

Overview of Neuropathic Pain and Pharmacological Approaches

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New York, New York

Peripheral Neuropathy Patient Conference

Foundation for Peripheral Neuropathy

AGENDA

- 8:30 AM Welcome:** *David M. Simpson, MD, FAAN*
- 8:35 AM: Opening Remarks:** *Louis Mazawey; Lindsay Colbert*
- 8:45 AM: Overview of Neuropathic Pain and Pharmacologic Approaches:**
David M. Simpson, MD, FAAN
- 9:15AM: Controlled Substances: What are the Roles of Opioids and Medical Marijuana in the Treatment of Neuropathic Pain:**
Jessica Robinson-Papp, MD
- 9:45AM: Q and A/Round Table**
- 10:15 AM: Break**
- 10:30 AM: Optimizing Communication With Your Provider and Beyond:**
Drugs: Non-Pharmacological Management of Neuropathic Pain:
Shanna Patterson, MD
- 11:00 AM: Research and Technology for Possible Options to Neuropathic Pain Treatment:** *Mary Catherine George, PhD*
- 11:30 AM: Q and A/Round Table**
- 12:15 PM: Adjourn**

Nociceptive vs Neuropathic Pain

Nociceptive Pain

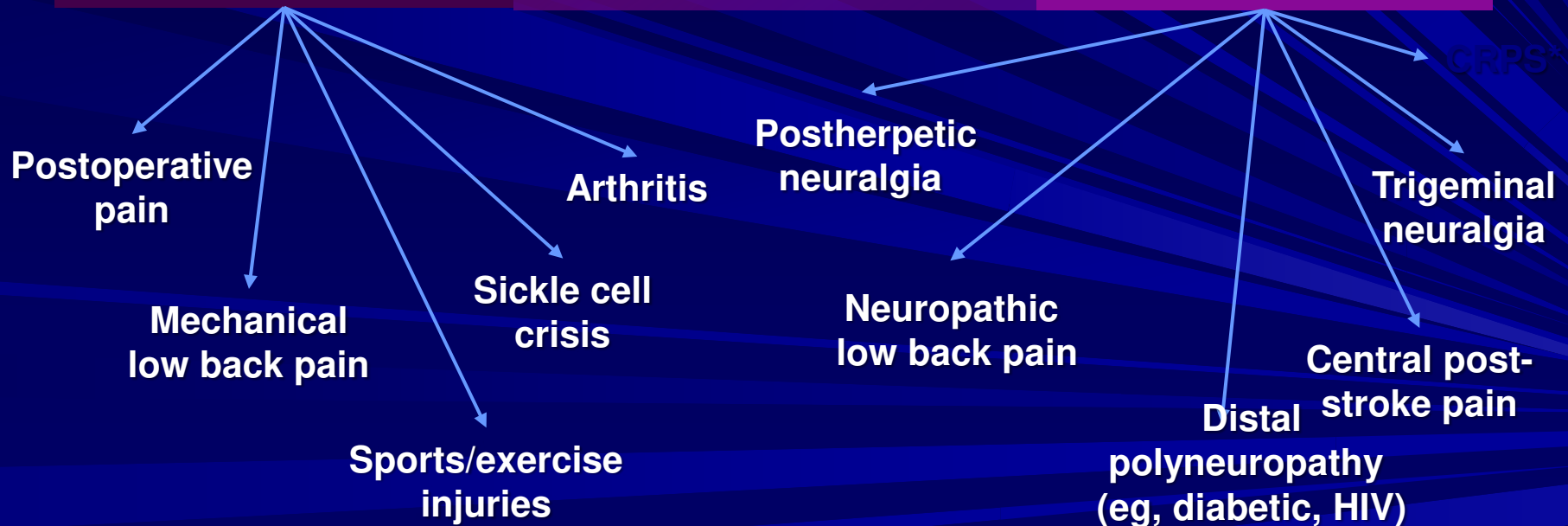
Caused by activity in neural pathways in response to potentially tissue-damaging stimuli

Mixed Type

Caused by a combination of both primary injury and secondary effects

Neuropathic Pain

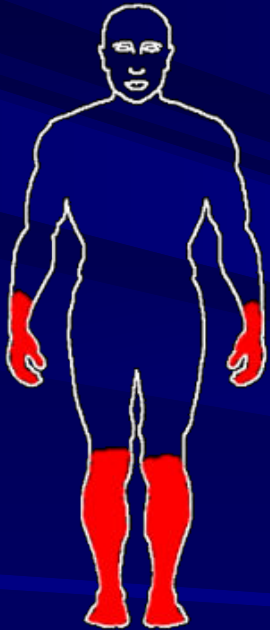
Initiated or caused by primary lesion or dysfunction in the nervous system



*Complex regional pain syndrome.

Types of Neuropathy

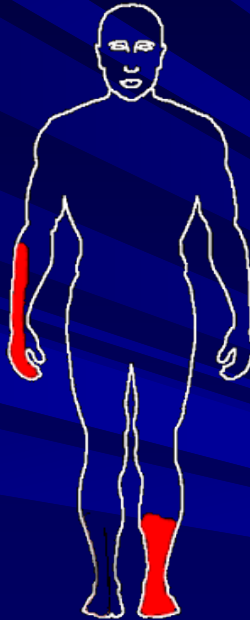
**Distal Symmetrical
Polyneuropathy**



**Mononeuropathy
Multiplex**



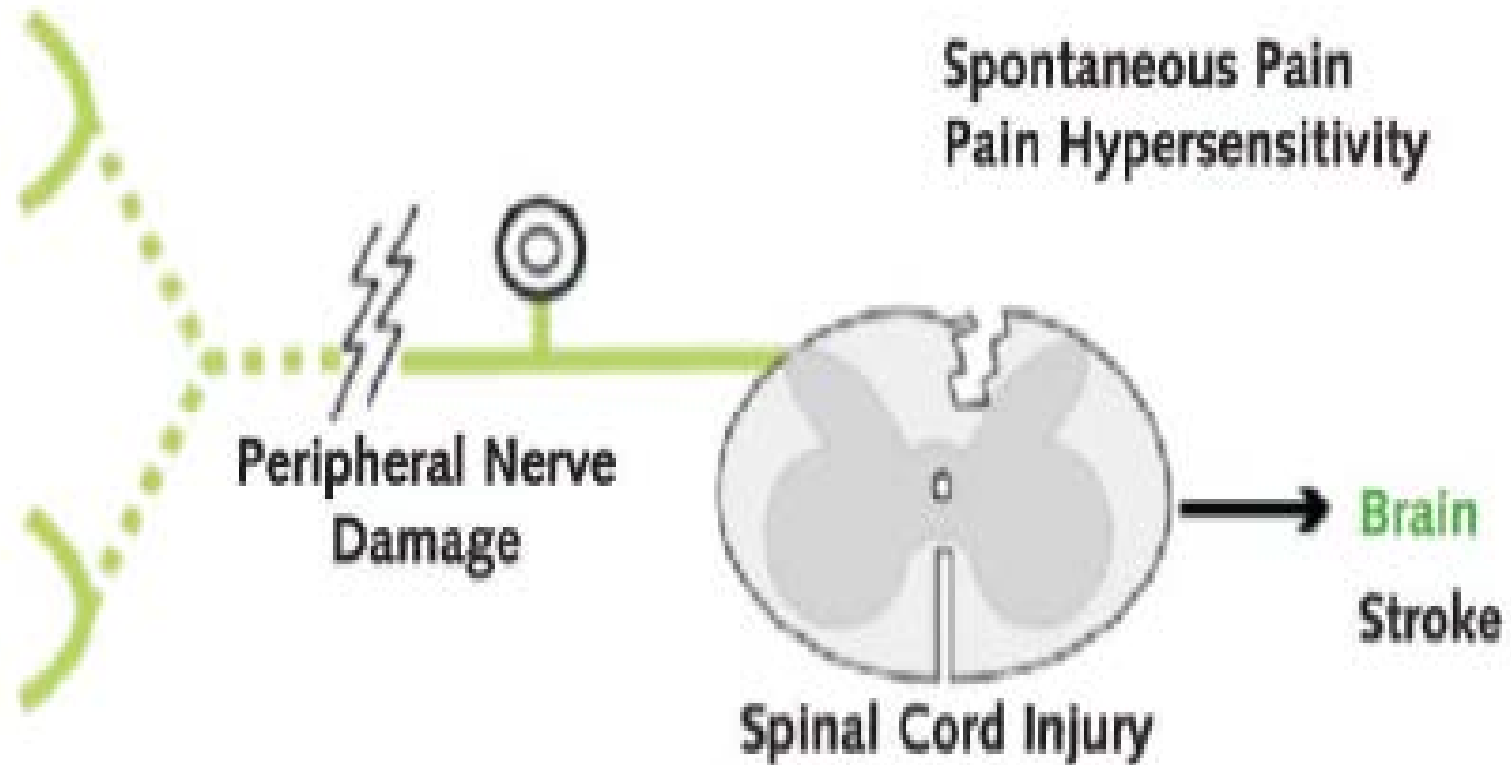
**Inflammatory
Demyelinating
Polyneuropathy**



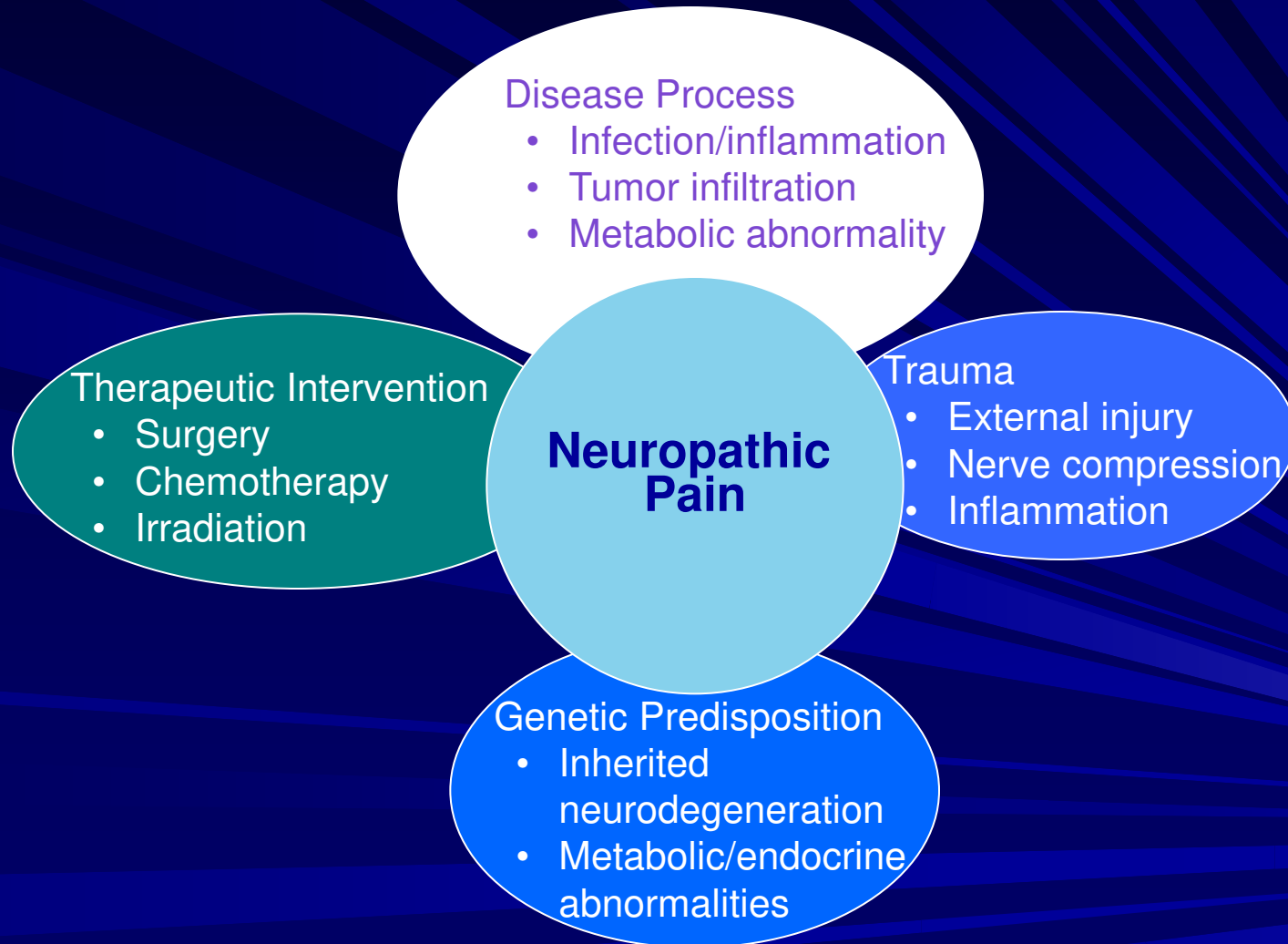
Mononeuropathy

**Brachial
Plexopathy**

Neuropathic Pain

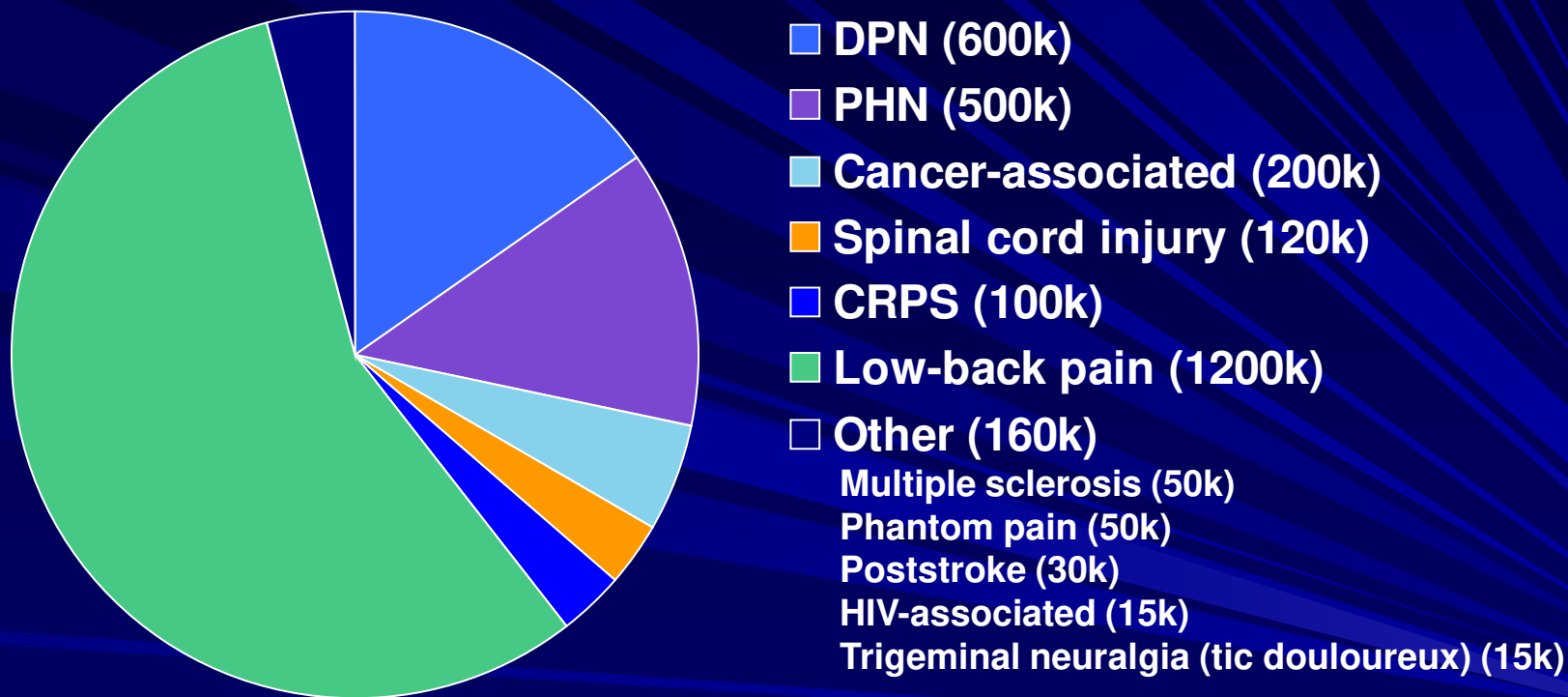


Common Causes of Neuropathic Pain



Estimated Prevalence of Neuropathic Pain in the United States*

Total Number of Cases of Neuropathic Pain: 3,780,000



DPN = diabetic peripheral neuropathy; PHN = postherpetic neuralgia; CRPS = complex regional pain syndrome.

*Based on population of 270 million.

Bennett GJ. *Hosp Pract (Off Ed)*. 1998;33:95-98, 101-104, 107-110.

Pain is a more terrible master of humankind than death itself

Albert Schweitzer (1922), *On the Edge of the Primeval Forest*





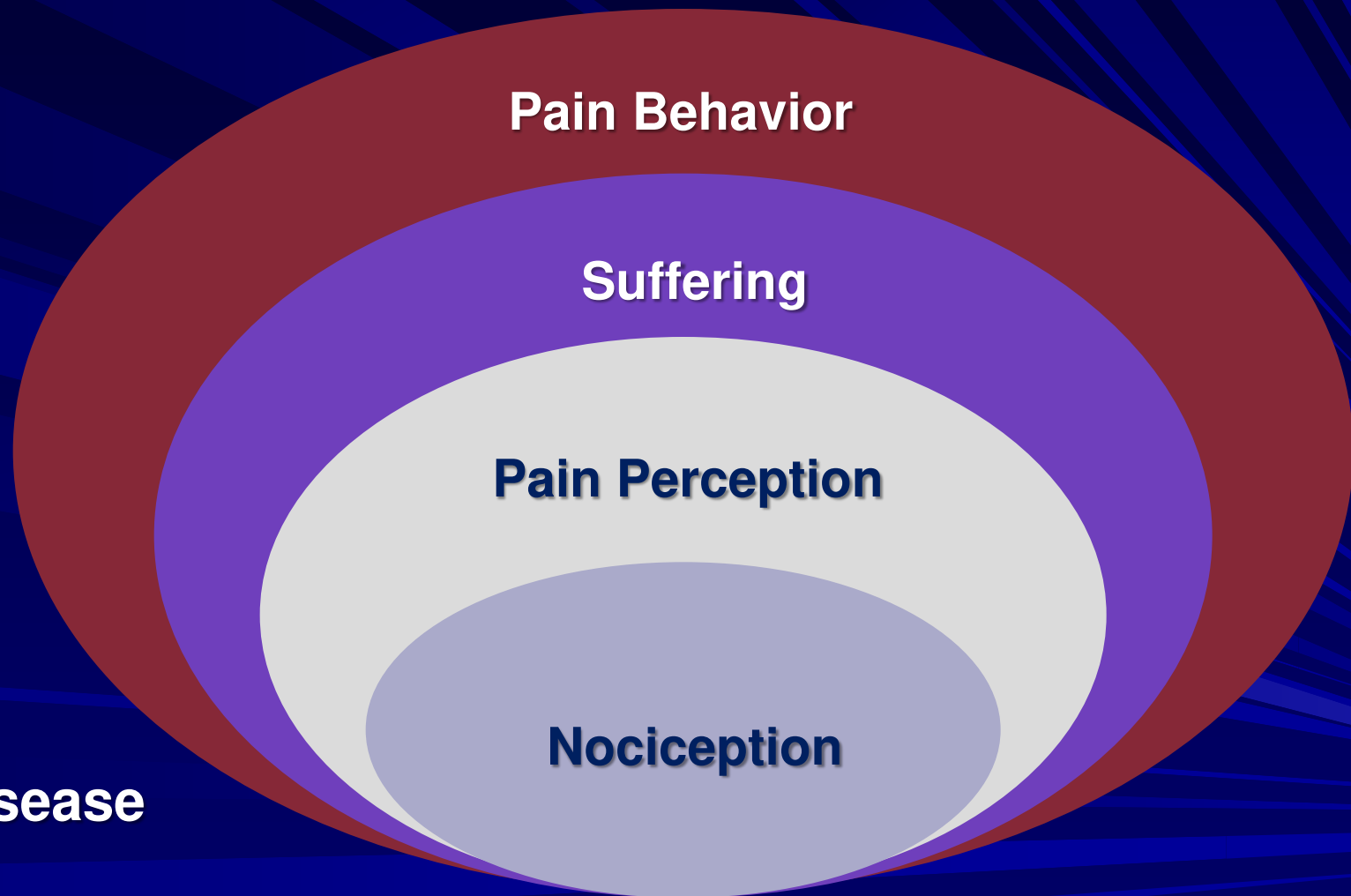
Pain: Issues and Challenges

- Most common type of medical symptom
 - 25% to 50% of all clinic visits
- Underassessment and undertreatment
- Patient not believed
- Complex pathophysiology
- Treatment choices suboptimal
- Interpatient variability in response to Rx

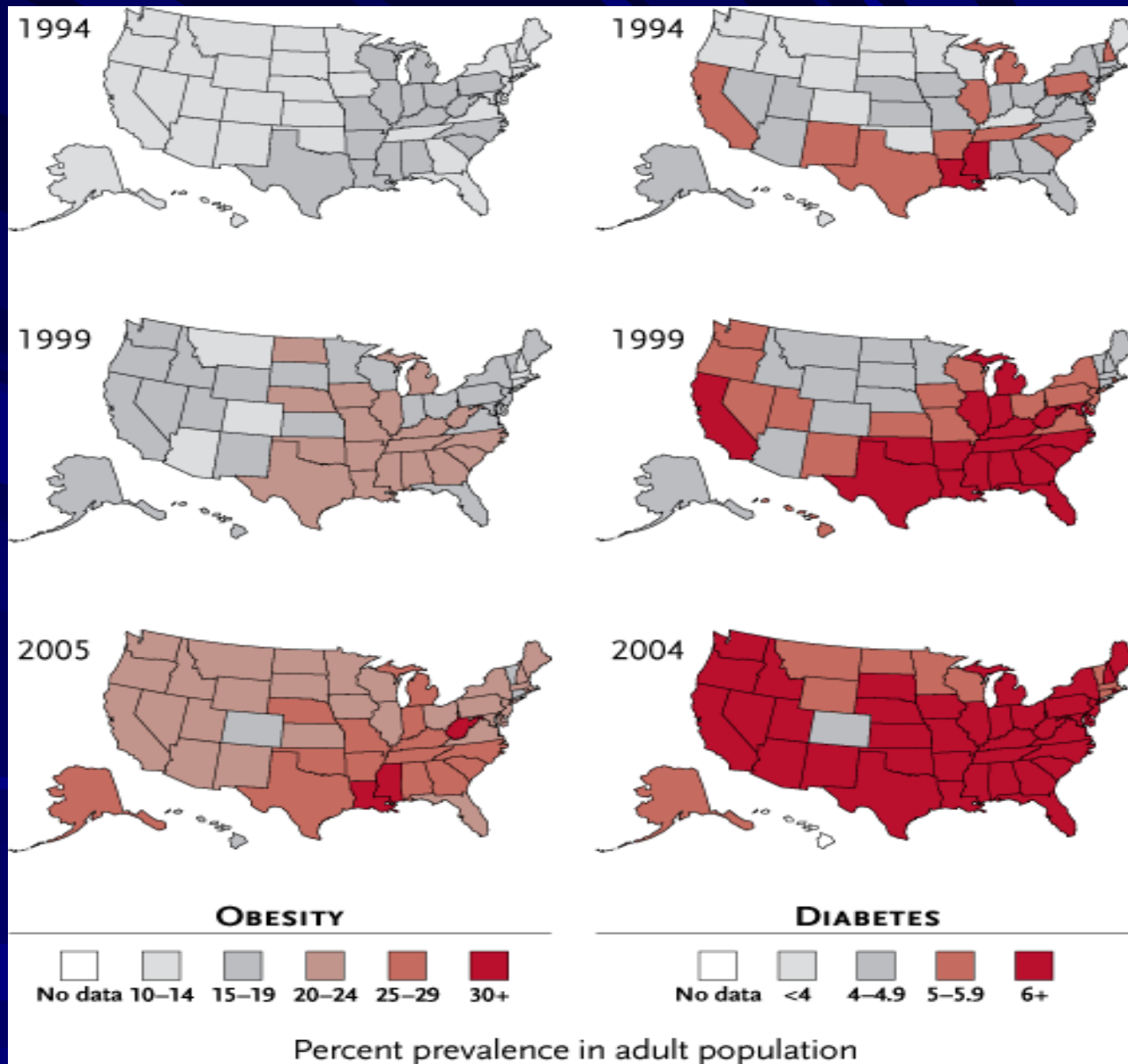
The Complex Nature of Pain

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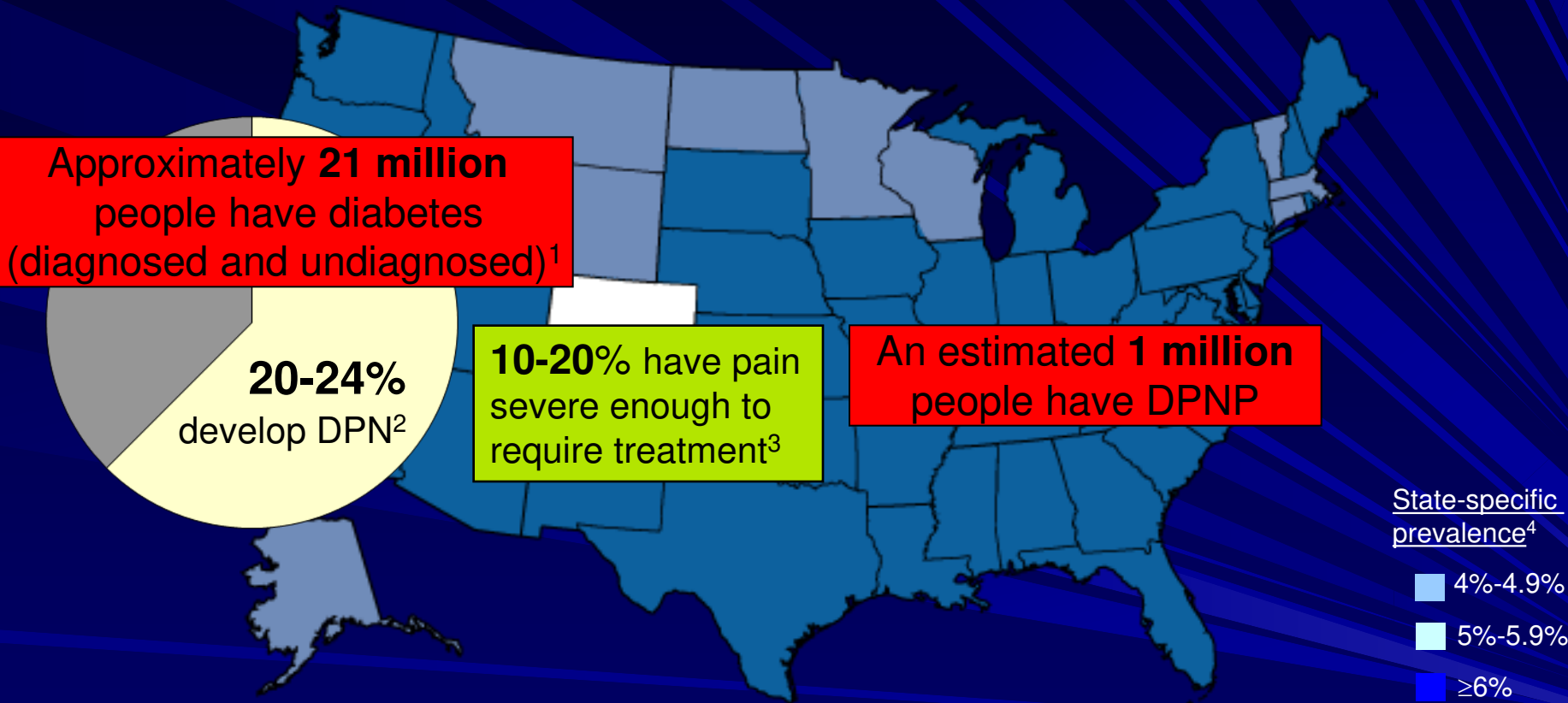
Disease



Obesity and Diabetes in US



Prevalence of Diabetes, Diabetic Neuropathy, and Diabetic Peripheral Neuropathic Pain



1. NDIC. Available at: <http://diabetes.niddk.nih.gov/dm/pubs/statistics/#7>. Accessed May 30, 2008.

2. Schmäder KE. *Clin J Pain*. 2002;18(6):350-354.

3. Boulton AJ, et al. *Diabetes Care*. 2004;27(6):1458-1486.

4. CDC. Available at: <http://www.cdc.gov/diabetes/statistics/prev/state/fPrev1994and2004.htm>. Accessed May 30, 2008.



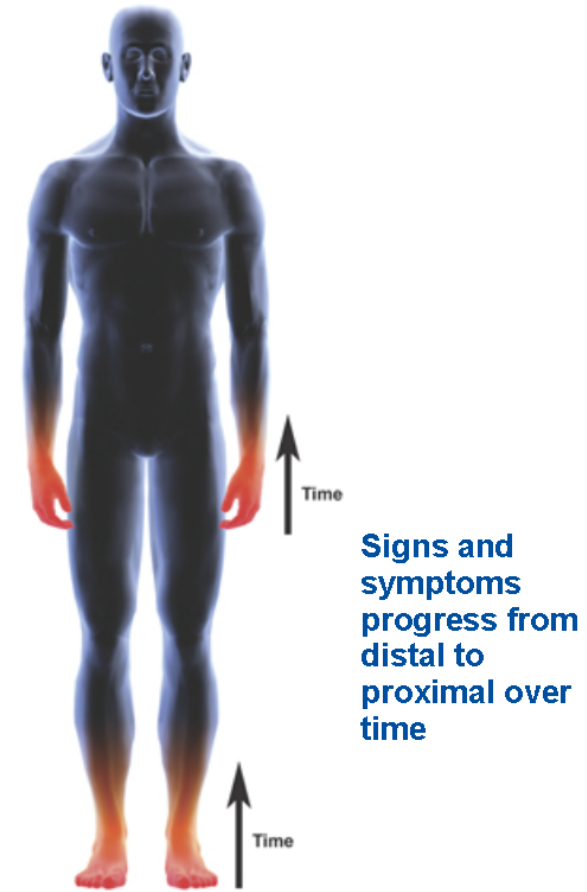
Diabetic Neuropathy: Risk Factors

- Aging
- Duration of diabetes
- Poor glycemic control
- Diastolic hypertension
- Reduced HDL cholesterol
- Increased triglycerides
- Hypertension
- Smoking

1. Gimbel JS et al. *Neurology*. 2003;60:927-934.
2. Schmader KE. *Clin J Pain*. 2002;18:350-354.
3. Tesfaye S et al. *Diabetologia*. 1996;39:1377-1384.

Clinical manifestations of diabetic peripheral neuropathy (DPN)^{1,2}

- Distal symmetrical sensorimotor polyneuropathy is the most common form of DPN
- Patients frequently complain of:
 - Pain (e.g. burning, shooting, stabbing)
 - Exacerbated by activities
 - Typically worse at night
 - “Pins and needles” (paresthesias)
 - Increased sensitivity (allodynia, hyperalgesia)
 - Numbness
 - Impaired balance (loss of proprioception)

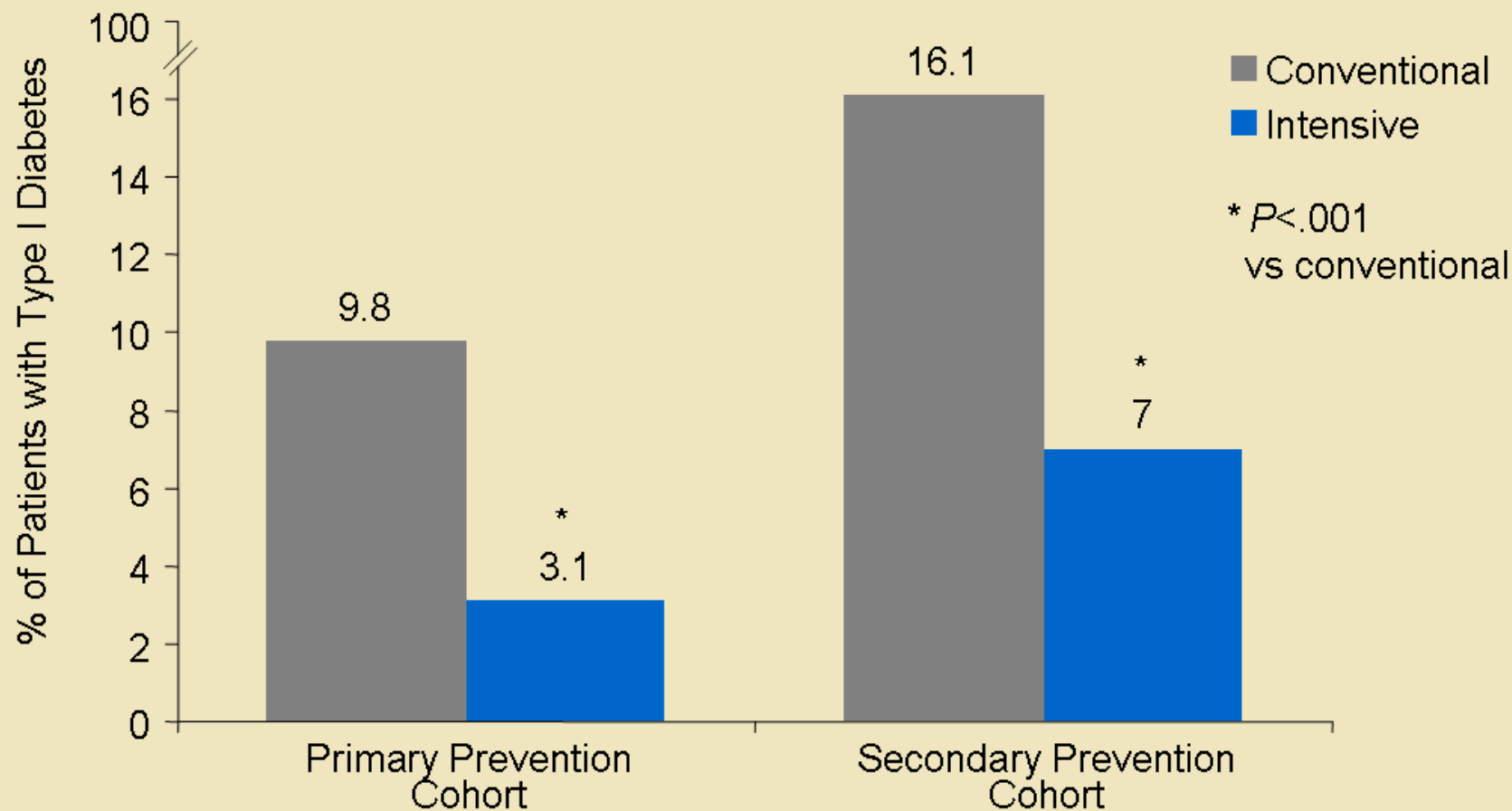


1. The National Institute of Diabetes and Digestive and Kidney Disease (NIDDK)

2. Boulton AJM, et al. *Diabetes Care*. 2004, 27(6):1458-1486

Glycemic control can decrease the risk of diabetic neuropathy

Effect of Diabetes Treatment on the Prevalence of Clinical Neuropathy at 5 years
(from the Diabetes Control and Complications Trial)



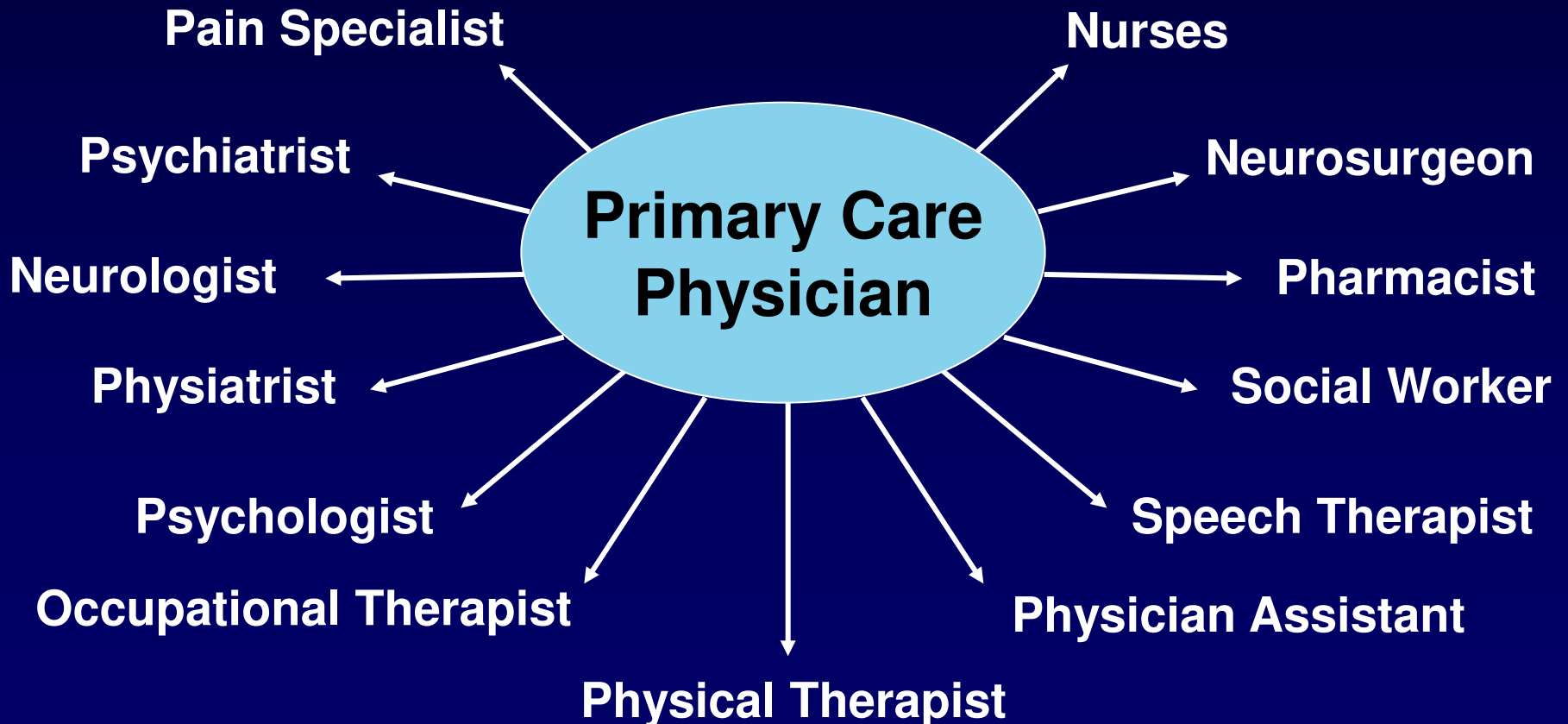


What Are the Goals of Clinical Assessment?

- Achieve diagnosis of pain
- Identify underlying causes of neuropathy
- Identify comorbid conditions
- Evaluate psychosocial factors
- Evaluate functional status (activity levels)
- Set goals
- Develop a targeted treatment plan
- Determine when to refer to specialist or multidisciplinary team (pain clinic)

Coordination of the Multidisciplinary Team

Integrated Coordinated Interdisciplinary



Can We Reliably Measure Pain?



Pain Assessment Process

- Physicians should address
 - Types of pain
 - Distribution of pain
 - Patient's current pain state
 - Effects of patient's current treatment
 - Appropriate tools available for pain evaluation

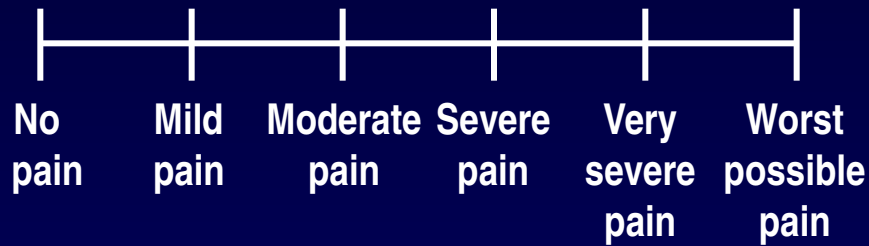
Pain Intensity: How Much It Hurts



“Ouch,” “D*#mn!,” and “G*% D*#mn!”

Pain Assessment Scales

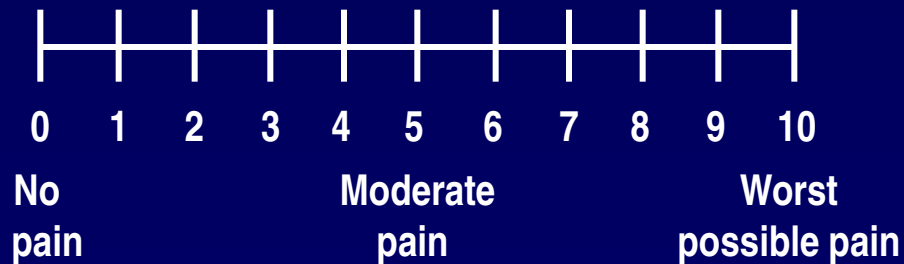
Verbal Pain Intensity Scale¹



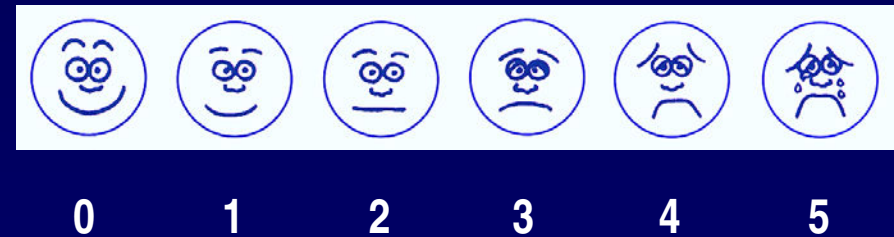
Visual Analog Scale¹



0–10 Numeric Pain Intensity Scale²

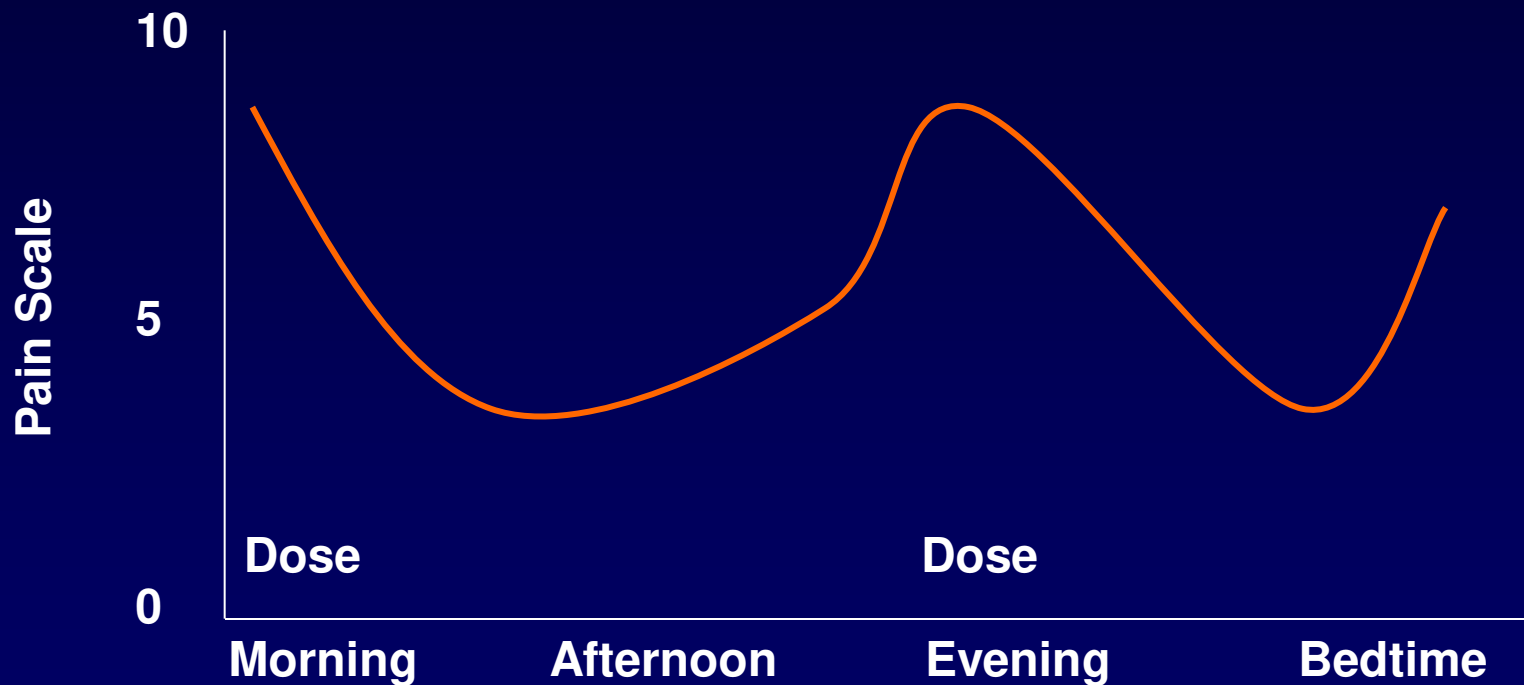


“Faces” Scale³



Patient Pain Diary

Utility of manual versus electronic diaries?



Pain Quality: How it Feels



Sharp/stabbing



Hot/burning



Electrical/
shocking

Diagnostic Studies and Limitations

Studies

- Blood studies
- X-ray, CT, MRI
- Electromyography (EMG)
- Nerve conduction velocity (NCV)
- Quantitative sensory testing (QST)
- Epidermal skin biopsy

Limitations of EMG/NCV

- Insensitive in acute injury
- Normal result does not rule out neuropathic pain
- Cannot assess function of small-fiber nerves involved in most neuropathic pain

Treatment of Neuropathic Pain

“Undertreatment of acute and chronic pain persists despite decades of efforts to provide clinicians with information about analgesics.”

Amer Pain Society Quality of Care Committee. JAMA 1995

Attitudes on Pain

To experience pain is to
have certainty; to hear
about pain is to have doubt

~ Elizabeth Scary

Well

HARD CASES | ABIGAIL ZUGER, M.D.

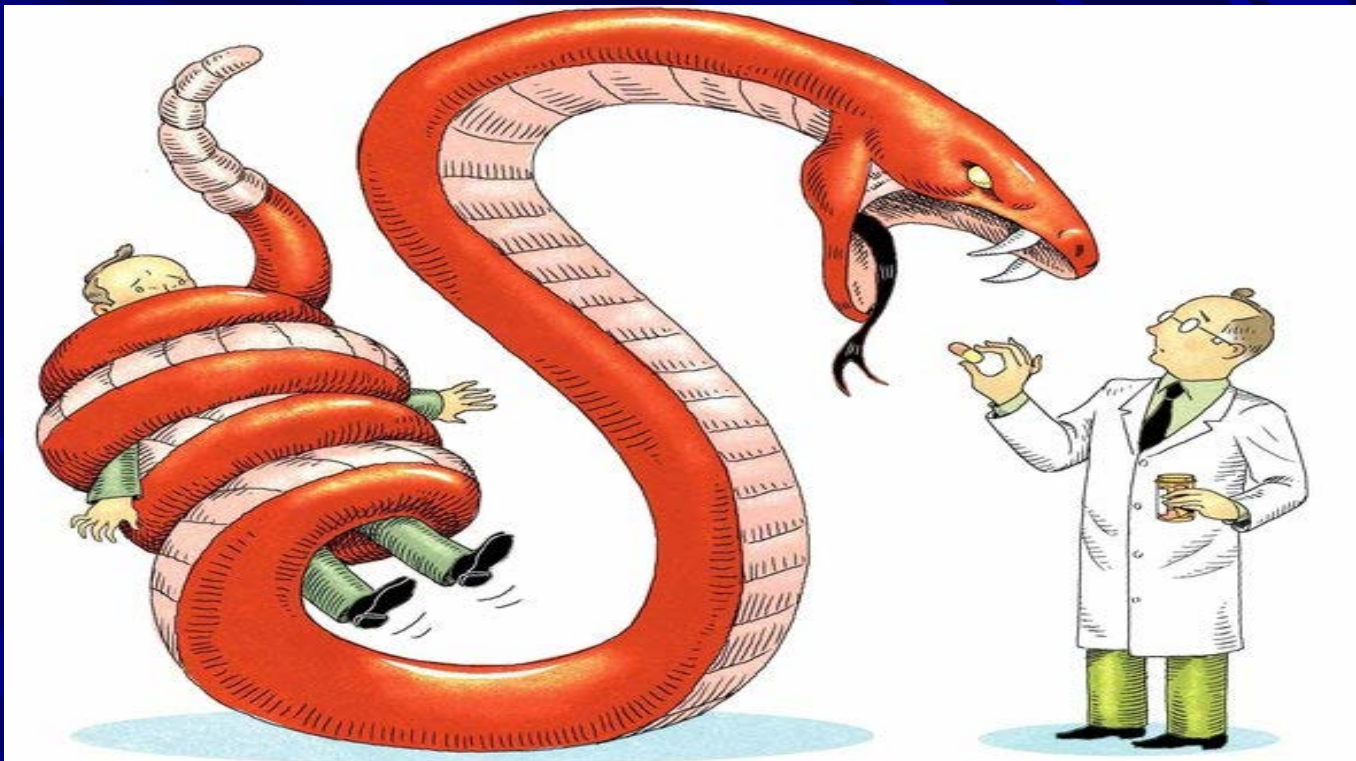
The Traps of Treating Pain

Doctors are rarely trained to manage discomfort, so they wind up following general guidelines.

measured or monitored, and varies wildly and unpredictably from person to person. We hate it because it can drag us closer to the perilous zones of illegal practice than any other complaint.

And we hate it most of all because unless we specifically seek out training in how to manage pain, we get virtually none at all,

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Neuropathic Pain

Barriers to Management

■ Patient-related

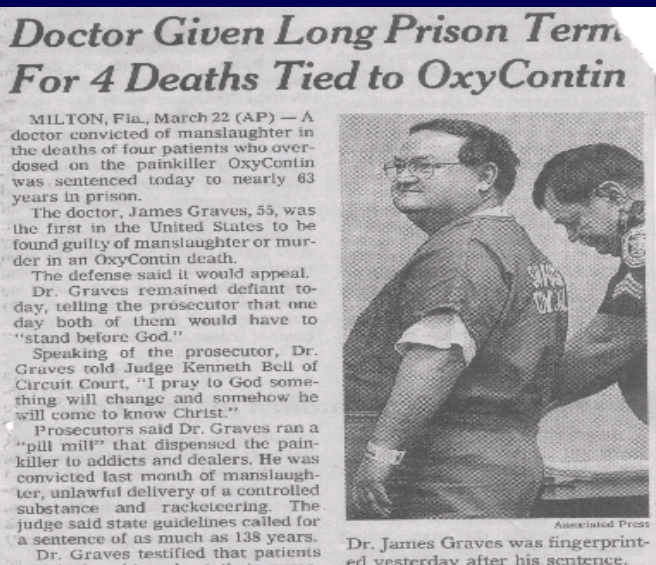
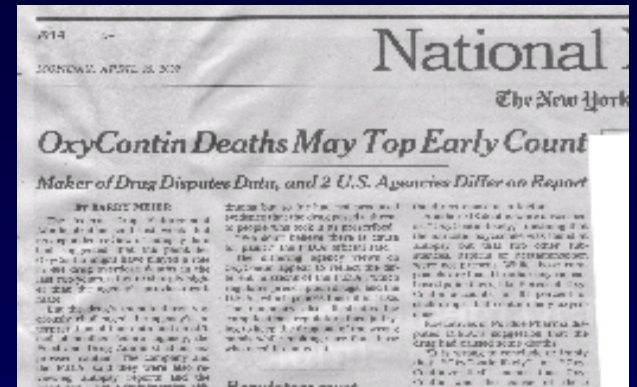
- Reluctance to report pain
- Substance abuse

■ Health care provider

- Fear of addiction
- Fear of being “scammed”

■ Health care system

- Triplicates, narcotic restrictions



To the Patient, the Impact of Pain Rx Goes Far Beyond the Pain

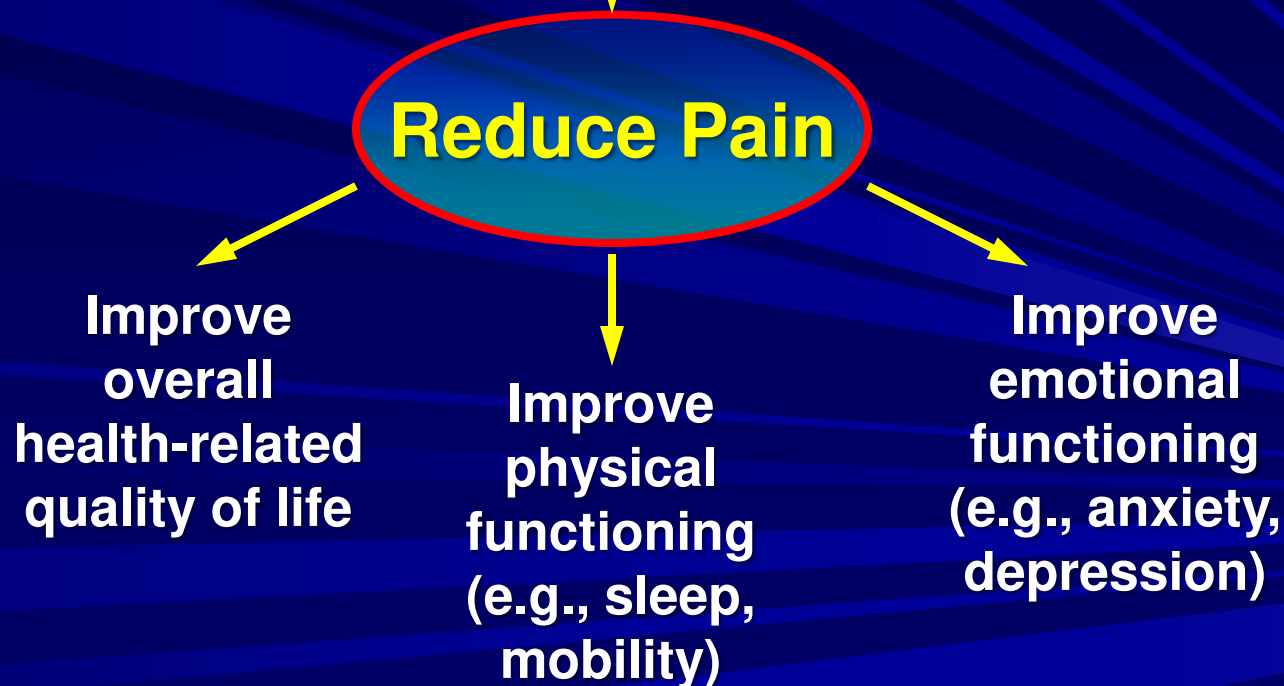
- Pain broadly interferes with daily functioning and quality of life¹⁻⁵
 - General activity, walking
 - Energy level
 - Social and leisure activities
 - Ability to sleep
 - Change in mood, ↑ feelings of depression and anxiety
 - Overall enjoyment of life

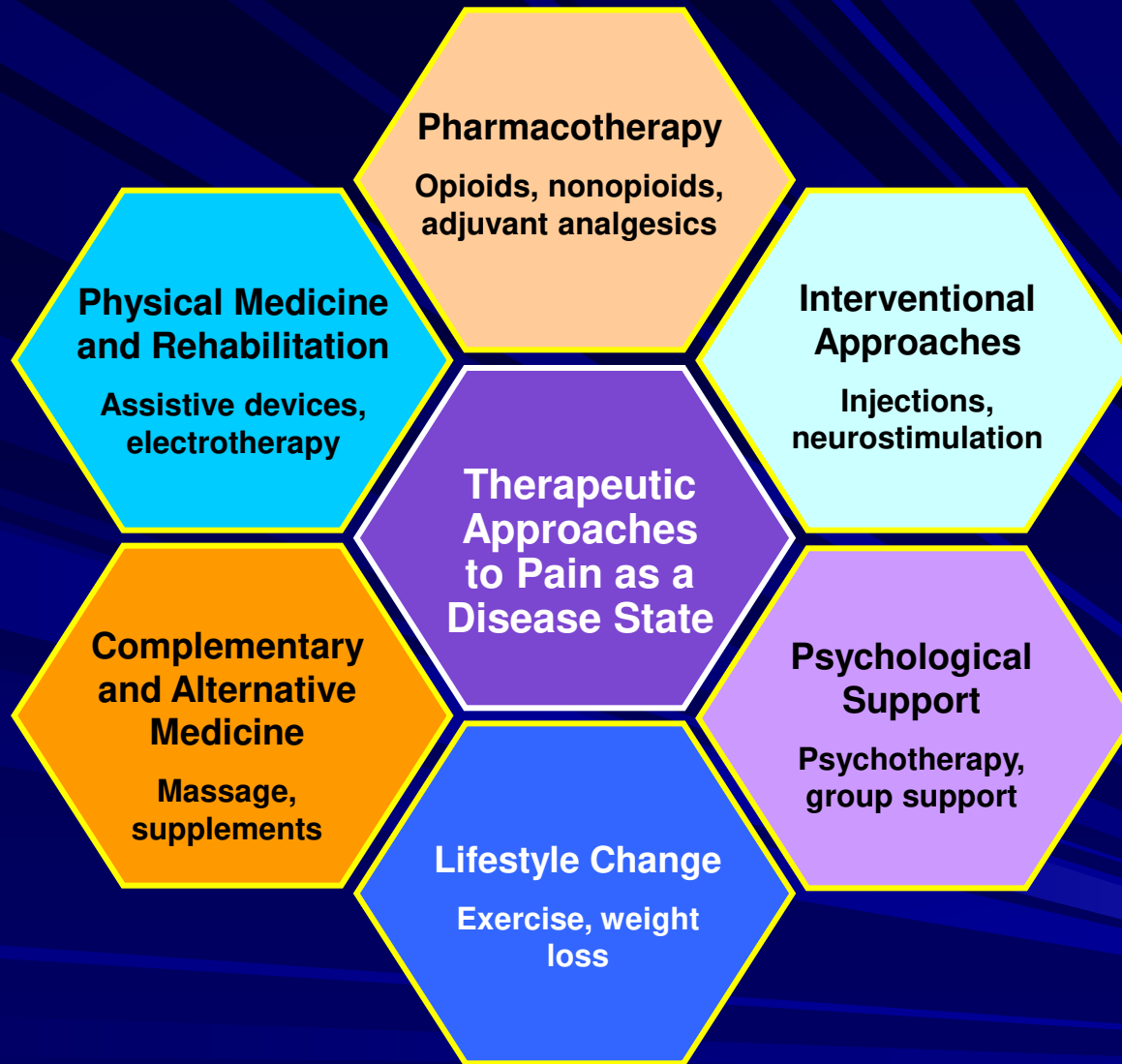


Overall Objectives of Treatment of Neuropathic Pain

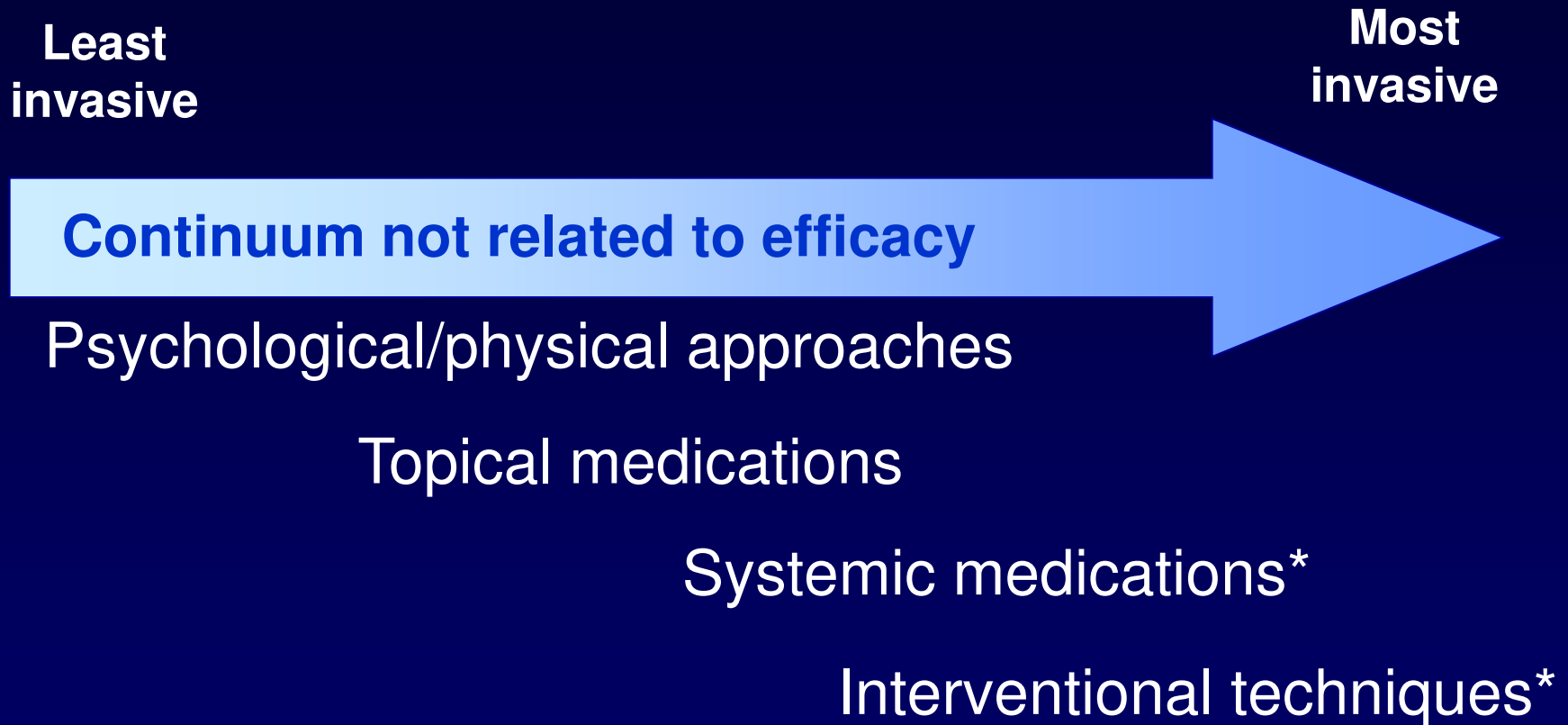
Diagnosis and assessment

If possible, treat underlying condition with disease-modifying therapy





Pain Treatment Continuum



*Consider referral if previous treatments were unsuccessful.

Pharmacologic Treatment for Neuropathic Pain

- Classes of systemic agents with efficacy demonstrated in multiple, randomized, controlled trials for neuropathic pain
 - Anticonvulsants (e.g. Gabapentin/Neurontin, Pregabalin/Lyrica)
 - Antidepressants (e.g. Amitriptyline/Elavil, Duloxetine/Cymbalta)
 - Opioids (e.g. Morphine, Oxycodone/Oxycontin, Percocet, Vicodin)

The Perils of Placebo

Of course, parachute design and testing should always be done with the **utmost** scientific rigor and diligence.



Hence the placebo groups.

FDA-Approved Treatments for Neuropathic Pain (Oct 2018)

- Lidocaine patch 5%

- PHN

- Gabapentin

- PHN

- Carbamazepine

- Trigeminal neuralgia

- Duloxetine

- PDN

- Pregabalin

- PHN

- PDN

- High-conc capsaicin patch

- PHN (US FDA)

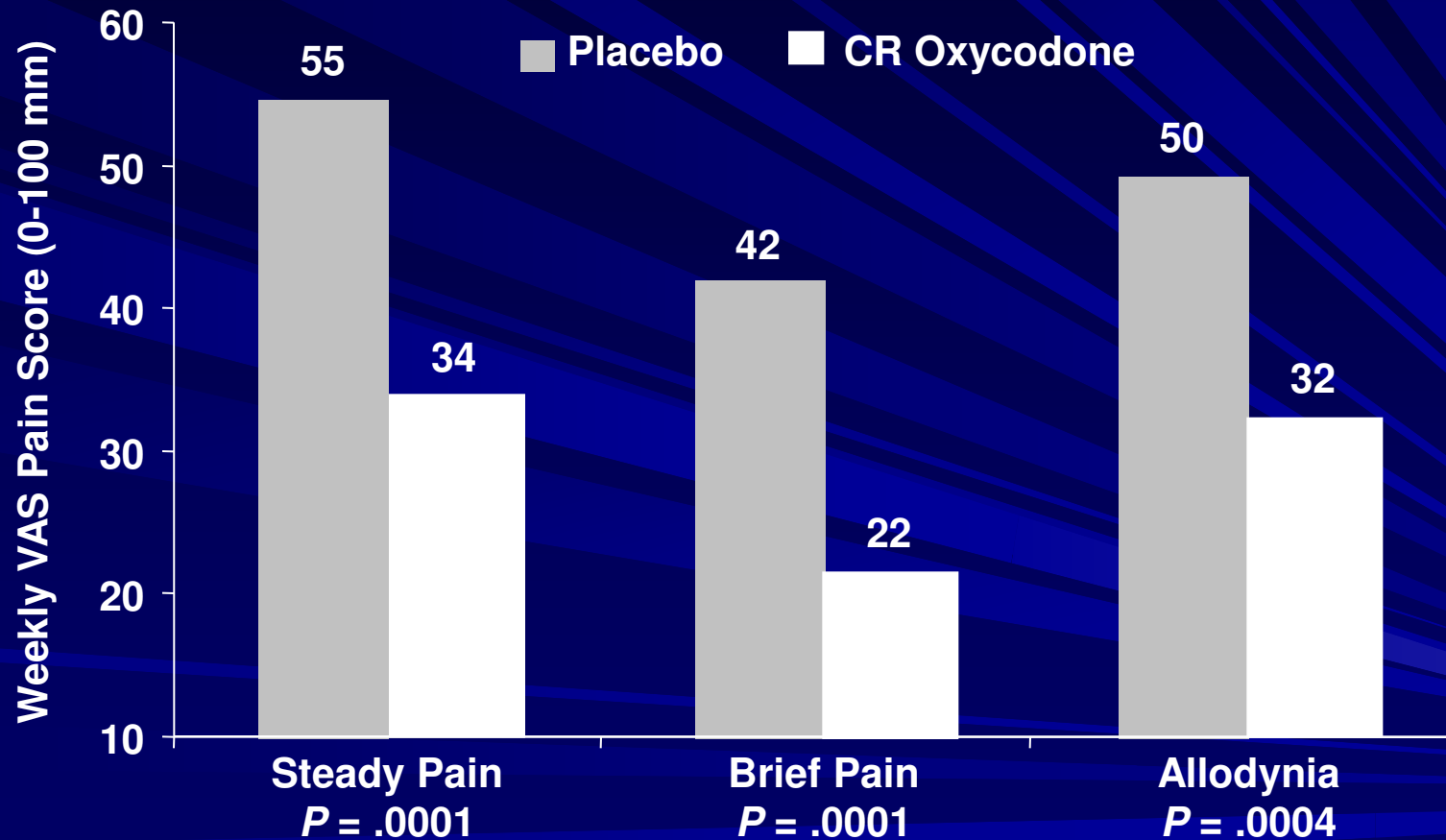
- Periph PN x DM (EMEA)

- Tapentadol

- DPN

Opioid Analgesics: Efficacy in Postherpetic Neuralgia

VAS Scores During Final Week of Treatment



N = 38

Reproduced with permission from Watson CPN, Babul N. *Neurology*. 1998;50:1837-1841.

Combination Therapy for Peripheral Neuropathic Pain

Possible Advantages

- Decreased adverse effects¹
- Increased efficacy^{1,2,4}

Possible Disadvantages

- Increased adverse effects^{3,4}
- Increased drug–drug interactions^{1,4}
- Complex drug regimens⁴
- Difficulty in determining cause of adverse effects^{3,4}

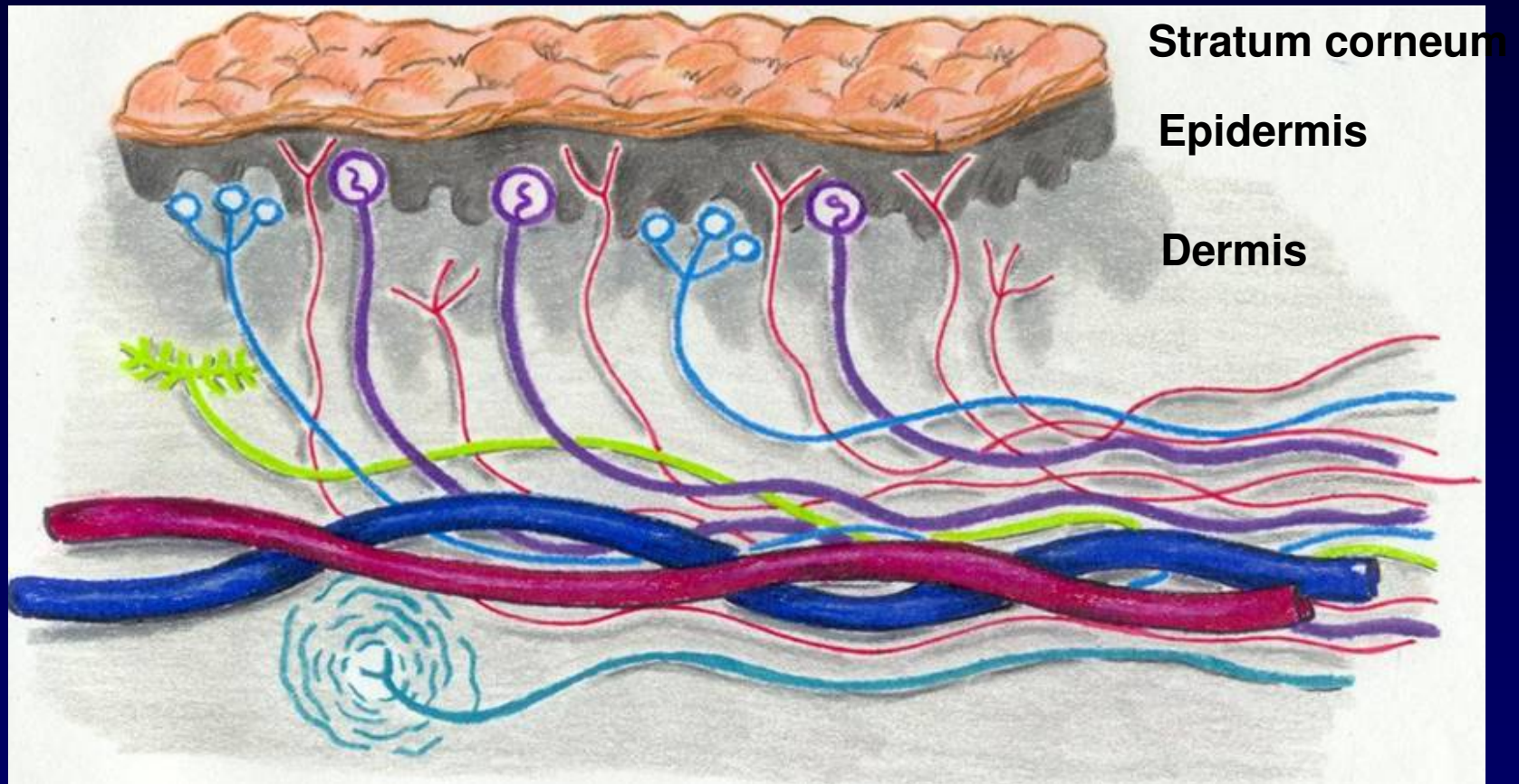
1. Namaka M et al. *Clin Ther*. 2004;26:951-979.

2. Dworkin RH et al. *Arch Neurol*. 2003;60:1524-1534.

3. Dworkin RH, Schmader KE. *Clin Infect Dis*. 2003;36:877-882.

4. Harden N, Cohen M. *J Pain Symptom Manage*. 2003;25:S12-S17.

Sensory System in Skin



Topical Treatments for Pain



Lidocaine Patch 5%



Capsaicin

Capsaicin Patch Neuropathy Treatment Procedure



Take Home Points

- Patients who present to their primary care physicians with pain require:
 - A thorough diagnostic evaluation
 - Targeted diagnostic testing
 - Aggressive cause-specific treatment
 - Lifestyle modification
 - Pain control

Summary

- ❑ Neuropathic pain is common, and a major cause of chronic pain and suffering
- ❑ Pain is underdiagnosed and undertreated
- ❑ A rational, mechanism-based approach to treatment of pain provides substantial improvement in quality of life
- ❑ Successful treatment requires long term close relationships with patients
- ❑ Successes are not measured by eliminating pain- but by improving ability to function.

Mount Sinai Neuropathy Research Program

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