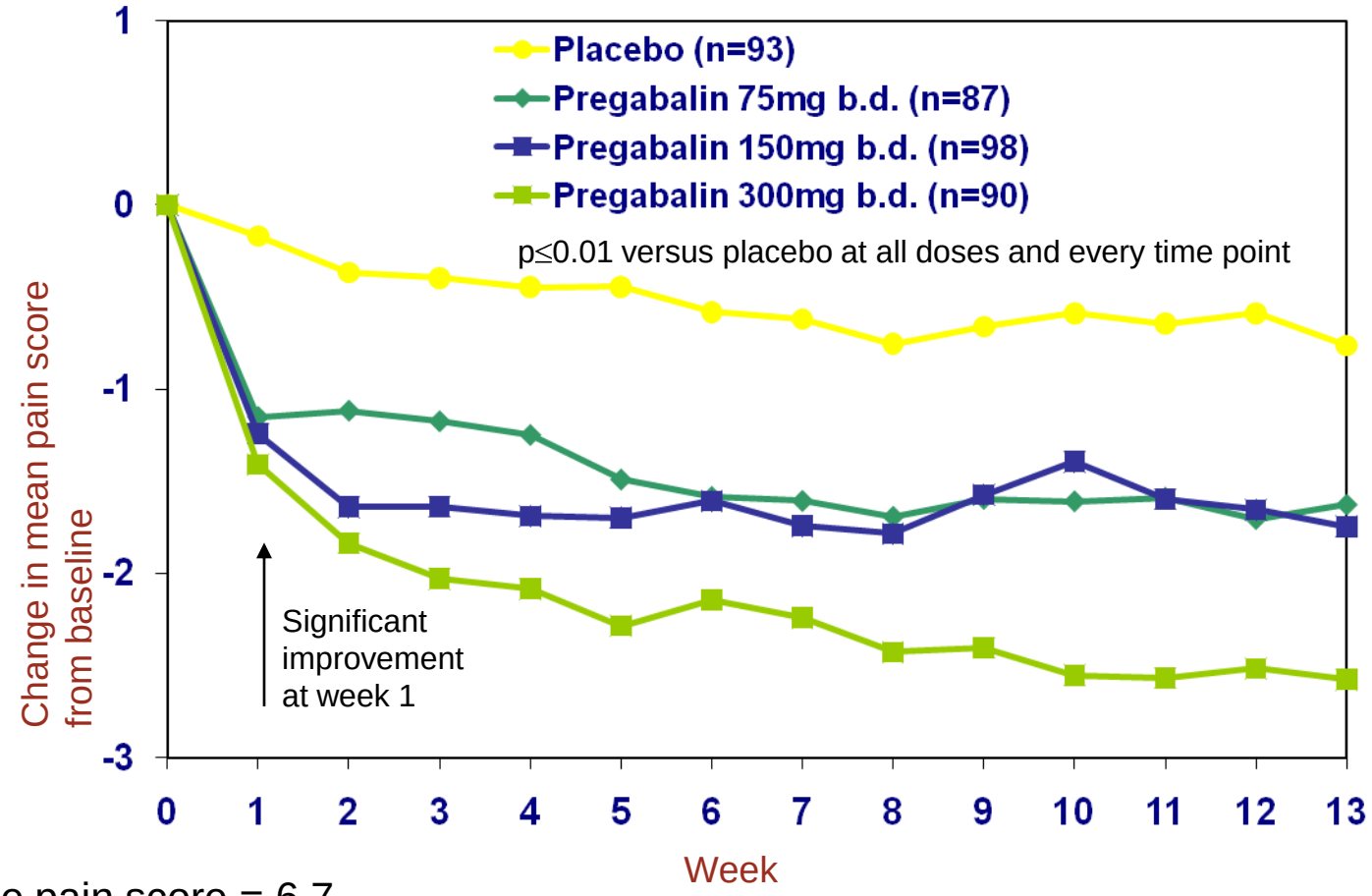
Topical Agents

- Lidocaine 5% patch
- Capsaicin 0.075% cream
- (Capsaicin 8% “Qutenza” Astellas)

Efficacy: Lack of efficacy?

Reduction in pain scores; is it enough?

Pain reduction over 13 weeks in postherpetic neuralgia



Baseline pain score = 6.7

1. Van Seventer R, Feister HA, Young JP Jr *et al*. Curr Med Res Opin 2006; 22(2): 375–384

Inneffective Drugs: Opioids?

Opioids in neuropathic pain

- Poor evidence for codeine, fentanyl, methadone, buprenorphine
- Better evidence for morphine, oxycodone, tramadol
- Problems with side-effects
- Need for protocols to avoid misuse

Tramadol

- Noradrenaline and Serotonin reuptake inhibitor
- Weak μ-receptor agonist
- 5 studies show efficacy in NP

Monotherapy vs combination therapy

Drugs in combination

- Morphine plus Gabapentin (vs active placebo or either alone)
  - improved analgesia
  - lower doses
  - less side effects

NEJM. 2005 Mar 31;352(13):1324-34.

New drugs

Antidepressants: Duloxetine

- Mixed serotonin and NA uptake inhibition (SNRI)
- Large study of duloxetine in diabetic neuropathic pain: NNT 4
- Less sedation than tricyclic antidepressants

Goldstein, Pain, 2005 , Volume 116, Issue 1, Pages 109-118

Qutenza: 8% topical capsaicin (Astellas)

- Prolonged efficacy (>16 weeks) in
  - PHN
  - HIV associated NP
- TRPV1 receptor agonist
- Reduction in sub-epithelial nociceptive nerve endings
- Application is hospital based
- ? Cost

M. Backonja *The Lancet Neurology*, 2008;7 12: 1106-1112

D. M. Simpson *Neurology* 2008;70: 2305-2313

Pain related effects

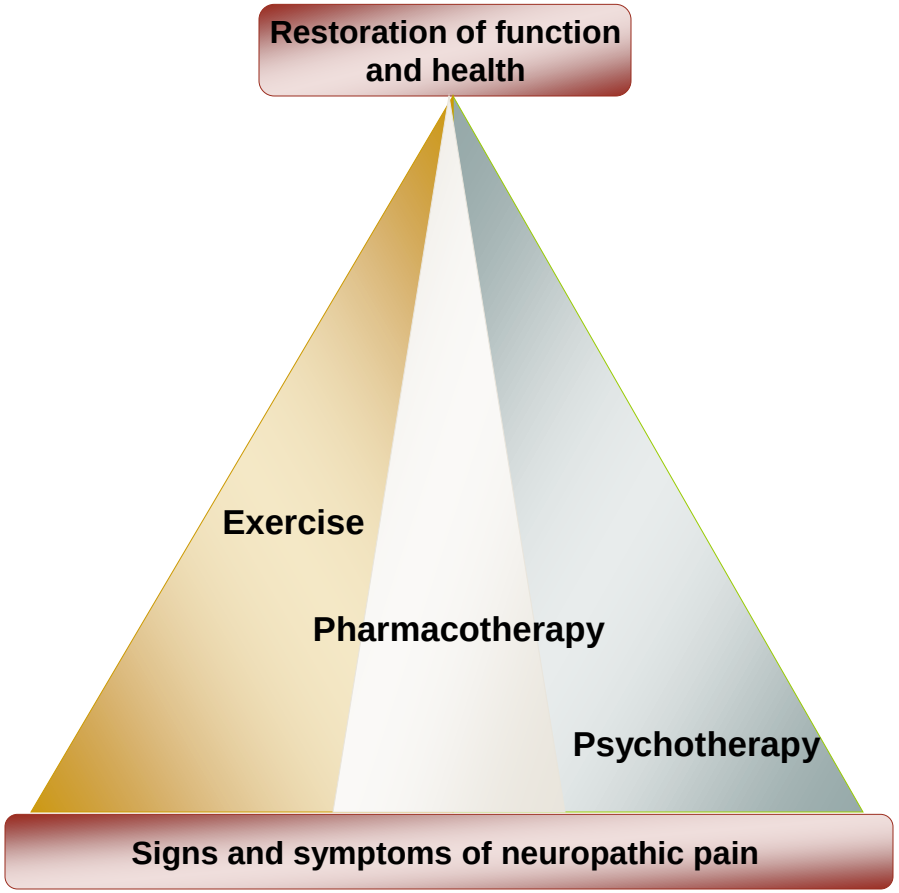
- Sleep
- Mood
- Relationships
- Activity
- Work

The 3 R's in the treatment of chronic pain

- ***R*** eassurance (psychotherapy)
- ***R*** elief (pharmacotherapy)
- ***R*** ehabilitation (physiotherapy)

Adapted from: Raja SN, Grabow TS. Anesthesiology 2002; 96(5): 1254–1260

Treatment should involve a three-pronged approach

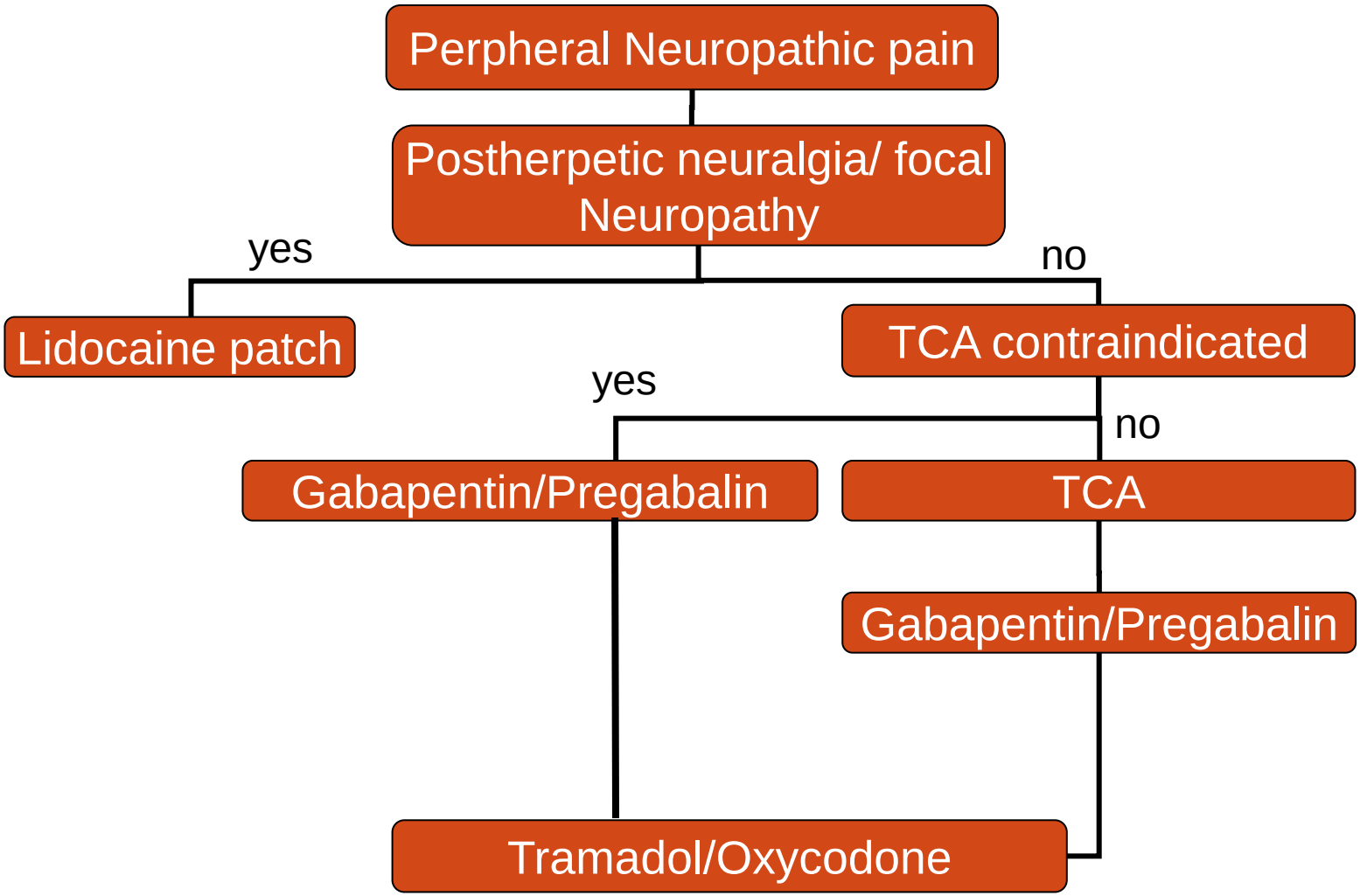


- The ultimate treatment goal is pain relief and restoration of function and health
- No single therapeutic modality achieves this goal in all patients
- Physiotherapy, pharmacotherapy and psychotherapy all play a role

Adapted from: Raja SN, Grabow TS. Anesthesiology 2002; 96(5): 1254–1260

Evidence based guidelines

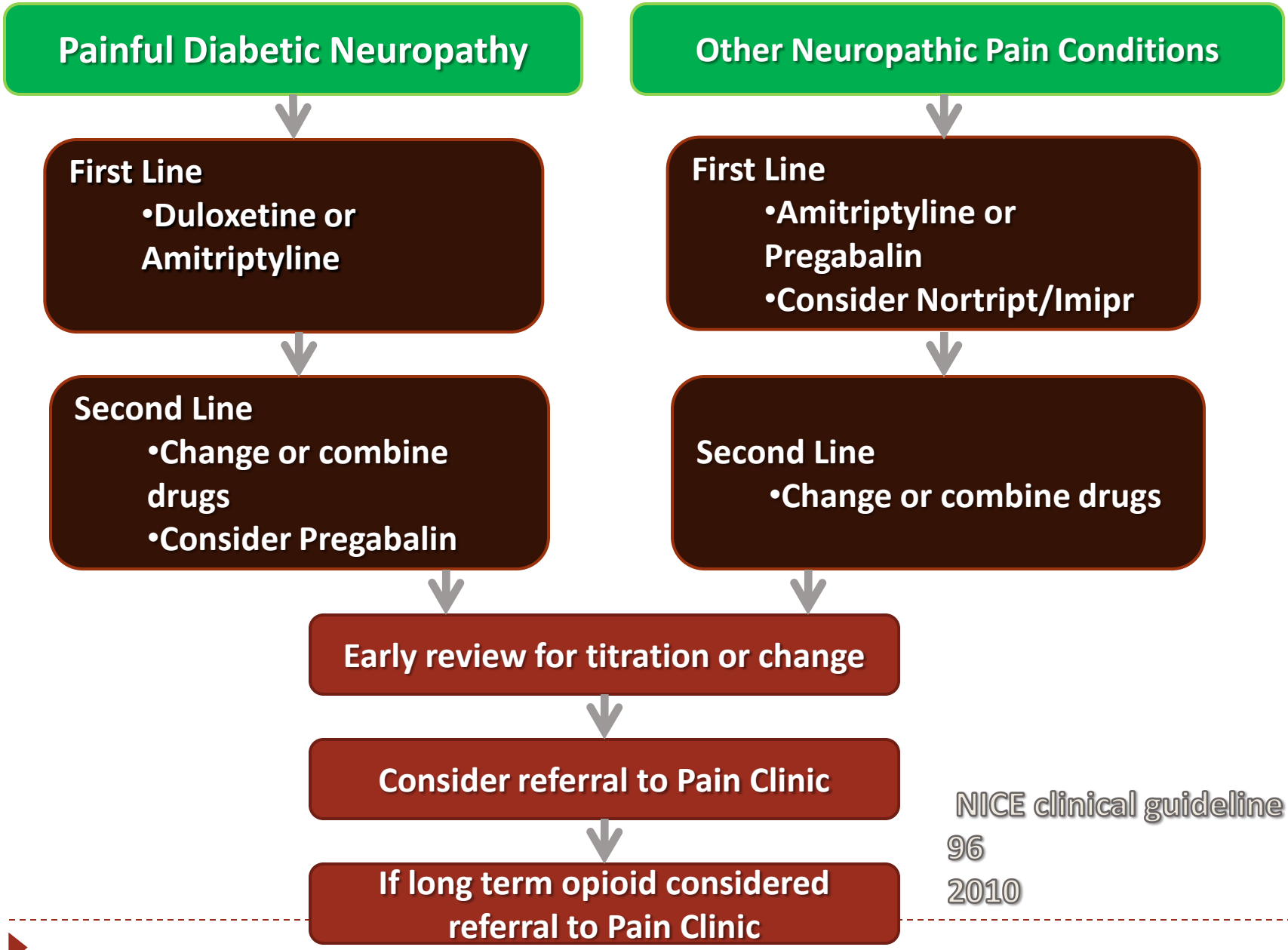
- Finnerup et al 2005
- European Federation of Neurological Societies (EFNS) 2006 & 2009
- National Institute of Clinical Excellence (NICE) UK 2010



After Finnerup NB et al 2005 Pain 118

Condition	Level A	Level B	1st line	2nd line
Painful	Gabapentin	Lamotrigine	Gabapentin	Lamotrigine
Peripheral	Opioids		Pregabalin	Opioids
Neuropathy	Pregabalin		TCA	SNRI
	SNRI			Tramadol
	TCA			
	Tramadol			
Post	Gabapentin	Capsaicin topical	Gabapentin	Capsaicin
Herpetic	Opioids	Lidocaine topical	Pregabalin	Opioids
Neuralgia	Pregabalin	Tramadol	Lidocaine topical	Tramadol
	TCA	Vaproate	TCA	Valproate
Trigeminal	CBZ	OXC	OXC	Surgery
Neuralgia			CBZ	
Central		Cannabinoids MS)	Amitriptyline	Cannabinoids
pain		Gabapentin (SCI)	Gabapentin	Lamotrigine
		Pregabalin (SCI)	Pregabalin	Opioids
		Amitriptyline(CPSP)		
		Lamotrigine(CPSP)		

2006 EFNS European Journal of Neurology 13, 1153–1169



NICE clinical guideline 96
2010

Problems

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  - Undertreatment
- Efficacy
- Pain associated symptoms
  - Sleep, mood, reduced exercise, social aspects
- Side effects
- Reliance on ineffective drugs
- Reliance on monotherapy
- Expense of non-pharmacological treatment

Solutions

- Better and earlier diagnosis
- Primary care diagnosis and treatment
- Early referral to pain clinic where ineffective
- Early dose titration and review of treatment
- Change drugs where ineffective
- Combine drugs where ineffective
- Multidisciplinary care
- New treatments