Host Information

Dr. Robert Klaassen - TranQol Instrument Author; Pediatric Hematologist and Oncologist, Clinical Investigator - CHEO Research Institute; Associate Professor, Faculty of Medicine/ Department of Pediatrics - University of Ottawa
Transfusion Quality of Life (TranQol)
Agenda

- Brief review of Thalassemia
- Brief review of QOL
- Development of the TranQol
- Validation of the TranQol
- Current translations
- Access to TranQol
Pathophysiology of Thalassemia

- Thalassemia = defective globin gene synthesis
- Results in unbalanced chain synthesis
- Unpaired chains are insoluble and adhere to the cytoskeleton
- Result is early cell death (ineffective erythropoiesis) or shortened red cell life span
- Thalassemia Disease states are either:
  - Transfusion-Dependent
  - Non-Transfusion Dependent
Bone Marrow

- Erythroblast

Mutations and deletions, chromosomes 11 (β-thal) and 16 (α-thal)

excess α chains (β-thal)

Inclusion Bodies

excess β chains

Hb.H Disease (α-thal)

Intra Medullary

Extra Medullary

- Apoptosis
  - Ineffective Erythropoiesis
- Target Cell
  - Hemolysis

Rachmilewitz et al Blood 2011
**Treatment: Transfusion-Dependent Thalassemia**

- **Transfusion** is the gold standard
  - to maintain adequate Hb levels
  - to suppress production of defective RBC’s
- **Transfuse every 2-5 wks**
- **Iron overload a significant problem after 10-20 transfusions**
  - Cardiac, liver and endocrine toxicity
- **Require chelation for long term survival**
  - Either subcutaneous infusion or oral
- **Please see review for more details**
  - Amid et al “Thalassaemia in children: from quality of care to quality of life”
  - Archives of Disease in Childhood 2015
What is QOL?

“Individuals’ perceptions 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.”

“The gap between ones life expectations and life experiences.”

(WHOQOL group, 1993 & 1995)

Quality of Life Research 1993; 2: 153-159
Social Science and Medicine 1995; 41: 1403-1409
Tool Development

- Initial investigator meeting generated 69 potential items.
- A further 74 possible items were generated through interviews with
  - 16 children with thalassemia and 22 parents
  - 15 adults with thalassemia
  - 9 adults with MDS.
- A second expert meeting was convened to refine the suggested items.
Developing of the TranQol

Initial Meeting of Investigators in Toronto (Phase 1)

Item Generation Interviews/Focus Groups

- 15 thalassemia children age 7.0–18
- 25 parents (10 child age 2-6.9, 15 child age 7.0–18)
- 15 thalassemia adults
- 15 MDS adults

Toronto Meeting to Develop Initial Measures

Cognitive Debriefing of the Developed Measures (Phase 2)

- 15 thalassemia children age 7.0–18
- 25 parents (10 child age 2-6.9, 15 child age 7.0–18)
- 15 thalassemia adults
- 15 MDS adults

Consensus Meeting in Toronto to Refine Measures
## Developing of the TranQol

<table>
<thead>
<tr>
<th>Category</th>
<th>Expert Item</th>
<th>Patient #1</th>
<th>Patient #2</th>
<th>Patient #3 M-M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Item Ranking#</td>
<td>Importance Rank</td>
<td>Importance Rank</td>
<td>Importance Rank</td>
</tr>
<tr>
<td><strong>Schooling</strong></td>
<td>Does having Thalassemia and having blood transfusions affect your academic performance?</td>
<td>1</td>
<td>1</td>
<td>.</td>
</tr>
<tr>
<td></td>
<td>Does having Thalassemia and having blood transfusions affect your social life at school (i.e. dances, parties, special events)</td>
<td>2</td>
<td>1</td>
<td>.</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td>Do you worry about your future?</td>
<td>3</td>
<td>8</td>
<td>.</td>
</tr>
<tr>
<td><strong>Sleep</strong></td>
<td>I have trouble sleeping because of my infusions</td>
<td>4</td>
<td>7</td>
<td>.</td>
</tr>
<tr>
<td><strong>Self esteem</strong></td>
<td>Do you feel different from other children?</td>
<td>5</td>
<td>6</td>
<td>.</td>
</tr>
<tr>
<td><strong>Disclosure</strong></td>
<td>Have you worried about telling a boyfriend/girlfriend about your Thalassemia?</td>
<td>6</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>To what extent do you feel that physical pain prevents you from doing what you need to do?</td>
<td>7</td>
<td>5</td>
<td>.</td>
</tr>
<tr>
<td><strong>Parent/Child interaction</strong></td>
<td>I fight with my parent(s) about my treatment</td>
<td>8</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td></td>
<td>I wish my parent/parents would allow me to make more decisions about my treatment</td>
<td>9</td>
<td>.</td>
<td>.</td>
</tr>
</tbody>
</table>
For each item please tell us how often these things happened to you in the past 4 weeks...

<table>
<thead>
<tr>
<th>We would like to know something about your physical health</th>
<th>Never</th>
<th>Almost never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I have had trouble sleeping...</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. I was free of pain or discomfort...</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Pain prevented me from doing what I need to do...</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. I had enough energy for daily activities...</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. I was limited in my ability to do the kind of moderate work or activities I take part in...</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. I was limited in my ability to do the kind of vigorous work or activities I take part in...</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. How often did you feel too tired to do the things you enjoy doing? (i.e. hobbies, crafts, sports, musical instruments etc)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. My health allows me to participate in as many social events as I wanted to...</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>We would like to know something about your emotional health</th>
<th>Never</th>
<th>Almost never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. I felt sad...</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Tool Development

- End result was 4 questionnaires:
  - Thalassemia child and proxy versions (proxy identical to the child version except for “my child” instead of “I”)
  - Thalassemia parent version (determines parental burden)
  - Thalassemia adult version
Cognitive Debriefing

- Debriefing was done in an additional:
  - 15 children and 21 parents
  - 15 adults with thalassemia
- 3 items were added
- one was deleted
- 16 of the questions were modified.
Introducing the Tran Qol: A New Disease-Specific Quality of Life Measure for Children and Adults with Thalassemia Major

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Abstract

Background: Patients with thalassemia major require red cell transfusions for survival and have to deal with iron overload and chelation. Chelation is burdensome, traditionally involving nightly prolonged subcutaneous infusion therapy. We developed a disease-specific tool for these patients (TranQol) to measure their unique quality of life issues.

Methods: Pediatric and adult thalassemia health care professionals and quality of life methodology experts generated 69 potential items. 74 further questions were generated through interviews with patients (pediatric and adult) and parents.

Results: 120 participants contributed: 16 healthcare workers, 31 children and 30 adults with thalassemia and 43 parents. Duplicate and infrequent questions were discarded leaving 58 items. Three self-reported questionnaires (child, parent and adult) and one child proxy-report for parents were developed. Questionnaire length ranged from 29 (child’s) to 39 (parent’s). Questions were grouped into four domains: physical health, emotional health, family functioning, and school and career functioning. A fifth category on sexual activity included only one item. Cognitive debriefing was done by interviewing additional children, parents, and adults. As a result, three items were added. one was deleted and 16 were modified.

Conclusion: The TranQol is a new disease-specific quality of life measure for thalassemia major patients developed using rigorous methodology.
TranQol Validation

Baseline (pre transfusion)

One week post transfusion

Prior to next transfusion

Table I. Sample characteristics by subgroup.

<table>
<thead>
<tr>
<th></th>
<th>Child N = 55</th>
<th>Adult N = 51</th>
<th>Total N = 106</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, N (%)</td>
<td>27 (51)</td>
<td>16 (31)</td>
<td>43 (41)</td>
</tr>
<tr>
<td>Age, years (range)</td>
<td>13-4 (7–18)</td>
<td>28-6 (19–51)</td>
<td>20-7 (7–51)</td>
</tr>
<tr>
<td>Adult marital status, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>9 (18)</td>
<td>9 (18)</td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>38 (75)</td>
<td>38 (75)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3 (6)</td>
<td>3 (6)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>20 (36)</td>
<td>13 (26)</td>
<td>33 (31)</td>
</tr>
<tr>
<td>Black</td>
<td>0 (0)</td>
<td>3 (6)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Asian</td>
<td>26 (47)</td>
<td>30 (59)</td>
<td>56 (53)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (18)</td>
<td>6 (12)</td>
<td>16 (15)</td>
</tr>
<tr>
<td>Transfusion frequency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Every 3 weeks</td>
<td>16 (29)</td>
<td>35 (6)</td>
<td>51 (48)</td>
</tr>
<tr>
<td>Every 4 weeks</td>
<td>38 (69)</td>
<td>9 (18)</td>
<td>47 (44)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (2)</td>
<td>6 (12)</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Co-morbidities, Y (%)</td>
<td>4 (7)</td>
<td>37 (73)</td>
<td>41 (39)</td>
</tr>
<tr>
<td>Chelator, N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desferal</td>
<td>15 (27)</td>
<td>27 (53)</td>
<td>42 (40)</td>
</tr>
<tr>
<td>Es jade</td>
<td>48 (87)</td>
<td>33 (65)</td>
<td>81 (76)</td>
</tr>
<tr>
<td>Ferriprox</td>
<td>0 (0)</td>
<td>8 (16)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Ferritin, pmol/l (range)</td>
<td>4017 (45–21,857)</td>
<td>5186 (921–20,403)</td>
<td>4579 (45–21,857)</td>
</tr>
<tr>
<td>Hepatic iron concentration, mg/g dry tissue (range)</td>
<td>5·2 (0·1–27)</td>
<td>6·6 (0·3–42)</td>
<td>5·9 (0·1–42)</td>
</tr>
<tr>
<td>TranQol score, mean (range)</td>
<td>77 (38 97)</td>
<td>63 (32 93)</td>
<td>71 (32 97)</td>
</tr>
</tbody>
</table>
TranQoL Score Distribution

(A)

(B)

Paediatric

Adult

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### TranQol Domains

**Table II.** Correlation of child TranQol and PedsQL domain scores at baseline.

<table>
<thead>
<tr>
<th>TranQol, mean (SD)</th>
<th>Emotional health 66.4 (25.2)</th>
<th>Family functioning 77.8 (15.7)</th>
<th>School functioning 81.2 (17.8)</th>
<th>Physical health 79.6 (15.9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PedsQL, mean (SD)</td>
<td>Emotional functioning 85.0 (17.4)</td>
<td>Social functioning 89.7 (15.8)</td>
<td>School functioning 75.9 (18.6)</td>
<td>Physical functioning 86.2 (15.6)</td>
</tr>
<tr>
<td>Domain correlation, $r$</td>
<td>0.65</td>
<td>0.50</td>
<td>0.43</td>
<td>0.69</td>
</tr>
</tbody>
</table>

**Table III.** Adult TranQol and SF-36 domain scores at baseline.

<table>
<thead>
<tr>
<th>TranQol, mean (SD)</th>
<th>Emotional health (EH) 62.1 (18.0)</th>
<th>Family functioning (FF) 61.5 (27.7)</th>
<th>School &amp; career functioning (SF) 65 (19.9)</th>
<th>Physical health (PH) 64.7 (18.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36 summary, mean (SD)</td>
<td>Mental component summary 45.5 (11.3)</td>
<td>Physical component summary 47.6 (7.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF-36 scales, mean (SD)</td>
<td>Role-emotional 77.1 (25.3)</td>
<td>Mental health 69.0 (19.5)</td>
<td>Vitality 52.3 (20.5)</td>
<td>Social functioning 79.0 (21.9)</td>
</tr>
<tr>
<td>Domain/scale correlation, $r$</td>
<td>EH 0.64</td>
<td>FF 0.62</td>
<td>PH 0.71</td>
<td>SF 0.68</td>
</tr>
</tbody>
</table>
TranQol Reliability

- Internal consistency
  - Cronbach’s alpha
    - child = 0.84
    - proxy = 0.89
    - adult = 0.96
  - Had to eliminate one item “Thalassemia postively affected my family” as <0.3

- Test-retest reliability
  - children = 0.89
  - Adults = 0.94
Fig 2. Changes in adult TranQol scores at 1 week post-transfusion by self-reported change in quality of life rating.
Validation and reliability of a disease-specific quality of life measure (the TranQol) in adults and children with thalassaemia major

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Summary

This study aimed to demonstrate the validity, reliability and responsiveness of a new disease-specific quality of life (QoL) questionnaire for children and adults with thalassaemia major, the Transfusion-dependent Qol questionnaire (TranQol). 106 participants (51 adults and 55 children) were recruited from six North American thalassaemia treatment centres with a mean age of 20.7 years (standard deviation [SD] 9, range 7–51 years). The mean total TranQol score was 71 (SD 17, 32–97) on a scale of 0–100. Patients with co-morbidities had significantly lower scores (63 vs. 75, P = 0.001). TranQol scores showed substantial agreement (P < 0.001) with the Health Utilities Index Mark 3 (all patients, r = 0.65), the Pediatric QoL (children, r = 0.77) and the Short Form (36) physical (adults, r = 0.69) and mental summary scores (r = 0.76). In the subgroup who rated their QoL as better, there was a 4–0 point (SD 9.4) improvement in TranQol scores, from baseline of 67.1–71.1 one week later (P = 0.008). Test-retest reliability was excellent (intra-class correlation coefficient, 0.93). The TranQol was valid, with acceptable correlation for all administered measures and was reliable and responsive to change. The TranQol can be incorporated into future studies of thalassaemia major.

Keywords: thalassaemia, quality of life, validation studies, reproducibility of results, questionnaires.
TranQol: Available Language Versions

- **Original language of development:**
  - English for North America (USA and Canada)

- **Available translations:**
  - Greek (Greece)
  - Italian (Italy)
  - Turkish (Turkey)
  - Arabic (Lebanon)
  - French (France)
  - Thai (Thailand)

- Translations produced by Mapi Language Services, following a full linguistic validation methodology
How to Access the TranQol

- Centralization of information and language versions
- Licensing process
- Distribution

handled by Mapi Research Trust on behalf of the TranQol’s authors
TranQol: Conditions of Use

- Conditions of use available and detailed on PROQOLID (www.proqolid.org)

- Process:
  - Signature of a User Agreement for each study
  
  - Free access for Non-Funded Academic Users:
    - Easy and quick access to the TranQol for Non-Funded Academic Users via Online Distribution process on PROQOLID
  
  - Payment of access fees if the TranQol is used in:
    - Funded academic research
    - Large non-commercial organization research and evaluation
    - Commercial studies

- When the process is completed, Mapi Research Trust delivers:
  - Needed language versions (if available)
  - Scoring instructions
TranQol: conditions of use

- For any questions on the TranQol:
  - please visit PROQOLID (www.proqolid.org)
  - Or send an email to our Information Support Unit (PROinformation@mapi-trust.org)
Key Discussion Topic
Key Discussion Points

1. TranQOl is a tool specifically designed for patients with transfusion-dependent thalassemia with input from patients and expert health care providers.
2. There are 4 versions—child, proxy, parent, and adult.
3. There are 4 domains—physical, emotional, family, and school and career.
4. There was clear construct and known group validity.
5. The TranQol is reliable and has good responsiveness.
6. It is currently translated into 6 languages in addition to North American English.
7. Ready access to the measure is available through PROQOLID.
Thank You!

Additional Questions? Ask our Webinar Hosts directly!

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