Insulin resistance, metabolic syndrome, and lung function in U.S. adolescents with and without asthma.

Online Supplement

Erick Forno, MD, MPH[1*], Yueh-Ying Han, PhD[1*], Radhika H Muzumdar, MD[2], Juan C Celedón, MD DrPH[1]

[1]Division of Pediatric Pulmonary Medicine, Allergy, and Immunology; and [2]Division of Pediatric Endocrinology, Children's Hospital of Pittsburgh of UPMC, University of Pittsburgh School of Medicine, Pittsburgh, PA.

*These authors contributed equally to this manuscript.

Corresponding author: Erick Forno, MD, MPH
Division of Pulmonary Medicine, Allergy and Immunology
Children's Hospital of Pittsburgh of UPMC
4401 Penn Avenue, Pittsburgh, PA 15224
Phone: 412.692.8429; Fax: 412.692.7636
Email: erick.forno@chp.edu

Supplemental Table 1 – Characteristics of study participants by "ever asthma" status

Characteristics	No asthma N=1334	Ever asthma N=315	P-value
Age (year)	14.54 ± 0.05	14.82 ± 0.12	0.031
Male gender	688 (50.03)	177 (53.95)	0.231
Race/ethnicity			
Non-Hispanic White	439 (60.51)	106 (61.68)	
Non-Hispanic Black	294 (13.34)	90 (16.07)	0.044
Hispanic	530 (19.55)	98 (14.79)	
Other	71 (6.61)	21 (7.47)	
Household income < $20,000/year	247 (13.81)	62 (13.75)	0.983
Health insurance coverage	1125 (88.45)	285 (94.01)	0.013
Family history of asthma	314 (22.42)	176 (51.99)	<0.001
ETS exposure	203 (15.04)	59 (20.48)	0.058
Hay fever	115 (10.02)	65 (21.90)	0.001
FEV_1 (L)[1]	3.40 ± 0.03	3.43 ± 0.05	0.003
FVC (L)[1]	3.93 ± 0.03	4.11 ± 0.05	0.561
FEV_1/FVC (%)	86.82 ± 0.22	83.52 ± 0.53	<0.001
C-reactive Protein	0.14 ± 0.02	0.11 ± 0.01	0.225
Body mass index (BMI) z-score	0.65 ± 0.04	0.79 ± 0.08	0.101
Percent body fat (PBF) z-score	0.24 ± 0.04	0.39 ± 0.06	0.046
Waist circumference (WC) z-score	-0.07 ± 0.04	0.09 ± 0.07	0.055
Waist-to-Height ratio (WHR) z-score	-0.11 ± 0.04	0.01 ± 0.07	0.145
Glucose-to-insulin ratio[2]	9.51 ± 0.38	8.19 ± 0.39	0.018
QUICKI[2]	0.33 ± 0.002	0.32 ± 0.002	0.032
HOMA-IR[2]	3.24 ± 0.11	3.49 ± 0.22	0.276
Metabolic syndrome[2]	58 (9.02)	14 (9.34)	0.920

Mean (SE) for continuous and N (%) for binary variables. Number may vary due to missingness. ETS = Environmental tobacco smoking. QUICKI = quantitative insulin-sensitivity check index. HOMA-IR=homeostasis model assessment - insulin resistance. [1]Adjusted for age, gender, height, and height^2. [2]Data analyzed only for children who were examined fasting, in morning sessions (n=701).

Supplemental Table 2 – Insulin sensitivity/resistance, metabolic syndrome, and lung function by adiposity status

	Glucose-to-insulin ratio	QUICKI[1]	HOMA-IR	Metabolic syndrome
PBF < 85th percentile (n=391)				
FEV_1 (ml	-2.10 (-13.37, 9.17)	-7.38 (-31.51, 16.73)	8.90 (-26.04, 43.84)	-198.72 (-460.68, 63.24)
FVC (ml)	-1.61 (-10.94, 7.71)	-3.13 (-24.67, 18.41)	0.67 (-37.94, 39.28)	-71.52 (-371.52, 228.49)
FEV_1/FVC (%)	-0.01 (-0.17, 0.15)	-0.13 (-0.45, 0.20)	0.22 (-0.25, 0.69)	-3.89 (-6.23, -1.55)**
PBF ≥ 85th percentile (n=118)				
FEV_1 (ml)	31.80 (1.16, 62.43)*	35.73 (0.18, 71.29)*	-25.41 (-51.95, 1.13)	233.96 (56.41, 411.51)*
FVC (ml)	36.47 (14.70, 58.24)**	44.40 (13.35, 75.45)**	-28.97 (-54.44, -3.50)*	395.01 (178.97, 611.06)**
FEV_1/FVC (%)	0.09 (-0.41, 0.60)	0.06 (-0.46, 0.58)	-0.09 (-0.42, 0.24)	-2.09 (-4.00, -0.18)*
WC < 85th percentile (n=457)				
FEV_1 $(ml)^2$	-0.13 (-9.50, 9.76)	-1.10 (-20.64, 18.45)	-6.53 (-26.12, 13.05)	-7.25 (-262.39, 247.88)
FVC $(ml)^2$	-0.11 (-8.25, 8.03)	1.58 (-15.87, 19.03)	-9.47 (-29.57, 10.62)	172.89 (-160.77, 506.55)
FEV_1/FVC (%)	0.01 (-0.14, 0.16)	-0.06 (-0.35, 0.24)	0.01 (-0.33, 0.35)	-4.30 (-6.47, -2.13)**
WC ≥ 85th percentile (n=84)				
FEV_1 (ml)	40.66 (-6.77, 88.09)	57.00 (2.66, 111.33)*	-22.76 (-49.18, 3.66)	298.01 (234.24, 361.78)**
FVC (ml)	68.26 (-1.29, 137.80)	87.71 (6.80, 162.63)*	-34.56 (-70.01, 0.90)	394.86 (364.19, 425.56)**
FEV_1/FVC (%)	-0.22 (-0.81, 0.38)	-0.12 (-0.67, 0.44)	0.06 (-0.23, 0.34)	-0.30 (-0.95, 0.34)
WHR < 85th percentile (n=453)				
FEV_1 $(ml)^2$	0.73 (-9.34, 10.80)	0.40 (-20.02, 20.83)	-8.85 (-30.68, 12.99)	-168.44 (-410.03, 73.15)
FVC $(ml)^2$	0.23 (-8.37, 8.83)	2.09 (-15.73, 19.91)	-9.18 (-30.80, 12.44)	-13.53 (-289.49, 262.43)
FEV_1/FVC (%)	0.02 (-0.13, 0.16)	-0.04 (-0.32, 0.24)	-0.04 (-0.37, 0.29)	-4.28 (-6.28, -2.29)**
WHR ≥ 85th percentile (n=88)				
FEV_1 (ml)	59.56 (38.21, 80.90)**	79.56 (55.23, 103.89)**	-37.16 (-57.56, -16.76)**	229.16 (181.16, 277.16)**
FVC (ml)	65.33 (19.72, 110.94)**	92.08 (43.92, 140.23)**	-47.35 (-75.12, -19.58)**	383.34 (357.78, 408.90)**
FEV_1/FVC (%)	0.15 (-0.56, 0.83)	0.15 (-0.64, 0.93)	0.01 (-0.37, 0.38)	-2.01 (-2.49, -1.53)**

Data presented as beta (95% CI). All models adjusted for age, gender, race/ethnicity, health insurance coverage, family history of asthma, ETS exposure, fasting hours, C-reactive protein, and current asthma. FEV_1 and FVC additionally adjusted for height and $height^2$. *p<0.05, **p<0.01. [1]Results shown per 0.01 unit of QUICKI increment in each lung function measure.

Supplemental Table 3 – Metabolic syndrome criteria and lung function by asthma and obesity status

	SBP ≥ 90th percentile	HDL < 50 mg/dL	Triglyceride ≥ 100 mg/dL	WC ≥ 75th percentile	Fasting glucose ≥ 110 mg/dL
FEV_1/FVC					
All participants[1]	-0.38 (-2.15, 1.40)	-0.65 (-2.08, 0.78)	-0.40 (-2.46, 1.66)	-1.65 (-3.37, 0.08)	-1.68 (-6.26, 2.90)
-Non-asthmatics	0.14 (-1.72, 2.01)	-0.63 (-2.14, 0.88)	-0.34 (-2.48, 1.80)	**-1.94 (-3.79, -0.10)***	-1.70 (-6.33, 2.93)
Asthmatics	**-12.73 (-16.97, -8.50)****	1.61 (-1.25, 4.47)	0.46 (-0.87, 1.80)	**2.82 (1.06, 4.57)****	n/a[2]
Normal weight[1]	-0.53 (-3.08, 2.03)	0.33 (-1.73, 2.39)	-0.51 (-3.45, 2.44)	n/a[2]	-2.85 (-8.79, 3.08)
Overweight/obese[1]	-0.12 (-2.64, 2.39)	**-1.93 (-3.66, -0.20)***	-0.20 (-2.10, 1.69)	-1.54 (-3.21, 0.23)	2.07 (-1.32, 5.45)
FEV_1					
All participants[1]	-83.48 (-187.63, 20.68)	92.85 (-1.31, 187.00)	0.83 (-100.50, 102.15)	71.40 (-38.99, 181.78)	5.63 (-232.87, 244.13)
Non-asthmatics	-101.58 (-215.95, 12.78)	84.44 (-14.10, 182.97)	22.96 (-74.20, 120.12)	82.32 (-32.58, 197.23)	10.55 (-229.17, 250.27)
Asthmatics	**-322.97 (-379.37, -266.57)****	151.86 (-52.38, 356.10)	**-450.61 (-523.61, -377.60)****	-71.00 (-206.91, 64.91)	n/a[2]
Normal weight[1]	-50.01 (-153.81, 53.79)	**150.53 (29.68, 271.38)***	-83.93 (-282.56, 114.70)	n/a[2]	160.96 (177.48, 499.40)
Overweight/obese[1]	-77.84 (-205.30, 49.62)	-75.34 (-213.64, 62.96)	144.75 (-52.07, 341.57)	**-200.70 (-372.33, -29.06)***	-114.66 (-510.55, 281.23)
FVC					
All participants[1]	-71.49 (-201.82, 58.83)	**121.29 (10.49, 232.10)***	17.19 (-125.09, 159.47)	**170.55 (40.73, 300.37)***	108.71 (-317.35, 534.77)
Non-asthmatics	**-125.14 (-247.89, -2.39)***	107.12 (-9.88, 224.13)	43.34 (-93.04, 179.71)	**202.11 (70.56, 333.65)****	114.76 (-323.20, 552.71)
Asthmatics	**282.05 (123.76, 440.33)****	**143.10 (47.3, 238.87)****	**-474.65 (-527.09, -422.21)****	**-101.12 (-163.14, -39.10)****	n/a[2]
Normal weight[1]	-25.97 (-156.59, 104.65)	132.25 (1.80, 262.70)	-84.30 (-292.06, 123.45)	n/a[2]	353.91 (-236.31, 944.14)
Overweight/obese[1]	-62.04 (-291.97, 167.89)	-10.92 (-131.2, 109.35)	189.72 (-40.84, 420.28)	-160.19 (-337.84, 17.45)	-219.07 (-624.66, 186.53)

Data presented as β (95% CI). All models adjusted for age, gender, race/ethnicity, health insurance coverage, family history of asthma, ETS exposure, fasting hours, and CRP. [1]Defined on basis of BMI z-score; additionally adjusted for current asthma. [2]All asthmatics had fasting glucose < 110mg/dL, and all children of normal weight had WC < 75th pct. *p<0.05, **p<0.01.

Supplemental Table 4 – Insulin sensitivity/resistance, metabolic syndrome, and percent-of-predicted FEV_1, FVC and FEV_1/FVC by asthma status among white, black and Mexican American participants

Outcome	Glucose:insulin ratio	QUICKI[1]	HOMA-IR	Metabolic syndrome
All Participants[2] (n=446)				
FEV_1 (%pred[3])	**3.11 (0.90, 5.33)****	**7.56 (2.67, 12.45)****	**-9.45 (-14.59, -4.31)****	-27.38 (-77.86, 23.10)
FVC (%pred[3])	**2.75 (0.73, 4.76)****	**7.84 (3.80, 11.87)****	**-9.16 (-13.36, -4.96)****	7.66 (-41.41, 56.74)
FEV_1/FVC (%pred[3])	<0.001 (-0.002, 0.002)	-0.03 (-0.36, 0.30)	<-0.001 (-0.003, 0.003)	**-0.02 (-0.05, -0.002)***
No asthma (n=421)				
FEV_1 (%pred[3])	**3.06 (0.78, 5.34)***	**7.37 (2.25, 12.48)****	**-9.18 (-14.66, -3.70)****	-26.50 (-75.79, 22.79)
FVC (%pred[3])	**2.64 (0.58, 4.69)***	**7.54 (3.35, 11.74)****	**-8.83 (-13.35, -4.32)****	3.73 (43.85, 51.32)
FEV_1/FVC (%pred[3])	<0.001 (-0.002, 0.002)	-0.02 (-0.35, 0.31)	<-0.001 (-0.003, 0.003)	-0.02 (-0.04, 0.005)
Current asthma (n=25)				
FEV_1 (%pred[3])	-5.33 (-12.78, 2.12)	-8.54 (-36.29, 19.20)	8.12 (-21.61, 37.86)	7.14 (-664.54, 678.82)
FVC (%pred[3])	1.06 (-26.19, 28.31)	4.17 (-56.56, 64.89)	0.48 (-50.10, 58.07)	106.24 (-372.10, 584.59)
FEV_1/FVC (%pred[3])	-0.01 (-0.04, 0.03)	-1.16 (-4.40, 2.08)	0.008 (-0.01, 0.03)	**-0.09 (-0.18, -0.03)***

Data presented as beta coefficient (95% CI). All models adjusted for age, gender, family history of asthma, ETS exposure, fasting hours, C-reactive protein, and BMI z-score. [§]p<0.1; *p<0.05, **p<0.01. [1]Results shown per 0.01 unit of QUICKI increment in each lung function measure. [2]Additionally adjusted for asthma status. [3]Percent-of predicted based on NHANES III equations.

Supplemental Table 5 – Insulin sensitivity/resistance, metabolic syndrome, and percent-of-predicted FEV_1, FVC and FEV_1/FVC by obesity status among white, black and Mexican American participants

Outcome	Glucose:insulin ratio	QUICKI[1]	HOMA-IR	Metabolic syndrome
BMI < 85th percentile (n=257)				
FEV_1 (%pred[2])	0.33 (-1.90, 2.55)	0.34 (-5.05, 5.73)	-1.40 (-12.36, 9.56)	12.21 (-51.87, 76.29)
FVC (%pred[2])	-0.40 (-1.82, 1.02)	-0.30 (-3.95, 3.55)	-1.39 (-8.37, 5.59)	28.23 (-13.44, 73.91)
FEV_1/FVC (%pred[2])	0.001 (-0.001, 0.003)	<0.001 (-0.004, 0.004)	-0.001 (-0.007, 0.006)	-0.01 (-0.07, 0.04)
BMI ≥ 85th percentile (n=191)				
FEV_1 (%pred[2])	**6.73 (2.23, 11.24)****	**10.95 (4.85, 17.05)****	**-7.84 (-11.69, 3.99)****	0.78 (-55.43, 56.99)
FVC (%pred[2])	**5.71 (3.18, 8.25)****	**9.08 (6.02, 12.14)****	**-5.79 (-7.44, -4.13)****	37.19 (-15.87, 90.25)
FEV_1/FVC (%pred[2])	<0.001 (-0.002, 0.004)	0.002 (-0.002, 0.006)	-0.002 (-0.005, 0.001)	**-0.03 (-0.05, -0.004)***

Data presented as beta (95% CI). All models adjusted for age, gender, family history of asthma, ETS exposure, fasting hours, C-reactive protein, and asthma status. *p<0.05, **p<0.01. [1]Results shown per 0.01 unit of QUICKI increment in each lung function measure. [2]Percent-of predicted based on NHANES III equations.

Supplemental Table 6 – Metabolic syndrome criteria and percent-of-predicted FEV_1/FVC by asthma and obesity status among white, black, and Mexican-American participants

	SBP ≥ 90th percentile	**HDL < 50 mg/dL**	**Triglyceride ≥ 100 mg/dL**	**WC ≥ 75th percentile**	**Fasting glucose ≥ 110 mg/dL**
All participants[1]	0.001 (-0.02, 0.02)	-0.002 (-0.02, 0.01)	-0.01 (-0.02, 0.01)	**-0.02 (-0.03, -0.01)****	-0.02 (-0.07, 0.03)
Non-asthmatics	0.01 (-0.01, 0.03)	-0.002 (-0.02, 0.01)	-0.004 (-0.02, 0.01)	**-0.02 (-0.04, -0.01)****	-0.02 (-0.07, 0.03)
Asthmatics	**-0.16 (-0.28, -0.05)****	0.06 (-0.05, 0.17)	0.03 (-0.28, 0.33)	**0.01 (0.001, 0.03)***	n/a[2]
Normal weight[1]	-0.002 (-0.02, 0.02)	0.01 (-0.01, 0.04)	-0.01 (-0.03, 0.01)	n/a[2]	-0.03 (-0.10, 0.03)
Overweight/obese[1]	0.001 (-0.02, 0.04)	-0.02 (-0.04, 0.002)	0.003 (-0.01, 0.02)	**-0.02 (-0.04, -0.01)****	0.01 (-0.02, 0.04)

FEV1/FVC as percent-of predicted based on NHANES III equations. Data presented as β (95% CI). All models adjusted for age, gender, family history of asthma, ETS exposure, fasting hours, and CRP. [1]Defined on basis of BMI z-score; additionally adjusted for current asthma. [2]All asthmatics had fasting glucose < 110mg/dL, and all children of normal weight had WC < 75th pct. *p<0.05, **p<0.01.

SUPPLEMENTAL FIGURE LEGENDS

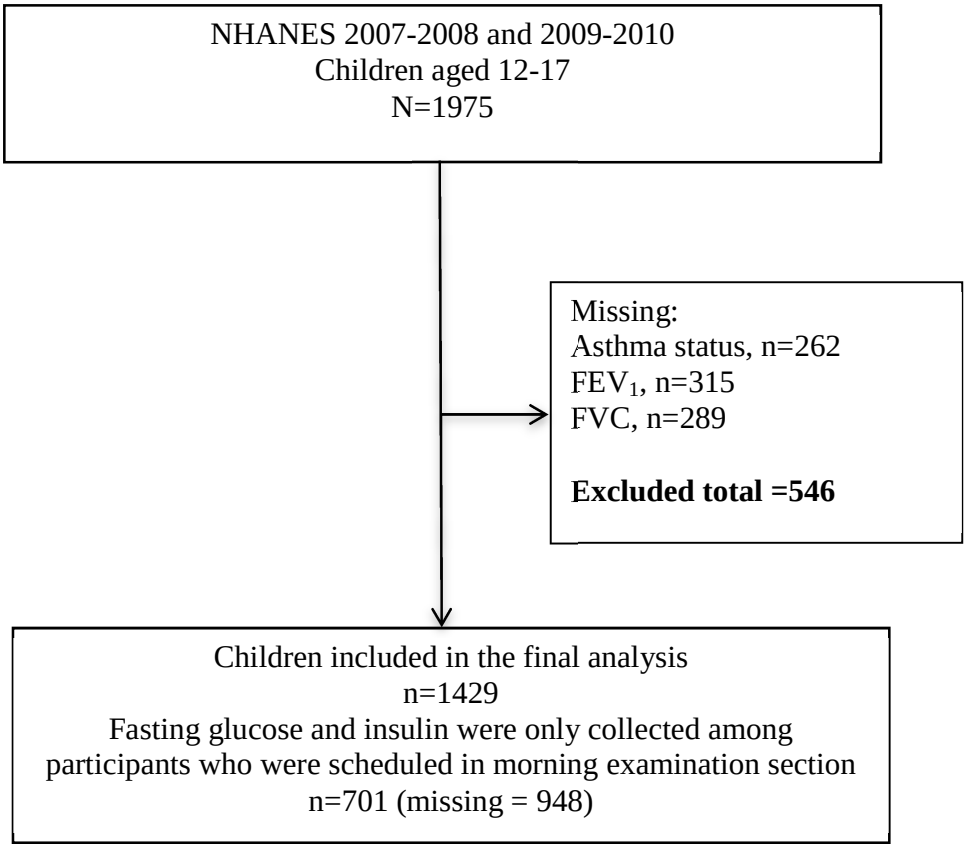
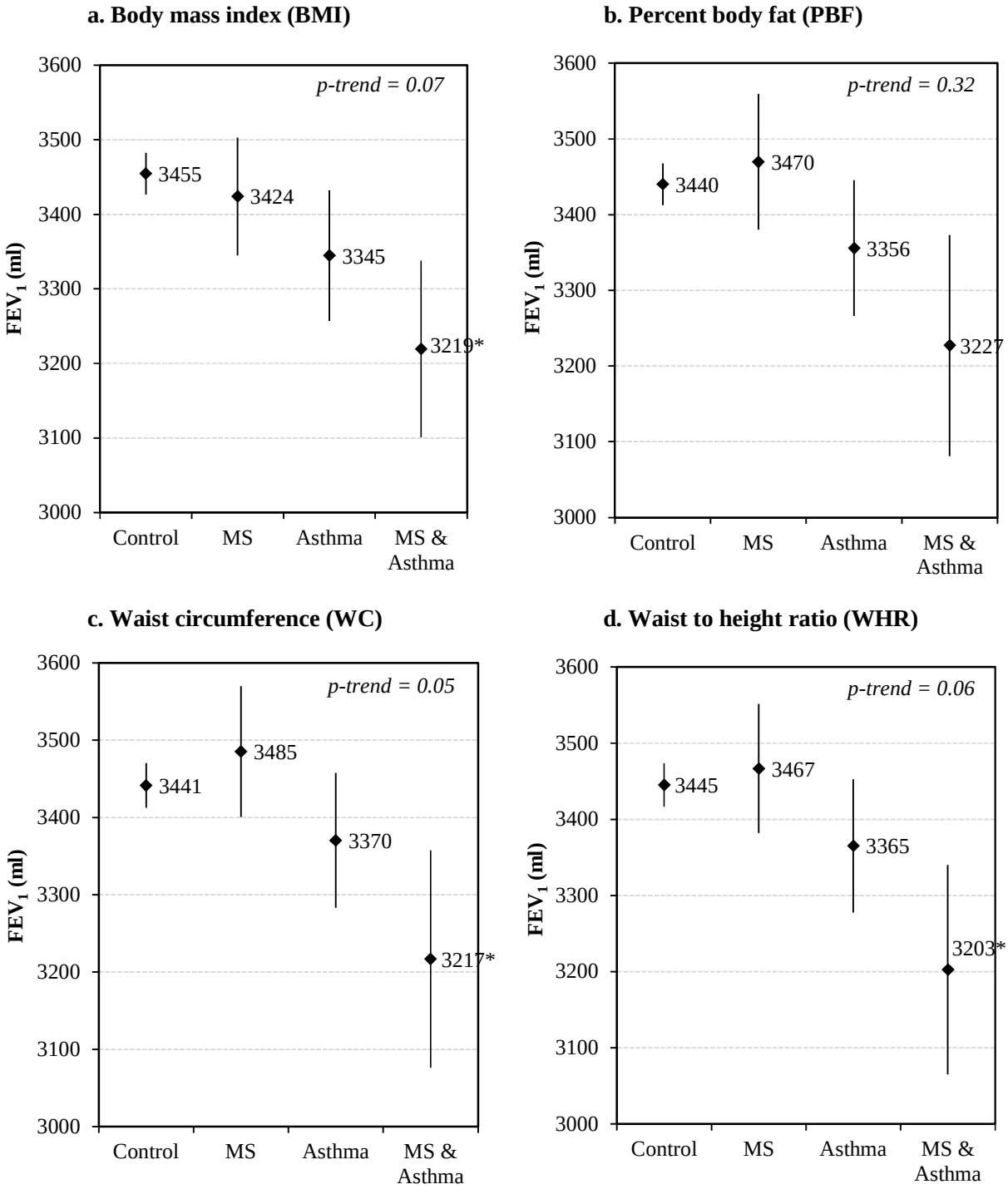
Supplemental Figure 1 – Derivation of study sample from NHANES 2007-2008 and 2009-2010

NHANES: National Health and Nutrition Examination Survey.

Supplemental Figure 2 – Predicted FEV_1 by asthma and metabolic syndrome status

All models adjusted for age, gender, race/ethnicity, health insurance coverage, family history of asthma, ETS exposure, fasting hours, C-reactive protein, and z-score for each respective adiposity indicator (BMI, PBF, WC, or WHR). MS=metabolic syndrome. No asthma & no MS n=496; MS only n=58; asthma only n=23; and MS & asthma n=7. *P<0.05 compared to control group (no asthma & no MS).

Supplemental Figure 1 – Derivation of study sample from NHANES 2007-2008 and 2009-2010



Supplemental Figure 2 – Predicted FEV_1 by asthma and metabolic syndrome status