Certificate

Diberikan kepada :

dr. I Putu Eka Widyadharma M.Sc, Sp.S(K)

Yang berperan serta sebagai :

Pembicara

Pada Seminar dan Lokakarya sehari,

SYMPOSIUM AND WORKSHOP
COMPREHENSIVE MANAGEMENT OF NEUROPATHIC PAIN

Sabtu, 2 Mei 2015, Hotel Harris Kelapa Gading, Jakarta

AKREDITASI IDI : Peserta 5 SKP, Pembicara 8 SKP, Moderator 2 SKP

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Ketua PP PERDOSSI

CHRONIC MIXED PAIN MANAGEMENT

I Putu Eka Widyadharma

CURICULUM VITAE

dr. I Putu Eka Widyadharma, M.Sc, Sp.S(K)

Pendidikan :

S1	:	Universitas Udayana Denpasar Tahun 1997
Profesi	:	Universitas Udayana Denpasar Tahun 1999
S2 –Clinical Medicine	:	Universitas Gadjah Mada Yogyakarta Tahun 2009
Spesialis Saraf	:	Universitas Gadjah Mada Yogyakarta Tahun 2009
Konsultan Nyeri	:	Kolegium Neurologi Indonesia Tahun 2014

Pelatihan/Workshop :

- Neuropathic pain Management, Manila, Phillipina, 2011
- Pain Management, Mumbai, India, 2012
- Diabetic Neuropathy Workshop, , Manila, Phillipina, 2012
- USG for Neurologist, Jakarta, 2012
- World Congress of Pain, Milan, Italy 2012
- USG Guidance for Interventional Pain management, Bandung 2012
- Pain Management Camp, Singapore 2013
- Interventional Pain Management, Medan 2013
- USG Guidance In Pain management, Yogyakarta 2014

Pekerjaan /Jabatan :

- Staf Subdivisi Nyeri dan Nyeri Kepala Bag/SMF Neurologi FK UNUD-RSUP Sanglah Denpasar
- Kepala Unit *Health Technology Assesment* (HTA) RSPTN Udayana
- Sekretaris PERDOSSI Cabang Denpasar
- Sekretaris *Indonesian Pain Society* Cabang Denpasar
- Anggota *International Association for the Study of Pain* (IASP)
- Anggota *Neuropathic Pain Special Interest Group of IASP* (NeuPSIG)
- Anggota *Pain Education Special Interest Group of IASP*
- Anggota *ASIA Neuropathic Pain Expert Panel*
- Anggota Kelompok Studi Nyeri PERDOSSI
- Anggota ICE-EBM Network
- Anggota Tim Penanggulangan Nyeri RSUP Sanglah Denpasar

Defining Pain

What is pain?

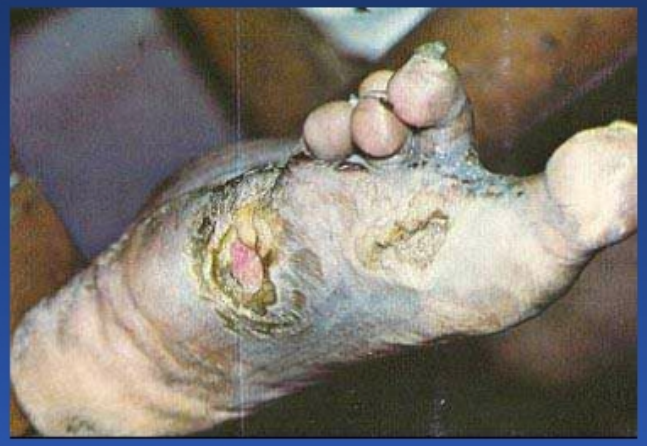
"An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."

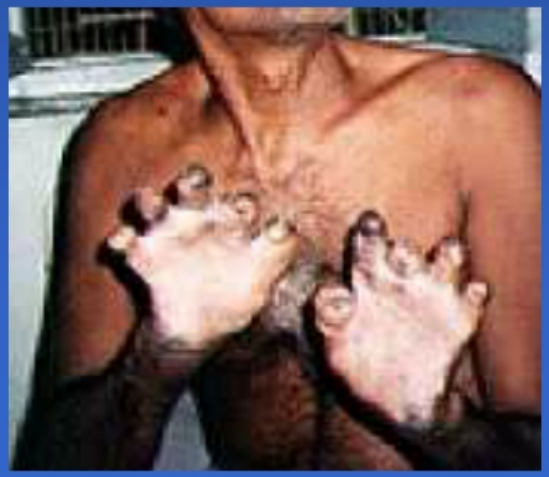
International Association for the Study of Pain (IASP) 1994
Kyoto Protocol IASP 2008

Merskey H et al. (Eds) In: Classification of Chronic Pain: Descriptions of Chronic Pain Syndromes and Definitions of Pain Terms. 1994:209-212.
Loeser JD, Treede RD. The Kyoto Protocol of IASP Basic Pain Terminology. *Pain* 2008;137:473-477.

Pain: good or bad?

Consequences Of Being Unable to Feel Pain

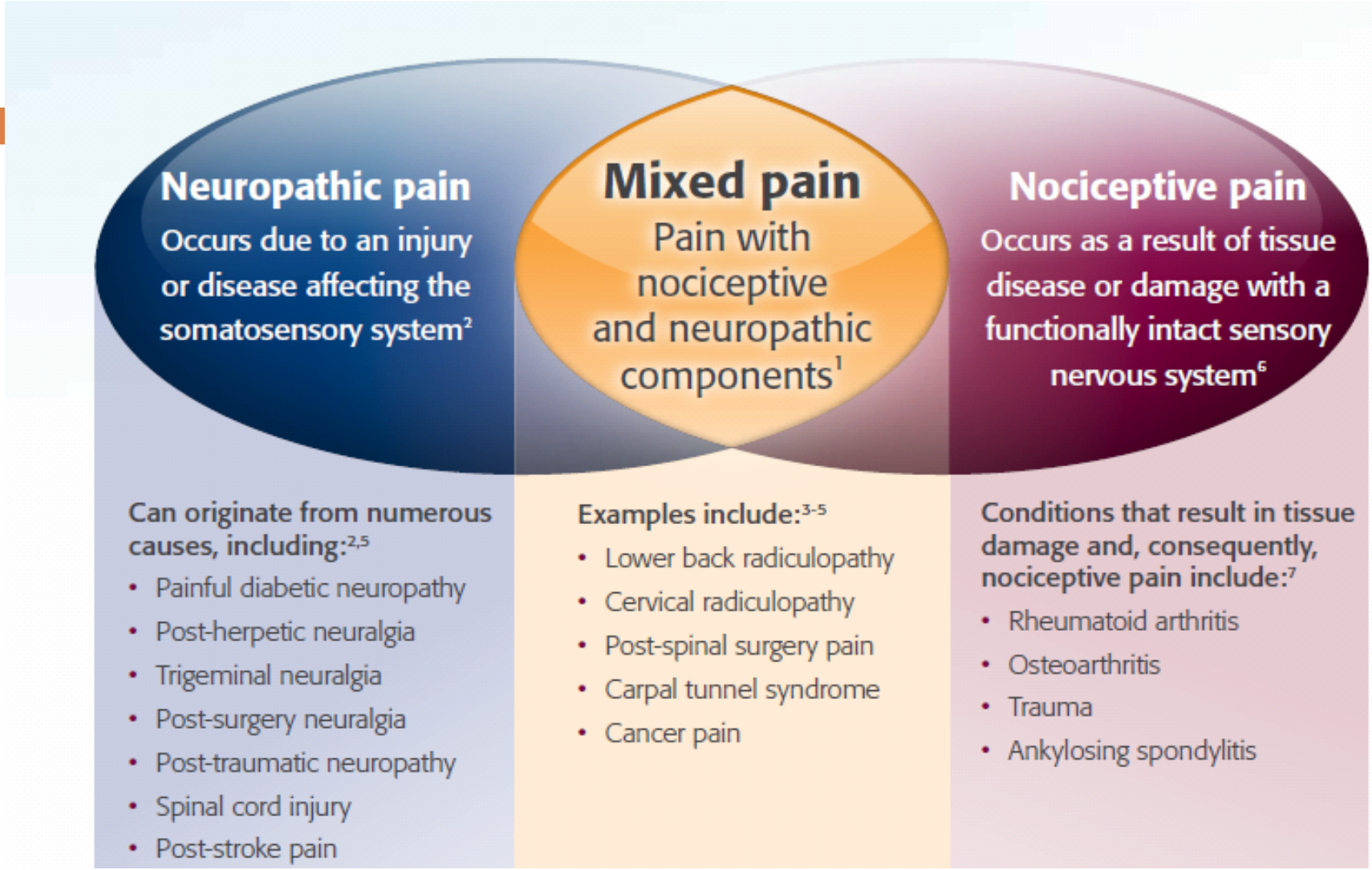




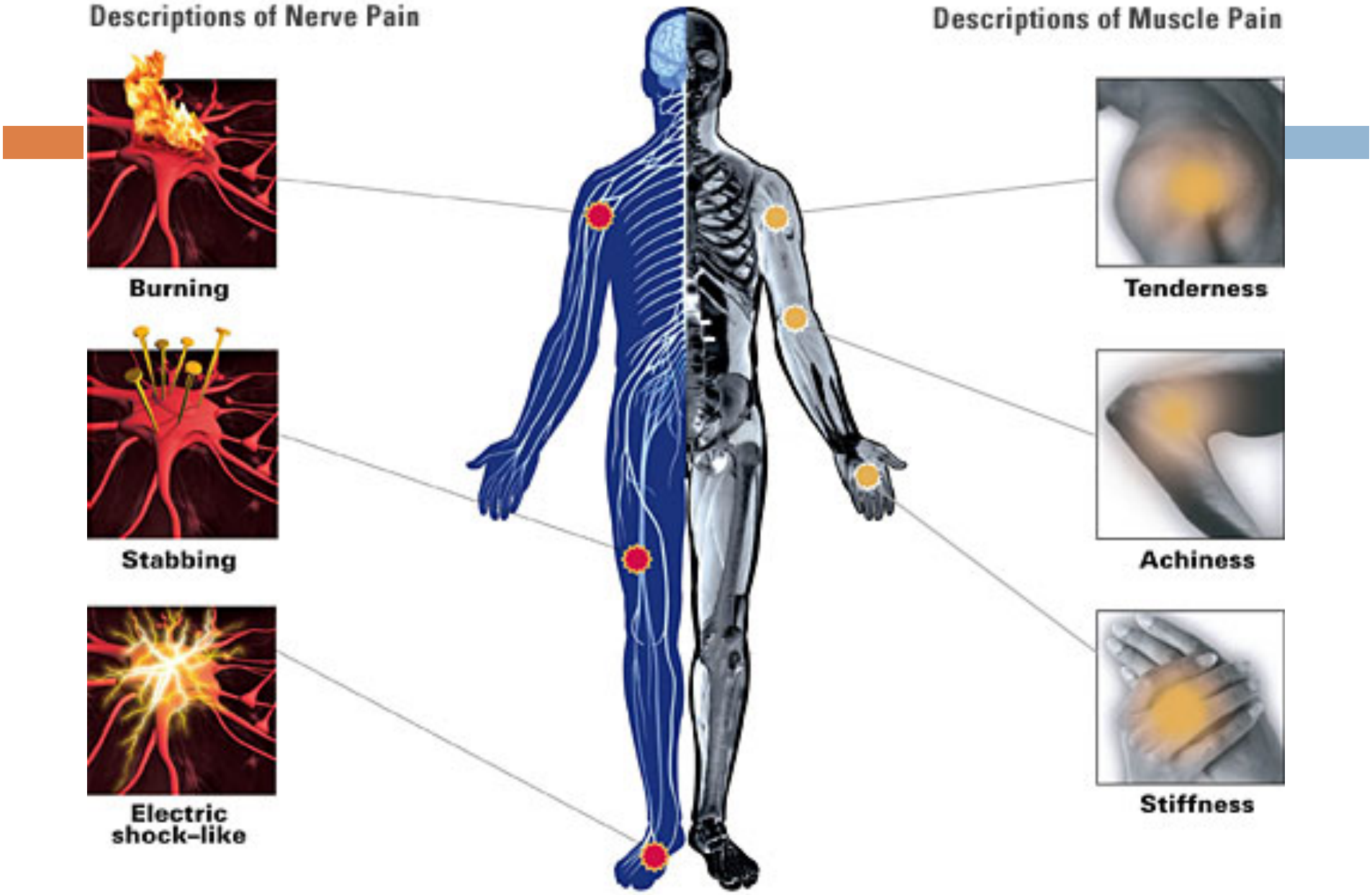
Consequences Of Being Unable to Feel Pain

From Fields 1987

Classification of Pain



References: 1. Baron R *et al.* Neuropathic pain: Diagnosis, pathophysiological mechanisms and treatment. *Lancet Neurol* 2010; 9: 807-9. **2.** Freynhagen R, Bennett MI. Diagnosis and management of neuropathic pain. *BMJ* 2009; 339: 391-95. **3.** Freynhagen R, Baron R. The evaluation of neuropathic components in low back pain. *Curr Pain Headache Rep* 2009; 13: 185-190. **4.** Davis MP, Walsh D. Epidemiology of cancer pain and factors influencing poor pain control. *Am J Hosp Palliat Care* 2004; 21: 137-42. **5.** Sadosky A *et al.* A review of the epidemiology of painful diabetic peripheral neuropathy, postherpetic neuralgia, and less commonly studied neuropathic pain conditions. *Pain Pract* 2008; 8: 45-56. **6.** Haanpaa ML *et al.* Assessment of neuropathic pain in primary care. *Am J Med* 2009; 122: S13-S21. **7.** The Merck Manual. Low back pain. April 2008. Available at: http://www.merck.com/mmhe/print/sec06/ch094/ch094b.html. Accessed April 6, 2009.


Descriptions of Nerve Pain
Burning
Stabbing
Electric shock–like
Descriptions of Muscle Pain
Tenderness
Achiness
Stiffness

Definition

- Mixed pain is a combination of nociceptive and neuropathic pain.
- The category of mixed pain should not be ignored as its pathogenesis is a combination of that for neuropathic and nociceptive pain

Chronic pain

- Nociceptive, Neuropathic or both.
- Psychological mechanisms play a major role.
- Attenuated neuroendocrine stress response and have prominent sleep and affective disturbances.

CHRONIC PAIN IS MULTI-FACTORIAL

- Psychologic factors – depression, anxiety, somatization
- Socioeconomic factors – cultural differences, urban poor, gender
- Spiritual factors – spiritual suffering, meaning of pain

- Physical factors – VERY complex neuroanatomy creating the pain sensation, from pain receptors to afferent nerves to spinothalamic tract, to thalamus to cortex with modulators all along the way

- Therefore best approach is multi-disciplinary

Low Back Pain

- is a good example of mixed pain.
- It may have resulted originally from a mechanical injury—which triggered nociceptive pain.
- That same injury may also have led to nerve compression—which produced neuropathic pain.
- Unfortunately, mixed pain types can also be more difficult for doctors to diagnose and treat.

Melnikova I. Pain market. Nat Rev Drug Discov 2010;9:589-90.

Osteoarthritis

- For years osteoarthritis pain has been assumed to be purely nociceptive not neuropathic but a growing body of literature suggests otherwise.
- Two research studies in patients with low back pain used screening tools for neuropathic pain that suggested that 37% and 54% of patients respectively had pain of predominantly neuropathic origin.
- These studies lend evidence to the fact that there is more pain of a mixed origin than was previously thought.

Diagnosis

- Pain assessment is critical to optimise pain management and or interventions.
- Pain of mixed origin is usually chronic.
- In the case of mixed pain syndromes, healthcare professionals are likely to hear elements of both neuropathic and nociceptive pain described by the patient

Diagnosis

- There are no clear guidelines for diagnosing mixed pain as a syndrome in its own right. So it seems reasonable to combine the diagnosis and management of the two components in this case.
- Guidelines recommend the use of diagnostic screening tools like DN4, pain detect or LANSS to differentiate between neuropathic and nociceptive pain

Douleur Neuropathique 4 Questions (DN4)

Bouhassira et al Pain 2005;114:29–36

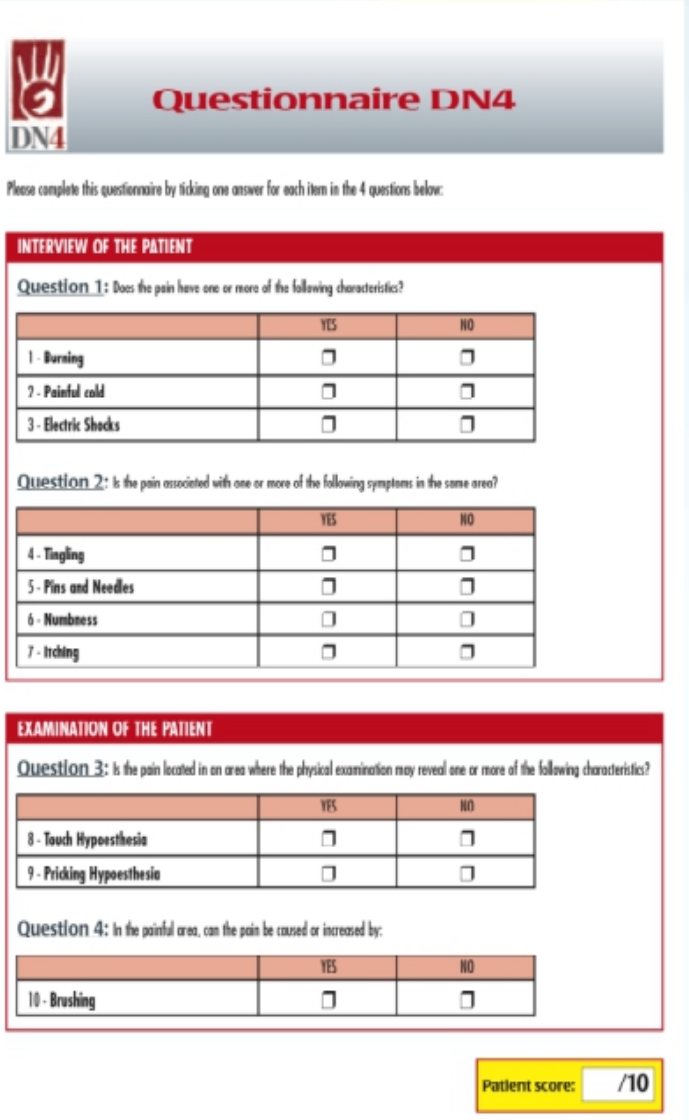
- 7 symptom questions
- 3 clinical examination questions

- Specificity 83%
- Sensitivity 90%

- Score > 4/10 = POPNO*

- 7 symptom questions can be used alone as self administration form

- Multiple validations in several languages



DN4

Questionnaire DN4

Please complete this questionnaire by ticking one answer for each item in the 4 questions below:

INTERVIEW OF THE PATIENT

Question 1: Does the pain have one or more of the following characteristics?

	YES	NO
1 - Burning	❒	❒
2 - Painful cold	❒	❒
3 - Electric Shocks	❒	❒

Question 2: Is the pain associated with one or more of the following symptoms in the same area?

	YES	NO
4 - Tingling	❒	❒
5 - Pins and Needles	❒	❒
6 - Numbness	❒	❒
7 - Itching	❒	❒

EXAMINATION OF THE PATIENT

Question 3: Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?

	YES	NO
8 - Touch Hypoesthesia	❒	❒
9 - Pricking Hypoesthesia	❒	❒

Question 4: In the painful area, can the pain be caused or increased by:

	YES	NO
10 - Brushing	❒	❒

Patient score: /10

* Pain of Predominantly Neuropathic Origin

Box 1: Examples of red flags

- Features of Cauda Equina Syndrome
- Severe worsening of pain, especially at night or when lying down
- Significant trauma
- Weight loss
- History of cancer
- Fever
- Use of intravenous drugs or steroids
- Patients over the age of 50 years

Box 2: Examples of yellow flags

- Attitudes and belief that all pain and activity are harmful
- The presence of "sickness behaviours"—avoidance, extended bed rest
- Low or negative moods
- Social withdrawal
- Compensation pending
- Heavy work, unsociable hours
- An overprotective family OR obvious lack of familial or social support.

Treatment

- From a pharmacological side, both neuropathic and non neuropathic agents will probably be needed in combination to treat mixed pain.

Treatment

- No clear guidelines specific to mixed pain are currently available.
- Mixed pain is likely to need a poly-pharmaceutical approach to manage the different types of pain.
- A combination of neuropathic treatments and NSAIDS and opiates may be needed to cover all aspects of the patient□s pain.

Chronic Pain Management Goals

- Improvements in **nociception, not** curing.
- Decrease pain and suffering
- Increase daily activity.
- Instill hope

THERAPEUTIC MODALITIES

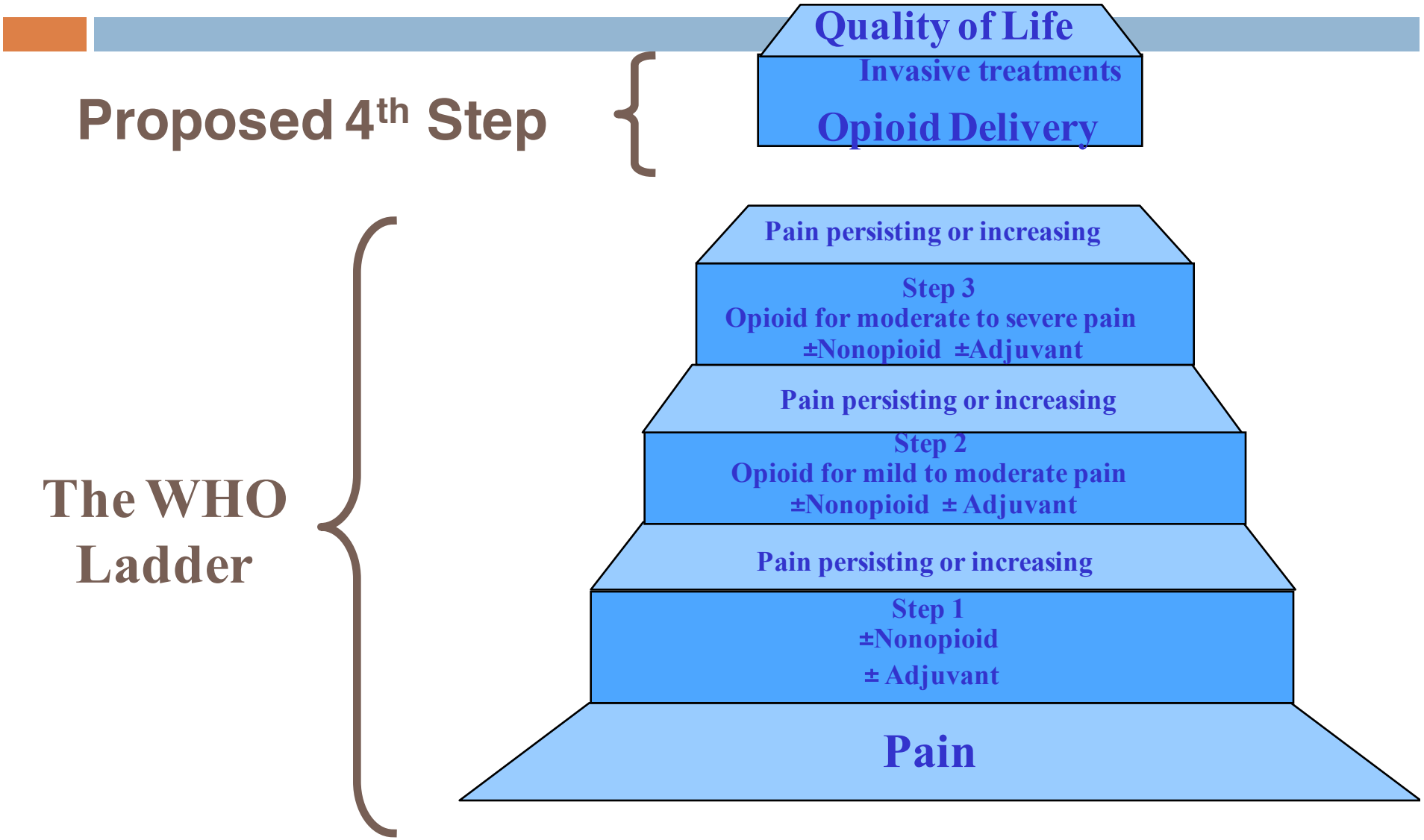
1. PHARMACOLOGICAL.
2. PHYSICAL MEASURES/NON PHARMACOLOGICAL.
3. PSYCHOLOGICAL MEASURES.
4. INVASIVE TECHNIQUES.

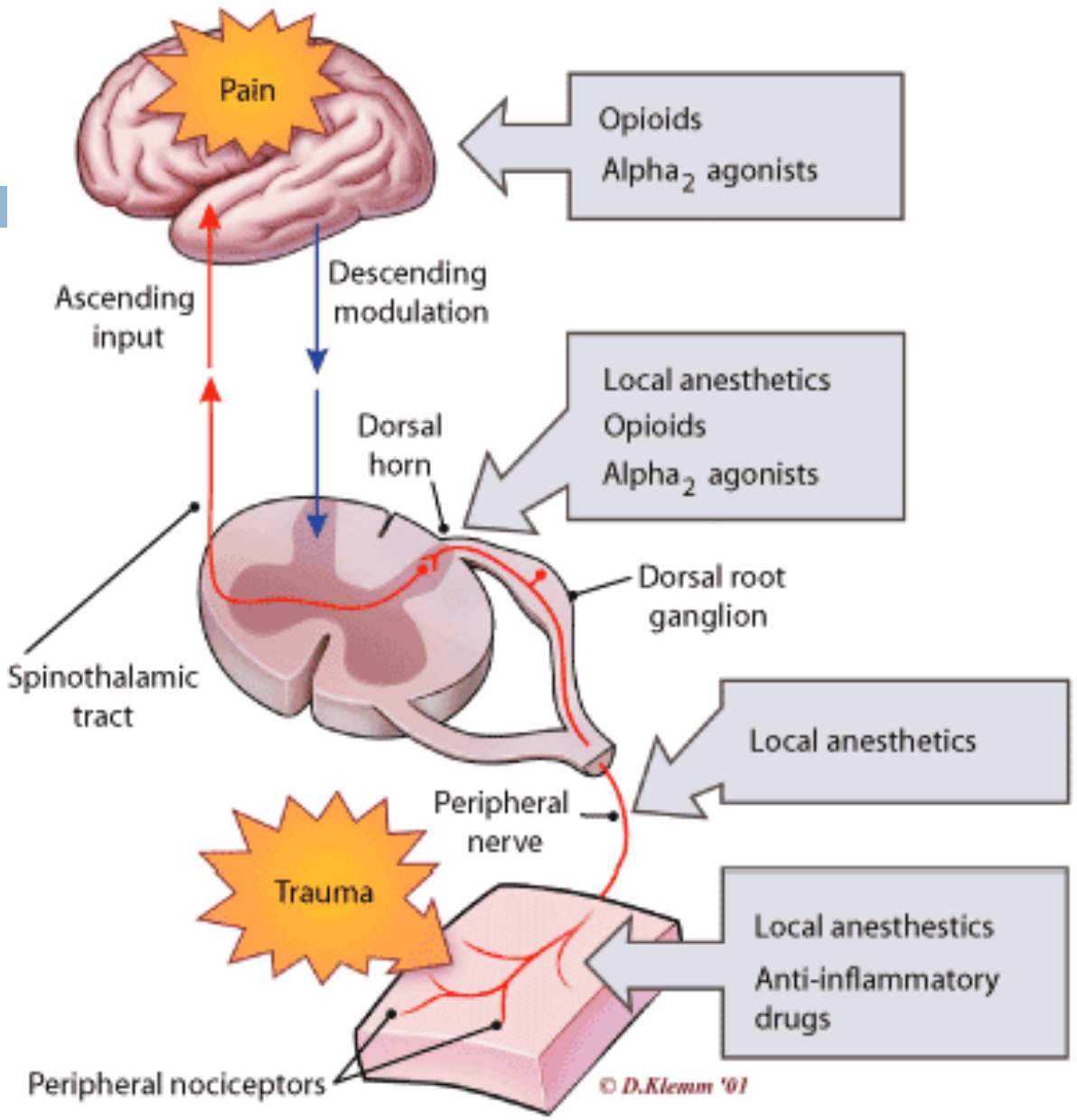
PHARMACOLOGIC CONTROL OF PAIN

- About half of hospitalized patients who have pain are under-medicated.
- Children are at particular risk of poor pain control methods.
- Medications are given as:
  - PRN – "as needed"
  - As a prescribed schedule

WHO PAIN RELIEF LADDER

Modified WHO Analgesic Ladder




Pain
Opioids
Alpha2 agonists
Ascending input
Descending modulation
Local anesthetics
Opioids
Alpha2 agonists
Dorsal horn
Dorsal root ganglion
Spinothalamic tract
Local anesthetics
Peripheral nerve
Trauma
Local anesthestics
Anti-inflammatory drugs
Peripheral nociceptors
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ANALGESIC MEDICATIONS

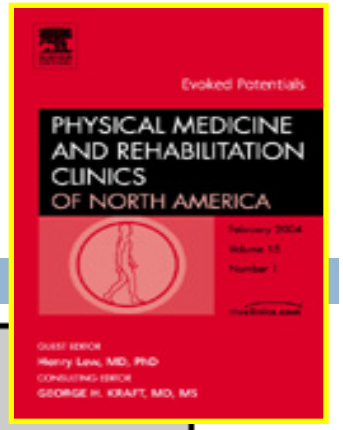


Table 2
Analgesic medications

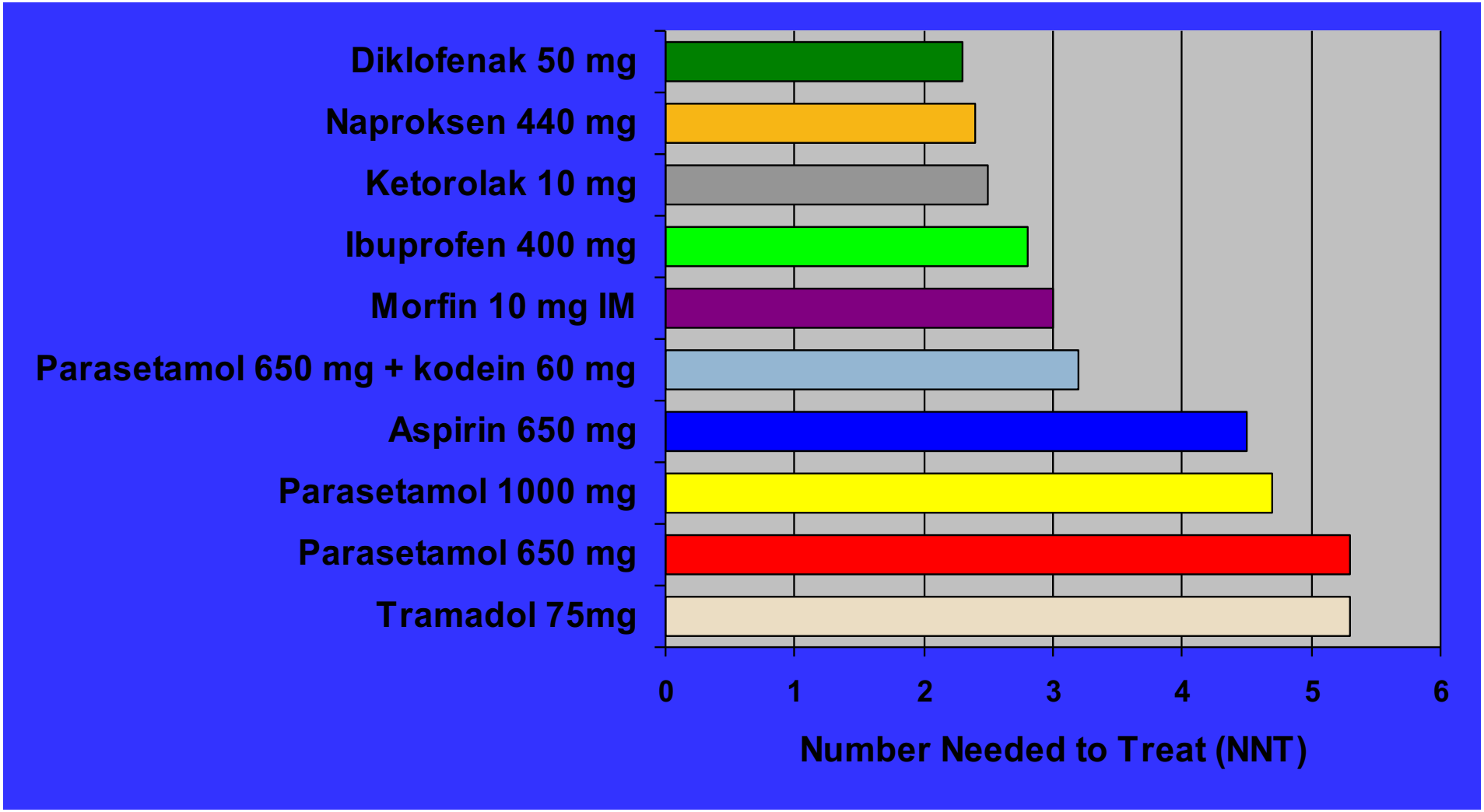
Drug	Recommended Maximum Dose
Acetaminophen	650 mg PO 5 × per day (3250 mg/24 h)
Ibuprofen	800 mg PO QID (3.2 g/24 hs)
Naproxen	500 mg PO BID (1 g/24 h)
Sulindac	200 mg PO BID (600 mg/24 h)
Indomethacin	50 mg PO TID (150 mg/24 h)
Salsalate	1500 mg BID (3 g/24 h)
Diclofenac	50 mg PO TID (150 mg/24 h)
Etodolac	500 mg PO BID (1000 mg/24 h)
Tolmentin	600 mg PO TID (1.8 g/24 h)
Tramadol	100 mg PO q6h (400 mg/24 h)
Celecoxib	100 BID (200 mg/24 h)
Meloxicam	15 mg PO daily (15 mg/24 h)

Abbreviations: BID, twice a day; PO, by mouth; q, every; QID, 4 times a day; TID, 3 times a day.

Pangarkar & Lee. Phys Med Rehabil Clin N Am 22 (2011) 503–520

Efikasi berbagai AINS berdasarkan nilai NNT (Number Needed to Treat)

Dwiprahasto, 2006



Analgesic agents commonly used for the treatment of acute pain

	Common routes of administration	Probable mechanisms of analgesic action	Potential relevant side-effects
Local anaesthetics (bupivacaine, lidocaine)	EA/SA, PNB/C, SC, TR	Inhibition of sodium channel	Hypotension, motor block, myotoxicity, systemic toxicity (seizures, cardiac dysrhythmias, cardiac arrest) in high doses
Opioids (fentanyl, morphine)	EA/SA, IV, SC, TR	μ-receptor agonist	Sedation, nausea, vomiting, pruritus, respiratory depression, immunosuppression
Paracetamol	PO, IV	Uncertain	Hepatic toxicity and liver failure at high doses, hypersensitivity
Non-steroidal anti-inflammatory agents (celecoxib, ibuprofen, ketorolac)	PO, IV	Inhibition of cyclo-oxygenase	Gastrointestinal irritation, platelet inhibition, renal insufficiency or failure, cardiovascular, hypersensitivity
Gabapentinoids (gabapentin, pregabalin)	PO	Inhibition of voltage-gated sodium channels	Sedation, peripheral oedema, gastrointestinal; decrease dose for renal insufficiency
α_2 agonists (clonidine, dexmedetomidine)	PO, IV	α_2- receptor agonist	Sedation, hypotension, bradycardia

EA/SA=epidural/spinal. PNB/C=peripheral nerve block/catheter. SC=subcutaneous. TR=transdermal. IV=intravenous. PO=oral.

Christopher L Wu, Srinivasa N Raja, ***Lancet , June 2011; 377: 2215–25***

OPIOIDS

- Commonly for chronic noncancer pain including neck pain
- May be effective for short-term pain relief
- Possibility of opioid-induced hyperalgesia (OIH)
- Suspect OIH when opioid treatment becomes less efficacious, particularly in the context of unexplained new pain, diffuse allodynia, or changes in quality of pain compared with that previously observed

Chu, et al. Clin J Pain 2008;24(6):479–96.

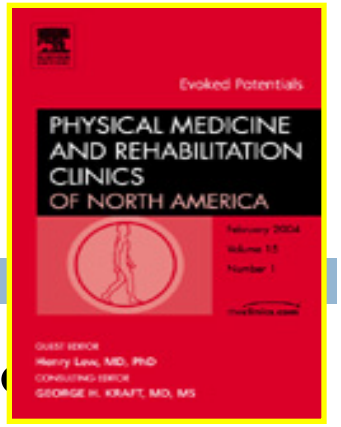
Equianalgesic doses of commonly used opioid agonists

Physical Medicine and Rehabilitation Clinics of North America

Opioid Agonist	Approximate equianalgesic oral dose	Approximate equianalgesic parenteral dose
Morphine	30 mg every 3–4 hours	10 mg every 3–4 hours
Codeine	130 mg every 3–4 hours	75 mg every 3–4 hours
Hydromorphone	7.5 mg every 3–4 hours	1.5 mg every 3–4 hours
Hydrocodone	30 mg every 3–4 hours	Not available
Meperidine	300 mg every 2–3 hours	100 mg every 3 hours
Oxycodone	30 mg every 3–4 hours	Not available

Nemat & Richeimer. Phys Med Rehabil Clin N Am 14 (2003) 629–641

TRAMADOL



- Tramadol has action on both mu-opioid receptor activ
  and on serotonin and norepinephrine reuptake inhibition.
- Tramadol can be considered for mild-moderate pain before using "weak" opioids.
- has led to abuse and dependence
- Warnings about renal failure, seizures, and potential serotonin syndrome when used with other serotonergic medications.

Pangarkar & Lee. Phys Med Rehabil Clin N Am 22 (2011) 503–520

ADJUVANT MEDICATIONS

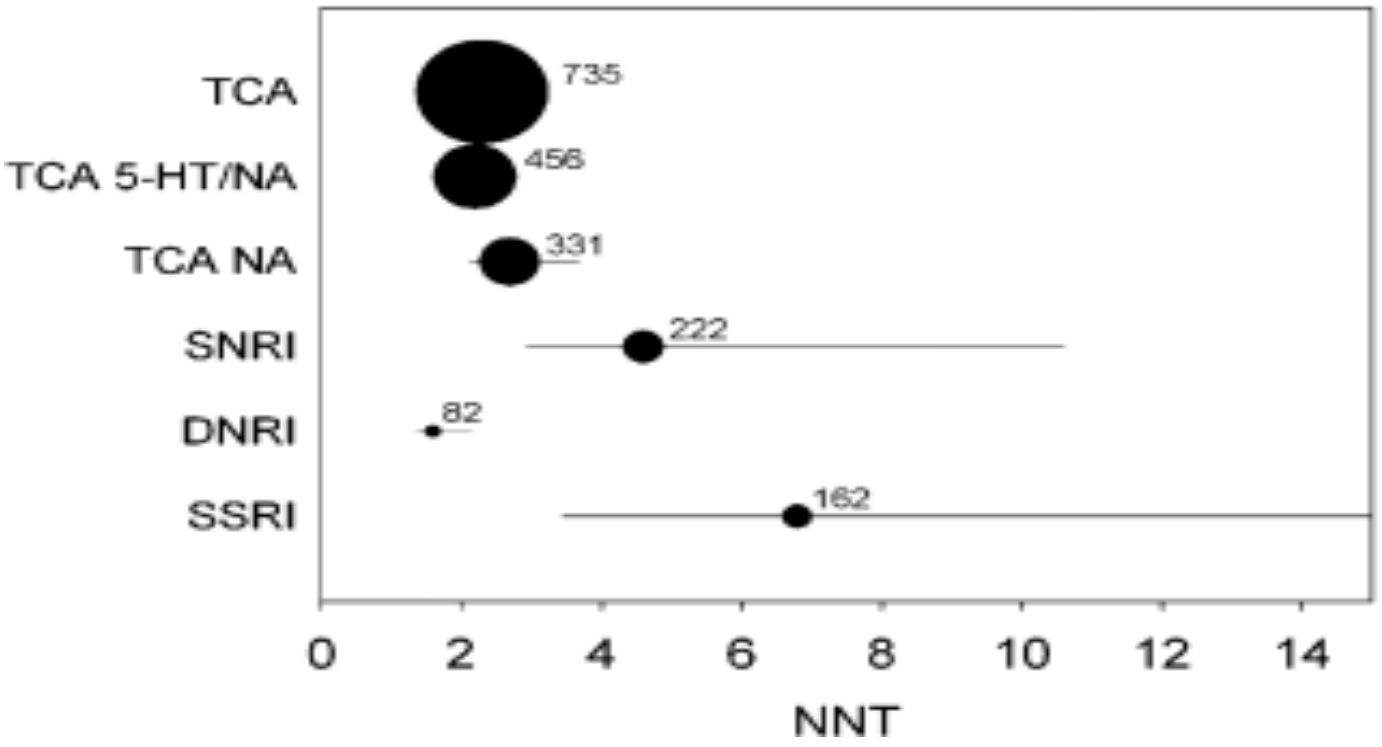
- Antidepressants
- Anticonvulsants
- Local anesthetics
- Miscellaneous agents

Antidepressants in the Treatment of Neuropathic Pain

Søren H. Sindrup[1], Marit Otto[1], Nanna B. Finnerup[2] and Troels S. Jensen[2]

[1]Department of Neurology, Odense University Hospital, Odense, Denmark, and [2]Danish Pain Research Center, Aarhus University Hospital, Aarhus, Denmark

AD in peripheral neuropathic pain



Sindrup, et al. Basic & Clinical Pharmacology & Toxicology 2005, **96, 399–409.**

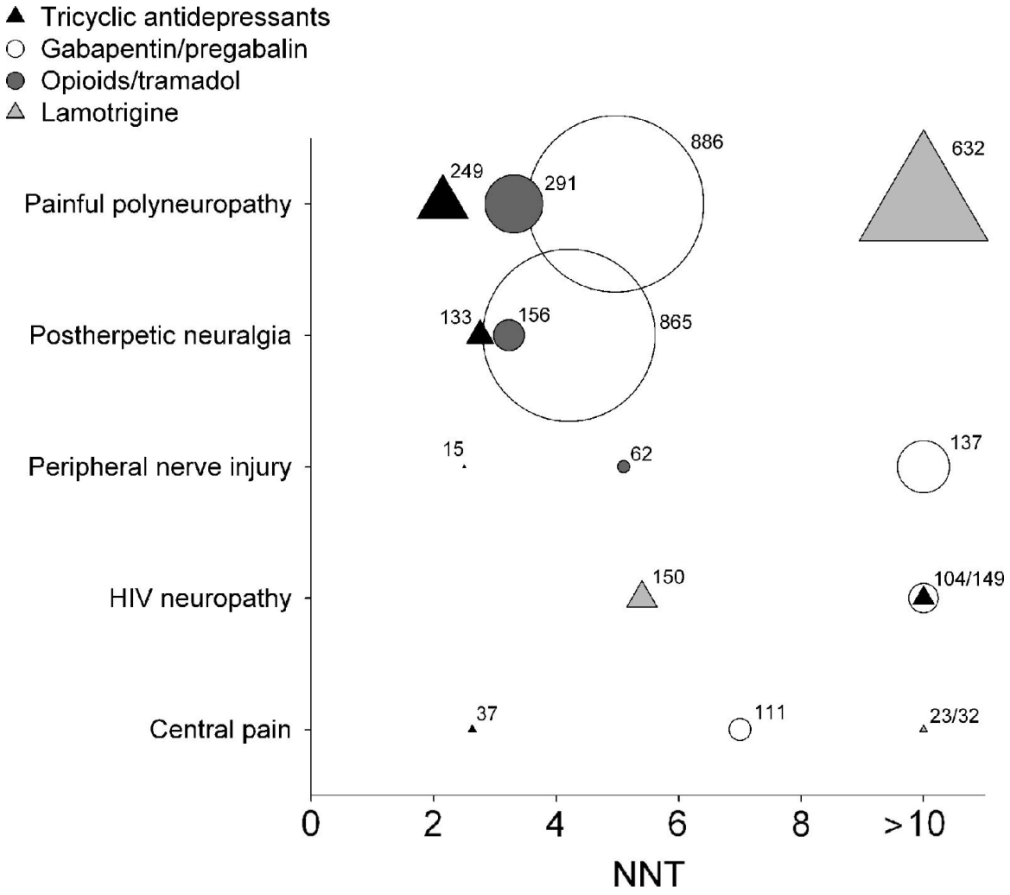
International Association for the Study of Pain
IASP
Working together for pain relief
International Association for the Study of Pain

PAIN® 150 (2010) 573–581

www.

The evidence for pharmacological treatment of neuropathic pain

Nanna Brix Finnerup [a,*], Søren Hein Sindrup [b], Troels Staehelin Jensen [a]



EFNS guidelines for the treatment of painful polyneuropathy

- Drugs with established efficacy include PREGABALIN, Gabapentin, TCAs, SNRIs, strong opioids and tramadol

First line therapy	PREGABALIN/gabapentin or TCAs/SNRIs (evidence level A)
Second line therapy	Opioids and lamotrigine (evidence level B)
Lack of or weak efficacy	SSRIs, capsaicin, mexiletine, oxcarbazepine and topiramate (evidence level A)
Low strength evidence or safety concerns	Carbamazepine and valproate

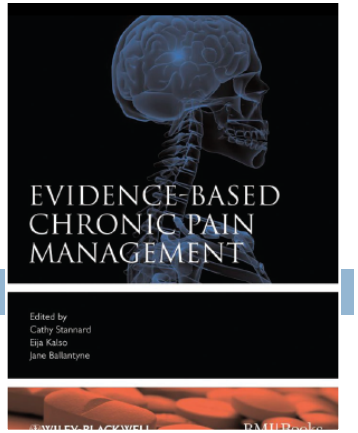
Attal et al., 2006, EFNS: European Federation of Neurological Societies

TOPICAL ANALGESICS

- There are 3 main types of topical analgesics: menthol/methylsalicylates, capsaicin, and anesthetics.
- Topical analgesics are absorbed through the skin and block local pain sensations.
- Menthol elicits a cooling sensation over painful areas.
- Anesthetics such as lidocaine relieve pain by blocking the sodium channels necessary for nerves to transmit pain signals

Wood, et al. J Neurobiol 2004;61(1):55–71.

Interventional therapies

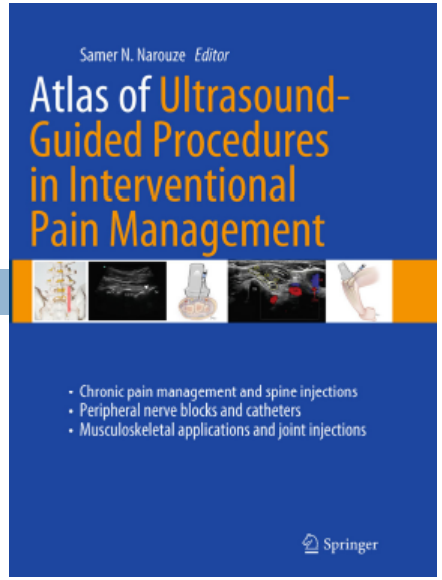


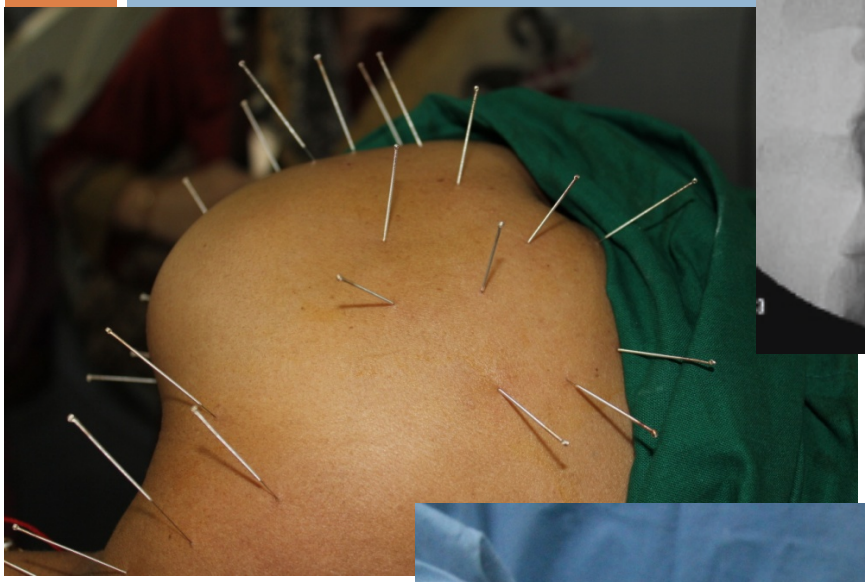
- Used in the management of chronic and malignant pain include various types of neural blockades and minimally invasive surgical procedures.
- These therapies are employed for a wide range of painful conditions, despite ongoing controversy about their effectiveness.
- Most of these procedures are performed on patients with chronic pain, which remains a poorly understood, complex clinical state associated with psychiatric, behavioral and neurobiologic implications.

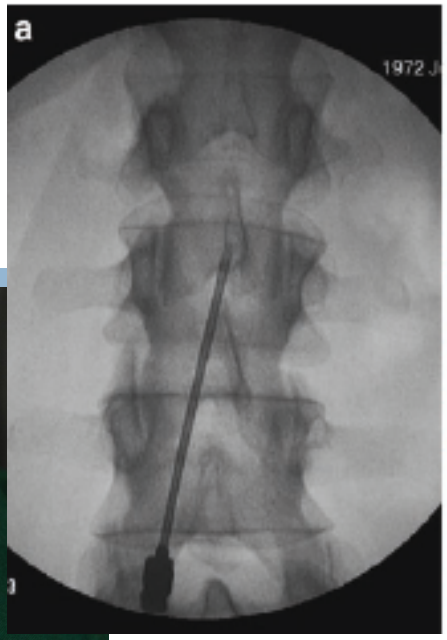
Dragovich & Cohen, 2010

Procedure	Guidance
Sympathetic blocks	
Stellate ganglion	Fluoroscopy
	US
Celiac plexus	CT, FDCT
	Fluoroscopy
Epidurals	
Caudal	Fluoroscopy
	US
Lumbar TF	Fluoroscopy
	DSA
	US
Lumbar IL	Fluoroscopy
	US

Procedure	Guidance
Cervical TF	Fluoroscopy
	DSA
	US
	CT
Lumbar medial branch block	Fluoroscopy
	US
Cervical medial branch block	Fluoroscopy
	US
Lumbar facet joint	Fluoroscopy
	US
Cervical facet joint	Fluoroscopy
	US



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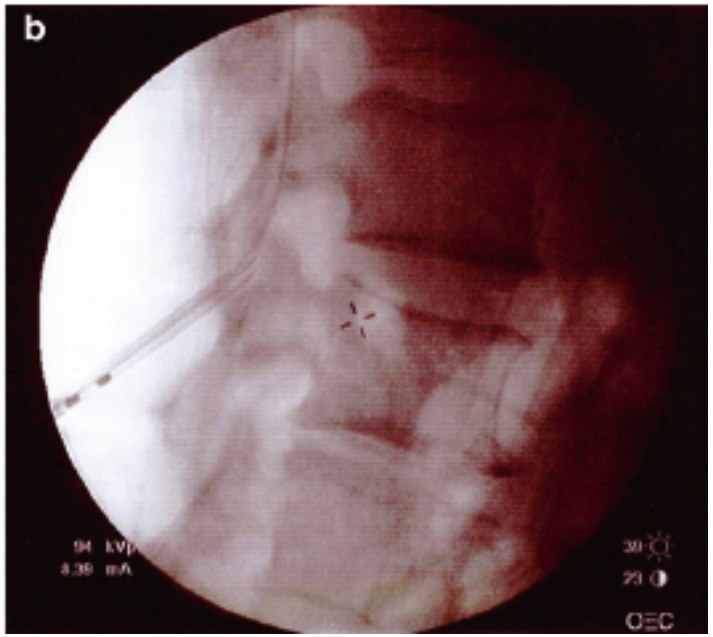
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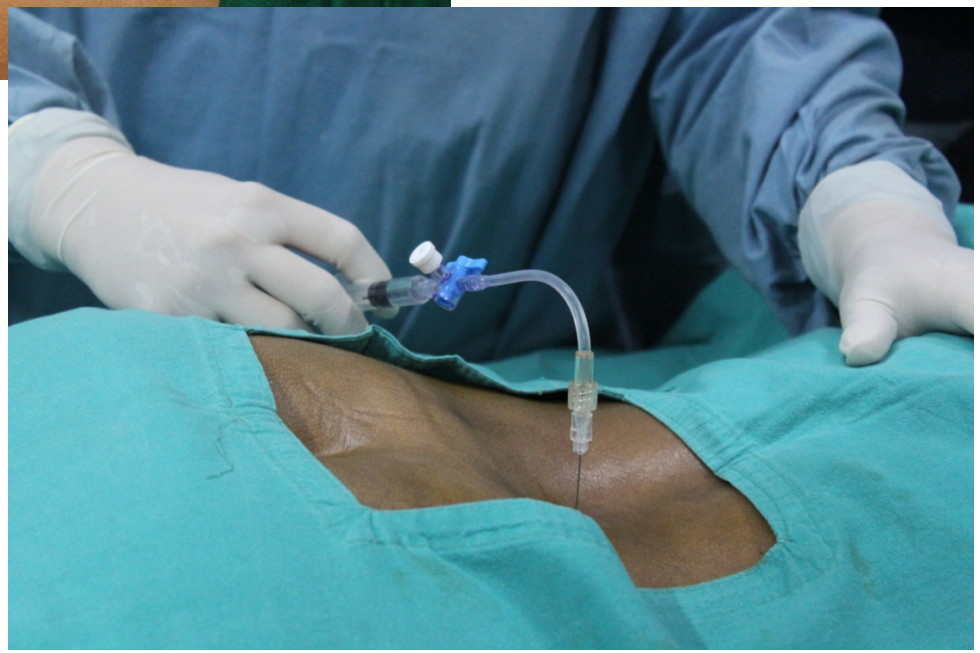

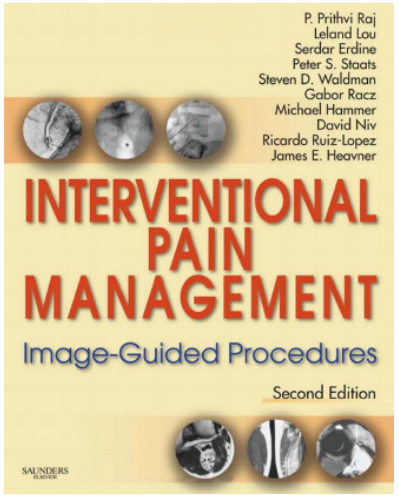
P. Prithvi Raj
Leland Lou
Serdar Erdine
Peter S. Staats
Steven D. Waldman
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INTERVENTIONAL PAIN MANAGEMENT
Image-Guided Procedures
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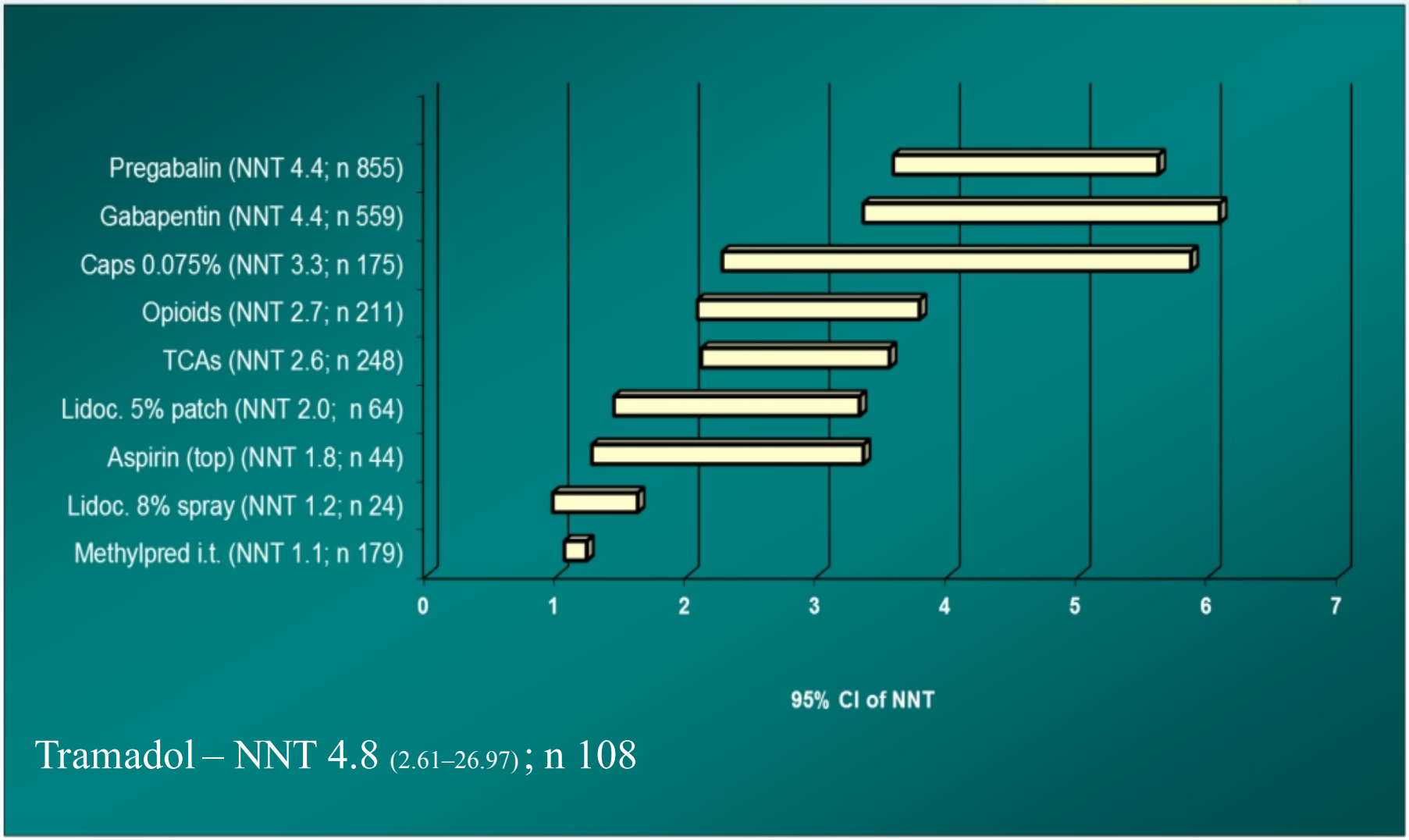
SAUNDERS

Efficacy (NNT< 5.0) in PHN

Hempenstall K et al PLOS-Medicine 2005;2(7):628-644

Updated March 2011



Tramadol – NNT 4.8 (2.61–26.97); n 108

Meta-analysis of RCTs for Analgesic Efficacy in HIV-SN

Phillips TJC et al PLoS ONE 2010;5: e14433

Efficacy

- NGF (s.c.) (McArthur 2000)
- Capsaicin 8% (Simpson 2008)
  (NNT30% 6.46)–
  – (NB Simpson et al 2012)
- Smoked cannabis (Abrams 2007; Ellis 2008)
  NNT30% 3.6–
  – NNT30% 3.5

No Evidence

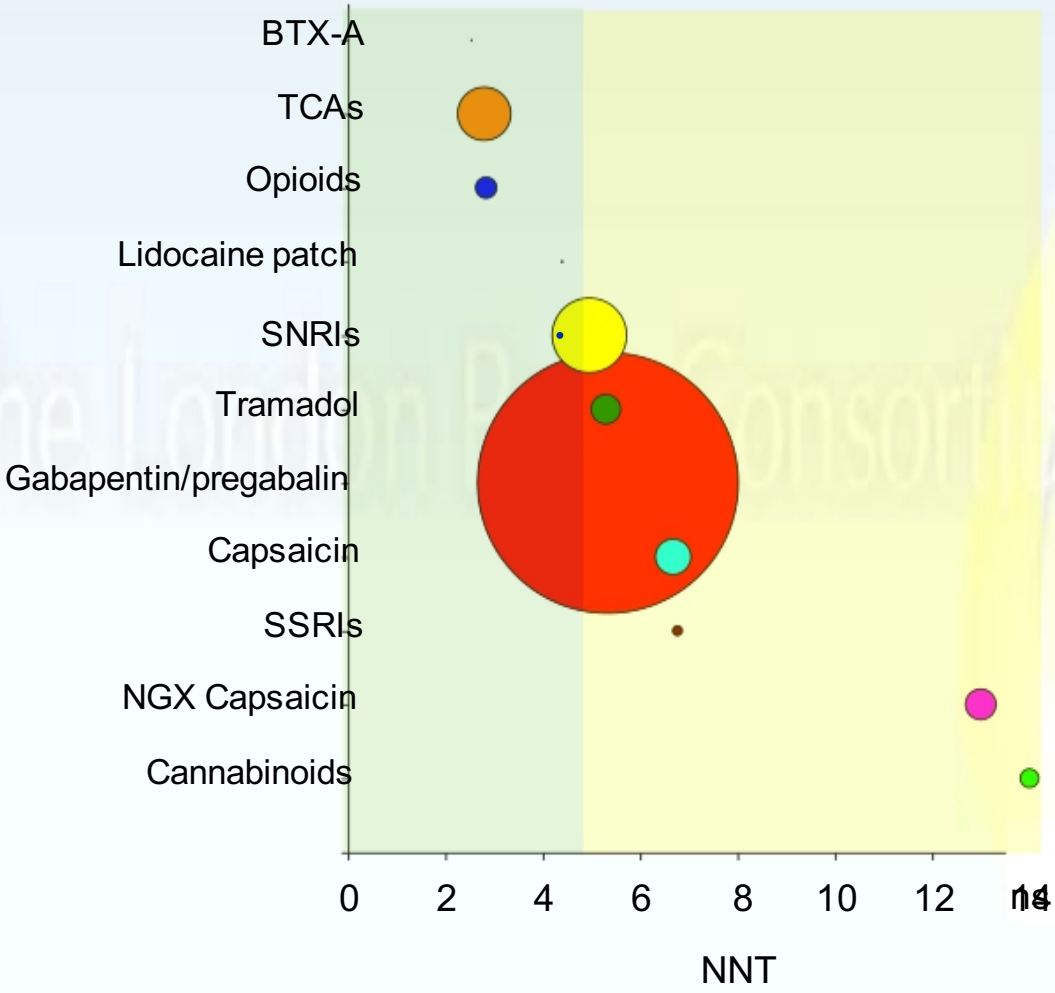
- Opioids

No Efficacy or Minor Effect

- Amitriptyline (Kieburtz 1998; Shlay 1998)
- Mexilitine (Kieburtz 1998)
- Acupuncture (Shlay 1998)
- Peptide T (Simpson 1996)
- Capsaicin 0.075% (Paice 2000)
- Prosaptide (Evans 2007)
- Acetylcarnitine (Youle 2007)
  _ Efficacy in EE population
- Lamotrigine (Simpson 2000 & 2003)
  Efficacy for ATN patients–
- Gabapentin (Hahn 2004)
- Pregabalin (Simpson 2010)

Meta-analysis of RCTs in Peripheral Neuropathic Pain

Finnerup et al Pain 2010:150:573-851



Slide Courtesy of Nanna Finnerup, Aarhus


THANK
YOU