



On December 15, 2023, the American Lung Association submitted the following feedback to the National Heart, Lung, and Blood Institute's (NHLBI) Request for Information: Strategic Vision Refresh. This request asked for perspective on critical research needs or compelling research questions for any of the refresh focus areas and for perspective on challenges or barriers that need to be addressed to support progress in any of the refresh focus areas.

**Focus Area 1: Harnessing data science and new technologies to drive scientific discovery and precision health.**

The American Lung Association believes in the importance of data science and precision medicine in developing treatments for chronic lung disease. NHLBI should prioritize ongoing research on asthma treatment within this focus area. There are several emerging asthma treatments that require and are driven by ongoing research and precision medicine. For example, the National Asthma Education and Prevention Program (NAEPP) recently updated their guidelines to include Single Maintenance and Reliever Therapy (SMART) to treat persistent moderate to severe asthma. NHLBI should prioritize research into the implementation of this recommendation to identify barriers to uptake. We urge NHLBI to pursue all relevant areas of study for asthma treatment. As these emerging therapies develop, NHLBI should focus continued research efforts on all chronic lung disease treatments with emphasis on SMART therapy and biologics for the treatment of asthma.

**Focus Area 2: Using novel approaches for addressing health disparities and tackling their biological underpinnings in heart, lung, blood, and sleep diseases and conditions.**

It is crucial that addressing health disparities be a central focus of NHLBI's research related to lung disease. Health disparities are identifiable in numerous aspects of lung disease. For example, Black individuals are 42% more likely to have asthma than white individuals.<sup>1</sup> Similar disparities can be seen in the smoking population, where about 27 of every 100 non-Hispanic American Indian/Alaska Native adults smoke (as opposed to 13 of every 100 non-Hispanic white adults) and nearly 20 of every 100 adults with a disability smoke (as opposed to 12 of every 100 adults without a disability).<sup>2</sup> And more women are living with chronic obstructive pulmonary disease (COPD) compared to men and deaths from COPD are higher in women than in men.<sup>3</sup> It is clear that further research and better strategies are needed in order to meet patients' needs across demographics.

NHLBI should work to develop better strategies for identifying and addressing these disparities. Research should leverage existing data on structural and sociocultural contexts (e.g., housing indices, distance to highways, air pollution levels, food insecurity), as well as individual and family level-behavior (e.g. medication use, health care utilization). This would allow us to better understand health disparities beyond race, gender, and ethnicity, and would identify areas for change that would promote health equity. As the aforementioned disparities persist, it is critical that more work is done to identify and mitigate the effects of these barriers to care.

Addressing health disparities and tackling their biological underpinnings requires an increased focus on improving the diversity of clinical trial participants. Research is needed to understand how to improve recruitment and retention in cohort studies and clinical trials, especially of individuals who are typically underrepresented in biomedical research, including women and historically underrepresented communities. Robust representation is necessary to better understand how lung diseases work. Current approaches to improving diversity in clinical trials

have seen limited success. While improving clinical trials is already included under Objective 6 of the current strategic vision, an increased, specific focus on addressing health disparities in this context would be beneficial for lung disease research.

#### **Focus Area 4: Furthering the science on the importance of lifestyle behaviors.**

The American Lung Association is concerned by the emerging threat that long-term vaping and e-cigarettes pose to lung health. When considering the importance of lifestyle behaviors, we urge NHLBI to continue to research new and emerging lung diseases linked to vaping and e-cigarettes.

The mid- to long-term health consequences of using e-cigarettes are not yet known, because these products have only been available in the U.S. for a little over a decade and the products themselves have continued to change. However, reports so far show that using e-cigarettes causes health risks and exposes others to dangerous secondhand e-cigarette emissions.<sup>4</sup> A recent study found that e-cigarette use is associated with an increased risk of emergency department visits and death.<sup>5</sup> Another study found that chronic e-cigarette use may increase the risk of heart disease.<sup>6</sup> E-cigarettes are the most popular tobacco product among both high school and middle school students.<sup>7</sup> It is clear that continued studies of the long-term effects of these products are needed. This topic requires ongoing research to allow us to understand the threats that e-cigarettes and vaping pose to lung health.

One notable example of the risk that e-cigarettes pose to lung health is EVALI, or E-cigarette or Vaping Use-Associated Lung Injury. While the initial spike in these cases from 2019-2020 has declined, it demonstrated the ongoing necessity of research into new and emerging lung diseases linked to e-cigarettes and vaping. The CDC did determine that a chemical found in some marijuana e-cigarettes, Vitamin E acetate, was responsible for the spike in EVALI cases in 2019-2020. However, there was and continues to be a smaller number of EVALI cases from nicotine e-cigarettes. There is a lack of understanding about the cause and how to best treat them. NHLBI should include EVALI in its research on nicotine e-cigarette use as a lifestyle behavior.

#### **Focus Area 6: Addressing and reducing the impact of “place” (geography, climate, rural/urban, neighborhood) on heart, lung, blood, and sleep health.**

There is an intrinsic link between lung health and the ‘place’ a person lives. To better understand this connection, it is crucial to continue research into how a geographic, climate-related, or rural or urban ‘place’ can impact lung health.

Research is clear that climate change can negatively affect health and exacerbate community vulnerabilities.<sup>8</sup> As climate change continues to impact numerous aspects of life, it is important that NHLBI devote research to understanding how these changes affect air quality and lung health. For example, climate change is expected to lead to higher incidence in allergic illnesses.<sup>9</sup> Further research could explore how these changes will impact the severity of lung disease and other illnesses over time. Further research could also explore the extent to which these impacts interact with other social determinants of health.

A number of additional research opportunities exist related to air quality. First, NHLBI should prioritize research on the impacts of wildfires and wildfire smoke exposure. NHLBI should evaluate additional protective measures, including masks and air-filtration devices that can be used in smoke-prone areas. Other research topics that NHLBI should prioritize related to air quality include the impact of air pollutants on the reproductive system and developing fetuses, the impact of particulate matter on the brain (including both physical harm and mental health



impacts), and the interaction between genetics and air quality and other environmental exposures.

Finally, NHLBI should explore additional research related to the workplace. There is limited research investigating the impact of occupational exposures on long-term lung health. Approximately 1 in 6 adult-onset asthma cases and 1 in 7 COPD cases are caused by occupational exposures.<sup>10,11</sup> NHLBI should expand its research into risk factors for workplace asthma, COPD, pulmonary fibrosis, and other lung diseases to better identify risks and protect workers from lung disease.

**Final Section: The relevance of the 8 objectives for the NHLBI Strategic Vision, and any critical questions or challenges that are not already incorporated in the NHLBI Strategic Vision.**

In addition to what has been covered by the six focus areas of the RFI, the American Lung Association would like to offer feedback on Objective 5 of the current Strategic Vision and some general input on how NHLBI addresses lung disease issues.

Objective 5 of the current Strategic Vision is to develop and optimize novel diagnostic and therapeutic strategies to prevent, treat, and cure heart, lung, blood diseases, and sleep disorders. Under this section, we encourage the NHLBI to prioritize the treatment of lung diseases that require oxygen therapy, including COPD. We also encourage NHLBI to continue their support for development of new oxygen therapy devices. Patients with lung disease who require supplemental oxygen often find they have limited treatment and equipment options. Oxygen therapy is often only provided at home, limiting patients' mobility and quality of life. There remains a need for further research on how to improve treatment and quality of care for patients who require supplemental oxygen.

Objective 5 of the current Strategic Vision also addresses research of comorbidities from patients with chronic disease by seeking the best strategy for reducing cardiac and vascular morbidity and mortality. This question could be expanded, however, to address several critical lung disease comorbidities. For example, there is very little research on patients with dual asthma and COPD diagnoses. Most patients are eliminated from asthma or COPD-specific studies if they have been diagnosed with both disorders, leading to limited research on how these diseases interact. Furthermore, as studies continue to emerge on COVID-19 and respiratory syncytial virus (RSV), there is an ongoing need for research on how these diseases interact with other lung diseases. In particular, NHLBI should focus additional research on how comorbidities affect older adults.

In addition to this expansion of the current vision, the Lung Association encourages NHLBI to expand its collaborations with other research institutes and federal agencies. Many lung health issues like supplemental oxygen and healthy air are broad and require collaboration between multiple stakeholders to properly address their more complex research needs. For example, better understanding of the links between air quality and lung disease can be reached by working with EPA, CDC and other agencies that can build upon and add to NHLBI's existing work. Ongoing lung health research at the NHLBI can also be improved through collaboration with other institutes, including the National Cancer Institute (NCI) to identify additional causes of cancer, including genetic and occupational risks; the National Institute on Minority Health and Health Disparities to better address health inequities found in lung disease; and the National Institute on Environmental Health Sciences on issues related to air pollution, wildfire smoke and similar exposures. The Lung Association encourages NHLBI to enhance its collaboration with organizations similarly committed to reducing death and disease caused by lung diseases.

NHLBI should also ensure that research advances are translated into clear guidelines and benchmarks for providers to develop treatment plans with their patients. For example, NHLBI has developed the 2020 Focused Updates to the Asthma Management Guidelines to provide evidence-based guidelines for asthma management. While the Lung Association works to verify state Medicaid coverage of these guidelines, it is common to find providers and insurers that are not familiar with the updated benchmarks, highlighting the need to improve dissemination of these important resources. Many patients use emergency departments as their only source of asthma care, and improved uptake of clinical guidelines could help to reduce hospital re-admissions. Treatment of other lung diseases, including COPD, would also benefit from clearer provider guidelines and patient resources. We urge NHLBI to continue its work to develop guidelines for the treatment of crucial lung diseases and to collaborate with stakeholders to ensure widespread implementation of best practices.

Finally, the Lung Association's work to study lung disease includes our Lung Health Cohort Study,<sup>12</sup> a pioneering study made possible with an NHLBI grant that will study the evolution of lung disease and how healthy lungs change over time. We are working to identify strategies for addressing lung disease and the origins of lung disease in order to prevent illness before it happens. Building off this work, the Lung Association encourages NHLBI to prioritize studies that not only focus on treating lung disease symptoms but healing lungs. This type of research could help move towards a world where patients living with COPD and other lung diseases don't just have to settle for slowing symptom progression but can see the damage to their lungs reversed.

Thank you for the opportunity to provide input on the National Heart, Lung, and Blood Institute's Strategic Vision refresh.

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- <sup>2</sup> Current Cigarette Smoking Among Adults. Centers for Disease Control and Prevention, March 2022. Available at: [https://www.cdc.gov/tobacco/data\\_statistics/fact\\_sheets/adult\\_data/cig\\_smoking/index.htm](https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm)
- <sup>3</sup> <https://www.lung.org/lung-health-diseases/lung-disease-lookup/copd/learn-about-copd#:~:text=Women%20are%20more%20vulnerable%20than,with%20less%20cigarette%20smoke%20exposure>
- <sup>4</sup> National Academies of Sciences, Engineering, and Medicine. 2018. [Public Health Consequences of E-Cigarettes](#). Washington, DC: The National Academies Press.
- <sup>5</sup> Goldberg Scott, Shauna et al. “Demographic, Clinical, and Behavioral Factors Associated With Electronic Nicotine Delivery Systems Use in a Large Cohort in the United States.” *Tobacco use insights* vol. 16 1179173X221134855. 5 Jan. 2023, doi:10.1177/1179173X221134855
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- <sup>9</sup> U.S. Global Change Research Program. Fourth National Climate Assessment. Accessed December 2023. Available at: <https://nca2018.globalchange.gov/>
- <sup>10</sup> American Lung Association. Asthma at work. Accessed December 2023. Available at: <https://www.lung.org/lung-health-diseases/lung-disease-lookup/asthma/managing-asthma/workplace>
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- <sup>12</sup> American Lung Association. Lung Health Cohort Study: Making History. Accessed December 2023. Available at: <https://www.lung.org/research/lung-health-cohort-study>