an individual patient. The idea is to combine and recombine drugs in response to repeated genomic sequencing of specific cancers at various stages of the disease process as opposed to the traditional one-drug-fits-all approach (10). These tools are providing a new twist to the Hippocratic emphasis on individualized care.

Physicians need to alternate between scientific principles and individualized care, two complementary systems of knowledge that reciprocate in a Yin–Yang manner. Scientific principles gained through research are collective in outlook (generalizable universal statements), whereas the clinician's gaze is concentrated on the solitary patient. The capacity to switch between these two systems demands equal proficiency in the use of a telescope and a microscope. ■

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References

1. Reichenbach H. The rise of scientific philosophy. Berkeley: University of California Press; 1951. pp. 5–7.
2. Kahn JM, Carson SS. Generating evidence on best practice in long-term acute care hospitals. *JAMA* 2013;309:719–720.
3. Ferguson ND, Cook DJ, Guyatt GH, Mehta S, Hand L, Austin P, Zhou Q, Matte A, Walter SD, Lamontagne F, *et al*.; OSCILLATE Trial Investigators; Canadian Critical Care Trials Group. High-frequency oscillation in early acute respiratory distress syndrome. *N Engl J Med* 2013;368:795–805.
4. Rothman KJ. Modern epidemiology. Boston: Little, Brown and Co; 1986. pp. 82–95.
5. Ellmann R. James Joyce, new and revised edition. Oxford: Oxford University Press; 1983. p. 505.
6. Doll R, Hill AB. The mortality of doctors in relation to their smoking habits; a preliminary report. *BMJ* 1954;1:1451–1455.
7. Levi P. The drowned and the saved. London: Abacus; 1988. p. 39.
8. Nuland SB. Doctors: the biography of medicine. New York: Knopf; 1988. p. 8.
9. Tobin MJ, Jubran A, Laghi F. Fighting the ventilator. In: Tobin MJ (editor). Principles and practice of mechanical ventilation, 3rd edition. New York: McGraw-Hill Inc.; 2012. pp. 1121–1136.
10. Gonzalez de Castro D, Clarke PA, Al-Lazikani B, Workman P. Personalized cancer medicine: molecular diagnostics, predictive biomarkers, and drug resistance. *Clin Pharmacol Ther* 2013;93:252–259.

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Developing a Research Agenda for Primary Prevention of Chronic Lung Diseases—An NHLBI Perspective

The idea that prevention is better than cure is a long-standing concept recognized by physicians from antiquity. Advances in public health have borne out the validity of this concept, and the National Heart, Lung, and Blood Institute (NHLBI) at the National Institutes of Health has been at the forefront of innovative interventions designed to prevent mortality from cardiovascular disease (CVD). The NHLBI research agenda for primary prevention of CVD has involved a balance of basic, translational, clinical, and population science. One important advance occurred when the Framingham Heart Study coined the term CVD "risk factors," which paved the way for the in-depth characterization of the "preclinical" pathobiology of CVD. The identification of preclinical biomarkers of CVD led to seminal scientific breakthroughs such as the elucidation of low-density lipoprotein metabolism and the identification of key drug targets for CVD preventive interventions. Over the past 25 years, this research agenda has changed the natural history of the disease, decreased coronary heart disease death rates by 60%, and added nearly 25 years to the lifespan of people in the United States since the 1950s. At the same time, recognition of exposure to tobacco smoke as a major risk for both heart and lung disease was critically important in the success of the CVD primary prevention agenda.

At this moment in history, despite the significant reductions in exposure to tobacco smoke and particulate and gaseous pollutants, and increased knowledge concerning etiology, the rates of chronic lung diseases are rising rather than falling. So one obvious question is, what are we missing, and should we consider new candidate paradigms for primary prevention to address this major public health problem? Is it time to engage the community in developing a research agenda for primary prevention that replicates the success achieved with CVD and "bends the curve" for better outcomes in chronic lung disease and improves overall respiratory health?

The NHLBI has a long history of supporting highly productive and pivotal research that has translated into new therapies and improved management for chronic lung diseases. To date, our greatest successes have derived from research focused on the treatment of existing diseases in symptomatic patients, and there has been less research attention on primary prevention of lung diseases. We are intrigued by the promise of new insights into chronic lung disease coming from continuing advances in genetics, the blossoming field of reparative biology, and the applications of new imaging and "omic" technologies in well-characterized patients and populations. These scientific advances embolden us to envision a future in which we challenge the prevailing concept of "chronic lung disease" and contemplate the development of preventive strategies that will preempt the progression to lung disease and/or promote its "remission" toward normal lung physiology and respiratory health.

NHLBI recognizes that to fully achieve the goal of improving the health of the nation, it is necessary for us to support research that seeks to define and promote optimal lung health, as well as research on the pathobiology and clinical management of physician-diagnosed lung disease. An intermediate goal for this research may be the identification of predictive and modifiable molecular, cellular, and physiologic events that represent a departure from optimal

Links to the articles in the NHLBI Workshop on the Primary Prevention of Chronic Lung Diseases will be available at www.atsjournals.org/page/NHLBI-Workshop

function and may represent an opportunity for intervention that restores health or abrogates progression to disease.

To move toward these aims, we convened a working group in July 2012 and a workshop in September 2013 to discuss the state of the art, identify key issues and knowledge gaps, and develop a strategy for promotion of lung health and prevention of lung diseases. Experts in the areas of lung health, asthma, bronchopulmonary dysplasia, chronic obstructive pulmonary disease, cystic fibrosis, interstitial lung disease, and pulmonary hypertension discussed this currently underemphasized aspect of lung research. While it was apparent that all disease areas could benefit from multidisciplinary research to develop markers of health and disease, identify targets for intervention, and test preventive concepts, researchers in some disease areas are already beginning to consider primary prevention interventions. Although disease prevention research was more mature in some areas than others, the principles of how to approach this major new effort are likely to be similar across the range of lung diseases. The conclusions and recommendations from the seven topics of primary prevention research are presented in the April supplement to the *Annals of the American Thoracic Society*, which will be published online on April 15, and will serve as the basis for the development of a staged strategy for primary prevention research by the NHLBI.

Major themes in this effort will be the definitions of lung health, preclinical, and disease states, which vary both on a biological continuum and over time. The concept of lung health, while consistent with the Barker hypothesis for the fetal origins of adult disease, must also consider biologic, behavioral, environmental, and socioeconomic influences on health and disease risk during the life of an individual or population, and even across generations. Emerging evidence indicates that environmental, behavioral, and socioeconomic influences impact respiratory and immune biology in a sustained manner that can accumulate and positively or negatively affect lung health outcomes for individuals and populations. Lung health is a complex concept that must expand beyond currently defined physiologic tests, and should be measurable at both individual and population levels. Temporal effects may be more complex than simply characterizing lung development and growth from gestation into adolescence and young adulthood; the life course of lung health likely includes critical periods when an exposure can have sustained effects on function and risk can accumulate over time or even across generations. Better understanding and definition of lung health, during the entire lifespan, promises to identify opportunities to intervene at pivotal points to increase and/or preserve lung health. Such interventions may be at the population or societal level as well as the level of the individual. It may be possible to both promote development of healthier lungs and slow decline of aging lungs. Even small improvements of average respiratory health (as defined by multiple measures) of a population will have a significant public health impact immediately and could be compounded over future generations.

A related important theme is the critical need for a better definition of "disease." Disease is typically tied to clinical variables and a doctor diagnosis, but the pathobiology that leads to disease is dynamic and on a continuum from health to detectable abnormalities (e.g., imaging and serum markers) to disease. As we gain a more integrated understanding of lung health–incorporating molecular, cellular, organ, and system information, it will become possible to identify critical risk factors and biologic events that represent a disruption in health and homeostasis. Comprehensive signatures of risk and perturbed healthy processes should be developed that define preclinical disease states as well as the points of disease origin, because these likely will illuminate modifiable targets for intervention in both general and disease-specific primary prevention strategies. Understanding susceptibility and inception of disease in susceptible versus "protected" individuals may also be revealing of beneficial approaches for promotion and optimization of respiratory health and primary prevention of lung disease.

We challenge ourselves and the pulmonary community to join together and create a new paradigm in which optimal, sustained respiratory health and primary prevention of lung diseases are viewed as feasible and practical goals at both the individual and population levels. Multidisciplinary approaches and teams will be needed for these investigations, and great creativity will be required for research that produces effective preventive strategies. NHLBI will continue to work, in partnership with our pulmonary community, to identify gaps, opportunities, and the best approaches in preventive research. We believe that primary prevention of chronic lung diseases is an achievable and obligatory goal for our nation. ■

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Cystic Fibrosis Transmembrane Conductance Regulator and *Pseudomonas*

Cystic fibrosis (CF) lung disease is characterized by chronic airway infection and a heightened immune response leading to airway damage and bronchiectasis (1). *Pseudomonas aeruginosa* is the species of bacteria most commonly associated with CF, with almost 80% of adults chronically infected (2). Chronic *P. aeruginosa* infection is associated with more rapid decline in lung function and decreased survival (3, 4). Inhaled antipseudomonal antibiotics are effective in eradicating early *P. aeruginosa* infection and appear