CHEST Online Supplement

Obstructive Lung Disease in Mexican Americans and Non-Hispanic Whites

An Analysis of Diagnosis and Survival in the National Health and Nutritional Examination Survey III Follow-up Study

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e-Appendix 1.

Methods

Study design

Briefly, The National Health and Nutrition Examination Survey (NHANES) III used a multi-stage stratified probability sampling design to ensure a representative sample of the U.S. population.[1] Mexican-Americans were oversampled to produce reliable health estimates for this minority. Questionnaires were administered in participants' households and standardized medical examinations were performed in NHANES III mobile examination centers (MEC). Questionnaires included demographic, socioeconomic, and medical history questions. Subjects took the survey in English or Spanish according to their preference.

Participant selection

The following were participant criteria selection for this analysis: a) self-reported as either Non-Hispanic White or Mexican-American, b) be at least 40 years old, and c) had the MEC or home examination and a reliable spirometric testing done. We chose a minimal age of 40 years, because at this age the risk for COPD

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starts to increase. Additionally, 40 years old is a commonly used threshold in epidemiologic investigations of this disease.[2]

Spirometric assessment

Lung function was measured either with a dry rolling seal spirometer in the MEC of NHANES III or a portable spirometer at a subject's home following the 1987 ATS guidelines.[3] No bronchodilator was administered to the participant. Forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) were expressed in milliliters and as a percentage of predicted values based on sex and race/ethnicity.[4]

Covariates

Age, gender, country of birth, number of years living in the U.S. (for immigrant Mexican-Americans), education, poverty-to-income ratio, lifetime smoking status, pack years smoked, exposure to secondhand smoking, work in a high-risk industry, high-risk occupation, and living in urban area were extracted from the Adult Questionnaire at baseline. Body mass index (BMI) was drawn from the examination file. Age was categorized for logistic analysis (40-55, 56-70, >70 years) and used as continuous measure for survival analysis. We collapsed age into these categories to balance sample sizes across them by race/ethnic group. Country of birth was coded as Mexico-born or US-born. Those who were born in neither country were assigned to the US-born group, which was the reference group. The number of years living in the U.S. was classified into 3 categories approximating the tertiles of this variable among non-US born Mexican-American: <15, 15-30, and >30 years (for this variable US-born Mexican-Americans were considered the reference group). BMI was divided into 4 categories: <18.5, 18.5-24.9, 25-29.9, and ≥30 kg/m^2.[5] BMI 18.5-24.9 was used as reference group and a dummy variable 0/1 was created for each of the additional categories. Education level was based on the number of years of education completed and categorized as ≥12 or <12 years. Poverty-to-income ratio was calculated as the ratio of household income to the federal

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poverty level as determined by the Census Bureau for the corresponding survey year and dichotomized as <1.00 or ≥1.00. A family income-to-poverty ratio less than 1 represents a household that earned less than the federal poverty level.[6] Access to health care was measured using a binary "yes/no" indicator with "yes" indicating that the participant responded "yes" to the question "Is there a particular clinic, health center, doctor's office, or other place that you usually go to if you are sick, need advice about your health, or for routine care?"[7] _ENREF_22 Heart attack, chronic heart failure, stroke, diabetes, and cancer were physician-diagnosed self-reported diseases. Non-melanoma skin cancer was not considered as comorbidity. Hypertension was coded based on self-reported antihypertensive medication use and/or systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on exam.[8] Hypertension, heart attack, chronic heart failure, and stroke were collapsed into a cardiovascular comorbidity, which was used as covariate in the survival analysis together with diabetes and cancer. We chose these comorbidities as in our unadjusted analysis all of them increased the risk for mortality (data not shown).

Risk factors for chronic airflow obstruction included asthma history, smoking history, exposure to secondhand smoking, high-risk occupation, high-risk industry, and a surrogate for exposure to air pollution. Asthma history was a self-reported physician diagnosis of the disease.[5] This variable was used as binary variable for logistic analysis. Never smokers were those who responded "No" to the question "Have you smoked at least 100 cigarettes during your entire life?" Ever smokers were further classified as current or former smokers. The number of pack-years smoked was used as continuous variable for the main analyses. Secondhand smoke exposure at home was coded as "yes" for participants who responded "Yes" to the question "Does anyone who lives here smoke cigarettes in the home?" Secondhand smoke exposure at work was assessed by the question "At work, how many hours per day are you close enough to people who smoke so you can smell the smoke?" If the subject responded 1 or more hours it was considered positive. A subject was considered to have secondhand smoking exposure if he/she was exposed to secondhand smoke either at

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home or at work.[9] High-risk occupation and high-risk industries indicators were coded "yes" for participants whose occupation or industry is known to be associated with increased risk for COPD.[10] Exposure to air pollution[6] was coded as "yes" for participants with an urban residence where urban is defined as "Metropolitan Statistical Area" per U.S. Department of Agriculture.

Statistical Analysis

Comparisons between ethnic groups were assessed by chi square or t-test as appropriate according variable type. Odds ratios for OLD were estimated using logistic regression analysis. The main predictor was ethnicity with White as the reference group. The following covariates were chosen a priori based on prior studies[10-12]: demographic factors (age [categorical], gender, country of birth, BMI); socioeconomic factors (education, poverty-to-income ratio, and access to health care); risk factors for chronic airflow obstruction (asthma history, lifetime smoking status, pack-years of smoking, secondhand smoke exposure, high-risk industry, high-risk occupation, and living in an urban area). Race-ethnicity differences in all-cause mortality for OLD cases only were assessed using Cox proportional hazard models. Time to event for all-cause mortality was censored at date of death certificate or at December 31, 2006 (time of last follow-up).[5] The following covariates were included in the Cox model based upon prior investigations showing that all of them are associated with mortality from COPD[5, 13-15]: age (continuous), male gender, education level, BMI, asthma, lifetime smoking status, pack-years of smoking, dyspnea, and FEV_1% predicted. Prior asthma was further categorized as childhood asthma or not with a "yes" indicator if the diagnosis was made when the subject was less than 18 years old. We used this approach because of mortality differences according to age at asthma diagnosis in our unadjusted analysis and to meet the proportionality assumptions. In an additional survival analysis, we included the following comorbidities: cardiovascular disease, diabetes, and cancer as covariates into the model. Since the participants with missing data were likely to be Mexican-American and had higher self-reported COPD (defined as self-reported chronic bronchitis or emphysema)

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prevalence than those with complete data, we performed a survival model including subjects with incomplete data who self-reported COPD assuming they had OLD and excluding FEV_1% predicted. We also performed a survival analysis to examine the effects of country of birth and time living in the U.S. on mortality in Mexican-American subjects with OLD. Finally, we performed a sensitivity analysis to address the potential bias of our HR estimates based on the assumption that some non-US born Mexican-Americans may have moved back to and died in Mexico without having a NDI death certificate. Based on a prior study[16] that demonstrated a 15.6- 56.2% range of emigration rate for Mexican immigrants, we selected those extremes values and a mid-point (35.9%) as return migration estimates and randomly assigned to 15.6%, 35.9%, and 56.2% of the non-US born Mexican-Americans a deceased status with no change in their follow-up time. All analyses incorporated sampling weights that adjusted for differences in selection probability, noncoverage, and nonresponse following the Analytic guidelines of NHANES III. Logistic and survival analyses were performed with *rlogist* and *surveyphreg* procedures of callable SUDAAN 10.1 (RTI International, Research Triangle Park, NC) and SAS 9.3 (SAS Institute, Cary, NC) statistical software, respectively. Unweighted prevalence ratios (also called risk ratios) for OLD were computed with SAS *proc genmod*.

Results

Compared to those with complete data, participants with missing data (N=904, e-Figure 1) were more likely to be older (57 ± 0.5 vs. 68 ± 0.7 y; P<0.0001) and Mexican-American (4.0 ± 0.3 vs. 5.2 ± 0.7%; P=0.03). These participants were also more likely to have ≤12 y of school (26 ± 1.4 vs. 46 ± 2.7%; P<0.0001) and higher prevalence of self-reported physician-diagnoses of both chronic bronchitis (8.0 ± 0.4 vs. 11.7 ± 1.4%; P=0.02) and emphysema (3.4 ± 0.3 vs. 8.7 ± 0.3%; P<0.0001). There was no difference in gender proportion and lifetime smoking status between these groups.

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Likelihood of OLD

When we added smoking duration and age at start of smoking to this model, smoking duration was collinear with pack-years of smoking and the main result remained unchanged [OR 0.71, [0.53 - 0.95]). Similarly, when country of birth was included in the final model, it was collinear with Mexican-American ethnicity, and there was essentially no change in the odds of OLD for Mexican-Americans (OR 0.62, [0.46-0.84). Among smokers only, Mexican-American smokers also had lower odds of OLD than smoking Whites (OR 0.57, [0.39 – 0.82]).

Survival Analysis among OLD subjects

Immigrant Mexican-Americans residing in the U.S. less than 15 years had a survival benefit compared to U.S.-born Mexican-Americans (HR 0.21, [0.07- 0.63]). In contrast, non-U.S. born Mexican-Americans who have lived in the U.S. longer than 30 years tended to have an increase risk for mortality (HR 1.70, [0.93 - 3.11]). The survival benefit for Mexican Americans living in the U.S. less than 15 years was no longer apparent after adjustment for age (HR 0.39, [0.12-1.25]).

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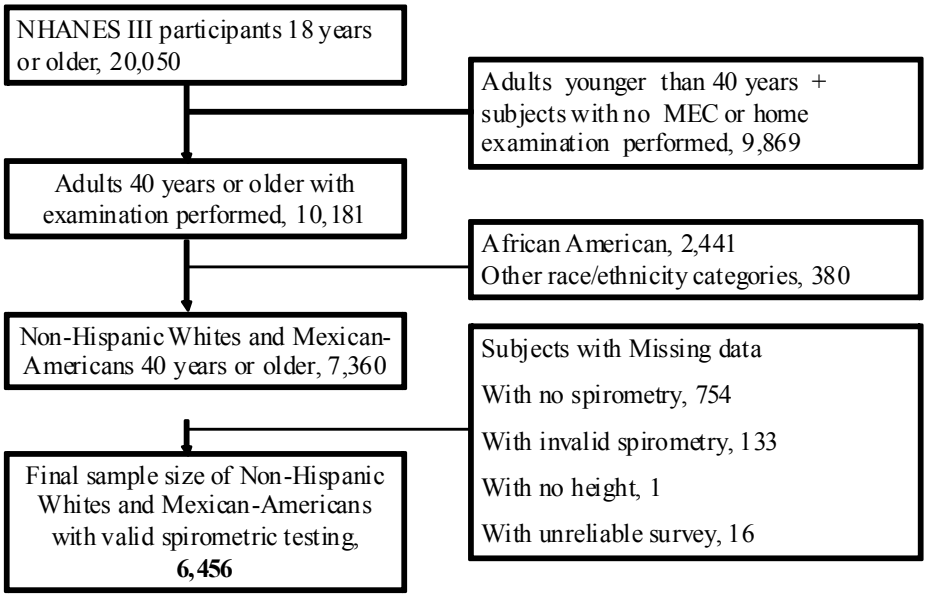

e-Figure 1 Flowchart showing the inclusion and exclusion criteria used to obtain the final sample size for the current analysis. NHANES III, Third National Health and Nutrition Examination Survey (1988-1994), National Center for Health Statistics. MEC, Mobile Examination Center of NHANES

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e-Table 1 Prevalence of OLD with alternate definitions of this condition by race/ethnic group.

OLD definition and ethnic groups	Total number of participants	Number of subjects meeting the OLD definition	OLD Prevalence Weighted % (SE)	P value
Definition: FEV_1/ FVC <0.7 and FEV_1 <80% predicted				<0.0001
Non-Hispanic White	4,554	677	12.4 (0.5)	
Mexican-American	1,902	134	5.3 (0.6)	
Definition: Lower limit of normal FEV_1/ FVC ratio				<0.0001
Non-Hispanic White	4,554	875	17.7 (0.8)	
Mexican-American	1,902	172	8.1 (0.6)	

Data from NHANES III, Third National Health and Nutrition Examination Survey (1988-1994), National Center for Health Statistics.

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e-Table 2 Univariate logistic analyses for predicting OLD.

		95% Confidence Interval		
	Odds Ratio	Lower Limit	Upper Limit	P value
Mexican-American ethnicity	0.43	0.36	0.52	<0.0001
Male gender	1.65	0.99	1.50	<0.0001
Age (y)				<0.0001
40-55	1.00	-	-	
56-70	3.14	2.56	3.85	
>70	4.55	3.72	5.58	
BMI (kg/m^2)				
≤18.5	2.58	1.43	4.66	0.001
18.6-24.9	1.00	-	-	
25-29	1.00	0.85	1.17	0.98
≥30	0.61	0.48	0.77	0.77
<12 years of school	1.50	1.27	1.76	<0.0001
Family income-to-poverty ratio <1.00	1.20	0.91	1.58	0.18
Access to healthcare	1.13	0.89	1.44	0.30
Self-reported asthma history	2.72	2.17	3.40	<0.0001
Smoking status				
Never smoking	1.00	-	-	
Former smoker	1.36	1.18	1.57	<0.0001
Current smoker	2.14	1.73	2.65	<0.0001
Pack-years of smoking	1.02	1.02	1.02	<0.0001
Secondhand smoke exposure	1.17	0.98	1.41	0.07
Living in urban area	0.84	0.73	0.96	0.008
High-risk industry	1.16	1.00	1.33	0.04
High-risk occupation	1.06	0.89	1.26	0.51

All logistic univariate models incorporated sampling weights.
Data from NHANES III, Third National Health and Nutrition Examination Survey (1988-1994), National Center for Health Statistics.

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e-Table 3 Prevalence ratio of OLD*.

	Prevalence ratio (95% CI)	P value	Odds Ratio (95% CI)	P value
Model 1 (univariate)				
Race/ethnicity				
Non-Hispanic White	1.00	-	1.00	-
Mexican-American	0.50 (0.45 - 0.56)	<0.0001	0.41 (0.36 - 0.47)	<0.0001
Model 2 (multivariate)†				
Race/ethnicity				
Non-Hispanic White	1.00	-		
Mexican-American	0.67 (0.59 - 0.77)	<0.0001	0.59 (0.49 - 0.71)	<0.0001

*OLD is defined as FEV_1/ FVC <0.7. All estimates were computed with *proc genmod* of SAS. Logistic models have no sampling weights.
†Model 2 included age [categorical], sex, BMI, education level, family income-to-poverty ratio, access to health care, asthma history, lifetime smoking status, pack-years of smoking, secondhand smoke exposure, high-risk industry, high-risk occupation, and living in urban area.
Data from NHANES III, Third National Health and Nutrition Examination Survey (1988-1994), National Center for Health Statistics.

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e-Table 4 Unadjusted Cox proportional hazards models for all cause mortality in OLD subjects.*

		95% Confidence Interval		
	Odds Ratio	Lower Limit	Upper Limit	P value
Mexican-American ethnicity	0.72	0.53	0.99	0.04
Male gender	1.04	0.85	1.27	0.71
Age (y)	1.09	1.08	1.10	<0.0001
BMI (kg/m^2)				
≤18.5	2.01	1.03	3.94	0.04
18.6-24.9	1.00			
25-29	1.03	0.80	1.33	0.80
≥30	0.78	0.57	1.07	0.12
<12 years of education	1.68	1.33	2.14	<0.0001
Self-reported asthma history	0.69	0.50	0.94	0.02
Asthma diagnosed at ≤17 yr old	0.36	0.20	0.65	0.001
Smoking status				
Never smoking	1.00			
Former smoker	1.13	0.93	1.38	0.21
Current smoker	0.91	0.75	1.12	0.37
Pack-years of smoking	1.006	1.004	1.008	<0.0001
Shortness of breath	1.78	1.43	2.13	<0.0001
FEV_1 % predicted	0.99	0.98	0.99	<0.0001

All survival models incorporated sampling weights.
Data from NHANES III, Third National Health and Nutrition Examination Survey (1988-1994), National Center for Health Statistics.

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Secondary Logistic and Survival Analyses Using Alternate Definitions of OLD

e-Table 5 Univariate and multivariate logistic analyses for predicting OLD defined as lower limit of normal FEV_1/ FVC ratio*

		95% Confidence Interval		
	Odds Ratio	Lower Limit	Upper Limit	P value
Model 1 (univariate)				
Race/ethnicity				
Non-Hispanic White	1.00	-	-	
Mexican-American	0.41	0.33	0.50	<0.0001
Model 2 (multivariate)†				
Race/ethnicity				0.003
Non-Hispanic White	1.00	-	-	
Mexican-American	0.61	0.45	0.84	
Gender				0.34
Female	1.00	-	-	
Male	1.14	0.86	1.52	
Age (y)				<0.0001
40-55	1.00	-	-	
56-70	1.79	1.41	2.28	
>70	2.19	1.63	2.94	
BMI (kg/m^2)				
≤18.5	2.58	1.06	6.29	0.04
18.6-24.9	1.00	-	-	
25-29	0.70	0.54	0.91	0.009
≥30	0.47	0.36	0.62	<0.0001
Self-reported asthma history				<0.0001
No	1.00			
Yes	4.74	3.36	6.69	
Smoking status				
Never smoker	1.00	-	-	
Former smoker	1.58	1.09	2.29	0.02
Current smoker	3.79	2.42	5.95	<0.0001
Pack-years of smoking	1.01	1.01	1.02	<0.0001

*All logistic models incorporated sampling weights.
†Model 2 included all the covariates showed in the table and education level, family income-to-poverty ratio, access to health care, secondhand smoke exposure, high-risk industry, high-risk occupation, and living in urban area.
Data from NHANES III, Third National Health and Nutrition Examination Survey (1988-1994), National Center for Health Statistics.

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e-Table 6 Results of univariate and multivariate logistic analyses for predicting OLD with low lung function defined as FEV_1/ FVC <0.7 and FEV_1 <80% predicted*.

		95% Confidence Interval		
	Odds Ratio	Lower Limit	Upper Limit	P value
Model 1 (univariate)				
Race/ethnicity				<0.0001
Non-Hispanic White	1.00	-	-	
Mexican-American	0.40	0.30	0.51	
Model 2 (multivariate)†				
Race/ethnicity				0.03
Non-Hispanic White	1.00	-	-	
Mexican-American	0.66	0.46	0.95	
Gender				0.77
Female	1.00	-	-	
Male	0.96	0.72	1.28	
Age (y)				<0.0001
40-55	1.00	-	-	
56-70	3.39	2.51	4.58	
>70	4.90	3.30	7.28	
BMI (kg/m^2)				
≤18.5	3.66	1.92	6.97	0.0002
18.6-24.9	1.00	-	-	
25-29	0.85	0.64	1.15	0.29
≥30	0.87	0.63	1.22	0.43
Self-reported asthma history				<0.0001
No	1.00			
Yes	4.08	2.82	5.90	
Smoking status				
Never smoker	1.00	-	-	
Former smoker	1.42	1.01	1.98	0.04
Current smoker	4.70	3.28	6.74	<0.0001
Pack-years of smoking	1.02	1.01	1.02	<0.0001
High-risk industry				0.049
No	1.00	-	-	
Yes	1.23	1.00	1.51	

*The main predictor is the race/ethnic group where Non-Hispanic White was the reference group. All logistic models incorporated sampling weights.
†Model 2 included all the covariates showed in the table and education level, poverty-to- income ratio, access to health care, secondhand smoke exposure, high-risk occupation, and living in urban area.
NHANES III, Third National Health and Nutrition Examination Survey (1988-1994), National Center for Health Statistics.

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Sensitivity Survival Analysis

e-Table 7 Adjusted Mexican-American hazard ratios for all-cause mortality in participants with OLD assuming different return migration rates among non-US born Mexican-Americans.*

	Odds Ratio	95% Confidence Interval Lower Limit	Upper Limit	P value
Scenario 1				
15.6% non-US born Mexican- Americans moved and died out of US	0.98	0.77	1.26	0.87
Scenario 2				
35.9% non-US born Mexican- Americans moved and died out of US	1.17	0.94	1.45	0.15
Scenario 3				
56.2% non-US born Mexican- Americans moved and died out of US	1.23	0.96	1.58	0.10

*The main predictor for all the models is the race/ethnic group where Non-Hispanic White was the reference group. Models were adjusted for age (continuous), sex (male=1), BMI (categorical), education level (<12 school years=1), asthma history (yes=1), age at asthma diagnosis (<18 years old=1), lifetime smoking status (categorical), pack-years of smoking (continuous), dyspnea (yes=1), and FEV_1 % predicted (continuous).
Survival analyses incorporated sampling weights.
Data from NHANES III, Third National Health and Nutrition Examination Survey (1988-1994) and its Linked Mortality File, National Center for Health Statistics.

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