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

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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.

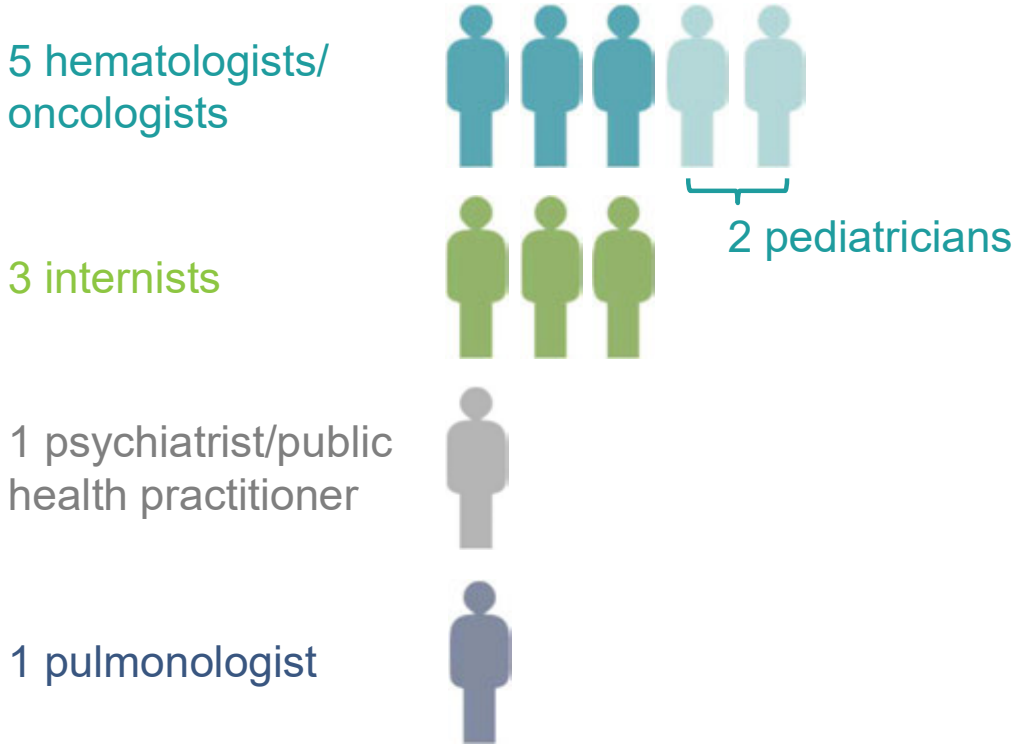
Objective

- **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.

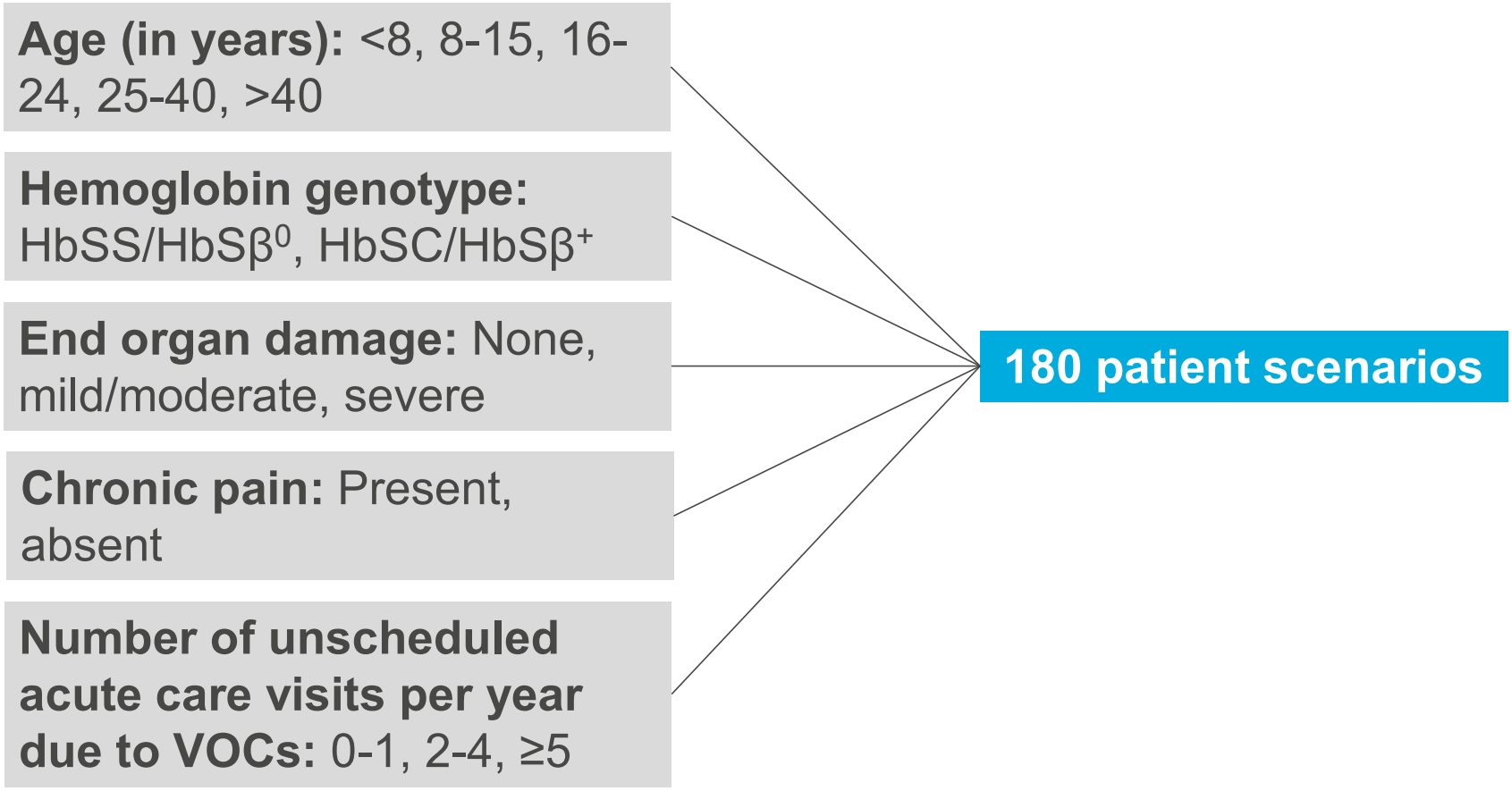
Method

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.



Variables included in 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 ≥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

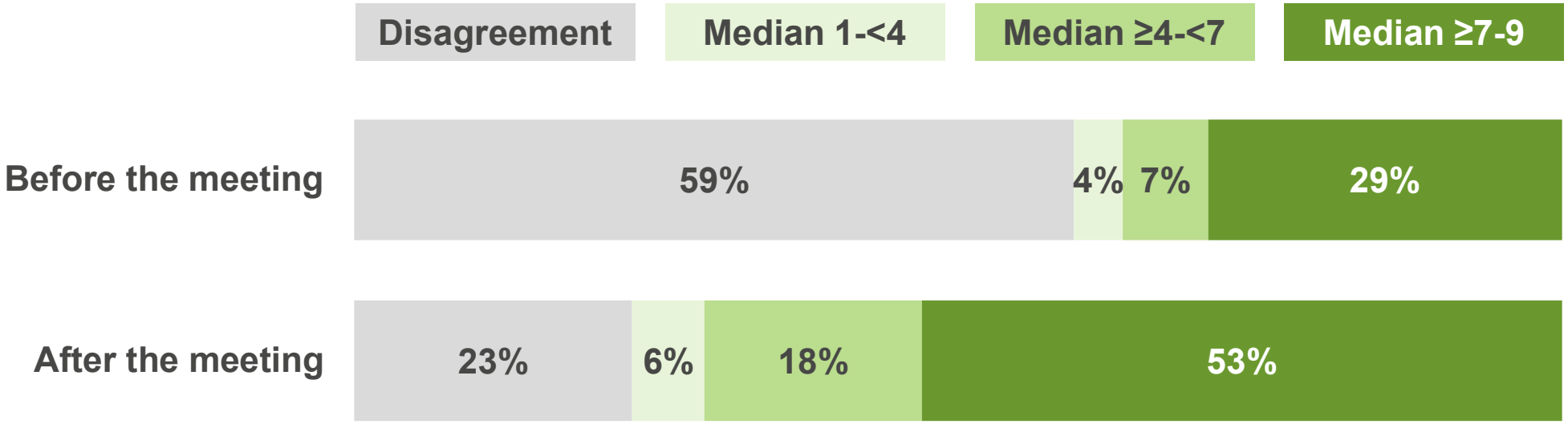
Convened in person to discuss ratings

- 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: ≥2 ratings outside the median category
Median 1-<4 without disagreement
Median ≥4-<7 without disagreement
Median ≥7-9 without disagreement

Results

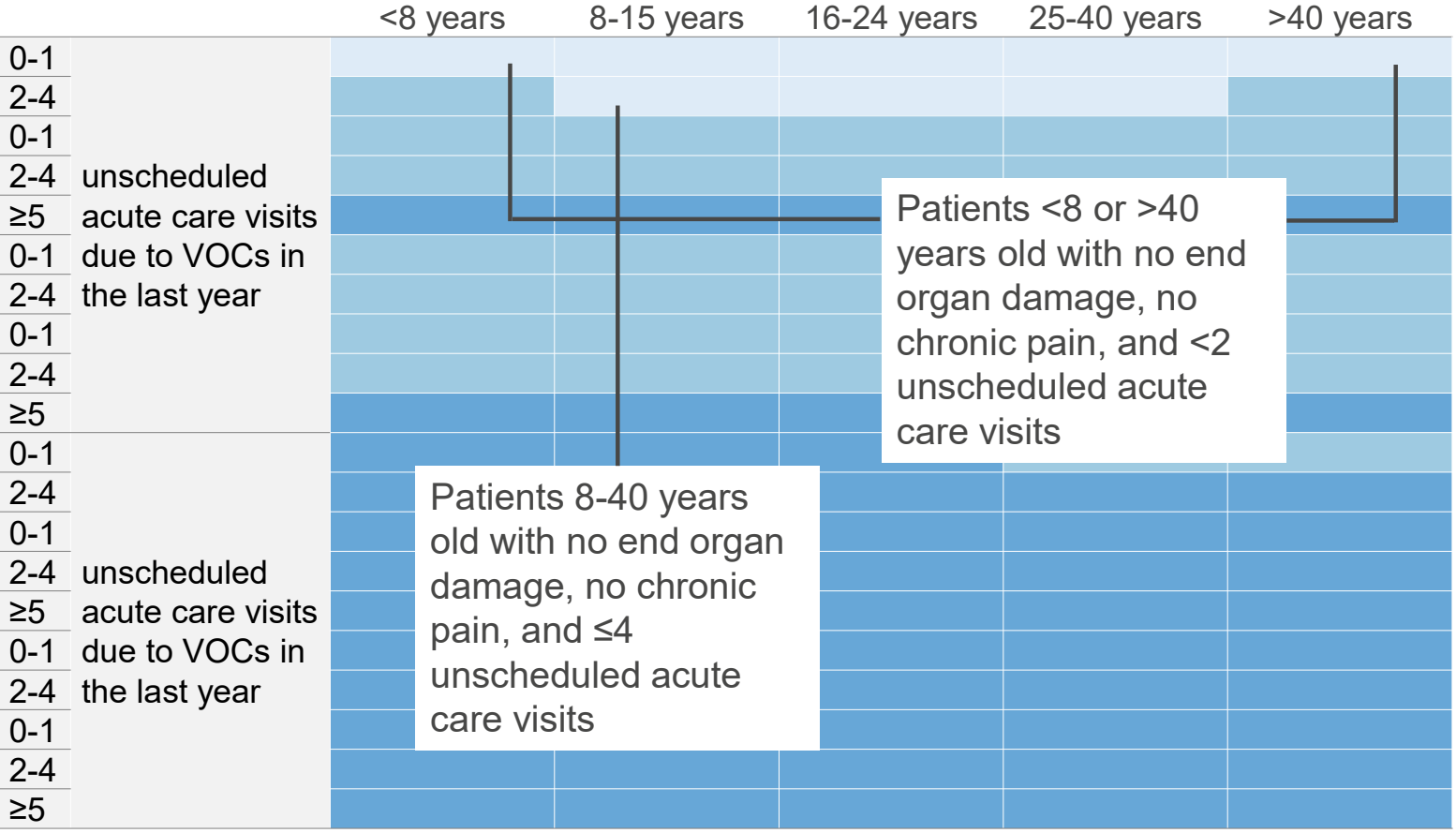
Overall disease severity ratings



Percent of scenarios in each rating category for overall disease severity

Class I (least severe)

Patient characteristics			
no end organ damage	no chronic pain	0-1	unscheduled acute care visits due to VOCs in the last year
		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	unscheduled acute care visits due to VOCs in the last year
		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	



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	unscheduled acute care visits due to VOCs in the last year					
		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	unscheduled acute care visits due to VOCs in the last year					
		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 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	unscheduled acute care visits due to VOCs in the last year					
		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	unscheduled acute care visits due to VOCs in the last year					
		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						

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.