References

1 Amin R, Sayal A, Syed F, Daniels C, Hoffman A, Moraes TJ, *et al*. How long does it take to initiate a child on long-term invasive ventilation? Results from a Canadian pediatric home ventilation program. *Can Respir J* 2015;22:103–108.
2 Baker CD, Martin S, Thrasher J, Moore HM, Baker J, Abman SH, *et al*. A standardized discharge process decreases length of stay for ventilator-dependent children. *Pediatrics* 2016;137:e20150637.
3 Solan LG, Beck AF, Brunswick SA, Sauers HS, Wade-Murphy S, Simmons JM, *et al*.; H_2O Study Group. The family perspective on hospital to home transitions: a qualitative study. *Pediatrics* 2015;136: e1539–e1549.
4 Edwards JD, Panitch HB, Nelson JE, Miller RL, Morris MC. Decisions for long-term ventilation for children: perspectives of family members. *Ann Am Thorac Soc* 2020;17:72–80.
5 Sherman JM, Davis S, Albamonte-Petrick S, Chatburn RL, Fitton C, Green C, *et al*. Care of the child with a chronic tracheostomy: this official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. *Am J Respir Crit Care Med* 2000;161:297–308.
6 Dal'Astra AP, Quirino AV, Caixêta JA, Avelino MA. Tracheostomy in childhood: review of the literature on complications and mortality over the last three decades. *Rev Bras Otorrinolaringol (Engl Ed)* 2017;83: 207–214.
7 Watters K, O'Neill M, Zhu H, Graham RJ, Hall M, Berry J. Two-year mortality, complications, and healthcare use in children with Medicaid following tracheostomy. *Laryngoscope* 2016;126:2611–2617.
8 Sterni LM, Collaco JM, Baker CD, Carroll JL, Sharma GD, Brozek JL, *et al*.; ATS Pediatric Chronic Home Ventilation Workgroup. An official American Thoracic Society clinical practice guideline: pediatric chronic home invasive ventilation. *Am J Respir Crit Care Med* 2016; 193:e16–e35.
9 Amar-Dolan LG, Horn MH, O'Connell B, Parsons SK, Roussin CJ, Weinstock PH, *et al*. "This is how hard it is": family experience of hospital-to-home transition with a tracheostomy. *Ann Am Thorac Soc* 2020;17:860–868.
10 Arnold J, Diaz MC. Simulation training for primary caregivers in the neonatal intensive care unit. *Semin Perinatol* 2016;40: 466–472.
11 Tofil NM, Rutledge C, Zinkan JL, Youngblood AQ, Stone J, Peterson DT, *et al*. Ventilator caregiver education through the use of high-fidelity pediatric simulators: a pilot study. *Clin Pediatr (Phila)* 2013;52: 1038–1043.
12 Thrasher J, Baker J, Ventre KM, Martin SE, Dawson J, Cox R, *et al*. Hospital to home: a quality improvement initiative to implement high-fidelity simulation training for caregivers of children requiring long-term mechanical ventilation. *J Pediatr Nurs* 2018;38: 114–121.
13 Casavant DW, McManus ML, Parsons SK, Zurakowski D, Graham RJ. Trial of telemedicine for patients on home ventilator support: feasibility, confidence in clinical management and use in medical decision-making. *J Telemed Telecare* 2014;20: 441–449.
14 Edwards JD, Morris MC, Nelson JE, Panitch HB, Miller RL. Decisions around long-term ventilation for children: perspectives of directors of pediatric home ventilation programs. *Ann Am Thorac Soc* 2017;14: 1539–1547.

Strange Bedfellows: The Interaction between COPD and Lung Cancer in the Context of Lung Cancer Screening

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It has been nearly 70 years since Doll first described the association between cigarette smoking and lung cancer (1), and later others followed by discovering the association of smoking with chronic obstructive pulmonary disease (COPD). Some smokers suffer the unfortunate "double whammy" of having preexisting COPD that increases the risk of developing lung cancer and are diagnosed with both. More recently, screening high-risk current and former smokers for lung cancer using radiation low-dose computed tomography (CT) has been added to the mix (2, 3). As screening is implemented globally, and given the increased risk of developing lung cancer in those suffering from COPD, there is a temptation to advocate screening all eligible patients with COPD with the hope of enriching the screened population with more patients likely to develop an early, curable cancer. To test that hypothesis in those eligible for screening, it would be important to know the prevalence and severity of COPD, the presence of respiratory symptoms, and the prevalence of other comorbid conditions to better understand their effect on screening outcomes. The study by Ruparel and colleagues (pp. 869–878) published in this issue of *AnnalsATS* goes some way to providing that information (4).

The study design was clever. Nearly 8,000 patients eligible for lung cancer screening by age, smoking history, or meeting certain thresholds for developing lung cancer using validated lung cancer risk models were invited to participate in a "lung

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health check," rather than just being offered a chest CT screen (4). In addition to a detailed medical history, they all had spirometry. Perhaps one of the most important aspects of this study was that it was undertaken in underserved communities, as evidenced by the fact that more than half had left school before the age of 15 years and there was a higher proportion than expected of current heavy smokers. These communities are where lung cancer screening is likely to have the most impact. The findings were eye opening, with more than half of the participants having spirometric evidence of COPD. Surprisingly, two-thirds of those did not have a documented prior history of the disease. Not surprisingly, the odds of having respiratory symptoms increased significantly as airflow obstruction worsened, and the presence of comorbidities was significantly higher in those with known versus undiagnosed COPD.

Now comes the tricky part. How do we convert the knowledge gained from this study into our practice of screening for lung cancer? We know that the risk of lung cancer increases in a linear relationship as the severity of airflow limitation worsens, which means those at greatest risk of lung cancer generally have the highest prevalence of COPD (5, 6). This observation underpins an important limitation of using a risk-based (i.e., age and pack-year history) approach to selecting smokers for screening. Increasing age and smoking history not only increases the likelihood of developing lung cancer but also increases the likelihood of getting COPD. This is important because COPD is associated with a number of other smoking-related diseases, such as coronary artery disease, and is a strong marker of reduced life expectancy among smokers (7–9). This translates to reduced gains from screening. Indeed a *post hoc* analysis of the NLST (National Lung Screening trial) reported that for those with COPD (the presence of airflow limitation on the basis of spirometry), the reduction in lung cancer mortality associated with the CT arm relative to the chest radiograph arm was about 15%, in contrast to those with normal lung function, where the reduction in lung cancer mortality was 28%, nearly twofold greater (6). In a further *post hoc* analysis, this reduced benefit for those with COPD was linked to lower surgical rates for early-stage cancer and greater deaths from non–lung cancer causes (6). In the same analysis, there was no screening benefit in those with Global Initiative for Chronic Obstructive Lung Disease 3 or 4 severity (6). These findings suggest that underlying (and unrecognized) COPD may contribute to both undertreatment, where surgery is inappropriately withheld, and overtreatment, where surgery is undertaken but no survival benefit is achieved.

Another feature of having preexisting COPD in the context of lung cancer is that it is associated with more aggressive forms of lung cancer (10). This means more aggressive biology reflected in both histology (more small-cell, squamous-cell, and non–small-cell subtypes) and shorter volume-doubling times (10, 11). This suggests that lung cancers developing in those with advanced COPD may be less amenable to early diagnosis by screening and confer only modest long-term survival after surgery (6).

If reducing lung cancer mortality and prolonging survival are the key determinants of successful screening, then it is likely that screening those at intermediate risk where life expectancy is greater (than for those at high risk) may be a more cost-efficient way to undertake screening. Although the routine use of spirometry in the setting of lung cancer screening may identify those with significant airflow limitation and greatest risk of lung cancer, it may have a greater utility in identifying who has severely limited life expectancy and who gains little from screening for lung cancer (e.g., Global Initiative for Chronic Obstructive Lung Disease 3–4 COPD) (6). In other words selection using a solely "risk-based" approach, with the aim to enrich the number of lung cancers identified through screening, may not improve the risk–benefit balance, particularly where the benefit ignores long-term survival. Recently, Cheung and colleagues developed a life-years–gained model, compared it to traditional risk-based screening, and found that using their approach would maximize the benefits of screening by including patients who have both a high risk of developing lung cancer and a long life expectancy (12).

Although all of these machinations seem like an exercise built for ivory tower academics, the reality on the ground is that <10% of those eligible for screening in the United States have been screened (13–15). Although spirometry is likely to be helpful in assessing a patient's risk of developing lung cancer and may provide information regarding the risk/benefit ratio from screening, one has to question whether it is feasible to add spirometry to a visit that already includes a shared decision-making component and a smoking cessation consultation for current smokers. Still, the concept of a "lung health check" is intriguing, as it may provide a forum for checking a patient for both COPD and lung cancer and present an opportunity for smoking cessation counseling to those with newly diagnosed disease. Following this cohort is critical, as it will add to our knowledge of how to interpret the effect COPD has on the outcomes of lung cancer screening and whether upfront spirometry should become a routine part of the screening visit. Stay tuned. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

References

1 Doll R, Hill AB. Smoking and carcinoma of the lung. *BMJ* 1950;221: 739–748.

2 Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, Fagerstrom RM, *et al*.; National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011;365:395–409.

3 de Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, *et al*. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med* 2020;382:503–513.

4 Ruparel M, Quaife SL, Dickson JL, Horst C, Tisi S, Hall H, *et al*. Prevalence, symptom burden, and underdiagnosis of chronic obstructive pulmonary disease in a lung cancer screening cohort. *Ann Am Thorac Soc* 2020;17:869–878.

5 Hopkins RJ, Duan F, Chiles C, Greco EM, Gamble GD, Aberle D, *et al*. Reduced expiratory flow rate among heavy smokers increases lung cancer risk: results from the National Lung Screening Trial-American College of Radiology Imaging Network Cohort. *Ann Am Thorac Soc* 2017;14:392–402.

6 Young RP, Hopkins RJ. Chronic obstructive pulmonary disease (COPD) and lung cancer screening. *Transl Lung Cancer Res* 2018;7:347–360.

7 Young RP, Hopkins R, Eaton TE. Forced expiratory volume in one second: not just a lung function test but a marker of premature death from all causes. *Eur Respir J* 2007;30:616–622.
8 Shavelle RM, Paculdo DR, Kush SJ, Mannino DM, Strauss DJ. Life expectancy and years of life lost in chronic obstructive pulmonary disease: findings from the NHANES III follow-up study. *Int J Chron Obstruct Pulmon Dis* 2009;4:137–148.
9 Rivera MP, Tanner NT, Silvestri GA, Detterbeck FC, Tammemägi MC, Young RP, *et al*.; American Thoracic Society Assembly on Thoracic Oncology. Incorporating coexisting chronic illness into decisions about patient selection for lung cancer screening: an official American Thoracic Society research statement. *Am J Respir Crit Care Med* 2018;198:e3–e13.
10 Young RP, Duan F, Chiles C, Hopkins RJ, Gamble GD, Greco EM, *et al*. Airflow limitation and histology shift in the National Lung Screening Trial: the NLST-ACRIN cohort substudy. *Am J Respir Crit Care Med* 2015;192:1060–1067.
11 Veronesi G, Maisonneuve P, Bellomi M, Rampinelli C, Durli I, Bertolotti R, *et al*. Estimating overdiagnosis in low-dose computed tomography screening for lung cancer: a cohort study. *Ann Intern Med* 2012;157:776–784.
12 Cheung LC, Berg CD, Castle PE, Katki HA, Chaturvedi AK. Life-gained-based versus risk-based selection of smokers for lung cancer screening. *Ann Intern Med* 2019;171:623–632.
13 Jemal A, Fedewa SA. Lung cancer screening with low-dose computed tomography in the United States-2010 to 2015. *JAMA Oncol* 2017;3:1278–1281.
14 Richards TB, Soman A, Thomas CC, VanFrank B, Henley SJ, Gallaway MS, *et al*. Screening for lung cancer: 10 States, 2017. *MMWR Morb Mortal Wkly Rep* 2020;69:201–206.
15 Zahnd WE, Eberth JM. Lung cancer screening utilization: a behavioral risk factor surveillance system analysis. *Am J Prev Med* 2019;57:250–255.