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Validation of the Seattle Angina Questionnaire in Women with Ischemic Heart Disease

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Abstract

Background—Although the Seattle Angina Questionnaire (SAQ) has been widely used to assess disease-specific health status in patients with ischemic heart disease, it was originally developed in a predominantly male population and its validity in women has been questioned.

Methods—Using data from 8892 men and 4013 women across 2 multicenter trials and 5 registries, we assessed the construct validity, test-retest reliability, responsiveness to clinical change, and predictive validity of the SAQ Summary Score (SS) and its 5 subdomains (Physical Limitation (PL), Anginal Stability (AS), Angina Frequency (AF), Treatment Satisfaction (TS), and Quality of Life (QoL)) separately in men and women.

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Results—Comparable correlations of the SAQ SS with Canadian Cardiovascular Society class was demonstrated in both men and women (-0.48 for men, -0.46 for women). Similar correlations between the SAQ PL scale with treadmill exercise duration and Short Form-12 (SF-12) Physical Component Summary were observed in women and men (0.34 – 0.63 and 0.40 – 0.63 , respectively). SAQ AS scores were significantly lower for both men and women with acute syndromes compared with 1 month later. The SAQ AF scale was strongly correlated with daily angina diaries (0.62 for men and 0.66 for women). The SAQ QoL scores were moderately correlated with the EQ5D visual analog scale and SF-12 general health question in men (0.43 – 0.50) and women (0.33 – 0.39). All SAQ scales demonstrated excellent reliability (intraclass correlation 0.78) in both men and women with stable CAD and were very sensitive to change after percutaneous coronary intervention (15 -point difference in scores, standardized response mean 0.67). The SAQ SS was similarly predictive of 1-year mortality and cardiac re-hospitalizations for both men and women.

Conclusion—The SAQ demonstrates similar psychometric properties in men and women with CAD. These findings provide evidence for validity of the SAQ in assessing women with IHD.

INTRODUCTION

The primary treatment goals in patients with ischemic heart disease (IHD) are to optimize secondary prevention and to minimize patients' symptoms of angina, maximize their function, and optimize their quality of life. The 19-item Seattle Angina Questionnaire (SAQ), and its shorter 7-item version,¹ have been extensively used in clinical trials and registries to quantify patients' symptoms, functional status and quality of life.² Furthermore, it has been endorsed by the International Consortium for Health Outcomes Measurement as a standardized outcome measure for patients with coronary artery disease³ and has been proposed as a performance measure by CMS for percutaneous coronary interventions (PCI) in stable IHD.⁴ Despite the widespread acceptance of the SAQ, there have been periodic concerns about its validity in women^{5–7} because it was originally developed in a cohort of patients that was 84% men.⁸

Although the SAQ was designed to be applicable across sex, race, and socio-economic status,⁴ there are important differences in the presentation and outcomes of men and women with IHD that could interfere with the psychometrics of the instrument. Women present with IHD at a later age, have a higher prevalence of “atypical” symptoms, and have poorer exercise tolerance as compared with men.⁹ They also have poorer quality of life and a greater burden of ischemic symptoms for the same degree of obstructive disease in addition to an increased prevalence of non-obstructive coronary disease, which is associated with a greater risk of poor outcomes than men.^{10, 11} Collectively, these findings suggest a distinct “female pattern” of ischemia⁷ that could potentially undermine the validity of the SAQ.

Given that the therapeutic goal for both men and women is to maximize function, minimize angina, and optimize patients' quality of life,¹² being able to validly and reliably measure these outcomes in both men and women is important. Because of the differences in pathophysiology, symptoms, presentation and prognosis between men and women with

ischemic heart disease, and limited comparisons on the validity of the SAQ between women and men, we sought to explicitly validate the SAQ and its subdomains in women.

Methods

Seattle Angina Questionnaire

The SAQ is a 19-item self-administered questionnaire measuring health status in patients with IHD across 5 domains: physical limitation (PL), angina stability (AS), angina frequency (AF), treatment satisfaction (TS), and quality of life (QoL).⁸ All domain scores and a summary score (SS; derived from the PL, AF, and QoL domains) range from 0 to 100, with higher scores indicating less angina, fewer physical limitations due to angina, and better QoL. The 7-item version excludes the TS and AS domains.¹

Data sources

We used data from 2 trials and 5 longitudinal cohort studies that enrolled patients with IHD and collected the SAQ (Table 1).^{13–17} These studies included patients with different presentations of IHD; stable ischemic heart disease, patients undergoing coronary revascularization, and acute coronary syndromes (unstable IHD).

Construct Validity

Table 2 summarizes the comparisons used to establish the psychometric properties of the SAQ in men and women. These are further described below.

SAQ Summary Score

The SAQ SS were compared with Canadian Cardiovascular Society classification of angina (CCSC), which is a physician-reported measure of angina-associated limitation with classes ranging 0–IV and higher classes denoting angina with progressively lower degrees of exertion.¹⁸ To evaluate this, we assessed the correlation between SAQ summary score and CCSC for both men and women with stable IHD population (PREMIER registry at month 12), using Kendall Tau-b rank correlation coefficient.

Physical Limitation scale

The SAQ PL scale assesses the degree of physical limitation over the past 4 weeks due to various activities representing mild, moderate and severe exertion.⁸ We assessed the correlation of SAQ PL scores with exercise treadmill test duration and exercise capacity using Pearson's correlation in patients enrolled in the MERLIN trial where the patients' 8-month exercise treadmill tests were used to capture a stable IHD population. We also assessed the cross-sectional correlation of the SAQ PL scale with other assessments of physical capacity –the Physical Component Summary score (PCS) of the Short-Form 12 (SF-12) and the Canadian Cardiovascular Society classification of angina (CCSC)– in patients with stable and unstable IHD (AMI) (Table 2), using Pearson's correlation and Kendall Tau-b rank correlation.

Angina Stability Scale

The SAQ AS scale assesses the change in patient symptoms over the past 4 weeks, with a score of 50 representing no change and lower scores indicating a recent worsening of patients' angina, while higher scores indicate fewer symptoms compared with 4 weeks ago. We compared mean SAQ AS scores between patients with unstable IHD (unstable angina patients undergoing PCI in PRISM, AMI patients in TRIUMPH and PREMIER registries) and patients with stable IHD (follow-up scores 1 month later), using paired t-tests both for men and women. We hypothesized that scores in stable IHD patients would be higher than scores in unstable patients.

Angina Frequency Scale

The SAQ AF scale measures the frequency of angina symptoms over the past 4 weeks with higher scores representing lesser angina burden. This domain has been previously validated against daily angina and sublingual nitroglycerin use with no difference between sexes.¹⁹ TERISA trial included patients with type 2 diabetes and stable angina wherein SAQ questionnaires and electronic angina diary responses were collected at study entry and 8 weeks (study end) or study withdrawal. The responses to the 2 SAQ angina frequency questions were correlated with angina diary responses of angina frequency and sublingual nitroglycerin use over previous 4 weeks at study end or week 8 using Spearman's correlation coefficient. The results of correlation stratified by sex are reproduced here.¹⁹

Treatment Satisfaction Scale

The SAQ TS scale evaluates the level of satisfaction with the treatment of the patient's angina. We compared SAQ TS scores with a separately-administered patient satisfaction questionnaire. Patients with AMI who were enrolled in the TRIUMPH registry were asked the following questions at 12 months: "Q1: How well does your doctor or care provider know you and your medical condition?" and "Q2: How good is your doctor or care provider or his or her staff at following up with you on appointment and test results?" Patients' responses were captured on a 5-point Likert scale, and dichotomized as "satisfied" (extremely well, fairly well) and "not satisfied" (somewhat well, not very well, not at all). For both men and women, SAQ TS scores were compared between those patients who were and were not satisfied using two-tailed t-tests.

Quality of Life scale

The SAQ QoL scale assesses how the patient perceives their CAD to be impacting his or her QoL. The SAQ QoL was compared with the general health question of the SF-12 ("how well is your general health?") and the Euro-Quality of Life Visual Analog Scale (EQ-5D VAS). We assessed these correlations separately for men and women, in different CAD states (stable CAD and elective PCI population) using Kendall Tau-b rank and Pearson's correlation coefficient.

Construct validity for patients with Myocardial infarction with non-obstructive coronary arteries (MINOCA)

Women are more likely to present with a distinct phenotype of non-obstructive ischemic heart disease, including Myocardial Infarction with non-obstructive coronary arteries (MINOCA).^{20, 21} To assess the construct validity of the SAQ in this population, we conducted a sub-analysis of patients presenting with myocardial infarction with absence of obstructive coronary artery disease (<50% left main or <70% any epicardial coronary stenosis) enrolled in the TRIUMPH and PREMIER AMI registries. We compared baseline SAQ PL, SAQ QoL and SAQ summary scores with SF-12 PCS, SF-12 general health question and CCSC using Pearson's correlation and Kendall Tau-b rank correlation coefficient.

Predictive Validity

Predictive validity was assessed by comparing the associations in men and women of SAQ scores (SS, AF, PL, and QOL domains) 1 month after an AMI with 12-month mortality and rehospitalization for acute coronary syndromes in the TRIUMPH study. Hazard ratios and 95% confidence intervals were calculated for ranges of the SAQ Scores; 0–49 (poor to fair), 50–74 (fair to good) and 75–100 (good to excellent)) using Cox proportional hazards models. C-statistics were calculated to assess discrimination for each subdomain in men and women.

Test-retest Reliability

Reliability was assessed in the PRESS study, where SAQ scores were collected monthly for 6 months after PCI. We compared the change in SAQ scores and the intraclass correlation coefficient between months 5 and 6 among clinically stable patients (defined as no ACS or repeat revascularization between months 5 and 6). Intra-class correlations describe the proportion of variability in scores due to between-patient differences compared to within-patient differences and range from 0–1 and higher intra-class correlations indicate greater reliability. Angina Stability scores were not compared for test-retest reliability as this metric represents a change in patient angina burden over the past 4 weeks and is therefore not appropriate for longitudinal analysis.

Responsiveness to Clinical Change

Responsiveness was assessed by comparing SAQ scores before and 1 month after PCI in the PRISM study, as this is a period where significant gains in health status are expected. As above, Angina Stability scores were not analyzed for this psychometric property, as changes in change scores are not readily interpretable. We calculated the mean (SD) change in scores and standardized response means (SRM; mean change/SD of change) for both men and women. Larger SRMs indicated greater responsiveness and an SRM > 0.8 is considered a large clinical change.

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RESULTS

Our analytic cohort was derived from 2 multinational clinical trials (MERLIN-TIMI 36 and TERISA) and 5 prospective registries (PRESS, OPS, PRISM, PREMIER, and TRIUMPH; Table 1). These studies included 8729 patients who were hospitalized with an acute coronary syndrome (5913 men and 2816 women), 2736 patients who underwent PCI (1964 men and 772 women) and 917 patients with stable angina (563 men and 354 women). Across all data sources, SAQ scores were available for 8440 men and 3952 women.

Construct Validity

SAQ Summary score—The SAQ SS showed strong correlations with CCS class in 1878 patients with stable IHD for both men and women, with correlations of -0.48 and -0.46 , respectively (Table 3).

SAQ Physical Limitation—For 1902 patients with stable IHD, the cross-sectional correlations between SAQ PL scores and both exercise duration and exercise capacity (METs) were moderately strong and similar for men and women (exercise duration correlations: men= 0.40 vs. women= 0.34 ; exercise capacity: men= 0.35 vs. women= 0.28 ; Table 4). The correlations between SAQ PL and the SF-12 PCS and CCSC were also moderately strong (correlation ranging from 0.51 to 0.63 for men and 0.59 to 0.63 for women) and similar for both men and women in stable and unstable (AMI) IHD settings (Table 4).

SAQ Angina Stability—Patients with unstable disease (i.e., presenting with MI or unstable angina) had significantly lower SAQ AS scores than the same patients 1 month later, and these differences were similar between men and women (men (n=3652): 43.2 ± 23.7 vs. 55.8 ± 18.6 ; $p < 0.0001$; women (n=1751): 41.4 ± 24.4 vs. 55.7 ± 19.7 , $p < 0.0001$).

SAQ Anginal Frequency—SAQ AF domain was previously validated in patients with stable angina in the TERISA trial, which enrolled 563 men and 354 women.¹⁹ The SAQ AF question responses were strongly correlated with daily angina diaries (correlation= 0.62 for men and 0.66 for women) and SL nitroglycerin use (0.67 for men and 0.73 for women).¹⁹

SAQ Treatment Satisfaction—Patients with stable IHD who reported being unsatisfied on the generic questions had lower SAQ TS scores than those who reported being satisfied, with similar differences in men and women (men (n=1568): Q1 89.5 ± 16.7 vs. 94.9 ± 10.3 , $p = 0.0004$; Q2: 85.7 ± 18.1 vs. 95.1 ± 10.1 , $p < 0.0001$; women (n=782) Q1: 83.7 ± 18.9 vs. 93.5 ± 12.4 , $p < 0.0001$; Q2: 80.5 ± 24.8 vs. 93.6 ± 11.43 , $p < 0.0001$).

SAQ Quality of Life—In patients with stable IHD, SAQ QoL scores had moderately strong correlations with the EQ5D visual analog scale and the SF-12 general health question (men: 0.50 and 0.43 ; women: 0.34 and 0.33 ; Table 5). The statistically significant correlations between the SAQ QoL scale and these general QoL scales were lower in women compared with men.

Myocardial infarction with non-obstructive coronaries (MINOCA)—In patients presenting with myocardial infarction but no evidence of obstructive coronaries on angiography, SAQ PL score, SAQ QoL score and SAQ summary scores showed moderately strong correlation which were similar in men and women with SF-12 PCS score (men: 0.63 and women: 0.64), SF-12 general health question (men: 0.41 and women: 0.42) and CCSC class (men: −0.55 and women: −0.52) respectively.

Predictive validity

The SAQ SS, AF, PL, and QoL domain scores demonstrated a graded inverse relationship with 12-month mortality and acute coronary syndrome rehospitalization for both men and women (Table 7). The PL scale was most strongly associated with 12-month mortality, particularly for women ($c=0.57$ for men and 0.77 for women), whereas all 3 domains and the summary score with similarly associated with risk of cardiac rehospitalization ($c=0.59$ to 0.60).

Test-retest Reliability

Among patients with stable IHD, the reliability of the SAQ domain and summary scores was excellent (ICC 0.78 , mean change of < 2.5 points for all scores) in both men and women (Table 8).

Responsiveness to clinical change

Among patients undergoing PCI, all SAQ domains, except TS, were highly responsive to the improvements in patients' health status after PCI in both men and women. A 15-point mean difference in scores (SRM 0.67 ; Table 8) was seen for all domains, although women had a greater change in SAQ PL score after PCI as compared with men (24.6 ± 28.6 vs. 17.5 ± 22.7). SAQ TS scores were high for both men and women at baseline (men = 93.7 ± 10.9 , women = 92.5 ± 11.5), as would be expected before and after revascularization.

The psychometric properties and results of the shorter version of SAQ, SAQ-7 were similar in men and women, and are presented in Supplement Tables 2–6.

DISCUSSION

Cardiovascular disease in women has historically received less attention^{7, 22}, despite the increased cost, morbidity, and mortality associated with it.^{11, 23, 24} As the health care landscape moves towards rewarding value, quality, and patient-centered care, patient-reported outcomes are becoming increasingly important. Instruments, such as the SAQ, that assess the impact of ischemic heart disease on patient's symptoms, function, and quality of life are ideally suited to become performance measures and tools to improve the quality of clinical care. However, the psychometric validation studies for the SAQ were performed in a predominantly male population primarily enrolled from Veteran's Affairs hospitals.^{8, 25} As such, even though the SAQ has been widely used to measure patient's health-related quality of life in multiple trials, registries, and clinical practice, a lack of explicit validation of the SAQ in women has been perceived as a weakness.⁷ While there has been some prior work with factor-analysis in 175 women with stable angina showing good internal consistency and

reliability of the SAQ in women, there has never been a comprehensive comparison of the psychometric properties of the SAQ between men and women.⁵ In the current study, we explicitly examined the psychometric properties of the SAQ, using patient data from multiple trials and prospective registries representing various different presentations of IHD, and found comparable performance in both men and women.

Women with cardiovascular disease have several notable differences in their presentation, symptoms, time to diagnosis, functional status and prognosis as compared with men.^{7, 9, 11} Anginal symptoms in women are often “atypical,” defined by lack of exertional component or unusual prodromal symptoms such as fatigue, sleep problems and shortness of breath.^{26, 27} Women have also been described to have a greater symptom burden, present more often for evaluation of their symptoms, but to be at a higher risk for delayed and under-diagnosis of their disease, although a recent study did not identify sex to be a significant predictor of under-recognition in a stable outpatient cohort with known IHD.^{9, 28} Thus, it is critically important to identify tools that could standardize angina symptom reporting by women and accurately quantify changes in symptoms with treatment. We found that the SAQ is not only good at identifying angina-related symptom severity, frequency, and the stability in women, but it was also highly reproducible in women with stable disease and highly sensitive to change when a clinical change occurs.

In examining the construct validity of the different SAQ scales, only the SAQ QoL score showed lower correlations with the selected criterion standards in women compared to men. In both the TRIUMPH and PRISM studies, used for these comparisons, the burden of comorbid conditions was greater in women than in men. Thus the generic health status questionnaires may be capturing the impact of these comorbidities in women, thus decreasing the strength of the associations between disease-specific and overall health status in women. Nevertheless, the SAQ QoL domain had similar reproducibility, responsiveness to change, and predictive validity between men and women, which suggests that it is a very good measure of the impact of IHD on women’s health status.

Patient-reported outcomes, such as the SAQ, are increasingly being advocated for use to measure the patient-centeredness and quality of care.^{2, 3} Accordingly, the 7-item version of SAQ has been proposed as a performance measure by CMS for PCI in stable IHD.⁴ Our study provides comprehensive evidence that the SAQ is a valid patient-reported instrument that reliably helps capture the symptoms, functional status and quality of life related to angina, while also providing useful prognostic information in women with CAD. The SAQ can be used as a quick, inexpensive, and reliable instrument to assess the sex-related disparities in symptoms, presentation, management, and outcomes related to ischemic heart disease in a standardized manner.

Our study should be interpreted in the context of the following potential limitations. First, there is no gold standard for quantifying the impact of IHD on patients’ symptoms, function, and QoL. We therefore had to rely on other measures, such as the SF-12 and physician-assigned CCSC, as our comparison standards. As such, it is important to note that we do not expect perfect correlations of the SAQ with these measures, as the SAQ is capturing something distinct from these measures. Second, the SAQ only includes questions regarding

angina symptoms, while women are more likely to present with shortness of breath or silent ischemia and therefore might respond differently to these questions. However, despite this theoretical concern, we were able to demonstrate that the SAQ performs similarly well in men and women across multiple different clinical settings. Nevertheless, we cannot exclude the possibility that the inclusion of other questions might further improve the performance of a disease-specific health status measure in women, although it would also have to be proven to similarly quantify the impact of IHD on men. There is increasing data supporting a distinct phenotype of ischemic heart disease in women, one associated with increased cardiovascular risk despite non-obstructive coronary disease,²¹ which might not have been captured in its entirety in the registries and trials used in this study. For example, we were able to identify a population of patients with MINOCA, but did not have data on patients with stable chest pain considered to be myocardial ischemia who were documented to not have obstructive coronary disease. Ongoing studies, such as the CIAO (NCT02347215) and the WARRIOR (NCT03417388) will provide additional opportunities to validate the SAQ in more stable patients without obstructive coronary disease. Nevertheless, a large recent study of young men and women with myocardial infarction showed that men and women present in a similar manner with chest pain as the predominant symptom, with women having greater non-chest pain symptoms in addition.²⁹ Also, our analyses showing comparable validity in MINOCA patients suggests that it works well in this population.

In conclusion, across a large number of patients with IHD in a broad range of clinical settings, analyses we found comparable psychometric performance of the SAQ in both men and women with CAD. These findings provide evidence for validity of the SAQ in assessing women with CAD and support its use in observational studies, clinical trials and for quality assessment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Chan PS, Jones PG, Arnold SA, Spertus JA. Development and validation of a short version of the Seattle angina questionnaire. *Circ Cardiovasc Qual Outcomes*. 2014; 7(5):640–7. [PubMed: 25185249]
2. Rumsfeld JS, Alexander KP, Goff DC Jr, Graham MM, Ho PM, Masoudi FA, et al. Cardiovascular health: the importance of measuring patient-reported health status: a scientific statement from the American Heart Association. *Circulation*. 2013; 127(22):2233–49. [PubMed: 23648778]
3. McNamara RL, Spatz ES, Kelley TA, Stowell CJ, Beltrame J, Heidenreich P, et al. Standardized Outcome Measurement for Patients With Coronary Artery Disease: Consensus From the International Consortium for Health Outcomes Measurement (ICHOM). *J Am Heart Assoc*. 2015; 4(5)
4. [Last accessed March 17, 2018] https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/MMS/Downloads/Hospital-Level-PRO-Based-PM-for-Patients-Undergoing-non-Emergent-PCI_Public-Comment-Summary-Report.pdf
5. Kimble LP, Dunbar SB, Weintraub WS, McGuire DB, Fazio S, De AK, et al. The Seattle angina questionnaire: reliability and validity in women with chronic stable angina. *Heart Dis*. 2002; 4(4): 206–11. [PubMed: 12147179]
6. Thompson DR, Ski CF, Garside J, Astin F. A review of health-related quality of life patient-reported outcome measures in cardiovascular nursing. *Eur J Cardiovasc Nurs*. 2016; 15(2):114–25. [PubMed: 27006403]
7. Pepine CJ. Ischemic heart disease in women: facts and wishful thinking. *Journal of the American College of Cardiology*. 2004; 43(10):1727–1730. [PubMed: 15145090]
8. Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Prodzinski J, McDonell M, et al. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. *J Am Coll Cardiol*. 1995; 25(2):333–41. [PubMed: 7829785]
9. Shaw LJ, Bairey Merz CN, Pepine CJ, Reis SE, Bittner V, Kelsey SF, et al. Insights from the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) Study: Part I: gender differences in traditional and novel risk factors, symptom evaluation, and gender-optimized diagnostic strategies. *J Am Coll Cardiol*. 2006; 47(3 Suppl):S4–S20. [PubMed: 16458170]
10. Gulati M, Cooper-DeHoff RM, McClure C, Johnson BD, Shaw LJ, Handberg EM, et al. Adverse cardiovascular outcomes in women with nonobstructive coronary artery disease: a report from the Women's Ischemia Syndrome Evaluation Study and the St James Women Take Heart Project. *Arch Intern Med*. 2009; 169(9):843–50. [PubMed: 19433695]
11. Bairey Merz CN, Shaw LJ, Reis SE, Bittner V, Kelsey SF, Olson M, et al. Insights from the NHLBI-Sponsored Women's Ischemia Syndrome Evaluation (WISE) Study: Part II: gender differences in presentation, diagnosis, and outcome with regard to gender-based pathophysiology of atherosclerosis and macrovascular and microvascular coronary disease. *J Am Coll Cardiol*. 2006; 47(3 Suppl):S21–9. [PubMed: 16458167]
12. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *Circulation*. 2012; 126(25):e354–471. [PubMed: 23166211]
13. Morrow DA, Scirica BM, Karwatowska-Prokopczuk E, Murphy SA, Budaj A, Varshavsky S, et al. Effects of ranolazine on recurrent cardiovascular events in patients with non-ST-elevation acute coronary syndromes: the MERLIN-TIMI 36 randomized trial. *JAMA*. 2007; 297(16):1775–83. [PubMed: 17456819]
14. Kosiborod M, Arnold SV, Spertus JA, McGuire DK, Li Y, Yue P, et al. Evaluation of ranolazine in patients with type 2 diabetes mellitus and chronic stable angina: results from the TERISA randomized clinical trial (Type 2 Diabetes Evaluation of Ranolazine in Subjects With Chronic Stable Angina). *J Am Coll Cardiol*. 2013; 61(20):2038–45. [PubMed: 23500237]

15. Spertus JA, Peterson E, Rumsfeld JS, Jones PG, Decker C, Krumholz H. The Prospective Registry Evaluating Myocardial Infarction: Events and Recovery (PREMIER)--evaluating the impact of myocardial infarction on patient outcomes. *Am Heart J.* 2006; 151(3):589–97. [PubMed: 16504619]
16. Arnold SV, Chan PS, Jones PG, Decker C, Buchanan DM, Krumholz HM, et al. Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status (TRIUMPH): design and rationale of a prospective multicenter registry. *Circ Cardiovasc Qual Outcomes.* 2011; 4(4):467–76. [PubMed: 21772003]
17. Spertus JA, Bach R, Bethea C, Chhatrwalla A, Curtis JP, Gialde E, et al. Improving the process of informed consent for percutaneous coronary intervention: patient outcomes from the Patient Risk Information Services Manager (ePRISM) study. *Am Heart J.* 2015; 169(2):234–241. e1. [PubMed: 25641532]
18. Campeau L. Letter: Grading of angina pectoris. *Circulation.* 1976; 54(3):522–3.
19. Arnold SV, Kosiborod M, Li Y, Jones PG, Yue P, Belardinelli L, et al. Comparison of the Seattle Angina Questionnaire With Daily Angina Diary in the TERISA Clinical Trial. *Circ Cardiovasc Qual Outcomes.* 2014; 7(6):844–50. [PubMed: 25249560]
20. Beltrame JF. Assessing patients with myocardial infarction and nonobstructed coronary arteries (MINOCA). *J Intern Med.* 2013; 273(2):182–5. [PubMed: 22998397]
21. Garcia M, Mulvagh SL, Merz CN, Buring JE, Manson JE. Cardiovascular Disease in Women: Clinical Perspectives. *Circ Res.* 2016; 118(8):1273–93. [PubMed: 27081110]
22. Bairey Merz CN, , Andersen H, , Sprague E, , Burns A, , Keida M, , Walsh MN. , et al. The Women's Heart Alliance 2017 Knowledge, Attitudes, and Beliefs Regarding Cardiovascular Disease in Women.
23. Gupta A, Wang Y, Spertus JA, Geda M, Lorenze N, Nkonde-Price C, et al. Trends in acute myocardial infarction in young patients and differences by sex and race, 2001 to 2010. *Journal of the American College of Cardiology.* 2014; 64(4):337–345. [PubMed: 25060366]
24. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Heart disease and stroke statistics-2013 update. *Circulation.* 2013; 127(1)
25. Spertus JA, Jones P, McDonnell M, Fan V, Fihn SD. Health status predicts long-term outcome in outpatients with coronary disease. *Circulation.* 2002; 106(1):43–9. [PubMed: 12093768]
26. Douglas PS, Ginsburg GS. The evaluation of chest pain in women. *N Engl J Med.* 1996; 334(20):1311–5. [PubMed: 8609950]
27. McSweeney JC, Cody M, O'Sullivan P, Elbersson K, Moser DK, Garvin BJ. Women's early warning symptoms of acute myocardial infarction. *Circulation.* 2003; 108(21):2619–23. [PubMed: 14597589]
28. Arnold SV, Grodzinsky A, Gosch KL, Kosiborod M, Jones PG, Breeding T, et al. Predictors of Physician Under-Recognition of Angina in Outpatients With Stable Coronary Artery Disease. *Circ Cardiovasc Qual Outcomes.* 2016; 9(5):554–9. [PubMed: 27531922]
29. Lichtman JH, Leifheit EC, Safdar B, Bao H, Krumholz HM, Lorenze NP, et al. Sex Differences in the Presentation and Perception of Symptoms Among Young Patients With Myocardial Infarction: Evidence from the VIRGO Study (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients). *Circulation.* 2018; 137(8):781–790. [PubMed: 29459463]

Table 1

Data sources

Study	Patient Population	Enrollment Time Frame	Number of patients	Time of SAQ assessments
MERLIN-TIMI 36	Multinational Randomized controlled trial of patients with NSTEMI-ACS	2004–2007	6560	Baseline, 4, 8, 12 months
TERISA	Multinational Randomized Controlled trial of patients with Type 2 Diabetes and chronic stable angina	2011–2012	917	Baseline, 8 weeks or study termination
PRESS	Single-center prospective PCI registry	1999	255	Baseline, 1, 2, 3, 4, 5, 6 mo
OPS	3-center prospective PCI registry	2009–2011	1901	Baseline, 6, 12 mo
PRISM	6-center prospective PCI registry	2010–2011	1398	Baseline, 1, 6, 12 mo
PREMIER	19-center prospective acute MI registry	2003–2004	2498	Baseline, 1, 6, 12 mo
TRIUMPH	24-center prospective acute MI registry	2005–2008	4340	Baseline, 1, 6, 12 mo

MERLIN (Metabolic Efficiency with Ranolazine for Less Ischemia in Non–ST-elevation acute coronary syndromes); TERISA (Type 2 Diabetes Evaluation of Ranolazine in Subjects With Chronic Stable Angina); PRESS (Post-Revascularization Recovery and Survival Study); OPS (Outcomes of PCI Study); PRISM (Patient Risk Information Services Manager); PREMIER (Prospective Registry Evaluating Outcomes after Myocardial Infarction: Events and Recovery); TRIUMPH (Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status)

Table 2

Analyses, Settings and Cohorts Used for Validation of SAQ

Objective	Reference measure	Analyses performed	Clinical settings analyzed (study, assessment)
Construct validity			
SAQ summary score	CCSC	Mean $\pm$ SD; R ² ; Kendall Tau-b rank correlation	Stable IHD (PREMIER month 12)
SAQ Physical limitation	ETT duration and exercise capacity in METS, SF-12 PCS, CCSC	Mean $\pm$ SD; Pearson's and Kendall Tau-b rank correlation	Stable IHD (MERLIN month 8, TRIUMPH/PREMIER month 12) Unstable IHD (Acute MI- TRIUMPH/PREMIER baseline)
SAQ Angina Stability	Difference in the score in unstable disease (PCI, AMI patients) and stable disease (follow-up scores during a stable state)	Paired t-test	Unstable (elective PCI OPS/PRISM baseline with diagnosis of unstable angina and acute MI (TRIUMPH/PREMIER baseline) Stable: scores at month 1 in above patients
SAQ Angina Frequency	Angina Diary and Sublingual Nitroglycerin use	Mean $\pm$ SD; Spearman's correlation	Stable IHD (TERISA cross-sectional week 8)
SAQ Treatment Satisfaction	Doctor satisfaction questionnaire	Mean $\pm$ SD	Stable IHD (TRIUMPH month 6 and 12)
SAQ Quality of Life	EQ5D VAS, SF-12 question 1	Mean $\pm$ SD; Pearson's and Kendall Tau-b rank correlation	Stable IHD (OPS/PRISM and TRIUMPH/PREMIER month 12)
Reliability	1 month change in SAQ scores	Mean $\pm$ SD; intraclass-correlation	Stable IHD (PRESS months 5 and 6)
Responsiveness to clinical change	1 month change in SAQ post-PCI	Mean $\pm$ SD of change, standardized response mean	Elective PCI (OPS/PRISM baseline, 1 month)
Predictive validity	1 year all-cause mortality, 1 year ACS hospitalization	C statistic	Post-MI (TRIUMPH month 1)

Table 3

Sex-specific construct validity of SAQ summary score

	Stable IHD (PREMIER mo 12) SAQ summary score	
CCSC class	Men (n=1276) Mean $\pm$ SD	Women (n=602) Mean $\pm$ SD
0	95 $\pm$ 7	94 $\pm$ 8
I	76 $\pm$ 14	72 $\pm$ 17
II	71 $\pm$ 15	67 $\pm$ 22
III	56 $\pm$ 16	57 $\pm$ 18
IV	54 $\pm$ 22	49 $\pm$ 19
Kendall Tau-b rank correlation coefficient	-0.48 P<0.0001	-0.46 P <0.0001

Table 4

Sex-specific construct validity of the SAQ Physical Limitation (PL) subdomain

	Setting	Men		Women	
		Mean $\pm$ SD SAQ PL score	Correlation coefficient (N)	Mean $\pm$ SD SAQ PL score	Correlation coefficient (N)
Exercise treadmill duration	Stable IHD (MERLIN mo 8)	79.5 $\pm$ 21.2	0.40 (N=1339)	80.0 $\pm$ 22.5	0.34 (N=563)
Exercise capacity (METs)	Stable IHD (MERLIN mo 8)	79.5 $\pm$ 21.2	0.35 (N=1339)	80.0 $\pm$ 22.5	0.28 (N=563)
SF-12 PCS	Stable IHD (TRIUMPH/PREMIER 12m)	94.6 $\pm$ 5.1	0.51 (N=2506)	90.7 $\pm$ 19.6	0.59 (N=932)
SF-12 PCS	Unstable IHD (Acute MI-TRIUMPH/PREMIER BL)	87.2 $\pm$ 21.3	0.63 (N=3988)	79.3 $\pm$ 6.6	0.63 (N=1708)
CCSC	Stable IHD (PREMIER 12m)	95.8 $\pm$ 12.9	-0.55 (N=1047)	93.5 $\pm$ 6.9	-0.56 (N=384)

p-values for all correlations <0.0001;

SF-12 PCS: Short Form-12 Physical Component Summary, CCSC: Canadian Cardiovascular Society Classification, METs: Metabolic Equivalents

Table 5

Sex-specific construct validity of SAQ Quality of Life (QOL) subdomain

	Settings	Men		Women	
		Mean $\pm$ SD SAQ QOL scores	Pearson's correlation coefficient (N)	Mean $\pm$ SD SAQ QOL scores	Pearson's correlation coefficient (N)
EQ5D VAS	Stable IHD (OPS/PRISM 12m)	81.8 $\pm$ 18.6	0.50 (N=1557)	77.9 $\pm$ 19.4	0.34 (N=607)
SF-12 question 1	Stable IHD (TRIUMPH/PREMIER 12m)	84.2 $\pm$ 19.0	0.43 (N= 3034)	80.4 $\pm$ 21.4	0.33 (N=1477)

p-values for all correlations <0.0001

EQ5D VAS: Euro QOL 5 Dimension Visual Analog Scale; SF-12: Short Form-12 Q1: "how well is your general health?", CCSC: Canadian Cardiovascular Society Classification of angina

Table 6

Sex-specific construct validity of SAQ in patients presenting with myocardial infarction with non-obstructive coronaries (MINOCA) enrolled in the TRIUMPH/PREMIER myocardial infarction registries at baseline

SAQ	Reference measure	Men		Women	
		Mean $\pm$ SD SAQ score	Correlation coefficient (N)	Mean $\pm$ SD SAQ PL score	Correlation coefficient (N)
SAQ PL	SF-12 PCS	82.74 $\pm$ 24.54	0.63 (N=146)	85.73 $\pm$ 24.07	0.64 (N=174)
SAQ QOL	SF-12 question1	59.48 $\pm$ 25.27	0.41 (N=146)	61.30 $\pm$ 23.11	0.42 (N=174)
SAQ SS	CCSC	75.76 $\pm$ 18.79	-0.55* (N=159)	77.90 $\pm$ 18.04	-0.52* (N=214)

p-values for all correlations <0.0001;

SF-12 PCS: Short Form-12 Physical Component Summary, SF-12: Short Form-12 Q1: "how well is your general health?", CCSC: Canadian Cardiovascular Society Classification. Correlations assessed using Pearson's correlation except * where Kendall Tau-b rank correlation was used.

Table 7

Sex-specific predictive validity of SAQ

	12-month mortality		12-month Cardiac Rehospitalization	
	Men (N=1956)	Women (N=984)	Men (N=1703)	Women (N=855)
Physical limitation				
Poor to fair (0 to <50)	3.1 (1.3, 7.0)	9.1 (3.5, 23.7)	2.4 (1.5, 4.0)	2.7 (1.6, 4.8)
Good (50 to <75)	1.4 (0.6, 3.5)	1.2 (0.3, 6.1)	2.1 (1.4, 3.1)	1.4 (0.7, 2.7)
Excellent (75 to 100)	Ref	Ref	Ref	Ref
C statistic	0.57	0.77	0.60	0.64
Anginal frequency				
Poor to fair (0 to <50)	1.9 (0.6, 6.1)	2.4 (0.9, 6.8)	2.5 (1.2, 5.0)	3.6 (1.8, 7.2)
Good (50 to <75)	1.3 (0.6, 2.6)	0.9 (0.4, 2.2)	2.3 (1.6, 3.4)	1.9 (1.2, 3.0)
Excellent (75 to 100)	Ref	Ref	Ref	Ref
C statistic	0.53	0.52	0.59	0.60
Quality of life				
Poor to fair (0 to <50)	1.8 (0.9, 3.5)	1.0 (0.5, 2.3)	2.8 (1.9, 4.1)	2.1 (1.3, 3.4)
Good (50 to <75)	1.3 (0.7, 2.3)	1.1 (0.5, 2.2)	1.3 (0.9, 1.8)	1.4 (0.9, 2.3)
Excellent (75 to 100)	Ref	Ref	Ref	Ref
C statistic	0.52	0.54	0.59	0.59
SAQ Summary score				
Poor to fair (0 to <50)	2.4 (1.1, 5.2)	2.0 (0.9, 4.6)	2.9 (1.8, 4.8)	3.1 (1.8, 5.2)
Good (50 to <75)	1.3 (0.7, 2.5)	1.5 (0.8, 2.9)	2.0 (1.4, 2.9)	1.8 (1.2, 2.8)
Excellent (75 to 100)	Ref	Ref	Ref	Ref
C statistic	0.56	0.59	0.61	0.62

Numbers in each cell represent Hazard Ratios for the outcome (95% confidence intervals) with excellent health status (SAQ summary and subdomain scores between 75–100) as the reference. SAQ scores used were collected 1 month post-AMI as we wanted scores representing stable disease.

Table 8

Reliability and responsiveness of SAQ to clinical change, according to patient sex.

Reliability (change from 5m to 6m in stable patients)				
	Men (n=115)		Women (n=50)	
SAQ domain	Mean change $\pm$ SD	ICC ¹	Mean change $\pm$ SD	ICC ¹
Physical limitation	-0.1 $\pm$ 10.8	0.88	-0.3 $\pm$ 14.4	0.82
Angina frequency	0.6 $\pm$ 13.1	0.78	1.2 $\pm$ 14.2	0.79
Treatment satisfaction	0.1 $\pm$ 10.7	0.80	1.1 $\pm$ 10.4	0.84
Quality of life	-0.6 $\pm$ 11.7	0.84	2.3 $\pm$ 12.1	0.88
Summary score	0.1 $\pm$ 9.7	0.86	1.5 $\pm$ 10.1	0.88
Responsiveness to change (change from before PCI to 1m after PCI)				
	Men (n=770)		Women (n=277)	
SAQ domain	Mean change $\pm$ SD	SRM ²	Mean change $\pm$ SD	SRM ²
Physical limitation	17.5 $\pm$ 22.7	0.77	24.6 $\pm$ 28.6	0.86
Angina frequency	21.3 $\pm$ 25.4	0.84	21.0 $\pm$ 24.7	0.85
Treatment satisfaction	-0.2 $\pm$ 11.6	-0.02	0.8 $\pm$ 13.9	0.06
Quality of life	21.6 $\pm$ 27.0	0.80	19.6 $\pm$ 29.4	0.67
Summary score	20.0 $\pm$ 20.6	0.97	19.8 $\pm$ 22.2	0.89

¹ICC (Intraclass correlation) = variability in scores due to between-patient differences (higher=more reliable).²SRM (Standardized response mean) = mean change divided by SD of change (higher = more responsive).