

Overview of Pain Mechanisms in Sickle Cell Disease

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Disclosures

- No Disclosures

Current Gaps and Failures in Pain Management for Sickle Cell Disease

Ineffective Acute Pain Management

- Emergency care protocols often fail to provide timely or adequate treatment for vaso-occlusive crises.

Chronic Pain Neglect

- Limited focus on the transition from acute to chronic pain management, especially neuropathic pain.

Provider Knowledge Gaps

- Insufficient training in understanding SCD pain mechanisms and individualized care.

Access Disparities

- Unequal availability of specialized pain clinics and multidisciplinary care.

Stigmatization of Patients

- Bias in healthcare settings leading to delayed treatment.

Need for Comprehensive Pain Models

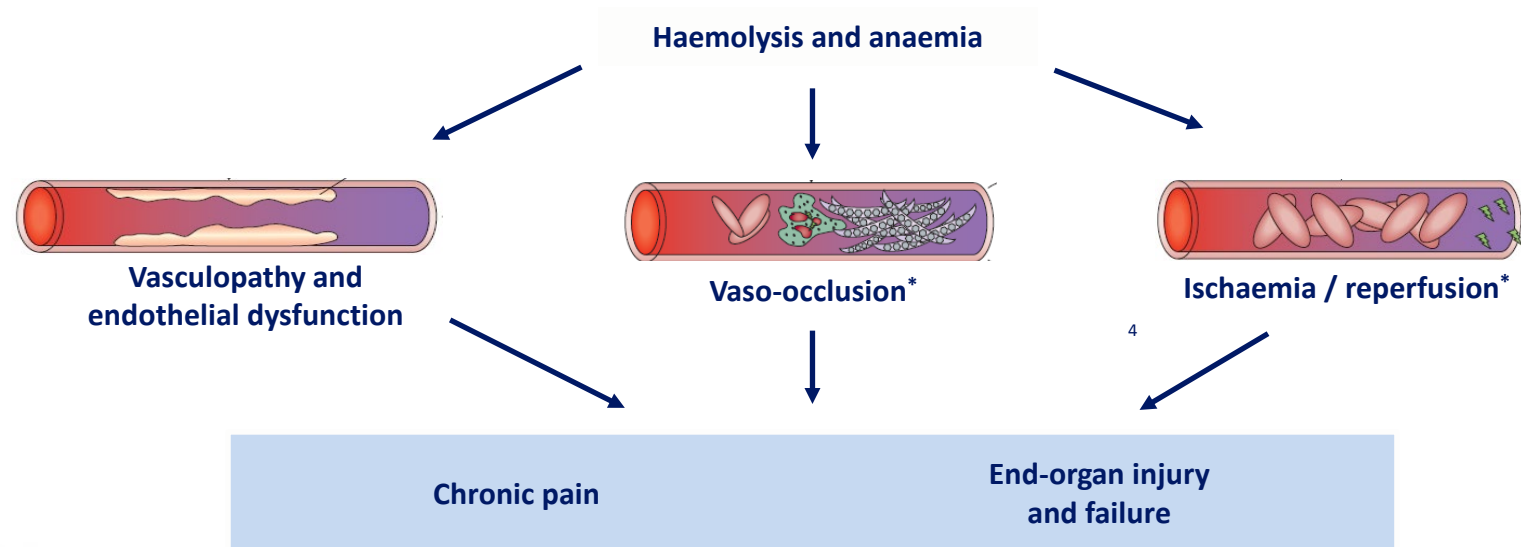
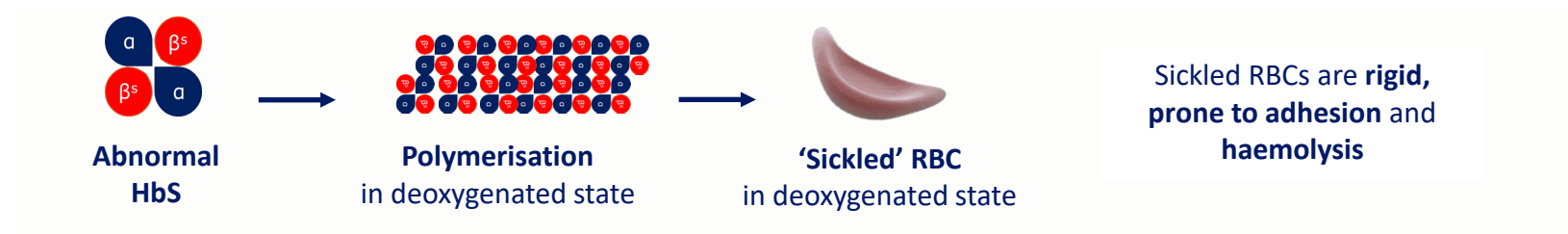
- Lack of integrated psychological and pharmacological approaches.

Sickle Cell Disease

Normal



Sickle Cell Disease: defect in the adult haemoglobin gene



Sources:

Hannemann A, Weiss E, Rees DC, Dalibalta S, Ellory JC, Gibson JS. The Properties of Red Blood Cells from Patients Heterozygous for HbS and HbC (HbSC Genotype). Anemia. 2011;2011:248527. doi: 10.1155/2011/248527. Epub 2010 Oct 13. PMID: 21490760; PMCID: PMC3066570.

SCD Pain can be categorized by

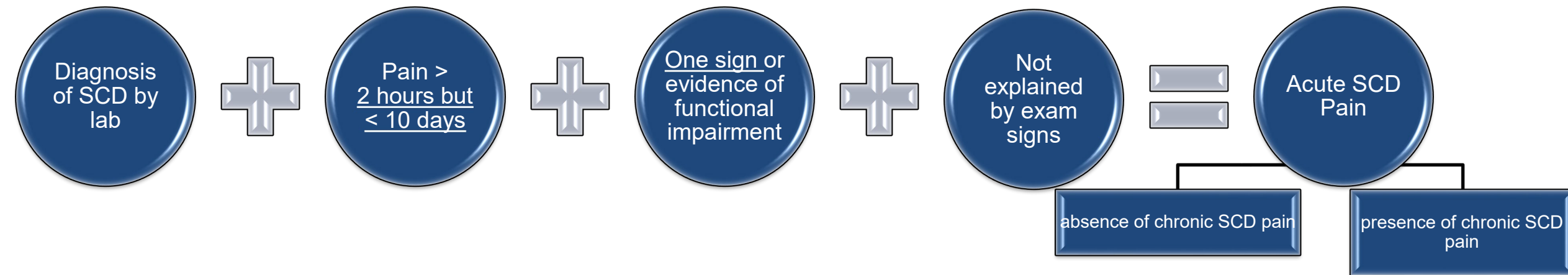
Clinical Presentations:

- **Acute:** Sudden onset, often severe, typically linked to vaso-occlusive crises.
- **Chronic:** Persistent, long-term pain that can be constant or fluctuate.
- **Acute-on-Chronic:** Acute exacerbation of underlying chronic pain.

Mechanistic Subtypes:

- **Nociceptive:** Pain due to tissue damage or inflammation (e.g., vaso-occlusive crisis).
- **Neuropathic:** Pain caused by nerve damage (e.g., chronic nerve injury from microvascular ischemia).
- **Nociplastic:** Pain without obvious tissue or nerve damage, possibly linked to altered pain processing (e.g., central sensitization).

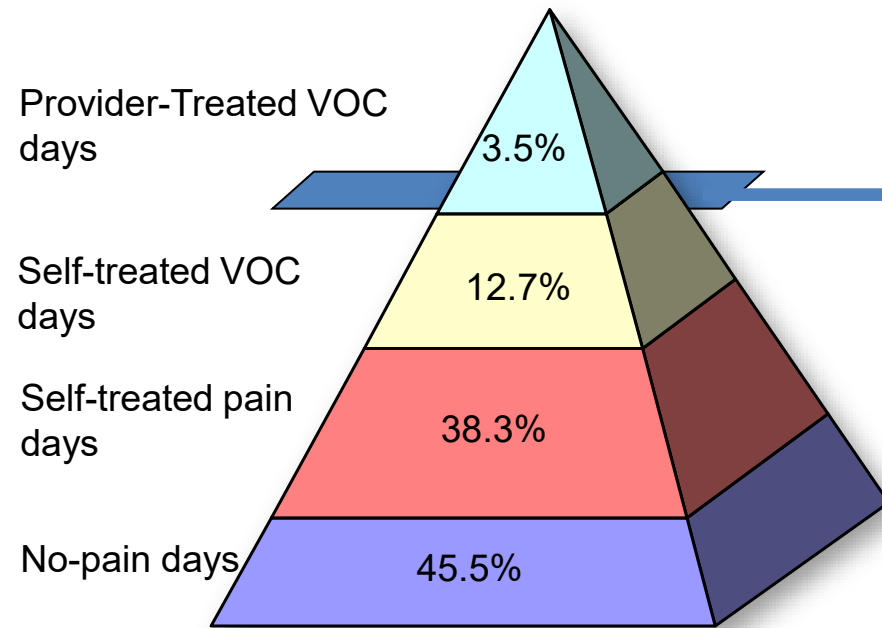
Acute SCD Pain Definition







Sources

1. Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks-American Pain Society Pain Taxonomy initiative.
2. Field JJ, Ballas SK, Campbell CM, Crosby LE, Dampier C, Darbari DS, McClish DK, Smith WR, Zempsky WT. Analgesic, Anesthetic, and 10.1016/j.jpain.2018.12.003. [Epub ahead of print] PubMed PMID: 30578848. Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks-American Pain Society-American Academy of Pain Medicine Pain Taxonomy Diagnostic Criteria for Acute Sickle Cell Disease Pain. J Pain. 2018 Dec 19; pii: S1526-5900(18)31017-4. doi:

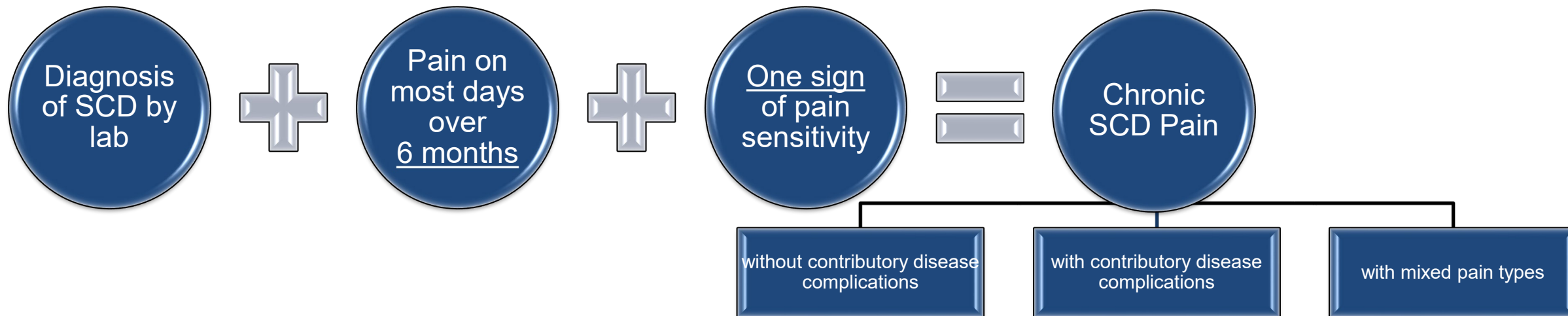
Only a Small % Days Spent in Acute Pain Managed in Hospital



Pain Intensity		Mean	Std Dev
	Utilization	5.9	0.1
	Crisis w/o utilization	5.0	0.1
	Pain w/o crisis or util.	3.9	0.1
	No Pain	0	0

*Percentage of days. Utilization= utilization with or without crisis or pain; Crisis= crisis without utilization; Pain= pain without crisis or utilization

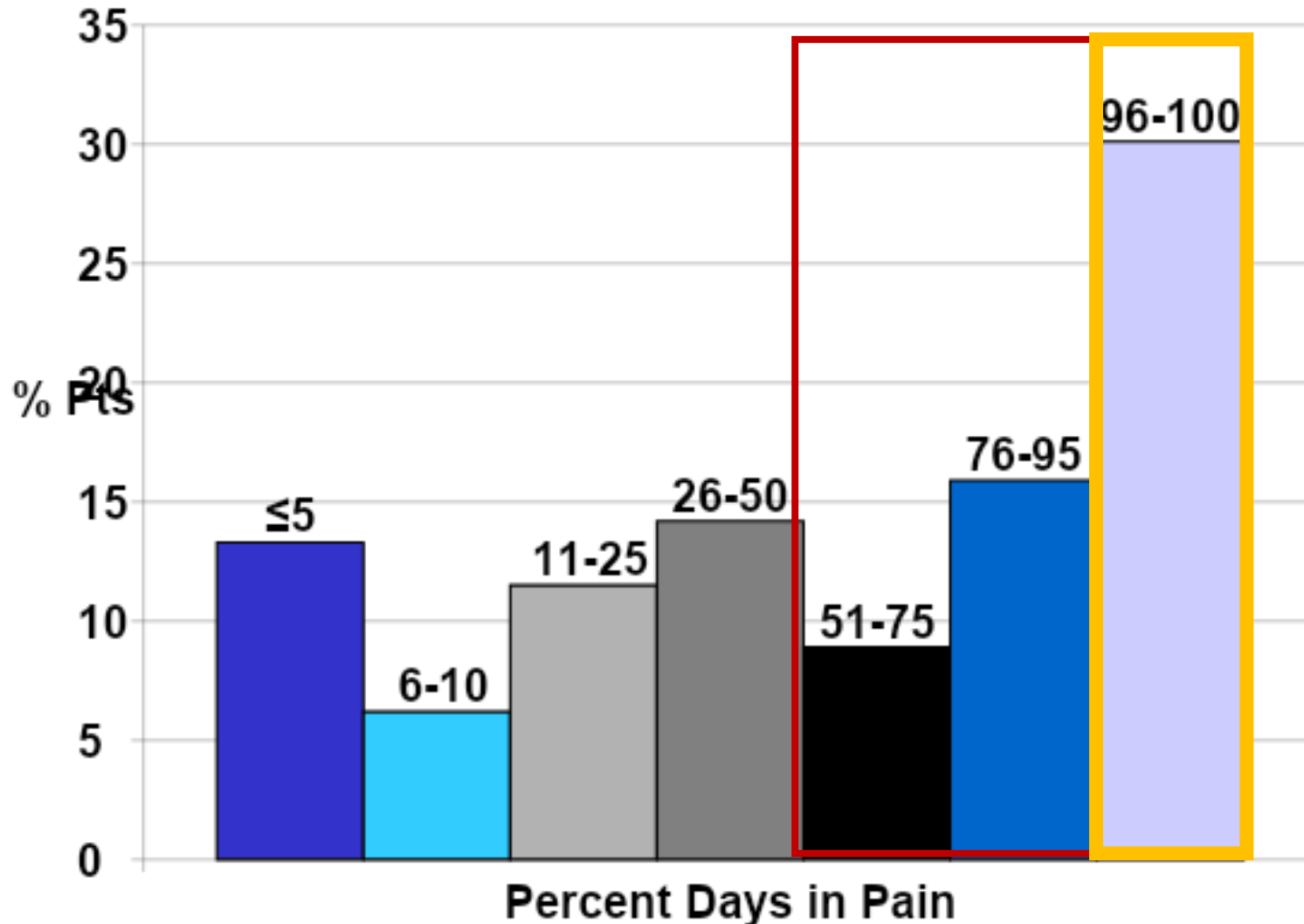
Chronic SCD Pain Definition



Sources:

Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks-American Pain Society Pain Taxonomy initiative. ; Dampier C, Palermo TM, Darbari DS, Hassell K, Smith W, Zempsky W. AAPT Diagnostic Criteria for Chronic Sickle Cell Disease Pain. J Pain. 2017 May;18(5):490-498. doi: 10.1016/j.jpain.2016.12.016. Epub 2017 Jan 5. PubMed PMID: 28065813.

Chronic Pain is Usual in SCD Adults



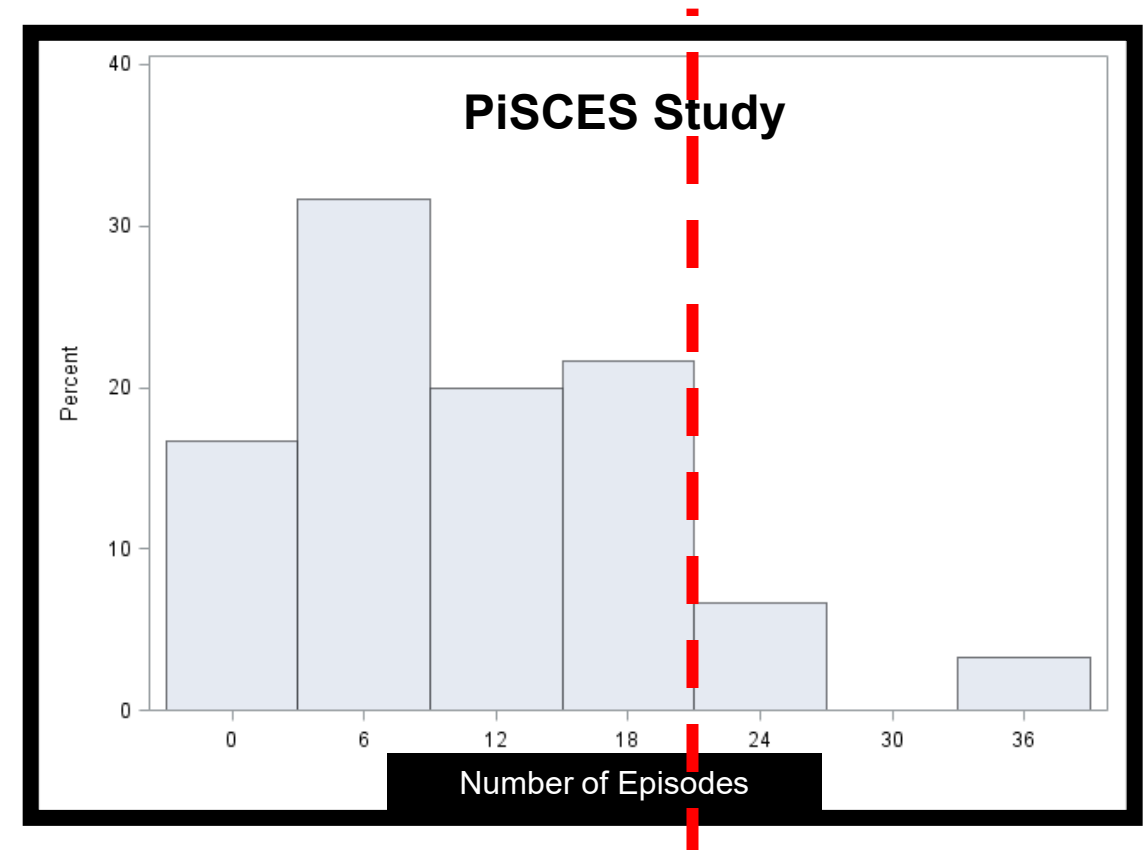
- Only 13% of subjects almost never had pain
- 55% had pain >half of days
- 30% pain essentially daily
- Likely AAPT “chronic pain with mixed pain types”
 - Neuropathic, nociceptive (vasculopathic, tissue injury) inflammatory
 - Adapted from Smith WR, et. al. Ann Intern Med 2008 Jan 15, 148(2):94-101

Acute-on-Chronic SCD Pain

Intensity Exacerbations of 2 or more on Likert Scale Often Occurred Without “Crisis”

The large majority of patients had 18 or fewer exacerbations of 2 or more on the Likert scale

The large majority of patients had 10 or fewer exacerbations of 3 or more on the Likert scale .



Nociceptive, Neuropathic, Nociplastic Pain



Nociceptive pain :
ongoing
inflammation and
damage of tissues



Neuropathic pain :
nerve damage



Nociplastic
(Central
Neuropathic) pain :

- augmented CNS pain, sensory processing, altered pain modulation
- Multifocal pain, widespread or intense, or both
- Other CNS-derived sx's: fatigue, sleep, memory, and mood problems

Pain Transformation in SCD

Usual Pain phenotype

- Usual pain sensitivity
- Afferent pain-modulation balance



15-20 Years of recurrent Vaso-occlusive damage to CNS neurons, glia

- Elevated cerebral blood flow from cerebral hypoxia



Hyper-nociceptive phenotype

- Afferent pain modulation imbalance
- Silent brain ischemia
- Cognitive deficits
- Altered pain cognition

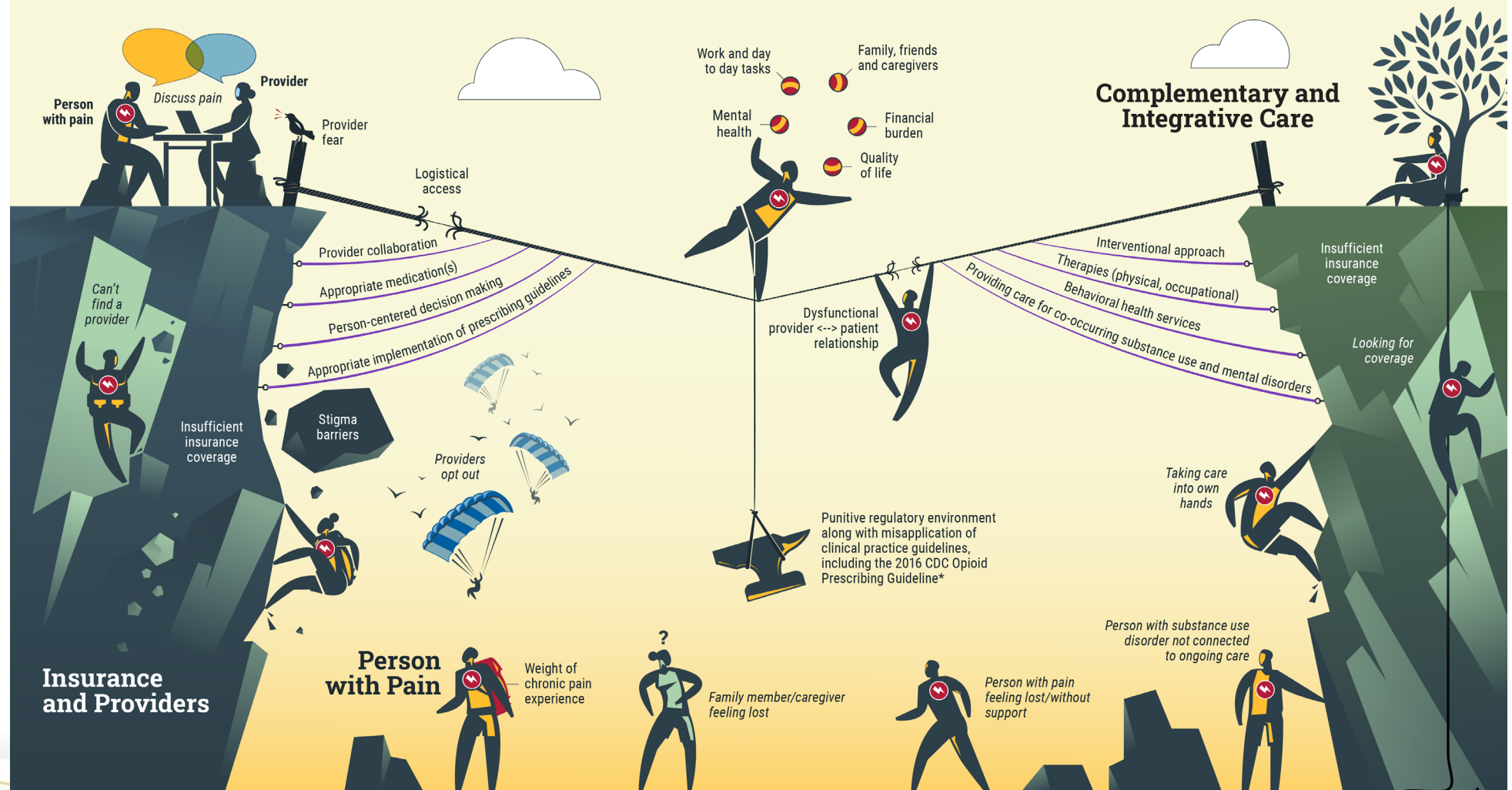


Patients' Plight: Whole-Person Pain Treatment is POOR

Chronic Pain Experience

Understand access to covered treatment and services for people with chronic pain.

This visual is derived from stakeholder interviews focusing on the experiences of those living with and treating chronic pain. Its intent is to highlight the most prominent barriers experienced by people accessing care and the influencers acting on providers, ultimately affecting the person with chronic pain, their quality of care, and their quality of life. These sentiments were derived from requests for information (RFIs) conducted by CMS and CDC, including as part of CDC's efforts to understand and integrate the lived experiences of patients and providers into their update to the 2016 opioid prescribing guideline.



* CDC is in the process of updating the 2016 CDC Guideline for Prescribing Opioids for Chronic Pain. The goal of the revised clinical practice guideline is to help advance effective, individualized, patient-centered care. The revision was designed with a focus on ensuring appropriate use as a clinical tool and to avoid misapplication of the guideline itself.