Barriers to Optimal Management of Sickle Cell Pain

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Learning Objectives

- Understand the uniqueness of sickle cell pain sometimes makes optimal management difficult
- Understand that racial disparities in pain management exist
- Understand the stigma patients feel associated with sickle cell pain
- Understand ignorance of health care professionals as a barrier to optimal pain management
- Understand pharmacokinetics and pharmacodynamics of opiates

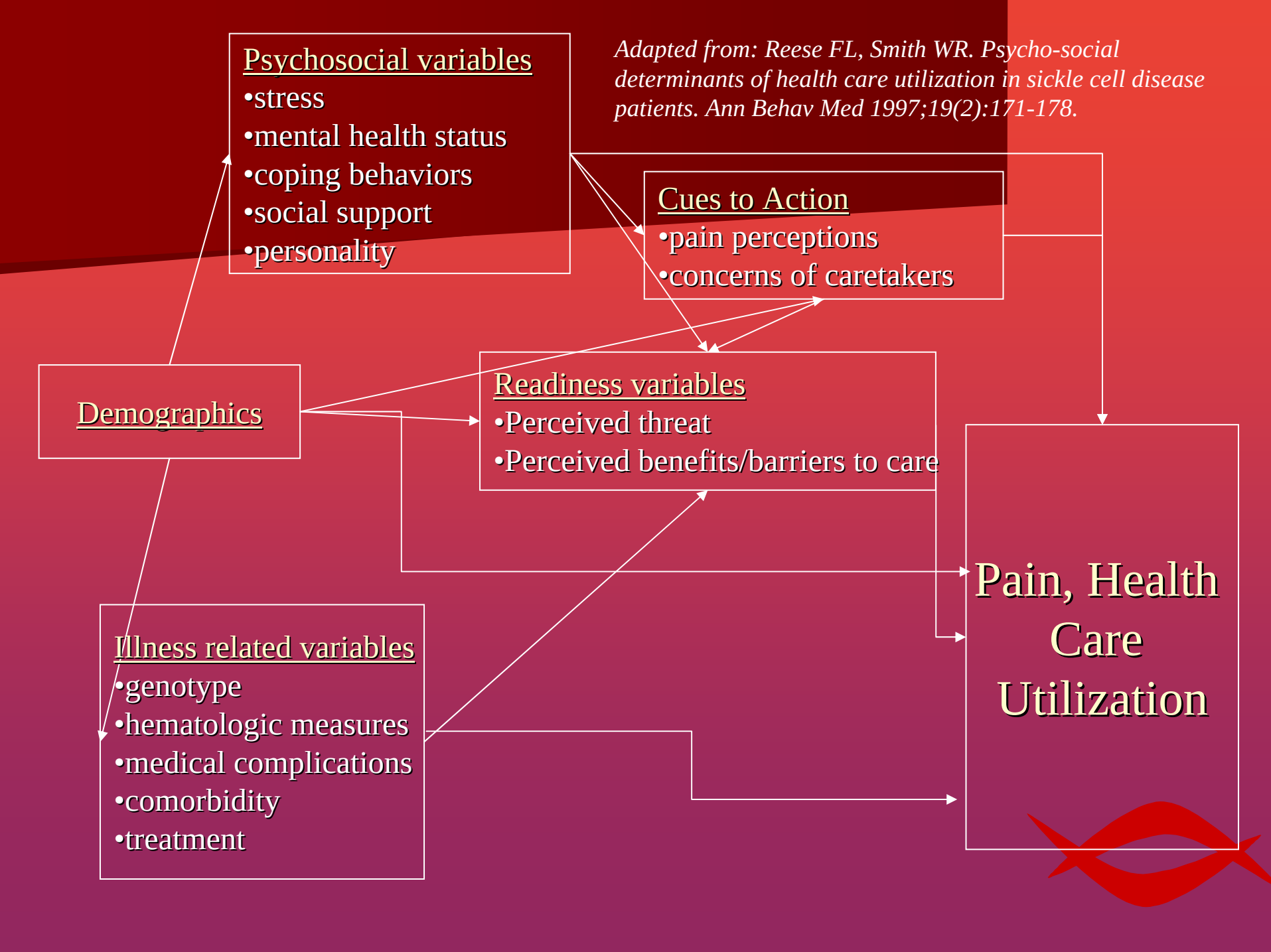
The uniqueness of sickle cell pain sometimes makes optimal management difficult.

Pain in Sickle Cell Disease

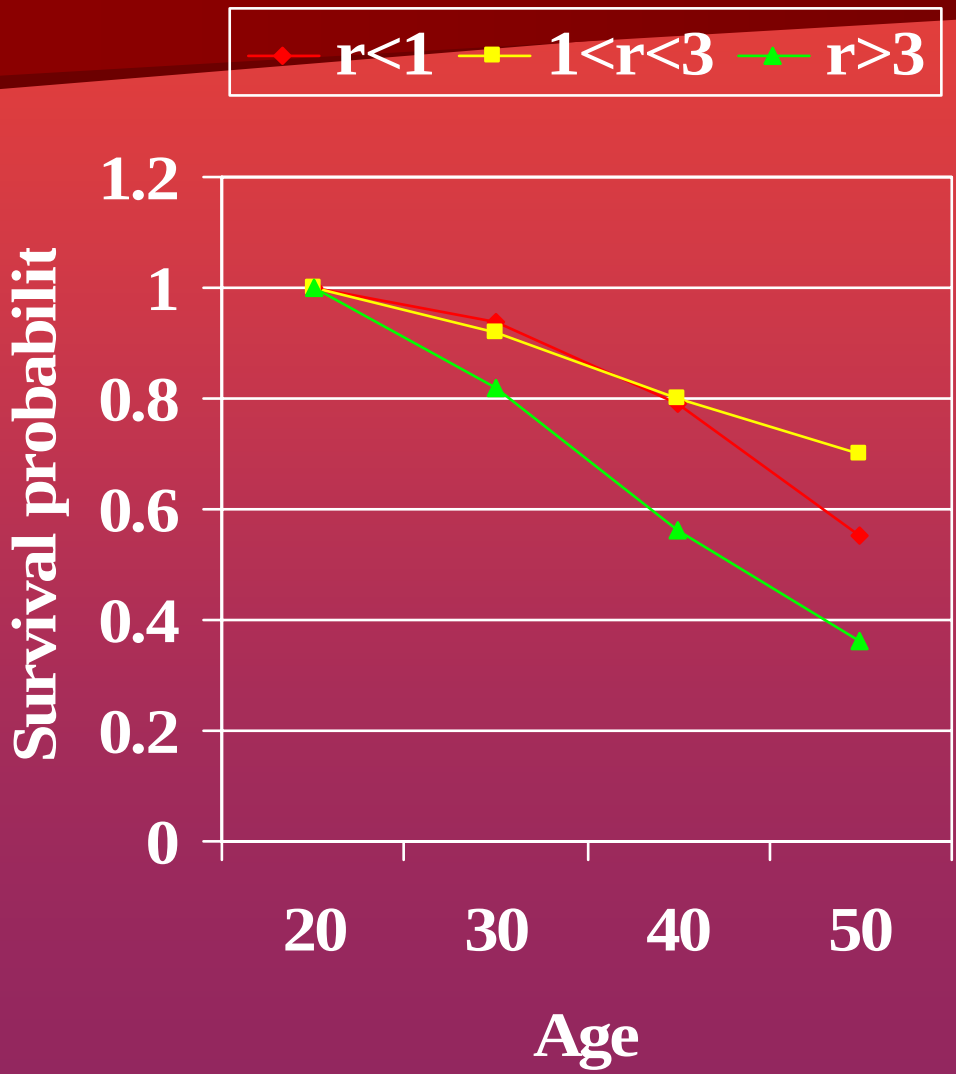
- Poorly understood
- Pain is variable
- Genotype and biological traits explain only part of these variances
- Little is known about differences in pain responses

Differences in Sickle Cell Pain and Cancer Pain

Cancer Pain	Sickle Cell Pain
Non-ischemic	Ischemic
Continuous	Intermittent
Progressive	Remitting
Predictable	Unpredictable
Terminal event	Throughout life
Not questioned	Questioned by MDs
Many objective correlates	Few objective correlates
May be absent	Prominent feature of disease
Few to no ER visits	Frequent ER visits
Older adults	Children, young adults
Longitudinal specialty care	Episodic care

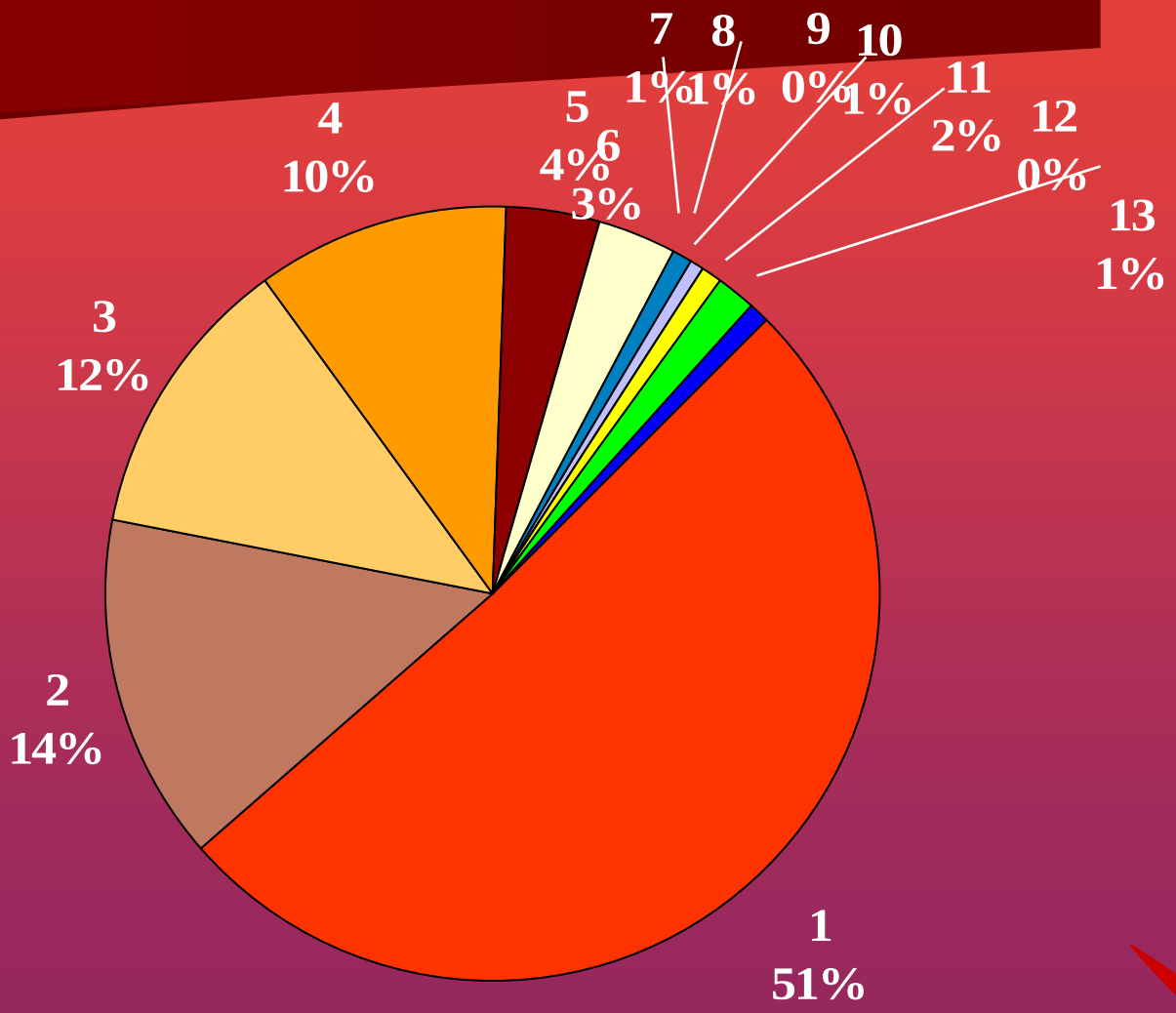

Psychosocial variables
•stress
•mental health status
•coping behaviors
•social support
•personality
Adapted from: Reese FL, Smith WR. Psycho-social determinants of health care utilization in sickle cell disease patients. Ann Behav Med 1997;19(2):171-178.
Cues to Action
•pain perceptions
•concerns of caretakers
Demographics
Readiness variables
•Perceived threat
•Perceived benefits/barriers to care
Pain, Health Care Utilization
Illness related variables
•genotype
•hematologic measures
•medical complications
•comorbidity
•treatment

Results of CSSCD: “Pain” rate above age 20 predicts death



- Adapted from: Platt, et.al. N Engl J Med; 1991;325:11-16.

A few patients responsible for most "pain" (i.e, visits)



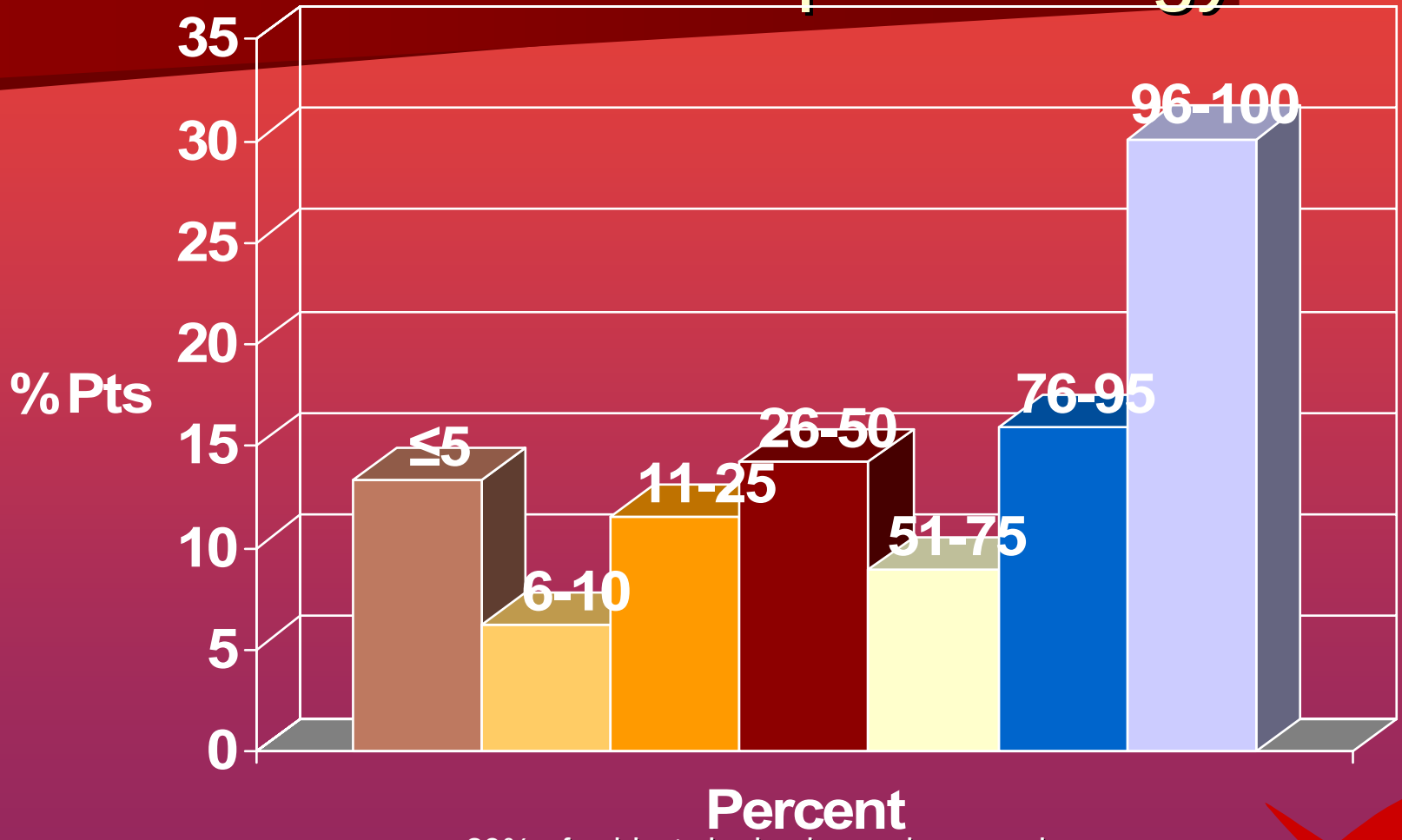
No. MCV Admits/Yr, 1990-91 (n=125)

The “Difficult Patient: “Chronic” Pain Syndrome

- Only a few high utilizer patients responsible for most ED visits, due to:
  - Coexisting disease, underlying medical problem
    - lupus, rheumatoid, gout, gum infection, thyroid disease, leg ulcer, etc.
  - Avascular necrosis of hip
    - this pain more responsive to non-steroidals
  - Recurrent but remitting sickling and crisis pain
    - Psychosocial overlay possible
    - Street drug abuse possible

% Days in Pain: Histogram

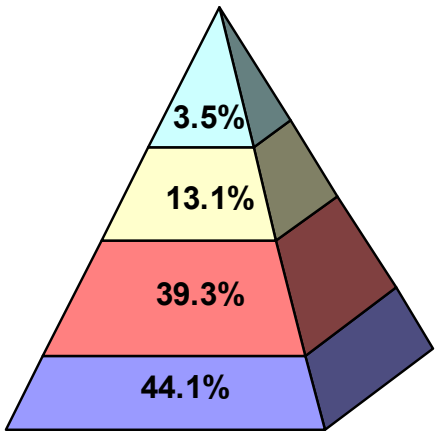
Pain in Sickle Cell Epidemiology Study



- 30% of subjects had pain nearly every day
- Only 13% of subjects almost never had pain

The Iceberg: Proportion of Days in Pain, Crisis, Utilization

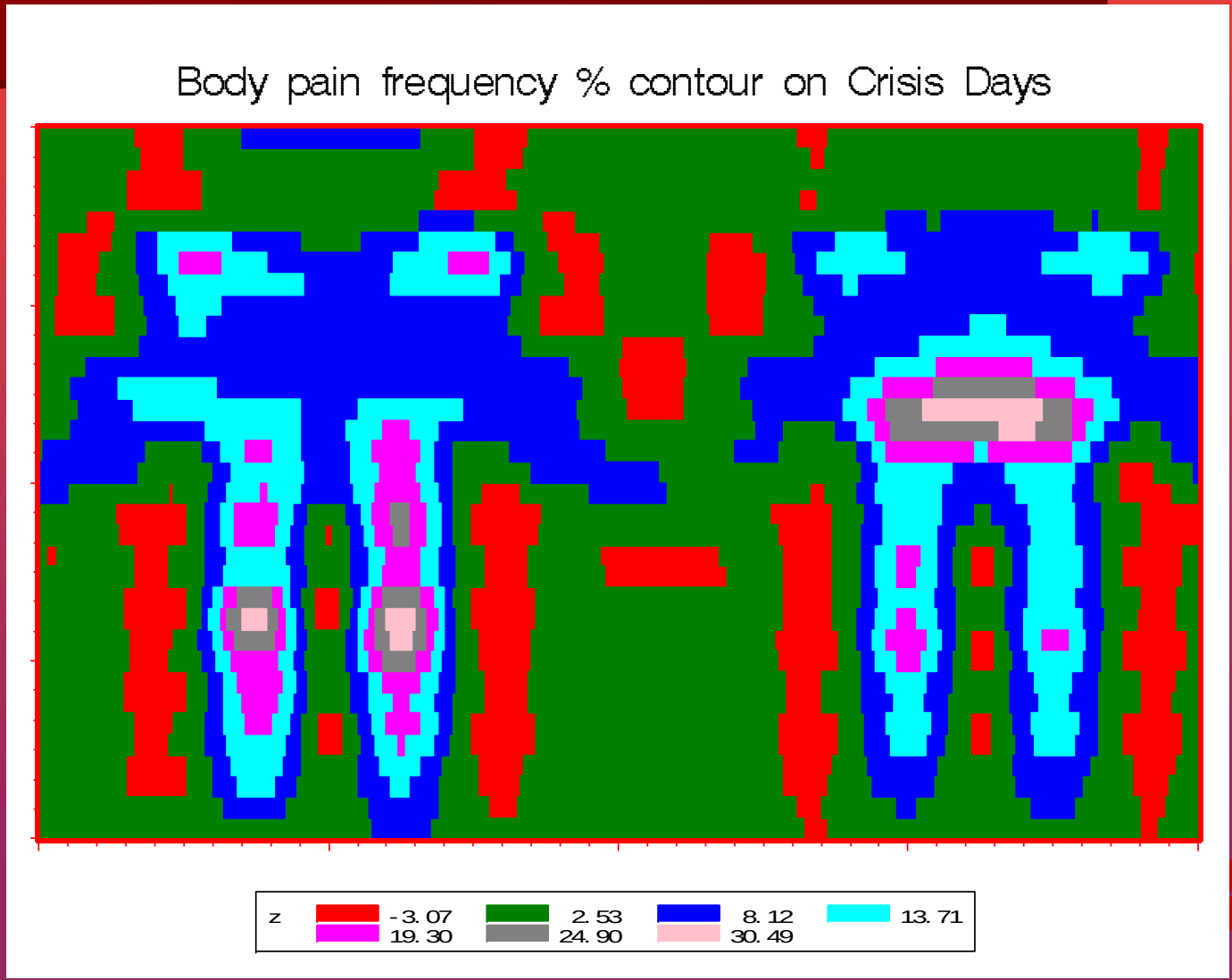
*Iceberg of Days With Utilization, Crises, and Pain in PiSCES**



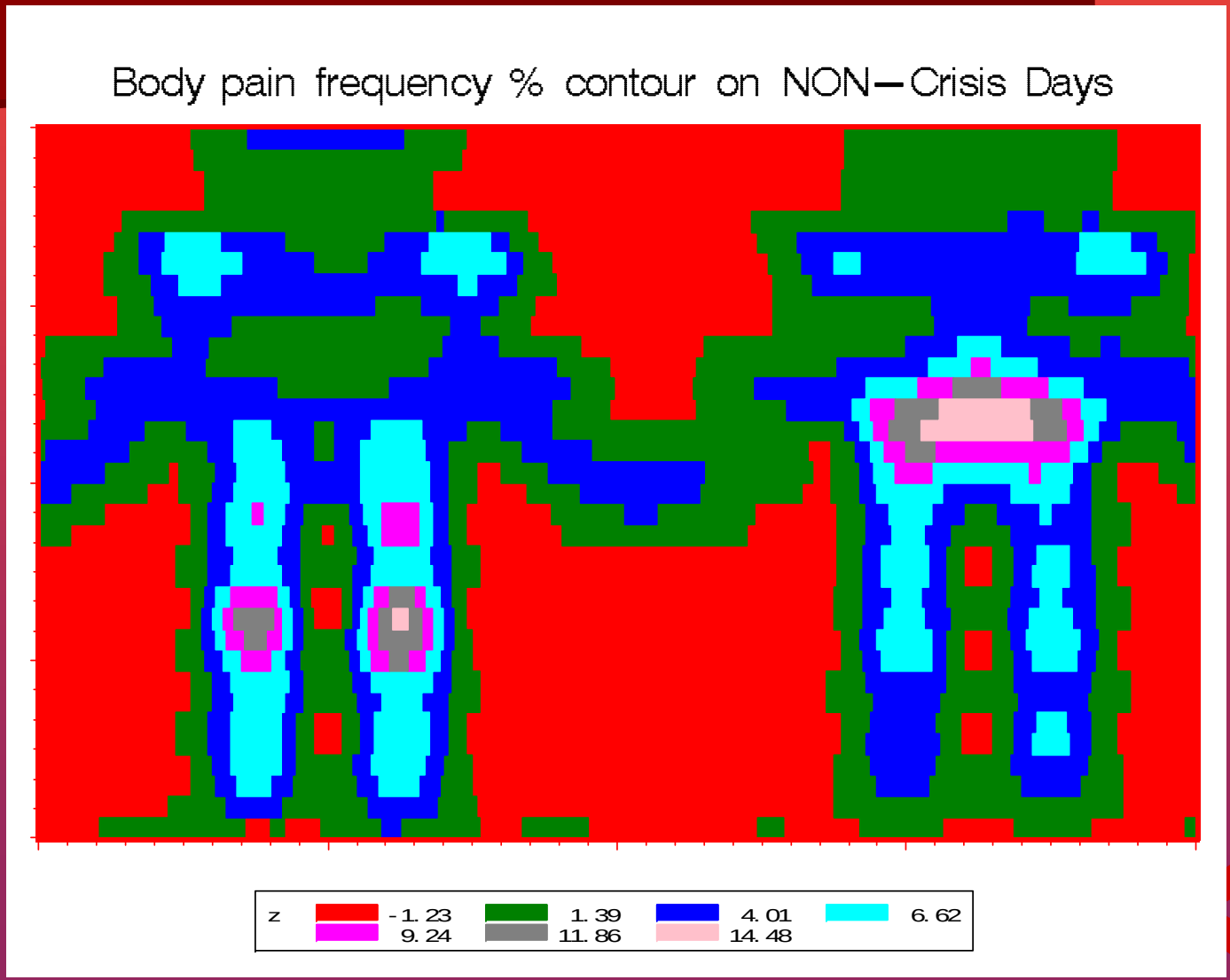
Pain Intensity	Mean	Std Dev
Utilization Days ± Crisis ± Pain	**6.5**	**2.3**
Crisis Days ± Pain	**5.5**	**2.1**
Pain Days-Crisis-Utilization	**4.2**	**2**
No Pain Days	**0**	**0**

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

Pain Location Frequency-crises



Pain location frequency—non-crisis

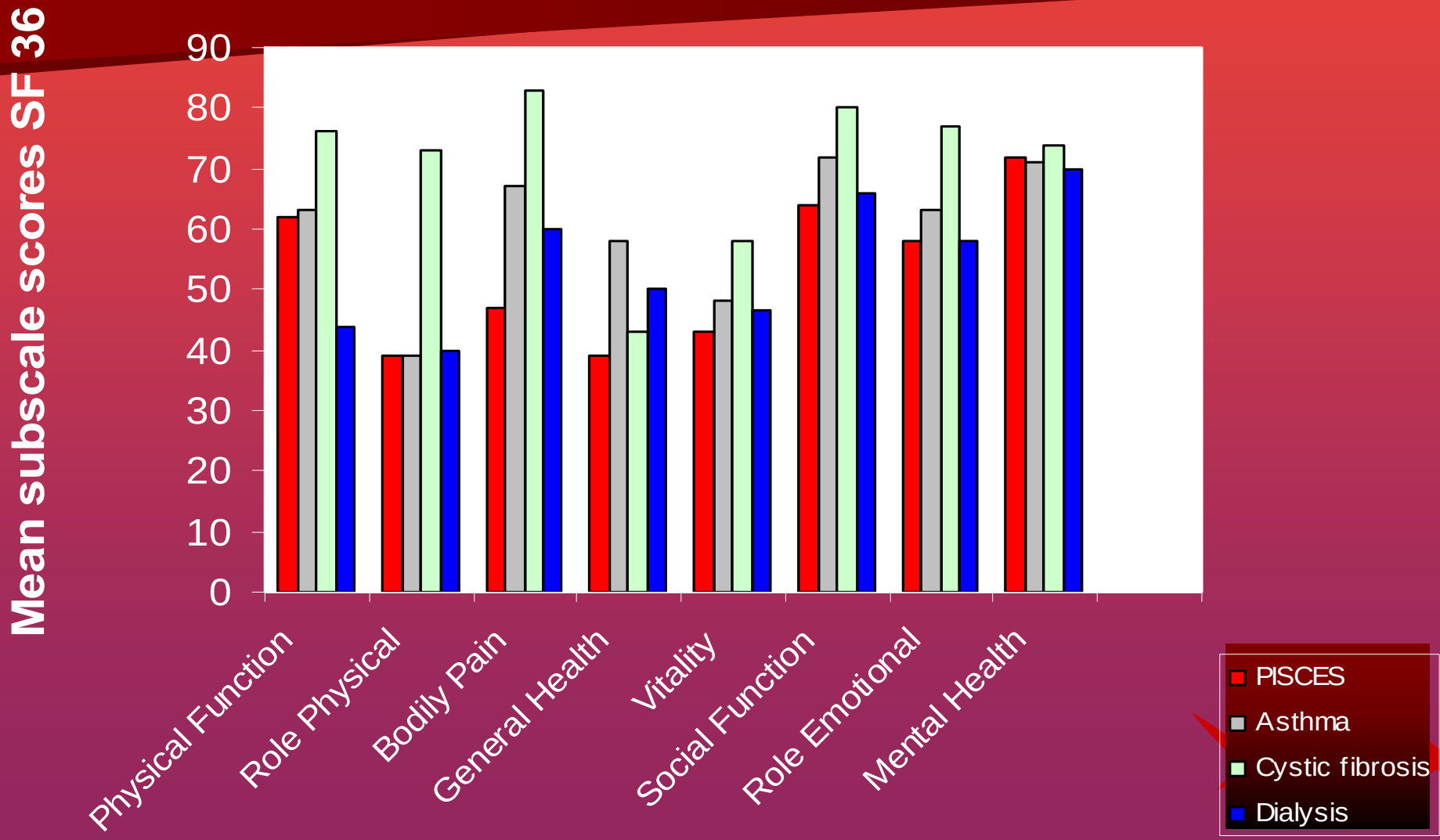


Patients feel a stigma associated with sickle cell disease and its pain.

Health outlook, medical care opinions may influence response to pain

- SCD satisfaction with, humaneness of care << asthma
  - Bobo L, Miller ST, Smith WR, Elam JT, Rosmarin PC, Lancaster DJ. Health perceptions and medical care opinions of inner-city adults with sickle cell disease or asthma compared with those of their siblings. Southern medical journal 1989;82(1):9-12.
- Treated rudely, or delays in care.
- Some try to avoid ED until extreme need.
  - Treat even severe pain “crises” at home.
    - Murray N, May A. Painful crises in sickle cell disease--patients' perspectives. Bmj 1988;297(6646):452-4.
- Documented disputes patients vs. staff
  - Patient behaviors raise staff concerns about analgesic misuse.
    - Elander J, Lusher J, Bevan D, Telfer P, Burton B. Understanding the causes of problematic pain management in sickle cell disease: evidence that pseudoaddiction plays a more important role than genuine analgesic dependence. J Pain Symptom Manage 2004;27(2):156-69.

Quality of Life, Sickle vs. Chronic Diseases



Depression, Alcohol, Anxiety

- Any depression 28.3%
  - Major depression 14.9%
  - Other depression 13.6%
- Any anxiety disorder 8.9%
  - Panic disorder 4.4%
  - Other anxiety 3.5%
  - 70% with anxiety also had depression
- ***Alcohol abuse 31.4%***

Racial disparities in pain management exist.

Ethnic basis for inadequate analgesia

- **ED long-bone fx:** Hispanic Adjusted OR for no analgesia 7.46[2.22-25.04]
  - JAMA 1993; 269:1537-39.
- **Cancer:** 65%, minorities, (esp. Hisp.s), w/o "guideline-recommended" analgesics (vs. 50% whites, p<.001)
  - Ann Intern Med 1997;127:813-816.
- **Post-op limb fx.:** Morphine equiv's Whites=22 mg/d, blacks=16 mg/d, Hisp=13 mg/d. (p<.005)
  - Psychosom Med 1996;58:125-129
- **PCA:** No Δ in *self-admin*. PCA across race; *prescribed* PCA White>Hisp; Black>Hisp or Asian (p<.01)
  - Pain 1996;66:9-12.

The ignorance of health care professionals is a barrier to optimal pain management.

Understanding the pharmacokinetics and pharmacodynamics of opiates is important to opiate prescribers.

Current Controversies About Opioids

- Type of pain
- Choice of drug
- Route and method of administration
- Tolerance
- Physical dependence
- Addiction (Psychological dependence)
  - MD concerns about the latter three tend to override their concerns about the former three
    - Foley, Kathleen, M.D., Mem. Sloan Kettering

Definitions

- *Tolerance* = Decreased analgesic response to same dose of drug
  - Earliest symptom is shortening of duration of effective analgesia
- *Physical dependence* = Production of withdrawal upon abrupt discontinuation, antagonist
- *Addiction* = Psychological dependence
  - manifested by dose escalation, use of opioids for purposes other than pain relief

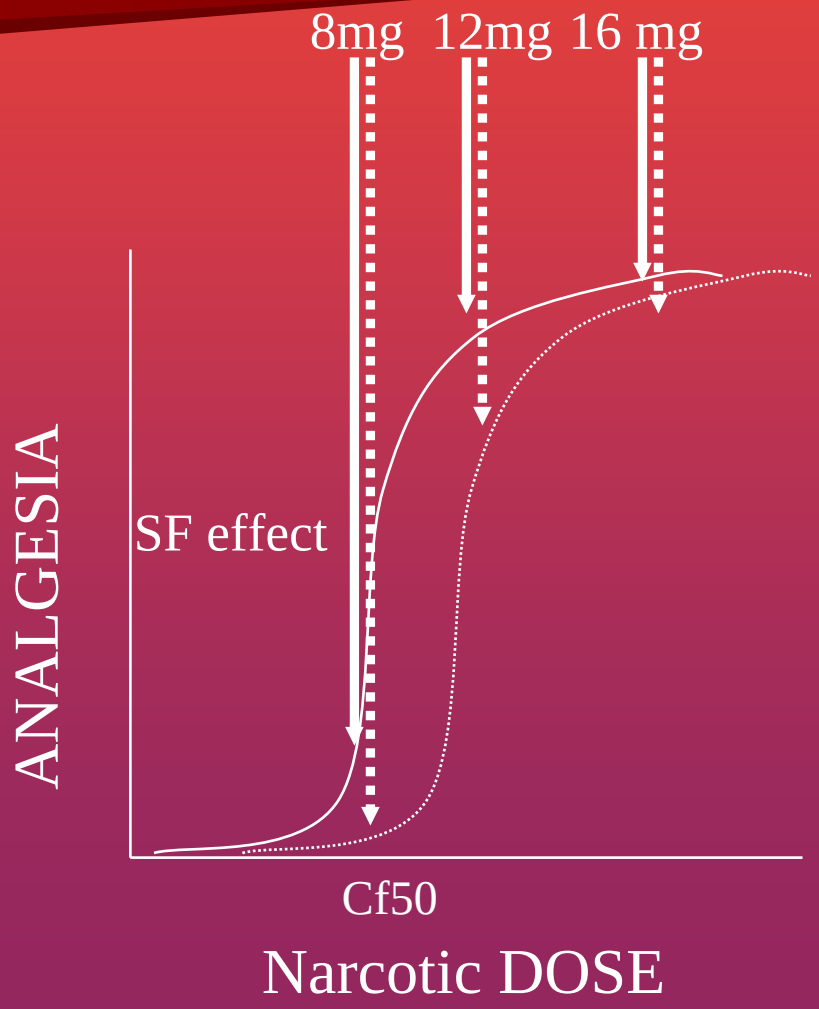
Pharmacokinetics vs. Pharmacodynamics

- *Pharmacokinetics:* drug dose --> drug concentration
- *Pharmacodynamics:* drug concentration --> drug effects (e.g. analgesia)
  - Sigmoid curve
  - Cf50 = half-maximal concentration
  - SF effect = effect from half-maximal concentration
  - Tailor infusions by measuring and aiming for target concentrations

Dose--> concentration--> effect

- Pharmacodynamic studies (relationship between dose, concentration, effect) not done in sickle cell disease
- Correlation between pain relief and sedation
  - On average, but NOT ALWAYS
  - Individualize analgesic dose based on these principles

Pharmacodynamic curve, tolerance greatly affect amount of analagesia



- TITRATE, TITRATE, TITRATE!!!

Characteristics of Tolerance

- Not equally frequent in all patients
- Different temporal rate of development between patients
- No limit to its degree
  - Often can safely double narcotic dose (shift of sigmoid curve to right)
- Side effects due to increased dose requirement
  - Sedation
  - Respiratory depression

Differential Dx. of Tolerance

- New or increased pain stimulus, dz. progression
  - Major reason for need to increase dose (in cancer)
- Cross Tolerance
  - Tolerance to other drugs of same type, especially opiates
  - Incomplete cross tolerance seen for opiates
  - Opiates may be selective for receptor subtype