EDITORIAL

Interpreting the diagnostic accuracy of tools for early detection of COPD

See linked articles by Sichletidis *et al.* on pg 184 and Frith *et al.* on pg 190

***Daniel Kotz^a**
Onno CP van Schayck^a

^a Department of General Practice, CAPHRI School for Public Health and Primary Care, Maastricht University Medical Centre, Maastricht, The Netherlands.

*Correspondence:
Dr Daniel Kotz,
Department of General Practice,
CAPHRI School for Public Health and Care,
Maastricht University Medical Centre,
P.O. Box 616,
6200 MD Maastricht,
Maastricht,
The Netherlands
Tel: +31 43 38 82893
Fax: +31 43 36 19344
E-mail: d.kotz@maastrichtuniversity.nl

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There has been increasing interest in recent years in developing and testing strategies for early detection of chronic obstructive pulmonary disease (COPD) in primary care. Proponents of early detection argue that COPD is underdiagnosed and should be detected early because of its irreversible and progressive nature.¹ Opponents, on the other hand, argue that early detection primarily yields subjects with mild to moderate airflow limitation and that medical services do not have the capacity to provide care for patients with borderline abnormal spirometry.² In this issue of the *PCRJ*, two studies present findings on a potential new tool for early detection of COPD – the PiKo-6® expiratory flow meter (or 'mini-spirometer') – and compare this with an existing strategy – a COPD diagnostic questionnaire.^{3,4}

The PiKo-6® (nSpire Health Inc.) is a relatively new and simple screening device that measures the forced expiratory volume in one and six seconds (FEV₁ and FEV₆, respectively) and the FEV₁/FEV₆ ratio. The device provides audio-visual feedback on the duration and quality of the exhalation manoeuvre and shows results immediately on a small display. Subjects below a certain threshold of FEV₁/FEV₆ (e.g., <0.70 pre- or post-bronchodilator) are considered "at risk" of COPD.

An international group of primary care specialists developed a COPD diagnostic questionnaire which has been implemented by the International Primary Care Airways Group (this questionnaire is further referred to as the "IPAG questionnaire" throughout this text).^{5,6} The questionnaire comprises eight items and its scoring system permits the calculation of an overall COPD risk score ranging from 0 - 38 points. Subjects with more than 16.5 points are considered "at risk" of COPD.⁶

In the two studies from Sichletidis *et al.*³ and Frith *et al.*⁴, the diagnostic accuracy of the IPAG questionnaire and the PiKo-6® were tested against the "gold standard" – i.e., spirometry according to ATS/ERS guidelines, with post-bronchodilator FEV₁/forced vital capacity (FVC) <0.70 defining COPD.⁷

In the first study, Sichletidis *et al.* screened 1,078 current, former and never-smoking patients aged older than 40 years without prior diagnosis of COPD, 49% of whom were current smokers.³ The prevalence of COPD was 10% (of which 84% was mild-to-moderate disease). For patients with PiKo-6® post-bronchodilator FEV₁/FEV₆ < 0.70, sensitivity (SN) and specificity (SP) were SN=80% and SP=95%. For patients with IPAG >16.5 points, these measures were SN=91% and SP=49%.

In the second study, Frith *et al.* screened 204 current and former smoking patients aged 50 or older without prior diagnosis of COPD, 45% of whom were current smokers.⁴ The prevalence of COPD was 28% (of which 95% was mild-to-moderate COPD). For patients with PiKo-6® pre-bronchodilator FEV₁/FEV₆ < 0.75, the diagnostic accuracy measures were SN=81% and SP=71%. For patients with IPAG > 16.5 points, these measures were SN=91% and SP=37%.

How can we interpret these different measures of diagnostic accuracy? Most diagnostic tests do not combine both a perfect SN and a perfect SP at the same time; there is usually a trade-off between the two – the higher the SN, the lower the SP, and *vice versa*. The question now is: which of the two do we find more important when screening for COPD? Do we want to be sure not to miss any patient with the disease (thus reducing the "false-

Table 1. Number of patients diagnosed false-negatively (in red) and false-positively (in bold) in an index population of 1,000 primary care patients screened for COPD with the IPAG questionnaire and the PiKo-6®.Based on results from Sichletidis *et al.*³

COPD*					COPD*				
		+	-				+	-	
IPAG	+	91	459	550	Piko-6	+	80	45	125
	-	9	441	450		-	20	855	875
		100	900	1000			100	900	1000
COPD prevalence:		10%			COPD prevalence:		10%		
SN:		91%			SN:		80%		
SP:		49%			SP:		95%		
1-SN (false-negative):		9%			1-SN (false-negative):		20%		
1-SP (false-positive):		51%			1-SP (false-positive):		5%		

Based on results from Frith *et al.*⁴

COPD*					COPD*				
		+	-				+	-	
IPAG	+	255	454	708	Piko-6	+	227	209	436
	-	25	266	292		-	53	511	564
		280	720	1000			280	720	1000
COPD prevalence:		28%			COPD prevalence:		28%		
SN:		91%			SN:		81%		
SP:		37%			SP:		71%		
1-SN (false-negative):		9%			1-SN (false-negative):		19%		
1-SP (false-positive):		63%			1-SP (false-positive):		29%		

SN = sensitivity, SP = specificity, *COPD (chronic obstructive pulmonary disease) diagnosed by "gold standard" (i.e., spirometry according to ATS/ERS guidelines)

negatives") or do we want to be sure not to misdiagnose any patient without the disease (thus reducing the "false-positives")? A negative result from a highly sensitive screening test will rule out COPD because the test produces very few false-negatives (a commonly used mnemonic is "SNout": a test with high SN, when negative, rules disease out).⁸ On the other hand, a positive result from a highly specific screening test will rule in COPD because the test produces very few false-positives ("SPin": SP when positives, rules in).⁸

For COPD screening, high SN is probably more important than high SP. We want to miss as few patients with COPD as possible, at the expense of diagnosing more patients "at risk" of COPD who in fact are healthy. We can afford to do so because the screening test is not designed to make a final diagnosis but as a triage of patients who will be referred for formal spirometry. Spirometry is a non-invasive diagnostic procedure that will have no negative consequences for patients who have initially been false-positively diagnosed according to the screening test. However, we should take into account that these patients might have been unnecessarily worried about their health. Furthermore, false-positive results from screening tests will result in avoidable use of health care resources and increased costs.

The magnitude of the problem with false-positive test results becomes apparent when we apply the figures for prevalence of COPD, and the SN and SP of the two screening instruments provided by Sichletidis *et al.* and Frith *et al.*, to an index population of 1,000

primary care patients screened (see Table 1). Screening 1,000 patients using the IPAG questionnaire results in 459 (Sichletidis) or 454 (Frith) avoidable spirometries. This is due to the low SP of the IPAG questionnaire, a problem that has been previously addressed in an external validation study of the questionnaire.⁹ The number of avoidable spirometries is much lower when using the PiKo-6 [45 (Sichletidis) and 209 (Frith); Table 1], but about twice as many patients with COPD would be missed compared with the IPAG questionnaire [20 (Sichletidis) and 53 (Frith), versus 9 (Sichletidis) and 25 (Frith); Table 1]. Furthermore, applying the PiKo-6® requires consultation with a health care professional which would have been avoidable in patients who do not have COPD [900 (Sichletidis), 720 (Frith); Table 1]. An advantage of the IPAG questionnaire is that it can be used without medical assistance, even on a mass scale. For example, the Dutch Asthma Foundation launched the questionnaire on the internet together with a media campaign which resulted in over 100,000 self-completed questionnaires during the first three weeks.¹⁰

The two studies do not give an answer to the question; what do clinicians have to offer to patients in order to detect early COPD by means of a screening program? An important principle for early detection of disease is the availability of an accepted treatment for newly diagnosed patients.¹¹ The studies by Sichletidis *et al.* and Frith *et al.* have shown that screening almost exclusively yields patients with mild to moderate COPD of whom less than half are current

smokers. The only effective intervention for these patients is smoking cessation. Unfortunately, there is not much evidence that COPD screening enhances smoking cessation in smokers newly detected with the disease. A recent randomised controlled trial showed that early detection of COPD followed by intensive smoking cessation treatment – including confrontation with the new diagnosis – was not more effective in increasing long-term abstinence rates than an equally intensive treatment without confrontation.¹² All smokers (regardless of spirometry testing) should be helped to quit, and there is a range of behavioural and pharmacological treatments available in primary care which have been proven to be effective in smokers with respiratory diseases.¹³

Newly detected COPD patients who have never smoked or have already quit successfully form an even more problematic group. The best clinicians have to offer is lifestyle advice towards avoidance of risk factors other than cigarette smoking, increasing or maintaining physical activity, and complying with a healthy diet.

The studies by Sichletidis *et al.*³ and Frith *et al.*⁴ show that early detection of COPD in primary care is possible by using simple methods like the IPAG questionnaire or the PiKo-6®. However, the health care costs for testing the large group of false-positives are considerable. The short-term effects of treating newly diagnosed COPD patients – in terms of smoking cessation – are disappointing so far. The proof of the pudding is in the eating. Proponents of early detection will need to prove the cost-effectiveness of their approach in terms of long-term prognosis and incremental quality adjusted life-years gained, both in newly detected smoking and non-smoking COPD patients.

Conflict of interest declaration

DK and OvS have nothing to declare. OvS is an Assistant Editor of the *PCRJ*, but was not involved in the editorial review of, nor the decision to publish, this article

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