History and Current State of PROs

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- Equity: Health Outcomes Sciences, LLC
Basic Definitions

- **Definition of a Patient-Reported Outcome**
  - *A PRO is a measurement of any aspect of a patient’s health status that comes directly from the patient*
  - i.e., without the interpretation of the patient’s responses by a physician or anyone else

- **Generic Health Status Measures**
  - Quantify impact of patients’ overall health

- **Disease-Specific Measures**
  - More sensitive in quantifying benefits of treatment
  - More interpretable to physicians

Defining and Measuring Health Status

- The manifestations of HF from patients’ perspectives

  - **Disease**
    - Myocardial Injury
    - RAAS Activation
    - LV dysfunction

  - **Symptoms**
    - Fatigue
    - Dyspnea
    - Edema

  - **Functional Limitation**
    - Physical
    - Emotional
    - Social

  - **Quality of Life**
    - Discrepancy between actual & desired health and functioning

<table>
<thead>
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<th>Myocardial Injury</th>
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The Range of Health Status in PROs
Key Attributes of Health Status Measures

- **Validity:**
  
  *Does the instrument measure what it is supposed to?*

- **Reliability:**
  
  *Are the results the same when given repeatedly to stable patients?*

- **Responsiveness:**
  
  *Do the results reflect changes in patients’ disease status?*

- **Interpretability:**
  
  *What does a given score or change in score mean?*

- **Translations:**
  
  *Are linguistically and culturally appropriate translations available?*

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Evolution to Shorter, More Feasible PROs

- **1981:** Sickness Impact Profile 136 items
- **1985:** Minnesota Living with Heart Failure Questionnaire 21 items
- **1988:** SF-36 36 items
- **1992:** Seattle Angina Questionnaire 19 items
- **1994:** SF-12 12 items
- **1995:** Sickness Impact Profile 68 items
- **1988:** SF-36 36 items
- **1992:** Seattle Angina Questionnaire 19 items
- **1994:** SF-12 12 items
- **2000:** Kansas City Cardiomyopathy Questionnaire 23 items
- **2005:** Seattle Angina Questionnaire 7 items
- **2014:** Kansas City Cardiomyopathy Questionnaire 12 items
- **2015:** PROMIS Computer Adaptive Testing – NIH/PCORI-funded

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*Generic* vs. *Cardiac-Specific*
How can we Use the Patient’s Voice

- As Outcomes in Clinical Trials
- Selecting Patients for Treatment/Disease Management
- As a Foundation for Shared Medical Decision-making
- As Tools in Routine Clinical Care
- As Performance Measures of Healthcare Quality

Evolving Standards in Clinical Care

- The ‘Gold Standard’ for Cardiac Physiology

- Limitations in…
  - Accuracy
  - Reproducibility
A Conceptual Framework for PROs

- The ‘Gold Standard’ for History of Symptoms and Impact

- Limitations in…
  - Accuracy
  - Reproducibility

The Key Challenge is Rendering Results Interpretable to Patients and Providers

PROs as Performance Measures in Heart Failure

- CHAMP-HF – 150-center outpatient US registry of 5000 patients with HFrEF

- Examined the proportion of patients in each practice with Monthly-No symptoms (KCCQ TSS >75)

- After adjusting for 28 patient characteristics, examined the variability across centers using MOR
Marked Variability in Symptom Control

Conclusions

- PROs quantify the disease from patients’ perspectives
- Disease-specific measures are more sensitive and relevant
- PROs have evolved into shorter, more feasible tools
- The value of reproducible measures of disease severity are myriad…
Treatment Goals for Stable Ischemic Heart Disease

**Principal Treatment Goals**

- **To Make Patients Live Longer**
  - Disease Progression
    - ACS Events
    - Heart Failure
    - Mortality
  - To Make Patients Feel Better
    - Patient’s “Health Status”
      - Symptoms
      - Functional Status
      - Quality of Life
Traditional Outcomes Studies

Trials focusing upon mortality describe a minority of patients...

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Articles

One-Year Results From the Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries (GUSTO-I) Trial

Robert M. Califf, MD; Harvey D. White, MB, DSc; Frans Van de Werf, MD; Zygmunt Sadowski, MD; Paul W. Armstrong, MD; Alec Vahanian, MD; Maarten L. Simes, MD; R. John Simel, MD; Kerry L. Lee, PhD; Eric J. Topol, MD; for the GUSTO-I Investigators

Duke University Medical Center, Durham, NC (R.M.C., K.L.L.); Green Lane Hospital, Auckland, New Zealand (H.D.W.); Institute Karolinka, Warsaw, Poland (Z.S.); University of Alberta, Edmonton, Canada (P.W.A.); Hospital Trinité, Paris, France (A.V.); Thoraxcenter, Erasmus University, Rotterdam, the Netherlands (M.L.S.); National Heart Medical Research Council Clinical Trials Centre, University of Sydney, Australia (R.J.S.); University Hospital Gaethestingeb, Leuven, Belgium (F. Van de W.); and the Cleveland (Ohio) Clinic Foundation (E.J.T.).

Correspondence to Robert M. Califf, MD, Box 33123, Duke University Medical Center, Durham, NC 27710.

Overall 1-year mortality in the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO-I) trial by treatment assignment

1-year GUSTO Results

What happened to the other 90%??

%.

The KC Cardiomyopathy Questionnaire

- 23/12 items that measure 5 clinically relevant domains
  - Physical Limitation
  - Symptoms: Frequency, Severity and Change over time
  - Social Limitation
  - Self-Efficacy
  - Quality of Life

- Represents the patient’s perspective of their HF
- Available in over 90 translations
- Established validity, reliability and responsiveness

Green et al, JACC 2000; 35:1245-55
Mapping the KCCQ Scales

Disease \(\Longrightarrow\) Symptoms \(\Longrightarrow\) Functional Limitation \(\Longrightarrow\) Quality of Life

Symptom Scales

Physical and Social Function Scales

Quality of Life Scale

KCCQ Overall Summary Scale

KCCQ Clinical Summary Scale

Improving the KCCQ’s Feasibility

The following questions refer to your heart failure and how it may affect your life. Please read and complete the following questions. There are no right or wrong answers. Please mark the arrow that best applies to your experience.

1. Heart failure affects different people in different ways. Some have shortness of breath while others feel tired. Please indicate how much you were limited by heart failure (clearness of breath or fatigue) in your activities over the past 2 weeks.

   - A. Somewhat limited
   - B. Moderately limited
   - C. Extensively limited
   - D. Not limited

2. Over the past 2 weeks, how many times did you have something in your bed, nightly or nap that you woke up in the morning?
   - A. More than 3 times per week
   - B. Less than 3 times per week
   - C. Not limited

3. Over the past 2 weeks, on average, how many times has fatigue limited your ability to do what you wanted?
   - A. More than 3 times per day
   - B. Less than 3 times per day
   - C. Not limited

4. How much does your heart failure affect your mobility? Please indicate how you heart failure may have limited your participation in the following activities over the past 2 weeks.

   - A. Moderate activity
   - B. Limited activity
   - C. No activity

5. How many times have you been forced to sleep using a chair or bed (or at least 3 inches) in your home or other residence, as a result of shortness of breath?
   - A. More than 3 times per week
   - B. Less than 3 times per week
   - C. Not limited

6. Over the past 2 weeks, how much has your heart failure limited your enjoyment of life?
   - A. A lot
   - B. A little
   - C. Not limited

Note: This is an excerpt from the KCCQ questionnaire used to assess the quality of life and functional status of patients with heart failure.
A Short Form SAQ for Routine Clinical Care

- Only 7 questions
- Takes <2 minutes

Using the KCCQ for Clinical Care

KCCQ Symptom Scores

Today’s Score

KCCQ Summary Scores

Today’s Score
Proportion with Excellent Health Status

Khariton, Circ Cardiovasc Qual Outcomes. 2018; 11: e004668

Distribution of KCCO-OS by Site

MOR = 70% ↑Risk (95% CI 54%, 200%; p < 0.001)

Conclusion

- PROs Meet All Requirements of Performance Measures
  - Important
  - Interpretable
  - Actionable
- Disease-specific measures can improve the process of delivering clinical care
  - Can bring the patients’ voices into care
  - Will be used to translate clinical trials into shared decision-making tools to improve care
- Blue Cross Should Lead the Evolution of PROs as PMs
Interpreting SAQ Angina Frequency Scores

Over the past 4 weeks, how often have you had angina?

- >4X/day
- 1-3X/day
- >3X/week
- 1-2X/week
- >1X/week
- Not at All

Using the SAQ Scores Clinically

SAQ Angina Frequency Score

- Daily Angina
- Weekly Angina
- Monthly Angina
- None

Today’s Score
Previous Score

SAQ Summary Scores

- Very Poor-Poor
- Poor-Fair
- Fair-Good
- Good-Excellent

Today’s Score
Previous Score
Do MDs Accurately Assess Angina?

- 24-center study of outpatients with CAD (n=1,257)
- To compare patient- and clinician-reported angina

Patient-reported Angina Frequency

- 68% Daily/Weekly
- 24% Monthly
- 8% No Angina
Dr:Pt Discordance – Frequent Angina

Overall Concordance between Patients and Physicians = 0.48 (95% CI = 0.44, 0.53)
Very Accurate Compared to Daily Diaries

Distribution of Diary Responses to Each of the SAQ AF Questions

<table>
<thead>
<tr>
<th>SAQ AF Q1: Over the past 4 weeks, on average, how many times have you had chest pain, chest tightness, or angina?</th>
<th>Expected Diary Range</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥4 times a day (n=7)</td>
<td>≥28</td>
<td>24.5 (13.3-25.7)</td>
</tr>
<tr>
<td>1-2 times a day (n=119)</td>
<td>7 to 21</td>
<td>9.3 (6.5-13.5)</td>
</tr>
<tr>
<td>≥2 times a week but not every day (n=232)</td>
<td>3 to 6</td>
<td>4.5 (3.3-6.7)</td>
</tr>
<tr>
<td>1-2 times per week (n=358)</td>
<td>1 to 2</td>
<td>2.4 (1.8-4.0)</td>
</tr>
<tr>
<td>Less than once per week (n=156)</td>
<td>&gt;0 to &lt;1</td>
<td>1.3 (0.8-2.5)</td>
</tr>
<tr>
<td>None in the last 4 weeks (n=45)</td>
<td>0</td>
<td>1.0 (0.0-1.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SAQ AF Q2: Over the past 4 weeks, on average, how many times have you had to take nitrates (nitroglycerin tablets) for your chest pain, chest tightness, or angina?</th>
<th>Expected Diary Range</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥4 times a day (n=6)</td>
<td>≥28</td>
<td>26.5 (21.0-31.0)</td>
</tr>
<tr>
<td>1-3 times a day (n=70)</td>
<td>7 to 21</td>
<td>10.1 (6.0-12.5)</td>
</tr>
<tr>
<td>≥2 times a week but not every day (n=181)</td>
<td>3 to 6</td>
<td>3.6 (2.5-5.8)</td>
</tr>
<tr>
<td>1-2 times per week (n=273)</td>
<td>1 to 2</td>
<td>1.6 (1.0-3.0)</td>
</tr>
<tr>
<td>Less than once per week (n=202)</td>
<td>&gt;0 to &lt;1</td>
<td>0.8 (0.3-1.3)</td>
</tr>
<tr>
<td>None in the last 4 weeks (n=184)</td>
<td>0</td>
<td>0.0 (0.0-0.5)</td>
</tr>
</tbody>
</table>

Arnold et al. – Analysis from the TERISA Trial of 917 diabetic patients with SIHD

Improving the KCCQ’s Feasibility
Patient Reported Outcome Instruments and Timing

**Instruments**

- The measure will use the following validated instruments:*
  - The Short Form Seattle Angina Questionnaire (SAQ-7)
  - The Rose Dyspnea Scale (RDS)

**Timing of Administration**

- The pre-procedure PROM assessment will be performed within 30 days of the PCI including the day of the procedure
- The post-procedure PROM assessment will be performed between 28 and 60 days following the PCI

*The inclusion of generic instruments such as the Veterans RAND-12 (VR-12) or the Patient-Reported Outcomes Measurement Information System-Global (PROMIS-Global) may be considered in future iterations of the measure. The TEP and Patient Working Group were divided on the incremental benefit of adding a generic PROM to the measure outcome.

Patient-Level Outcome

**Approach to Defining Patient Improvement**

- Patients are considered to have improved if they achieve a pre-specified change in their PROM score between baseline and follow up. This change represents the minimally important difference (MID)

**MID Definition**

- Either a five point improvement in the SAQ-7 summary score or a one point improvement in the RDS without a five point worsening of the SAQ-7 summary score
- MIDs defined using both empirical data and input from measure developer, patients, and other experts