



Normal capillary



Sickle Cell Anemia

Changes in Health-Related Quality of Life after Bone Marrow Transplantation for Severe Sickle Cell Disease

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HARVARD
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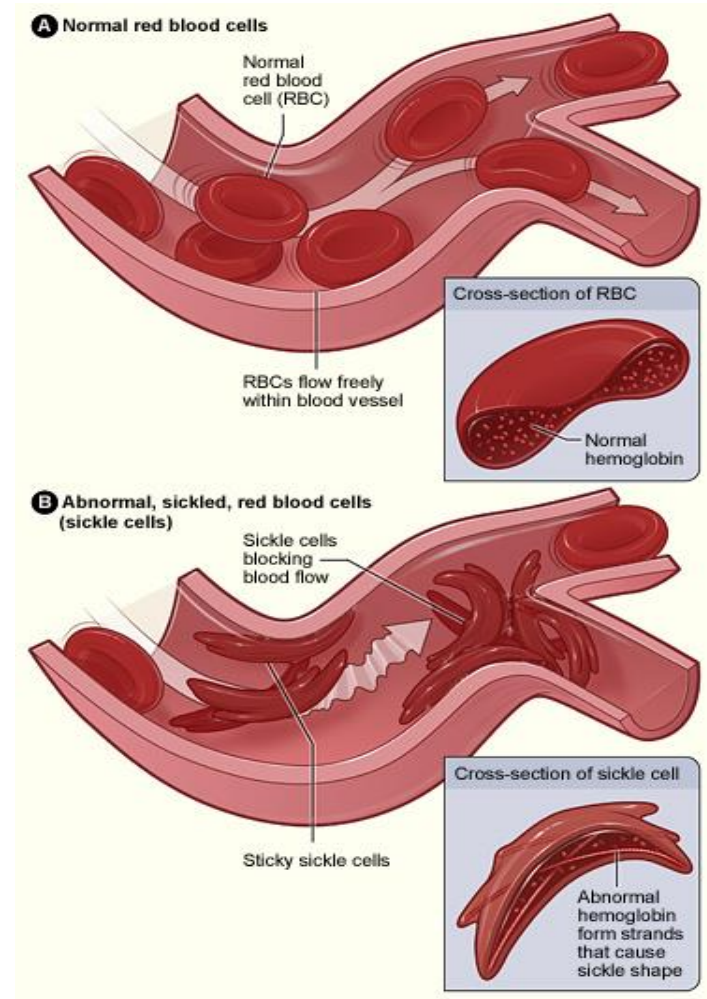
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Overview

- ❖ What is sickle cell disease (SCD)?
- ❖ Clinical trial of bone marrow transplantation to cure SCD
- ❖ Analysis of Health-Related Quality of Life (HRQoL)
 - Methods
 - Results
 - Limitations and implications

What does this disease do?

- Vaso-occlusive crises
- Stroke
- Pulmonary hypertension
- Acute chest pain



What causes SCD?

First a step back...

4

Everyone has DNA.

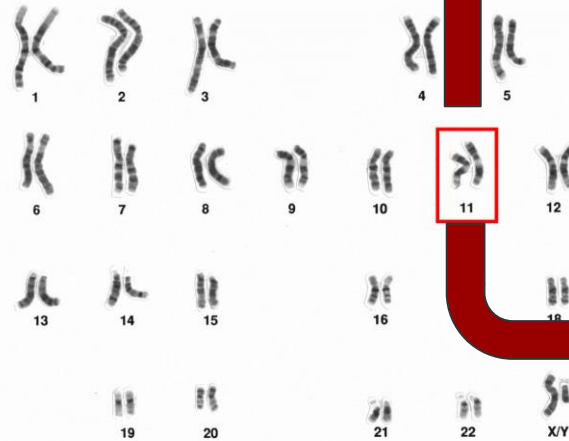
- 23 pairs of chromosomes
- 24,000 genes
- **3,200,000,000** nucleotides



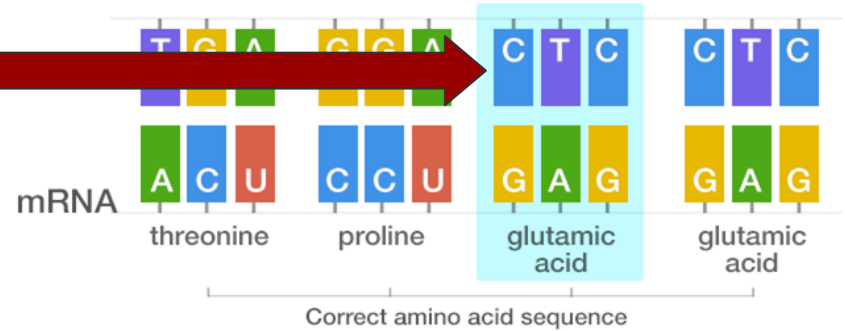
Now back to the question...

What is SCD caused by?

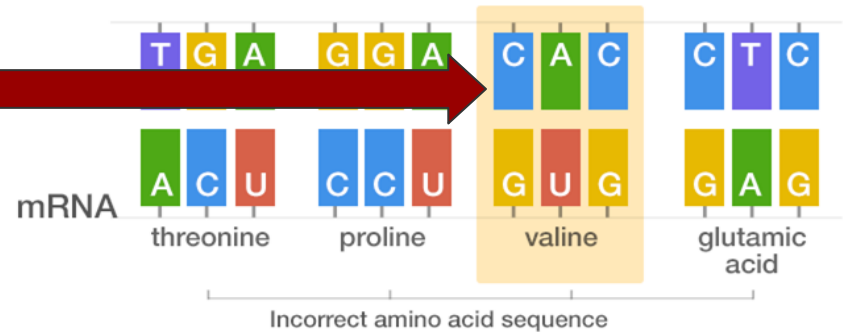
A Single Nucleotide Polymorphism (SNP) in a specific location.



Normal DNA sequence (HbA)

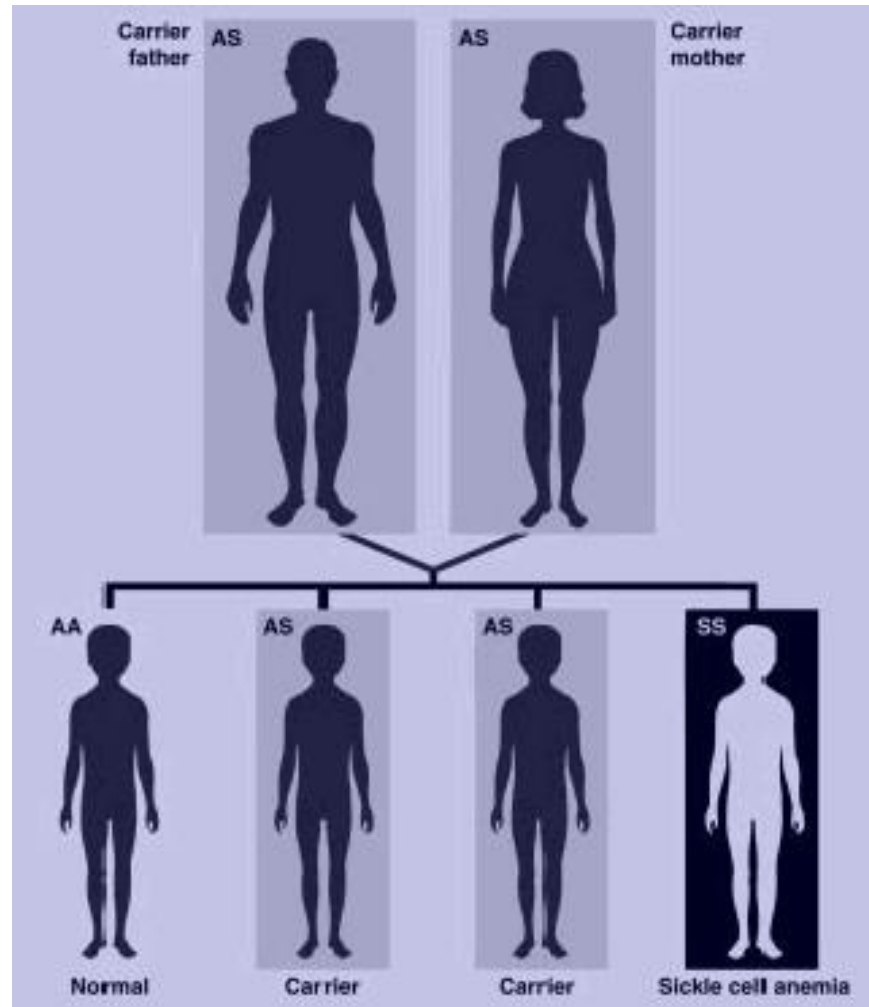


Mutated DNA sequence (HbS)



Inheritance

- Recessive hereditary disease.
- 1 in every 13 African-Americans are carriers of SCD
- Evolutionary advantage
- Approximately 100,000 Americans



The Study

- Pilot study of 22 patients with severe SCD
 - Eligibility criteria for severity reviewed prior to enrollment
 - Age: 15-40 years
- Treatment
 - Chemotherapy
 - Bone marrow transplantation
- Endpoints:
 - Survival at 1 year without redevelopment of disease
 - Our focus: change in quality of life
- Assessments
 - HRQoL using PROMIS-57 survey
 - Baseline, 6 months, 1 year

**Eligibility
Criteria**

Red Blood Cell
Transfusions
(n = 5)

OR

Strokes/Neurological
Events
(n = 2)

OR

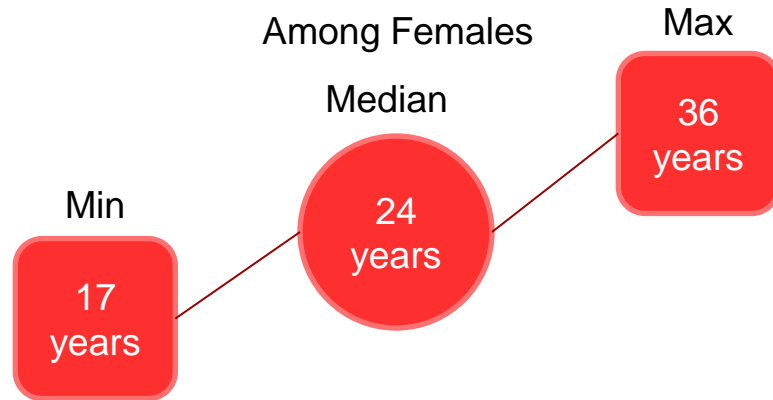
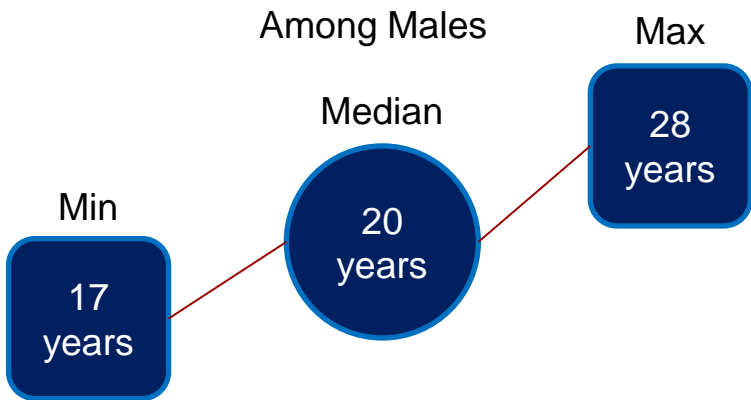
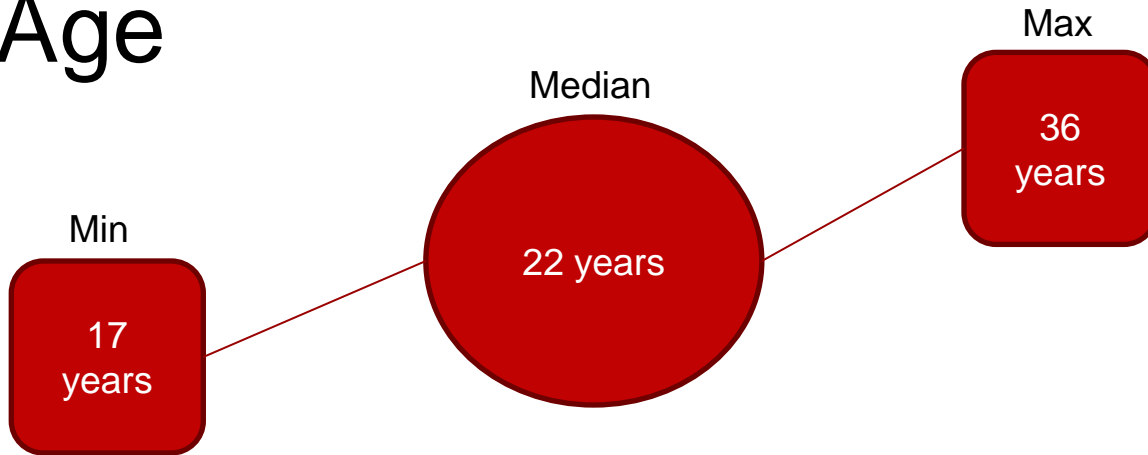
Tricuspid Regurgitant Jet
Velocity (TRJV)
(n = 5)

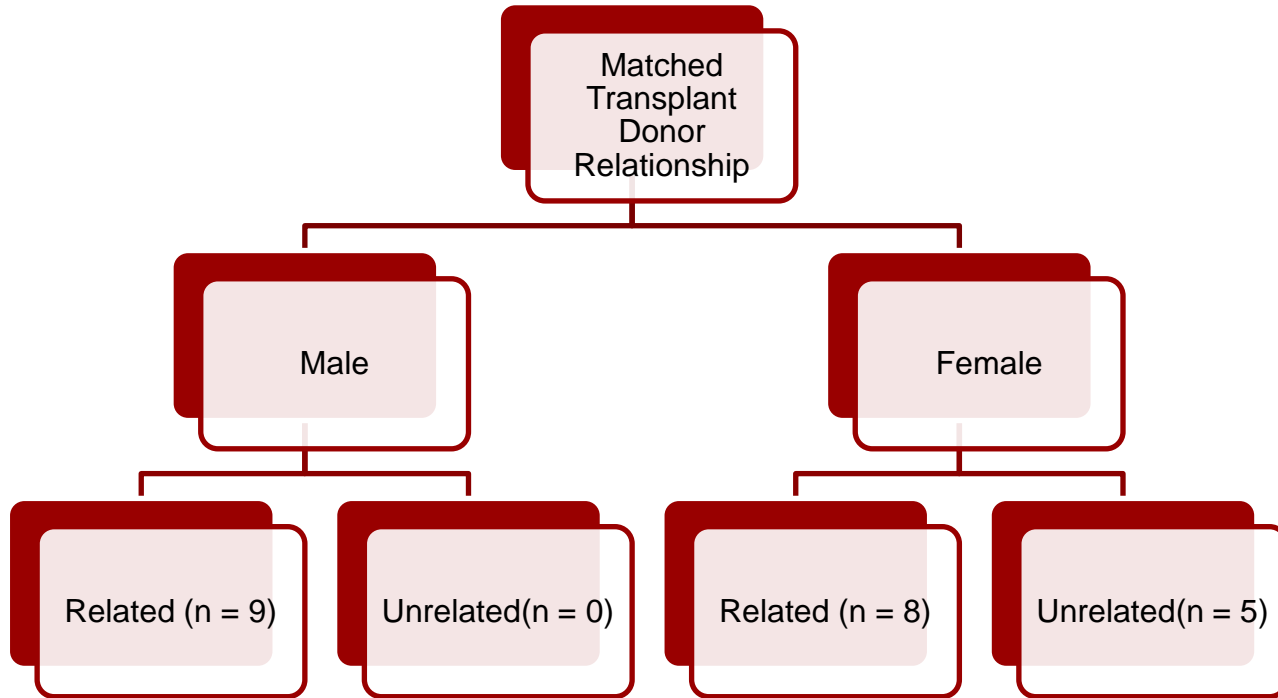
OR

Acute Chest Syndrome
(ACS) or Pain Crises
(n = 18)

OR

Age





Measuring HRQoL

- PROMIS - 57
(Patient Reported Outcomes Measurement Information System)
 - 8 items each scored 1-5
 - Anxiety
 - Depression
 - Fatigue
 - Pain interference
 - Physical function
 - Satisfaction with participation in social roles
 - Sleep disturbance
 - 1 item scored 0-10
 - Pain intensity

PROMIS-57 Profile v2.0

Please respond to each question or statement by marking one box per row.

	<u>Physical Function</u>	Without any difficulty	With a little difficulty	With some difficulty	With much difficulty	Unable to do
1	Are you able to do chores such as vacuuming or yard work?.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2	Are you able to go up and down stairs at a normal pace?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	Are you able to go for a walk of at least 15 minutes?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4	Are you able to run errands and shop?.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>



Question of Interest

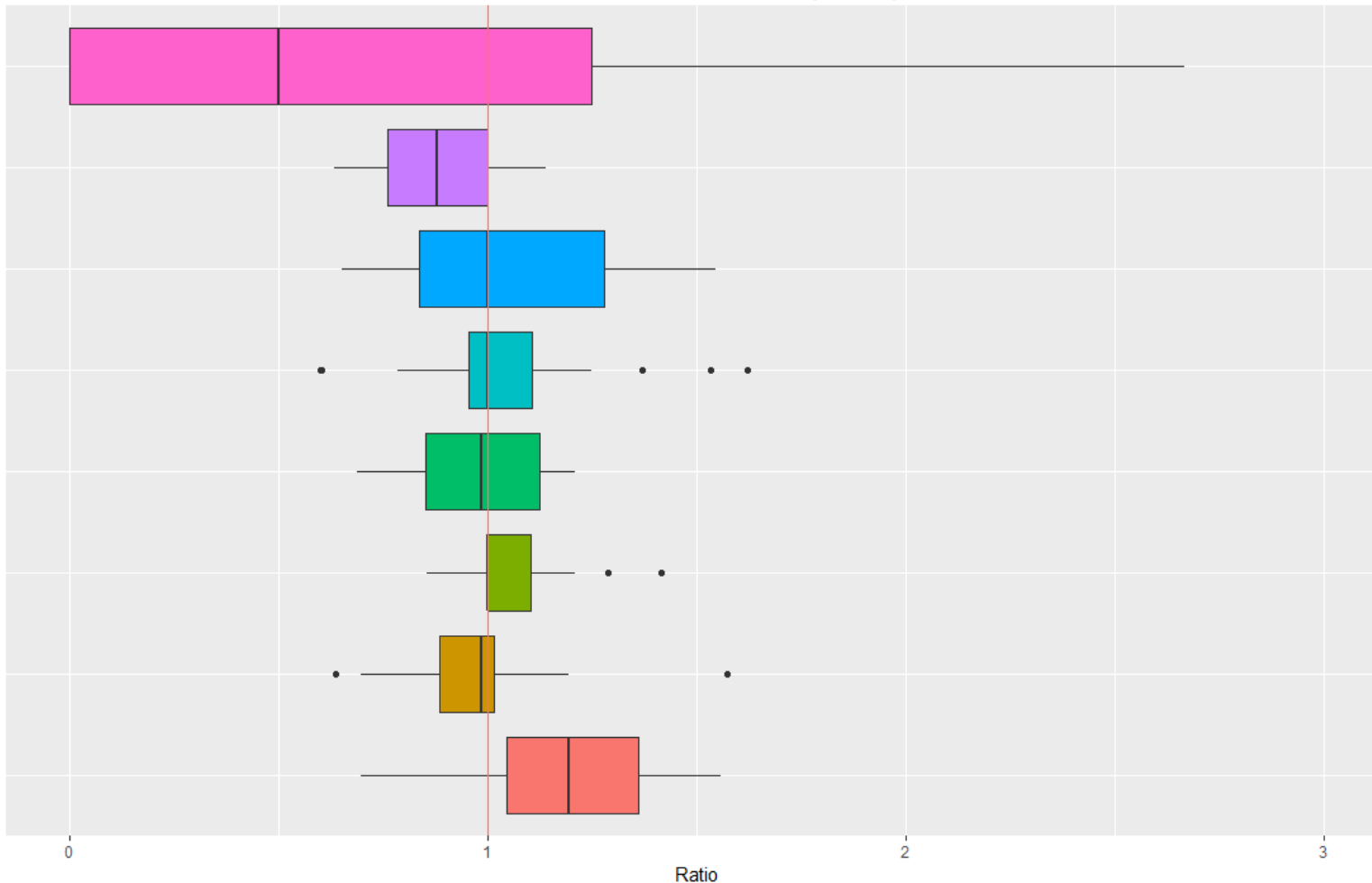
How is quality of life impacted by bone marrow transplantation in patients with severe sickle cell disease?

Methods

- ❖ One sample one-sided T-test
 - Ratios comparing 12-month to Baseline
 - Differences of Baseline from 12-month
 - ACS or Pain Crises eligibility
- ❖ Two sample Wilcoxon Rank Sum Test with continuity correction for tied ranks
 - Comparing gender
 - Comparing age categories

Table 2. Summary Statistics by Time for PROMIS-57 HRQoL Domains				
		Month		
	All Pts N=16	0	6	12
Physical Function				
Mean (SD)	46.8 (±10.7)	43.7 (±8.3)	46.2 (±11.7)	50.5 (±11.3)
Anxiety				
Mean (SD)	48.3 (±10.3)	50.1 (±10.1)	46.5 (±10.7)	48.1 (±10.5)
Depression				
Mean (SD)	45.9 (±8.9)	44.2 (±6.6)	46.6 (±9.7)	46.9 (±10.3)
Fatigue				
Mean (SD)	47.7 (±12.8)	47.3 (±10.6)	49.9 (±14.9)	46.0 (±13.4)
Sleep disturbance				
Mean (SD)	46.9 (±10.7)	46.2 (±10.8)	47.7 (±12.2)	46.9 (±9.6)
Satisfaction with Participation in Social Roles				
Mean (SD)	50.0 (±12.5)	51.8 (±12.0)	45.7 (±13.0)	52.4 (±12.3)
Pain Interference				
Mean (SD)	52.9 (±11.4)	57.6 (±9.9)	50.8 (±11.8)	50.1 (±11.6)
Pain Intensity				
Mean (SD)	2.5 (±3.0)	2.9 (±3.3)	2.1 (±2.7)	2.4 (±3.0)



Ratio of 12-months to Baseline (N = 16)



- T-Score Ratios
- Raw Pain Intensity Ratios
 - T-Score Pain Interference Ratios
 - T-Score Sleep Ratios
 - T-Score Social Ratios
 - T-Score Fatigue Ratios
 - T-Score Depression Ratios
 - T-Score Anxiety Ratios
 - T-Score Physical Ratios

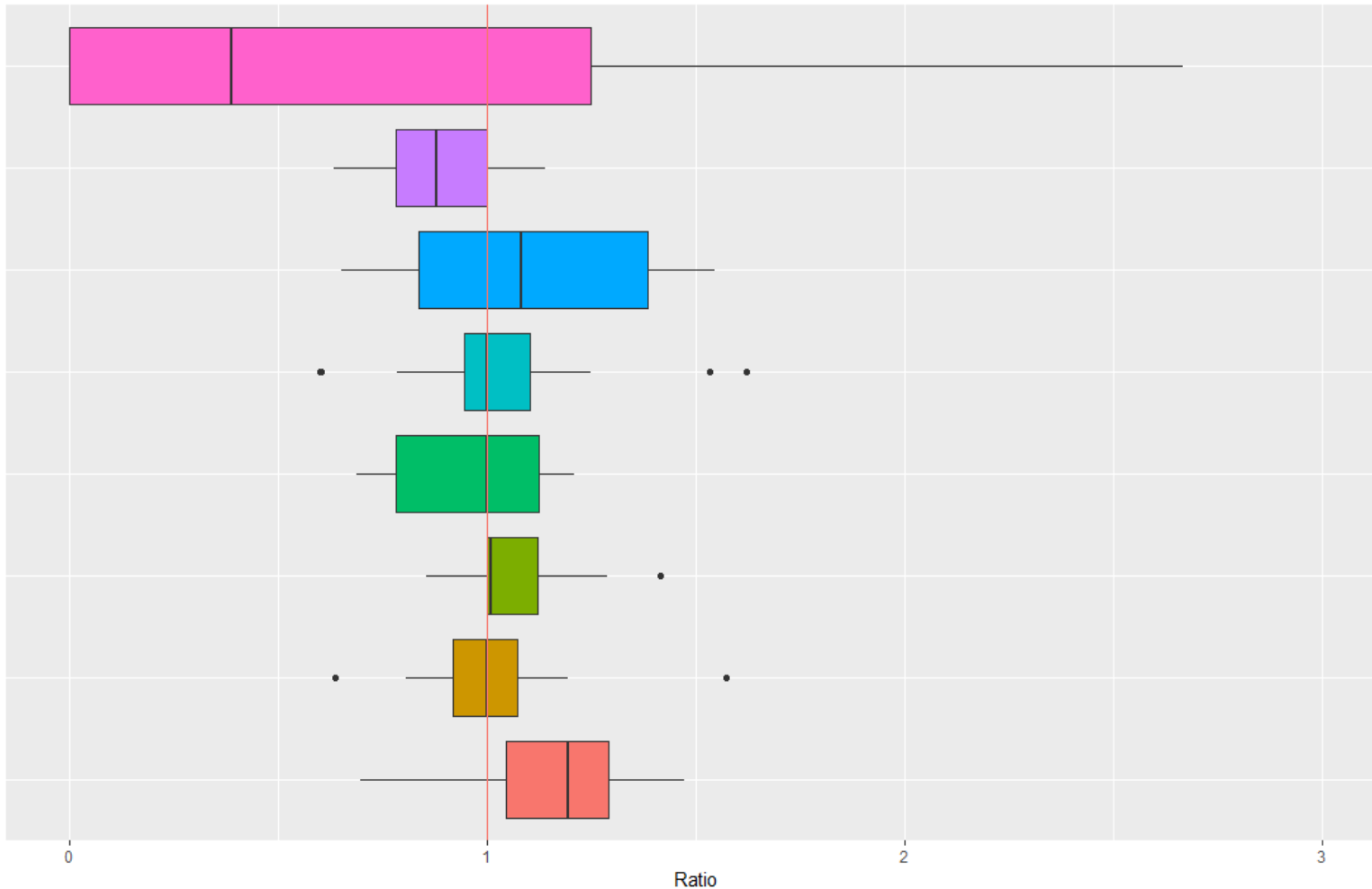
* 2 outliers not shown at value of 10 for raw pain intensity

Table 3. Evaluating the Impact of Bone Marrow Transplantation on Health-Related Quality of Life Using the Ratio of 12-month to Baseline

	Mean (± SD) (N = 16)	Range	Median	P-value
T-Score Physical	1.173 (± 0.069)	(28.3 - 59.2)	59.2 	0.018
T-Score Anxiety	0.977 (± 0.056)	(37.1 - 67.7)	46.85	0.676
T-Score Depression	1.057 (± 0.039)	(38.2 - 67.7)	41.45	0.139
T-Score Fatigue	0.974 (± 0.042)	(33.1 - 77.8)	43.55	0.515
T-Score Social	1.045 (± 0.077)	(26.2 - 65.6)	52.05	0.538
T-Score Sleep	1.056 (± 0.076)	(30.5 - 74.1)	44.6	0.447
T-Score Pain Interference	0.876 (± 0.041)	(40.7 - 77)	45.95 	0.005
Raw Pain Intensity	1.765 (± 0.881)	(0 - 8)	1	0.369

All p-values computed with one-sided t-test, since, by the distribution of ratios, improvement was the possibly significant outcome.


Ratio of 12-months to Baseline with Eligibility Pain or ACS (N = 11)



- T-Score Ratios
- Raw Pain Intensity Ratios
 - T-Score Pain Interference Ratios
 - T-Score Sleep Ratios
 - T-Score Social Ratios
 - T-Score Fatigue Ratios
 - T-Score Depression Ratios
 - T-Score Anxiety Ratios
 - T-Score Physical Ratios

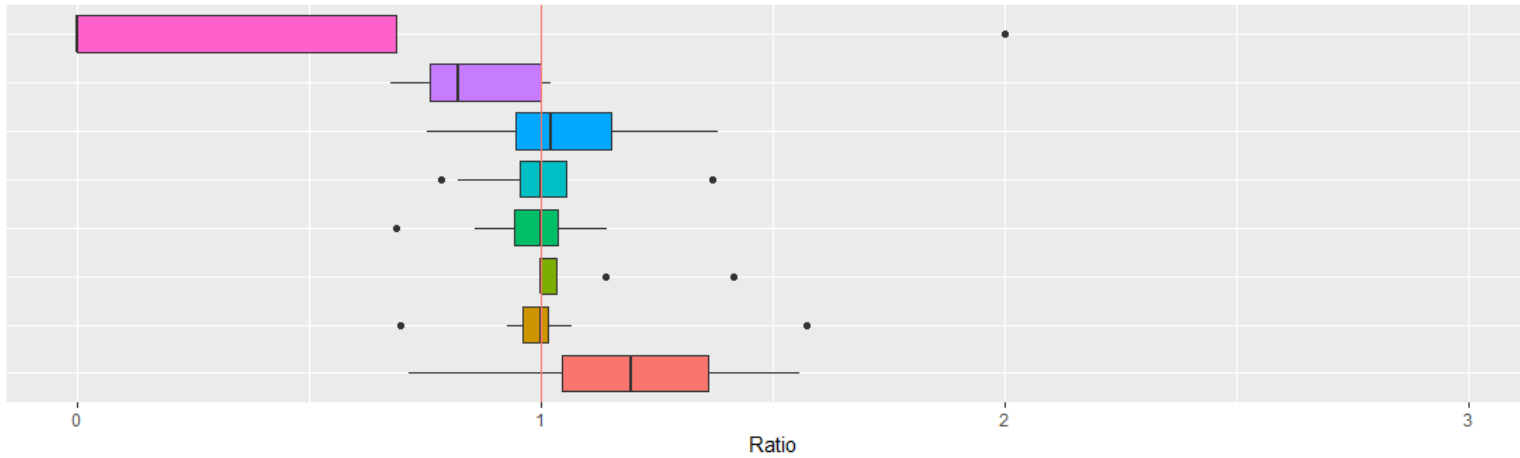
* 1 outlier not shown at value of 10 for raw pain intensity

Table 4. Evaluating the Impact of Bone Marrow Transplantation on Health-Related Quality of Life Using the Ratio of 12-month to Baseline among Patients Eligible under Acute Chest Syndrome or Pain Crisis

	Mean (\pm SD) (N=11)	Range	Median	P-value
T-Score Physical	1.156 (\pm 0.082)	(28.3 - 59.2)	59.2	0.059
T-Score Anxiety	1.017 (\pm 0.079)	(37.1 - 67.7)	47.8	0.814
T-Score Depression	1.084 (\pm 0.054)	(38.2 - 67.7)	49.4	0.113
T-Score Fatigue	0.971 (\pm 0.061)	(33.1 - 77.8)	42.8	0.609
T-Score Social	1.041 (\pm 0.11)	(26.2 - 65.6)	52.5	0.685
T-Score Sleep	1.12 (\pm 0.107)	(30.5 - 74.1)	43.9	0.239
T-Score Pain Interference	0.875 (\pm 0.052)	(40.7 - 77)	51.2	 0.023
Raw Pain Intensity	1.568 (\pm 2.938)	(0 - 8)	2	0.536

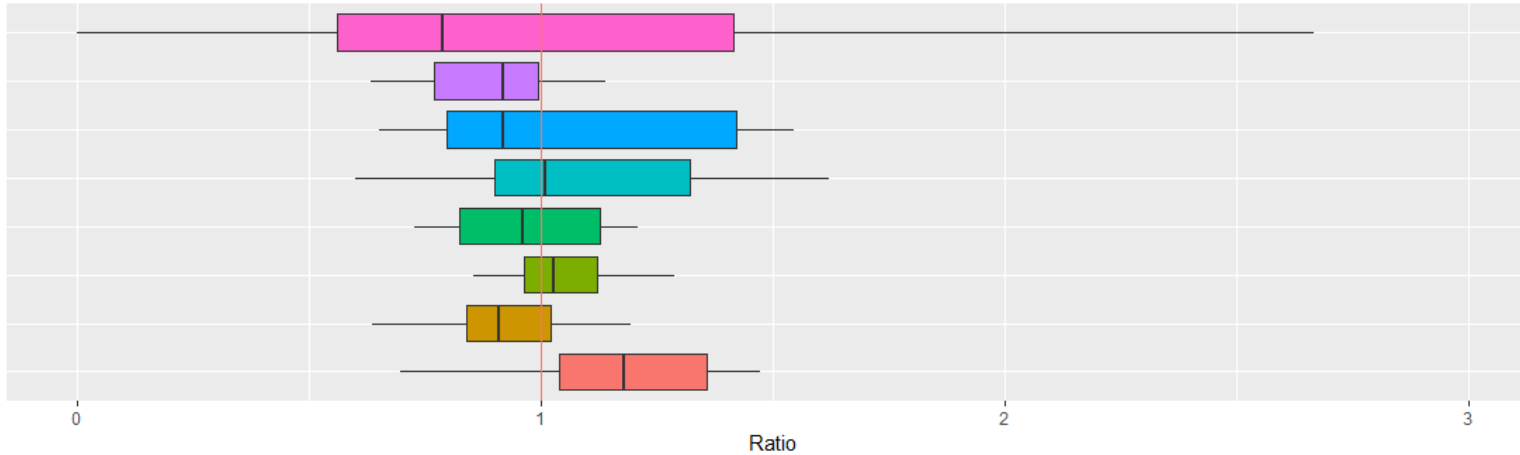
All p-values computed with one-sided t-test, since, by the distribution of ratios, improvement was the possibly significant outcome.

Male Ratios Comparing 12-months to Baseline (N = 8)



- T-Score Ratios
- Raw Pain Intensity Ratios
 - T-Score Pain Interference Ratios
 - T-Score Sleep Ratios
 - T-Score Social Ratios
 - T-Score Fatigue Ratios
 - T-Score Depression Ratios
 - T-Score Anxiety Ratios
 - T-Score Physical Ratios

Female Ratios Comparing 12-Months to Baseline (N = 8)



- T-Score Ratios
- Raw Pain Intensity Ratios
 - T-Score Pain Interference Ratios
 - T-Score Sleep Ratios
 - T-Score Social Ratios
 - T-Score Fatigue Ratios
 - T-Score Depression Ratios
 - T-Score Anxiety Ratios
 - T-Score Physical Ratios

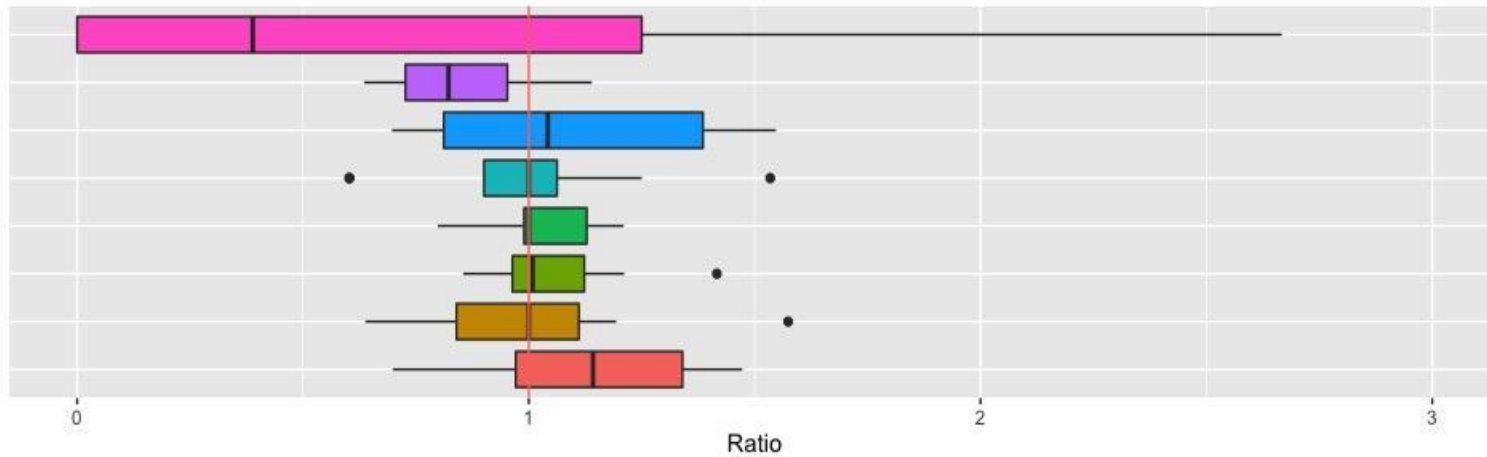
* 1 outlier in both Male and Female Ratios not shown at value of 10 for raw pain intensity

Table 5. Evaluating the Impact of Gender on Health-Related Quality of Life Using the Ratio of 12-months to Baseline

	Gender: Mean(± SD)		P-value	Female: Range	Male: Range	Female: Median	Male: Median
	F n = 8	M n=8					
T-Score Physical	1.163(±0.27)	1.183(±0.26)	0.96	(28.3 - 59.2)	(42.4 - 59.2)	43.5	59.2
T-Score Anxiety	0.925(±0.17)	1.030(±0.24)	0.34	(37.1 - 67.7)	(37.1 - 58.4)	47.8	41.5
T-Score Depression	1.045(±0.15)	1.069(±0.14)	0.78	(38.2 - 67.7)	(38.2 - 54.1)	51.75	38.2
T-Score Fatigue	0.971(±0.17)	0.976(±0.14)	0.79	(41 - 77.8)	(33.1 - 46.9)	50.25	33.1
T-Score Social	1.079(±0.37)	1.011(±0.177)	0.79	(26.2 - 65.6)	(47.9 - 65.6)	49.35	59.05
T-Score Sleep	1.059(±0.36)	1.053(±0.19)	0.83	(40.4 - 74.1)	(30.5 - 52.4)	49.1	42.2
T-Score Pain Interference	0.896(±0.17)	0.856(±0.13)	0.79	(40.7 - 77)	(40.7 - 52.3)	55.8	40.7
Raw Pain Intensity	1.999(±3.33)	1.531(±3.49)	0.23	(0 - 8)	(0 - 2)	4	0

All p-values calculated with two sample Wilcoxon rank sum test with continuity correction for tied ranks

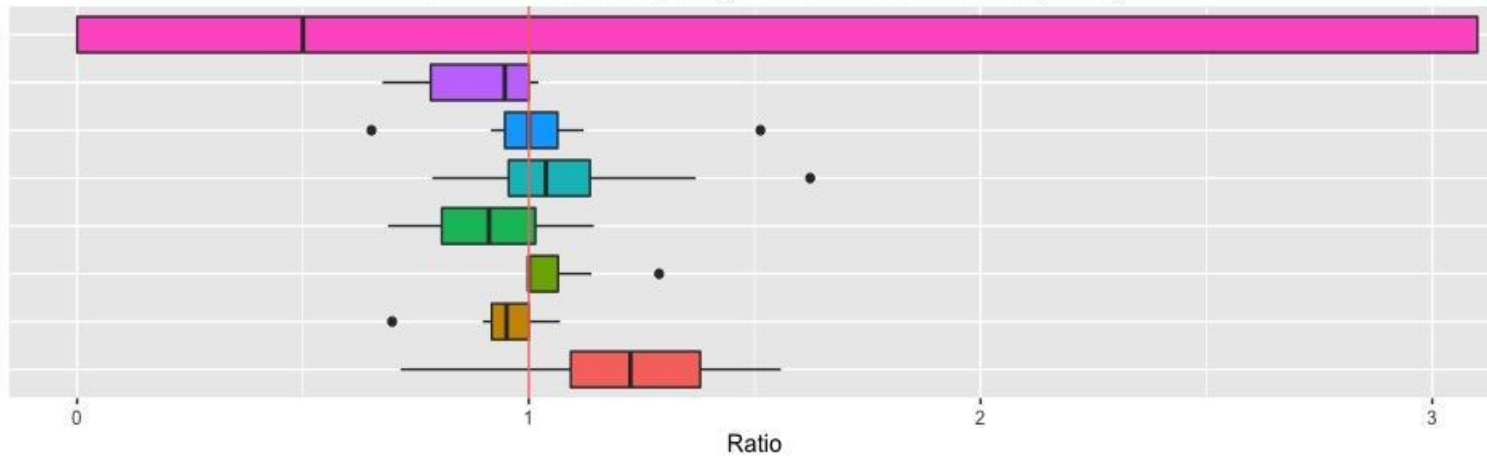
21 and Over Ratios Comparing 12-months to Baseline (N = 8)



T-Score Ratios

- Raw Pain Intensity Ratios
- T-Score Pain Interference Ratios
- T-Score Sleep Ratios
- T-Score Social Ratios
- T-Score Fatigue Ratios
- T-Score Depression Ratios
- T-Score Anxiety Ratios
- T-Score Physical Ratios

Under 21 Ratios Comparing 12-Months to Baseline (N = 8)



T-Score Ratios

- Raw Pain Intensity Ratios
- T-Score Pain Interference Ratios
- T-Score Sleep Ratios
- T-Score Social Ratios
- T-Score Fatigue Ratios
- T-Score Depression Ratios
- T-Score Anxiety Ratios
- T-Score Physical Ratios

* 2 outliers in under 21 not shown at value of 10 for raw pain intensity

Limitations

- PILOT study with small sample and no controls
- Only 15 complete all three timepoints
- Self-selection bias
- 1 patient's mother filled out surveys
- 1 patient's bone marrow graft failed and patient received re-transplantation
- 2 patients deceased

Implication of HRQoL Results

- ❖ Second clinical trial
 - Approximately 200 individuals
 - Controls
- ❖ Promising for those who have no other SCD treatment options
- ❖ Potential to cure thousands of individuals affected by severe SCD and significantly improve their quality of life

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Questions?

