

Quality of Life for Severe Aplastic Anemia

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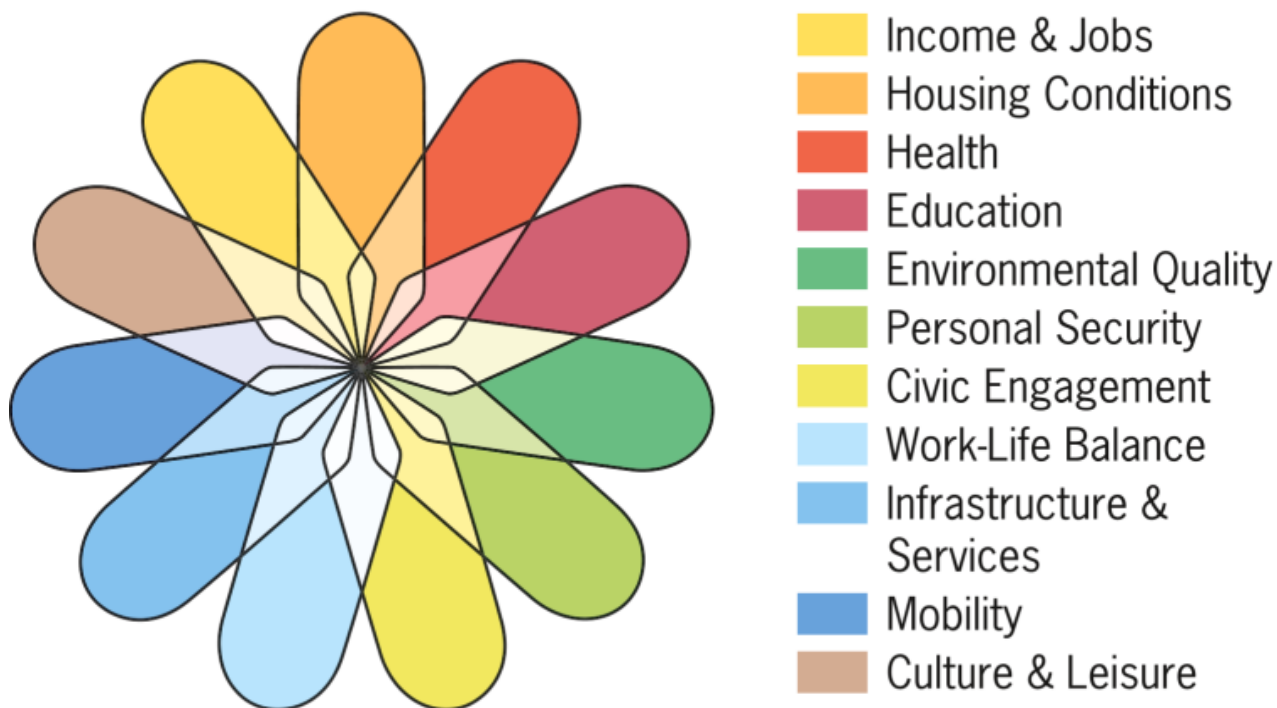
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Quality of Life

According to the [World Health Organization](#), quality of life (QoL) is described as:

“an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.”

Quality of life dimensions



Source: OECD (2014), How's Life in Your Region?: Measuring Regional and Local Well-being for Policy Making, OECD Publishing, Paris;
Design adapted by the FSO

Health Related Quality of Life

- Health related quality of life (HRQoL) is the health aspect of quality of life that focuses on people's level of ability, daily functioning and ability to experience a fulfilling life.
- Examples of influencing factors:
 - Disease
 - Injury
 - Impairment
 - Health perceptions
 - Health care and treatments
 - Policy

Rationale for HRQoL in SAA

- Disease related
 - Fatigue
 - Isolation and fear due to infection risk
 - Anxiety and depression
- Treatment related toxicity
 - Weight gain due to steroid treatment
 - Increased hair growth
 - GI symptoms with eltrombopag
- Caregiver concerns about decision making and outcomes

HRQoL in SAA

- Single institution study
 - Compared 155 patients on immunosuppressive therapy (IST) to 52 patients getting hematopoietic cell transplantation (HCT)
 - Included adult and pediatric patients age 2-74yrs
 - Similar survival, event-free survival, and quality-adjusted time without symptoms and toxicity after 15 years
 - HCT patients had longer periods free from symptoms

Viollier R, et al. Quality-adjusted survival analysis shows differences in outcome after immunosuppression or bone marrow transplantation in aplastic anemia. *Ann Hematol.* 2005;84(1):47-55.

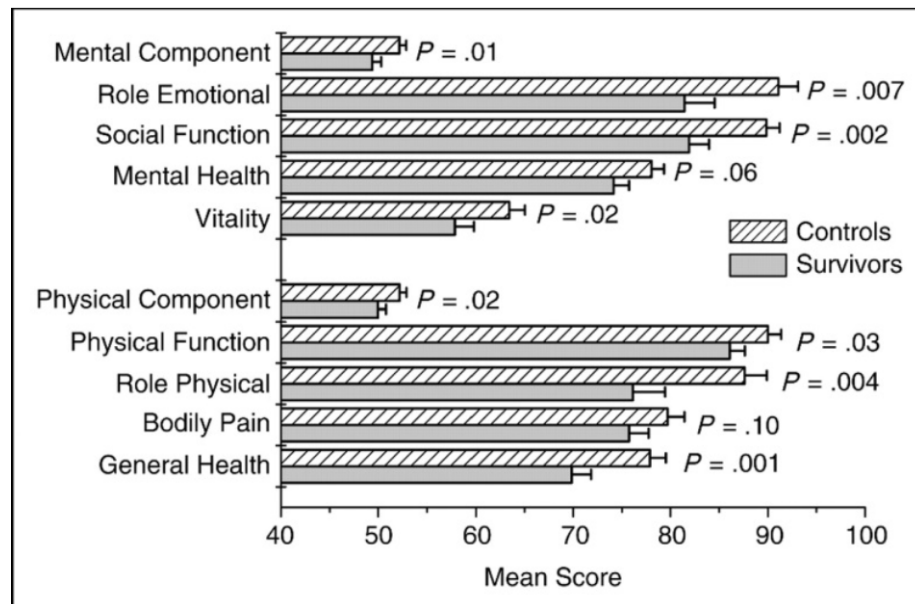
HRQoL in SAA

- Large national study of HCT recipients
 - 152 adult and pediatric patients age 7-55yrs
 - Analyzed the presence of chronic graft versus host disease (GVHD), pulmonary diseases, malignancy, and hepatitis
 - 49 adults (>18yrs) completed the Short Form-36 assessments
 - Found similar physical and mental function, educational status, work or school status, financial situation, or marital status
 - Higher denial of life and health insurance in survivors

Sanders JE, et al. Late effects among pediatric patients followed for nearly 4 decades after transplantation for severe aplastic anemia. *Blood*. 2011;118(5):1421-1428..

HRQoL in HCT

- HCT survivors for malignancies have poorer general health than suitably matched controls who had not undergone HCT⁴⁻⁷.
 - Similar rates of hospitalization and marital satisfaction
 - Survivors reported more denial of life and health insurance



Syrjala KL, et al. Delivering care to long-term adult survivors of hematopoietic cell transplantation. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2012;30(30):3746-3751.

Syrjala KL, et al. Late effects of hematopoietic cell transplantation among 10-year adult survivors compared with case-matched controls. *J Clin Oncol*. 2005;23(27):6596-6606.

Stein KD, et al. Physical and psychological long-term and late effects of cancer. *Cancer*. 2008;112(11 Suppl):2577-2592.

Martin PJ, et al. Life expectancy in patients surviving more than 5 years after hematopoietic cell transplantation. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2010;28(6):1011-1016

Unrelated Donor Transplant versus Immune Therapy (TransIT) in Pediatric Severe Aplastic Anemia

Aplastic Anemia Treatment

Figure 1: Treatment Schema for SAA

Establish diagnosis of Acquired SAA

YES

Consider MUD BMT or other treatment options, in context of trial

TransIT



- Consortium of ~45 pediatric hematology programs
- Collaborate on both clinical care and research protocols



- Established in 2001 to conduct large multi-institutional clinical trials
- Goal of addressing important issues in HCT

TransIT phase I

- **Screening Protocol Analysis-all patients suspected of SAA**

- Initially open 8 centers
- 67 consented for screening, 10 not SAA
- 57 SAA patients screened, 23 (40%) were randomized
- Reasons for patients not accepting randomization

Outcome of Screening	Number (Percentage)
Not Interested in Randomization	6 (10.5%)
Did Not Want BMT	4 (6%)
Did Not Want IST	3 (5%)
Medical Issues: Too Sick to wait/telomeres Too Low	1 (2%) “too sick” 2 (3.5%) “telomeres too low”
Sibling Donor Available	11 (19%)
MUD Donor Not Available	7 (12%)

TransIT phase I

- **11 pts randomized to IST**
 - 3 failed IST requiring HCT, 1 responding poorly
- **13 pts randomized to HCT**
 - 10/13 HCT as first therapy
 - Median time from randomization to admission 34d (23-70d)
 - 1 late rejection, rescued with second HCT
- **Transplant Related Mortality (TRM)**
 - 100% of patients alive
 - Median followup 18mths (1-33mths)
- **GVHD**
 - 2/9 acute GVHD (skin grade 2, skin grade 1)
 - 2/9 limited cGVHD

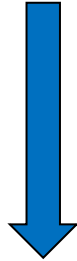
TransIT phase I Conclusions

- Can we arrive at a uniform diagnosis quickly?
 - *Modified approach was successful*
- Will patients and families be willing to randomize?
 - *40% of SAA patients screened enrolled*
- Will patients randomized to HCT receive it?
 - *Cross over to IST rate low*
- Will it take excessive time for donor clearance?
 - *Median time to HCT admit under 5 weeks*
- Will cGVHD with 9/10 donors be an issue?
 - *No extensive cGVHD to date, patients off IS*
- Will early rejection or TRM occur?
 - *5% expected, a single late graft failure occurred*

TransIT Phase III Trial

Possible Aplastic Anemia

3 weeks



Consistent work-up
Correlative biology studies
HLA typing, sibs
Rapid donor search

Eligibility for Trial Determined

1. FA ruled out, DC and SDS evaluation negative if clinically indicated
2. No MRD available
3. Possible 9/10 or 10/10 MUD confirmed



Consent/

Randomization

IST

MUD HSC

Donor not available

or

BMT cannot be started within 8 weeks

Current HRQoL Research in SAA

- Pilot study investigating HRQoL in SAA
 - 16 centers
 - Via online platform
 - *Qualitative excerpts*
 - *Participating in this study has really shown me how things have changed throughout treatment*
 - *I can't wait to do my surveys because I look forward to the gift card*
- TransIT phase III
 - PIs: David Williams and Michael Pulsipher
 - HRQoL CoPIs: Staci Arnold and Thomas Michiniacki

Current HRQoL Research in SAA

Proposed Instruments
PROMIS® Short Forms
Mental Health
Anger
Anxiety
Depressive Symptoms
Physical Health
Fatigue
Mobility
Pain Interference
Cognitive Function
Social Health
Peer Relationships
PedsQL 4.0
PedsQL Transplant Module Self-Image
Reproductive concerns
Financial burden assessment
Service utilization survey

Pediatric Global Health 7+2

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



		Excellent	Very Good	Good	Fair	Poor
Global01R1	In general, would you say your health is:.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
Global02R1	In general, would you say your quality of life is:.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
Global03R1	In general, how would you rate your physical health?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
Global04R1	In general, how would you rate your mental health, including your mood and your ability to think?	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
		Never	Rarely	Sometimes	Often	Always
PedGlobal05R1	How often do you feel really sad?	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
		Always	Often	Sometimes	Rarely	Never
PedGlobal06R1	How often do you have fun with friends?	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
PedGlobal07R1	How often do your parents listen to your ideas?.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
	In the past 7 days...					
		Never	Almost Never	Sometimes	Often	Almost Always
3876R1r	I got tired easily	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
3792R1r	I had trouble sleeping when I had pain.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5

Pediatric Global Health 7+2

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

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Global04R1	In general, how would you rate your mental health, including your mood and your ability to think?	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
		Never	Rarely	Sometimes	Often	Always
PedGlobal02R1	How often do you feel really sad?	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
		Always	Often	Sometimes	Rarely	Never
PedGlobal03R1	How often do you have fun with friends?	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
PedGlobal04R1	How often do your parents listen to your ideas?	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
	In the past 7 days...					
		Never	Almost Never	Sometimes	Often	Almost Always
2870R1r	I got tired easily	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5
3793R1r	I had trouble sleeping when I had pain.....	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5



In the past **ONE month**, how much of a **problem** has your teen had with ...

TREATMENT ANXIETY (problems with...)	Never	Almost Never	Some-times	Often	Almost Always
1. Getting anxious about going to see the doctor	0	1	2	3	4
2. Getting anxious about going to the hospital	0	1	2	3	4
3. Getting anxious about having needle sticks (i.e., injections, blood tests, IV's)	0	1	2	3	4
4. Getting anxious when he/she has to have medical treatments/procedures (i.e., biopsy)	0	1	2	3	4

PERCEIVED PHYSICAL APPEARANCE (problems with...)	Never	Almost Never	Some-times	Often	Almost Always
1. Not liking other people to see his/her scars	0	1	2	3	4
2. Worrying that his/her medicines will change the way he/she looks	0	1	2	3	4
3. Being embarrassed when other people see his/her body	0	1	2	3	4

COMMUNICATION (problems with...)	Never	Almost Never	Some-times	Often	Almost Always
1. Difficulty telling the doctors and nurses how he/she feels	0	1	2	3	4
2. Difficulty asking the doctors and nurses questions	0	1	2	3	4
3. Difficulty explaining his/her transplant to other people	0	1	2	3	4
4. Difficulty understanding what the doctors and nurses are telling him/her	0	1	2	3	4

Financial Hardship

Health Insurance and Medical Costs

1. Are you currently covered by any of the following types of health insurance or health coverage plans? Please check all that apply.

- Insurance through a current or former employer or union (of you or another family member)
- Insurance purchased directly from an insurance company (of you or another family member)
- Medicare, for people 65 and older, or people with certain disabilities
- Medicaid
- VA or TRICARE or other military health care

2. How satisfied are you with your current insurance coverage? Please circle one.

Not satisfied 2 3 4 5 Completely satisfied
 1

3. About how much of your own money did you spend last year for your medical care (including prescriptions, co-payments, deductibles, and premiums)?

\$ _____ dollars per month

4. The next questions are about costs associated with your SAA that are not direct medical costs. How difficult has it been for you to pay for the following costs? Please circle one number or "N/A" if you did not have the type of cost.

	Not difficult					Extremely difficult	Not Applicable
Paying for transportation to and from your appointments (gas, parking).....	1	2	3	4	5		N/A
Paying for SAA-related changes at home (cleaning, special food)	1	2	3	4	5		N/A
Paying for care services for children or parents usually in my care.....	1	2	3	4	5		N/A

5. How difficult is it for you to pay your medical bills (including prescriptions, co-payments, premiums, and deductibles)? Please circle one.

Not difficult at all 2 3 4 5 Extremely difficult
 1

6. The following questions ask about things that may make your life more difficult or stressful.

During the last year, how much have each of the following added stress in your life?

Never Rarely Sometimes Often Always

Conclusions

- Existing data are limited by small sample size
- Findings will guide future research to focus on prospectively determining differences in treatment outcomes that patients would consider important
- Results will inform future patient/caregiver education, allocation of resources, and policy

*Help us improve the lives of our patients
and families*

Amtmann D, et al. Minimally important differences for Patient Reported Outcomes Measurement Information System pain interference for individuals with back pain. *J Pain Res.* 2016;9:251-255.

Hays Rdet al. Approaches and recommendations for estimating minimally important differences for health-related quality of life measures. *COPD.* 2005;2(1):63-67.

Kroenke K, et al. Operating characteristics of PROMIS four-item depression and anxiety scales in primary care patients with chronic pain. *Pain Med.* 2014;15(11):1892-1901.

Thissen D, et al. Estimating minimally important difference (MID) in PROMIS pediatric measures using the scale-judgment method. *Qual Life Res.* 2016;25(1):13-23.

Yost KJ, et al. Minimally important differences were estimated for six Patient-Reported Outcomes Measurement Information System-Cancer scales in advanced-stage cancer patients. *J Clin Epidemiol.* 2011;64(5):507-516

Discussion/Questions



Appendix



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