

# The ‘missing millions’: Where do we find them?

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Improving rates for early diagnosis of chronic obstructive pulmonary disease (COPD) remains a challenge. As the natural history of the disease is largely insidious, permanent airway limitation has already occurred before symptoms of dyspnoea, cough and lower respiratory tract infections are present. Existing studies put the number diagnosed in the United Kingdom at 900,000 but also suggest a further two million people have the disease without a confirmed diagnosis.<sup>1</sup> Furthermore, the rate of underdiagnoses in COPD is higher when compared to other chronic diseases such as hypertension and hyperlipidemia.<sup>2</sup>

Therefore, strategies on how to find the “missing millions” are still being evaluated. The Copenhagen COPD screening project used a questionnaire with high response rates (81.2%) and detected undiagnosed COPD in 18% of the total participants.<sup>3</sup> Using a telephone questionnaire to stratify patient into moderate and high risk of having COPD followed by spirometry yielded a COPD diagnosis in 15.7% and 30.6%, respectively.<sup>4</sup> Similar efforts to find undiagnosed cases in primary care practices in Scotland by carrying out spirometry in high-risk subjects had a yield of 19%.<sup>5</sup> Others focused on capturing potential COPD subjects through community pharmacies to identify high-risk patients through five-item questionnaires, capturing up to 24% of subjects with a Forced expiratory volume in the first second (FEV1)/Forced Vital Capacity (FVC) ratio <0.7.<sup>6</sup>

The complex nature of comorbidity in COPD is well recognized<sup>7</sup> with studies reporting up to 69% of COPD patients having two other comorbidities.<sup>8</sup> Therefore, the use of screening questionnaires followed by spirometry in high-risk groups to find undiagnosed cases in patients visiting clinics for these comorbidities had been explored. A recent study on patients attending HIV clinics found that 25% of high-risk subjects had evidence of airflow limitation on spirometry.<sup>9</sup>

Targeting non-respiratory chronic conditions makes practical sense; 22.6% of patients with

established cardiovascular disease were found to have airflow limitation indicative of COPD not previously diagnosed,<sup>10</sup> while 19.8–32.1% of patients with heart failure also have COPD.<sup>11</sup> In patients with hypertension, 16.1%<sup>12</sup> have comorbid COPD. Therefore, a case finding programme for undiagnosed COPD among subjects with long-term conditions appears to be a realistic prospect. The article in this issue by Halpin et al.<sup>13</sup> took the approach of basing their selection criteria from attendees at long-term conditions clinics in primary care as the case-finding setting. Initial steps screened ever smokers for symptoms using a validated questionnaire, followed by the use of microspirometry in those with high questionnaire scores. Of the 1133 participants, 46% had high symptom scores and 22% had an FEV1 below the lower limit of normal. The majority of these (78%) had an FEV1 of 50–80%, which is perhaps not entirely surprising; however, 17% had FEV1 of 30–50% (severe airflow limitation). The diagnostic yield for this approach is comparable to that of other case-finding studies. Although participants with evidence of low FEV1 on microspirometry did not have full spirometry evaluations using the gold standard method, the correlation between the two methods had previously been tested.<sup>14,15</sup> It is also likely that the 22% yield was slightly overexpressed due to the lack of pretest bronchodilation.

Irrespective of these considerations, there remains an unmet need in COPD diagnosis and case-finding interventions certainly increase the diagnostic yield, but the exact methodology on the best approach to achieve best results remains the subject of deliberation. The balance between effectiveness, cost, and

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reliability remains poorly defined in screening/case-finding studies and more is needed to better understand this relationship to then apply best interventions. The paradox of low availability of spirometry in primary care still needs to be addressed.

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