

Occupation and Computed Tomography Measurements of  
Chronic Obstructive Pulmonary Disease

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**Abstract**

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Environmental & Occupational Health Sciences

Introduction

Occupational exposures have been linked to the development of chronic obstructive pulmonary disease (COPD). However, there are no studies reporting associations between occupation and computed tomography (CT) measures of COPD, such as airway wall thickness and lung density.

Methods

We analyzed data from a cross-sectional hospital and population-based study of current and past smokers conducted in Bergen, Norway between 2003 and 2005. 951 subjects completed an occupational questionnaire and underwent chest CTs to evaluate lung density (% low attenuation areas - %LAA950) and airway wall thickness (AWT) as a measure of chronic bronchitis. An industrial hygienist assigned a categorical dust exposure measure, 0 (none, n=444), 1 (low,

n=308), 2 (medium, n=129) or 3 (high, n=50), based on job title and work type. We assessed the relationship between dust exposure and CT measures using multivariable regression, adjusting for age, sex, smoking and percent total lung capacity (airway obstruction-adjusted) as a measure of breath hold on CT.

## Results

When compared to no dust exposure, the three dust exposure categories had a 20% (0.99%, 46%), 54% (18%, 102%), and 33% (0.92%, 93%) increase in geometric mean %LAA950, respectively, after adjusting for covariates. This suggests more emphysematous change in the dust exposure categories. When testing the association between dust exposure and AWT, the other COPD phenotype, the high dust category had a mean 0.092mm (.002, .181) greater AWT compared to no dust exposure, after adjusting for covariates.

## Conclusion

Dust exposure, as defined by occupational title and work type, was associated with more areas of low lung density, reflecting more lung emphysema. Lack of power in the high dust category limited the ability to detect a statistically significant dose-response relationship through all levels of dust exposure. The association of high dust exposure with airway wall thickness suggests that there is an association with chronic bronchitis at high dust levels only. Future studies using a job exposure matrix may allow more precise exposure estimation and quantification of the associations with CT measures of COPD.

The views expressed in this thesis are those of the author and do not reflect the official policy or position of the United States Air Force, Department of Defense, or the U.S. Government

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) results from inflammation of small airways leading to destruction of lung tissue most commonly from cigarette smoking but also from occupational exposures to various respirable particles. In a large Canadian-based population study, it was found over 14 years, that individuals 35 and older had a 1 in 4 chance of being diagnosed with COPD, with greater cumulative incidence among men, rural habitants, and lower socioeconomic status.(Gershon, Warner, Cascagnette, Victor, & To, 2011) In 2013 it was estimated that, in the next 7 years, COPD will rank 3rd in worldwide mortality and will be the 5th most burdensome disease in the world.(Vestbo et al., 2013)

Occupational exposure to dust has correlated well with decreased lung function(de Meer, Kerkhof, Kromhout, Schouten, & Heederik, 2004; Kauffmann, Drouet, Lellouch, & Brille, 1982; Oxman et al., 1993), increased respiratory symptoms(Eagan, Gulsvik, Eide, & Bakke, 2004; Korn, Dockery, Speizer, Ware, & Ferris, 1987; MacNee, 2012) and increased mortality due to COPD.(Bergdahl et al., 2004; Blanc, 2012; Torén & Järholm, 2013) In 2003, and again in 2007, the American Thoracic Society published a statement indicating that 15% of COPD cases were directly attributed to occupational exposures.(Balmes et al., 2003; Blanc & Toren, 2007) Among non-smokers, the occupational attributable risk of COPD has ranged between 26-30%, while the mortality due to COPD has been reported between 43-53%.(Blanc, 2012) In a Russian study that was assessing the prevalence of COPD in their industrial workers, they found that the non-smoking occupationally exposed workers had a similar prevalence as smokers who did not have occupational exposures.(Mazitova, Saveliev, Berheeva, & Amirov, 2012) In addition, a study conducted in South Africa calculated a 2.1 odds of COPD among those exposed to biological

dust, after accounting for odds of disease from tuberculosis and smoking.(Govender, Lalloo, & Naidoo, 2011)

Recent epidemiologic data has established a causal link to occupational exposures and COPD based on defined spirometry definitions for COPD (FEV1/FVC <0.70 and FEV1 < 80% predicted) as outlined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), where FEV1 is the forced expiratory volume in 1 second and the FVC is the forced vital capacity.(Mehta et al., 2012) In this prospective cohort study, they evaluated the incidence of COPD as based on spirometry data among certain occupations in Switzerland. They used a job exposure matrix and compared this with the self-reported exposure data from their study subjects in order to assess the association with spirometry specific diagnoses. They found that occupational exposure to high levels of vapors, gas, dust and fumes was statistically significantly associated with the development of COPD. Earlier this year, Omland et al. published a literature review and found abundant evidence relating to inorganic and organic dust exposures with strong patterns of dose response and consistent evidence to support a causal association with the development of COPD.(Omland et al., 2014)

Computed tomography (CT) has been used both diagnostically and in preparation for lung volume reduction surgery in those patients with severely advanced COPD. The CT helps define the morphologic condition of the lung both visually and quantitatively using computed algorithms. Typical quantitative measures that are used to assess the two main phenotypes of COPD (emphysema and chronic bronchitis) are measures of low attenuation areas and airway wall thickness, respectively. Low attenuation areas less than -950 Hounsfield units (LAA<-950 HU) on high-resolution CT have been shown to correlate well with emphysema changes as seen on pathologic specimens.(Gevenois, de Maertelaer, De Vuyst, Zanen, & Yernault, 1995; Kim et

al., 2011; Lynch & Al-Qaisi, 2013; Wang, Cherng, Perng, Lee, & Wang, 2013) Airway wall thickness is calculated as a standardized “hypothetical” bronchus with an internal perimeter of 10mm that is taken from the regression line between the square root of the wall area and the internal perimeter of each measured bronchus.(Kim, et al., 2011; Lynch & Al-Qaisi, 2013)

There has been a recent study identifying increased mortality in individuals with greater airway wall thickness (AWT) at increasing levels of emphysema (as measured by a higher percentage of LAA<-950).(Johannessen, Skorge, et al., 2013) Also, respiratory complaints of dyspnea, cough or wheezing have been associated with AWT and lung density measured on CT.(Grydeland et al., 2010) Finally, self-reported exposure to dust-gas was associated with a higher percentage of low-attenuation area in subjects with COPD after adjusting for age, sex, and pack-years of smoking, but there was no association with any self-reported exposure and AWT after adjusting for covariates.(Vedal, Grydeland, Coxson, Gulsvik, & Bakke, 2010)

While there are studies on the risk of COPD associated with occupational exposures, there are no studies comparing occupation and quantitative CT measures of COPD. The objective of this study is to derive an occupational dust exposure variable using job title and work type of each study participant. Then, to assess the association between the derived dust exposure variable and quantitative CT measures of COPD.

### **Research Hypothesis**

We hypothesize that there is a positive association between a worker’s level of dust exposure, as characterized by a job exposure measure based on job title and work type and lung disease as defined by low lung density (a measure of emphysema) and increased average airway wall

thickness (a measure of chronic bronchitis) on CT. Additionally, we expect to see a higher level of spirometric lung disease among the workers exposed to greater dust.

The first aim was to derive a meaningful dust exposure variable based on an individual's job title and type of work he/she performed for the longest duration. As a means of performing internal validation of the derived dust exposure measure, we plan to compare the derived dust exposure measure and the subject's self-reported exposure to dust. We anticipated that the derived dust exposure measure, based on the industrial hygienist's (IH) understanding of the subject's occupational title and type of work that was conducted would closely approximate the individual's self-reported exposure to dust. However, we ascribe more interpretive weight to the IH assignment of exposure because it is less subjective.

Null Hypothesis: There is no association between the IH-derived dust exposure measure and self-reported dust exposure.

The second aim was to determine if there was an association between the derived dust exposure measure and the outcomes of interest on CT scan (low lung density and airway wall thickness). As a secondary analysis, because we also have spirometry data on each participant, we hypothesize that with greater dust exposure there is a greater proportion of individuals with COPD as defined by spirometry.

## **METHODS**

We analyzed de-identified data from a Norwegian cross-sectional hospital-based study and a population-based study of current and past smokers that was conducted in Bergen, Norway between 2003 and 2005. 951 subjects completed an occupational questionnaire and underwent chest CT scan to evaluate:

- 1). lung density (% low attenuation areas - %LAA950) as a measure of emphysema
- 2). airway wall thickness (AWT) as a measure of chronic bronchitis.

### Study design and participants

Cross-sectional analysis of a Norwegian hospital and population-based study was conducted on a sub-set of participants (N=951) who had a voluntary high-resolution computed tomography (HRCT) scan of the chest and had completed an occupational questionnaire (Figure 1). The subjects used for this analysis were part of a much larger population study (N=1909) conducted in Bergen, Norway from January 2003 to January 2005. The larger study design recruited participants from 1 of 2 population surveys(Gulsvik, Humerfelt, Bakke, Omenaas, & Lehmann, 2008), voluntary recruits, as well as from a hospital patient registry (Figure 1).(Grydeland, et al., 2010; Johannessen, Nilsen, et al., 2013) The main purpose of the GenKOLS study was to compare past and current smokers with and without COPD for possible genetic differences.

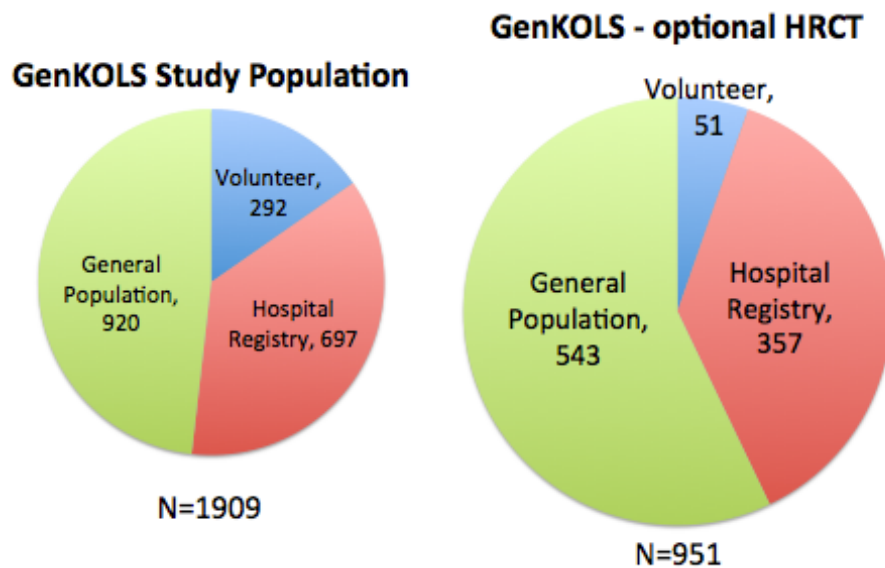


Figure 1: Population distribution of recruitment for the Norwegian study conducted between 2003-2005.

HRCT – High Resolution Computed Tomography.

## **Dust Exposure Measure**

Each of the participants completed a self-administered respiratory and occupational questionnaire during the study period (2003-2005). For the purpose of this study, we chose to focus on the question that asked “what has been your usual job, i.e., the one you have worked at the longest?” in order to derive a dust exposure variable. The participants were asked to provide job title, type of work done and the type of industry/business they worked in. For our study we recruited the assistance of an industrial hygienist, who was blinded to the clinical outcomes of interest, to assign a dust exposure level based on his understanding of the study participant’s particular job title and work type. If a particular job task was administrative, this typically was assigned a “0” (none) level exposure. However, if the same administrative job task was performed in a “dusty” environmental setting, i.e., one in which work is being done in areas where people are likely exposed above a particular permissible exposure level (PEL) or working in an industry with a low probability of high exposures, then the exposure measure was assigned a “1” (low). For individuals who indicated that their job title or work type involved areas that were likely over the PEL of some particulate agent, then a “3” (high) level of dust exposure was assigned. Then, anyone who was felt to have more than low level of dust exposure, but not a high level of dust exposure, were assigned a “2” (medium) level of dust exposure. Finally, for individuals who indicated their job title as some form of manager/supervisor, their dust exposure was lowered by one level when compared to an individual who may have the same job title, but who is performing, rather than managing, the majority of the work. There were 6 individuals who did not fill out this information and 8 others who indicated a job title or work type that could not be classified either because of poor description or were not classified because of lack of familiarity with dust exposure corresponding to their job.

Also, we had self-reported information from each participant indicating whether they worked in a dusty job for more than 1 year by indicating a “yes”, “no” or “don’t know.” For those participants who indicated “don’t know” (total number 18), these were treated as a “no” because they did not go on to answer the question of exposure to dust: “mild”, “moderate” or “severe”. Therefore, there were a total of 503 who indicated “no” exposure to dust. The other 433 participants indicated dust exposure and there were 15 participants who left this question blank. The self reported exposure information was used to perform internal validation analysis with the derived dust exposure measure based on their job title and work type.

### **Computed tomography (CT) outcome measures**

CT scans were performed with a single scanner and under the same full-inspiration protocol using 1 mm slice thickness at 20 mm intervals, as described by (Grydeland et al., 2011). Percentage of low attenuation areas, corresponding to areas in the lungs with <-950 Hounsfield Units, is a marker for emphysematous changes. A standardized “theoretical airway” measure of average airway wall thickness for a bronchus with internal perimeter of 10mm was calculated for each individual, which was based off the regression between the square root of an airway wall thickness and the internal perimeter of airways 6 mm or greater in diameter. This CT measure is a marker/surrogate for chronic bronchitis, the other COPD phenotype.

### **Definition of COPD**

COPD was defined by spirometry as FEV1/FVC <0.70 and FEV1 < 80% predicted, as outlined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) category 2 or greater,

where FEV1 is the forced expiratory volume in 1 second and the FVC is the forced vital capacity during spirometry.

### **Data Analysis**

Analyses were conducted using Stata version 12.1 (StataCorp College Station, TX 2013).

Differences in proportions and means were tested with  $\chi^2$  test and analysis of variance (ANOVA), respectively. To control for a participant's breath volume during the CT, independent of COPD status, the CT volume (percent total lung capacity - % TLC) was regressed against an individual's severity of COPD as referenced by their GOLD classification (0, 2, 3, or 4). The residuals from this regression were then used as an "obstruction-adjusted" measure of breath volume.

Multiple linear regression models, adjusted for age, gender, smoking history (including pack-years and current smoking status), and the obstruction-adjusted CT lung volume (% TLC), were used to determine the association between the derived dust exposure measure and the outcomes of interest (%LAA950) and AWT. Because %LAA950 and AWT are on the pathway to the development of COPD, we did not want to control for an individual's COPD status. The association between the derived dust exposure measure and the presence of COPD as a binary outcome was examined with logistic regression, adjusted for same covariates previously mentioned.

### **RESULTS**

A total of 951 study subjects completed CT of the chest. However, 20 subjects were excluded from analysis because their job title and/or work type was incomplete or missing, or an

occupational dust exposure could not be derived. Table 1 shows the 4x4 results of IH-derived dust exposure measure and self-reported dust exposure. Because the specific dust exposure question asked of the study participant was conceptually different from the assigned level of dust exposure based on the IH, the groups are binary for analysis. We conclude that there is a non-random association between the IH-derived dust exposure measure and the self-reported dust exposure to a high level of statistical significance ( $p < 0.001$ ).

		IH-derived dust exposure measure		
		No	Yes	Total
Self-reported dust exposure	No	335	159	494
	Yes	106	318	424
Total		441	477	918

Table 1: IH-derived dust exposure measure and self-reported dust exposure based on binary outcome of dust exposure. Chi-squared test of non-random association of the two variables yields  $p < 0.001$ .

Of the 931 quantitative chest CTs, 927 had complete information on %LAA950, while 876 had complete data for AWT measurement. There were higher proportions of men working in higher dust-exposed jobs ( $p < 0.001$ ). On average, dust exposed subjects were older with more pack-years of smoking and had smaller breath volumes as defined by percent total lung capacity (% TLC), after accounting for obstruction-adjusted CT lung volume. There was no statistically significant difference in prevalence of current smokers among the derived dust exposure groups.

Tables 2 and 3 show the distribution of the study participants in relation to dust exposure group and the distribution between the dust exposure and outcomes of interest, respectively. The distribution of %LAA950 was right-skewed; therefore this variable was log-transformed before performing the regression analysis.

Tables 4 and 5 show the analyses from multiple linear regression. After accounting for age (years – range from 40.1 to 86.2), gender (male=1), pack-years of smoking (range from 2.5 to 118.8), current smoking status (yes/no) and the derived breath volume measure (% TLC), there was a dose-response relationship with %LAA950 with the first two dust exposure groups, though this was significant only in the medium exposed participants ( $p=0.002$ ). When assessing the association of the derived dust exposure with AWT, after adjusting for the same covariates, only the high level of dust exposure showed a higher airway wall thickness compared to no dust exposure ( $p=0.044$ ).

	Dust Exposure Category				
	None	Low	Medium	High	
Subjects (n)	444	308	129	50	
Age (years; mean [SD])	58.9 [10.4]	60.0 [9.95]	61.5 [10.2]	62.4 [12.0]	<b>p=0.019</b>
Gender (Male; n [%])	195 [44%]	193 [63%]	110 [85%]	50 [100%]	<b>p&lt;0.001</b>
Current Smokers (n [%])	189 [43%]	158 [51%]	52 [40%]	23 [46%]	p=0.068
Pack-years (mean [SD])	22.9 [16.3]	26.1 [16.7]	26.4 [15.6]	28.4 [16.3]	<b>p=0.009</b>
CT lung volume <sup>§</sup> (mean [SD])	0.079 [1.01]	-0.010 [0.99]	-0.202 [1.04]	-0.067 [0.92]	<b>p=0.042</b>

Table 2: Characteristics of study population by dust exposure measure and covariates of interest. <sup>§</sup>Obstruction-adjusted CT lung volume is used as a measure of breath volume and correlates to the percent total lung capacity. p values represent ANOVA for mean[SD] and Chi-squared test for proportional variability

### Dust Exposure by Occupational Title and Work Type

		None	Low	Medium	High
% Low-attenuation areas < -950 HU	Subjects (n)	442	306	129	50
	Median [IQR]	1.08 [0.33-4.86]	1.78 [0.51-8.81]	3.02 [0.82-10.88]	3.25 [1.25-14.76]
AWT-Pi10 (mm)	Subjects (n)	421	287	121	47
	Mean [SD]	4.80 [0.32]	4.89 [0.33]	4.90 [0.27]	5.04 [0.35]

Table 3: Distribution of derived dust exposure by quantitative CT outcome variables. % Low-attenuation areas < -950 HU is a marker of emphysema. Because this was skewed, log-transformation of %LAA950 was used in the linear regression analysis. AWT-Pi10 is a standardized measure of airway wall thickness at 10mm internal perimeter, a marker of chronic bronchitis.

Log %LAA -950 HU			
	Coefficient	95% C.I.	p-value
None (reference category)			
Low	0.185	(-0.0112, 0.381)	p=0.065
Med	<b>0.425</b>	(0.165, 0.704)	<b>p=0.002</b>
High	0.233	(-0.111, 0.687)	p=0.157
age	<b>0.069</b>	(0.06, 0.078)	<b>p&lt;0.001</b>
gender	<b>0.847</b>	(0.652, 1.04)	<b>p&lt;0.001</b>
current smokers	<b>-0.186</b>	(-0.369, -0.003)	<b>p=0.047</b>
pack-years	<b>0.014</b>	(0.009, 0.02)	<b>p&lt;0.001</b>
CT lung volume	<b>0.716</b>	(0.627, 0.805)	<b>p&lt;0.001</b>
Intercept	-0.03	(-0.20, 0.15)	p=0.762

Table 4: Effect estimates for dust exposure measures and covariates for log %LAA950. Intercept term represents log %LAA950 in females with no dust exposure who have quit smoking and are of mean age, mean pack-year smoking history and have mean obstruction-adjusted CT lung volume (percent total lung capacity).

AWTPi10 (mm)			
	Coefficient	95% C.I.	p-value
None (reference category)			
Low	0.028	(-0.016, 0.071)	p=0.219
Med	-0.013	(-0.074, 0.047)	p=0.661
High	<b>0.092</b>	(0.002, 0.181)	<b>p=0.044</b>
age	0.0002	(-0.0018, 0.0022)	p=0.844
gender	<b>0.23</b>	(0.19, 0.28)	<b>p&lt;0.001</b>
current smokers	0.023	(-0.017, 0.064)	p=0.261
pack-years	<b>0.003</b>	(0.0017, 0.0042)	<b>p&lt;0.001</b>
CT lung volume	<b>-0.061</b>	(-0.081, -0.04)	<b>p&lt;0.001</b>
Intercept	<b>4.70</b>	(4.66, 4.74)	<b>p&lt;0.001</b>

Table 5: Effect estimates for dust exposure measures and covariates for Airway Wall Thickness, measure of chronic bronchitis. The intercept term represents AWT in females with no dust exposure who have quit smoking and are of mean age, mean pack-year smoking history and have mean obstruction-adjusted CT lung volume (% TLC).

## Secondary analysis

Logistic regression models, adjusted for age (10 year increment), gender, pack-years (10 pack-year increment), and current smoking status between the derived dust exposure measure and spirometry diagnosed presence or absence of COPD showed higher odds of COPD at all levels of derived dust exposure as shown in Figure 2, though only statistically significant for the low and medium exposure groups. Compared to no dust exposure, there was a 1.63 (1.16, 2.30), 2.40 (1.49, 3.88), and 1.95 (0.94, 4.03) odds of spirometry-defined COPD for low, medium and high dust exposures, respectively.

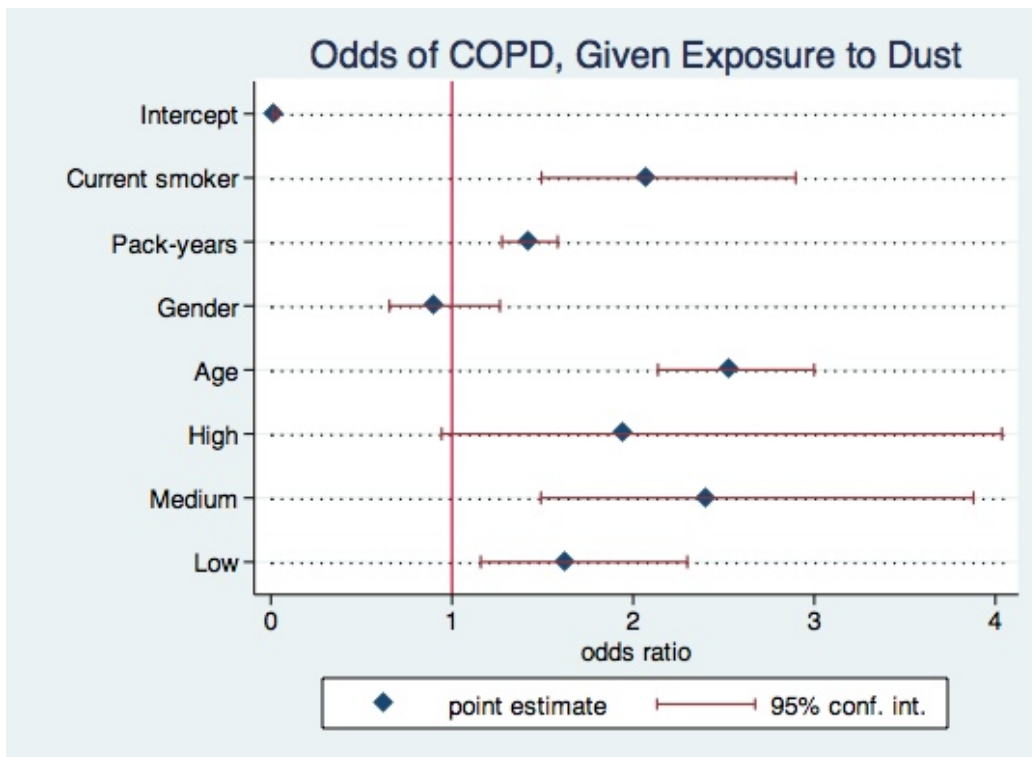


Figure 2: Logistic regression provides information regarding the odds of COPD as it relates to increasing levels of dust exposure, which is statistically significant at low and medium levels. The intercept term represents odds ratio in females with no dust exposure who have quit smoking and are in the earliest decade of life (ages 45 to 55), and have the lowest 10 pack-year smoking history (2.5 to 12.5).

## **DISCUSSION**

This was a large Norwegian general population and hospital based study, which showed that dust exposure, as defined by occupational title and work type, was associated with more areas of low lung density, reflecting more lung emphysema. There may also be an association with chronic bronchitis but at high dust levels only. These results add to the evidence that occupational dust exposure is independently associated with both phenotypes of COPD (emphysema and chronic bronchitis). Because the data was from a general population study, there is less likelihood for healthy worker bias effect as seen in occupational studies. Also, because the CT scans were performed using the same scanner and inspiratory protocol for each patient, this helped reduce misclassification in our outcome variables.

Because we had a good smoking history, with their pack-year use as well as current smoking status, we were able to adjust well for the effect of smoking on the outcomes in our linear and logistic regression models. When we adjusted for smoking in the model, we showed that the independent effect of smoking was significant with high level of confidence, thereby increasing the validity of our study results. Current smokers were found to have significantly less emphysematous changes on CT scan and this is likely as a result of “healthy smoker effect” or a “survivor effect” where a current smoking individual is likely less susceptible to the effects of smoking and therefore continues to smoke because the health impact is not noticeable whereas those with advancing disease would likely reduce their smoking or quit. This is consistent with a recent study that showed current smokers appear to have lower levels of emphysema.(Grydeland et al., 2009; Lynch & Al-Qaisi, 2013)

The lack of a linear dose response relationship for %LAA950 in the highest dust exposed category is likely due to the small sample size (N=50). It is also possible that the smaller effect

size could be related to individuals who are more prone to working in higher dust exposed environments are more likely to wear personal protective equipment and therefore reduce their exposure effect. Unfortunately, the respiratory questionnaire did not include questions on the utilization of personal protective equipment while working. It has been discussed that the biological plausibility between a worker's exposure to dust and the development of COPD should lead to greater regulation to decrease exposures.(Meldrum, Rawbone, Curran, & Fishwick, 2005) In a study looking at the mortality due to COPD among non-smokers, it was estimated that a reduction of workplace exposure to inorganic dust would prevent one out of eleven deaths due to COPD, regardless of smoking.(Bergdahl, et al., 2004) More recently, Naidoo as well as Diaz-Guzman report that the evidence for causality between dust and development of COPD in conjunction with significant morbidity and mortality is such that there should be greater public health concern through the implementation of workplace interventions to help manage work-related COPD.(Diaz-Guzman, Aryal, & Mannino, 2012; Naidoo, 2012) A greater proportion of men worked in the higher dust exposed occupations in our study population and had greater percentage of low lung density as well as thicker airway walls, when compared to females in our study. Grydeland et al. published similar sex differences among current and past smokers for both individuals with and without COPD.(Grydeland, et al., 2009) In a study looking at gender differences of quantitative measures on CT among smokers, they found that males had greater percentage of low lung density, while there was no significant difference between a standardized airway wall at 10 mm internal perimeter across gender.(Kim, et al., 2011) In a large multi-city general US population study looking at the exposure response relationship between duration of dust exposure and symptom reporting, they found that men and women had similar risks of symptoms, but men had a higher prevalence of COPD with

occupational dust exposure.(Korn, et al., 1987) In a cross-sectional Australian community based study looking at the occupational risk factors and development of COPD, they found that women had a significantly higher risk when exposed to biological dust, but not mineral dusts.(Matheson et al., 2005) It has also been shown in National Health Interview Survey data that females have an increased prevalence of COPD(Bang, Syamlal, Mazurek, & Wassell, 2013) and this has also been shown in an earlier UK cross-sectional study, although they were unsure if the females were more exposed or just more susceptible.(Melville, Pless-Mulloli, Afolabi, & Stenton, 2010) Finally, in a Swiss cohort study, it was found that COPD was observed mainly among men over 40 years and that men were more likely to report occupations with high levels of dust, gases or fumes exposures in these settings.(Mehta, et al., 2012)

## **LIMITATIONS**

One significant limitation to this study is the crude derived dust exposure measure, which is subject to exposure misclassification. However, the available methodology that was used was the best available to us at the present time. The first initial attempt was in trying to use a validated job exposure matrix like the Finish Job Exposure Matrix (FJEM) especially because it would likely offer a better indicator of historical exposures for the Nordic regions to more accurately assign the exposure variable. However, in discussion with the lead scientist who manages the release and utilization of the FJEM, he indicated that at the present time the matrix is not codified for general “dust” exposures, but that this was a current project that was in the development stages and possibly available in the near future. It has been described that the use of a JEM is more likely to randomly misclassify and therefore create a non-differential misclassification with a bias more towards the null.(Blanc et al., 2009)

Another consideration that was made was the possibility of using O\*Net as a means of better characterizing the exposure to dust based on the occupation the individual listed. However, it was found that the O\*Net classification was for “exposure to contaminants (pollutants, gases, dust or odors).” The problem with this definition is two-fold: first, the contaminants include other exposures like pollutants, gases and odors and second, the values, based on a 100% scale, did not identify which contaminant was being given the value and therefore was not specific to dust exposure.

Therefore, it was felt that utilizing the assistance of a trained exposure scientist in industrial hygiene would be the next best alternative for defining the exposure measure. The use of industrial hygienists to provide an exposure assessment specifically as it relates to dust exposure and COPD has been reported.(Weinmann et al., 2008) One potential way to improve exposure misclassification would have been to obtain measured dust exposure data on each individual. Alternatively, we could have utilized the assistance of a Norwegian industrial hygienist, who is more familiar with the specific exposures and personal protective use practices for the exposed industries.

When we compared the exposure assessment that was defined by the industrial hygienist there was a statistically significant level of agreement with the self-reported exposures to dust ( $\chi^2=229.4$ ,  $p < 0.001$ ). However, the highly significant association was primarily driven by the agreement amongst the individuals in the non-exposed groups.

Another limitation is the fact that we used the “longest usual job” as a means of defining dust exposure. If we had utilized the full occupational history, it is possible we could have had a better cumulative exposure measure based on their entire work history. However, the number of years worked in their “longest usual job” averaged 24 years (+/- 11 years), so this may not be a

significant concern. It has been described, when using the longest held job for exposure assignment, that this helps ensure that there is sufficient exposure time to precede the onset of disease.(Blanc, et al., 2009)

Finally, because the original study design of the GenKOLS study was to assess the genetic variation among smokers susceptible to the development of COPD, it is possible that the recruitment from the general populous, volunteers and the hospital registry, and selection due to the voluntary performance of high resolution CT scan of the chest could further bias the disease-exposure relationship.(Sørheim et al., 2010)

## **CONCLUSION**

This is one of the first studies to show that occupational dust exposure (as defined by occupational title and work type) is associated with COPD, based on CT measures of emphysema and chronic bronchitis. Although there were several limitations to this study, we attempted to account for these in the analysis but recognize that there could be additional confounding of the relationship between dust exposure and computed tomography measures of COPD. Future studies could be conducted and designed to attempt to avoid the study limitations by using a validated JEM, occupational questionnaire that is filled out with assistance to help provide complete work histories, include information regarding the use of personal protective equipment and training as well as include non-smokers in the study population.

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