



## Editorial

## COPD in Women: Future Challenges



### Background

Chronic obstructive pulmonary disease (COPD) has been a leading cause of death worldwide, but has not garnered the attention it deserves as a major contributor to morbidity and mortality from both a funding and public health perspective. This may be due to misconceptions held both by the medical and lay communities. COPD has traditionally been considered a disease of older men who smoke rather than being recognized as a ubiquitous disease affecting men and women, young and old, smokers and non-smokers. Even the two most recognizable pictorial representations of COPD in the medical literature, the “Blue Bloater” and “Pink Puffer,” depict older men. Meta-analyses estimate the global prevalence of COPD among men is 9–14% and among women 6–8%.<sup>1,2</sup> However, over time, differences in prevalence of COPD between men and women appear to be lessening. Further, women have not experienced the same improvements in mortality that have been seen among men.<sup>1,3,4</sup>

### Smoking, E-Cigarettes and Nicotine Exposures

While smoking remains the leading cause of COPD in all sexes,<sup>5</sup> only some of the increase in COPD among women is explained by proportional increases in smoking.<sup>4</sup> Even when comparing individuals with similar tobacco exposures, women are at greater risk for developing COPD as compared to men.<sup>6,7</sup> Studies have also shown that women develop COPD with less cigarette exposure and have more severe disease at younger ages than men.<sup>7</sup> There are several theories to explain this finding including smaller lung size of women (higher proportion of smoke/particle exposure per given amount of lung tissue), hormonal differences (decline in estrogen levels after menopause leads to alveolar loss), and genetics/epigenetics (altered cell function and pro-inflammatory pathways as a result of various exposures or infections), among others.<sup>1,3,4,6,7</sup>

Despite progress toward decreasing traditional combustion smoking over time, a novel threat to the lung health of future generations has risen: increasing use of E-cigarettes. As many as 1 in every 2 adolescents in some countries have reported using E-cigarettes at least once.<sup>8</sup> We still do not fully understand the long-term impact of E-cigarettes on lung health. However, we know that they contain as many, if not more, hazardous chemicals than conventional combustion cigarettes.<sup>9</sup> Some of these chemicals may ultimately prove to be as harmful as vitamin E acetate, the believed

cause of E-cigarette or Vaping Use-Associated Lung Injury (EVALI). In addition, E-cigarettes typically deliver as high or higher amounts of nicotine than combustion cigarettes.<sup>9</sup> Evidence suggests that E-cigarette use may serve as a gateway exposure to nicotine in other forms, as it has been associated with increased rates of traditional cigarette smoking over time.<sup>10,11</sup>

The potential for E-cigarettes to increase nicotine exposure in prenatal settings is another cause for concern which could perpetuate COPD in the next generation. While fetuses do not breathe in the traditional sense, nicotine is able to cross the placenta and nicotine receptors are plentiful in lung tissue.<sup>9</sup> Exposure to nicotine in-utero has been associated with impaired lung function in children as old as 12 years, higher rates of asthma and respiratory illnesses, as well as genetic/epigenetic changes (i.e. DNA methylation).<sup>12</sup> Nicotine itself can cause collagen deposition and impacts fetal airway development leading to longer and more tortuous airways that predispose to airflow obstruction.<sup>9</sup> Hence, increased nicotine exposure among pregnant women today could significantly increase the risk for COPD in the next generation. This is yet another reason that the long-term consequences of widespread E-cigarette use among young people is truly unknown.

### Non-Tobacco Exposures

Unfortunately, data show women are also prone to developing COPD without smoking. Among never-smokers with COPD, more than three-quarters are women.<sup>4</sup> The reasons for this are not completely clear. However, men and women do experience differences in exposure to polluted air within the home and at work.<sup>5</sup> At an international level, women have historically had greater exposure to indoor pollution caused by biomass fuels/indoor cooking.<sup>4</sup> The combustion of these fuels produces fine particles that can be breathed deeply into lungs, especially in poorly ventilated spaces. Other sources of pollution that women may be exposed to in the home include cleaning products, mold/mildew, asbestos, paint, and radon.<sup>9</sup> Outside the home, some traditionally female-dominated fields such as textiles, ceramics, and occupations like nail technician or hair dresser can result in exposure to harmful airborne chemicals and particulate matter.<sup>4</sup> While it may not be possible to avoid home and occupational exposures altogether, some of the harmful effects could be mitigated by improved ventilation, use of personal protective equipment such as masks, and air purification systems.

Outdoor air pollution is another major future threat for the development of COPD among women.<sup>5</sup> The WHO estimates that

99% of the world's population breathes air that exceeds safe pollution limits.<sup>13</sup> Environmental pollution is a global crisis which affects many health conditions, but for obvious reasons is particularly worrisome for those of us focused on lung disease. Extreme weather, natural disasters, wildfires, and droughts can cause very high particle levels in the air, even hundreds of miles away from the event itself. Data suggest women may also have increased sensitivity to these environmental exposures.<sup>14</sup>

### COPD Diagnosis and Treatment

In addition to aforementioned issues relating to prevention of COPD, there is also room for improvement of recognition and management of COPD in female patients. Women may not present with the same symptoms or comorbidities as men; they are more likely non-smokers who experience less coughing and phlegm production than men, but have more dyspnea and associated anxiety and depression.<sup>4,15</sup> Women are also more likely to endorse a delay in diagnosis and greater difficulty in reaching their doctors than men. This is concerning given several studies reporting women also experience more frequent exacerbations than men.<sup>15</sup> Providers should be further educated about this data, but we should also continue to investigate and invest in systems-level changes that could improve care delivery and management for COPD in women.

### Next Steps

It is true that collectively we face formidable challenges in the fight against COPD including rising nicotine use heralded by E-cigarettes and worsening air quality. Yet, the good news is that women are uniquely positioned to serve as advocates for themselves and the lung health of their children. We can defend the air that future generations will breathe by supporting initiatives such as adoption of cleaner energy strategies for transportation and manufacturing, safer housing (improved ventilation, smoking restrictions, mold mitigation, etc.), anti-idling policies in schools, restrictions on easily inhaled chemicals, and stronger regulation of tobacco products. In the future, we look forward to seeing women taking a stronger role in leadership, not only in politics but also within medicine, as we all work towards reducing the current and future burden of COPD.

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