Online Supplement
The Association of Multiparity with Lung Function and Chronic Obstructive Pulmonary Disease (COPD)-Related Phenotypes

COPDGene is a multicenter observational study which primarily consists of smokers with and without COPD (Regan et al., 2011). Subjects in COPDGene have at least 10 pack-years of smoking (except for a smaller group of nonsmoking controls, who were excluded from the analyses in this manuscript).

Lynch, MB; John D. Newell, Jr., MD; Elizabeth A. Regan, MD, PhD; James C. Ross, PhD; Raul San Jose Estepar, PhD; Joyce Schroeder, MD; Jered Sieren; Douglas Stinson; Berend C. Stoel, PhD; Juerg Tschirren, PhD; Edwin Van Beek, MD, PhD; Bram van Ginneken, PhD; Eva van Rikxoort, PhD; George Washko, MD; Carla G. Wilson, MS;

PFT QA Center, Salt Lake City, UT: Robert Jensen, PhD

Data Coordinating Center and Biostatistics, *National Jewish Health, Denver, CO*: Douglas Everett, PhD; Jim Crooks, PhD; Camille Moore, PhD; Matt Strand, PhD; Carla G. Wilson, MS

Epidemiology Core, *University of Colorado Anschutz Medical Campus, Aurora, CO*: John E. Hokanson, MPH, PhD; John Hughes, PhD; Gregory Kinney, MPH, PhD; Sharon M. Lutz, PhD; Katherine Pratte, MSPH; Kendra A. Young, PhD

Mortality Adjudication Core: Surya Bhatt, MD; Jessica Bon, MD; MeiLan K. Han, MD, MS; Barry Make, MD; Carlos Martinez, MD, MS; Susan Murray, ScD; Elizabeth Regan, MD; Xavier Soler, MD; Carla G. Wilson, MS

Biomarker Core: Russell P. Bowler, MD, PhD; Katerina Kechris, PhD; Farnoush Banaei-Kashani, Ph.D

COPDGene® Investigators – Clinical Centers

Ann Arbor VA: Jeffrey L. Curtis, MD; Carlos H. Martinez, MD, MPH; Perry G. Pernicano, MD

Baylor College of Medicine, Houston, TX: Nicola Hanania, MD, MS; Philip Alapat, MD; Mustafa Atik, MD; Venkata Bandi, MD; Aladin Boriek, PhD; Kalpatha Guntupalli, MD; Elizabeth Guy, MD; Arun Nachiappan, MD; Amit Parulekar, MD;

Brigham and Women's Hospital, Boston, MA: Dawn L. DeMeo, MD, MPH; Craig Hersh, MD, MPH; Francine L. Jacobson, MD, MPH; George Washko, MD

Columbia University, New York, NY: R. Graham Barr, MD, DrPH; John Austin, MD; Belinda D'Souza, MD; Gregory D.N. Pearson, MD; Anna Rozenshtein, MD, MPH, FACR; Byron Thomashow, MD

Duke University Medical Center, Durham, NC: Neil MacIntyre, Jr., MD; H. Page McAdams, MD; Lacey Washington, MD

HealthPartners Research Institute, Minneapolis, MN: Charlene McEvoy, MD, MPH; Joseph Tashjian, MD

Johns Hopkins University, Baltimore, MD: Robert Wise, MD; Robert Brown, MD; Nadia N. Hansel, MD, MPH; Karen Horton, MD; Allison Lambert, MD, MHS; Nirupama Putcha, MD, MHS

Los Angeles Biomedical Research Institute at Harbor UCLA Medical Center, Torrance, CA: Richard Casaburi, PhD, MD; Alessandra Adami, PhD; Matthew Budoff, MD; Hans Fischer, MD; Janos Porszasz, MD, PhD; Harry Rossiter, PhD; William Stringer, MD

Michael E. DeBakey VAMC, Houston, *TX*: Amir Sharafkhaneh, MD, PhD; Charlie Lan, DO

Minneapolis VA: Christine Wendt, MD; Brian Bell, MD

Morehouse School of Medicine, Atlanta, GA: Marilyn G. Foreman, MD, MS; Eugene Berkowitz, MD, PhD; Gloria Westney, MD, MS

National Jewish Health, Denver, CO: Russell Bowler, MD, PhD; David A. Lynch, MB

Reliant Medical Group, Worcester, MA: Richard Rosiello, MD; David Pace, MD

Temple University, Philadelphia, PA: Gerard Criner, MD; David Ciccolella, MD; Francis Cordova, MD; Chandra Dass, MD; Gilbert D'Alonzo, DO; Parag Desai, MD; Michael Jacobs, PharmD; Steven Kelsen, MD, PhD; Victor Kim, MD; A. James Mamary, MD; Nathaniel Marchetti, DO; Aditi Satti, MD; Kartik Shenoy, MD; Robert M. Steiner, MD; Alex Swift, MD; Irene Swift, MD; Maria Elena Vega-Sanchez, MD

University of Alabama, Birmingham, AL: Mark Dransfield, MD; William Bailey, MD; Surya Bhatt, MD; Anand Iyer, MD; Hrudaya Nath, MD; J. Michael Wells, MD

University of California, San Diego, CA: Joe Ramsdell, MD; Paul Friedman, MD; Xavier Soler, MD, PhD; Andrew Yen, MD

University of Iowa, Iowa City, IA: Alejandro P. Comellas, MD; Karin F. Hoth, PhD; John Newell, Jr., MD; Brad Thompson, MD

University of Michigan, Ann Arbor, MI: MeiLan K. Han, MD, MS; Ella Kazerooni, MD; Carlos H. Martinez, MD, MPH

University of Minnesota, Minneapolis, MN: Joanne Billings, MD; Abbie Begnaud, MD; Tadashi Allen, MD

University of Pittsburgh, Pittsburgh, PA: Frank Sciurba, MD; Jessica Bon, MD; Divay Chandra, MD, MSc; Carl Fuhrman, MD; Joel Weissfeld, MD, MPH

University of Texas Health Science Center at San Antonio, San Antonio, TX: Antonio Anzueto, MD; Sandra Adams, MD; Diego Maselli-Caceres, MD; Mario E. Ruiz, MD

Supplementary Tables

eTable S1: Specific questions used to obtain exposure and socioeconomic measures.

Question	Answer Choices
How old were you when you became pregnant for at least 6mo (years)?	
How many times have you been pregnant for at least 6mo?	
How old were you when your periods stopped? (years)	
How old were you when your monthly menstrual periods started (years)	

Highest degree or level of school completed	1=8th grade or less
	2=High school, no diploma
	3=High school graduate or GED
	4=Some college or technical school, no degree
	5=College or technical school graduate (Bachelor's or Associate degree)
	6=Master's or Doctoral degree
Do you have health insurance or a health care plan?	1=Yes
	0=No
	3=Uncertain
Income	1=Under $15,000
	2=$15,000-35,000
	3=$35,000-50,000
	4=$50,000-75,000
	5=More than $75,000
	6=Decline to answer

eTable S2: Characteristics of NHANES participants (n=418), stratified by never smokers and those with lower smoking exposure.

Variable	Never Smokers	Lower smoking exposure
n	321	97
Age, years (mean (SD))	66.26 (11.71)	59.03 (10.19)
Race (No. (%) non-Hispanic white)	321 (100.0)	97 (100.0)
Education (%)		
Less than 9th grade	17 (5.3)	2 (2.1)
9-11th grade (and 12th grade without diploma)	35 (10.9)	13 (13.4)
High schoool graduate/GED or equivalent	80 (24.9)	23 (23.7)
Some college or AA degree	97 (30.2)	38 (39.2)
College graduate or above	92 (28.7)	21 (21.6)
BMI (kg/m2, mean (SD))	29.29 (7.37)	28.72 (6.14)
Pack years of smoking (mean (SD))	0.00 (0.00)	8.77 (15.17)
Current smoking (No. (%))	0 (0.0)	34 (35.1)
Age started smoking in years (mean (SD))	NaN (NA)	18.61 (7.04)
Number of pregnancies (No. (%))		
1 or less	39 (12.1)	11 (11.3)
2	125 (38.9)	38 (39.2)
3 or more	157 (48.9)	48 (49.5)
Age in years of first pregnancy (mean (SD))	23.78 (4.68)	21.92 (4.56)
Multiparous (No. (%))	282 (87.9)	86 (88.7)
FEV1 % predicted (mean (SD))	95.63 (15.89)	96.62 (10.75)
FEF25-75/FVC (mean (SD))	70.65 (26.77)	63.36 (23.73)
FVC % predicted (mean (SD))	96.07 (14.34)	99.62 (11.48)
FEV1/FVC (mean (SD))	76.93 (6.68)	75.53 (5.73)

eTable S3: The association of number of pregnancies and multiparity with FEV$_1$/FVC ratio in COPDGene participants. The results of regression coefficients and 95% confidence intervals are displayed for the overall analysis (n-1,820) and stratified analyses. All models were adjusted for age, body-mass index, current smoking status, smoking history in pack-years, age at which smoking was started, and level of education completed. In the analysis including all COPDGene subjects, models were additionally adjusted for a variable indicated COPD case-control status.

Predictor	All		No or mild obstruction		PRISm		GOLD 2-4	
	Adj β (95% CI)	p-value	Adj β (95% CI)	p-value	Adj β (95% CI)	p-value	Adj β (95% CI)	p-value
2 pregnancies	-0.013 (-0.031, 0.0043)	0.14	-0.0016 (-0.011, 0.0075)	0.73	-0.014 (-0.032, 0.0046)	0.14	-0.017 (-0.041, 0.0062)	0.15
3 or more pregnancies	-0.016 (-0.033, 0.00034)	0.055	-0.0023 (-0.011, 0.0066)	0.61	-0.017 (-0.034, -0.00083)	0.04	-0.008 (-0.03, 0.014)	0.48
Multiparity (>1 pregnancy)	-0.015 (-0.03, 0.00052)	0.058	-0.002 (-0.01, 0.006)	0.63	-0.016 (-0.032, -0.00047)	0.043	-0.012 (-0.033, 0.009)	0.27

eTable S4: The association of number of pregnancies and multiparity with % LAA < -950 HU in COPDGene participants. The results of regression coefficients and 95% confidence intervals are displayed for the overall analysis (n-1,820) and stratified analyses. All models were adjusted for age, body-mass index, current smoking status, smoking history in pack-years, age at which smoking was started, and level of education completed. In the analysis including all COPDGene subjects, models were additionally adjusted for a variable indicated COPD case-control status.

Predictor	All		No or mild obstruction		PRISm		GOLD 2-4	
	Adj β (95% CI)	p-value	Adj β (95% CI)	p-value	Adj β (95% CI)	p-value	Adj β (95% CI)	p-value
2 pregnancies	-0.29 (-1.6, 0.98)	0.65	0.37 (-0.059, 0.81)	0.09	0.29 (-1.7, 2.3)	0.77	-0.58 (-2.8, 1.6)	0.6
3 or more pregnancies	0.93 (-0.29, 2.2)	0.14	0.19 (-0.24, 0.63)	0.38	-0.66 (-2.5, 1.1)	0.47	0.88 (-1.2, 2.9)	0.4
Multiparity (>1 pregnancy)	0.38 (-0.75, 1.5)	0.51	0.29 (-0.1, 0.67)	0.15	-0.33 (-2, 1.4)	0.7	0.29 (-1.6, 2.2)	0.77

eTable S5: The association of number of pregnancies and multiparity with Pi10 in COPDGene participants. The results of regression coefficients and 95% confidence intervals are displayed for the overall analysis (n-1,820) and stratified analyses. All models were adjusted for age, body-mass index, current smoking status, smoking history in pack-years, age at which smoking was started, and level of education completed. In the analysis including all COPDGene subjects, models were additionally adjusted for a variable indicated COPD case-control status.

Predictor	All		No or mild obstruction		PRISm		GOLD 2-4	
	Adj β (95% CI)	p-value	Adj β (95% CI)	p-value	Adj β (95% CI)	p-value	Adj β (95% CI)	p-value
2 pregnancies	0.052 (-0.076, 0.18)	0.43	-0.11 (-0.24, 0.019)	0.092	-0.11 (-0.67, 0.45)	0.68	0.31 (0.1, 0.52)	0.0039
3 or more pregnancies	0.093 (-0.035, 0.22)	0.15	-0.043 (-0.18, 0.096)	0.54	-0.0058 (-0.5, 0.49)	0.98	0.19 (-0.0062, 0.39)	0.058
Multiparity (>1 pregnancy)	0.072 (-0.044, 0.19)	0.22	-0.083 (-0.2, 0.037)	0.18	-0.037 (-0.51, 0.43)	0.87	0.24 (0.048, 0.42)	0.014

eTable S6: The association of number of pregnancies and multiparity with FEV$_1$/FVC ratio in NHANES participants. The results of regression coefficients and 95% confidence intervals are displayed for never smokers (n=321) and the lower smoking exposure group (n=97). All models were adjusted for age, body-mass index, pack-years of smoking, current smoking, and level of education completed.

Predictor	Never Smokers			Lower smoking exposure		
	Adj ß	95% CI	p-value	Adj ß	95% CI	p-value
2 pregnancies	-2.1	(-5.4,1.1)	0.2	-1.4	(-6.6,3.9)	0.6
3 or more pregnancies	0.05	(-3.1,3.2)	0.97	-0.45	(-5.4,4.5)	0.86
Parity (≥ 2 pregnancies)	-0.87	(-3.8,2.1)	0.56	-0.79	(-5.6,4)	0.74