9-29-2016

The Effect of Seasonality on Pulmonary Function Tests

Nicholas James Cotter
University of South Florida, Nicholas76@mail.usf.edu

The Effects of Seasonality on Pulmonary Function Test Outcomes

by

Nicholas James Cotter

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Public Health (Toxicology and Risk Assessment)
Environmental and Occupational Health
College of Public Health
University of South Florida

Major Professor: Giffe Johnson, Ph.D.
Marie Bourgeois, Ph.D.
Raymond Harbison, Ph.D.

Date of Approval:
March 22, 2017

Keywords: allergies, seasons, respirator, fitness

TABLE OF CONTENTS

LIST OF TABLES

ABSTRACT

Lung spirometry data from three working-class industry populations were analyzed using logistic and linear regression to see if seasonality adversely affected test outcomes. Populations included emergency responders, general industry, and shipwrights. The data was organized into allergy and non-allergy seasons using NOAA meteorological data and regression and logistic analysis was run on these separate populations to test for demographic and seasonal effects on lung spirometry test outcomes. The American Thoracic Society gold standard was as a point for determining impaired lung function ($FEV_1/FVC > 0.80$). It was found that seasonality imparted a slight linear effect on the predictive values of FEV_1 and FVC for determining impaired lung function FEV_1 and FVC values were $Pr > 0.0003$ and $Pr > 0.0002$, respectively. For demographic variables, age imparted the greatest linear effect for FEV_1 and FVC, with significant p-values of 0.0002 and <0.0001, respectively.

CHAPTER ONE:

INTRODUCTION

An often seemingly benign and under-played problem effecting millions throughout the United States, daily, are allergies. More than 50 million Americans suffer from this chronic illness; totaling up to a cost of $18 billion dollars annually (CDC.gov, 2011). While many of us know someone in our families or amongst our friends with allergies, this seems to be seen as commonplace and is often not looked into any further concerning possible further ramifications or consequences other than a continued and mild annoyance for the sufferer.

Allergies are the result of an over-responsive immune system reacting to seemingly harmless substances that would normally elicit a biological response in a human (CDC.gov, 2011). These responses range from coughing, sneezing, runny nose, and even hives or difficulty breathing. All ages are at risk for allergies. Given the wide variety of genetic make up for individuals as well as the nature of allergies, it is becoming more uncommon to find individuals that do not have some sort of allergy or sensitization. Allergies can range from an in-born allergy an infant may have to cow's milk or an adult male that has reoccurring allergic dermatitis when coming in contact with latex (CDC.gov, 2011). Allergies can also differ in their nature; being that they can be seasonal, which is typically limited to pollen produced in growing seasons by specific plants or from mold spores. Allergies can also be perennial, causing allergy sufferers to be affected year-round by dust mites, pet hair or dander, cockroaches, or molds (ACCAI.org, 2014). There are noted differences between the specific types of illnesses that allergies can cause. Contact dermatitis occurs when a specific allergen makes physical contact with the skin or mucosa and the skin reacts by swelling and turning red. Allergic rhinitis is associated with runny nose and itchy, watery eyes and is most often concurrent with pollen blooms in allergy seasons. Occupational rhinitis and dermatitis are associated with occupational contact with aggravating dusts, allergens, or chemicals that can sensitize individuals that come in contact with them. Allergic rhinitis, the most common of these, is often overlooked due to this very reason.

From an occupational standpoint, asthma and allergies can be debilitating to workers, potentially leading them to fail lung spirometry tests and suffer from distracting symptoms while at work. Lung spirometry is used in the industry as a form of health surveillance and can often detect if any workers are developing prodromal symptoms relating to their occupation (CDC.NIOSH.gov, 2011). Because of underlying allergy symptoms, these tests can give false positives and be misleading to Risk Management and health sections in the industry. As a result, workers could potentially fail fitness tests and be labeled as unfit for duty, even though they may not be at risk for occupational illnesses. The goal of this research is to investigate if there is an increase in workers failing lung spirometry tests coinciding with allergy seasons in the Southeastern United States.

Pulmonary Function Tests (PFTs) are a battery of tests that are used to assess how well a patient's lungs are functioning. A type of PFT, Lung Spirometry, measures airflow by having a patient exhale into a mouthpiece that is connected to a spirometer. The spirometer measures the maximum amount of air that a patient can forcefully exhale, usually measured in an interval of seconds. Patient safety precautions must be taken into consideration during this battery of tests. Given that spirometry tests can be physically demanding, Miller et al recommends that patients are made comfortable and placed in an environment that would mitigate the likelihood of injury through syncope. It is recommended that the patients remain seated while taking the tests. If a standing test is required, fall prophylaxis should be employed. It should be noted that the tests should try to replicate the conditions, in repeat testing, that were present in the first test. If the patient performed the lung spirometry testing while standing, they should perform the repeat testing in the standing position as well. Several important values are derived from this test that indicate the total amount of air expired and the total amount of air expired in one second, the forced vital capacity (FVC) and the forced expiratory volume in one second (FEV1). A ratio between the FVC and FEV1 is taken to and measured against a gold standard set by the American Thoracic Society. This standard stipulates that any FEV1/FVC value below 80% of the average FEV1/FVC ratio indicates that there is an obstructive or restrictive disease within the patient. Allergies come into play because chronic exacerbation can cause asthma, a restrictive lung disease. In a study conducted by Cushen et al, a cohort of Irish farmers was investigated for their prevalence of restrictive and obstructive lung diseases. Obstructive and restrictive disease were found in equal prevalence among smokers and non-smokers, with most these cases being related to allergies acquired in the workplace. The majority of these farmers were livestock farmers that were exposed to mildew and mold spores. There is further evidence to suggest that allergy-induced asthma, due to chronic exacerbations, still effect patients even outside of the allergy season. A study by Bake et al showed that patients that exhaled the highest quantity of nitrous oxide (an inflammation indicator) were patients that had allergy-related asthma due to pollen. These higher values of exhaled nitrous oxide also persisted out of the allergy season, indicating that the chronic allergy exacerbations lead to prolonged damage in the exchange surfaces within the lungs. Regarding spirometry, asthmatic patients compared to controls did not have significantly differing FEV_1/FVC values until subjected to bronchodilators. Upon subjecting the asthmatics to bronchodilators during the allergy season, these values changed slightly. Though this change was slight in the spirometry testing, it was significant. This change reinforces the previously mentioned chronic damage that allergies can perniciously inflict upon the exchange surfaces in the lungs. The data provided from the previous studies is lung spirometry testing from three different industries. These groups consist of Utility workers, Emergency Response personnel, and Boat Makers. This data will be examined using logistic regression and multiple linear regression. Logistic regression will be used to determine how much known pulmonary function predictor variables will lower FEV_1/FVC ratios. Lung spirometry data sets will be divided up between the tree industries chosen and data points will be further sub-divided depending on allergy seasonings in the southeastern United States. Lung spirometry data within and between the three industries will be compared for the active allergy seasons and the inactive allergy seasons. The key is to determine if recorded FEV_1/FVC ratios for workers being tested is, on average, lower during the allergy seasons. This would indicate that these workers with the lower ratios are, possibly, suffering from allergies which would reduce their overall FEV_1/FVC ratios. Possible retesting for these workers in the future to compare spirometry values before and after bronchodilator use would be recommended. Further investigation into factors that normally change FEV_1/FVC ratios such as age, weight, and height are suggested for future research should a significant correlation be found between allergy seasons and lowered values for these ratios. The primary allergens to be examined in this study are mold and pollen allergens. Being that these allergens follow the most distinct seasons, segregating the worker data for spirometry testing occurring during these allergy months would be the most exact. Typically, outdoor airborne mold spores are at their peak from the months of May to November (Kołodziejczyk et al, 2016).

CHAPTER TWO:

METHODS

Lung spirometry data was taken from three separate industries in the southeastern United States. These three industries were general industry, emergency medical response, and shipwrights. The hypothesis that seasonal allergies lend to a decrease in spirometry scores was tested by segregating the data from each of these industries into four distinct allergy seasons. These seasons were decided using meteorological data from NOAA. Seasons were decided based upon the beginning and ending of solstices and equinoxes. For instance, the meteorological start date for summer would be the beginning of the summer solstice, which falls between June 21 and 22. Under this convention, the allergy dates range between April 1st and end at November 30th and the non-allergy dates start at December 1st and end at March 30th. However, adjustments were made to optimize statistical analysis. Being that most the PFTs were taken in November, under the previously prescribed convention, it left only 29 subjects in the non-allergy season and 430 in the allergy season. To better fit the data, the date ranges were modified so that the non-allergy season would begin November 1st and end March 30th. This led to a more evenly distributed data set, leaving 195 patients in the allergy season and 142 in the non-allergy season, and considering that November is on the cusp of the end of the allergy season, the potential for misclassification of subjects was limited. The frequency procedure was used in SAS to enumerate these populations, which are listed in Table 1 on page 12. After the data was properly segregated, Multiple Linear Regression and Logistic Regression were run using SAS on the allergy and non-allergy seasons. Demographic variables were used for the regression analysis and included: Race (African American, Caucasian, and Hispanic), Height at test (above or below the median), smoking history (yes/no), Sex, FVC score above or below 80, age (above or below the median) and FEV1 score above or below 80. Odds ratios were also calculated to determine the likelihood that each variable would impart on the odds of scoring above or below the PFT score of 80. FVC/FEV1 scores below 80 were considered abnormal regarding pulmonary function.

After the data was properly segregated, Multiple Linear Regression and Logistic Regression were run using SAS on the allergy and non-allergy seasons. Demographic variables were used for the regression analysis and included: Race (African American, Caucasian, and Hispanic), Height at test (above or below the median), smoking history (yes/no), Sex, FVC score above or below 80, age (above or below the median) and FEV1 score above or below 80. Odds ratios were also calculated to determine the likelihood that each variable would impart on the odds of scoring above or below the PFT score of 80. FVC/FEV1 scores below 80 percent predicted were considered abnormal regarding pulmonary function.

CHAPTER THREE:

RESULTS

The Frequency procedure in SAS was used again to enumerate the populations demographic variables and divide them into allergy season versus non-allergy season. This showed that the baseline data had some discrepancies between the allergy and non-allergy seasons regarding variable distribution. In the Table 2 on page 8, it was found that there were slightly more females in the non-allergy season than in the allergy season, 28 compared to 13, respectively. The distribution between races was even, the only slight discrepancy that existed was that there were more African Americans in the allergy season versus the non-allergy season, 17 compared to 7, respectively. Regarding smoking history, there were twice as many smokers in the allergy season than there were in the non-allergy season (80 vs. 40). Data by height revealed that there were more people taller than 70 inches in the allergy season than there were in the non-allergy season, 116 compared to 67, respectively. The division of members scoring above and below 80% for FEV1 and FVC was an even distribution of 169 in the allergy season and 130 in the non-allergy season. These tables are listed below. Logistic regression run on the data revealed promising results. Age was a significant predictor variable for determining FVC score. Smoking history and age were significant predictor variables in determining whether a subject's FEV1 score would be below eighty percent. Multiple linear regression results revealed a subtle linear effect for seasonality, a Pr>F value of 0.0002 in regards to FVC score. Age was also had a linear effect on FVC score, with a Pr>F score of <0.0001. Linear effects for FEV1 were found in the age variable (0.0002 Pr>F), Sex (0.0139 Pr>F), Smoking history (0.0090 Pr>F), and in Season (0.0003 Pr>F). Season, for FEV1 had a subtle linear effect. These tables are listed below on pages 12 to 15.

CHAPTER FOUR:

DISCUSSION

The hypothesis posed at the beginning of this study was proven to be correct. Seasonality had a subtle linear effect but was not a determining factor for whether or not a subject would have an abnormal PFT score. Age, sex, and smoking history are well-established biologically plausibilities and were expected to influence FEV1 scores.

CHAPTER FIVE:

CONCLUSION

Within the purview of this study, it was shown that seasonality is associated with a subtle modulation of lung function tests. While the data, using the convention for determining seasons in this study design, was evenly divided, there could perhaps be more a determining affect from seasonality during peak pollen seasons or among highly sensitive individuals. Also, while this study was focused solely on industries in the southeastern united states, results could vary over differing climates; however, further research would be necessary to verify this.

Table 1. Allergy Months

Month	Frequency	Percent	Cumulative Frequency	Cumulative Percent
11	83	24.63	83	24.63
9	76	22.55	159	47.18
3	44	13.06	203	60.24
8	29	8.61	232	68.84
4	26	7.72	258	76.56
6	26	7.72	284	84.27
10	20	5.93	304	90.21
5	9	2.67	313	92.88
7	9	2.67	322	95.55
1	7	2.08	329	97.63
12	5	1.48	334	99.11
2	3	0.89	337	100
Season	**Frequency**	**Percent**	**Cumulative Frequency**	**Cumulative Percent**
Allergy	195	57.86	195	57.86
Non-Allergy	142	42.14	337	100

Table 2. Season by Sex			
Season	Sex		
Allergy	Male	Female	Total
Frequency	182	13	195
Percent	54.01	3.86	57.86
Row Percent	93.33	6.67	
Column Percent	61.49	31.71	
Non-Allergy	Male	Female	Total
Frequency	114	28	142
Percent	33.83	8.31	42.14
Row Percent	80.28	19.72	
Column Percent	38.51	68.29	
	296	41	337
Total	87.83	12.17	100

Table 3. Season by Height			
Season	Height		
Allergy	≥70 inches	≤ 70 Inches	Total
Frequency	116	79	195
Percent	34.42	23.44	57.86
Row Percent	59.49	40.51	
Column Percent	63.39	51.3	
Non-Allergy	≥70 inches	≤ 70 Inches	Total
Frequency	67	75	142
Percent	19.88	22.26	42.14
Row Percent	47.18	52.82	
Column Percent	36.61	48.7	
	183	154	337
Total	54.3	45.7	100

Table 4. Season by Race				
Season	Race			
Allergy	Caucasian	Hispanic	African American	Total
Frequency	162	16	17	195
Percent	48.07	4.75	5.04	57.86
Row Percent	83.08	8.21	8.72	
Column Percent	57.45	51.61	70.83	
Non-Allergy	Caucasian	Hispanic	African American	Total
Frequency	120	15	7	142
Percent	35.61	4.45	2.08	42.14
Row Percent	84.51	10.56	4.93	
Column Percent	42.55	48.39	29.17	
	282	31	24	337
Total	83.68	9.2	7.12	100

Table 5. Season by Smoking History			
Season	Smoking History		
Allergy	No	Yes	Total
Frequency	115	80	195
Percent	34.12	23.47	57.86
Row Percent	58.97	41.03	
Column Percent	53	66.67	
Non-Allergy	No	Yes	Total
Frequency	102	40	142
Percent	30.27	11.87	42.14
Row Percent	71.83	28.17	
Column Percent	47	33.33	
	217	120	337
Total	64.39	35.61	100

Table 6. Season by FVC			
Season	**FVC**		
Allergy	**> 80%**	**< 80%**	**Total**
Frequency	169	26	195
Percent	50.15	7.72	57.86
Row Percent	86.67	13.33	
Column Percent	56.33	70.27	
Non-Allergy	**> 80%**	**< 80%**	**Total**
Frequency	131	11	142
Percent	38.87	3.26	42.14
Row Percent	92.25	7.75	
Column Percent	43.67	29.73	
	300	37	337
Total	89.02	10.98	100

Table 7. Season by FEV1			
Season	**FEV1**		
Allergy	**> 80%**	**< 80%**	**Total**
Frequency	169	26	195
Percent	50.15	7.72	57.86
Row Percent	86.67	13.33	
Column Percent	56.52	68.42	
Non-Allergy	**> 80%**	**< 80%**	**Total**
Frequency	130	12	142
Percent	38.58	3.56	42.14
Row Percent	91.55	8.45	
Column Percent	43.48	31.58	
	299	38	337
Total	88.72	11.28	100

Table 8. Odds Ratio Estimates, FVC*			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
Age	1.071	1.031	1.13
Sex	0.215	0.024	1.885
Caucasian vs. All others	0.835	0.269	2.588
Smoking History Yes vs. No	0.753	0.366	1.55
Height	1.003	0.876	1.148
Allergy vs. Non-Allergy	0.664	0.307	1.436
**to produce <80% predicted FVC or Abnormal pulmonary Function*			

Table 9. Odds Ratio Estimates, FEV1*			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
Age	1.091	1.048	1.135
Sex	1.229	0.300	5.03
Caucasian vs. All others	0.943	0.300	2.963
Smoking History Yes vs. No	0.373	0.18	0.771
Height	1.029	0.897	1.181
Allergy vs. Non-Allergy	0.682	0.311	1.493
**to produce <80% predicted FVC or Abnormal pulmonary Function*			

Table 10. Multiple Linear Regression: FEV1						
Source	**DF**	**Parameter Estimate**	**Type I SS**	**Mean Square**	**F Value**	**Pr > F**
Age	1	-0.28035	3668.952	3668.952	13.94	0.0002
Sex	1	1.16993	1608.354	1608.354	6.11	0.0139
White vs. all others	1	-0.23938	40.353	40.353	0.15	0.6957
Smoking History (Y/N)	1	-3.83109	1817.146	1817.146	6.9	0.0090
Height	1	-0.58491	795.320	795.320	3.02	0.0831
Season (Allergy/ Non-allergy	1	-6.78501	3574.262	3574.262	13.58	0.0003

Table 11. Multiple Linear Regression: FVC						
Source	**DF**	**Parameter Estimate**	**Type I SS**	**Mean Square**	**F Value**	**Pr > F**
Age	1	-0.35702	5837.352	5837.352	25.09	<0.0001
Sex	1	3.73278	2626.809	2626.809	11.29	0.0009
White vs. all others	1	-3.10984	577.252	577.252	2.48	0.1162
Smoking History (Y/N)	1	-1.58466	507.731	507.731	2.18	0.1406
Height	1	-0.47917	531.251	531.251	2.28	0.1317
Season (Allergy/ Non-allergy	1	-6.62142	3403.985	3403.985	14.63	0.0002

REFERENCES

"Allergies." Centers for Disease Control. U.S. Department of Health & Human Services, 2 Feb. 2011. Web. 10 Mar. 2016. <http://www.cdc.gov/healthcommunication/ToolsTemplates/EntertainmentEd/Tips/Allergies.html>.

Bake, Björn, Emilia Viklund, and Anna-Carin Olin. "Effects of Pollen Season on Central and Peripheral Nitric Oxide Production in Subjects with Pollen Asthma." *National Center for Biotechnology Information*. U.S. National Library of Medicine, 9 July 2014. Web. 01 Aug. 2016.

"Common Seasonal Allergy Triggers." ACCAI.Org. American College of Allergies, Asthma, & Immunology, 2014. Web. 10 Mar. 2016. <http://acaai.org/allergies/types/seasonal>.

Cushen, Breda, Imran Sulaiman, Noreen Donaghue, Donna Langran, Tara Cahill, Eimear Nic Dhonccha, Olivia Healy, Fiona Keegan, Mark Browne, and Anthony O'Regan. "High Prevalence of Obstructive Lung Disease in Non-smoking Farmers: The Irish Farmers Lung Health Study." *Respiratory Medicine* 115 (2015): 13-19. *Science Direct*. Web. 6 June 2016..

Kołodziejczyk, Krzysztof, Andrzej Bożek, Jerzy Jarząb, and Radosław Gawlik. "The Clinical Differences of Asthma in Patients with Molds Allergy."*Pneumologia I Alergologia Polska* 84.2 (2016): 81-86. *Pubmed.gov*. US National Library of Medicine. Web. 3 Aug. 201

Miller, M. R., R. Crapo, and J. Hankinson. "General Considerations for Lung Function Testing." *European Respiratory Journal* 26.1 (2005): 153-61.*National Center for Biotechnology Information*. Pubmed.gov, 2005. Web. 15 July 2016. <http://www.thoracic.org/statements/resources/pft/PFT1.pdf>.

Miller, M.R., J. Hankinson, V. Brusasco, R. Casaburi, F. Burgos, and A. Coates. "Standardisation of Sprometry." *European Respiratory Journal* 26 (2005): 319-38. *ERS Journals*. European Respiratory Journal, 23 Mar. 2005. Web. 23 June 201

"Meteorological Versus Astronomical Summer-What's the Difference?"*National Centers for Environmental Information (NCEI) Formerly Known as National Climatic Data Center (NCDC)*. National Centers for Environmental Information, n.d. Web. 20 Sept. 2016.

"Pulmonary Function Tests." *U.S. National Library of Medicine*. Medline Plus, n.d. Web. 15 June 2016.

"Spirometry." National Institute for Occupational Safety and Health, 2011. Web. 10 Mar. 2016. http://www.cdc.gov/niosh/topics/spirometry/default.html