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# Gender, tobacco and chronic obstructive pulmonary disease: analysis of the 2020 National Health Interview Survey

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#### ABSTRACT

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Dr Alexander W Steinberg; alexws@uw.edu Rationale Recent studies describe an increasing prevalence of chronic obstructive pulmonary disease (COPD) and higher COPD exacerbation rates among women compared with men despite lower average cigarette use, which has raised the question of whether women are more susceptible to the effects of tobacco smoke. We examined associations between gender. cigarette smoking and COPD in a national dataset. Methods We used cross-sectional data for US respondents aged ≥40 years from the 2020 National Health Interview Survey (NHIS). Weighted multivariable logistic regressions assessed the relationship between gender and respondent-reported physician-diagnosed COPD, adjusting for tobacco use and sociodemographic covariates. Additional analyses were performed to determine if the relationship between cigarette smoking and COPD was modified by gender.

**Results** Women had a higher COPD prevalence (7.8%) than men (6.5%) despite lower cigarette smoke exposure. Women were less likely to have ever smoked, and among respondents who had smoked, women had a lower average pack-year history compared with men. In multivariable regressions, female gender was associated with a higher risk of COPD (adjusted risk ratio 1.47, 95% CI 1.30 to 1.65) and the relative risk was similar for respondents both with and without a history of smoking. Moreover, there was no significant interaction between gender and smoking status or gender and pack-year exposure relating to COPD prevalence. **Conclusions** Among adults aged ≥40 years, women had a roughly 50% greater risk of COPD than men. Higher

a roughly 50% greater risk of COPD than men. Higher susceptibility to cigarette smoking in women did not explain the difference.

#### INTRODUCTION

Despite significant declines in cigarette use over the last 50 years, chronic obstructive pulmonary disease (COPD) remains a leading cause of mortality in the USA.<sup>1</sup> While cigarette smoking has decreased significantly among both men and women over that time, smoking rates are declining more slowly for women<sup>23</sup> and the prevalence of COPD among women is approaching that of men.<sup>4-6</sup> Projections of COPD prevalence to 2050 suggest this

#### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Despite lower average cigarette use, women have high rates of COPD, indeed higher than men with similar smoke exposure. This has led to the conclusion that women are more vulnerable to cigarette smoke than men.

#### WHAT THIS STUDY ADDS

⇒ This study provides an updated estimate of the prevalence of self-reported physician-diagnosed COPD and re-demonstrates the higher risk for COPD in women compared with men when controlled for known risk factors. No interaction was found between gender and smoking status or gender and cigarette pack-year exposure. This research raises uncertainty about the common assumption that increased vulnerability to cigarette smoke is driving the gender divide in COPD.

# HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

 $\Rightarrow$  These findings suggest that further research is needed to understand what factors drive the high rates of COPD in women and how we can address them.

trend will continue.<sup>7</sup> Compared with men, women have more early-onset severe COPD,<sup>89</sup> more severe dyspnoea, more frequent exacerbations and worse quality of life for a given percent decrease in airflow on spirometry.<sup>910</sup> Women with COPD are younger on average and have a lower average pack-year smoking exposure than men.<sup>9-12</sup> This has raised the question of whether women are more susceptible to cigarette smoke.<sup>13</sup> Indeed, prior work has suggested that the dose-response relationship between smoking and COPD may vary by gender, with a more rapid decline in airflow seen in women.<sup>12</sup><sup>14</sup> However, other studies have shown no difference in the progression of airflow obstruction by gender.<sup>15</sup> <sup>16</sup> Only very limited research has focused on COPD in adults who have never smoked cigarettes,



but overall suggests higher rates of COPD among women compared with men.  $^{17\mathchar{-}20}$ 

To further elucidate the relationship between gender, cigarette smoke exposure and COPD and to update prior estimates of the prevalence and burden of disease, we used a large nationally representative dataset to determine whether the association between cigarette exposure and COPD prevalence differs by gender. Some of these results have been reported previously as a conference abstract.<sup>21</sup>

#### **METHODS**

#### Dataset

We used data for US respondents aged  $\geq$ 40 years from the 2020 National Health Interview Survey (NHIS), a cross-sectional health survey conducted by the National Centre for Health Statistics (NCHS) under the Centres for Disease Control and Prevention.<sup>22</sup> <sup>23</sup> NHIS survey questions cover a broad range of health topics including tobacco use.

#### **Primary outcome**

Respondent self-reported lifetime diagnosis of COPD was used as the primary outcome. The survey asked: "Have you ever been told by a doctor or other health professional that you had chronic obstructive pulmonary disease, COPD, emphysema or chronic bronchitis?"

#### **Cigarette and other tobacco use**

Respondents were asked about their smoking history including if they had ever smoked cigarettes, defined as having smoked more than 100 cigarettes in their lifetime; the age they started smoking regularly; the usual number of cigarettes consumed daily; and if and when they had quit smoking. These questions were used to categorise respondents by cigarette use (never, former or current). To assess lifetime risk related to smoking, respondents with former and current smoking were combined into a category of ever smoking. This categorisation (never, ever) was used in the multivariable regression described below. Among those with ever lifetime smoking, packyears were calculated by multiplying the number of years of smoking by the usual number of packs (number of cigarettes/20) smoked daily. Additionally, respondents were surveyed about whether they had ever used electronic cigarettes (e-cigarettes), cigars, pipe tobacco or smokeless tobacco products.

#### **Covariates**

NHIS collected data on demographics including gender, age, race, county of residence and family income. Survey respondents were asked: "Are you male or female?" without specific categorisation for transgender or nonbinary respondents. Age was used to group individuals by decade: 40–49, 50–59, 60–69, 70–79 and ≥80 years. Race was categorised as white, black/African American and other/multiple. County was used to define the respondents' US region and to assign urban-rural classification based on the 2013 NCHS Urban-Rural Classification Scheme for Counties.<sup>24</sup> Family annual income was used to calculate the ratio of family income to the poverty threshold: 0.00–1.99, 2.00–3.49, 3.50–4.99, 5.00+ (in 2020, a family of four with an income at the poverty line (US\$26200) would have a poverty threshold score of 1.0).

#### **Statistical analysis**

Weighted descriptive statistics examined COPD prevalence by gender, cigarette use and age. We calculated adjusted relative risk ratios (ARRs) and 95% confidence intervals (CIs) for the association between female gender and COPD while adjusting for cigarette use and sociodemographic covariates using multivariable-weighted Poisson regressions. Additionally, we stratified models by cigarette smoking status (never, ever) to directly compare the relative risk of COPD for men and women who had never smoked cigarettes separately from those with a history of cigarette use. Finally, we performed separate interaction analyses for gender\*pack-years and gender\*cigarette smoking status to determine whether the relationship between smoking and COPD was modified by gender. From the original sample, a total of 6.3%of the adults aged  $\geq 40$  years were missing data on one or more study variables (see online supplemental figure 1). As the use of multiple imputation may not provide a substantial benefit when missingness is below 10%,<sup>25</sup> respondents with missing data were excluded from weighted multivariable analyses using listwise deletion, resulting in a complete case analysis.<sup>26</sup> All analyses were performed by Westat using Stata version 17.0.

#### Patient and public involvement statement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination of this research except as involved with NHIS. For more information, please refer to the official NHIS website (https://www.cdc.gov/nchs/nhis) and survey description.<sup>22</sup>

#### RESULTS

#### **Sample description**

The study respondents consisted of 12638 women and 10390 men aged 40 years and older, with demographics representative of the US population (table 1). The sample was equally distributed between the fourth, fifth and sixth decades of life with fewer respondents aged 70–79 and >80 years. A higher proportion of women were aged >80 years, and more women reported a family income-to-poverty ratio of <2.0 compared with men.

#### **Cigarette use and COPD**

Women reported lower rates of both current and former cigarette, cigar, pipe and smokeless tobacco use but had

Table 1 COPD prevalence, cigarette use and sociodemographic characteristics by gender in 2020 NHIS respondents aged ≥40 years

≥+0 years				
	Total (n=23028)	Men (n=10390)	Women (n=12638)	
	Weighted % (or weighted mean)	Weighted % (or weighted mean)	Weighted % (or weighted mean)	
Lifetime COPD diagnosis				
Yes	7.2	6.5	7.8	
No	92.8	93.5	92.2	
Gender				
Men	47.3	-	_	
Women	52.7	-	-	
Cigarette use				
Never	58.6	52.9	63.7	
Former	28.6	33.2	24.4	
Current	12.8	13.9	11.8	
Pack-year exposure*	(22.4)	(24.4)	(20.2)	
Geographic location				
Large central metro	29.0	28.8	29.2	
Large fringe metro	24.8	25.0	24.7	
Medium and small metro	30.3	30.7	29.9	
Non-metropolitan	15.8	15.5	16.2	
Region				
Northeast	18.5	19.0	18.0	
Midwest	20.7	20.3	21.0	
South	37.9	37.4	38.5	
West	22.9	23.3	22.5	
Age				
40–49	25.5	26.3	24.8	
50–59	26.3	27.2	25.5	
60–69	24.4	24.6	24.3	
70–79	15.7	15.0	16.3	
>80	8.1	7.0	9.0	
Race				
White only	74.6	74.9	74.4	
Black/AA only	11.2	10.6	11.7	
Other race/multiple	14.2	14.5	13.9	
Family poverty ratio†				
0.00–1.99	26.2	23.1	28.9	
2.00–3.49	23.0	22.6	23.5	
3.50-4.99	18.3	18.7	18.1	
5.00+	32.5	35.6	29.6	

\*Among respondents who have ever smoked more than 100 cigarettes in their lifetime.

†Categorises families with respect to household income and the US poverty line, which was US\$26200 in 2020. For example, a family of four with an income of US\$32000 would be in the lowest category, which includes household incomes up to US\$52138 for a family of four. AA, African American; COPD, chronic obstructive pulmonary disease; NHIS, National Health Interview Survey.

similar rates of e-cigarette use compared with men. The weighted prevalence of COPD was 7.8% for women and 6.5% for men. When the study population was limited

to those with a diagnosis of COPD (online supplemental table 1), the demographics shifted towards a more elderly, white, female population, more commonly from

	Men		Women		
	No COPD	COPD diagnosis	No COPD	COPD diagnosis	
	Weighted % (or weighted mean)				
Cigarette use					
Never	55.5	14.3	66.9	26.4	
Former	31.8	53.3	23.0	41.0	
Current	12.7	32.4	10.1	32.5	
Cigarettes per day*	(15.7)	(21.7)	(12.3)	(17.6)	
Pack-year exposure†	(22.0)	(41.8)	(17.4)	(34.8)	
Age at onset of smoking†					
<15	7.5	28.0	4.2	19.1	
15–24	33.2	54.4	24.7	47.3	
≥25	3.2	3.1	3.7	6.8	
Other tobacco use					
Ever cigar	41.6	55.6	11.5	20.9	
Ever pipe	18.2	35.1	3.9	7.8	
Ever e-cigarette	10.3	19.7	8.3	26.4	
Ever smokeless	18.9	25.5	1.9	4.6	

\*Among respondents who currently smoke cigarettes.

†Among respondents who have ever smoked >100 cigarettes in their lifetime.

COPD, chronic obstructive pulmonary disease; NHIS, National Health Interview Survey.

the Midwest or South, living in non-metropolitan areas and reporting a lower average income. Among respondents with COPD, women were more likely to have never smoked cigarettes (26.4% vs 14.3%). They reported using fewer cigarettes per day than men (mean 17.6 vs 21.7), had lower pack-year exposure (mean 34.8 vs 41.8) and were less likely to have started smoking before the age of 15 years (19.1% vs 28.0%) (table 2). Women with COPD were also less likely to use all other tobacco products except for e-cigarettes (26.5% for women, 19.7% for men).

As shown in figure 1, the prevalence of COPD was almost twice as high in women who had never smoked cigarettes than in men who had never smoked (3.2% (95% CI 2.8% to 3.7%) vs 1.7% (95% CI 1.3% to 2.1%)). The prevalence of COPD was also higher for women who had ever smoked than for men who had ever smoked (15.9% (95% CI 14.6% to 17.2%) vs 11.5% (95% CI 10.3% to 12.7%)). Figure 2 shows the prevalence of COPD stratified by age and smoking status, and illustrates that a higher COPD prevalence in women is consistent across age decades within each smoking status category. Gender differences were statistically significant for respondents aged 40-49 who had ever used cigarettes and respondents aged 70-79 who had never smoked, with women having a higher prevalence than their respective male counterparts.

#### **Multivariable analyses**

In weighted multivariable analyses, female gender was associated with a significantly higher risk of COPD diagnosis, with an adjusted risk ratio (ARR) of 1.47 (95% CI 1.30 to 1.65) (table 3). This association persisted even when stratified by cigarette smoking history, with an ARR for women (vs men) of 1.62 (95% CI 1.22 to 2.15) among those who had never smoked and 1.43 (95% CI 1.25 to 1.63) for respondents who had ever smoked. Among those who had ever smoked, the risk of COPD increased for each additional 10 pack-years of cigarette use similarly for women and men (ARR 1.18 (95% CI 1.16 to 1.22) and 1.19 (95% CI 1.16 to 1.23), respectively). There was no significant interaction between gender and pack-years or gender and smoking status (p>0.05).

#### DISCUSSION

In this large nationally representative sample of adults aged  $\geq$ 40 years, after accounting for demographics and cigarette use, women had a roughly 50% greater risk of COPD than men. The higher risk of COPD in women was not explained by higher susceptibility to cigarette smoke as measured by either smoking status or pack-year exposure. In fact, women had a nearly identical increase in risk of COPD for every 10 pack-years of cigarette use when compared with men. An increased risk of COPD among women was present among those who had never



Figure 1 Weighted chronic obstructive pulmonary disease (COPD) prevalence with 95% CI by gender and smoking status in 2020 National Health Interview Survey (NHIS) respondents aged ≥40 years.

smoked and across all age groups from 40 to >80 years, regardless of smoking status. These results are consistent with previous research which showed a high burden of disease in women despite less cigarette smoking in comparison to men, with fewer women ever smoking

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cigarettes, an older average age of starting smoking and a lower average pack-year smoking history.

Our findings can help to update estimates of prevalence. By comparison, the National Health and Nutrition Examination Survey (NHANES) study showed



Figure 2 Weighted chronic obstructive pulmonary disease (COPD) prevalence with 95% CI grouped by age, gender and smoking status.

Table 3 Relative risk of COPD by cigarette use and gender among 2020 NHIS respondents aged ≥40 years overall and stratified by smoking status

		Relative risk		95% CI	P value
	COPD prevalence	Unadjusted	Adjusted*	(adjusted)	(adjusted)
Male	6.5%	Ref	Ref	Ref	Ref
Female	7.8%	1.21	1.47	1.3 to 1.65	<0.001
Male, never smoked	1.7%	Ref	Ref	Ref	Ref
Female, never smoked	3.2%	1.88	1.63	1.22 to 2.15	<0.001
Male, ever smoked	11.5%	Ref	Ref	Ref	Ref
Female, ever smoked	15.9%	1.38	1.43	1.25 to 1.63	<0.001

\*Adjusted for age, race, family poverty ratio, urban/rural county, pack-year cigarette exposure (per 10 pack-years), age started smoking and e-cigarette use. The overall model was further adjusted for smoking status. COPD, chronic obstructive pulmonary disease; NHIS, National Health Interview Survey.

a higher prevalence of COPD in men than in women, with increasing rates among women and decreasing rates among men between 1971 and 1994.<sup>27 28</sup> Between 1988 and 1994, using spirometry, NHANES estimated the prevalence among women to be 4.8% for mild COPD and 5.8% for moderate COPD. Compared with the current study population, the NHANES cohort included younger adults (aged  $\geq 17$  years) with more prevalent cigarette use. Our estimate of COPD prevalence of 7.8% among women is similar to the reported prevalence published in more recent studies, including a global meta-analysis that included over 150 studies representing roughly 3 million COPD cases and reported a COPD prevalence among women in North America of 7.3%.<sup>5</sup> The estimate of risk per 10 pack-years is similar to prior findings from the BOLD Initiative, which estimated an OR of 1.16 per 10 pack-years for men and 1.28 for women.<sup>6</sup> This matches our findings in the approximate numerical estimate and our conclusion that risk per 10 pack-years does not significantly differ between men and women.

Additionally, the pattern of higher rates of COPD among women (vs men) who never smoked cigarettes is consistent with prior findings.<sup>17 18</sup> In a 1995 study that combined subjects over the age of 18 from NHANES I and NHANES II, and the Hispanic Health and Nutrition Examination Survey (HHANES) who had never smoked, the prevalence of COPD was estimated to be 5.6% for women and 3.7% for men.<sup>17</sup> This study included 12980 adults who had never smoked, with the majority under the age of 50 years. The Canadian National Population Health Survey, with a study population between the ages of 35 and 64 years, reported a COPD prevalence of 0.8%for men and 2.1% for women who had never smoked cigarettes,<sup>18</sup> possibly underestimating the true prevalence by excluding those aged >65 years in whom COPD is more common. Given these prior limitations, our finding of a COPD prevalence among US respondents aged  $\geq$ 40 years who have never smoked of 3.2% for women and 1.7% for men may be more accurate than earlier estimates.

These findings should raise questions about whether differing susceptibility to tobacco smoke is the key factor driving the increased COPD prevalence in women in the USA. If women were more susceptible to the effects of smoking, we would not expect to see a nearly identical risk per 10 pack-year exposure, nor would we expect to see a similarly increased relative risk among those who had never smoked. Our analysis found no interaction between pack-years or smoking status and gender. This then begs the important question of what is driving high rates of COPD among women. Multiple theories have been suggested, including gender-related exposures as well as biological factors.<sup>29</sup>

Studies have suggested that increased inhalation exposure from traditionally female-predominated occupations, home heating and cooking, aerosolised hair and beauty products and household cleaning products may contribute to higher rates of COPD in women.<sup>20 30</sup> Globally, the use of biomass fuels is a major contributor<sup>31 32</sup> and, even in the USA, home heating with coal has been found to be an independent risk factor for COPD among adults without smoking exposure.33 The incremental risk to women from indoor pollution may be obscured when combined with smoking, as in a Canadian cohort study which found that coal heating was associated with increased COPD in women who had never smoked but not in those who had.<sup>20</sup> Similarly, the SPIROMICS AIR study found that, among those with COPD and prior cigarette use, indoor pollution was not differently associated with an accelerated decline in forced expiratory volume in 1 second for women compared with men.<sup>34</sup>

A recent meta-analysis divided biological sex-related variables that have been implicated in COPD progression into three categories: structural/physiological differences, inflammatory mediators and dysregulated immune function.<sup>35</sup> Women have smaller average airway diameter<sup>36 37</sup> and have been found to have more collapsible central airways than men,<sup>38 39</sup> both of which may predispose them to obstructive physiology. A 2016 study showed increases in lipid mediators of inflammation in women with COPD compared with men, but found no genderbased differences in study participants who had never smoked nor among those who smoked but had normal

spirometry.<sup>40</sup> This may suggest a gender-specific inflammatory response in the context of disease rather than a difference related to tobacco smoke. Sex steroid receptors are expressed in the lungs and androgens and oestrogens are thought to modulate aspects of lung maturation and may influence a number of pulmonary diseases.<sup>41</sup> An analysis of the UK Biobank showed an increased risk of COPD-related hospitalisations and death with increased parity (>3), late menarche (>15 years), early menopause (<47 years) and a decreased risk with oral contraceptive use.<sup>42</sup> Other research has suggested a closer tie between sex hormones and the response to tobacco smoke. A mouse model showed a more rapid relative decline of lung function for female mice when exposed to tobacco smoke that disappeared when the mice underwent bilateral oophorectomy.<sup>43</sup> Future research is needed to clarify how each of these potential factors may contribute to the increased prevalence of COPD in women, which may modulate the body's response to inhalational exposures.

COPD is a heterogeneous condition that can include both airways and parenchymal processes leading to progressive obstructive physiology and respiratory symptoms.<sup>44</sup> The definition has changed over time with our understanding of its pathophysiology leading to updated GOLD and ATS definitions in recent years.<sup>45</sup> NHIS surveys used a broad definition, asking respondents if they had ever been diagnosed with COPD, chronic bronchitis or emphysema. While this phrasing means we are unable to describe the patterns with more nuance around the aetiology or physiology of disease, this formulation is inclusive of the wide breadth of disease included in the modern definition of COPD.

Additional limitations to this work include dependence on a self-reported COPD diagnosis that can misrepresent true diagnoses by spirometry measures. Without spirometry to confirm the diagnosis, it is possible to both under-diagnose or over-diagnose COPD.<sup>46</sup> Studies have shown that primary care physicians are less likely to consider COPD in women compared with men presenting with similar symptoms,<sup>47</sup> that use of spirometry can correct this bias,<sup>48</sup> but that unfortunately women undergo spirometry testing less frequently than men.<sup>49</sup> This combination may bias the current research to underestimate the prevalence of COPD in women. On the other hand, there is some evidence that survey data could be biased towards higher rates of COPD in women. In the NHANES III cohort there was limited agreement between reduced lung function and a reported history of obstructive lung disease (including asthma, chronic bronchitis and emphysema), with women reporting higher rates of obstructive lung disease while men were more likely to have reduced lung function on spirometry.<sup>27</sup> It is possible that the spectrum of COPD with women experiencing higher rates of chronic bronchitis<sup>37</sup> and more symptomatic disease<sup>9</sup> influences the likelihood of their seeking out medical evaluation. Symptoms affecting quality of life might even

increase an individual's desire to respond to survey questions about respiratory disease. This difference in the characteristics of COPD between men and women could therefore lead to underestimating disease among men by comparison. Self-reported tobacco use and pack-year history may under-represent true exposure, including secondhand smoke that was not surveyed in NHIS.

Data may have also been limited by binary 'female' and 'male' gender reporting, which does not allow for accurate data about transgender and non-binary Americans. Understanding of COPD prevalence in this population has been historically limited by data collection techniques and prejudices creating barriers to care.<sup>50 51</sup> An important area for ongoing research will be how variable hormonal exposure with different patterns in contraceptive use, particularly in this population who also have relatively high rates of tobacco use.<sup>52</sup>

Physical and telephone surveys require a household address and telephone number and therefore responses are limited to housed individuals, which could exclude much of the population with unstable housing and residents of long-term medical facilities. Groups with a known higher prevalence of tobacco use, including those with psychiatric diagnoses, may therefore have been under-represented in the analysis.<sup>53</sup> The reliance on survey data without additional information such as hormonal influences, familial history, infectious, occupational or environmental inhalational exposures limits our ability to identify the underlying causes driving these findings.

Despite these limitations, our findings from a large nationally representative population demonstrate a consistent pattern, further elucidating the increased risk and under-recognition of COPD in women. Our findings refine prior estimates of COPD among those without a smoking history and re-emphasise the high burden of COPD in women, underscoring the need for thoughtful efforts to prevent, diagnose and treat their disease. Additionally, our research raises uncertainty about the common assumption that increased vulnerability to cigarette smoke is driving the gender divide in COPD.

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