

Daily Pain in Sickle Cell Disease: The Pain in Sickle Cell Epidemiology Study

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Learning Goals

- The learner will be familiar with recent research on daily pain, quality of life, and functional status in adults with sickle cell disease
- The learner will be familiar with the impact of recent revelations about daily pain in sickle cell disease



Pain in Sickle Cell Disease

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



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Pain in Sickle Cell Disease is Unique

- Hallmark of disease
- Intermittent (crises) and chronic
- Ischemic and others
- Secondary to erythrocyte (rather than platelet) vaso-occlusion
- Ubiquitous
- Present throughout life



Pain of Variable Frequency

- Unpredictable (within patient)
- 40% of patients with less than 1 crisis/year
- Small number of patients (5%) responsible for large number of painful crises (40%)
- Hemoglobin type predicts pain frequency
 - Hemoglobin SS 0.8/year
 - Hemoglobin SC, S β Thal 0.4/year
 - More Hemoglobin F, fewer α hemoglobin chain genes decreases frequency

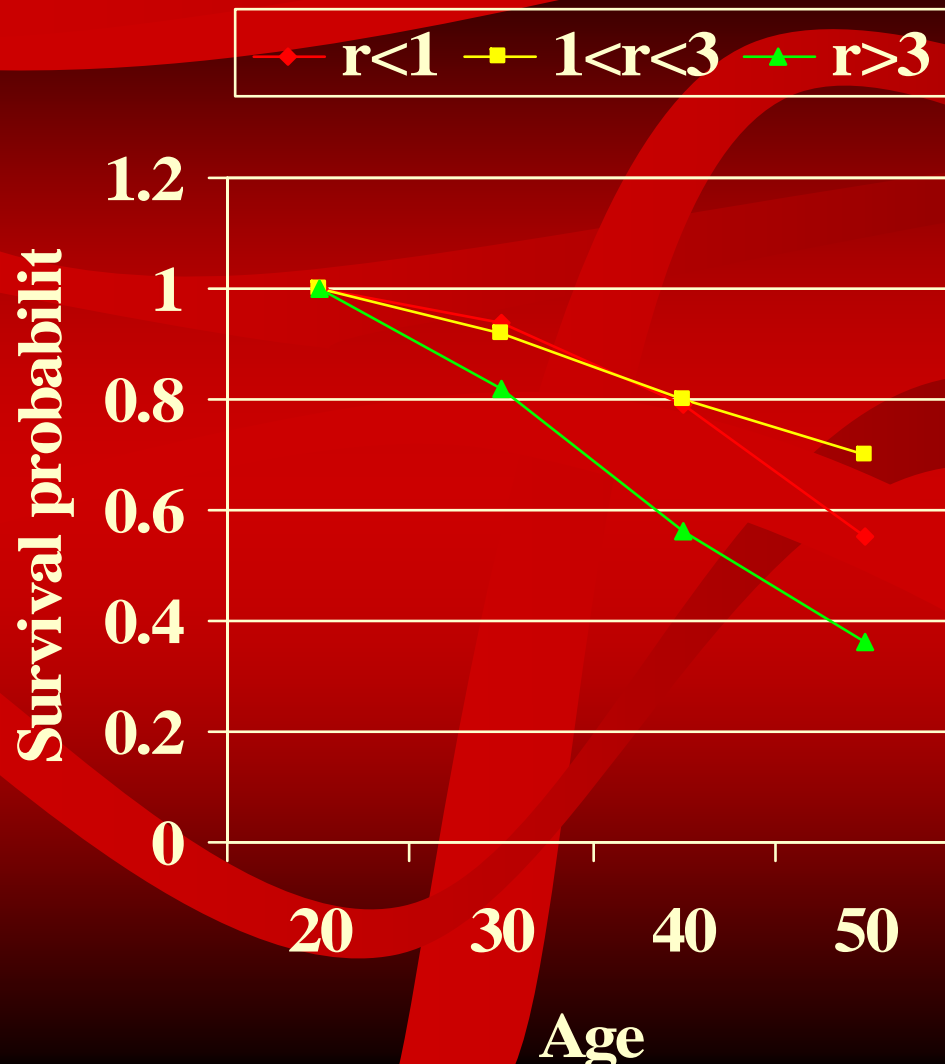


Adult SCD → High-Volume, Emergency Hospitalizations

- SCD discharges < 2% of the 39,163,834 US hospital discharges in 2005.
 - 1.12% of age 1-17 discharges; 0.48% or less of all other discharges
- % of SCD discharges in 18-44 yr age category >> % of non-SCD discharges in 18-44 yr (P<0.0001).
- Disproportionate % of SCD admissions (vs. all 2005 admissions) from the ED.
 - Most disproportionate % = 18-44 yr age category: 77.37%, vs. 34.37%



Pain rate above age of 20 is predictor of death

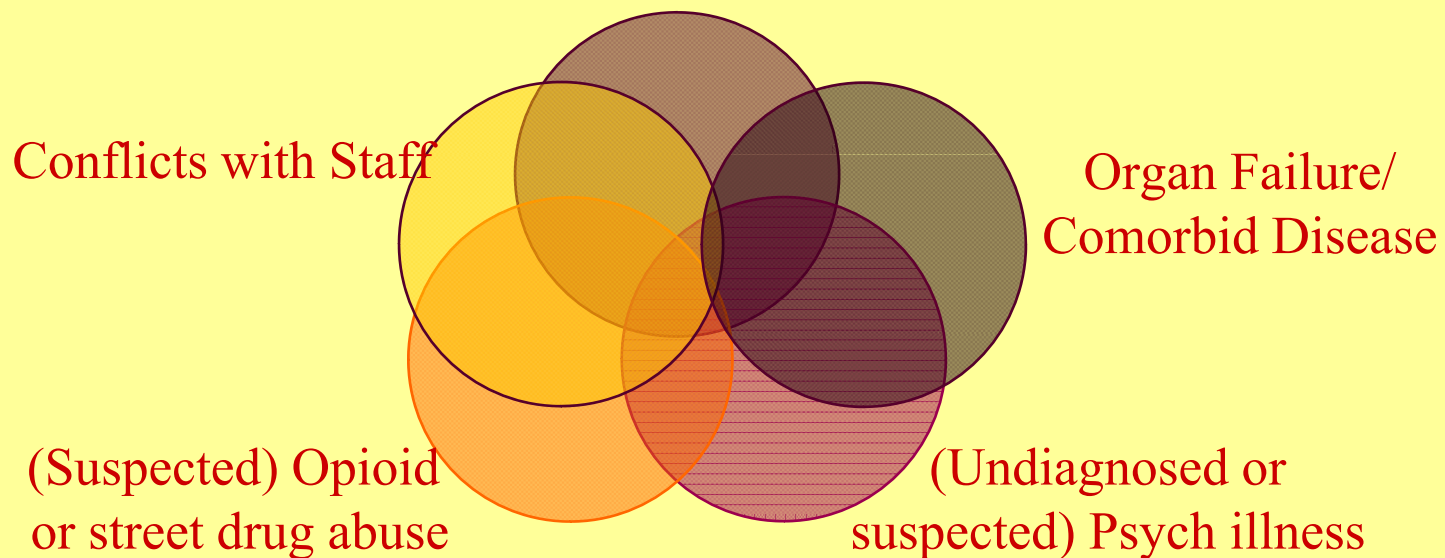


- Adapted from:
Platt, et.al. N
Engl J Med;
1991;325:11-16.

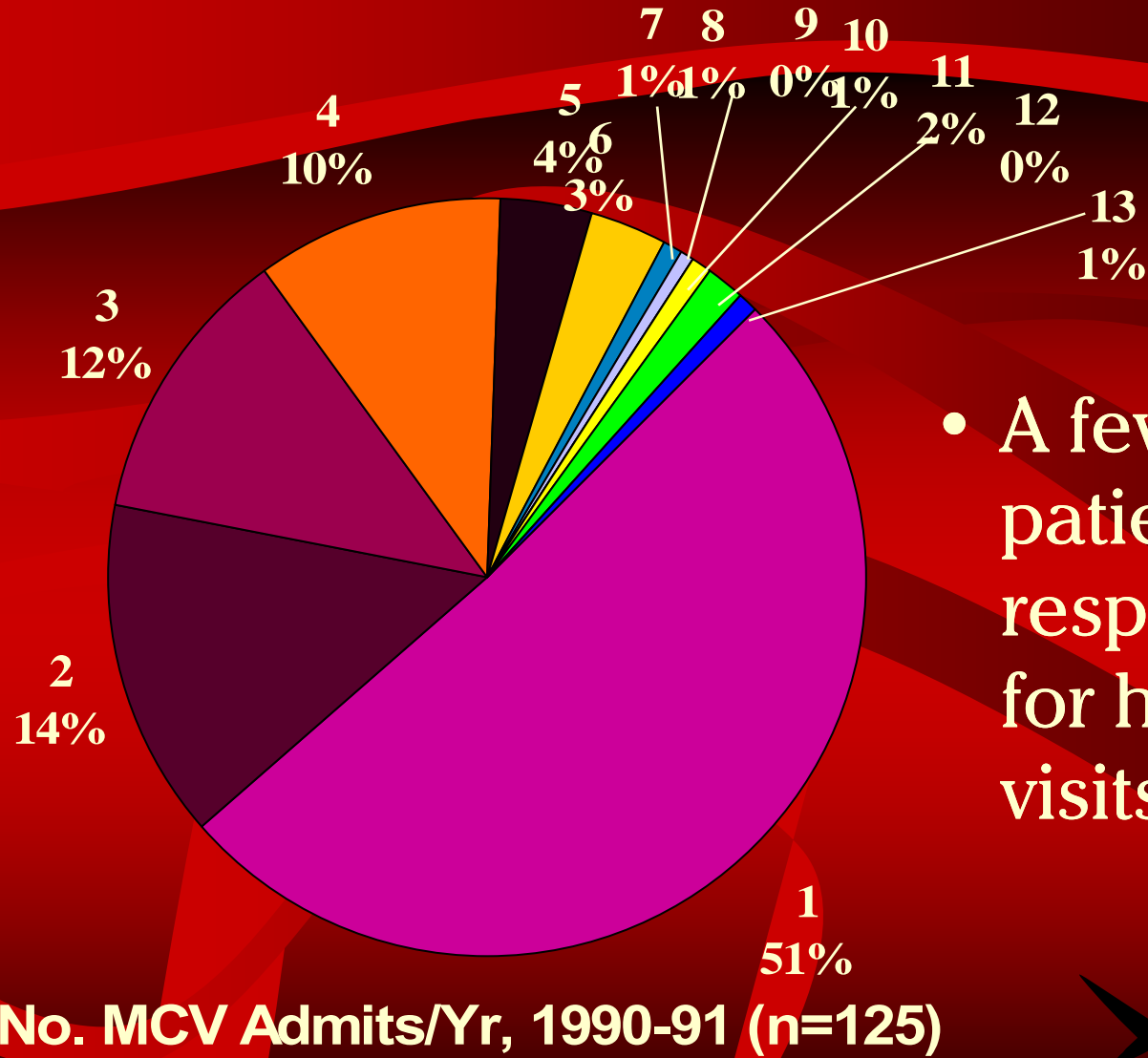


The “Difficult” SCD Patient

High Utilizer/High treatment requirements



High Utilizer/High Rx Requirement



- A few patients responsible for half of visits



Organ Failure/ Comorbid Disease → Different Pain Syndromes

- End-organ failure
 - Lung
 - Kidney
 - Heart
 - Liver
- SCD chronic pain complication
 - Avascular necrosis
 - Gout
 - Leg ulcer
 - Degenerative joint disease
 - Priapism
- Coexisting disease
 - Lupus
 - Rheumatoid arthritis
 - Infection
 - Thyroid disease
 - Diabetes
 - Hypertension



Psych Illness/Psychosocial Overlay → Complex Pain syndromes

- Depression/Anxiety/Somatization
- Stress
 - From caring for the illness
 - From strained relationships
 - Family
 - Others
- Personality Disorders
- Schizophrenia/Mania



(Suspected) Street Drug, Opioid Abuse

- Of 19 subjects surveyed in Richmond, VA
 - 6 screened positive on POMI (screener for risk of opioid misuse)
 - 0 screened positive on PDUQ (confirmatory survey for substance abuse or substance dependency)
- POMI
 - 4 subjects admitted to early refills (possible therapeutic dependence)
- PDUQ
 - 5 subjects had >1 provider of opioid medication
 - 3 subjects had taken analgesics prescribed for others
- Low rate of urine positivity for street drugs

Conflicts With Medical Staff: A Vicious Cycle

- Perception of a high prevalence of addiction → inadequate analgesia.
 - 53% of ED physicians , 23% of hematologists said > 20% of adult SCD “addicted”
 - 22% of ED physicians 9% of hematologists said > 50% addicted [22].
- SCD pts may be under-medicated in the ED [25, 26]
 - may report more pain and have increased rates of hospital utilization.
- Undertreatment → behaviors of *pseudoaddiction*
 - (drug-seeking behaviors that resolve when pain is adequately treated) which are often misunderstood and reinforce the misconceptions of addiction [27.]
- Inadequate analgesia → communication barriers, ↓ trust in the provider.
 - Most patients have had negative experiences in the acute care setting
 - Many report providers did not give them enough medication or frequent enough doses
 - Many report did not seem to understand how much pain they were experiencing.



Differences in Sickle Cell Pain and Cancer Pain

Cancer Pain

Non-ischemic

Continuous

Progressive

Predictable

Terminal event

Not questioned

Many objective correlates

May be absent

Few to no ER visits

Older adults

Longitudinal specialty care

Sickle Cell Pain

Ischemic

Intermittent

Remitting

Unpredictable

Throughout life

Questioned by MDs

Few objective correlates

Prominent feature of disease

Frequent ER visits

Children, young adults

Episodic care



Managing the Difficult Patient with SCD

- Sickle-associated painful morbidities
 - Avascular necrosis of hip
 - Ischemic ulcers of ankle, leg
- Coexisting disease, underlying medical problem
 - Ψ dz, lupus, rheumatoid, gout, infection, thyroid disease
- ***Chronic, or recurrent but remitting, pain**
 - Psychosocial overlay possible
 - Hyperalgesia? Central sensitization?
 - From opioids?
- ***Street drug abuse (cocaine)?**
 - *Recently documented or under study**

← Treat with non-steroidals

← Diagnose comorbid disease

← Measure and treat chronic pain

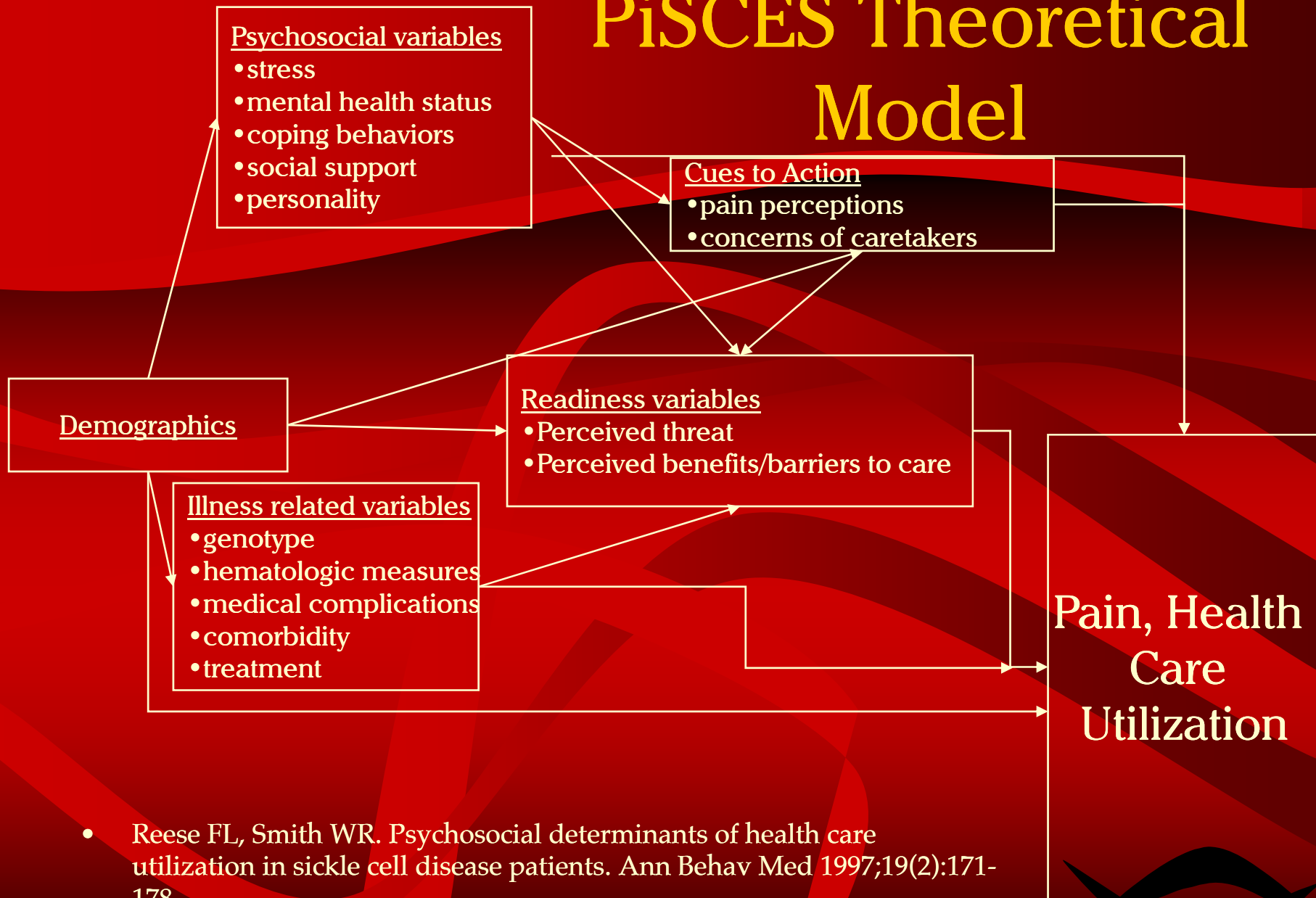
← Detect, co-manage abuse, counsel staff on pt needs

Pain in Sickle Cell Epidemiology Study

- National Institutes of Health
 - National Heart Lung and Blood Institute
- Funding for 3.5 years



PiSCES Theoretical Model



- Reese FL, Smith WR. Psychosocial determinants of health care utilization in sickle cell disease patients. *Ann Behav Med* 1997;19(2):171-178.

Four Possible Utilization Patterns

		Pain	
		High (or +)	Low (or -)
Utilization	High (or +)	High utilizers (or episode of utilization) explained by pain	High utilizers (or episode of utilization) unexplained
	Low (or -)	Home managers (or no episode of utilization) despite pain	Low utilizers (or no episode) explained by low pain



Aims of PISCES study

- Follow patients every day for six months via diaries
- Measure pain and response to pain in sickle cell disease
- Explain both *within-patient* and *between-patient* differences in pain and response to pain



Study Content

- Initial survey (50 min's)
- Blood draw and urine sample
- Diaries each day for six months
- Chart review
- Brief final survey



Diary Content

- Recall the prior 24 hours
 - How much pain? Rate 0-9
 - How much distress? Rate 0-9
 - How much disability? Rate 0-9
 - How much various types of utilization?
 - Non-narcotic analgesics
 - Narcotic analgesics
 - Office visits
 - Emergency department (ED) visits
 - Hospitalization
 - Check off pain locations (on a body locator map)

SICKLE CELL PAIN DIARY



1021

First: _____

M.I.

Last: _____

Study ID: _____ Entry Date: _____ / _____ / _____

1. Select yesterday's month and date with an X (like this). Month: jan feb mar apr may jun jul aug sep oct nov dec
 Date: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

2. Were medications taken yesterday? Yes No
 If no pills were taken, go to #3 below.
 Cross-out (X) the **total number of pills** taken yesterday for sickle cell pain. Write total number of pills if more than 10. Enter any new drug name (and strength) taken yesterday.

Drug Name / Strength	Yesterday's Pill Count	If >10
_____	1 2 3 4 5 6 7 8 9 10 _____	_____
_____	1 2 3 4 5 6 7 8 9 10 _____	_____
_____	1 2 3 4 5 6 7 8 9 10 _____	_____
_____	1 2 3 4 5 6 7 8 9 10 _____	_____
_____	1 2 3 4 5 6 7 8 9 10 _____	_____
_____	1 2 3 4 5 6 7 8 9 10 _____	_____
_____	1 2 3 4 5 6 7 8 9 10 _____	_____
_____	1 2 3 4 5 6 7 8 9 10 _____	_____
_____	1 2 3 4 5 6 7 8 9 10 _____	_____
_____	1 2 3 4 5 6 7 8 9 10 _____	_____

Phone number: _____
 (_____) _____ - _____

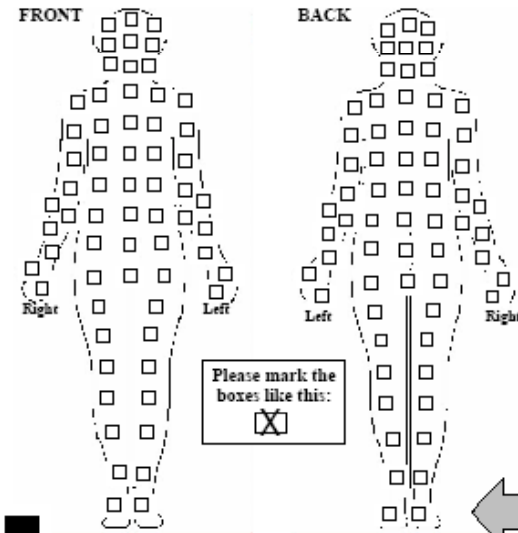
Office Use Only

3. Fill out the diary for what happened yesterday. Exclude non-sickle cell pain, like arthritis or regular headache. Include pain in hip, penis, gall bladder, pain from leg ulcers, and gout. Cross-out **one** number for yesterday's worst:
 Pain: 0 1 2 3 4 5 6 7 8 9
 (none) (unbearable)
 (how badly I hurt)
 Distress: 0 1 2 3 4 5 6 7 8 9
 (none) (total) (extremely)
 (how upset I felt because of pain)
 Interference: 0 1 2 3 4 5 6 7 8 9
 (how much the pain kept me from work, school, housework, family/friends)

4. Check all boxes that apply, about what happened yesterday:
 Yesterday, I went for a scheduled sickle cell doctor or clinic visit
 I was in a pain "crisis"
 I went for an unplanned (emergency, sudden) doctor's office or clinic visit
 I went to the emergency room
 I was in the hospital overnight
 I _____

(write what else may have happened in the box above)

5. Cross-out (X) **one** number for yesterday's BEST relief from pain treatments or medications:
 0 1 2 3 4 5 6 7 8 9
 (no relief) (complete)



6. On the body diagrams, place an X in each box where, due to sickle cell pain, you hurt yesterday.

HRQOL Measure

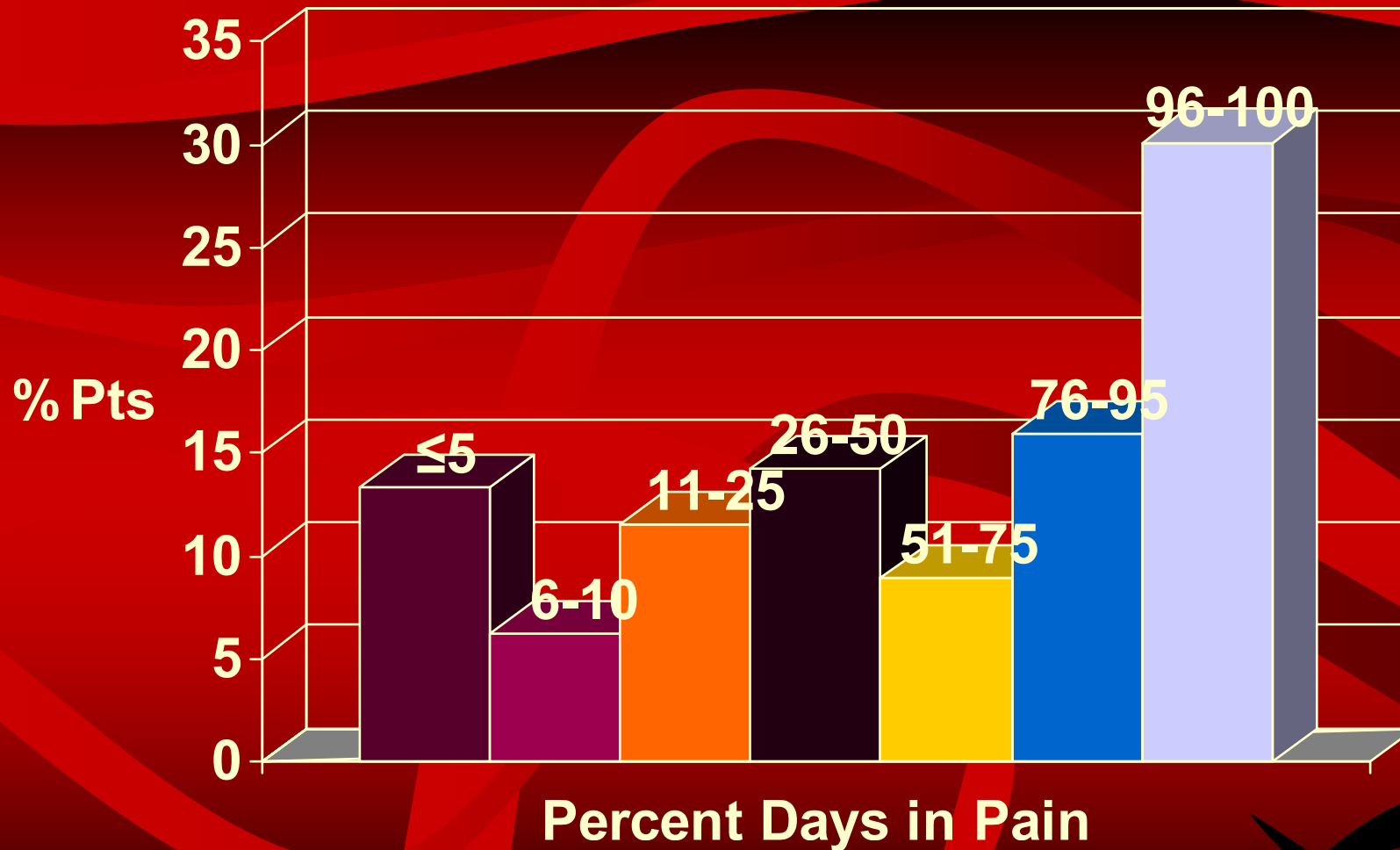
- Medical Outcomes Study 36-item Short-Form (MOS SF-36) Survey
 - 8 subscales measured on a 0-100 scale
 - Physical Function (PF)
 - Role Physical (RP)
 - Role Emotional (RE) Function
 - Bodily Pain (BP)
 - Vitality (VT)
 - Social Function (SF)
 - Mental Health (MH)
 - General Health (GH)



PiSCES: Number of Diaries Submitted

- 29,839 submitted diaries
- 141 pts. (62%) submitted >70% of diaries
- Pain on 16,586 diaries (55.6%)
- Crisis on 4,429 diaries (14.8%)

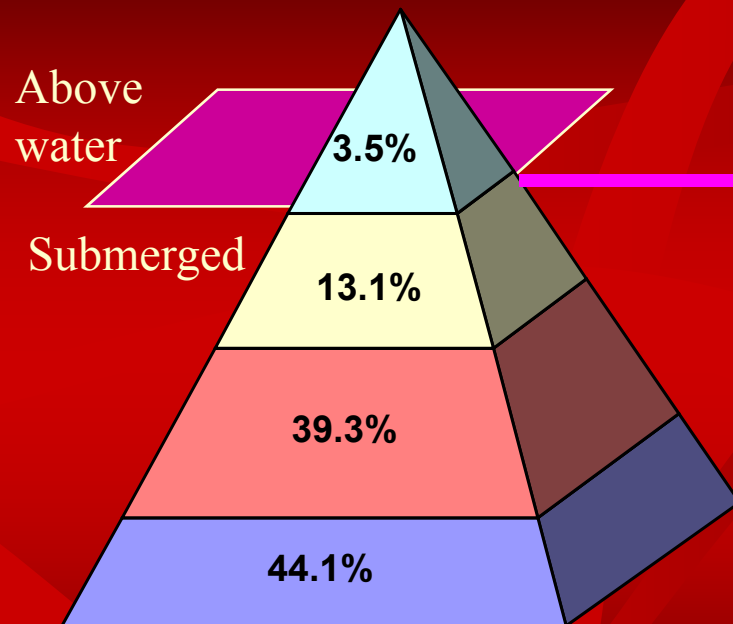
Pain Frequency: Histogram



- **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



Intensity	Mean	Std Dev
Utilization	6.5	2.3
Crisis w/o utilization	5.5	2.1
Pain w/o crisis, util.	4.2	2
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

Adapted from Smith WR, et. al. Ann Intern Med 2008 Jan 15, 148(2):94-101



Summary of Findings: Pain, Crises, And Utilization In Sickle Cell Disease

- 55% of patients had pain on more than half of their diary days
- 30% had pain essentially daily
- 4,429 crisis days (14.8%)
- In contrast, patients reported only 1,057 utilization days (3.5%)



Summary of Findings: (cont'd)

- Pain score correlated with proportion of pain days
 - (not shown, w/opioid utilization days and utilization days)
- Pain higher on utilization days, both on crisis and non-crisis pain days



Summary of Findings: (cont'd)

- Most crisis days, episodes not associated with utilization
 - Utilization days coincided with crisis days but not beyond chance
 - Utilization episodes occurred within or overlapped only 21% of crisis episodes
 - Crisis episodes occurred within or overlapped only 58% of utilization episodes.
- Results did not vary with % of diary completion or the length of time in study.

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%***

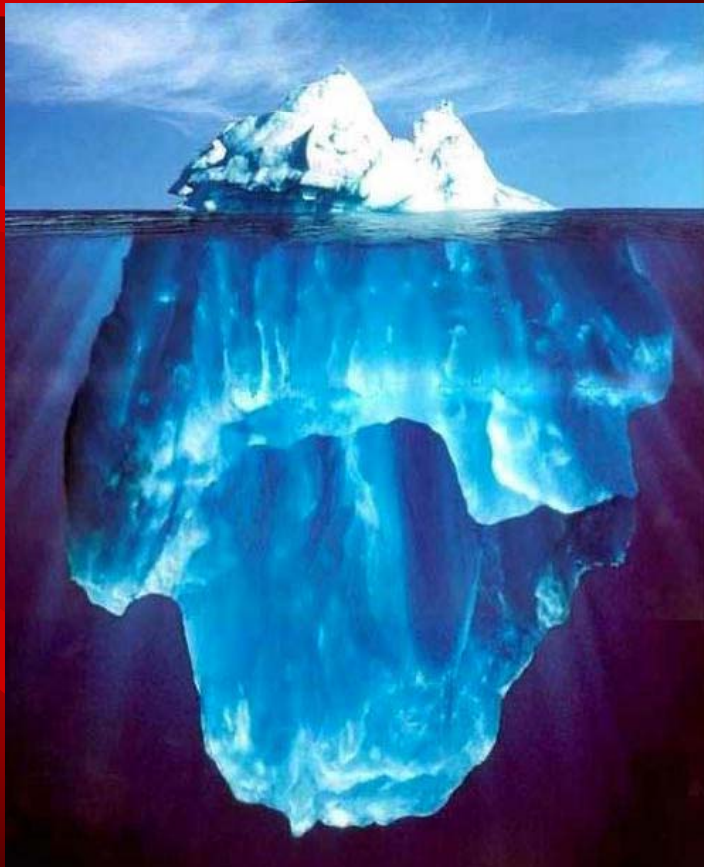


Conclusions

- Pain in sickle cell disease is the rule rather than the exception.
- (Severe) sickle cell pain occurs on a much higher proportion of days than previously reported
 - Much of sickle cell pain is not called a “crisis” by patients.
 - Utilization is the exception rather than the rule for response to pain in sickle cell disease.



Conclusions



- The largely “submerged” iceberg of pain in SCD is not seen by most caregivers, but is managed outside medical facilities.
 - Most sickle cell pain, though severe, is not severe enough to be called “crisis” pain
 - Most crises are not associated with utilization

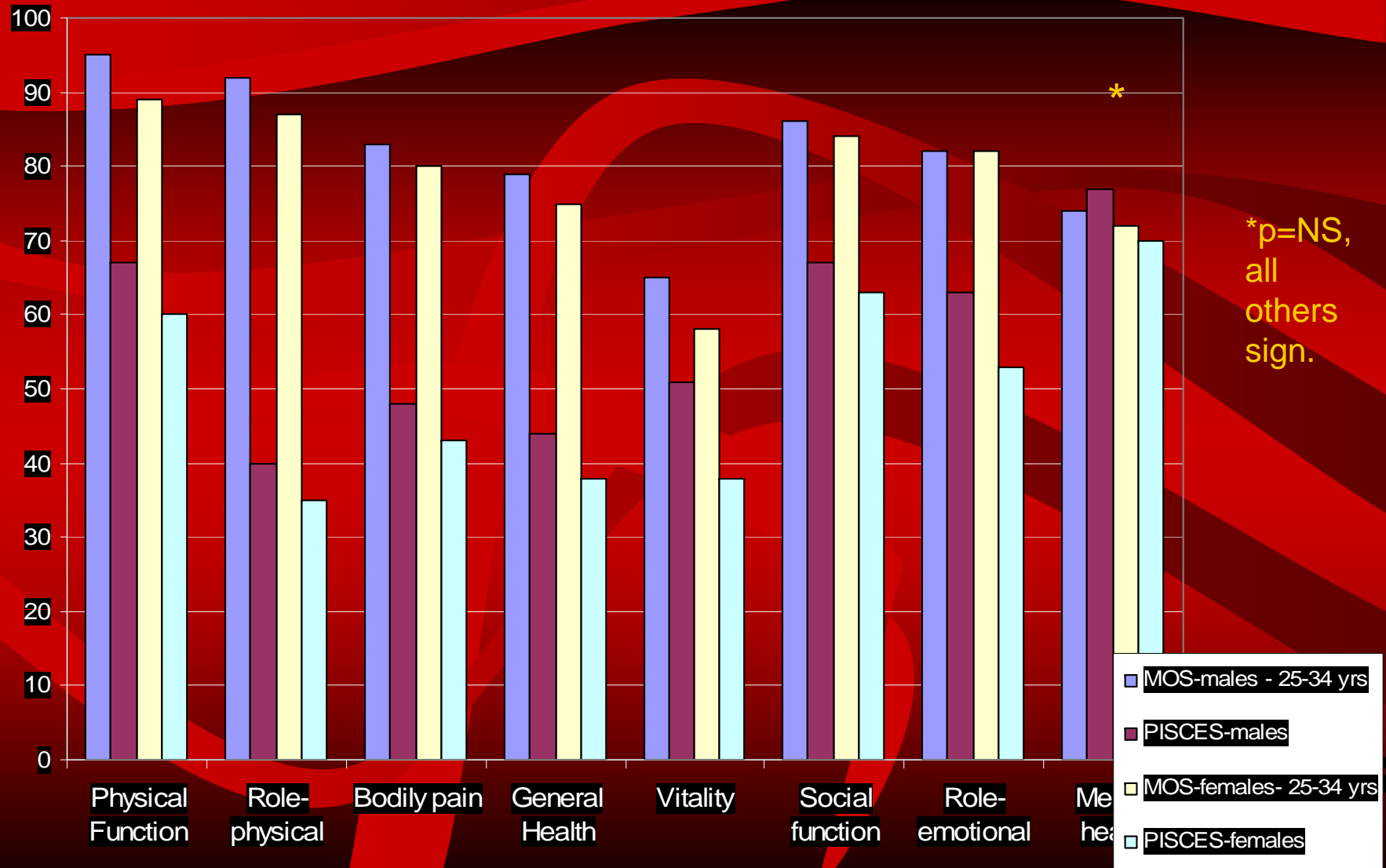


Implications: Treatment

- Pain in sickle cell disease is vastly under-recognized & undertreated, probably because physicians aren't seeing patients on most pain days



SF-36: PiSCES vs. National Norms



SF-36: PiSCES vs. Dialysis

