

# Severity Classification for Sickle Cell Disease: A RAND/UCLA Modified Delphi Panel

Nirmish Shah<sup>1</sup>, David Beenhouwer<sup>2</sup>, Michael S Broder<sup>2</sup>, Lanetta Bronte-Hall<sup>3</sup>,  
Laura M De Castro<sup>4</sup>, Sarah N Gibbs<sup>2</sup>, Victor R Gordeuk<sup>5</sup>, Julie Kanter<sup>6</sup>, Elizabeth S  
Klings<sup>7</sup>, Thokozeni Lipato<sup>8</sup>, Deepa G Manwani<sup>9</sup>, Brigid Scullin<sup>10</sup>, Irina Yermilov<sup>2</sup>,  
Wally R Smith<sup>8</sup>

<sup>1</sup>Duke University; <sup>2</sup>Partnership for Health Analytic Research (PHAR), LLC; <sup>3</sup>Foundation for Sickle Cell Disease Research; <sup>4</sup>University of Pittsburgh Medical Center; <sup>5</sup>University of Illinois at Chicago; <sup>6</sup>University of Alabama at Birmingham; <sup>7</sup>Boston University School of Medicine; <sup>8</sup>Virginia Commonwealth University; <sup>9</sup>Albert Einstein College of Medicine; <sup>10</sup>University of North Carolina

# Background

- Researchers have developed models to predict complications and mortality in sickle cell disease (SCD):
  - Cooperative Study of Sickle Cell Disease (Miller et al. NEJM 2000)
  - Sickle Cell Disease Assessment Instrument (Day. Pediatr Nurs 2004)
  - Network analysis model (Sebastiani et al. Blood 2007)
  - Pediatric SCD severity index (van den Tweel et al. Am J Hematol 2010)
- These models have a large number of complex variables, making them less useful in a clinical setting.
- There is currently no accepted classification system of overall SCD severity.

# Objective

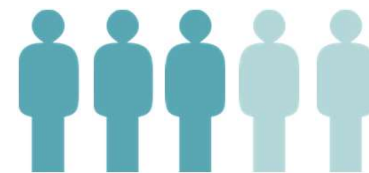
- **Our goal was to develop a severity classification system for SCD** that in the future could be both implemented in a clinical setting and tested as a clinical outcome predictor.
- The RAND/UCLA modified Delphi panel method is a valid, reliable, and reproducible method that can be used to generate consensus.

# Method

## Used a RAND/UCLA modified Delphi panel method

- Convened 10 expert clinicians from various backgrounds.
- Average professional experience: 20 years.
- Provided experts with a review of evidence primarily drawn from the 2014 National Heart, Lung, and Blood Institute Expert Panel Report.

5 hematologists/  
oncologists



3 internists



1 psychiatrist/public  
health practitioner



1 pulmonologist



2 pediatricians



# Variables included in patient scenarios

**Age (in years):** <8, 8-15, 16-24, 25-40, >40

**Hemoglobin genotype:**  
HbSS/HbS $\beta^0$ , HbSC/HbS $\beta^+$

**End organ damage:** None, mild/moderate, severe

**Chronic pain:** Present, absent

**Number of unscheduled acute care visits per year due to VOCs:** 0-1, 2-4,  $\geq 5$

**180 patient scenarios**

VOCs=vaso-occlusive crises

# Rated each scenario on multiple axes



**How high is this patient's risk of any additional serious complications or death in the next 10 years (5 years for patients  $\geq 16$  years old)?**

Low risk for this patient's age

Standard/typical risk for this patient's age

Significant/high risk for this patient's age

**How much is this patient's quality of life impacted by their disease?**

Minimal to no impact (the best quality of life you can expect in a patient this age)

Medium impact

Devastating impact (as severe as you can imagine in a patient this age)

**How would you rate this patient's overall level of disease severity?**

Mild

Moderate

Severe

## Convened in person to discuss ratings

- Ratings were completed independently before a full-day in-person meeting.
- Areas of disagreement were discussed at the meeting.
- Ratings were completed a second time at the conclusion of the meeting.

**Disagreement:  $\geq 2$  ratings outside the median category**

**Median 1-<4 without disagreement**

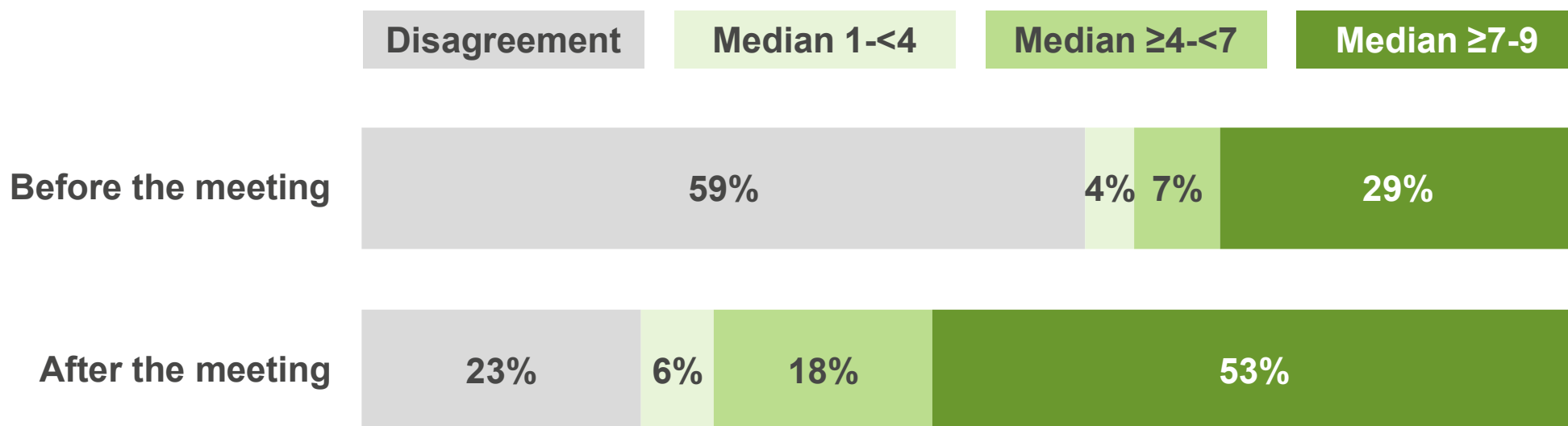
**Median  $\geq 4$ -<7 without disagreement**

**Median  $\geq 7$ -9 without disagreement**



# Results

# Overall disease severity ratings



Percent of scenarios in each rating category for overall disease severity

# Class I (least severe)

Patient characteristics			<8 years	8-15 years	16-24 years	25-40 years	>40 years
no end organ damage	no chronic pain	0-1 2-4					
	chronic pain	0-1 2-4 ≥5					
mild or moderate end organ damage	no chronic pain	0-1 2-4					
	chronic pain	0-1 2-4					
		≥5					
severe damage to bone or retina	no chronic pain	0-1 2-4					
	chronic pain	0-1 2-4					
		≥5					
severe damage to heart, lung, kidney, or brain	no chronic pain	0-1 2-4					
	chronic pain	0-1 2-4					
		≥5					

Patients <8 or >40 years old with no end organ damage, no chronic pain, and <2 unscheduled acute care visits

Patients 8-40 years old with no end organ damage, no chronic pain, and ≤4 unscheduled acute care visits

# Class III (most severe)

Patient characteristics			<8 years	8-15 years	16-24 years	25-40 years	>40 years
no end organ damage	no chronic pain	0-1					
		2-4					
	chronic pain	0-1					
		2-4	unscheduled acute care visits due to VOCs in the last year				
		≥5					
mild or moderate end organ damage	no chronic pain	0-1					
		2-4					
	chronic pain	0-1					
		2-4					
		≥5					
severe damage to bone or retina	no chronic pain	0-1					
		2-4					
	chronic pain	0-1					
		2-4	unscheduled acute care visits due to VOCs in the last year				
		≥5					
severe damage to heart, lung, kidney, or brain	no chronic pain	0-1					
		2-4					
	chronic pain	0-1					
		2-4					
		≥5					

Patients any age with ≥5 unscheduled acute care visits

Patients any age with severe damage to bone, retina, heart, lung, kidney, or brain

# Class II

Patient characteristics			<8 years	8-15 years	16-24 years	25-40 years	>40 years
no end organ damage	no chronic pain	0-1					
		2-4					
	chronic pain	0-1					
		2-4					
		≥5					
mild or moderate end organ damage	no chronic pain	0-1					
		2-4					
	chronic pain	0-1					
		2-4					
		≥5					
severe damage to bone or retina	no chronic pain	0-1					
		2-4					
	chronic pain	0-1					
		2-4					
		≥5					
severe damage to heart, lung, kidney, or brain	no chronic pain	0-1					
		2-4					
	chronic pain	0-1					
		2-4					
		≥5					

unscheduled acute care visits due to VOCs in the last year

unscheduled acute care visits due to VOCs in the last year

All other patients

Patients ≥25 years old with severe damage to bone or retina, no chronic pain, and 0-1 unscheduled acute care visits

# Limitations

- Patient scenarios were simplified patient histories that did not use patient-reported outcomes, lab data, or account for severity of acute visits.
- We developed a single system applicable to both adults and children, which may make it less specific for either group.
- The panel consisted of a relatively small number of clinicians who brought their individual clinical judgement, expertise, and experience to the process.
- The relationship between our system and outcomes has yet to be demonstrated.

# Conclusions

- A valid, reliable, and reproducible method was used to develop a classification system for SCD severity consistent with existing literature.
- Advantages of the classification system:
  - Consolidates patient characteristics into homogenous groups of patients with respect to disease state.
  - Uses few patient characteristics easily obtained during a clinical visit.
  - Its simplicity may improve adoption and hence utility.
- Studies to validate this system and further refine the tool using patient reported and clinical outcomes are planned.