History and Current State of PROs

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Saint Luke's MID AMERICA HEART INSTITUTE

Disclosures

- Speaker's Bureaus: None
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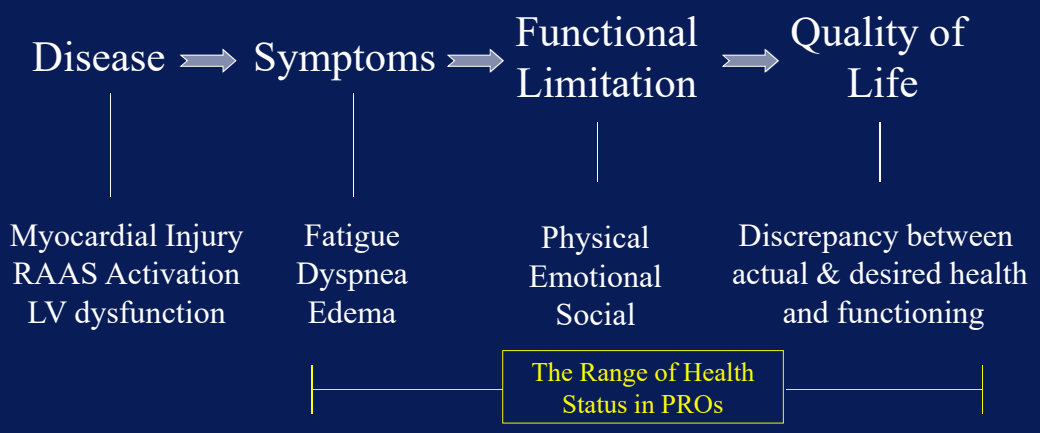
- Consultant: United Healthcare, Bayer, Novartis, Vwave, Corvia
- Copyrights/Patents: SAQ, KCCQ, PAQ, *e*PRISM
- Equity: Health Outcomes Sciences, LLC

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

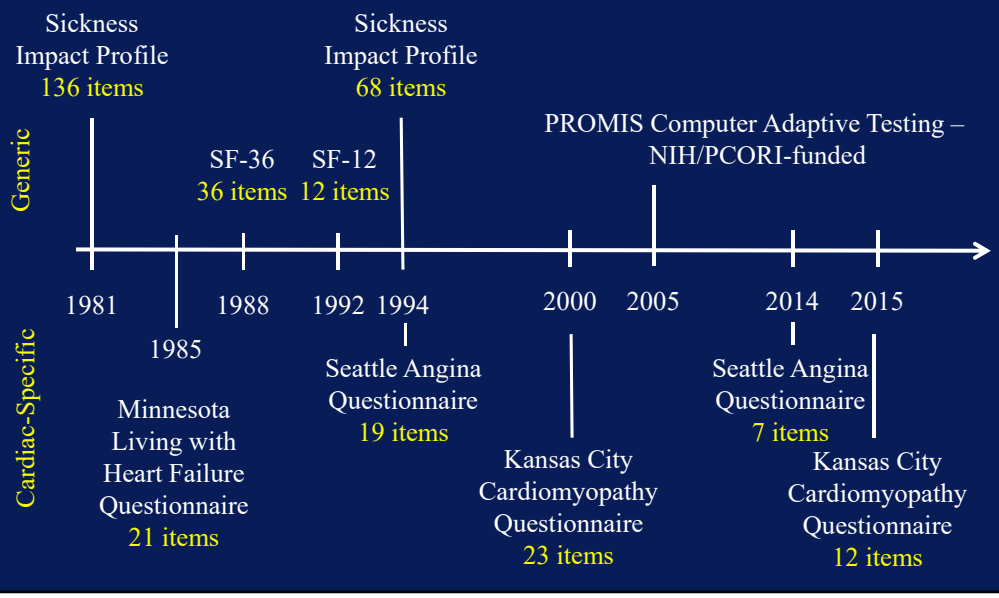
- The manifestations of HF from patients' perspectives



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?

Evolution to Shorter, More Feasible PROs



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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

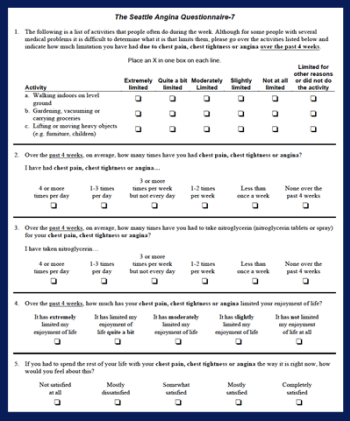
Evolution

- Limitations in…
  - Accuracy
  - Reproducibility

A Conceptual Framework for PROs

- The 'Gold Standard' for History of Symptoms and Impact

Evolution



The Seattle Angina Questionnaire-7

1. The following is a list of activities that people often do during the week. Although for some people with several medical problems it is difficult to determine what it is that limits them, please go over the activities listed below and indicate how much limitation you have had due to chest pain, chest tightness or angina over the past 4 weeks:

Place an X in one box on each line.

Activity	Extremely limited	Quite a bit limited	Moderately Limited	Slightly limited	Not at all limited	Limited for other reasons or did not do the activity
a. Walking indoors on level ground	❑	❑	❑	❑	❑	❑
b. Gardening, vacuuming or carrying groceries	❑	❑	❑	❑	❑	❑
c. Lifting or moving heavy objects (e.g. furniture, children)	❑	❑	❑	❑	❑	❑

2. Over the past 4 weeks, on average, how many times have you had chest pain, chest tightness or angina?

I have had chest pain, chest tightness or angina…

4 or more times per day	1-3 times per day	3 or more times per week but not every day	1-2 times per week	Less than once a week	None over the past 4 weeks
❑	❑	❑	❑	❑	❑

3. Over the past 4 weeks, on average, how many times have you had to take nitroglycerin (nitroglycerin tablets or spray) for your chest pain, chest tightness or angina?

I have taken nitroglycerin…

4 or more times per day	1-3 times per day	3 or more times per week but not every day	1-2 times per week	Less than once a week	None over the past 4 weeks
❑	❑	❑	❑	❑	❑

4. Over the past 4 weeks, how much has your chest pain, chest tightness or angina limited your enjoyment of life?

It has extremely limited my enjoyment of life	It has limited my enjoyment of life quite a bit	It has moderately limited my enjoyment of life	It has slightly limited my enjoyment of life	It has not limited my enjoyment of life at all
❑	❑	❑	❑	❑

5. If you had to spend the rest of your life with your chest pain, chest tightness or angina the way it is right now, how would you feel about this?

Not satisfied at all	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
❑	❑	❑	❑	❑

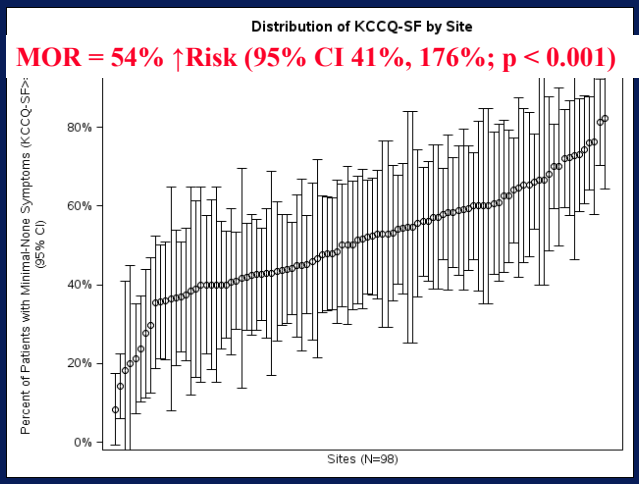
- Limitations in…
  - Accuracy
  - Reproducibility

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

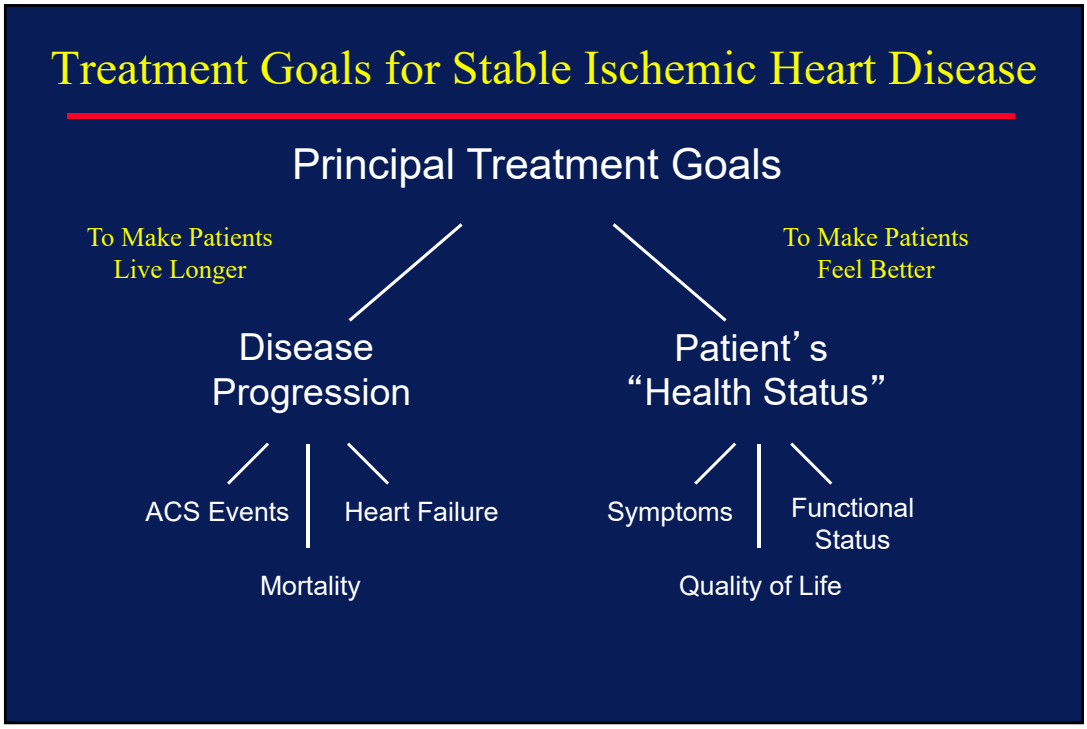


Khariton, *Circ Cardiovasc Qual Outcomes*. 2018; 11: e004668

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



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Traditional Outcomes Studies

- Trials focusing upon mortality describe a minority of patients…

(*Circulation*. 1996;94:1233-1238.)
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Articles

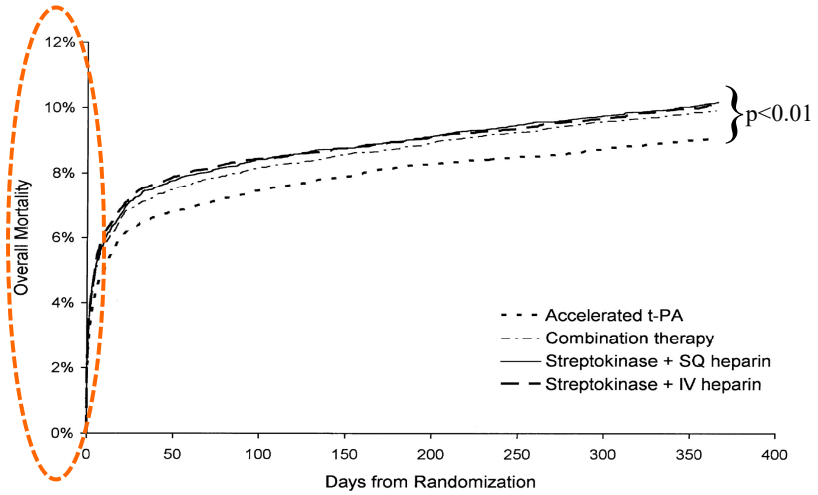
One-Year Results From the Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries (GUSTO-I) Trial

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. Simoons, MD; R. John Simes, 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.); Institut Kardiologu, Warszawa, Poland (Z.S.); University of Alberta, Edmonton, Canada (P.W.A.); Hospital Tenon, Paris, France (A.V.); Thoraxcenter, Erasmus University, Rotterdam, the Netherlands (M.L.S.); National Health Medical Research Council Clinical Trials Centre, University of Sydney, Australia (R.J.S.); University Hospital Gasthuisberg, Leuven, Belgium (F. Van de W.); and the Cleveland (Ohio) Clinic Foundation (E.J.T.).

Correspondence to Robert M. Califf, MD, Box 31123, 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



Califf, R. M. et al. Circulation 1996;94:1233-1238

Circulation

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American Heart Association
Learn and Live

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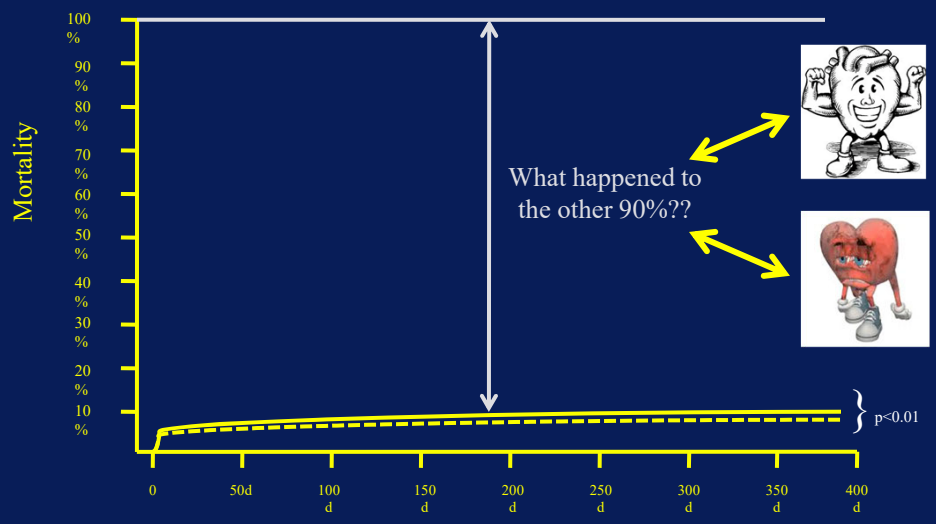
1-year GUSTO Results



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 ⟹ Symptoms ⟹ Functional Limitation ⟹ Quality of Life

- Symptoms → Symptom Scales
- Functional Limitation → Physical and Social Function Scales
- Quality of Life → Quality of Life Scale

KCCQ Clinical Summary Scale

KCCQ Overall Summary Scale

Improving the KCCQ's Feasibility

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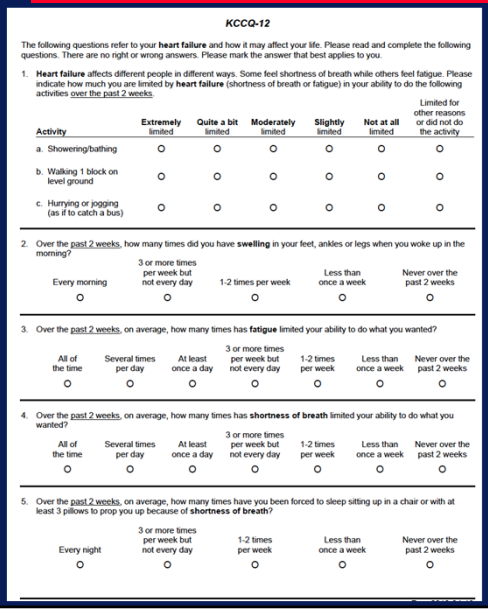


KCCQ-12

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 answer that best applies to you.

1. **Heart failure** affects different people in different ways. Some feel shortness of breath while others feel fatigue. Please indicate how much you are limited by **heart failure** (shortness of breath or fatigue) in your ability to do the following activities over the past 2 weeks.

Activity	Extremely limited	Quite a bit limited	Moderately limited	Slightly limited	Not at all limited	Limited for other reasons or did not do the activity
a. Showering/bathing	○	○	○	○	○	○
b. Walking 1 block on level ground	○	○	○	○	○	○
c. Hurrying or jogging (as if to catch a bus)	○	○	○	○	○	○

2. Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

Every morning	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○

3. Over the past 2 weeks, on average, how many times has **fatigue** limited your ability to do what you wanted?

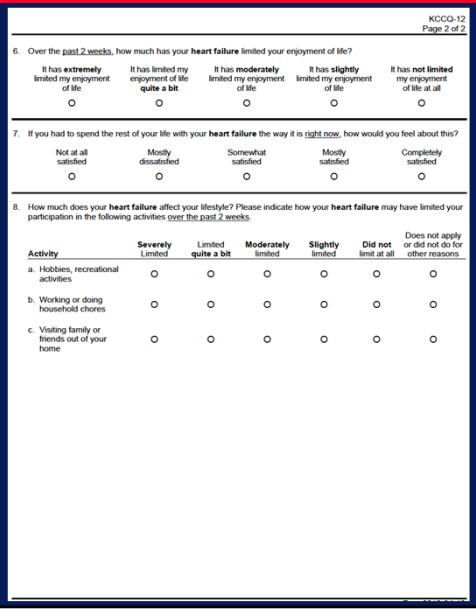
All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○	○	○

4. Over the past 2 weeks, on average, how many times has **shortness of breath** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○	○	○

5. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?

Every night	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○



KCCQ-12
Page 2 of 2

6. Over the past 2 weeks, how much has your **heart failure** limited your enjoyment of life?

It has **extremely** limited my enjoyment of life	It has limited my enjoyment of life **quite a bit**	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **not limited** my enjoyment of life at all
○	○	○	○	○

7. If you had to spend the rest of your life with your **heart failure** the way it is right now, how would you feel about this?

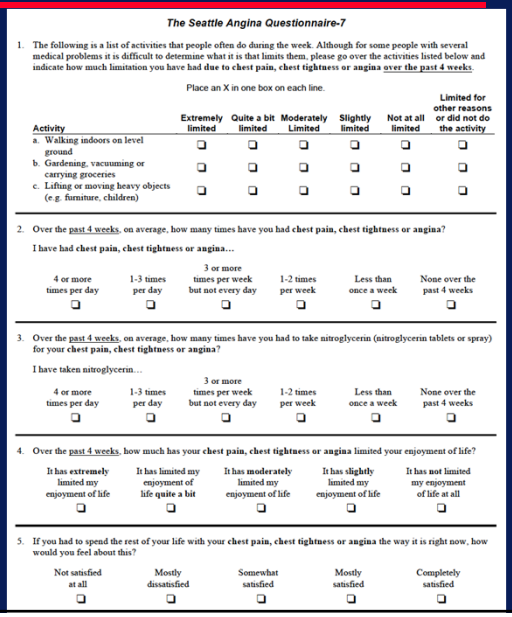
Not at all satisfied	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
○	○	○	○	○

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

Activity	Severely Limited	Limited **quite a bit**	Moderately limited	Slightly limited	Did not limit at all	Does not apply or did not do for other reasons
a. Hobbies, recreational activities	○	○	○	○	○	○
b. Working or doing household chores	○	○	○	○	○	○
c. Visiting family or friends out of your home	○	○	○	○	○	○

A Short Form SAQ for Routine Clinical Care

- Only 7 questions
  - Takes <2 minutes



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Place an X in one box on each line.

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a. Walking indoors on level ground	❑	❑	❑	❑	❑	❑
b. Gardening, vacuuming or carrying groceries	❑	❑	❑	❑	❑	❑
c. Lifting or moving heavy objects (e.g. furniture, children)	❑	❑	❑	❑	❑	❑

2. Over the past 4 weeks, on average, how many times have you had **chest pain, chest tightness or angina**?

I have had **chest pain, chest tightness or angina**…

4 or more times per day	1-3 times per day	3 or more times per week but not every day	1-2 times per week	Less than once a week	None over the past 4 weeks
❑	❑	❑	❑	❑	❑

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I have taken nitroglycerin…

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❑	❑	❑	❑	❑	❑

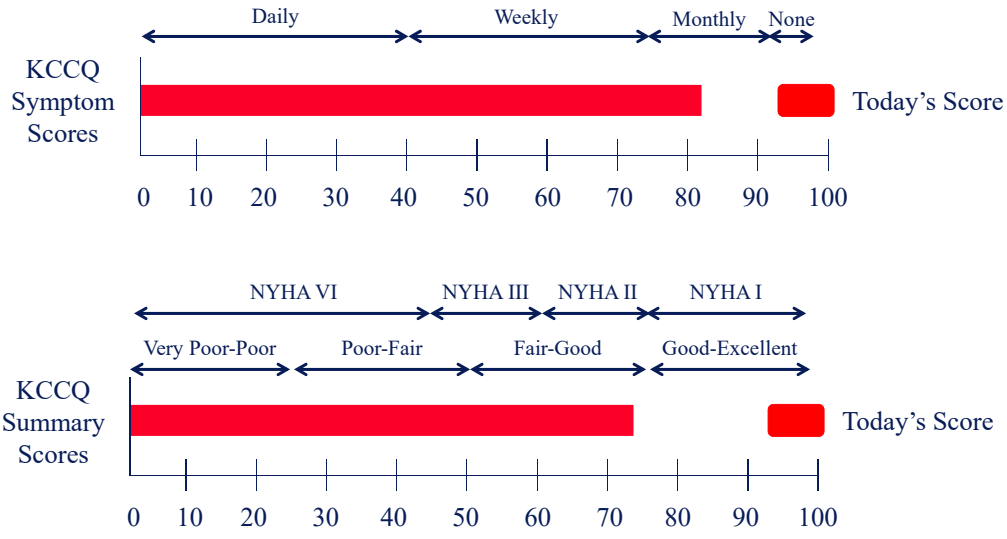
4. Over the past 4 weeks, how much has your **chest pain, chest tightness or angina** limited your enjoyment of life?

It has **extremely** limited my enjoyment of life	It has limited my enjoyment of life **quite a bit**	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **not** limited my enjoyment of life at all
❑	❑	❑	❑	❑

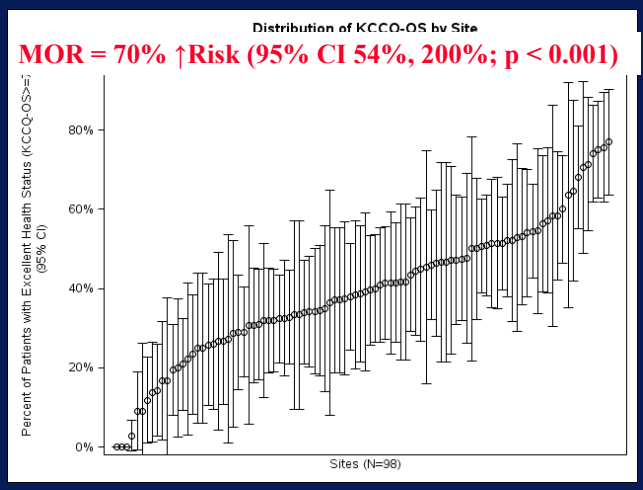
5. If you had to spend the rest of your life with your **chest pain, chest tightness or angina** the way it is right now, how would you feel about this?

Not satisfied at all	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
❑	❑	❑	❑	❑

Using the KCCQ for Clinical Care



Proportion with Excellent Health Status



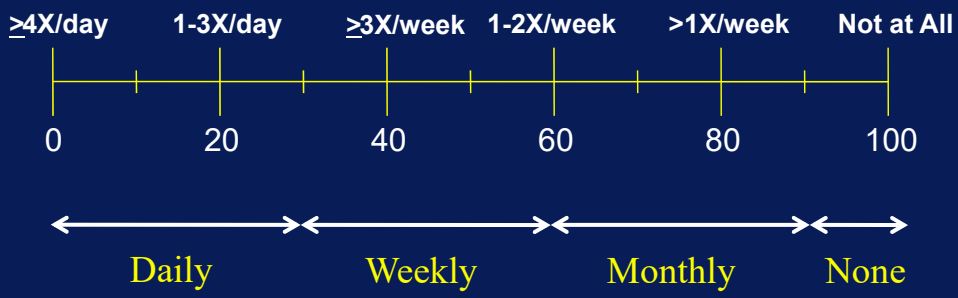
Khariton, *Circ Cardiovasc Qual Outcomes*. 2018; 11: e004668

Conclusion

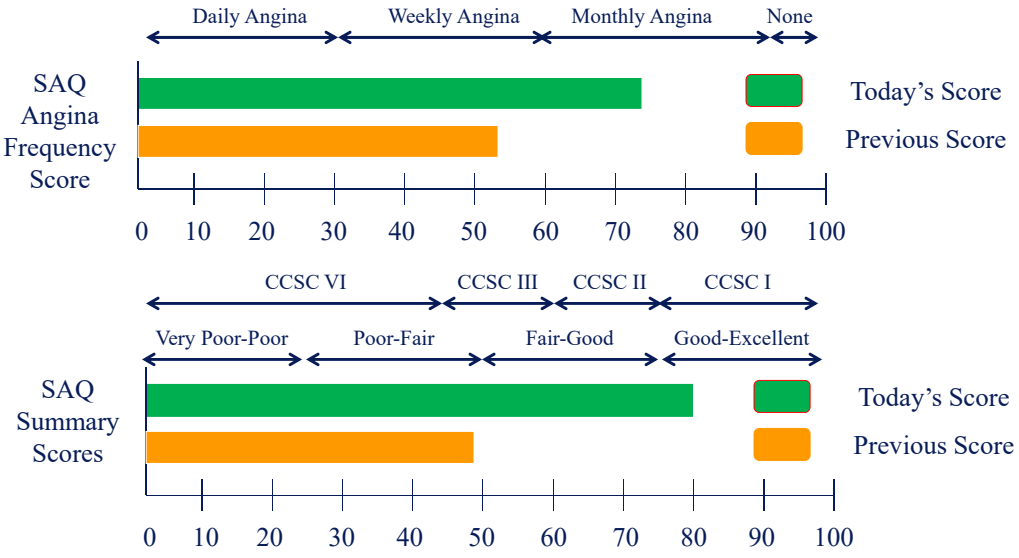
- PROs Meet All Requirements of Performance Measures
  - Important
  - Interpretable
  - Actionable
- Disease-specific measures can improve the process of delivering clinical care
  - Can bring the patients' voices into care
  - Will be used to translate clinical trials into shared decision-making tools 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?

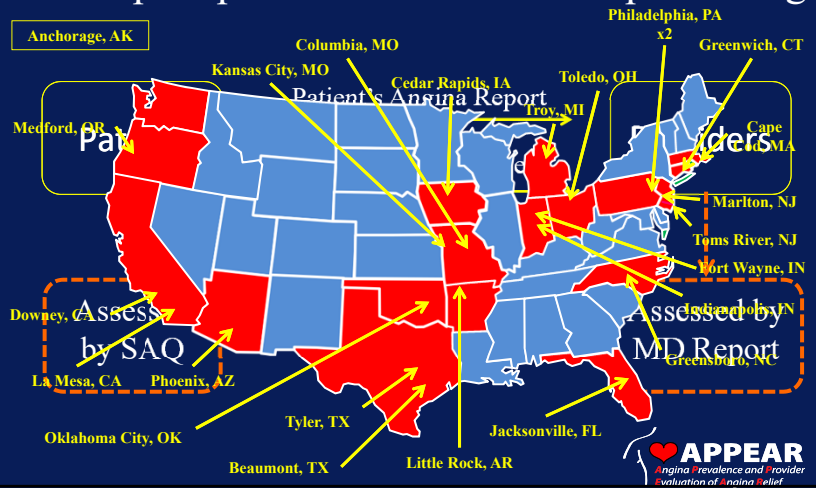


Using the SAQ Scores Clinically

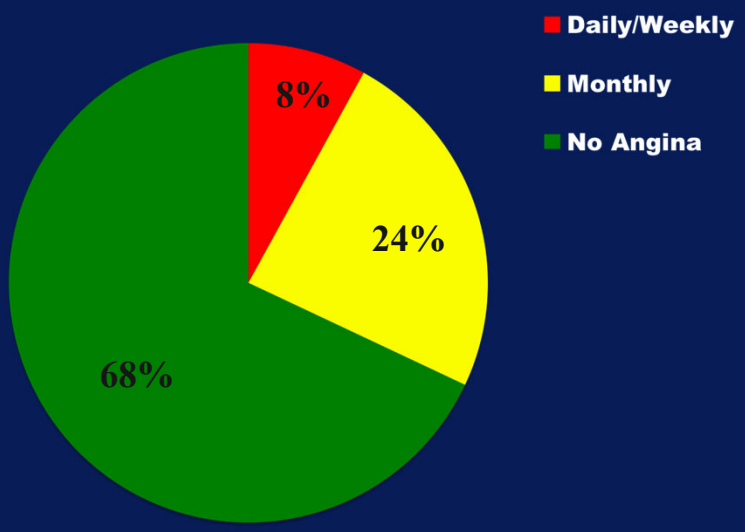


Do MDs Accurately Assess Angina?

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



Patient-reported Angina Frequency



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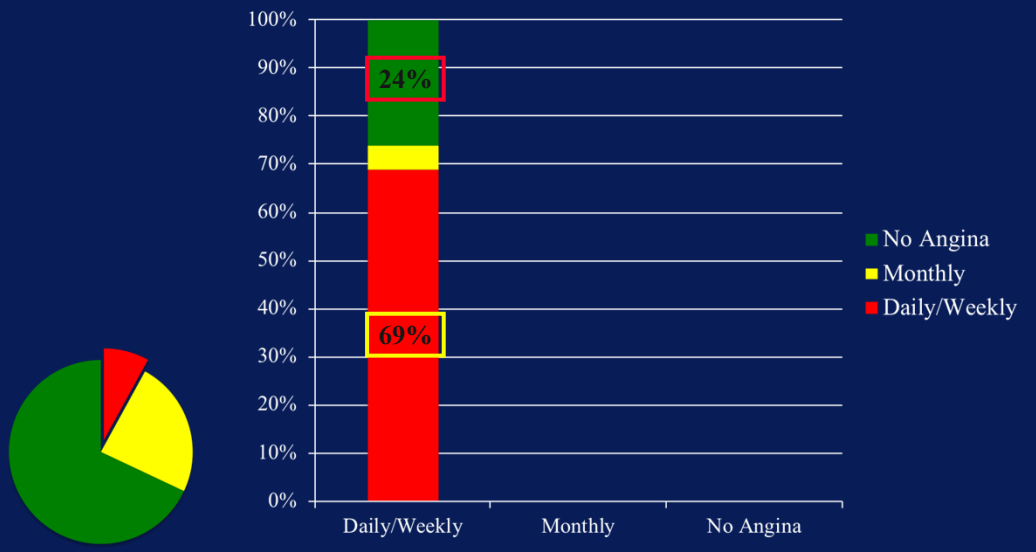
Dr:Pt Discordance – Frequent Angina



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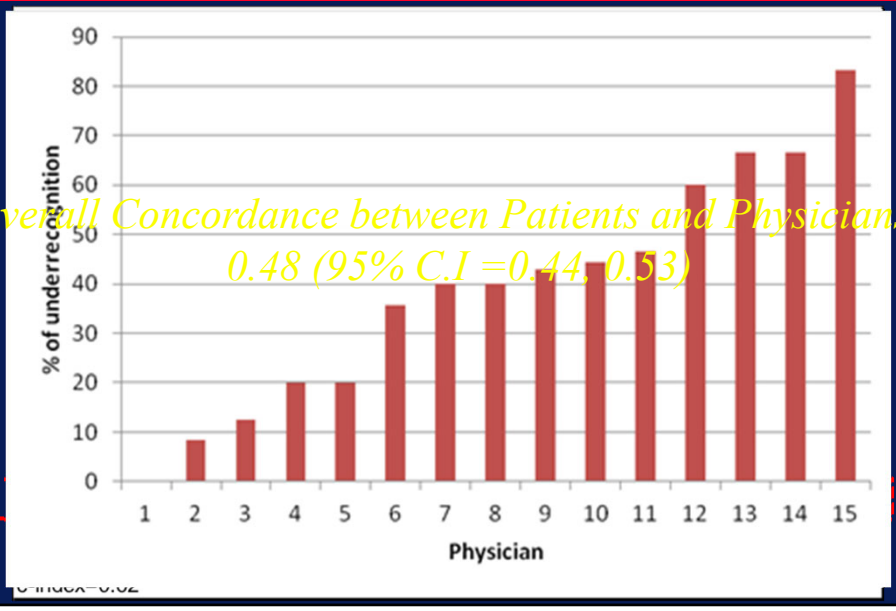
Predictors of Under-Recognition



Overall Concordance between Patients and Physicians = 0.48 (95% C.I =0.44, 0.53)

Very Accurate Compared to Daily Diaries

Distribution of Diary Responses to Each of the SAQ AF Questions

	Expected Diary Range	Median (IQR)
SAQ AF Q1: Over the past 4 weeks, on average, how many times have you had chest pain, chest tightness, or angina?		
≥4 times a day (n=7)	≥28	24.5 (13.3-25.7)
1-3 times a day (n=119)	7 to 21	9.3 (6.5-13.5)
≥3 times a week but not every day (n=232)	3 to 6	4.5 (3.3-6.7)
1-2 times per week (n=358)	1 to 2	2.5 (1.8-4.0)
Less than once per week (n=156)	>0 to <1	1.3 (0.8-2.5)
None in the last 4 weeks (n=45)	0	1.0 (0.0-1.8)
SAQ AF Q2: Over the past 4 weeks, on average, how many times have you had to take nitros (nitroglycerin tablets) for your chest pain, chest tightness, or angina?		
≥4 times a day (n=6)	≥28	26.5 (21.0-31.0)
1-3 times a day (n=70)	7 to 21	10.1 (6.0-12.5)
>3 times a week but not every day (n=181)	3 to 6	3.6 (2.3-5.8)
1-2 times per week (n=273)	1 to 2	1.6 (0.8-3.0)
Less than once per week (n=202)	>0 to <1	0.8 (0.3-1.3)
None in the last 4 weeks (n=184)	0	0.0 (0.0-0.5)

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

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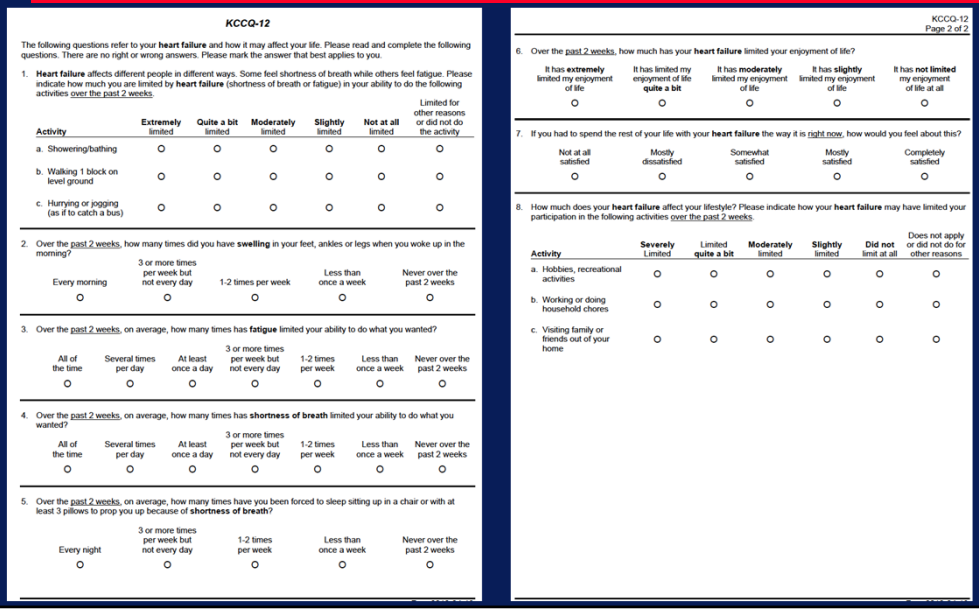
Improving the KCCQ's Feasibility



KCCQ-12

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Activity	Extremely limited	Quite a bit limited	Moderately limited	Slightly limited	Not at all limited	Limited for other reasons or did not do the activity
a. Showering/bathing	○	○	○	○	○	○
b. Walking 1 block on level ground	○	○	○	○	○	○
c. Hurrying or jogging (as if to catch a bus)	○	○	○	○	○	○

2. Over the past 2 weeks, how many times did you have **swelling** in your feet, ankles or legs when you woke up in the morning?

Every morning	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○

3. Over the past 2 weeks, on average, how many times has **fatigue** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○	○	○

4. Over the past 2 weeks, on average, how many times has **shortness of breath** limited your ability to do what you wanted?

All of the time	Several times per day	At least once a day	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○	○	○

5. Over the past 2 weeks, on average, how many times have you been forced to sleep sitting up in a chair or with at least 3 pillows to prop you up because of **shortness of breath**?

Every night	3 or more times per week but not every day	1-2 times per week	Less than once a week	Never over the past 2 weeks
○	○	○	○	○

KCCQ-12
Page 2 of 2

6. Over the past 2 weeks, how much has your **heart failure** limited your enjoyment of life?

It has **extremely** limited my enjoyment of life	It has limited my enjoyment of life **quite a bit**	It has **moderately** limited my enjoyment of life	It has **slightly** limited my enjoyment of life	It has **not limited** my enjoyment of life at all
○	○	○	○	○

7. If you had to spend the rest of your life with your **heart failure** the way it is right now, how would you feel about this?

Not at all satisfied	Mostly dissatisfied	Somewhat satisfied	Mostly satisfied	Completely satisfied
○	○	○	○	○

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

Activity	Severely Limited	Limited quite a bit	Moderately limited	Slightly limited	Did not limit at all	Does not apply or did not do for other reasons
a. Hobbies, recreational activities	○	○	○	○	○	○
b. Working or doing household chores	○	○	○	○	○	○
c. Visiting family or friends out of your home	○	○	○	○	○	○

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