ORIGINAL ARTICLE

Population-Based Screening for Chronic Obstructive Pulmonary Disease Using the St. George's Respiratory Questionnaire in Resource-Limited Settings

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Abstract

Rationale: Spirometry, although necessary for the diagnosis of chronic obstructive pulmonary disease (COPD), remains a scarce and costly resource worldwide. Screening questionnaires may help to bridge the diagnostic gap.

Objectives: We evaluated the performance of the St. George's Respiratory Questionnaire (SGRQ) as a screening tool using spirometry-confirmed COPD as a gold standard.

Methods: We screened adults aged 40 years and older for COPD in Bhaktapur, Nepal; Lima, Peru; and Nakaseke, Uganda. Participants completed SGRQs and prebronchodilator peak expiratory flow (PEF). We defined COPD as a postbronchodilator FEV_1/FVC *Z*-score less than −1.645, evaluated the discriminative performance of the SGRQ using receiver operating characteristic curves, and identified the best threshold to screen for spirometry-confirmed COPD.

Measurements and Main Results: We screened 10,709 participants (mean age, 56.3 yr; 49.7% male; 15.4% current smokers). After exclusion for missing data and implausible values, we analyzed the data of 10,008 (94%) participants. Prevalence of spirometry-confirmed COPD was 9.5%; mean SGRQ scores were 7.9 points (SD = 11.9) for the total population, 20.3 points (SD = 19.4) for participants with COPD, and 6.6 points (SD = 9.9) for participants without COPD. The area under the curve for SGRQ as a screening tool for COPD was 0.77 (95% confidence interval, 0.75–0.79), and the best threshold was 10.75 points. When the SGRQ was combined with prebronchodilator PEF stratified by sex, the area under the curve increased to 0.84 (95% confidence interval, 0.82–0.85). A screening test that combined a total SGRQ score of 12 points and higher and/or prebronchodilator PEF <400 L/min for men and <250 L/min for women yielded a sensitivity of 91%, a specificity of 47%, and negative predictive value of 98% to identify spirometry-confirmed COPD.

Conclusions: SGRQ is an alternative screening tool for spirometry-confirmed COPD. Screening with the SGRQ in combination with PEF may help to identify people at risk for COPD in resource-limited settings where spirometry is not readily available.

Keywords: COPD; diagnosis; low- and middle-income countries

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A complete list of GECo study investigators members may be found before the beginning of the References.

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At a Glance Commentary

Scientific Knowledge on the Subject: Spirometry, although necessary for the diagnosis of chronic obstructive pulmonary disease (COPD), remains a scarce and costly resource worldwide. Screening questionnaires may help to bridge the diagnostic gap.

What This Study Adds to the Field: The St. George's Respiratory Questionnaire is a simple, inexpensive, and efficient screening tool for spirometry-confirmed COPD. Screening with the St. George's Respiratory Questionnaire in combination with peak expiratory flow may help to identify people at risk for COPD in resource-limited settings where spirometry is not readily available.

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide (1, 2). In 2019, it was estimated that there were over 212 million cases of COPD and that COPD was responsible for 3.3 million deaths and 74.4 million disability-adjusted life years lost, with most of the burden of COPD in low- and middle-income countries (LMICs) (1, 2). By 2050, the prevalence of COPD is expected to increase by 23%, with the number of cases approaching 600 million and with the largest growth in burden projected in LMICs (3). However, these statistics may be an underestimate of the true burden, as many parts of the world lack spirometry and healthcare workers trained to perform spirometry.

Indeed, although a diagnosis of COPD is characterized by respiratory symptoms, lung function abnormalities, and alterations in imaging, current guidelines recommend the identification of non–fully reversible airflow obstruction by spirometry for confirmation (4). Despite these recommendations and the high burden of chronic respiratory disease, spirometry remains a limited resource worldwide, and it is not available in many resource-limited settings (5–9). Many individuals have a diagnosis of COPD, both in high-income countries and in LMICs, without having ever had a spirometry test performed (10). A recent report identified access to spirometry as a "best buy" intervention that should be prioritized by governments (11). Although policy and the political mechanisms are set in place to strengthen the surveillance and diagnosis of chronic respiratory disease, screening questionnaires and simple lung function assessments may help to bridge the gap when spirometry is not available or limited. For example, the Asthma Screening Questionnaire has been utilized in adults to diagnose asthma with 96% sensitivity and 100% specificity, but further data are needed for COPD and among large population-based studies (12).

We and others have tested various COPD-screening questionnaires in both community-based studies and healthcare facilities (13–19). However, to our knowledge, none of these previous studies have evaluated whether the St. George's Respiratory Questionnaire (SGRQ) can be used for screening in population-based studies. The SGRQ has become a standard tool in epidemiological studies for COPD and as a patient-centered outcome in randomized controlled trials of potential interventions to assess health-related quality of life (20–25). The SGRQ has recently been incorporated into the Food and Drug Administration's guidance on recommended COPD clinical outcomes (26). The SGRQ is widely used and has been validated in more than 70 languages (27). However, the SGRQ has not been tested as a screening tool. We evaluated the performance of the SGRQ to screen for spirometry-confirmed COPD in a large, population-based cohort of adult participants in three resource-limited settings: Nepal, Peru, and Uganda.

Methods

Study Setting and Design

The Global Excellence in COPD outcomes (GECo) study was conducted in three geographically diverse LMIC settings (Table 1), described in detail elsewhere (28). We used the available household census data at each of the study areas of each setting to identify and invite an age- (40–44, 45–54, 55–64, and 65–95 yr) and sex-stratified random sample of adults ages 40 years and older for a sample target of 10,500 participants, with equal numbers of participants per stratum. Census data consisted of age, sex, and vital status of all household members for all houses in the study area of each setting. We used a computerized algorithm to select a random list of participants within each age and sex stratum until the maximum number of 460 participants were enrolled in any stratum. Only one participant per household was allowed to participate. Eligibility criteria are described in detail elsewhere (17, 28). Briefly, we invited participants who lived in the study areas who were not pregnant, did not have active pulmonary tuberculosis, or were receiving antituberculosis treatment, and who did not have absolute or relative contraindications for spirometry at the research assessment (28). Participants were enrolled between January 5, 2018, and March 9, 2020. We obtained written informed consent before enrollment. The study was approved by the ethics committees of University College London in the United Kingdom; the School of Medicine at Johns Hopkins University in Baltimore, Maryland; the Nepal Health Research Council in Kathmandu, Nepal; A.B. PRISMA in Lima, Peru; and the Uganda National Council for Science and

Author Contributions: W.C. conceived the study question, conducted the analysis and interpretation, and wrote the first draft of the manuscript with input from all authors. M.Y. verified values in the dataset, replicated statistical analysis, and conducted data visualization. N.M.R. contributed to the writing and interpretation of the manuscript. A.K.S., R.K.C., L.S., S.K.D., B.K., P.A., G.G., T.S., S.L.P., S.Q., N.R., O.F.-F., J.R.H., and R.A.W. discussed the results and contributed to the final manuscript. W.C., J.R.H., T.S., and S.L.P. were responsible for study design and data collection. W.C. is ultimately responsible for the accuracy of the data and results presented in the manuscript.

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This article has a related editorial.

A data supplement for this article is available via the Supplements tab at the top of the online article.

Artificial Intelligence Disclaimer: No artificial intelligence tools were used in writing this manuscript.

Table 1. Geographical Differences in the Three Settings of the Global Excellence in Chronic Obstructive Pulmonary Disease Study

Setting	Population Size (Year)	Population Density*	GDP per Capita, US$ (Year; Reference)	Degree of Urbanization	Geography†	Elevation‡
Bhaktapur district, Nepal	432,132 (2021)	3,631	880 (2016; 49)	Urban	Temperate, dry winter, hot summer	1,401
Lima metropolitan area, Peru	11,362,000 (2023)	315	6,164 (2016; 49)	Urban	Dry, arid desert, hot	0
Nakaseke district, Uganda	191,100 (2012)	55	112 (2017; 50)	Rural	Tropical, monsoon	1,200

Definition of abbreviation: GDP = gross domestic product.
*Measured as number of individuals per square kilometer.
†According to the Köppen climate classification scheme.
‡Measured as meters above sea level.

Technology and the Makerere School of Medicine in Kampala, Uganda.

Assessment of Respiratory Symptoms with the SGRQ

The SGRQ is a 50-question, disease-specific instrument designed to measure impact on overall health, daily life, and perceived well-being in patients with obstructive airway disease. We obtained permission from St. George's University to use the SGRQ. The interviewers who administered the SGRQ were trained to reassure participants, to paraphrase or rephrase questions for clarity, to provide contextual clarifications, and to use a neutral tone and open-ended prompts. We used questions with a recall period of 3 months that were language-validated questionnaires across all three settings (29). For Peru, we used a Spanish-validated translation available from St. George's University. For Nepal and Uganda, our team conducted translation, back-translation, and validation of the SGRQ in Nepali (30) and Luganda (31), respectively. Although the SGRQ is designed to be self-administered, a member of the research team read aloud all questions without prompting and recorded answers into an electronic database (REDCap). We used the scoring algorithm provided by St. George's University to calculate SGRQ scores (32), and we administered the SGRQ on the same day that we conducted spirometry.

Conduct of Spirometry

For all participants, height was assessed in triplicate to the nearest millimeter using a standardized protocol, followed by pre- and postbronchodilator spirometry (EasyOne Air spirometer; ndd Medical Technologies). We used 400 μg inhaled salbutamol delivered through a spacer and waited 15–20 minutes before postbronchodilator testing. We followed standard guidelines for the conduct of spirometry (33–35). We calculated *Z* scores using the 2012 Global Lung Function Initiative mixed-ethnic reference population (36). Lung function values with *Z* scores less than −6 or greater than 6 SD were considered implausible and were excluded. We defined COPD as a postbronchodilator FEV_1/FVC *Z* score less than −1.645 SD (i.e., *Z* score corresponding to the fifth percentile) (37).

We measured prebronchodilator peak expiratory flow (PEF) twice on the same day during the study (i.e., using the Piko-1 peak flow meter and spirometry-based PEF measurements). We measured PEF using a single assessment with the Piko-1 peak flow meter (nSPIRE Health). The Piko-1 is a small, handheld, easy-to-use meter with a mechanical spring and electronic interface (38). Measuring PEF with the Piko-1 takes less than 5 minutes. We used the values obtained from the Piko-1 in our primary analyses. A single assessment of PEF, however, may be affected by intersubject variability (i.e., it may underestimate the true PEF), even if it passed quality criteria programmed into the electronic peak flow meter. We used best (highest) available prebronchodilator PEF values obtained from multiple assessments during spirometry to determine agreement between Piko-1 PEF and spirometry-derived PEF and to determine whether the spirometry-derived assessment of PEF performed better than a single assessment by Piko-1 when screening for spirometry-confirmed COPD.

Biostatistical Methods

We first conducted exploratory analyses summarizing the total SGRQ scores and its subscores by age, sex, and COPD status. We calculated means and SDs (or 95% confidence intervals [CIs]) for the total SGRQ score or *Z* scores for prebronchodilator FEV_1 and FEV_1/FVC as summary statistics. We conducted similar exploratory analyses for prebronchodilator PEF. We calculated a wealth index as the first principal component (which explained 88% of the total variance) of a principal-component analysis that included access to safe water and sanitation, availability of electricity, asset ownership (mattress, chair, table, television, refrigerator, bank account, gas or electric stove), household construction material (floor and roof), and number of children under age 5 living in the house as variables. We used multiple imputation by chained equations for missing data. We provide the code used to calculate the wealth index elsewhere (*see* the online supplement).

We then measured the diagnostic performance of the total SGRQ score to identify spirometry-confirmed COPD. We used standard methods to calculate sensitivity and specificity at different total SGRQ scores and plot receiver operating characteristic curves and used the Youden index to determine the best threshold for the total SGRQ score. We calculated the area under the curve (AUC) and corresponding 95% CIs as a measure of discrimination. We then used multivariable logistic regression models to build a screening algorithm and calculated the AUCs for combinations of total SGRQ scores and sex-specific prebronchodilator PEF values at different thresholds to determine whether we could improve classification of spirometry-confirmed COPD. We ran models for PEF by Piko-1 and spirometry separately. We used the Hosmer-Lemeshow test and plotted the observed (based on spirometry-confirmed COPD) against predicted probabilities (based on the screening algorithm) as a measure of calibration.

We used the Youden index to identify the best thresholds for total SGRQ and sex-specific prebronchodilator PEF for sensitivities 90% and higher. Data were missing in less than 1% (91/10,709) of cases, and we assumed that they were missing at random. Therefore, we conducted complete case analyses. We conducted statistical analyses in R, Version 4.2.2, named "Innocent and Trusting" (39).

Results

Participant Characteristics

We obtained SGRQ scores and spirometry data in 10,709 participants. Of these, 20 participants (0.2%) were missing SGRQ scores, 12 were missing height data (0.1%), 15 were missing prebronchodilator PEF assessments by the Piko-1 (0.14%), 52 (0.5%) were missing prebronchodilator assessments by spirometry, and 45 (0.4%) were missing postbronchodilator spirometry assessments, for a total of 91 participants with missing data (some participants were missing more than one data point). A total of 596 participants (5.6%) did not have postbronchodilator spirometry that met quality criteria. Of the remaining 10,022 (94%) participants, 14 (0.1%) had implausible values and were excluded from analyses, leaving 10,008 participants. There were no differences in age (mean, 57.0 vs. 56.3 yr; $P = 0.11$), sex (male, 50% vs. 50%; $P = 0.09$), of total SGRQ score (mean, 8.4 vs. 7.9 points; $P = 0.32$) between participants who were included in our analysis compared with those who were excluded.

Of the 10,008 participants, 948 (9.5%) met spirometric criteria for COPD (18.0% in Bhaktapur, 2.7% in Lima, and 7.5% in Nakaseke). We summarized differences in participant characteristics by COPD status in Table 2. Participants with COPD were, on average, older; were more likely to be men; had higher total SGRQ scores and subscores; were more likely to be smokers; and had a lower prebronchodilator PEF and worse socioeconomic status (a higher wealth index indicates worse socioeconomic status) than those without COPD. Mean total SGRQ score was 7.9 points (SD = 11.9) for the study sample; mean total SGRQ scores were 8.7 points (SD = 10.5) for Bhaktapur, 7.3 points (SD = 12.0) for Lima, and 7.6 points (SD = 13.0) for Nakaseke. Differences in mean total SGRQ scores across sites were even smaller when limited to participants without COPD (6.7 in Bhaktapur, 7.0 in Lima, and 6.1 in Nakaseke), suggesting that differences by setting were more likely driven by the prevalence of COPD. Mean prebronchodilator PEF determined by Piko-1 was 325 L/min (SD = 115); means were 315 L/min (SD = 112) for Bhaktapur, 377 L/min (SD = 126) for Lima, and 282 L/min (SD = 80) in Nakaseke. Site-specific means were 43 L/min lower to 52 L/min higher than the study sample mean.

Table 2. Participant Characteristics for the Global Excellence in COPD Outcomes Study

Characteristic	COPD ($n = 948$)	Non-COPD ($n = 9,060$)	*P* Value
Age range, yr, *n* (%)			<0.001
40–44	105 (11.1)	2,273 (25.1)	
45–54	145 (15.2)	2,456 (27.1)	
55–64	268 (28.3)	2,224 (24.5)	
65–95	430 (45.4)	2,107 (23.3)	
Age, yr, mean (SD)	62.6 (11.8)	55.6 (11.5)	<0.001
Sex, *n* (%)			<0.001
Male	553 (58.3)	4,402 (48.6)	
Female	395 (41.7)	4,658 (51.4)	
SGRQ, mean (SD)			
Total	20.3 (19.4)	6.6 (9.9)	<0.001
Symptoms	24.1 (19.4)	11.6 (12.8)	<0.001
Impact	13.1 (19.6)	3.4 (9.0)	<0.001
Activity	31.0 (26.0)	9.7 (16.0)	<0.001
Prebronchodilator PEF in L/min, mean (SD)			
PEF by Piko-1	236.8 (95.4)	334.7 (113.2)	<0.001
PEF by spirometry	255.0 (109.6)	418.1 (122.8)	<0.001
Smoking status, *n* (%)			<0.001
Never smoker	473 (49.9)	6,003 (66.3)	
Former smoker	193 (20.4)	1,777 (19.6)	
Current smoker	281 (29.7)	1,279 (14.1)	
Current biomass fuel use, *n* (%)			
Yes	243 (25.6)	2,585 (28.6)	0.06
No	705 (74.4)	6,458 (71.4)	0.06
Years of education, mean (SD)	6.9 (3.7)	7.9 (3.8)	<0.001
Wealth index, mean (SD)	3.2 (21.3)	−0.1 (16.3)	<0.001

Definition of abbreviations: COPD = chronic obstructive pulmonary disease; PEF = peak expiratory flow; Piko-1 = peak flow meter; SGRQ = St. George's Respiratory Questionnaire.

Determinants of SGRQ and Prebronchodilator Lung Function

Both age and sex were important determinants of the SGRQ score (Figure 1). The mean total SGRQ score was 12.7 points (95% CI = 11.9–13.4) higher in participants with COPD than in those without COPD, 2.2 points (95% CI = 1.8–2.6) higher in men than in women, and 1.7 points (95% CI = 1.5–1.9) higher for each older decade of age. When evaluating for interactions with sex, the mean total SGRQ scores were 12.0 points (95% CI = 11.0–13.0) and 15.6 points (95% CI = 14.5–16.8) higher for men and women with COPD when compared with those without COPD, respectively. The mean symptom, activity, and impact subscores of the SGRQ were, respectively, 11.5 points (95% CI = 10.5–12.4), 20.0 points (95% CI = 18.8–21.1), and 8.8 points (95% CI = 8.1–9.5) higher in participants with COPD than in those without COPD when adjusted for age and sex.

Age and sex were also important determinants of prebronchodilator PEF as assessed by Piko-1 (Figure 1). Participants with COPD had a mean PEF that was 89 L/min (95% CI = 83–96) lower than that of participants without COPD; men had a mean PEF that was 109 L/min (95% CI = 106–113) higher than that of women; and mean PEF was 27 L/min (95% CI = 26–29) lower for each older decade in age. When evaluating for interactions with sex, mean PEFs were 110 L/min (95% CI = 102–118) and 176 L/min (95% CI = 166–185) lower in men and women with COPD, respectively, when compared with those without COPD.

SGRQ scores were also associated with lower prebronchodilator FEV_1 and FEV_1/FVC *Z* scores for participants with

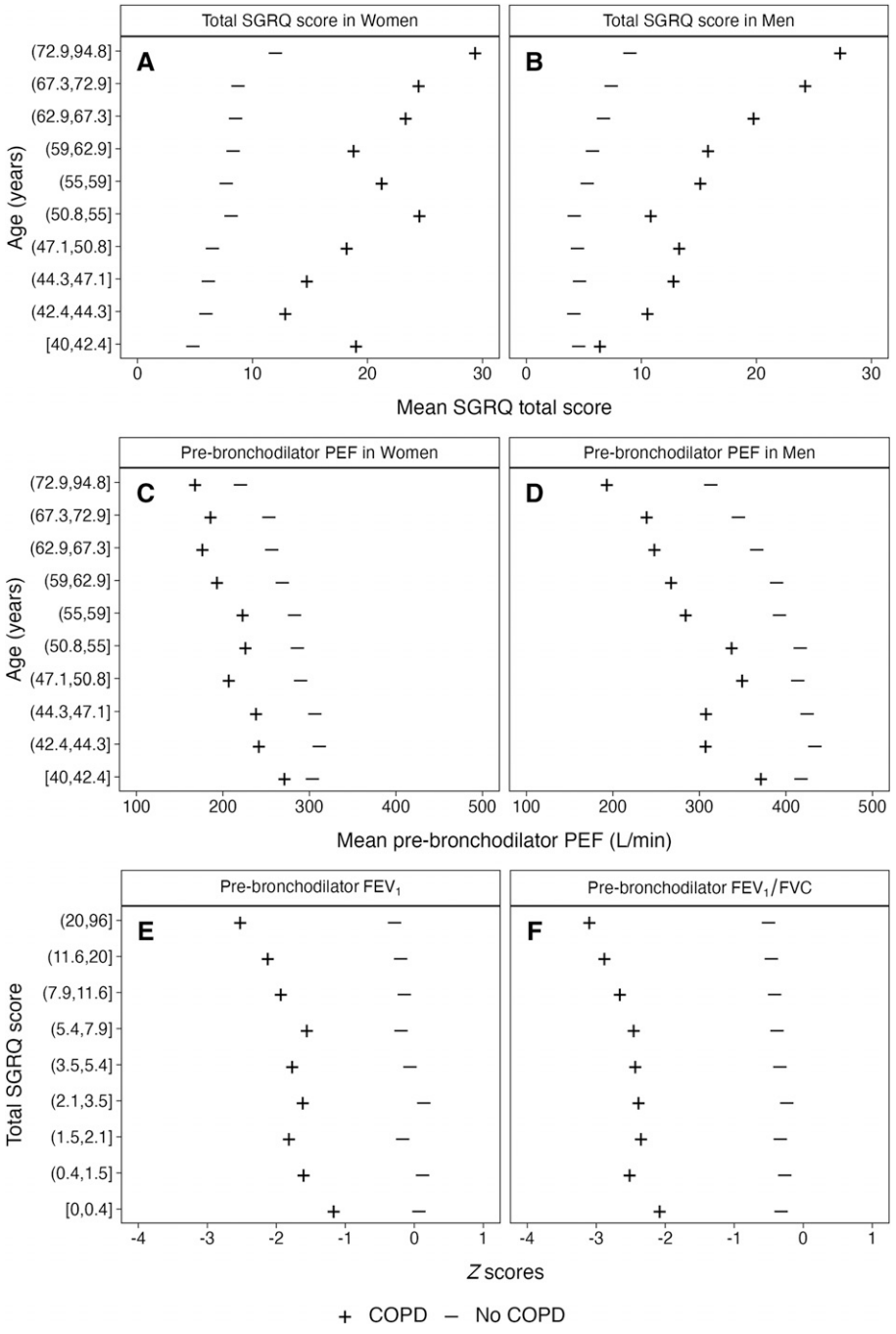

Figure 1. Association between age, sex, and chronic obstructive pulmonary disease (COPD) status on (*A* and *B*) the total St. George's Respiratory Questionnaire (SGRQ) score and (*C* and *D*) a simple prebronchodilator peak expiratory flow (PEF) assessment by a peak flow meter; and association between the SGRQ and prebronchodilator (*E*) FEV_1 *Z* score and (*F*) FEV_1/FVC *Z* score using the Global Lung Function Initiative 2012 mixed-ethnic population. We plotted: mean values for total SGRQ score (on the *x*-axis) by deciles of age (on the *y*-axis) stratified by sex (*A*: female participants; *B:* male participants) and COPD status (represented as + for participants with COPD and – for those without COPD); mean values for PEF (on the *x*-axis) by deciles of age (on the *y*-axis) stratified by sex (*C*: female participants; *D*: male participants) and COPD status; and mean *Z* scores (on the *x*-axis) for (*E*) FEV_1 and (*F*) FEV_1/FVC by deciles of total SGRQ score (on the *y*-axis) stratified by COPD status.

and without COPD (Figure 1). Mean prebronchodilator FEV_1 *Z* scores were 0.18 (95% CI = 0.14–0.22) and 0.10 (95% CI = 0.08–0.13) lower in participants with and without COPD, respectively, for every 10-point increase in the total SGRQ score. Mean prebronchodilator FEV_1/FVC ratios were 0.14 (95% CI = 0.11–0.17) and 0.07 (95% CI = 0.05–0.08) *Z* scores lower in participants with and without COPD, respectively, for every 10-point increase in the total SGRQ score.

Screening for COPD

We plotted the bivariate relationship between SGRQ and prebronchodilator PEF using the Piko-1 assessment by COPD status in Figure 2. The odds of having COPD were positively associated with the total SGRQ score; however, this relationship was not linear. Odds of COPD were 3.41 (95% CI = 3.04–3.83) times higher for a 10-point difference in SGRQ score up to 20 points after adjusting for age and sex. Thereafter, there was an inflection point, and the odds of COPD were 1.18 (95% CI = 1.09–1.26) times higher for a 10-point difference in SGRQ score above 20 points. For example, the odds of having COPD were 3.41 times higher between 15 and 5 points but only 1.18 times higher between 35 and 25 points in the SGRQ score; and the odds of having COPD were 7.4 times higher between 30 and 5 points and 8.7 times higher between 40 and 5 points in the total SGRQ score. The odds of COPD were 1.9 times higher (95% CI = 1.83–2.03) for a 50 L/min lower difference in prebronchodilator PEF.

We plotted the receiver operating characteristic curves for combinations of SGRQ scores, prebronchodilator PEF assessed by the Piko-1, and sex-specific values of prebronchodilator PEF assessed by the Piko-1 (Figure 3). The AUC for the total SGRQ score as a screening tool for COPD was 0.77 (95% CI = 0.75–0.79), with a best threshold of 10.75 points, a specificity of 81%, and a sensitivity of 61%. Stratified by sex, the AUC for men was 0.78, and the best threshold was 7.75 points; and the AUC for women was 0.77, and the best threshold was 11.35 points in the SGRQ score. However, stratifying the total SGRQ score by sex did not improve the AUC significantly ($P = 0.39$). The AUC for prebronchodilator PEF assessed by the Piko-1 as a screening tool for COPD was 0.76 (95% CI = 0.74–0.77), and the best threshold was 242 L/min, with a specificity of 79% and sensitivity of 59%. Stratified by sex, the AUC for men was 0.80, and the best threshold was 310 L/min; and the AUC for women was 0.79, and the best threshold was 224 L/min. The AUC improved significantly when PEF was stratified by sex ($P < 0.001$). When the total SGRQ and sex-specific pre-bronchodilator PEF assessed by the Piko-1 were combined into a single model, the AUC increased to 0.84 (95% CI = 0.82–0.85). The Hosmer-Lemeshow test indicated that a screening test that included total SGRQ test, prebronchodilator PEF, and sex had a good fit ($P = 0.21$) and predicted probabilities for COPD followed the observed probabilities closely (Figure 4). A screening tool that combined a total SGRQ score of 12 points

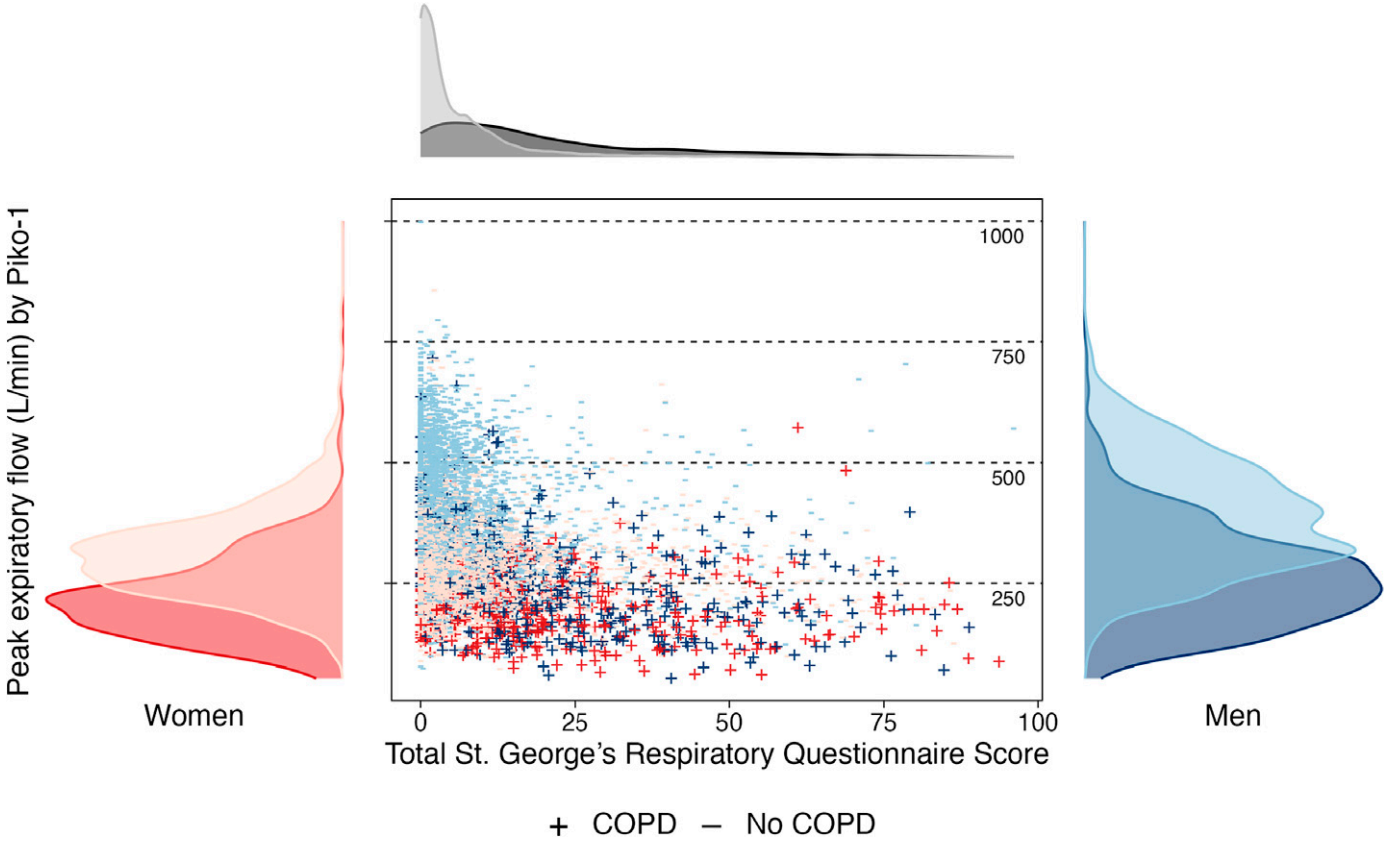

Figure 2. Bivariate relationship between the total St. George's Respiratory Questionnaire (SGRQ) score and simple prebronchodilator peak expiratory flow (PEF) assessment by a Piko-1 stratified by chronic obstructive pulmonary disease (COPD) status and sex. We plotted a scatterplot of prebronchodilator PEF by the total SGRQ score stratified by COPD status (represented as + for participants with COPD and – for those without COPD) and sex (scatterpoints in blue for men and red for women). We also display the density distributions for SGRQ stratified by COPD status (dark gray, participants with COPD; light gray, those without COPD) along the *x*-axis and for sex-specific PEF stratified by COPD status among participants with COPD (dark blue, men; dark red, women) and among those without COPD (light blue, men; light red, women) on the *y*-axis. Piko-1 = peak flow meter.

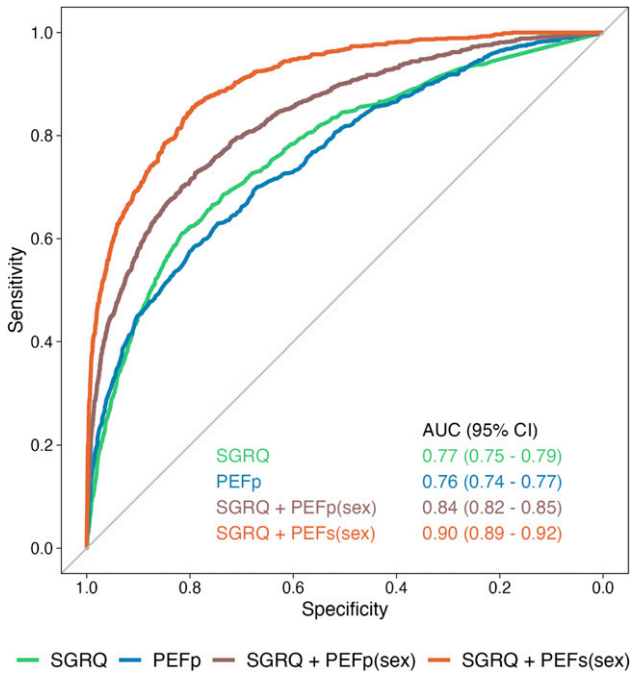

Figure 3. Receiver operating characteristic (ROC) curves for combinations of the total St. George's Respiratory Questionnaire (SGRQ) score and prebronchodilator peak expiratory flow (PEF) assessment by a peak flow meter (Piko-1) or spirometry used to screen for chronic obstructive pulmonary disease. Here, we plotted the ROC curves for SGRQ score, PEF assessed by Piko-1 (PEF_p), SGRQ plus PEF_p stratified by sex, and SGRQ plus PEF_s stratified by sex. Values for the AUC and corresponding 95% CIs are displayed in the bottom right corner. AUC = area under the ROC curve; CI = confidence interval; PEF_s = peak expiratory flow by spirometry.

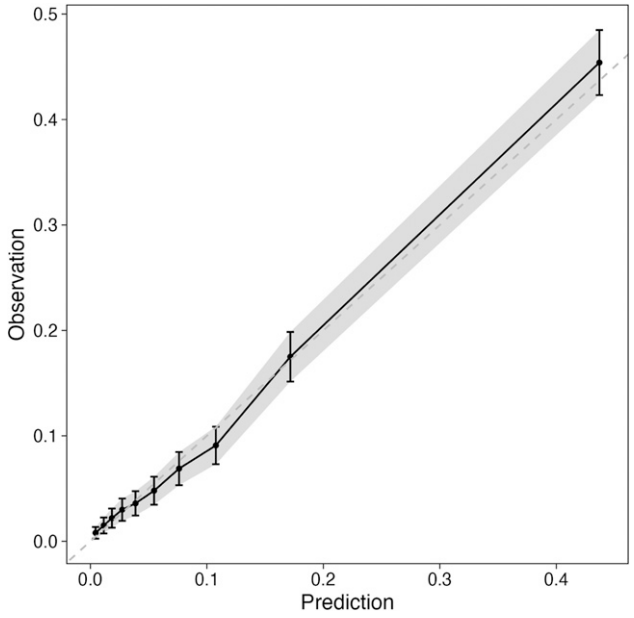

Figure 4. Calibration plot for a logistic regression model for chronic obstructive pulmonary disease as an outcome and the total St. George's Respiratory Questionnaire score, prebronchodilator peak expiratory flow assessment by a peak flow meter and sex. We plotted predicted versus observed averages of the proportion stratified into 10 bins.

or more and/or Piko-1–assessed prebronchodilator PEFs <400 L/min for men and <250 L/min for women yielded a sensitivity of 91%, a specificity of 47%, a positive predictive value of 15%, and a negative predictive value of 98%.

Prebronchodilator PEF assessed by the Piko-1, however, underestimated prebronchodilator PEF assessed by spirometry (Figure 5). Indeed, prebronchodilator PEF assessed by the Piko-1 was 66 L/min lower, on average, than prebronchodilator PEF assessed by spirometry, and there was evidence of a proportional bias (i.e., the mean underestimation was greater with higher values of PEF). We had prebronchodilator PEF assessed by spirometry in a subset of 8,037 participants (20% missing overall; 59% missing in Uganda, 2.3% missing in Peru, and 0.4% missing in Nepal). When we used prebronchodilator PEF assessed by spirometry instead, the AUC increased to 0.84 (95% CI = 0.82–0.85), and the best threshold was 301 L/min, with a specificity of 70% and sensitivity of 82%. Stratified by sex, the AUC for men was 0.90 (sensitivity, 85%; specificity, 77%), and the best threshold was 419 L/min; and the AUC for women was 0.90 (sensitivity, 85%; specificity, 80%), and the best threshold was 274 L/min. When the total SGRQ and sex-specific prebronchodilator PEF assessed by spirometry were combined into a single model, the AUC increased to 0.90 (95% CI = 0.89–0.92). A screening tool that combined a total SGRQ score of 12 points or more and/or spirometry-assessed prebronchodilator PEFs less than 450 L/min for men and less than 300 L/min for women yielded a sensitivity of 92%, a specificity of 61%, a positive predictive value of 21%, and a negative predictive value (NPV) of 99%. These results suggest that the prebronchodilator PEF obtained from multiple assessments may perform better than the prebronchodilator PEF from a single assessment.

Discussion

Here, we demonstrate that the SGRQ, alone or in combination with a simple assessment of prebronchodilator PEF, can be used as an alternative screening tool for spirometry-confirmed COPD in settings where spirometry is not readily available. A total SGRQ score of 12 points or more and/or a

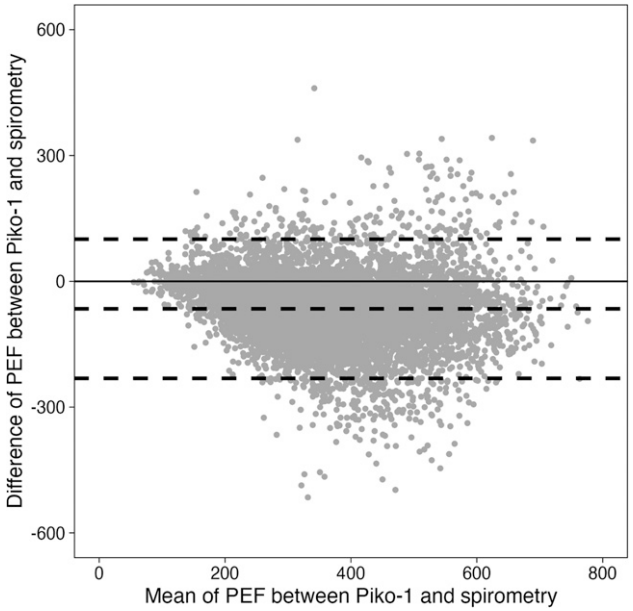

Figure 5. Bland-Altman plot of the agreement between prebronchodilator peak expiratory flow (PEF) by a peak flow meter (Piko-1) and spirometry. We plotted the difference between PEF assessed by Piko-1 and spirometry on the *y*-axis against their mean on the *x*-axis, indicated with gray dots. The broken lines indicate the mean bias (−66 ml; 95% confidence interval [CI], −67 to −64 ml), the upper limit of agreement (100 ml; 95% CI, 97 to 104 ml), and the lower limit of agreement (−231 ml; 95% CI, −235 to −228 ml).

simple assessment for prebronchodilator PEF less than 400 L/min for men and less than 250 L/min for women identified spirometry-confirmed COPD with a sensitivity of 91% and an NPV of 98% in a heterogeneous population of adults in three LMICs. Although other screening tools are available, none are widely known and used in large population-based epidemiological studies of COPD and randomized controlled trials of interventions for COPD as is the SGRQ, which has appeared in more than 2,200 articles in PubMed.

Previous studies have examined the use of screening tools for spirometry-confirmed COPD using either retrospectively collected data or in small samples from a select group of participants with an established history of respiratory disease. The "Could it be COPD?" questionnaire had a sensitivity of 40–63% and an NPV of 85–94% (13). This questionnaire was designed retrospectively using data from the third U.S. National Health and Nutrition Examination Survey (or, NHANES III) of 7,701 individuals ages 35–75 years, 13.3% of whom had spirometry-confirmed COPD. Another contemporary study, conducted in a U.K. primary clinic, evaluated the use of questions based on age, dyspnea on exertion, and respiratory symptoms and achieved a sensitivity of 77.4–87.1%, with an AUC of 0.80–0.85; however, this study included a highly selective group of 369 participants (16.8% had COPD-diagnosed spirometry) ages 40 years and older who were former or current smokers, had recent respiratory medication use, or had a history of asthma with no current medications (14). The COPD Population Screener Questionnaire, which assessed respiratory symptoms, smoking history, and age, was developed through expert opinion and tested using data from pulmonary and primary care clinics. When tested in 697 participants ages 35 years and older, 113 (38%) of whom had spirometry-diagnosed COPD, a COPD Population Screener Questionnaire score greater than 5 was associated with a positive predictive value of 56.8%, an NPV of 86.4%, and an AUC of 0.81 (16). Another study developed and tested the Lung Function Questionnaire, including items on age, respiratory symptoms, and tobacco use, in a sample of 387 participants ages 40 years and older and found an AUC of 0.72 with a sensitivity of 73% and specificity of 58% (19). However, these studies developed and implemented respiratory questionnaires that *1*) targeted patient populations that had a varying prevalence of COPD and were limited by small sample sizes, *2*) were used in healthcare settings rather than in population settings with healthier individuals, and *3*) have overall poor specificity.

Two recent studies incorporated the use of PEF as a screening tool for COPD. The first use of PEF in a case-control design compared 186 participants with COPD and at least one exacerbation in the past year or an FEV_1 less than 60% of predicted without an exacerbation in the past year against 160 participants with no COPD or mild COPD (15). The five-item COPD Assessment in Primary Care to Identify Undiagnosed Respiratory Disease and Exacerbation Risk Questionnaire (CAPTURE) was used to assess environmental exposures, breathing difficulties, tiring easily with physical activity, and acute respiratory illnesses in the past year (15). The CAPTURE alone had an AUC of 0.79, and use of PEF (<350 L/min in male participants and <250 L/min in female participants) in participants scoring between 2 and 4 improved classification to an AUC of 0.91 (15). A subsequent study conducted by our team, used a random population-based cohort of 1,173 adults ages 35 years and older in Uganda to test the COPD in Low- and Middle-Countries Assessment (COLA). The COLA score was based on symptoms, exposure (tobacco smoking and biomass smoke), tiring easily or hospitalizations due to respiratory concerns, age, and PEF finding an AUC of 0.83 (18). A COLA score of 2 or higher had a sensitivity of 96% and an NPV of 100% (18). We have previously tested several of these screening questionnaires (two including PEF measurements) in the GECo cohort, with AUCs ranging between 0.72 and 0.79 and sensitivities from 34% to 64% (17). Score thresholds for the COLA-6, CAPTURE, and the Lung Function Questionnaire to achieve a sensitivity of more than 90% had specificities from 10% to 30% (17).

Our analysis shows that the SGRQ, in combination with sex-specific PEF, outperforms previous screening tools; however, one must consider the benefits and drawbacks of the SGRQ in population based–settings. First, the SGRQ was developed as a research tool to measure well-being for people with lung disease and has been used in thousands of epidemiological studies of COPD. A minimum clinically

important difference of 4 points in the total SGRQ score is now considered a standard in trials that evaluate interventions for COPD (40). Second, some may argue that scoring the SGRQ is complex and it requires a weighted calculation compared with other questionnaires with fewer items (41). The SGRQ takes up to 15 minutes to complete when self-administered and up to 30 minutes when administered by an interviewer; this is significantly shorter than conducting pre- and postbronchodilator spirometry, which requires more instrumentation, staff expertise, setup, a waiting period after the administration of bronchodilators, and quality control effort (32, 41, 42). We have observed this in our epidemiological studies of COPD across LMICs, with colleagues favoring shorter questionnaires such as the COPD and Airways Assessment Test (CAAT; previously known as the COPD Assessment Test) (17, 43–46) and the Clinical COPD Questionnaire (47, 48). We did not collect the CAAT in our population sample. There remains a gap in literature of the use of the CAAT and Clinical COPD Questionnaire in LMIC settings (44, 48). Future studies could consider using the CAAT in population-based studies. However, given the wide use and availability of the SGRQ in over 70 languages and accessibility to free scoring programs, the SGRQ could be considered a reasonable screening tool across multiple settings, and the scores can allow for interstudy and intercountry comparisons.

Our study has several strengths. First, we tested the SGRQ in a heterogenous population spanning three languages and with a range of ages 40 years and older with a disparate prevalence of COPD and risk factors across settings. Second, our study was a large randomly selected population-based sample of over 10,000 participants, regardless of symptoms or prior diagnoses in contrast to studies with more selective patient populations based in clinical settings. Third, we conducted standardized spirometry according to American Thoracic Society/European Respiratory Society guidelines and quality control across these settings to guarantee the highest quality of spirometry. There are some potential shortcomings. First, we were unable to determine the average SGRQ completion time; however, previous estimates report an average of 15 minutes. Second, our data also show that a simple assessment of PEF by a peak flow meter may underestimate the true PEF when compared with that obtained by spirometry. On the basis of these results, screening PEF may require multiple assessments and standard guidelines to obtain maximal effort. The thresholds for PEF identified in this study may be dependent on the COPD prevalence in our study population and may not be generalizable to other settings. However, we found that the mean total SGRQ score among participants without COPD was similar across our three settings and lessens concerns about heterogeneity. Nonetheless, identifying a screening threshold may require testing across multiple settings to determine whether a single threshold is sufficient or multiple thresholds according to setting are needed to screen for COPD.

In conclusion, the SGRQ, in combination with PEF, may serve as an alternative screening tool for COPD in LMIC settings, especially in settings where either resources or skills are not available. Further research is needed to test its implementation in other settings and whether screening and earlier diagnosis is associated with better outcomes in COPD. ■

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