Cost-Accuracy Analysis of Chronic Obstructive Pulmonary Disease Screening in Low- and Middle-Income Countries

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Introduction

The global burden of COPD disproportionately affects low- and middle-income countries (LMIC). Among well-recognised challenges to the mitigation of COPD in LMIC include the absence[1] and poor implementation[2] of COPD guidelines, and lack of access to diagnostic spirometry. Screening and case-finding tools may provide an effective way to target scarce resources to those most likely to benefit, and we have recently reported the diagnostic accuracy of three COPD screening tools in LMIC settings[3]. Cut-points on screening tools can be adjusted to prioritise sensitivity or specificity, which impacts diagnostic pick-up and the downstream need for confirmatory spirometry and thus further healthcare use and costs. We now report a cost-accuracy analysis of three COPD screening tools in LMIC settings.

Methods

The trial methodology has been previously reported[4]. Individuals aged over 40 years were randomly selected from the population in semi-urban Bhaktapur, Nepal, urban Lima, Peru, and rural Nakaseke, Uganda. We tested CAPTURE (COPD Assessment in Primary Care To Identify Undiagnosed Respiratory Disease and Exacerbation Risk, which includes peak expiratory flow, PEF), COLA-6 (COPD in LMICs Assessment-6, which includes PEF) and the Lung Function Questionnaire (LFQ, which does not include PEF). To characterise diagnostic pathways, we used a structured decision tree (Figure 1) to consider the likelihood of reaching individuals for the screening visit, prevalence of COPD, and screening tool accuracy. We estimated the overall accuracy of the tools, and a sensitivity analysis used site-specific accuracy estimates with thresholds for the tools adjusted to return a sensitivity ≥90%. The likelihood of individuals accessing the healthcare system for a spirometry-confirmed diagnosis, and the availability of spirometry were also considered. Each step was costed from a health-system perspective using time taken to deliver CAPTURE, COLA-6 and LFQ, and externally sourced costs including the cost of spirometry, and of a clinician visit for those testing positive. We present three metrics – 1) cost of diagnostic workup per 100 individuals screened, 2) cost per correctly identified negative or positive case, and 3) cost per correctly diagnosed positive case. To reflect those who could benefit from treatment, metrics 2 and 3 considered only positive cases that accessed the health system. Permissions were obtained and participants provided written consent as reported in the parent study[3,4]. A detailed description of the Methodology is provided in the Supplement.

FIGURE 1: *Decision tree for screening using a case-finding questionnaire (CFQ), assuming that confirmatory diagnosis with spirometry subsequently takes place.*

Results

The patient demographic and diagnostic accuracy of the three tools at the three sites have been previously reported[3]. In brief, we screened 10709 people, with a mean (SD) age of 56.3(11.7) years, 50.3% female. The overall unweighted prevalence of COPD was 9.4% but this varied by site and was 18.2% in Nepal, 2.7% in Peru and 7.4% in Uganda. More than 95% of cases were previously unaware of their diagnosis despite 49.3% having GOLD group[5] B, C or D disease and therefore clinically significant COPD. The AUC for the three screening tools were similar[3].

Administration of the case-finding instruments in participant homes took a mean (SD) of 6.5 (0.28) minutes for LFQ, 7.8 (0.42) minutes for CAPTURE and 8.7 (0.61) minutes for COLA-6 inclusive of introductory conversations. The cost-accuracy analyses are reported in Table 1 (2019 USD). The total diagnostic pathway cost per 100 individuals screened was similar across the three instruments but lowest for COLA-6 (at around $700). COLA-6 also had the lowest cost per correct diagnosis, negative or positive, because of its higher specificity. Analysis by site showed that the costs of the diagnostic pathways were heterogeneous: highest in Peru ($1,567 per 100 individuals screened on average across the three questionnaires), followed by Nepal ($308 per 100 individuals screened), then Uganda ($295 per 100 individuals screened), associated with differences in prevalence and unit costs across sites.

Results of the sensitivity analysis, where thresholds for the instruments were adjusted to return a sensitivity ≥90% indicate that, due to lower specificity, 74-89% of patients screened would be positive on the screening tools. This would improve the identification of patients with COPD (from 2.8-3.6 to 5.8-6.0, per 100 screened), but significantly increase the downstream diagnostic workup costs (from around $700 to around $1,100, per 100 patients screened).

TABLE 1: *Cost-Accuracy Analysis of three COPD Screening Tools in three LMIC Settings.*

Site (number targeted/ 100 screened)	**Screening tool (ST)**	**Number of individuals per 100 screened...**			**Cost (2019 USD) per…**		
		... positive to ST *	**…with correct positive diagnosis ****	**… with correct negative diagnosis *****	**…100 individuals screened**	**…correct positive or negative diagnosis **,***	**…correct positive diagnosis**
Main analysis for LFQ, CAPTURE and COLA-6 using trial estimates (pooled across sites) of sensitivity/specificity: 58.8%/78.9% (LFQ), 60.0%/81.5% (CAPTURE) and 45.6%/86.6% (COLA-6).							
Nepal (159)	**LFQ**	28.0	6.9	68.8	305.4	4.0	44.0
	CAPTURE	26.0	7.1	70.4	315.6	4.1	44.5
	COLA-6	19.3	5.4	73.6	303.4	3.8	56.3
Uganda (171)	**LFQ**	23.9	2.8	76.2	309.3	3.9	109.9
	CAPTURE	21.6	2.9	78.2	307.3	3.8	106.9
	COLA-6	15.8	2.2	82.2	269.2	3.2	123.2
Peru (181)	**LFQ**	22.1	1.0	81.3	1,590.9	19.3	1,525.5
	CAPTURE	19.6	1.1	83.3	1,580.0	18.7	1,483.3
	COLA-6	14.3	0.8	87.1	1,526.7	17.4	1,886.3
Overall (150)	**LFQ**	24.7	3.6	75.4	735.2	9.1	559.8
	CAPTURE	22.4	3.7	77.3	734.3	8.9	544.9
	COLA-6	16.4	2.8	81.0	699.8	8.1	688.6
Sensitivity analysis for LFQ and COLA-6 using site-specific thresholds defined to return a sensitivity ≥90%. Sensitivity/specificity values for LFQ were: Nepal 95.7%/27.5%, Peru 92.6%/30.4% and Uganda 90.4%/25.2%. Sensitivity/specificity values for COLA-6 were: Nepal 98.4%/11.6%, Peru 97.9%/12.4% and Uganda 96.5%/10.7%.							
Nepal (159)	**LFQ**	76.7	11.3	37.2	403.8	8.3	35.7
	COLA-6	90.2	11.6	27.4	446.5	11.4	38.4
Uganda (171)	**LFQ**	75.9	4.3	34.3	665.1	17.2	153.6
	COLA-6	89.8	4.6	23.0	775.4	28.0	167.7
Peru (181)	**LFQ**	70.2	1.6	44.5	2,109.4	45.7	1,284.4
	COLA-6	87.9	1.7	30.9	2,320.6	71.2	1,335.2
Overall (150)	**LFQ**	74.3	5.8	38.7	1,059.4	23.7	491.2
	COLA-6	89.3	6.0	27.1	1,180.8	36.9	513.8

Costs presented here consider i) the resources required to perform screening (in the community) and ii) any subsequent procedures/resources needed to achieve a diagnosis (at health facilities).

* includes false positives

** a correct positive diagnosis includes individuals that were identified as positive to the screening tool, accessed the health system and have conducted spirometry where available (hence, excludes false positives identified via spirometry). Note that it was assumed that only a proportion of those testing positive to the screening questionnaire would follow-through to the health system.

*** a correct negative diagnosis includes individuals that were true negatives to the screening questionnaire and any false positives which received spirometry.

Discussion

We have recently reported the diagnostic accuracy of three screening tools for COPD in LMIC settings[3]. The tools tested had similar, moderate accuracy. Here we report the cost-accuracy of the tools, which are dependent on tool performance (and selected thresholds), COPD prevalence, and local costs.

In choosing among screening instruments, a policymaker needs to consider the trade-offs between specificity (reducing health-system burden from false positives) and sensitivity (identifying more cases). Our cost-accuracy analysis makes these trade-offs explicit by quantifying diagnostic-workup savings from the increased specificity of COLA-6. However, consideration needs to be given to long-term benefits arising from the increased detection of COPD using CAPTURE and LFQ (which had a higher sensitivity), and whether these offset the additional costs arising from reduced specificity. Part of the cost of administering screening tools is incurred attempting to reach targeted individuals. Programs designed to better target and reach individuals at risk of COPD could improve cost-accuracy.

We demonstrate that maximising sensitivity to >90% increased identification of COPD to 6%, but resulted in 74-89% of all screened cases returning a positive result. Even if only 65% of these individuals accessed the health-system (as considered in our analyses), this is likely unaffordable.

Arguments against screening for COPD in high-income settings have centred around the lack of disease-modifying interventions in milder disease[6]. This does not hold in LMIC settings where many participants have clinically significant disease[3]. Moreover, availability of cost-effective interventions for COPD in LMIC is increasing, including pulmonary rehabilitation[7], and with the recent inclusion of long-acting anti-muscarinic drugs on the WHO Essential Medicines List (EML)[8]. It is important to remark that the presence of a medicine on an EML does not necessarily imply that there is access to affordable drug in the community[9].

In conclusion, COPD screening in LMIC identifies clinically significant, previously undiagnosed disease, which presents a high-burden to patients and health systems. COPD prevalence varies by setting and this cost-accuracy analysis highlights the trade-offs between sensitivity and specificity, number of cases accessing downstream services and costs. Further research should be conducted to quantify the burden of unidentified COPD, and the potential for reducing this with cost-effective interventions. This would allow extending our analyses to consider full cost-effectiveness which, by determining the net impacts of the sensitivity/specificity profiles of the different screening tools, would be able to explicitly inform policy decisions on the value of the alternative approaches.

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