

Phenotyping Chronic Pain Patients

SYMPTOMS, SIGNS, AND UNDERLYING
MECHANISMS

Clifford Woolf



Pain Phenotype

Disease

Age

Gender

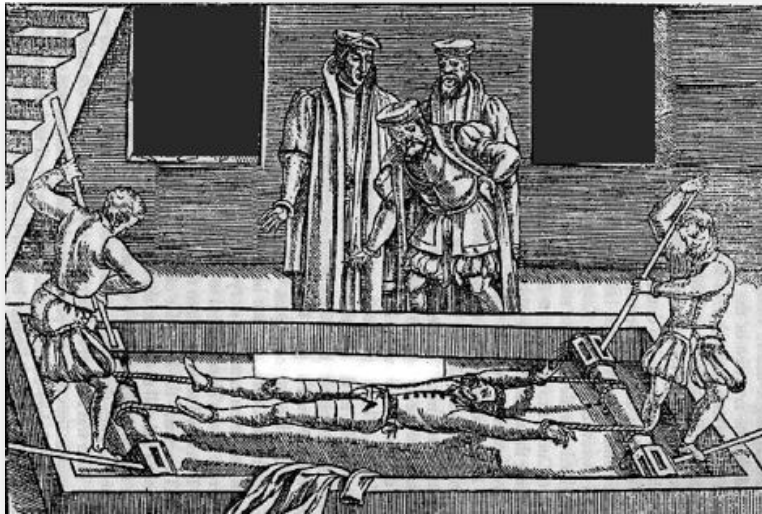
Symptoms – amplitude, distribution and quality

Signs

Psychosocial factors

Pain severity

Stimulus – response relationship



No Pain
Mild
Moderate
Severe

The Worst Imaginable Pain

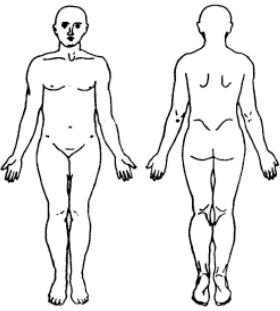
No Pain

Pain quality

McGill Pain Questionnaire

Patient's Name _____ Date _____ Time _____ am/pm

PRI: S _____ A _____ E _____ M _____ PRI(T) _____ PPI _____
 (1-10) (11-15) (16) (17-20) (1-20)

<table border="1" style="width: 100%; border-collapse: collapse;"> <tbody> <tr><td style="width: 50%;">1 FLICKERING</td><td style="width: 50%;">11 TIRING</td></tr> <tr><td>QUIVERING</td><td>EXHAUSTING</td></tr> <tr><td>PULSING</td><td>12 SICKENING</td></tr> <tr><td>THROBBING</td><td>SUFFOCATING</td></tr> <tr><td>BEATING</td><td>13 FEARFUL</td></tr> <tr><td>POUNDED</td><td>FRIGHTFUL</td></tr> <tr><td>2 JUMPING</td><td>TERRIFYING</td></tr> <tr><td>FLASHING</td><td>14 PUNISHING</td></tr> <tr><td>SHOOTING</td><td>GRUELLING</td></tr> <tr><td>3 PRICKING</td><td>CRUEL</td></tr> <tr><td>BORING</td><td>VICIOUS</td></tr> <tr><td>DRILLING</td><td>KILLING</td></tr> <tr><td>STABBING</td><td>15 WRETCHED</td></tr> <tr><td>LANCINATING</td><td>BLINDING</td></tr> <tr><td>4 SHARP</td><td>16 ANNOYING</td></tr> <tr><td>CUTTING</td><td>TROUBLESOME</td></tr> <tr><td>LACERATING</td><td>MISERABLE</td></tr> <tr><td>5 PINCHING</td><td>INTENSE</td></tr> <tr><td>PRESSING</td><td>UNBEARABLE</td></tr> <tr><td>GNAWING</td><td>17 SPREADING</td></tr> <tr><td>CRAMPING</td><td>RADIATING</td></tr> <tr><td>CRUSHING</td><td>PENETRATING</td></tr> <tr><td>6 TUGGING</td><td>PIERCING</td></tr> <tr><td>PULLING</td><td>18 TIGHT</td></tr> <tr><td>WRENCHING</td><td>NUMB</td></tr> <tr><td>7 HOT</td><td>DRAWING</td></tr> <tr><td>BURNING</td><td>SQUEEZING</td></tr> <tr><td>SCALDING</td><td>TEARING</td></tr> <tr><td>SEARING</td><td>19 COOL</td></tr> <tr><td>8 TINGLING</td><td>COLD</td></tr> <tr><td>ITCHY</td><td>FREEZING</td></tr> <tr><td>SMARTING</td><td>20 NAGGING</td></tr> <tr><td>STINGING</td><td>NAUSEATING</td></tr> <tr><td>9 DULL</td><td>AGONIZING</td></tr> <tr><td>SORE</td><td>DREADFUL</td></tr> <tr><td>HURTING</td><td>TORTURING</td></tr> <tr><td>ACHING</td><td>PPI</td></tr> <tr><td>HEAVY</td><td>0 NO PAIN</td></tr> <tr><td>10 TENDER</td><td>1 MILD</td></tr> <tr><td>TAUT</td><td>2 DISCOMFORTING</td></tr> <tr><td>RASPING</td><td>3 DISTRESSING</td></tr> <tr><td>SPLITTING</td><td>4 HORRIBLE</td></tr> <tr><td></td><td>5 EXCRUCIATING</td></tr> </tbody> </table>	1 FLICKERING	11 TIRING	QUIVERING	EXHAUSTING	PULSING	12 SICKENING	THROBBING	SUFFOCATING	BEATING	13 FEARFUL	POUNDED	FRIGHTFUL	2 JUMPING	TERRIFYING	FLASHING	14 PUNISHING	SHOOTING	GRUELLING	3 PRICKING	CRUEL	BORING	VICIOUS	DRILLING	KILLING	STABBING	15 WRETCHED	LANCINATING	BLINDING	4 SHARP	16 ANNOYING	CUTTING	TROUBLESOME	LACERATING	MISERABLE	5 PINCHING	INTENSE	PRESSING	UNBEARABLE	GNAWING	17 SPREADING	CRAMPING	RADIATING	CRUSHING	PENETRATING	6 TUGGING	PIERCING	PULLING	18 TIGHT	WRENCHING	NUMB	7 HOT	DRAWING	BURNING	SQUEEZING	SCALDING	TEARING	SEARING	19 COOL	8 TINGLING	COLD	ITCHY	FREEZING	SMARTING	20 NAGGING	STINGING	NAUSEATING	9 DULL	AGONIZING	SORE	DREADFUL	HURTING	TORTURING	ACHING	PPI	HEAVY	0 NO PAIN	10 TENDER	1 MILD	TAUT	2 DISCOMFORTING	RASPING	3 DISTRESSING	SPLITTING	4 HORRIBLE		5 EXCRUCIATING	<table border="1" style="width: 100%; border-collapse: collapse;"> <tbody> <tr><td>BRIEF _____</td><td>RHYTHMIC _____</td><td>CONTINUOUS _____</td></tr> <tr><td>MOMENTARY _____</td><td>PERIODIC _____</td><td>STEADY _____</td></tr> <tr><td>TRANSIENT _____</td><td>INTERMITTENT _____</td><td>CONSTANT _____</td></tr> </tbody> </table> <div style="text-align: center; margin: 20px 0;">  </div> <div style="text-align: center; border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> E = EXTERNAL I = INTERNAL </div> <div style="border: 1px solid black; padding: 10px; margin-top: 20px;"> <p>COMMENTS:</p> </div>	BRIEF _____	RHYTHMIC _____	CONTINUOUS _____	MOMENTARY _____	PERIODIC _____	STEADY _____	TRANSIENT _____	INTERMITTENT _____	CONSTANT _____
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Pain phenotype as marker of disease pathology

Rheumatoid arthritis Osteoarthritis Postoperative Pain Post-traumatic Pain
Painful peripheral diabetic neuropathy Postherpetic neuralgia HIV neuropathy
Axial low back pain Lumbar radiculopathy Spinal Stenosis Spondylolisthesis
Fibromyalgia Interstitial Cystitis Irritable Bowel Disease Non cardiac chest pain
Migraine Tension type headache Cluster headache Trigeminal neuralgia
Angina Claudication Vulvodynia Cancer Pain Atypical facial pain
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Pain phenotype as marker of mechanism

- Nociception
- Peripheral sensitization
- Ectopic excitability
- Phenotypic switch
- Central sensitization
- Altered circuitry
- Disinhibition
- Increased facilitation
- Neuroimmune interactions

Neurobiological mechanisms & Pain Phenotype

Peripheral sensitization

Heat allodynia

Ectopic excitability in nociceptors

Spontaneous pain

Central sensitization

Dynamic tactile allodynia

Secondary hyperalgesia

Measuring Pain Phenotype

History - Symptoms

Physical examination - Signs

Quantitative sensory tests

Clinical Electrophysiology

Imaging

Genotype

A Novel Tool for the Assessment of Pain: Validation in Low Back Pain

Joachim Scholz^{1*}, Richard J. Mannion², Daniela E. Hord¹, Robert S. Griffin¹, Bhupendra Rawal³, Hui Zheng³, Daniel Scoffings⁴, Amanda Phillips⁵, Jianli Guo¹, Rodney J. C. Laing², Salahadin Abdi⁶, Isabelle Decosterd⁷, Clifford J. Woolf¹

April 2009

Pain Phenotype

Standardized Interview

Current pain state
Pain location
Onset and time course
Temporal characteristics
Pain-evoking stimuli
Quality of the pain
Effect of drug therapy and other pain-alleviating conditions
Non-painful sensations
Sensory deficits

Physical examination

Skin and appendages, subcutaneous tissue

Skin lesions
Swelling
Change of skin color
Altered sweating
Trophic changes
Pressure sensitivity of deep tissues

Sensory nervous system

Response to punctuate mechanical stimuli
Response to pressure
Response to a dynamic mechanical stimulus
Pinprick pain
Sense of vibration
Response to thermal stimuli
Temporal summation
Sense of position and response to movement

Each individual has 85 tags defining their pain “universe”

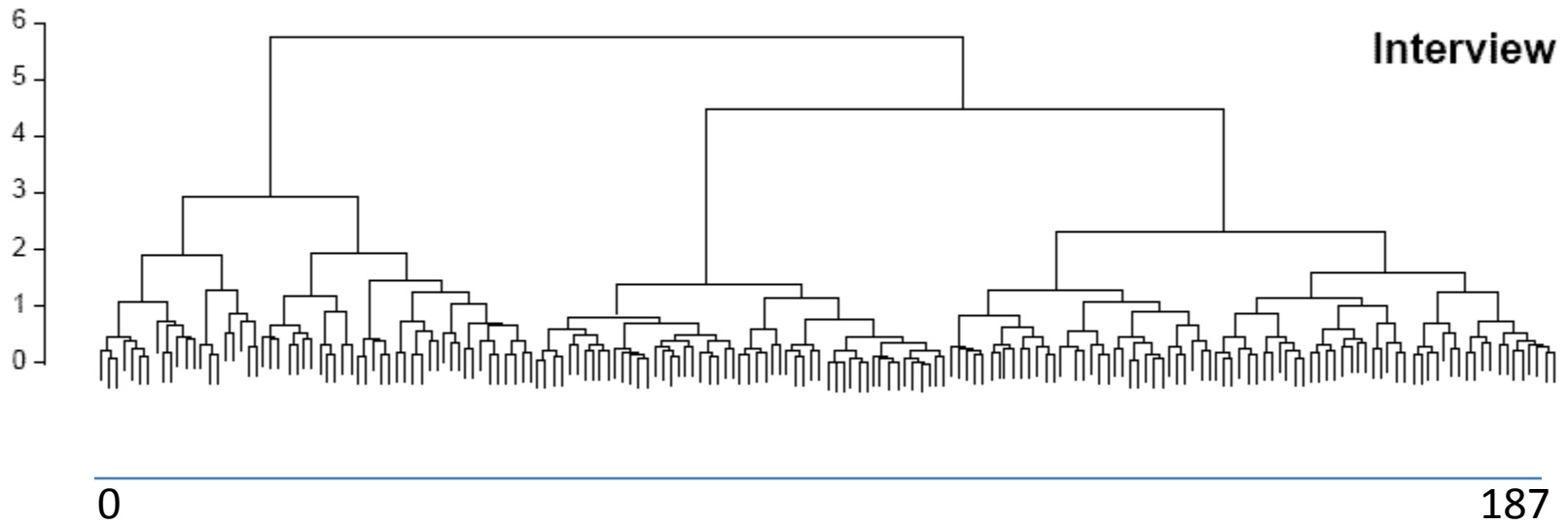
Enrollment

- Postherpetic neuralgia **23**
- Painful diabetic polyneuropathy **50**
- Low back pain with signs of nerve root damage **rLBP 57**
- Axial low back pain w/o radicular symptoms or signs **aLBP 57**

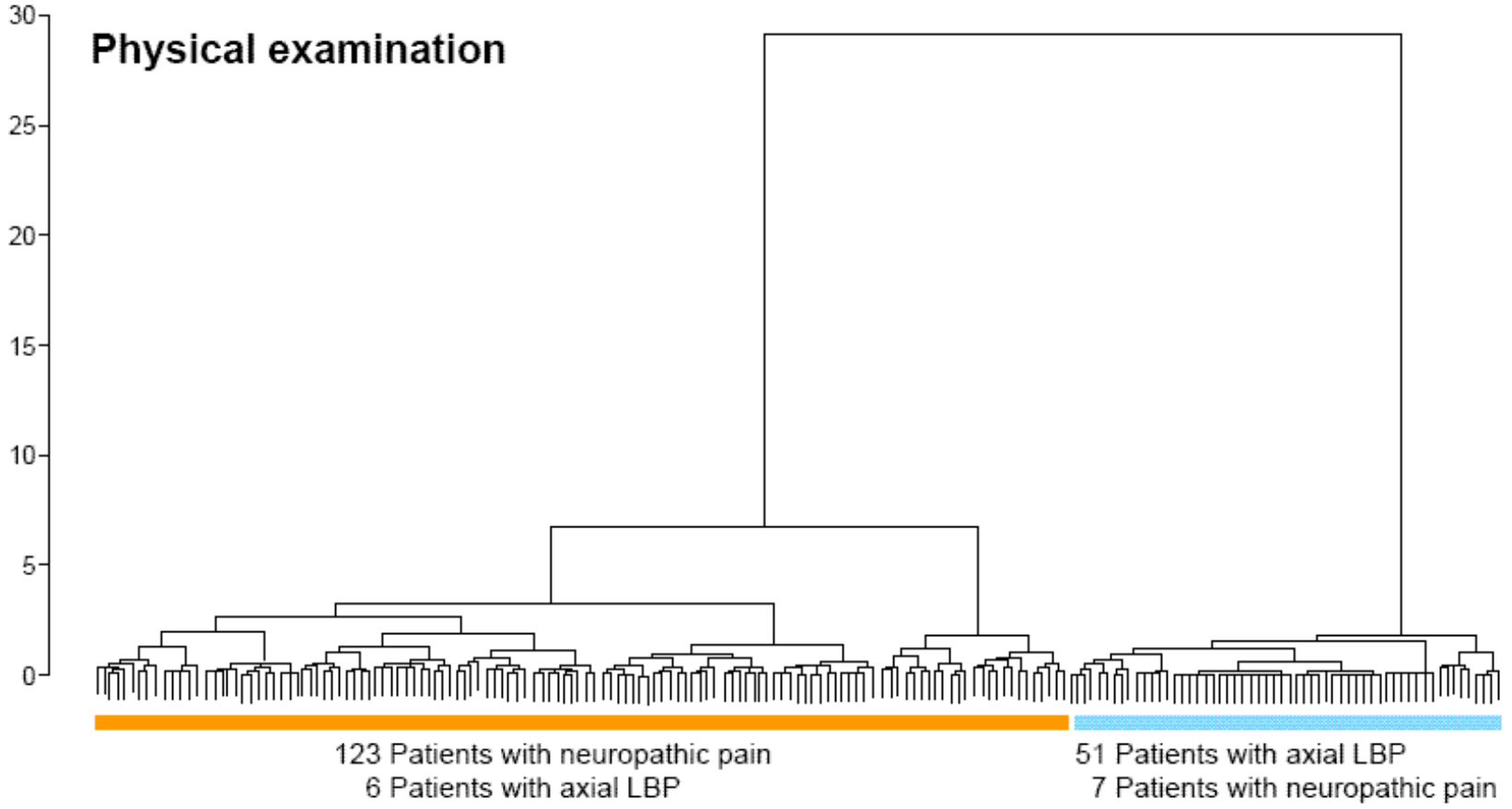
Total 187

Inclusion criteria:

- At least **18** years of age
- Chronic pain (**≥ 3 months**)
- Average pain intensity rated **6/10 or higher** on a numerical rating scale

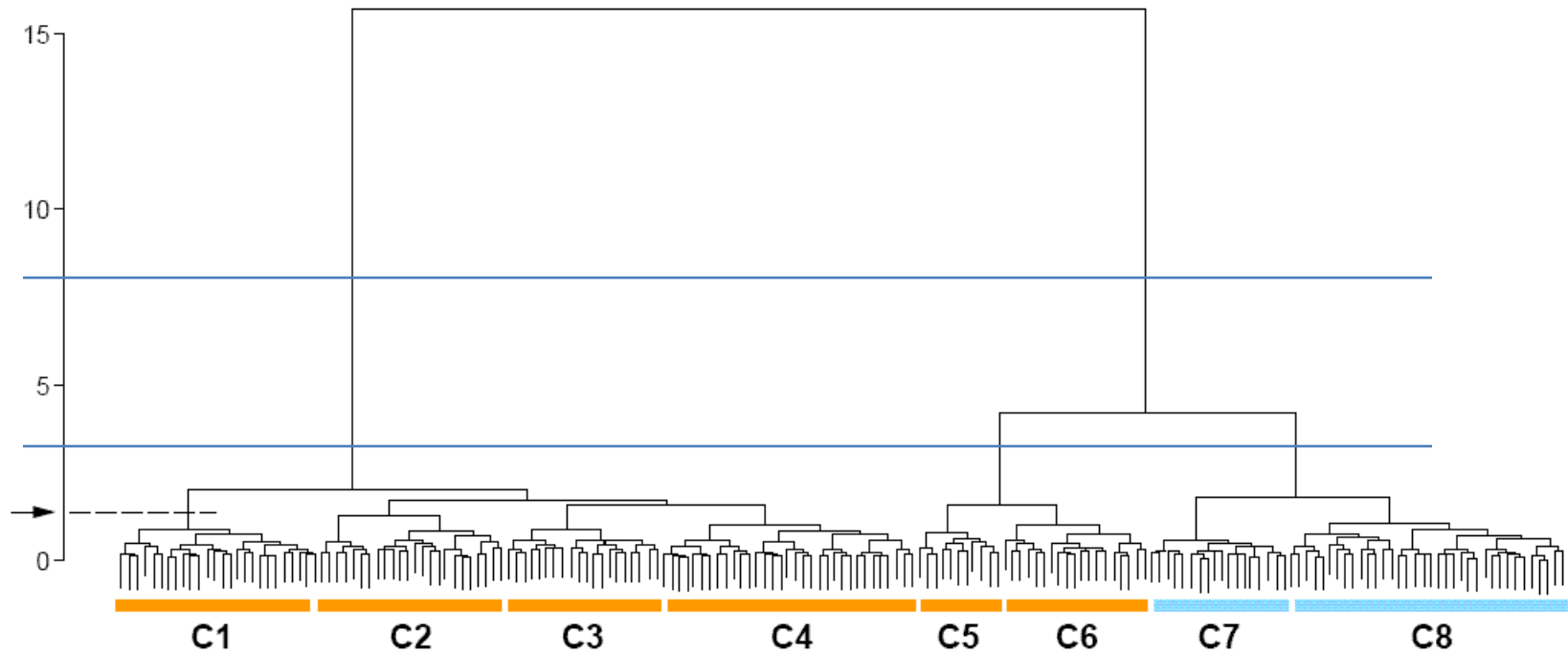


Standardized interview 46 items

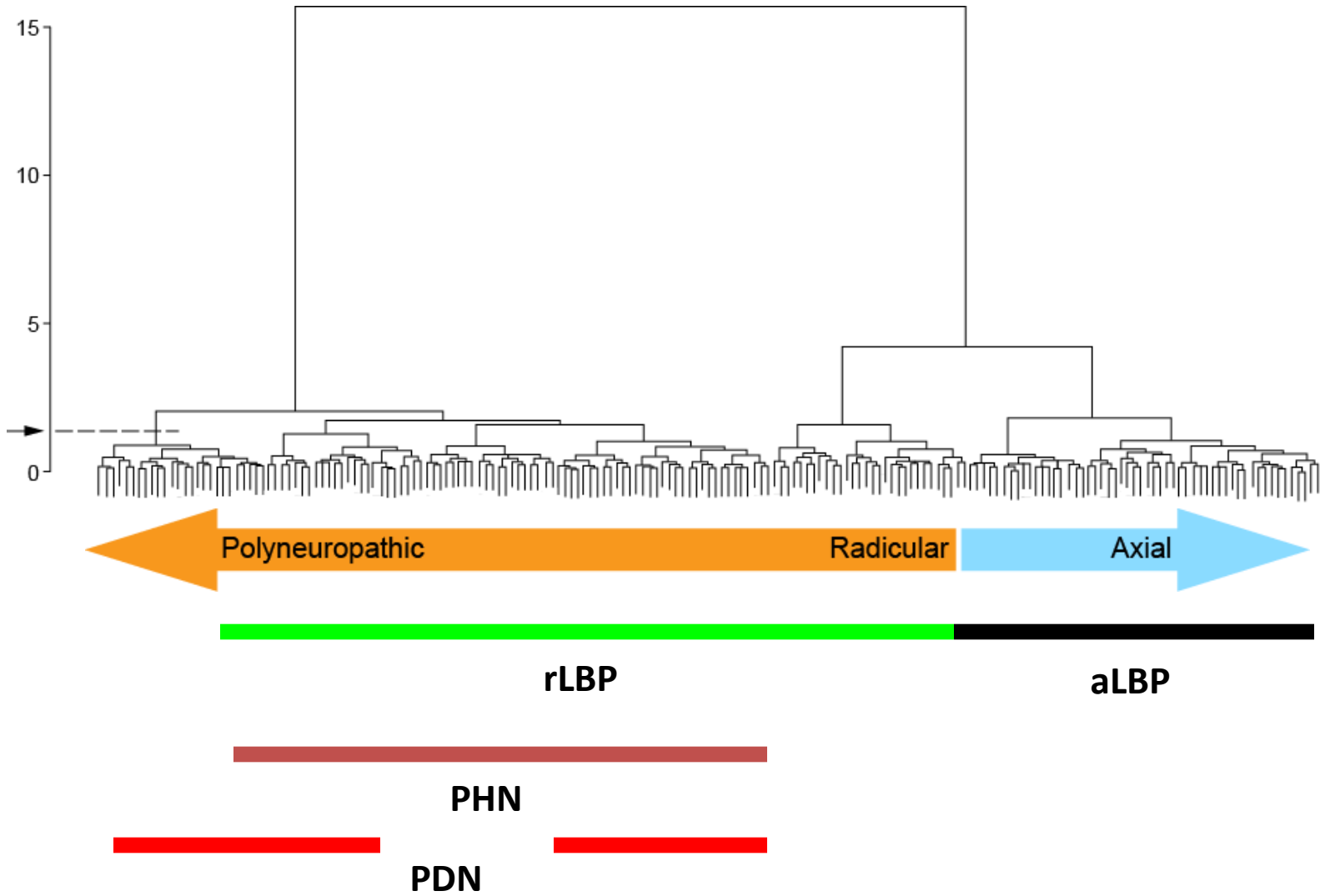


Physical examination 39 items

Combined history and examination



Diagnosis	Patient cluster							
	C1	C2	C3	C4	C5	C6	C7	C8
DN	24	14	1	10	0	1	0	0
PHN	1	5	12	3	0	2	0	0
Radicular LBP	1	5	5	19	9	14	0	4
Axial LBP	0	0	2	1	2	2	18	32
Total	26	24	20	33	11	19	18	36



Unbiased Screen

Interview

Superficial pain

Deep pain

Ongoing pain

Intermittent pain episodes

Series of consecutive pain episodes

Evoked pain (general)

Aftersensations

Trigger zones

Activity-evoked pain

Touch-evoked pain

Pain evoked by moving stimuli

Pressure-evoked pain

Warmth-evoked pain

Cold-evoked pain

Pain quality

- Throbbing, pounding, pulsating

- Shooting, radiating

- Cramping, squeezing

- Stabbing, sharp

- Aching, dull

- Painful pins and needles, stinging

- Burning, hot

Dysesthesia (total)

Ongoing dysesthesia

Intermittent episodes of dysesthesia

Quality of dysesthesia

- Tingling

- Itching

- Warm or cold

Numb skin areas

Physical Examination

Skin

Swelling

Color change

Abnormally dry skin

Excessive sweating

Trophic changes

Sensory nervous system

Decreased response to stimulation with von Frey filaments

Pain evoked by stimulation with von Frey filaments

Decreased response to blunt pressure

Blunt pressure-evoked pain

Increased pressure sensitivity of deep tissues

Decreased response to brush movement

Brush movement-evoked pain

Decreased response to pinprick

Pinprick hyperalgesia

Decreased response to vibration

Decreased response to warmth

Warmth-evoked pain

Decreased response to cold

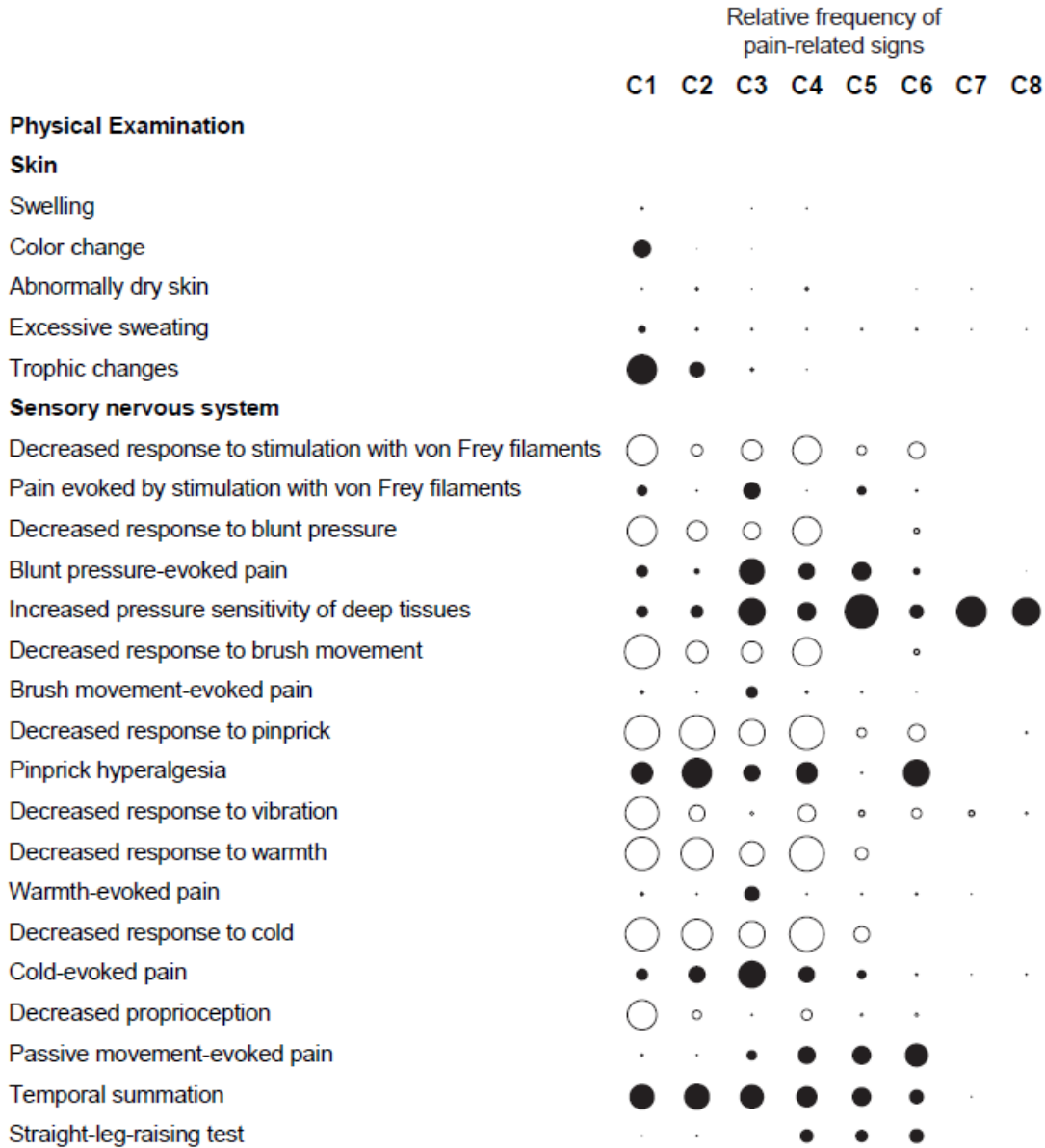
Cold-evoked pain

Decreased proprioception

Passive movement-evoked pain

Temporal summation

Straight-leg-raising test



Physical Examination

Skin

Swelling

Color change

Abnormally dry skin

Excessive sweating

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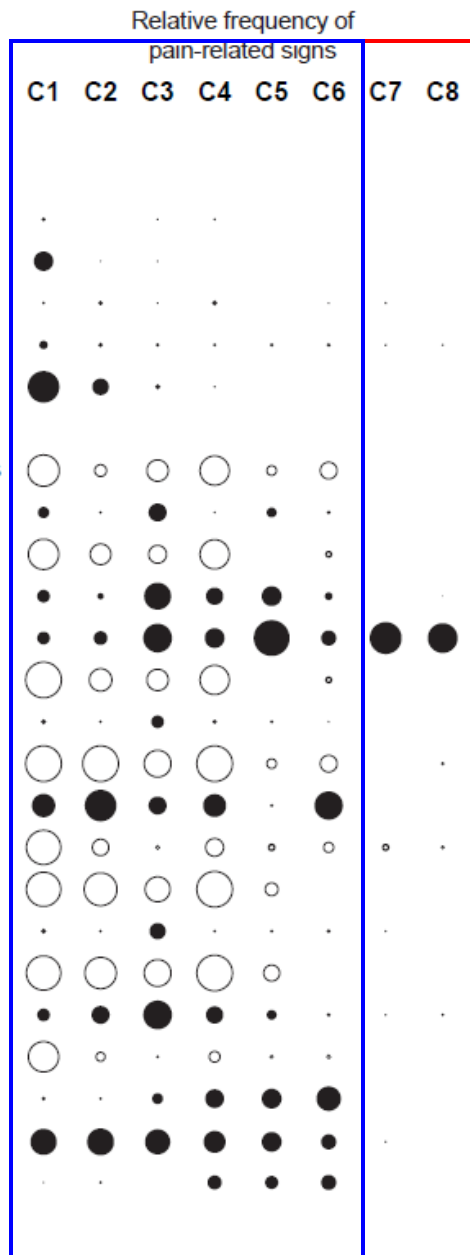
Cold-evoked pain

Decreased proprioception

Passive movement-evoked pain

Temporal summation

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Relative frequency of
pain-related signs

C1 C2 C3 C4 C5 C6 C7 C8

Physical Examination

Skin

Swelling

Color change

Abnormally dry skin

Excessive sweating

Trophic changes

Sensory nervous system

Decreased response to stimulation with von Frey filaments



Pain evoked by stimulation with von Frey filaments



Decreased response to blunt pressure



Blunt pressure-evoked pain



Increased pressure sensitivity of deep tissues



Decreased response to brush movement



Brush movement-evoked pain



Decreased response to pinprick



Pinprick hyperalgesia



Decreased response to vibration



Decreased response to warmth



Warmth-evoked pain



Decreased response to cold



Cold-evoked pain



Decreased proprioception



Passive movement-evoked pain

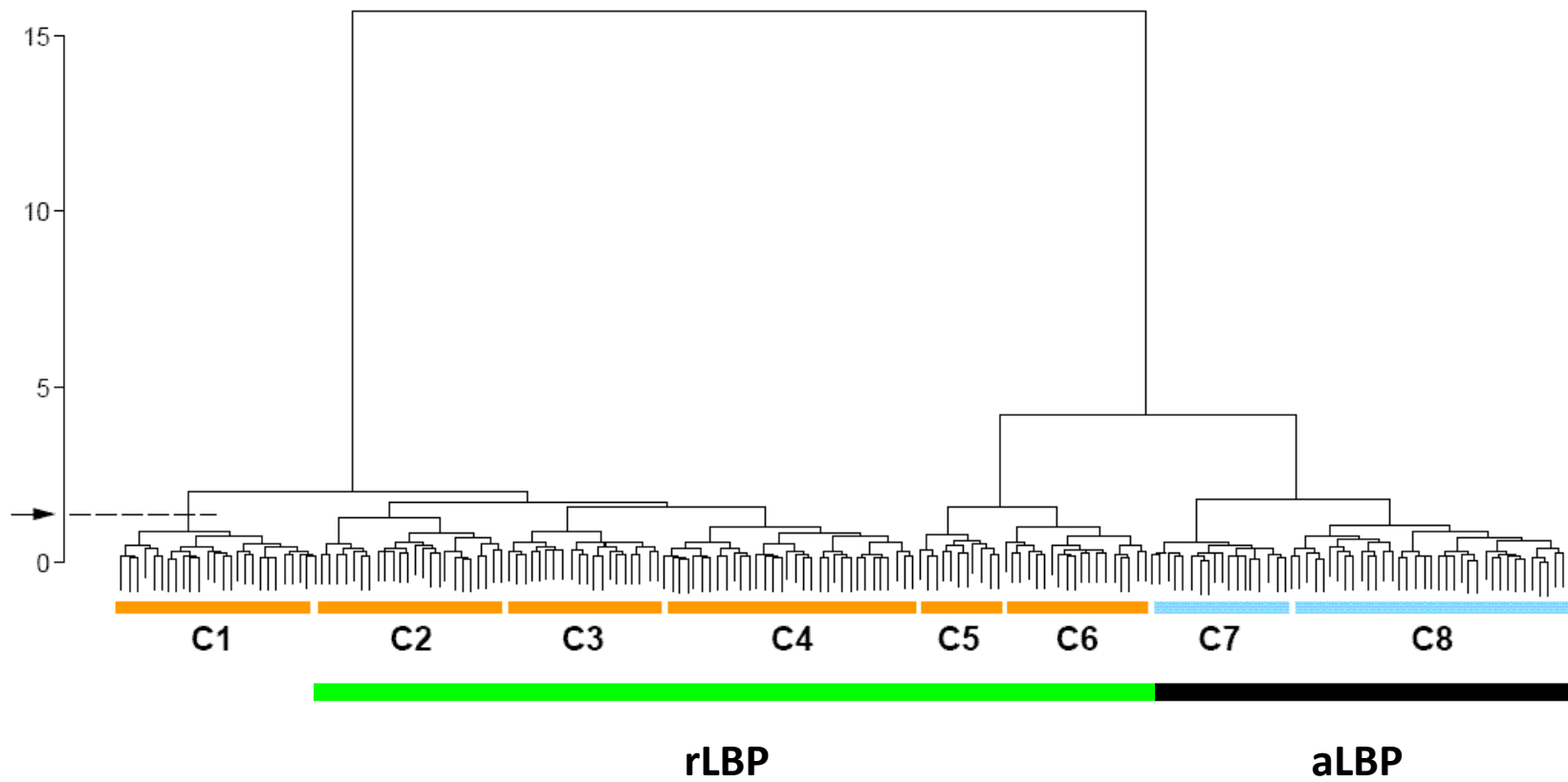


Temporal summation

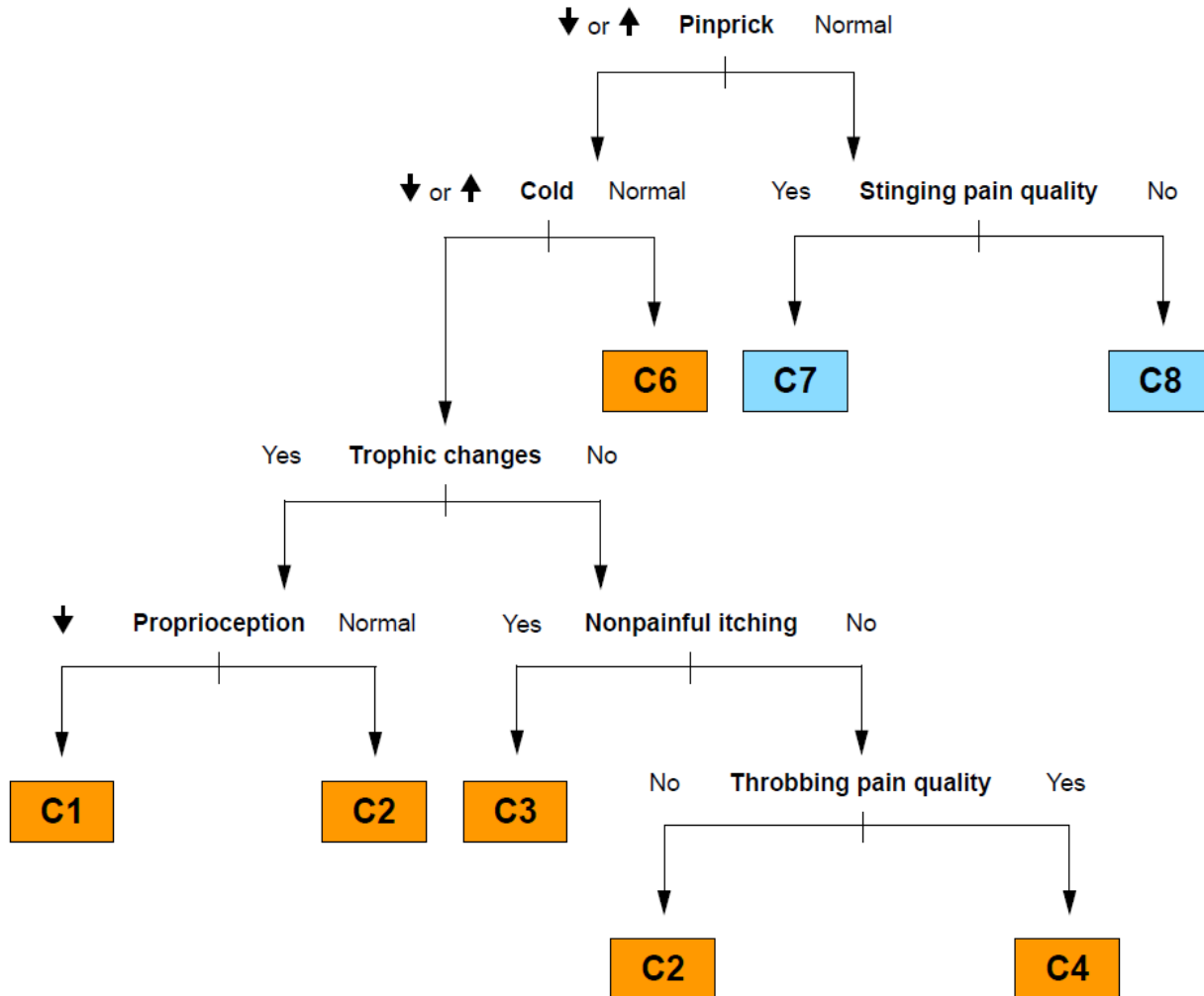


Straight-leg-raising test



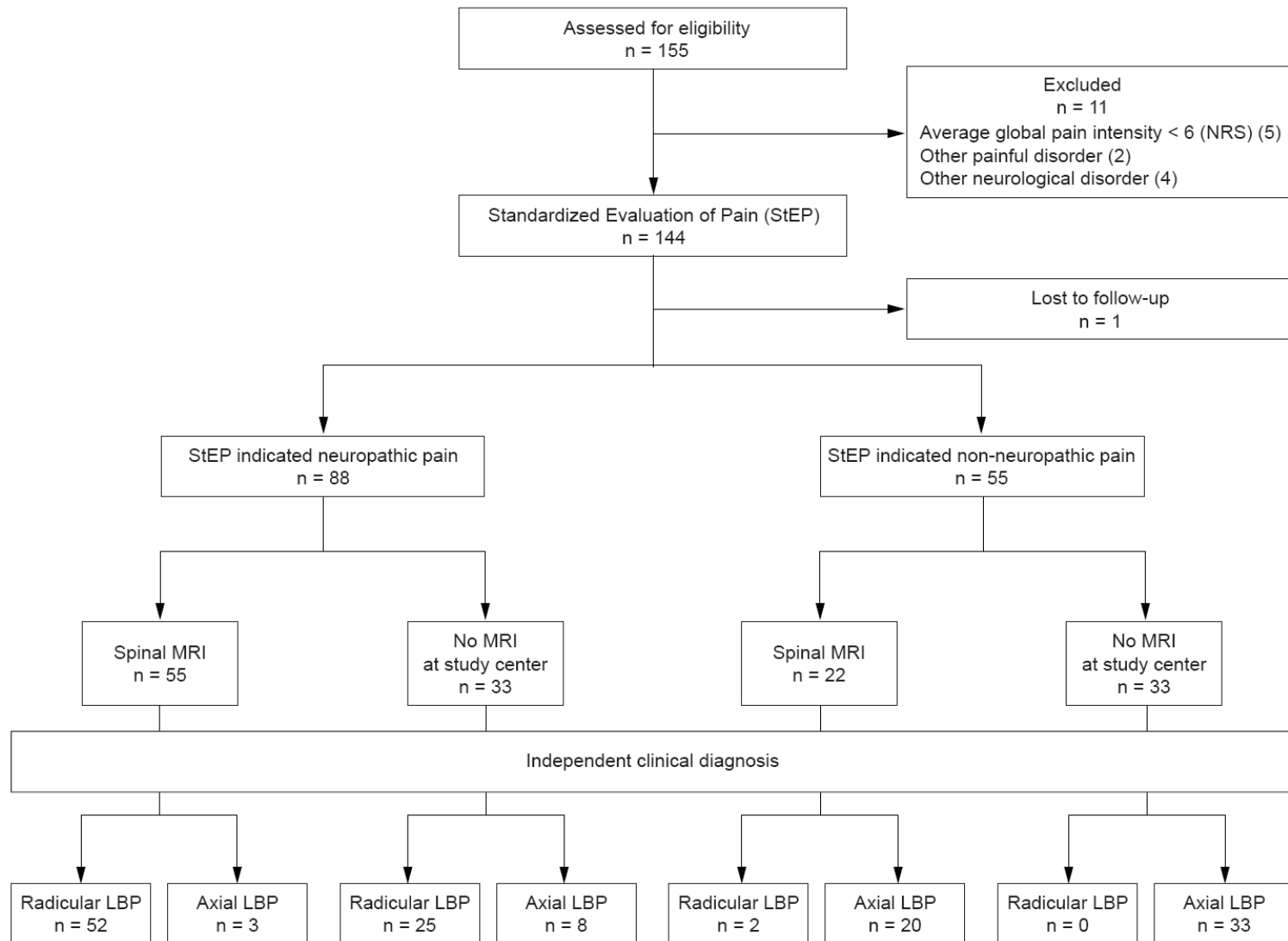


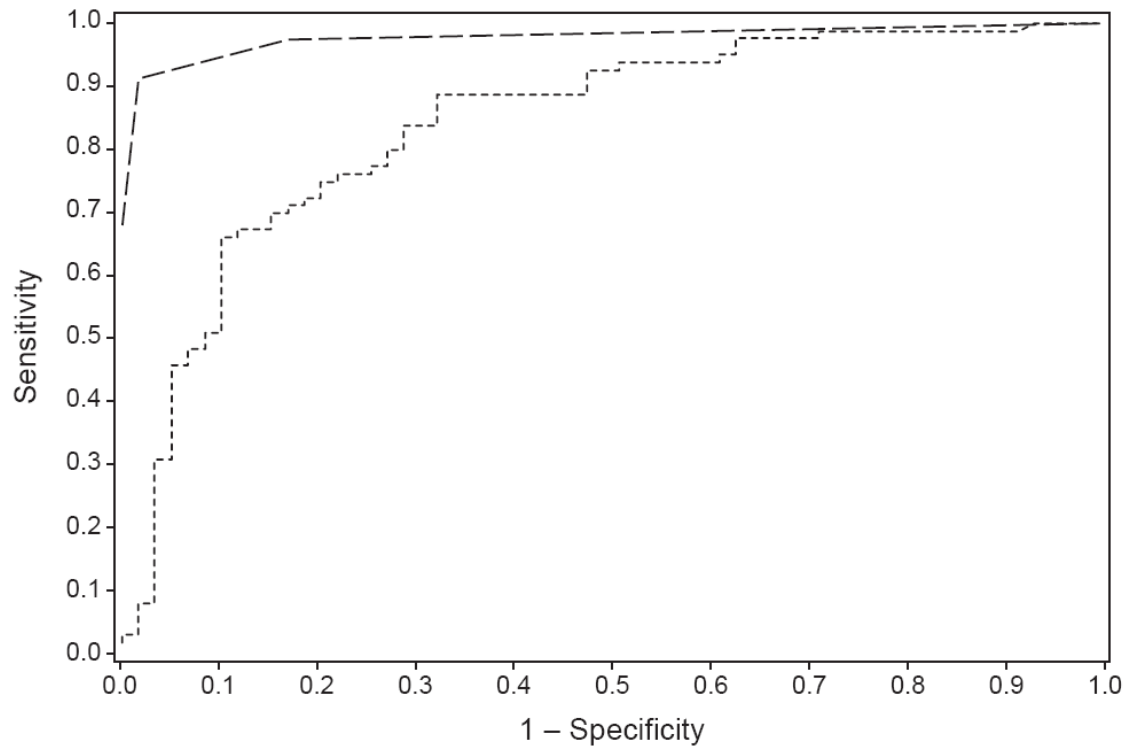
Classification Tree Analysis



StEP = 6 interview & 10 examination items

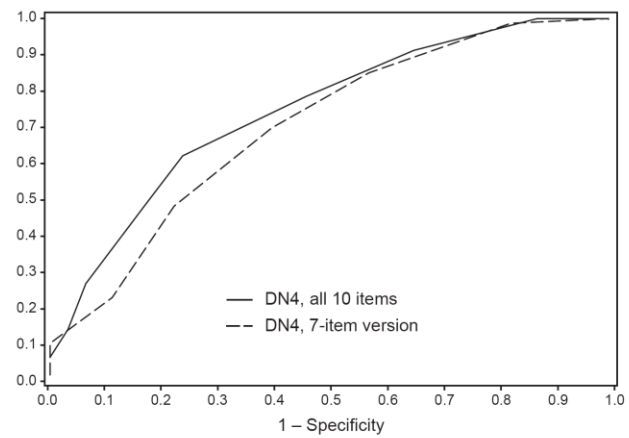
Trial 2 to test if StEP can distinguish aLBP from rLBP



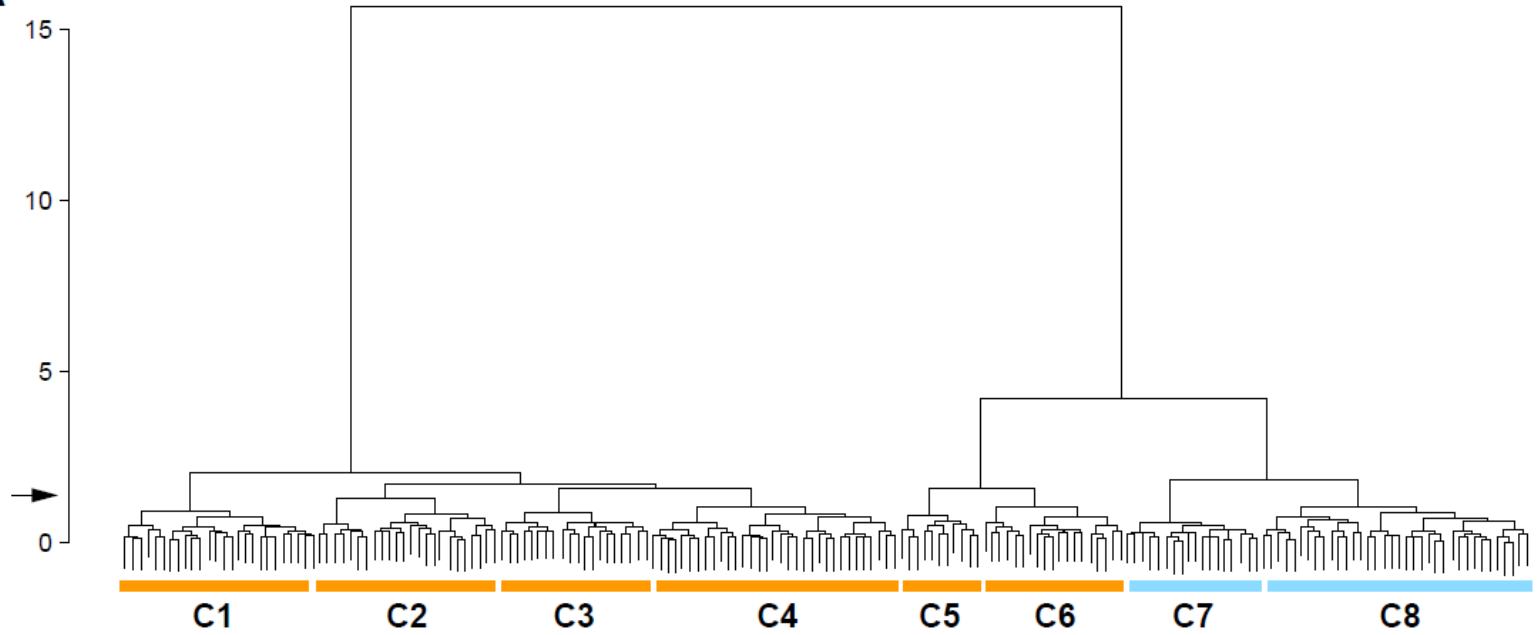


StEP

Douleur Neuropathique



A



Peripheral sensitization

Central sensitization

Disinhibition

Ectopic activity





Joachim Scholz



Richard Mannion