Updates in Pain Medicine

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Conflict of Interest

NONE

Why Update

Conversation about opioids has evolved since the 2016 CDC opioid guidelines

Pain medicine is evolving to be more biopsychosocial

Treatment of pain is evolving to be more holistic

Why Update?

2016 CDC OPIOID GUIDELINES LIMITED OPIOID TREATMENT OF CHRONIC PAIN

THE PANDEMIC CHANGED THE COURSE OF OPIOID CRISIS

NEW EMPHASIS ON HOLISTIC TOOLS TO MANAGE PAIN

From: **Estimated Rates of Incident and Persistent Chronic Pain Among US Adults, 2019-2020**

JAMA Netw Open. 2023;6(5):e2313563. doi:10.1001/jamanetworkopen.2023.13563

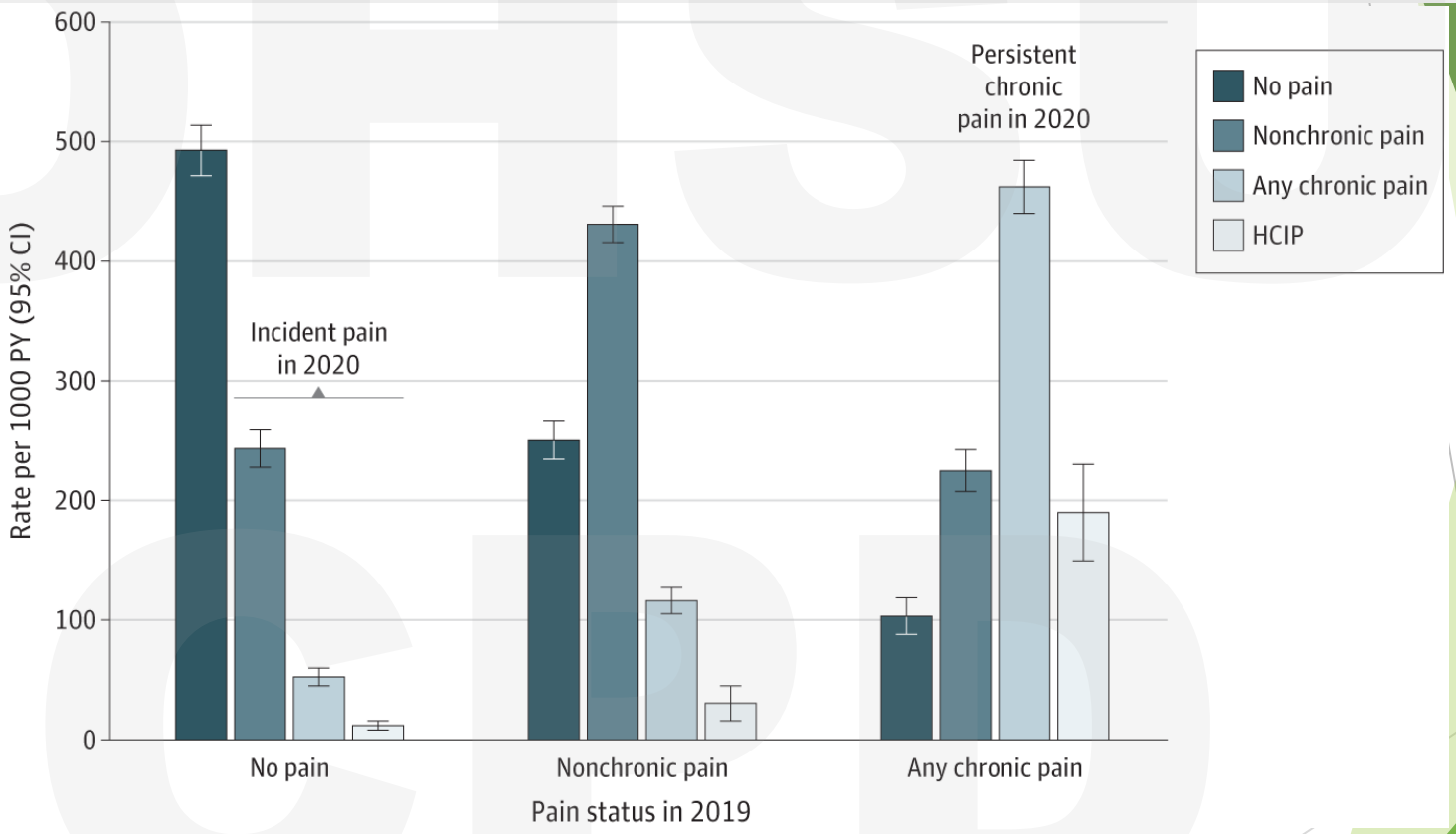


Figure Legend:

Rates of Pain in 2020 by Pain Status in 2019 No pain was defined as no pain in the past 3 months, nonchronic pain as pain on some days in the past 3 months, and chronic pain as pain on most days or every day in the past 3 months. High-impact chronic pain (HICP) was defined as chronic pain that limited life or work activities on most days or every day during the past 3 months. Rates were estimated using longitudinal survey weights supplied by the National Center for Health Statistics (10 415 participants included in the analysis; total weighted population of 250.9 million adults who were age standardized to the age distribution of the US population in 2010). The whiskers represent 95% CIs. PY indicates person-years.

Incidence and Prevalence of Cancer Related Pain

- prevalence 33% in patients after curative treatment
- 59% in patients receiving anticancer treatment
- 64% in patients with metastatic, advanced or terminal disease
- Pain has a high prevalence earlier in disease in specific cancer types such as pancreatic (44%) and head and neck cancer (40%)
- POOR QUALITY OF LIFE

Fallon, Marie, et al. "Management of cancer pain in adult patients: ESMO Clinical Practice Guidelines." *Annals of Oncology* 29 (2018): iv166-iv191.

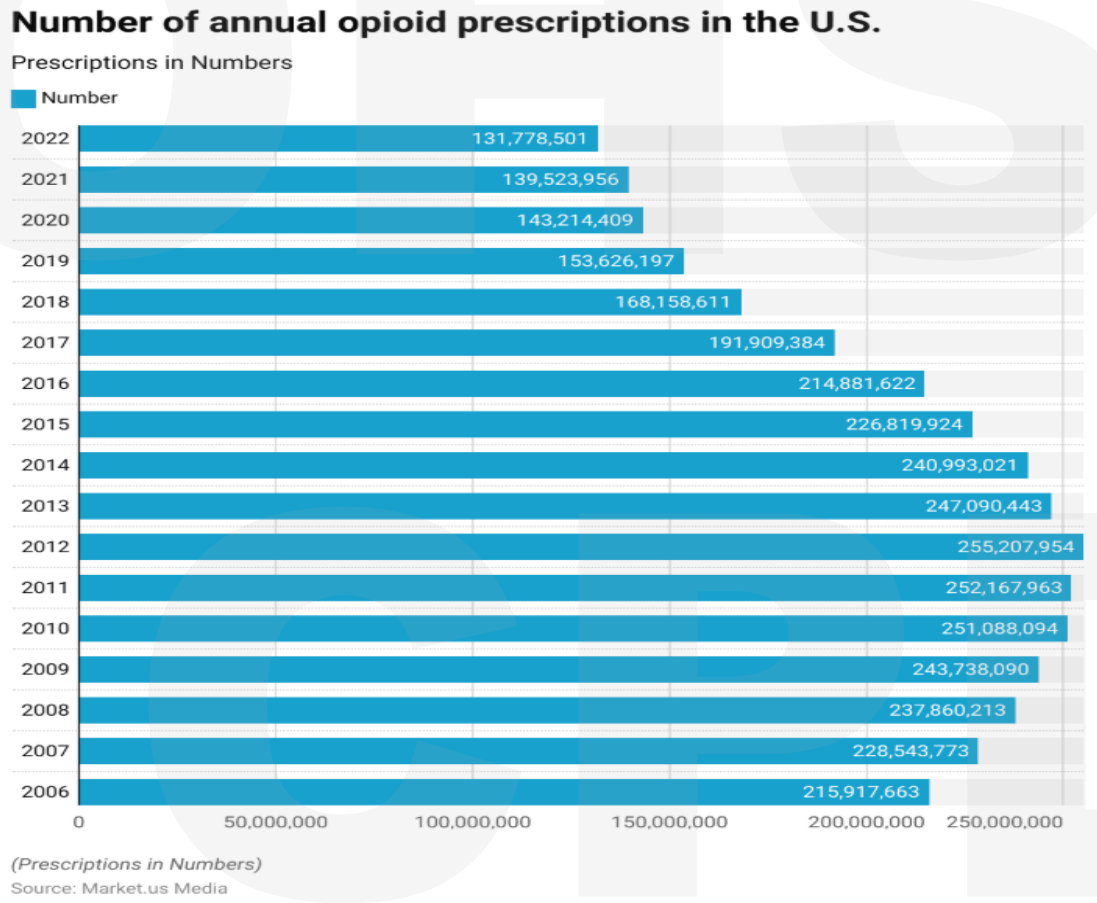
Cancer Related Pain

- 10,637 studies, of which 444 were included between 2014-2021
- The overall prevalence of pain was 44.5%. Moderate to severe pain was experienced by 30.6% of the patients, a lower proportion compared to previous research.
- **Increased attention to the assessment and management of pain might have fostered the decline in the prevalence and severity of pain**

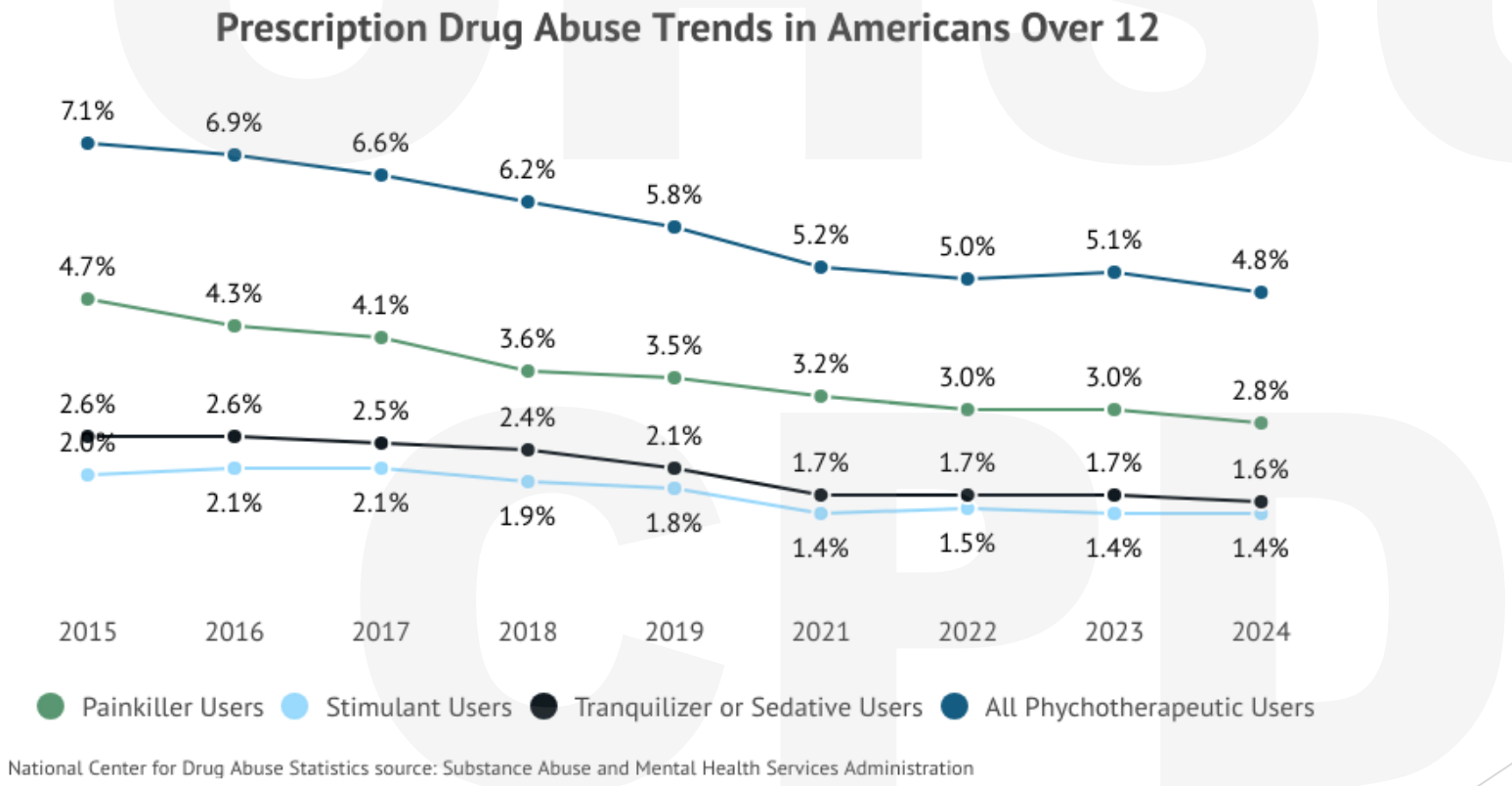
Snijders, R.A.H.; Brom, L.; Theunissen, M.; van den Beuken-van Everdingen, M.H.J. Update on Prevalence of Pain in Patients with Cancer 2022: A Systematic Literature Review and Meta-Analysis. *Cancers* **2023**, *15*, 591. https://doi.org/10.3390/cancers15030591

Good Job!

Opioid Prescription Rates

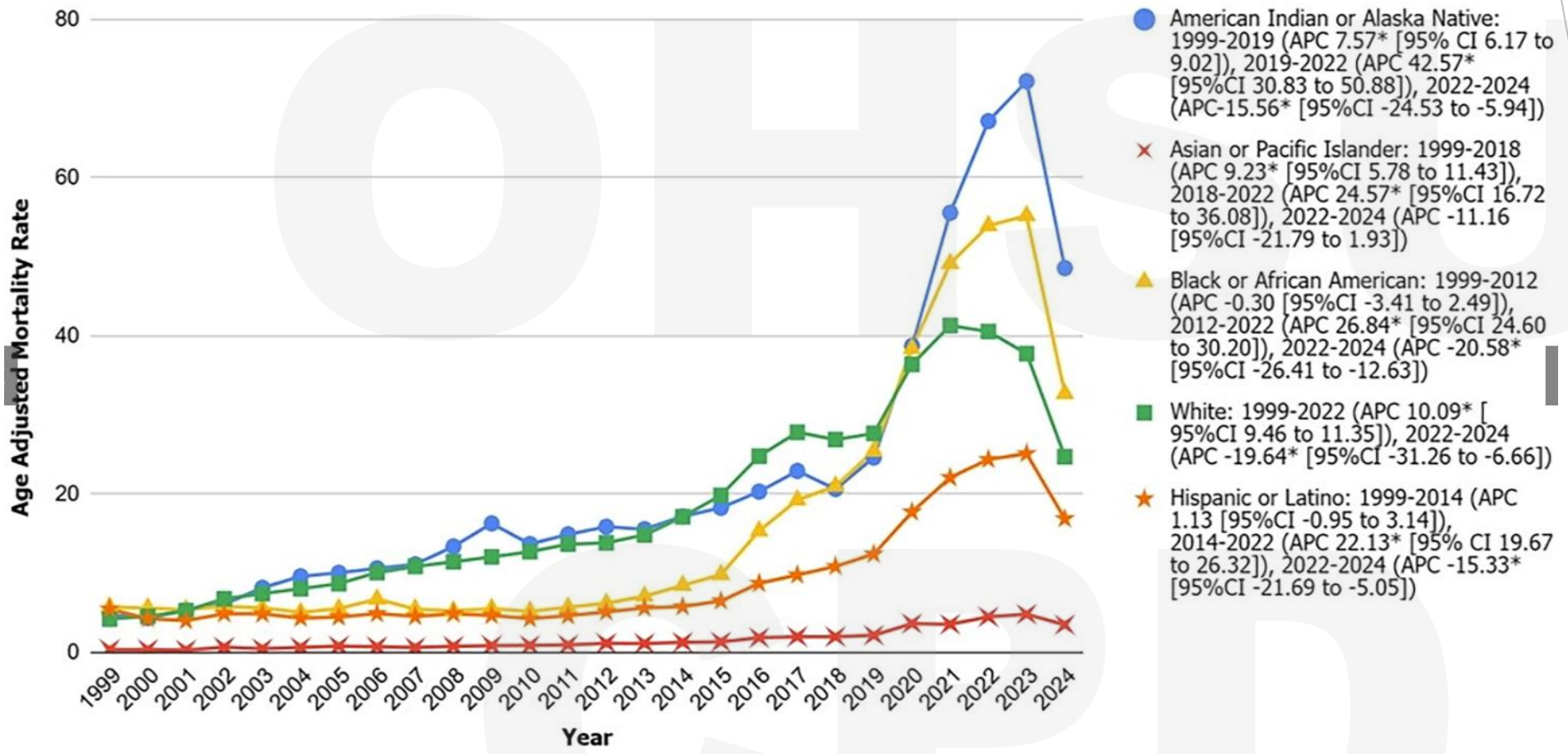


Prescription Drug Abuse Trends



National Center for Drug Abuse Statistics source: Substance Abuse and Mental Health Services Administration

Pandemic Changed Opioid Crisis



Ahmed, Sophia, et al. "Mortality Due to Opioid Overdose in the United States: Trends from a CDC WONDER Analysis (1999–2024)." *Population Health Management* (2025).

Hypothesis about Flattening the Curve

Increased recognition and treatment of addiction

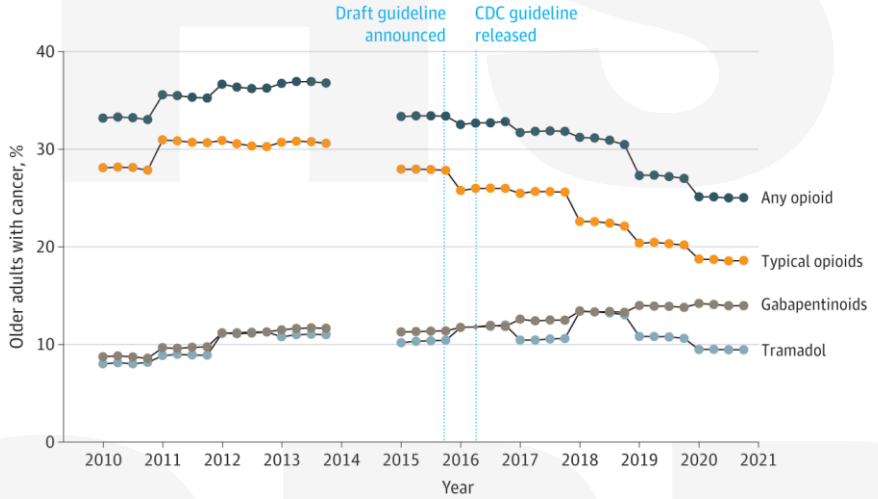
Like other epidemics, the disease had ran its course

the federal government cracked down on Mexican cartels and working with the Chinese to curtail import of Fentanyl precursors.

- Side effects of the 2016 CDC Guidelines for Prescribing Opioids for Chronic pain

From: **The 2016 CDC Opioid Guideline and Analgesic Prescribing Patterns in Older Adults With Cancer**

JAMA Netw Open. 2025;8(5):e259043. doi:10.1001/jamanetworkopen.2025.9043



Analgesic Prescribing in Older Adults With Any Cancer, 2010 to 2020

From: **Long-term Risk of Overdose or Mental Health Crisis After Opioid Dose Tapering**

JAMA Netw Open. 2022;5(6):e2216726. doi:10.1001/jamanetworkopen.2022.16726

Table 3. Adjusted IRRs of Overdose or Mental Health Crisis in the Postinduction Compared With the Pretaper Period by Patient or Period Subgroups[a]

Patient or period subgroup	Overdose or withdrawal		Overdose		Mental health crisis	
	IRR (95% CI)	*P* value[b]	IRR (95% CI)	*P* value[b]	IRR (95% CI)	*P* value[b]
Baseline dose, MME[c]						
50-89	1.24 (0.98-1.58)	.01	1.04 (0.75-1.44)	.15	1.26 (0.97-1.63)	<.001
90-149	1.54 (1.24-1.90)		1.43 (1.08-1.91)		1.18 (0.93-1.49)	
150-299	1.47 (1.23-1.75)		1.40 (1.11-1.76)		1.49 (1.21-1.82)	
≥300	2.03 (1.67-2.47)		1.71 (1.31-2.24)		2.54 (1.95-3.30)	
Postinduction achieved dose vs baseline[d]						
Discontinued	1.09 (0.88-1.36)	<.001	0.86 (0.62-1.20)	<.001	1.17 (0.91-1.50)	.13
1%-49%	1.32 (1.08-1.61)		1.07 (0.82-1.39)		1.58 (1.26-1.97)	
50%-84%	1.93 (1.61-2.32)		1.86 (1.46-2.37)		1.77 (1.43-2.19)	
85%-114%	2.16 (1.71-2.73)		1.93 (1.43-2.62)		1.59 (1.23-2.06)	
≥115%	1.56 (1.00-2.43)		1.64 (0.94-2.87)		1.28 (0.76-2.16)	
Early vs later in postinduction period						
Early (months 13-16)	1.56 (1.32-1.84)	.94	1.32 (1.05-1.67)	.53	1.56 (1.28-1.89)	.77
Later (months 17-24)	1.57 (1.41-1.75)		1.42 (1.24-1.64)		1.51 (1.33-1.71)	

Abbreviations: IRR, incidence rate ratio; MME, morphine milliequivalents.

[a] Data were estimated using fixed-effects negative binomial regression (21 515 tapers among 19 377 patients).

[b] *P* values are for χ^2 tests for significant heterogeneity in IRRs across subgroups.

[c] Stratum-specific IRRs were estimated by fitting models with interaction terms between pretaper vs posttaper period and baseline dose categories.

[d] Defined as the average opioid dose (in MME) during the first postinduction 60-day period divided by the average opioid dose during the 12-month stable baseline period.

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CDC Updated Guidelines 2022 (latest)

1. Maximize non-opioid treatments for acute pain
2. Non-opioids are preferred over opioids
3. Start with immediate release opioids
4. Lowest effective dose, avoid escalation
5. **opioid therapy should not be discontinued abruptly, and clinicians should not rapidly reduce dose**
6. no greater quantity than needed for the expected duration of pain
7. evaluate within 1–4 weeks
8. evaluate risk for opioid-related harms
9. PDMP
10. toxicology testing
11. caution when prescribing opioid and benzodiazepines concurrently
12. **Detoxification without medications for opioid use disorder is not recommended**

Oregon – Oregon Medical Board 2022

- All Oregon Medical Board licensees must complete the Oregon Pain Management Commission's (OPMC) continuing education course Changing the Conversation About Pain“ at initial licensing and then every 2 years.

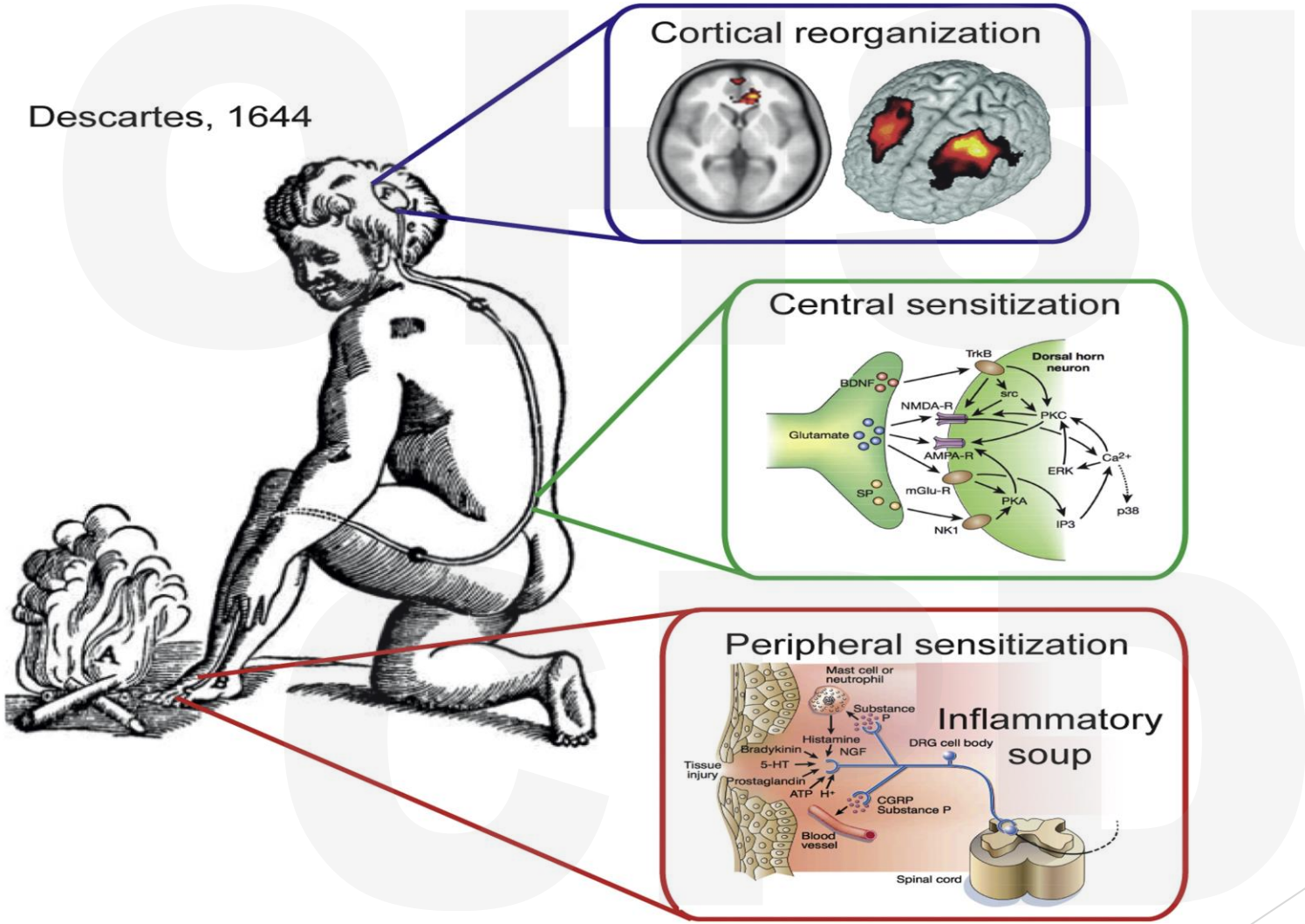
- Visit OregonPainGuidance.org/paineducationtoolkit to access the toolkit. A clinician-focused version is also available at OregonPainGuidance.org/paineducationtoolkitforclinicians.

The changing conversation of pain management

1. The evolution of pain from nociception to biopsychosocial pain

2. The treatment of pain to include psychological and social pain.

Pain as Nociception



Baliki, Marwan N., and A. Vania Apkarian. "Nociception, pain, negative moods, and behavior selection." *Neuron* 87.3 (2015): 474-491.

The Definition of Pain -- IASP

“An unpleasant sensory and emotional experience associated with, or resembling... actual or potential tissue damage,”

https://www.iasp-pain.org/publications/iasp-news/iasp-announces-revised-definition-of-pain/

Old Nomenclature

- Chronic Pain Syndrome – Not only do patients have chronic pain, they also have a psychological and emotional **preoccupation** with the pain that limits function.

Florence, David W. "The chronic pain syndrome: a physical and psychologic challenge." *Postgraduate Medicine* 70.5 (1981): 217-228.

The New Biopsychosocial Aspects of Chronic pain -2020 IASP Update

- **Normalizing the** psychosocial aspect of pain.
- Pain is always a **personal experience** that is influenced to varying degrees by **biological, psychological, and social factors.**
- Pain and **nociception** are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.

https://www.iasp-pain.org/publications/iasp-news/iasp-announces-revised-definition-of-pain/

New Nomenclature of Chronic Pain

- MG30.0 Chronic primary pain
- MG30.1 Chronic cancer-related pain
- MG30.2 Chronic postsurgical or posttraumatic pain
- MG30.3 Chronic secondary musculoskeletal pain
- MG30.4 Chronic secondary visceral pain
- MG30.5 Chronic neuropathic pain
- MG30.6 Chronic secondary headache or orofacial pain

Beatrice Korwisi, International Association for the Study of Pain (IASP) in 6/14/23 World Health Organization Unlocking the potential of ICD-11 for chronic pain. (https://www.who.int/news-room/events/detail/2023/06/14/default-calendar/who-webinar-on-unlocking-the-potential-of-icd-11-for-chronic-pain)

New Pain Classification -- Nociplastic Pain

- central sensitization is the major underlying mechanism of nociplastic pain, which is a pain phenotype.

Chronic Primary Pain

- **emotional distress or functional disability**
- **Chronic pain as a health condition**

Examples are:

1. **Chronic widespread pain (CWP)**/fibromyalgia
2. **Complex regional pain syndrome**
3. Chronic **headaches and orofacial pain**: migraine, tension-type headache, trigeminal autonomic cephalgias, temporomandibular disorders, burning mouth, orofacial pain
4. **Chronic visceral pain**: chest pain syndrome, epigastric pain syndrome, irritable bowel syndrome, abdominal pain syndrome, bladder pain syndrome, pelvic pain syndrome
5. **Chronic musculoskeletal pain** (other than orofacial): cervical pain, thoracic pain, low back pain, limb pain

Chronic Secondary Pain

- Chronic pain as a symptom of an underlying disease
- **No correlation between pain severity and disease**
- Requires **interdisciplinary pain treatment**

How Did the Conversation Change:

Assess pain as a biopsychosocial disease instead of nociception:

Physical pain, an aversive state related to actual or potential injury and disease;

Social pain, an aversive emotion associated to social exclusion;

Psychological pain, a negative emotion induced by incentive loss.

Papini MR, Fuchs PN, Torres C. Behavioral neuroscience of psychological pain. Neurosci Biobehav Rev. 2015 Jan;48:53-69. doi: 10.1016/j.neubiorev.2014.11.012. Epub 2014 Nov 25. PMID: 25446953.

Treatment of Pain focuses on Behavioral Contributions and Functional Improvement

- Sleep
- Nutrition
- Activity
- Mood
- Social connections
- Flare-ups
- Medications

Poor Sleep is an Independent Risk Factor of Poorly Controlled Pain

- patients with both chronic pain and sleep disturbances have greater pain severity,
- longer duration of pain,
- greater disability,
- are less physically active
- more likely to have concurrent depression, catastrophizing, anxiety, and suicidal ideation.

Aubrey J Husak, Matthew J Bair, Chronic Pain and Sleep Disturbances: A Pragmatic Review of Their Relationships, Comorbidities, and Treatments, *Pain Medicine*, Volume 21, Issue 6, June 2020, Pages 1142–1152

Treat Both Chronic Pain and Insomnia

Study	No.	Treatment, Duration	Pain Outcome	Sleep Outcome
Arnold et al. (2008) [50]	745	Pregabalin vs placebo, 14 wk	Improved pain score compared with placebo ($P < 0.001$)	Improved sleep quality compared with placebo ($P < 0.001$)
Crofford et al. (2005) [51]	529	Pregabalin vs placebo, 8 wk	Improved pain score compared with placebo ($P < 0.001$)	Improved sleep quality compared with placebo ($P < 0.001$)
Mease et al. (2008) [52]	748	Pregabalin vs placebo, 12 wk	Improved pain score compared with placebo ($P = 0.007$)	Improved sleep quality compared with placebo ($P < 0.0001$)
Pauer et al. (2011) [53]	747	Pregabalin vs placebo, 14 wk	Improved pain score compared with placebo ($P = 0.013$)	Decreased sleep disturbance compared with placebo ($P \leq 0.015$)
Roth et al. (2012) [54]	102	Pregabalin vs placebo, 86 d	Improved pain score compared with placebo ($P = 0.0084$)	Improved total sleep time and sleep efficiency compared with placebo ($P < 0.0001$)

Sleep

Goforth et al. (2014) [55]	52	Eszopiclone vs placebo, 1 mo	Improved pain score compared with placebo ($P < 0.004$)	Improved total sleep time, sleep efficiency, and sleep quality compared with placebo ($P \leq 0.001$)
Vidor et al. (2013) [59]	32	Melatonin vs placebo, 4 wk	Improved pain score compared with placebo ($P < 0.001$)	Improved sleep quality compared with placebo ($P < 0.001$)
Carette et al. (1995) [60]	22	Amitriptyline vs placebo, 16 wk	Improved pain score compared with placebo ($P = 0.02$)	Improved sleep quality compared with placebo ($P < 0.05$)
Moldofsky et al. (2011) [62]	36	Cyclobenzaprine vs placebo, 8 wk	Improved pain score compared with placebo ($P = 0.044$)	Improved total sleep time and sleep efficiency compared with placebo ($P \leq 0.023$)
Kosinski et al. (2007) [65]	815	Tramadol vs placebo, 12 wk	Improvement in pain score compared with placebo ($P < 0.001$)	Improved sleep quality compared with placebo ($P = 0.002$)
Russel et al. (2011) [66]	548	Sodium oxybate vs placebo, 14 wk	Improved pain score compared with placebo ($P < 0.001$)	Improved sleep quality compared with placebo ($P < 0.001$)
Scharf et al. (2003) [67]	24	Sodium oxybate vs placebo, 92 d	Improved pain score compared with placebo ($P < 0.005$)	Improved sleep latency compared with placebo ($P < 0.05$)
Spaeth et al. (2012) [68]	573	Sodium oxybate vs placebo, 14 wk	Improved pain score compared with placebo ($P \leq 0.001$)	Improved sleep quality compared with placebo ($P < 0.001$)

Nutrition -Macronutrients

Carbohydrates promote release of serotonin, synthesis of endogenous oSpioids, but excessive consumption promotes inflammation and pain

Protein facilitates tissue healing and anti-inflammatory processes

Fats such as omega-3 fatty acids can be anti-inflammatory while saturated fats are proinflammatory

Bautista, A., Lee, J., Delfino, S. *et al.* The Impact of Nutrition on Pain: A Narrative Review of Recent Literature. *Curr Pain Headache Rep* **28**, 1059–1066 (2024).

Nutrition - Micronutrients

- Vitamin D modulates the immune system and reduces inflammation. Small studies showing Vitamin D supplementation for patients with chronic wide-spread pain. Doses range from 1200-2400 (Haddad HW, Jumonville AC, Stark KJ, et al. The role of vitamin D in the management of chronic pain in fibromyalgia: a narrative review. Health Psychol Res. 2021;9(1):25208.)
- Magnesium has NMDA antagnoist properties. malignancy-related neurologic symptoms, diabetic neuropathy, postherpetic neuralgia, and chemotherapy-induced peripheral neuropathy. In addition, magnesium treatment is reportedly able to alleviate fibromyalgia, dysmenorrhea, headaches, and acute migraine attacks. (Shin HJ, Na HS, Do SH. Magnesium and pain. Review. Nutrients. 2020;12(8):1–13.)
- B1 (Thiamine) ,B6 (Pyridoxine), B9 (Folate), B12 (Cobalamin)

Nutrition -- Supplements

- S-adenosylmethionine: improves knee arthritis pain and function comparable to celecoxib (Najm WI, Reinsch S, Hoehler F, Tobis JS, Harvey PW. S-adenosyl methionine (SAMe) versus celecoxib for the treatment of osteoarthritis symptoms: a double-blind cross-over trial. [ISRCTN36233495]. BMC Musculoskelet Disord. 2004 Feb 26;5:6. doi: 10.1186/1471-2474-5-6. PMID: 15102339)
- Alpha-Lipoic Acid: ALA showed efficacy for the treatment of headache, carpal tunnel syndrome and burning mouth syndrome. Meta-analysis was conducted only with the studies using diabetic polyneuropathy. Compared to placebo, ALA treatment decreased the total symptom score (TSS) (Cassanego G, Rodrigues P, De Freitas Bauermann L, Trevisan G. Evaluation of the analgesic effect of α-lipoic acid in treating pain disorders: A systematic review and meta-analysis of randomized controlled trials. Pharmacol Res. 2022 Mar;177:106075. doi: 10.1016/j.phrs.2022.106075. Epub 2022 Jan 10. PMID: 35026405.)

Nutrition -- Supplements

- Acetyl-L-Carnitine improves various neuroapthic pain conditions. (Di Stefano G, Di Lionardo A, Galosi E, Truini A, Cruccu G. Acetyl-L-carnitine in painful peripheral neuropathy: a systematic review. J Pain Res. 2019 Apr 26;12:1341-1351. doi: 10.2147/JPR.S190231. PMID: 31118753; PMCID: PMC6498091.)
- Glucosamine and chondroitin: 2016 multinational study called 'the MOVES trial' found the combination of glucosamine and chondroitin as effective at relieving knee OA pain and swelling as celecoxib (Arthritis foundation)
- Methylsulfonylmethane (MSM) may help with soft tissue synthesis and lessen pain. 500mg tid. (Toguchi A, Noguchi N, Kanno T, Yamada A. Methylsulfonylmethane Improves Knee Quality of Life in Participants with Mild Knee Pain: A Randomized, Double-Blind, Placebo-Controlled Trial. Nutrients. 2023 Jun 30;15(13):2995. doi: 10.3390/nu15132995. PMID: 37447322; PMCID: PMC10346176.)

Activity - Niederstrasser, Nils Georg, and Nina Attridge. "Associations between pain and physical activity among older adults." *PLoS One* 17.1 (2022): e0263356.

	β (SE)	Odds Ratio (95% Confidence Interval)
Intercept	1.27 (0.30)	
Reference category: No current musculoskeletal pain		
Existing musculoskeletal pain	1.53 (0.06)**	4.60 (4.01–5.20)
Age	-0.00 (0.00)	1.00 (1.00–1.01)
Reference category: sedentary PA		
mild PA	-0.16 (0.22)	0.85 (0.55–1.30)
moderate PA	-0.32 (0.22)	0.72 (0.47–1.10)
high PA	-0.52 (0.22)*	0.59 (0.38–0.91)
Reference category: normal weight		
underweight	-0.05 (0.40)	0.95 (0.43–2.03)
overweight	0.29 (0.07)**	1.34 (1.16–1.55)
obese	0.61 (0.08)**	1.85 (1.58–2.16)
Reference category: male gender		
female gender	0.44 (0.06)**	1.55 (1.38–1.75)
Reference category: Low Income		
Low to Middle	-0.18 (0.11)	0.84 (0.68–1.04)
Middle	-0.46 (0.11)**	0.63 (0.51–0.78)
Middle to High	-0.38 (0.10)**	0.68 (0.56–0.83)
High	-0.51 (0.10)**	0.60 (0.49–0.73)

R^2 for final regression equation = .23 (Nagelkerke), Model $x^2(13) = 1079.50$, $p < .01$;
N = 5802;
* $p < .05$;
** $p < .01$;
Beta weights are from the final regression equation;

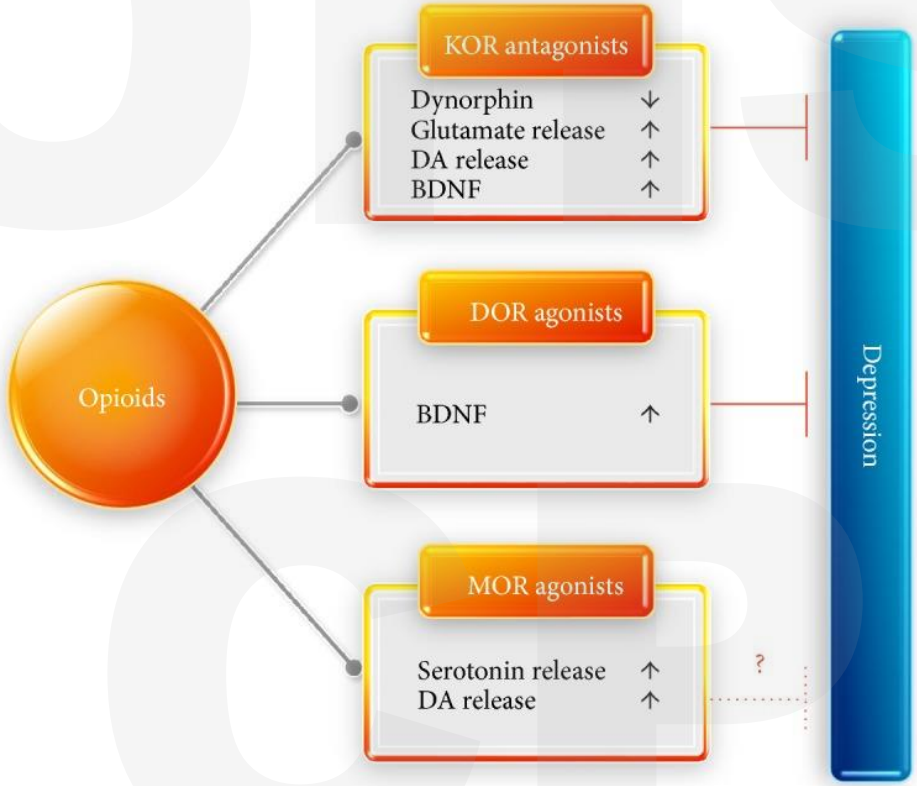
https://doi.org/10.1371/journal.pone.0263356.t003

Mood

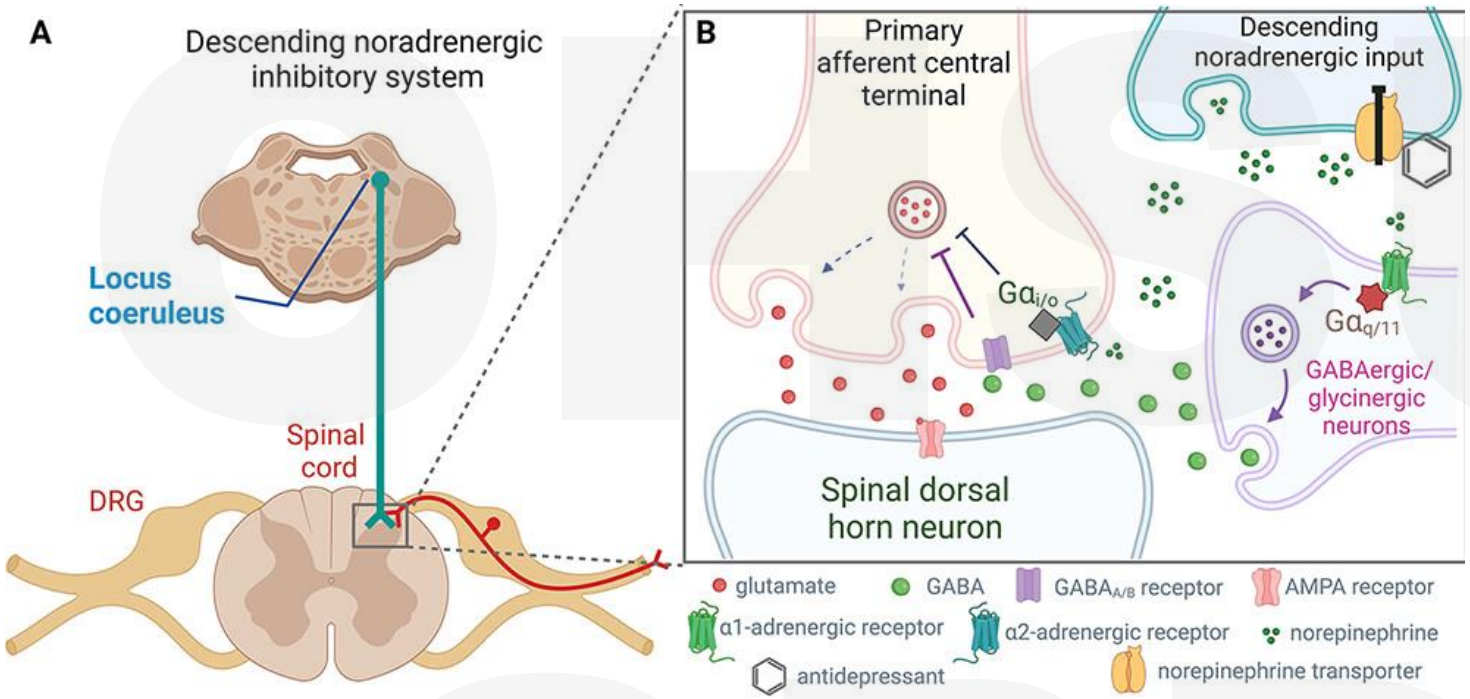
- Injury to sensory pathways of body pains share the same brain regions as mood management,
- insular cortex,
- prefrontal cortex,
- anterior cingulate,
- thalamus,
- hippocampus, and
- Amygdala

Sheng J, Liu S, Wang Y, Cui R, Zhang X. The Link between Depression and Chronic Pain: Neural Mechanisms in the Brain.

Mood: Opioid as antidepressant



Sheng J, Liu S, Wang Y, Cui R, Zhang X. The Link between Depression and Chronic Pain: Neural Mechanisms in the Brain. Neural Plast. 2017;2017:9724371. doi: 10.1155/2017/9724371. Epub 2017 Jun 19. PMID: 28706741; PMCID: PMC5494581.



Mood and Pain – Tricyclic antidepressants

Huang, Yuying, et al. "Duloxetine and amitriptyline reduce neuropathic pain by inhibiting primary sensory input to spinal dorsal horn neurons via α1-and α2-adrenergic receptors." *ACS chemical neuroscience* 14.7 (2023): 1261-1277.

Mood and Pain -- Duloxetine

- Duloxetine is effective in reducing pain in painful diabetic neuropathy, fibromyalgia, and pain in major depressive disorder

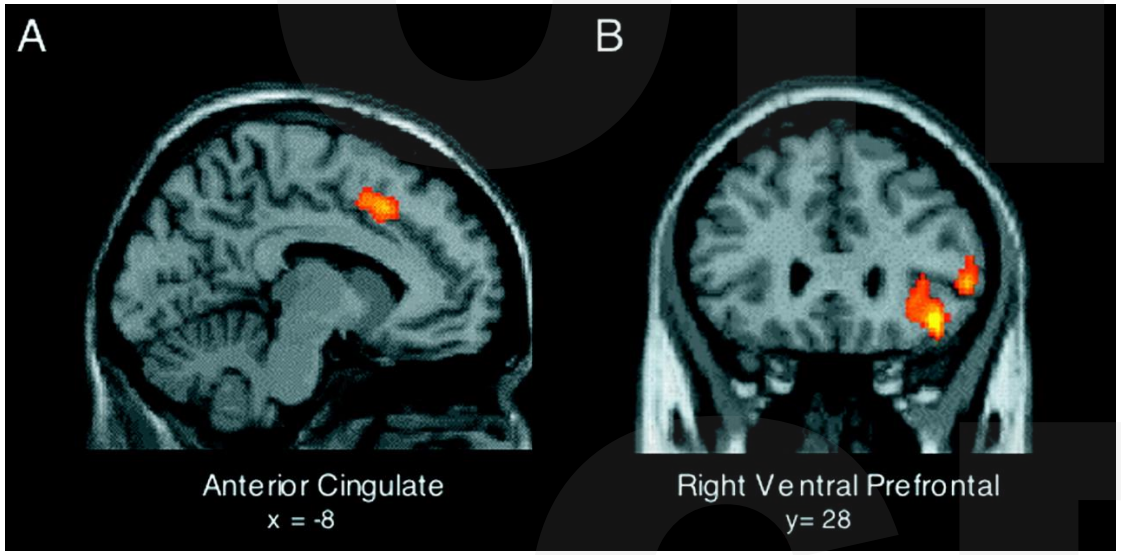
Lunn MPT, Hughes RAC, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD007115. DOI: 10.1002/14651858.CD007115.pub3. Accessed 07 February 2026.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Duloxetine				
Number with ≥ 50% pain relief at 12 weeks or less Follow-up: 12 weeks	**360 per 1000**	**493 per 1000** (428 to 572)	**RR 1.37** (1.19 to 1.59)	1023 (2 studies)	⊕⊕⊕⊖ **moderate**[1]	NNTB for ≥ 50% pain relief at < 12 weeks 60 mg duloxetine daily: 8 (95% CI 5 to 14)
Number with ≥ 30% pain relief at 12 weeks or less	**467 per 1000**	**593 per 1000** (537 to 654)	**RR 1.27** (1.15 to 1.4)	1359 (3 studies)	⊕⊕⊖⊖ **low**[1,2]	NNTB for ≥ 30% pain relief at < 12 weeks 60 mg duloxetine: 8 (95% CI 4- to 14)
Mean improvement in pain at 12 weeks or less Visual analogue scale. Scale from: 0 to 10. Follow-up: 12 weeks	The mean mean improvement in pain at 12 weeks or less in the control groups was **1.23**	The mean mean improvement in pain at 12 weeks or less in the intervention groups was **0.55 lower** (0.75 to 0.35 lower)		1359 (3 studies)	⊕⊕⊖⊖ **low**[1,2]	
Mean improvement in Patient Reported Global Impression of Change at 12 weeks or less	See comment	See comment	Not estimable	-	See comment	Outcome not measured
Adverse events	See comment	See comment	Not estimable	-	See comment	See pooled adverse events in 'Summary of findings' table 1

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RR:** risk ratio; **NNTB**: number needed to treat for an additional beneficial outcome

Social Pain potentiates Physical Pain



- Social pain is defined as the pain of perceived threat or real rejection

Eisenberger, Naomi I., Matthew D. Lieberman, and Kipling D. Williams. "Does rejection hurt? An fMRI study of social exclusion." *Science* 302.5643 (2003): 290-292.

Social Pain reduction

- mindfulness training (eng S-L, Tan HH: Effects of Brief Mindfulness and Loving-Kindness Meditation Inductions on Emotional and Behavioral Responses to Social Rejection among Individuals with High Borderline Personality Traits. *Behav. Res. Ther.* 2018;100(January):44–53.)

Social Pain Reduction

- **Psilocybin** double-blind, randomized, counterbalanced, cross-over study assessed the neural response to social exclusion after the acute administration of Psi (0.215 mg/kg) or placebo (Pla) in 21 healthy volunteers by using functional magnetic resonance imaging (fMRI) and resting-state magnetic resonance spectroscopy (MRS).
- Participants reported a reduced feeling of social exclusion after Psi vs. Pla administration,
- Neural response to social exclusion was decreased in the dorsal anterior cingulate cortex (dACC) and the middle frontal gyrus, key regions for social pain processing

Preller, Katrin H., et al. "Effects of serotonin 2A/1A receptor stimulation on social exclusion processing." *Proceedings of the National Academy of Sciences* 113.18 (2016): 5119-5124.

Social Pain Reduction – Cognitive Behavioral Model

- Model of loneliness holds that implicit hypervigilance for social threat exerts a powerful influence on perceptions, cognitions, and behaviors,
- Loneliness may be diminished by reducing automatic perceptual and cognitive biases that favor over-attention to negative social information in the environment.
- Interventions that targeted maladaptive social cognition (e.g., cognitive behavioral therapy that involved training to identify automatic negative thoughts and look for disconfirming evidence, to decrease biased cognitions, and/or to reframe perceptions of loneliness and personal control) would be more effective than interventions that targeted social support, social skills, or social access

(Hawkley LC, Cacioppo JT. Loneliness matters: a theoretical and empirical review of consequences and mechanisms. Ann Behav Med. 2010 Oct;40(2):218-27. doi: 10.1007/s12160-010-9210-8. PMID: 20652462; PMCID: PMC3874845.)

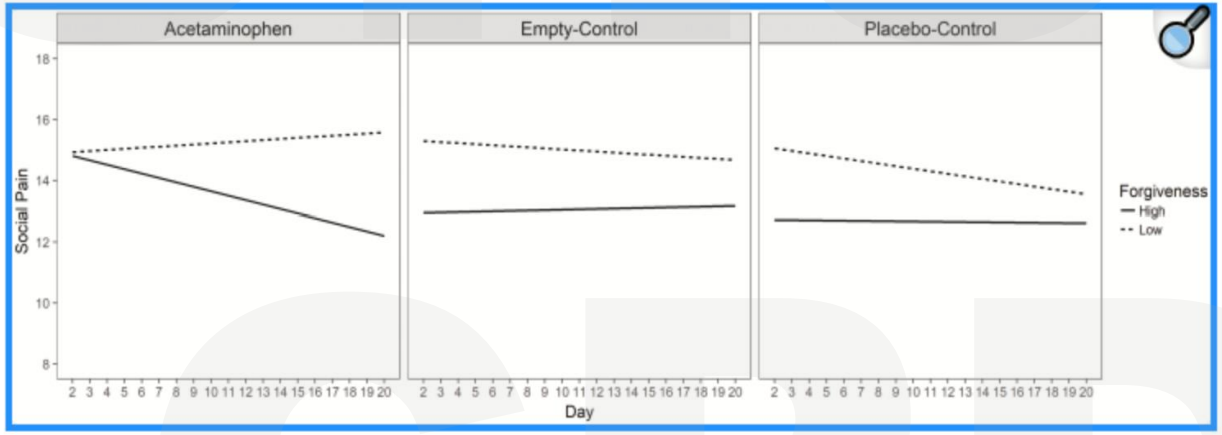
Acetaminophen

- acetaminophen decreases neural responses to social rejection in brain regions that represent the affective component of physical pain (DeWall CN, MacDonald G, Webster GD, et al. Acetaminophen reduces social pain: Behavioral and neural evidence. Psychol Sci. 2010;21:931–937)
- Slavich GM, Shields GS, Deal BD, Gregory A, Toussaint LL. Alleviating Social Pain: A Double-Blind, Randomized, Placebo-Controlled Trial of Forgiveness and Acetaminophen. Ann Behav Med. 2019 Nov 9;53(12):1045-1054. doi: 10.1093/abm/kaz015. PMID: 31050715; PMCID: PMC6845385.

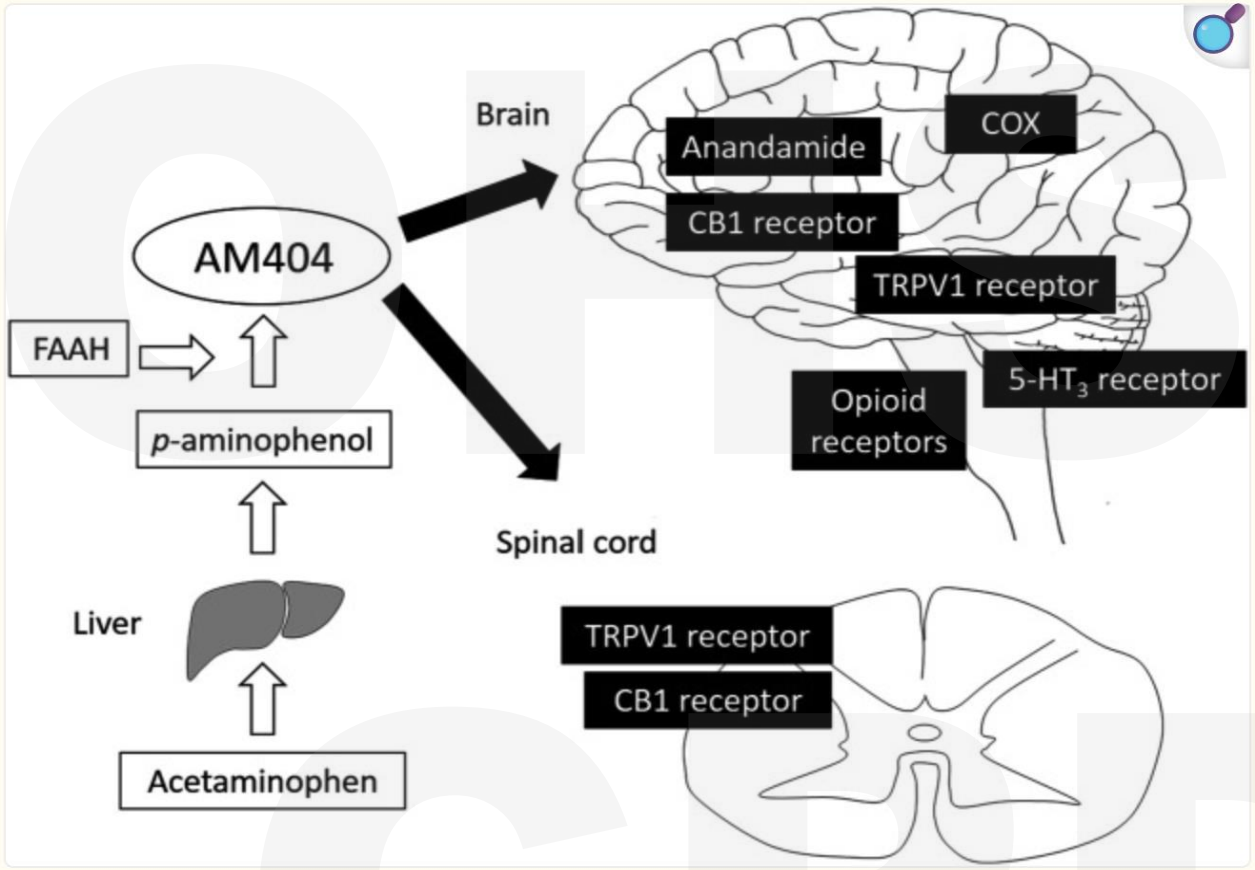
Acetaminophen Alleviating Social Pain

Ann Behav Med. 2019 May 3;53(12):1045–1054. doi: 10.1093/abm/kaz015

Fig. 2.



Forgiveness × Experimental Condition × Time effect on levels of social pain over 20 days. Acetaminophen reduced participants' levels of social pain over time, and this effect was significantly greater in persons exhibiting high levels of forgiveness ($B = -.14$, $p = .003$) than for those exhibiting low levels of forgiveness ($B = .03$, $p = .18$), $p = .003$. In contrast, forgiveness was not related to changes in social pain over time in the placebo-control or empty-control condition, $ps > .344$. The lines for high and low forgiveness represent model estimates, not distinct participant groups ($n = 42$).

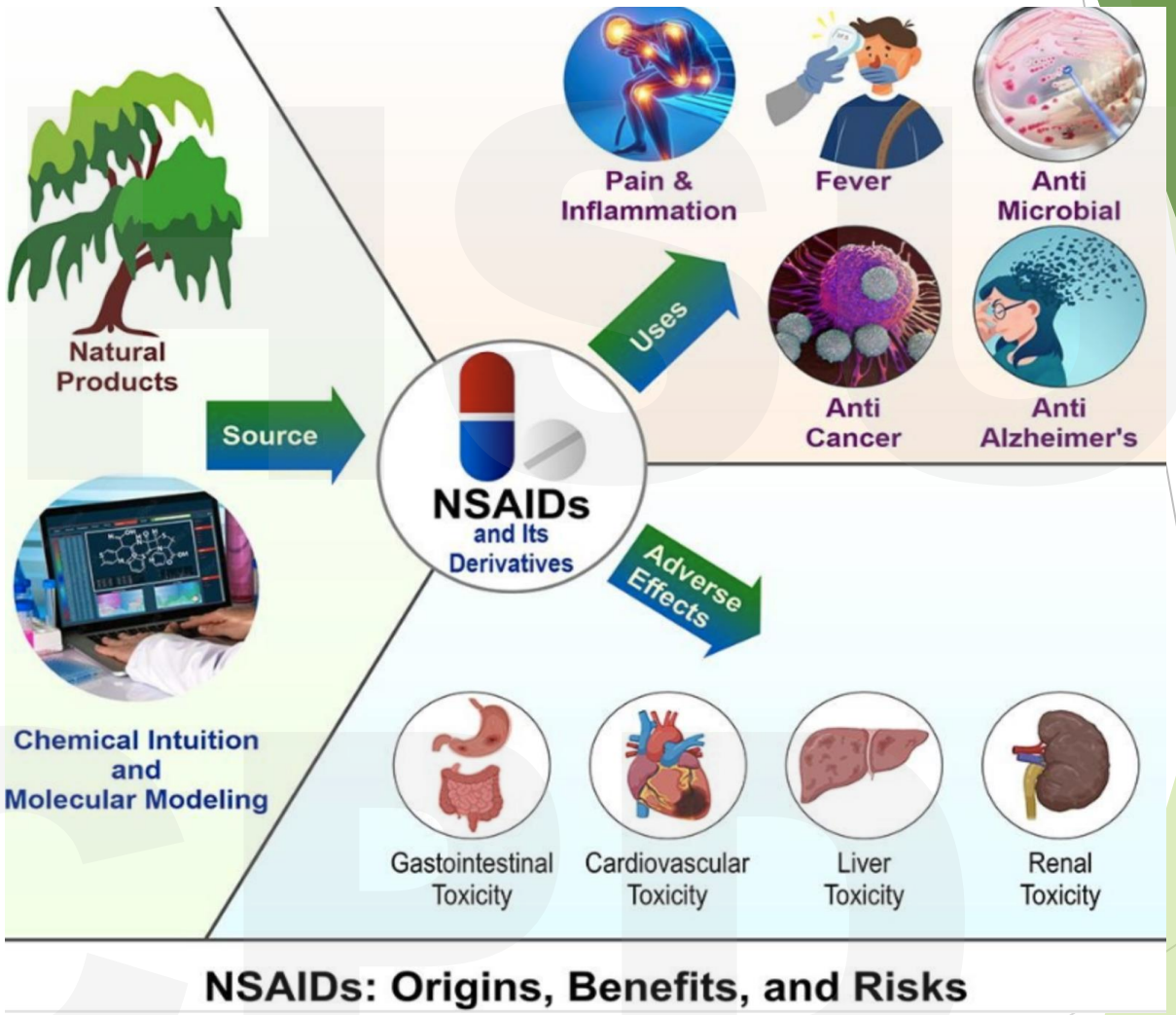


Acetaminophen --Acetaminophen is metabolized to p-aminophenol, which easily crosses the blood-brain barrier and is converted to AM404 by FAAH. AM404 mainly acts on both the brain and spinal cord via COX, anandamide, CB1, TRPV1, opioid, and 5-HT3 receptors. (Ohashi N, Kohno T. Analgesic Effect of Acetaminophen: A Review of Known and Novel Mechanisms of Action. Front Pharmacol. 2020 Nov 30;11:580289. doi: 10.3389/fphar.2020.580289. PMID: 33328986; PMCID: PMC7734311.)

Multimodal Analgesia

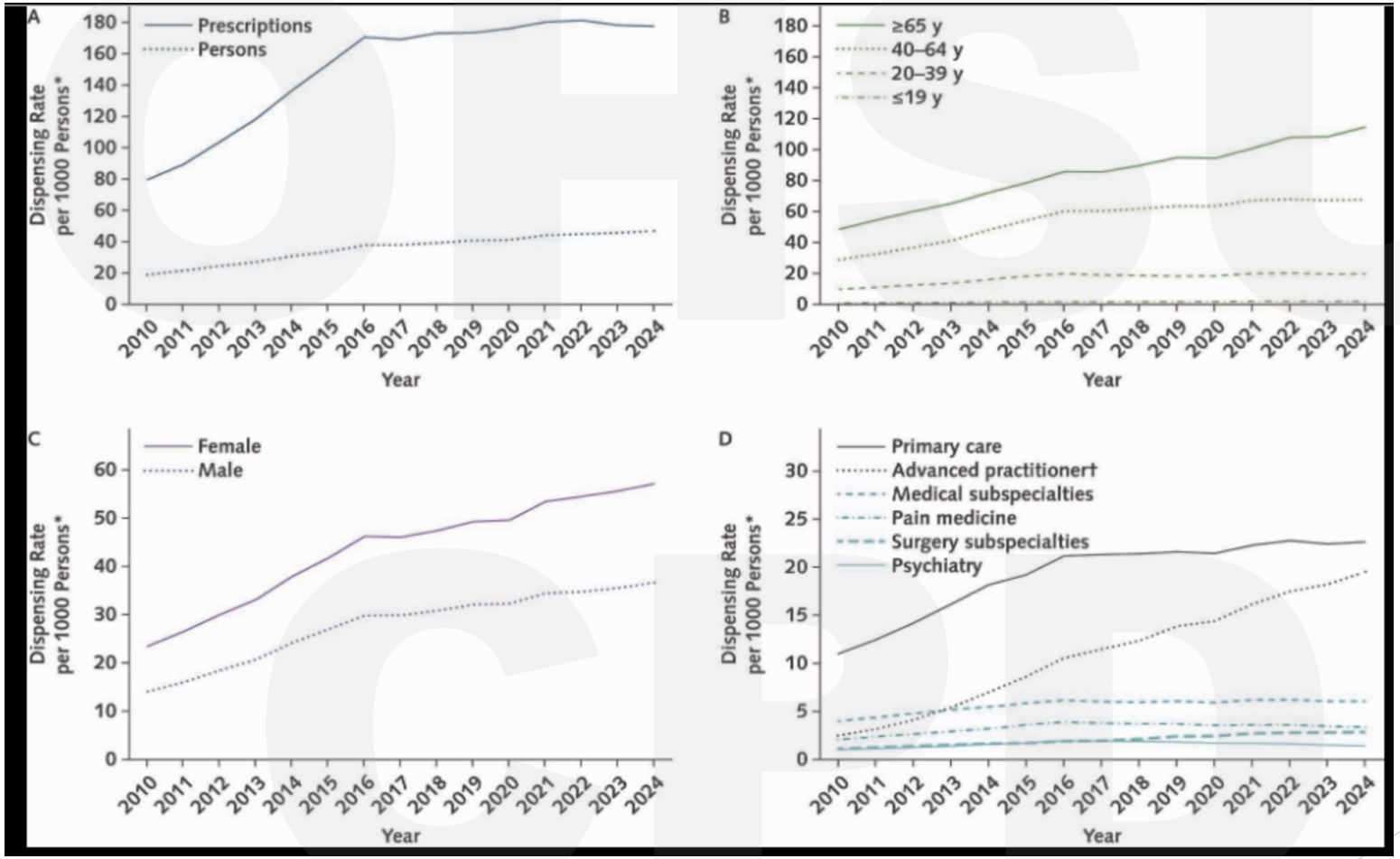
- Acetaminophen
- NSAIDS
- Gabapentinoids
- Pain relieving antidepressants
- Centrally acting muscle relaxants
- Opioids
- Ketamine
- Suzetrigine

NSAIDS



- Arfeen, Minhajul, et al. "Design, classification, and adverse effects of NSAIDs: A review on recent advancements." *Bioorganic & Medicinal Chemistry* 112 (2024): 117899.

Gabapentinoids



Strahan, Andrea E., et al. "Trends in dispensed gabapentin prescriptions in the United States, 2010 to 2024." Annals of Internal Medicine 178.12 (2025): 1816-1818.

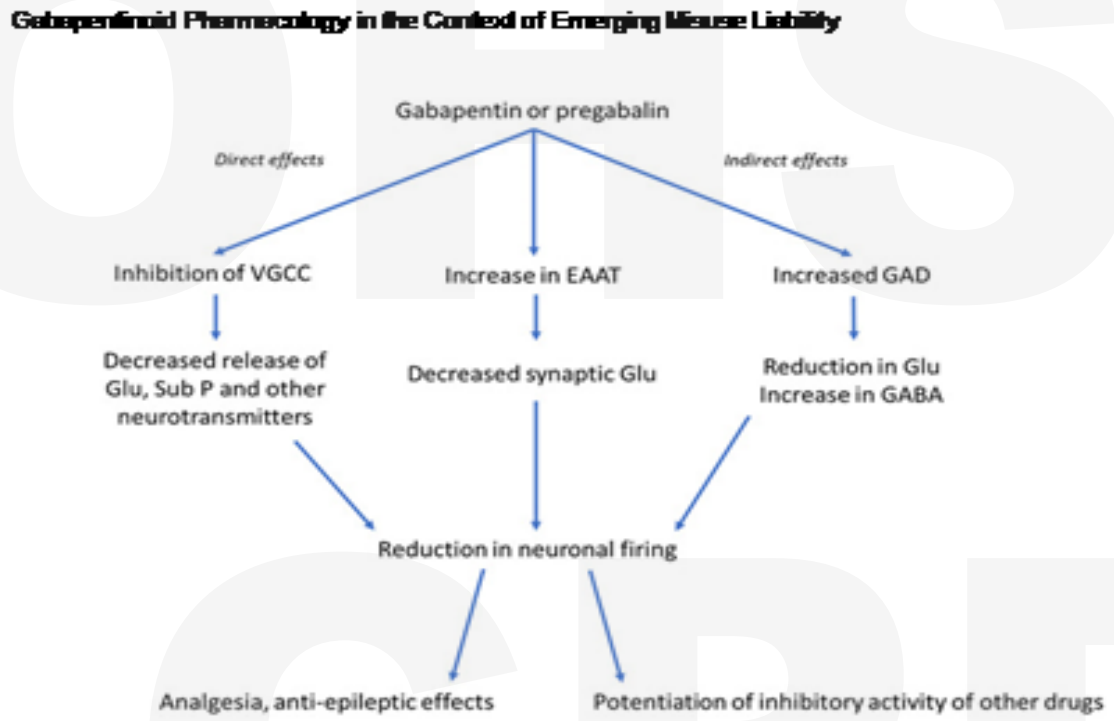
Gabapentinoids

- 24 186 175 (79.5 per 1000 persons) in 2010 to 58 868 142 (177.6 per 1000 persons) in 2024;
- persons dispensed gabapentin increased from 5 764 112 (18.9 per 1000 persons) in 2010 to 15 541 680 (46.9 per 1000 persons) in 2024

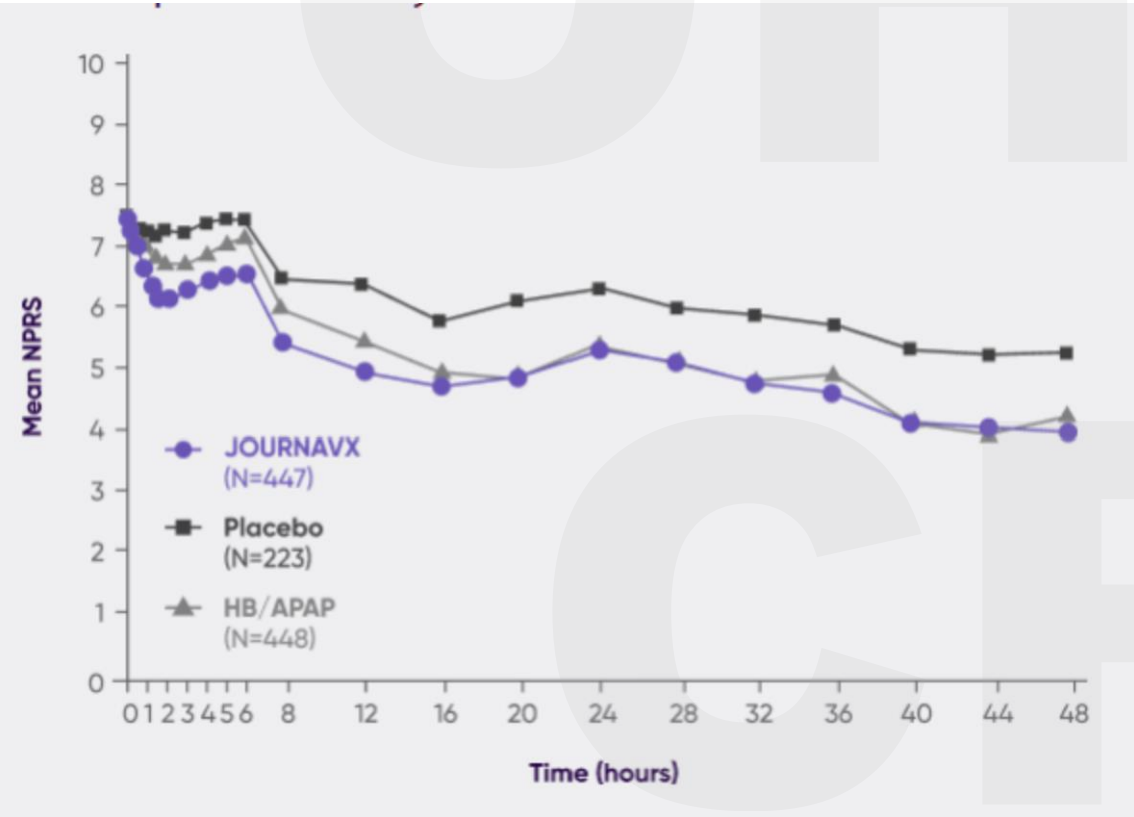
Gabapentinoids

- Misuse -- use of a drug for purposes not indicated, through a route of administration that is unprescribed/not recommended
- Abuse refers to repeated and inappropriate use of a drug accompanied by negative consequences (physical or psychological)
- Among opioid abusers, the prevalence of gabapentin misuse ranged from 15% to 22%, and that of gabapentin abuse (with a prescription of gabapentin) ranged from 40% to 65% in the US and UK. Further, utilization patterns of gabapentin were similar to that of medications with known abuse potential (R.V. Smith, J.R. Havens, S.L. Walsh. Gabapentin misuse, abuse, and diversion: a systematic review. Addict. (Abingdon, Engl.), 111 (7) (2016), pp. 1160-1174)
- The abuse rate was higher in gabapentin users with prolonged duration of use (≥ 120 days), particularly among those with concurrent use of opioids\
- Gabapentin misuse and abuse were associated with increased risks withdrawal and overdose.
- when misused or abused with opioids, gabapentin was associated with elevated risks of opioid overdose, respiratory suppression and death.

Gabapentinoids



Medications – Suzetrigine—First in its class



- sodium channel blocker highly selective for $Na_V1.8$
- Blocks peripheral nerve transmission
- Approved for moderate to severe acute pain
- Contraindicated in patients who are on strong CYP3A inhibitors

Updates in Interventional Pain Treatment

- Interventional pain management options provide effective and long-lasting pain relief to patients not responding to medical management.

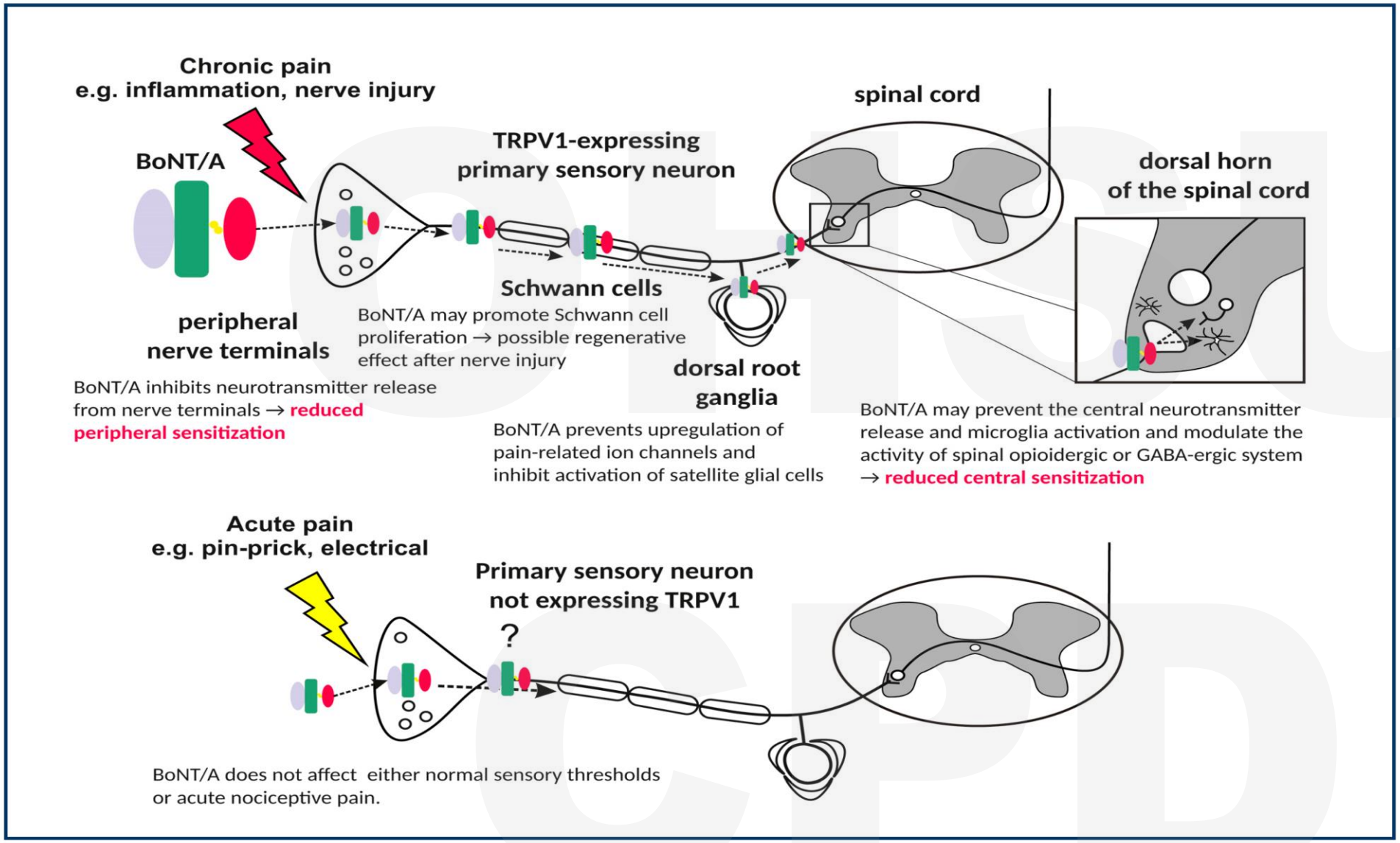
Cohen, Steven P., Lene Vase, and William M. Hooten. "Chronic pain: an update on burden, best practices, and new advances." *The Lancet* 397.10289 (2021): 2082-2097.

Interventions – Indications

- Procedures might be used for diagnostic purposes such as nerve root blocks
- to facilitate other treatments (such as sympathetic blocks to facilitate physical therapy for complex regional pain syndrome.)
- Best procedure candidate would not have much central sensitization (peripheral nerve blocks do not work well for phantom limb pain)

lindividuals without secondary gain, and lower degrees of disease burden (eg, those taking opioids, and with high baseline disability scores)

- Patient decompensated neuropathic conditions.



Matak, Ivica, et al. "Mechanisms of botulinum toxin type A action on pain." *Toxins* 11.8 (2019): 459.

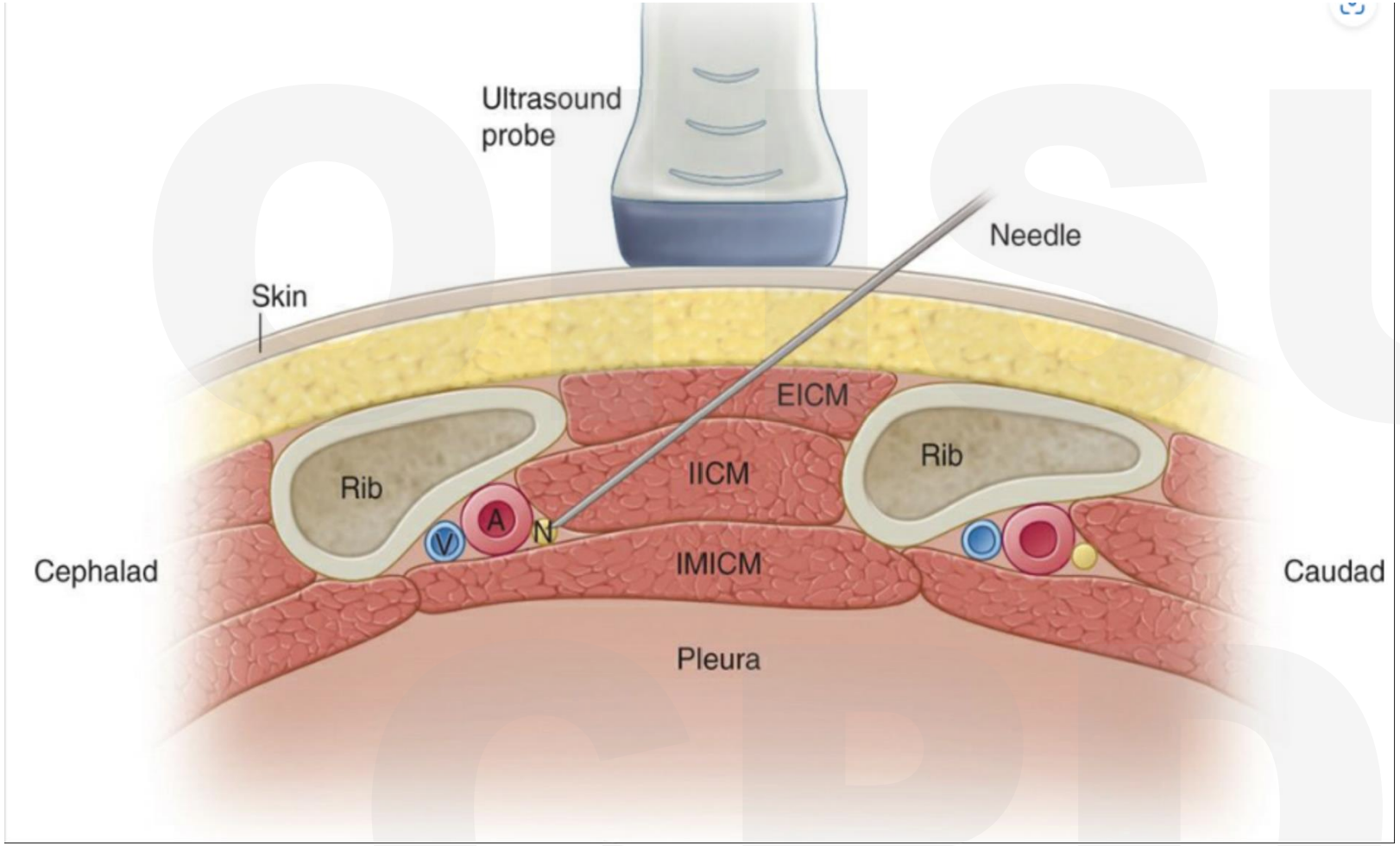
Uses of Botulinium toxin in Pain Medicine

- **reducing spasticity, improving passive and active mobility, reducing pain, and improving upper limb comfort care** (Hareb, Farid, et al. "Botulinum toxin in children with cerebral palsy: an update." *Neuropediatrics* 51.01 (2020): 001-005.)
- Botulinum toxin (BoNT) is currently considered the **treatment of choice for cervical dystonia and can lead to an improvement in pain and dystonic symptoms in up to 90% of patients** (Camargo, Carlos Henrique Ferreira, Lígia Cattai, and Hélio Afonso Ghizoni Teive. "Pain relief in cervical dystonia with botulinum toxin treatment." *Toxins* 7.6 (2015): 2321-2335.)
- **Elongation of abdominal wall prior to reconstruction (6cm)** (Timmer, Allard S., et al. "A systematic review and meta-analysis of technical aspects and clinical outcomes of botulinum toxin prior to abdominal wall reconstruction." *Hernia* (2021): 1-13.)

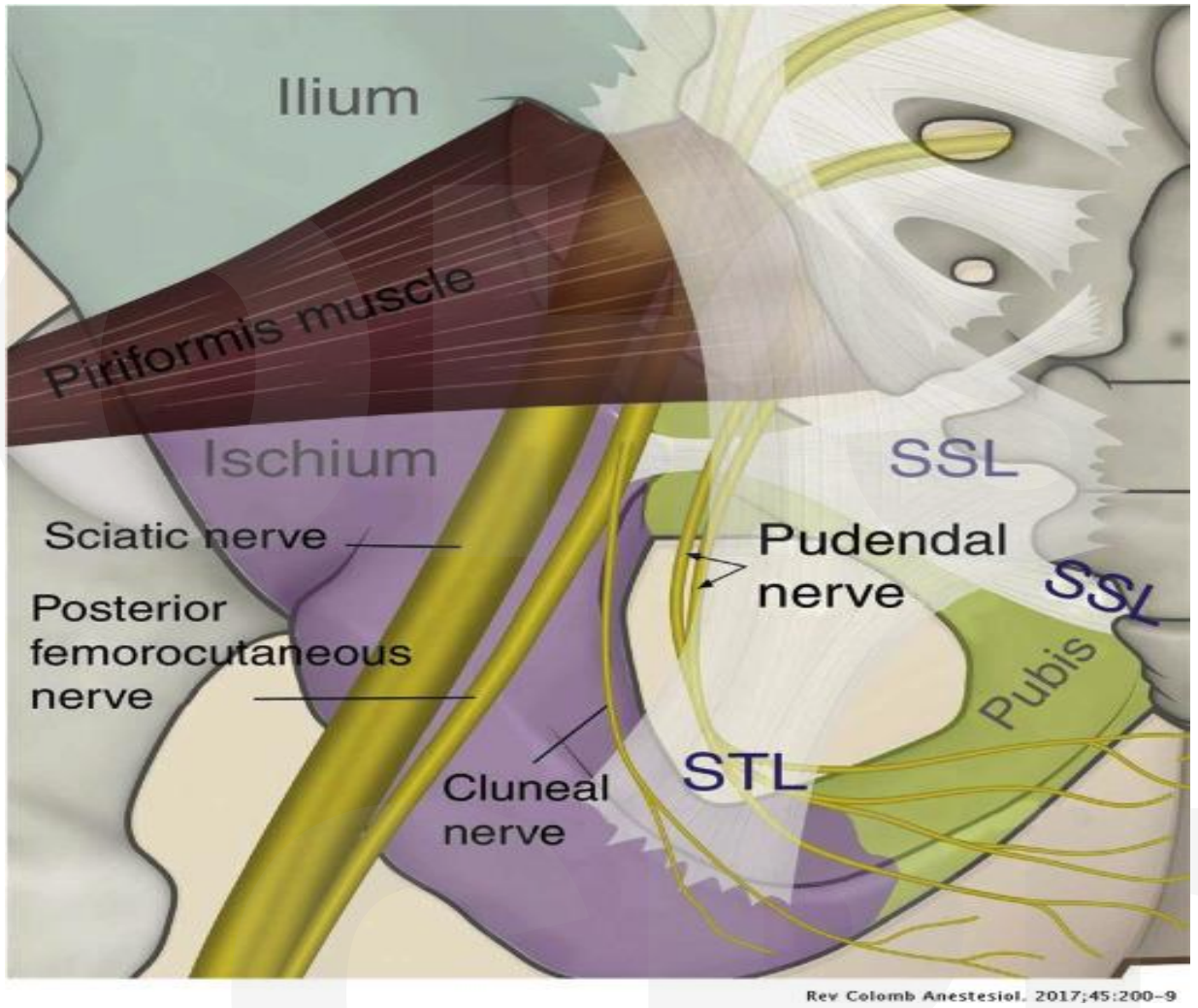
Cryoanalgesia

- Cryoanalgesia causes Wallerian degeneration of nerve; but leaves the myelin sheath and endoneurium intact.
- May be superior to other methods of ablation (like heat or chemical) because it does not cause neuritis or neuralgia
- Indications include:
  - Intercostal neuralgia from rib fractures, post thoracotomy pain or post-herpetic neuralgia
  - Occipital neuralgia and other types of cephalgias
  - Ilioinguinal neuralgia postsurgery
  - Genitofemoral neuralgia
  - Pudendal neuralgia

Trescot, Andrea M. "Cryoanalgesia in interventional pain management." *Pain physician* 6.3 (2003): 345.



Intercostal Nerve Block | Anesthesia Key (aneskey.com)



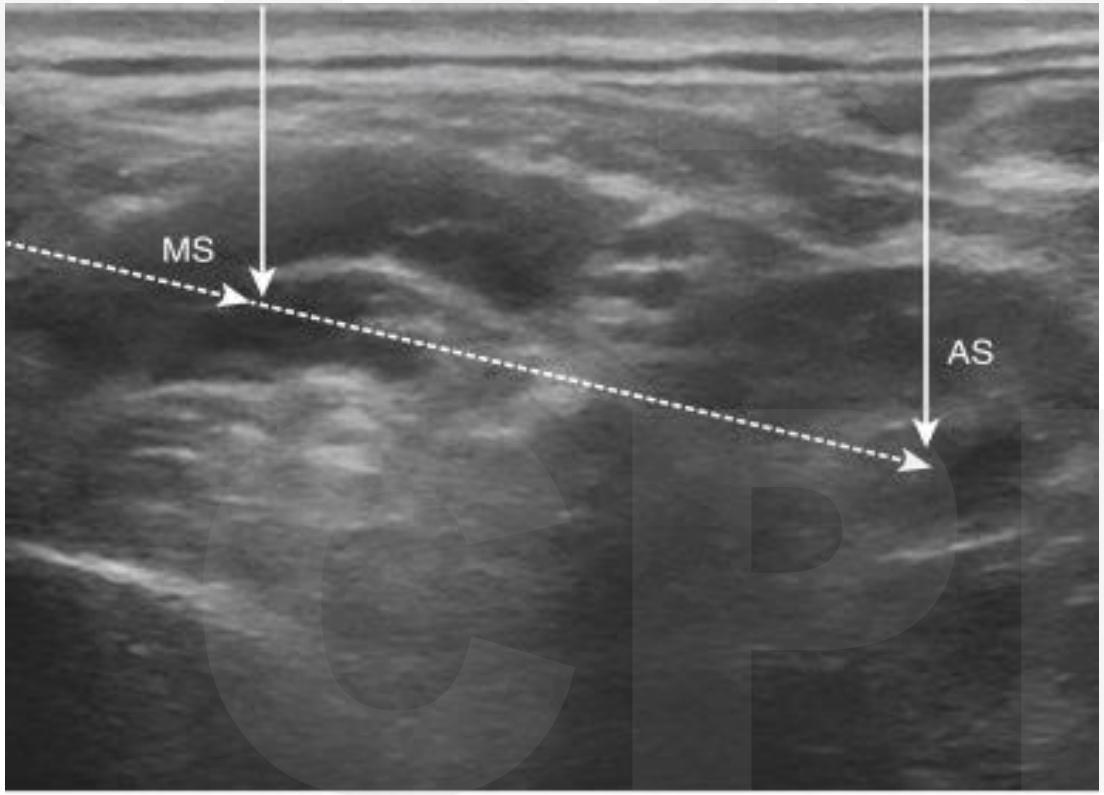
Rana, AL-Jumah, and Krishna B. Shah. "Pudendal Neuralgia." *Interventional Management of Chronic Visceral Pain Syndromes*. Elsevier, 2021. 53-61.

Scalenes Block for Thoracic Outlet Syndrome

Fereydooni, Arash, et al. "Impact of Scalene Muscle Botulinum Toxin Injection With and Without Surgery in Neurogenic Thoracic Outlet Syndrome." *Clinical Journal of Sport Medicine* 33.2 (2023): 116-122.

- With Botulinium toxin injection 77.9% reported subjective relief, confirmed by an improved QDASH disability score.
- Thirty-one patients (40.3%) then went on to have further persistent symptoms and proceeded with first rib resection. 96.8% reported symptomatic relief

Nelson, Ariana, Honorio T. Benzon, and Juan Francisco Asenjo. "Deep Muscle Injections: Piriformis, Scalene Muscle, Iliopsoas Injections." *Essentials of Pain Medicine*. Elsevier, 2018. 737-748.



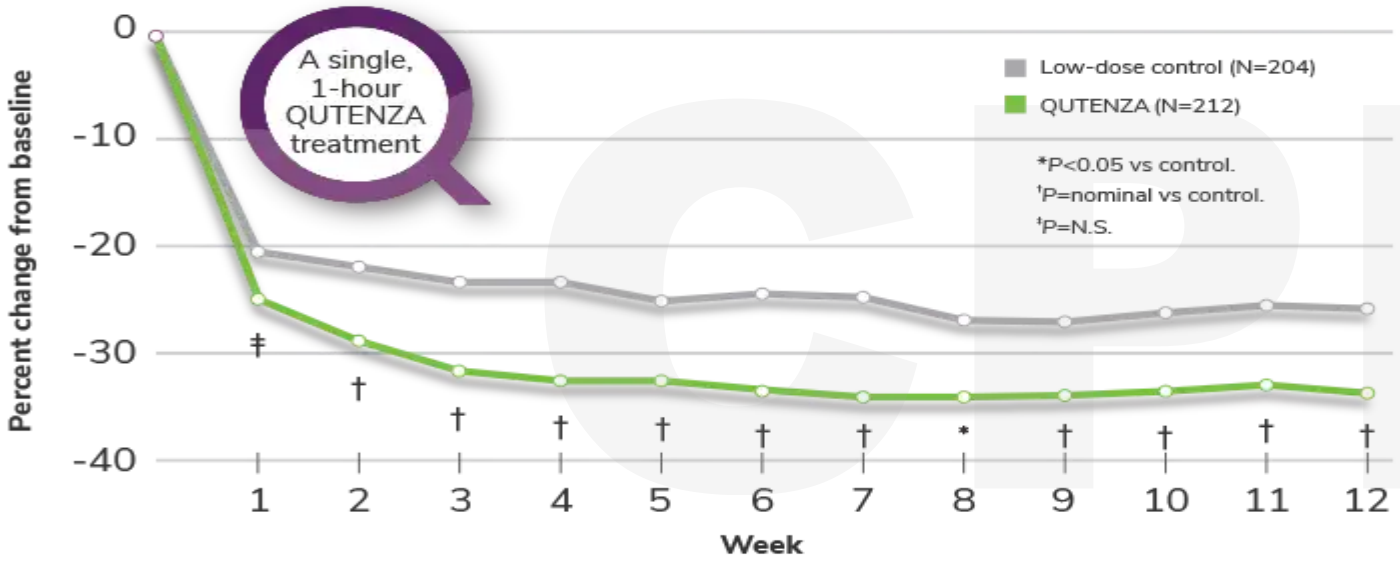
MS = Middle scalene muscle, AS = Anterior scalene muscle
Arrows display location of injection: Solid line = Out-of-plane technique
Dashed line = In-plane technique

Capsaisin 8% system

- For diabetic neuropathy
- Post-herpetic neuralgia
- Peripheral neuropathy

Pain scores decreased about 30% and sustained through Week 12[1]

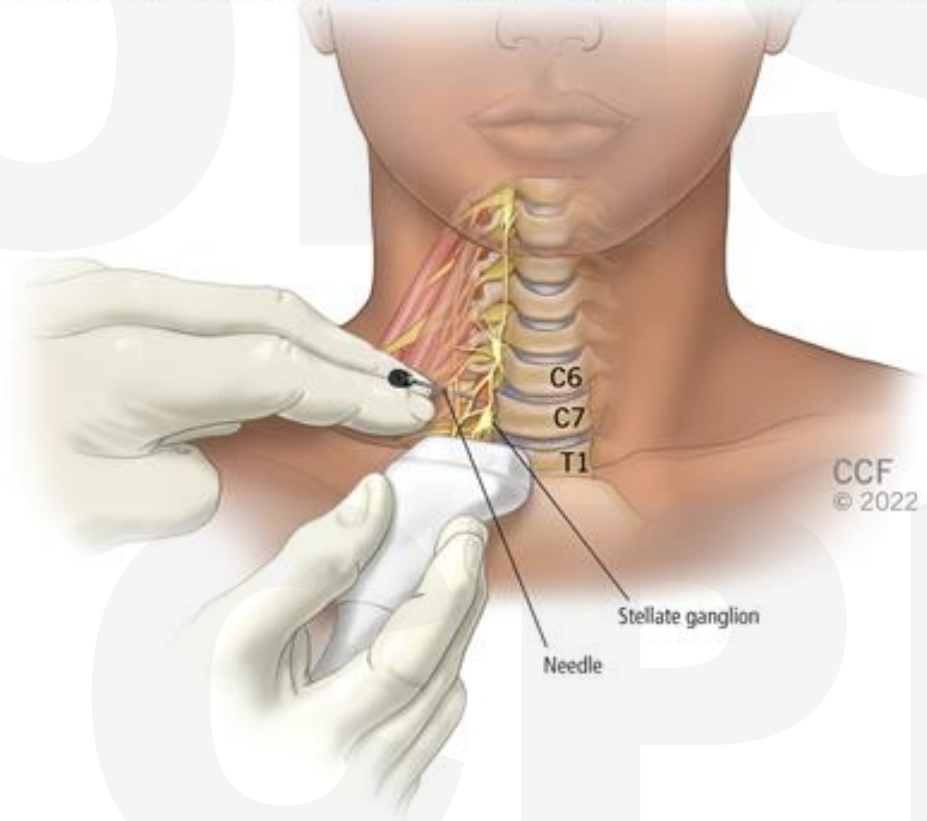
PHN Study 2[3]: Percent change in average pain for the past 24 hours NPRS scores by week



Mean percent changes in NPRS scores from baseline to Week 8 were -33% for QUTENZA vs -26% for control (*P*=0.011).

Stellate Ganglion Block

In stellate ganglion block, anesthetic is injected under ultrasonographic or fluoroscopic guidance into the stellate ganglion at the C6 or C7 vertebral level, targeting the sympathetic nerve chain that runs anterior to the transverse processes of the seventh cervical vertebra and



Yeoncoo Sara Lee et al. CCJM 2022;89:147-153

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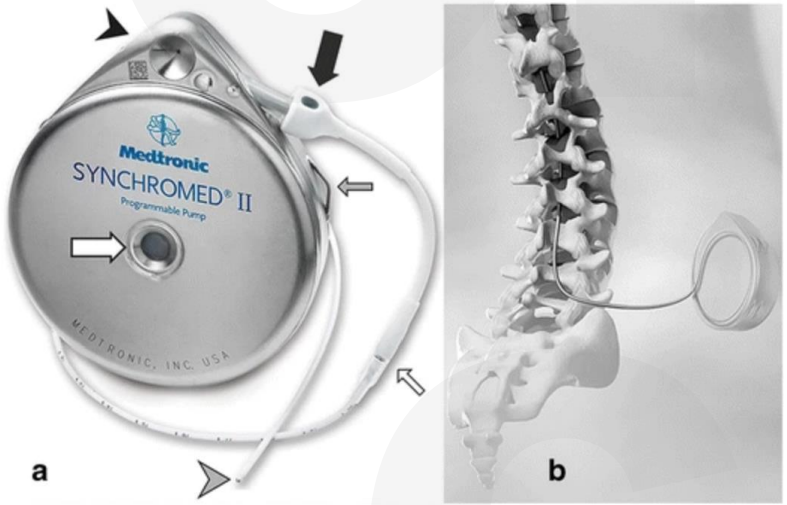
Indications for Stellate Ganglion Block

- PTSD (Olmsted, Kristine L. Rae, et al. "Effect of stellate ganglion block treatment on posttraumatic stress disorder symptoms: a randomized clinical trial." *JAMA psychiatry* 77.2 (2020): 130-138.)
- Refractory Ventricular Tachycardia (Sanghai, Saket, et al. "Stellate ganglion blockade with continuous infusion versus single injection for treatment of ventricular arrhythmia storm." *Clinical Electrophysiology* 7.4 (2021): 452-460.)
- Refractory Cerebral Vasospasm (Wendel, Christopher, et al. "Stellate Ganglion Block and Intraarterial Spasmolysis in Patients with Cerebral Vasospasm: A Retrospective Cohort Study." *Neurocritical Care* (2023): 1-9.)

Intrathecal Pumps

Fig. 1



Implanted, programmable pump system. External view (**a**) and drawing of implanted pump and intrathecal catheter 8731SC (**b**). Pump with the catheter access port (*black arrowhead*), pump catheter connection (*thick black arrow*), refill membrane (*thick white arrow*) and suture loops for fixation (*thin grey arrow*), catheter–catheter segment connection (*thin white arrow*) and titanium catheter end (*grey arrowhead*)

- Can contain baclofen for spasticity,
- Opioids, ziconitide and local anesthetic for cancer pain,

Delhaas, E.M., Harhangi, B.S., Frankema, S.P.G. *et al.* Plain radiography in patients treated with intrathecal drug delivery using an implantable pump device. *Insights Imaging* **8**, 499–511 (2017).

Conclusion

- Conversation about pain shifts from nociceptive model to a biopsychosocial model
- Conversation about pain treatment shifts away from opioids to lifestyle medicine, minimally invasive and invasive treatments.
- Treatment of pain is aimed at the underlying disease and aims to improve quality of life