Zoom Webinar: Severe Asthma and Health Disparities in Hispanic Communities

October 5th / 2 p.m. ET

This webinar focuses on the health disparities that Hispanics may face when accessing treatment and care for severe asthma and highlights strategies and solutions to address these barriers.

JUAN C. CELEDÓN, MD, DRPH, ATSF

Professor of Medicine
University of Pittsburgh

BERT E. JOHANSSON, MD, PHD, FAAP

Executive Board Member
National Hispanic Medical Association

Learn more and register at:

bit.ly/NHMAAsthmaWeb

NHMA
National Hispanic Medical Association

Welcome

Bert Johansson, MD, PhD, FAAP
Executive Board Member
National Hispanic Medical Association

Housekeeping

- All participant microphones will be muted, but please feel free to use the raised hand feature to be unmuted to ask a question or type your question into the Q & A box for the panelists to address during our Q & A session at the end.
- The recording will be housed on NHMAmd.org and our YouTube channel.
- The recording and slides will be sent out one week after the event.

AMGEN

NHMA
National Hispanic Medical Association

Agenda & Learning Objectives

Agenda

- Overview of Health Disparities of Severe Asthma among Hispanics – Dr. Juan C. Celedon, MD, DrPH, ATSF
- Q & A from Audience
- Closing Remarks – Dr. Bert Johannson

Learning Objectives

- To educate health advocates about the health disparities that Hispanic face with Severe Asthma.

AMGEN

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National Hispanic Medical Association

Asthma in Hispanic Adults

Juan Carlos Celedón, M.D., Dr.P.H.
Niels K. Jerne Professor of Pediatrics and Medicine
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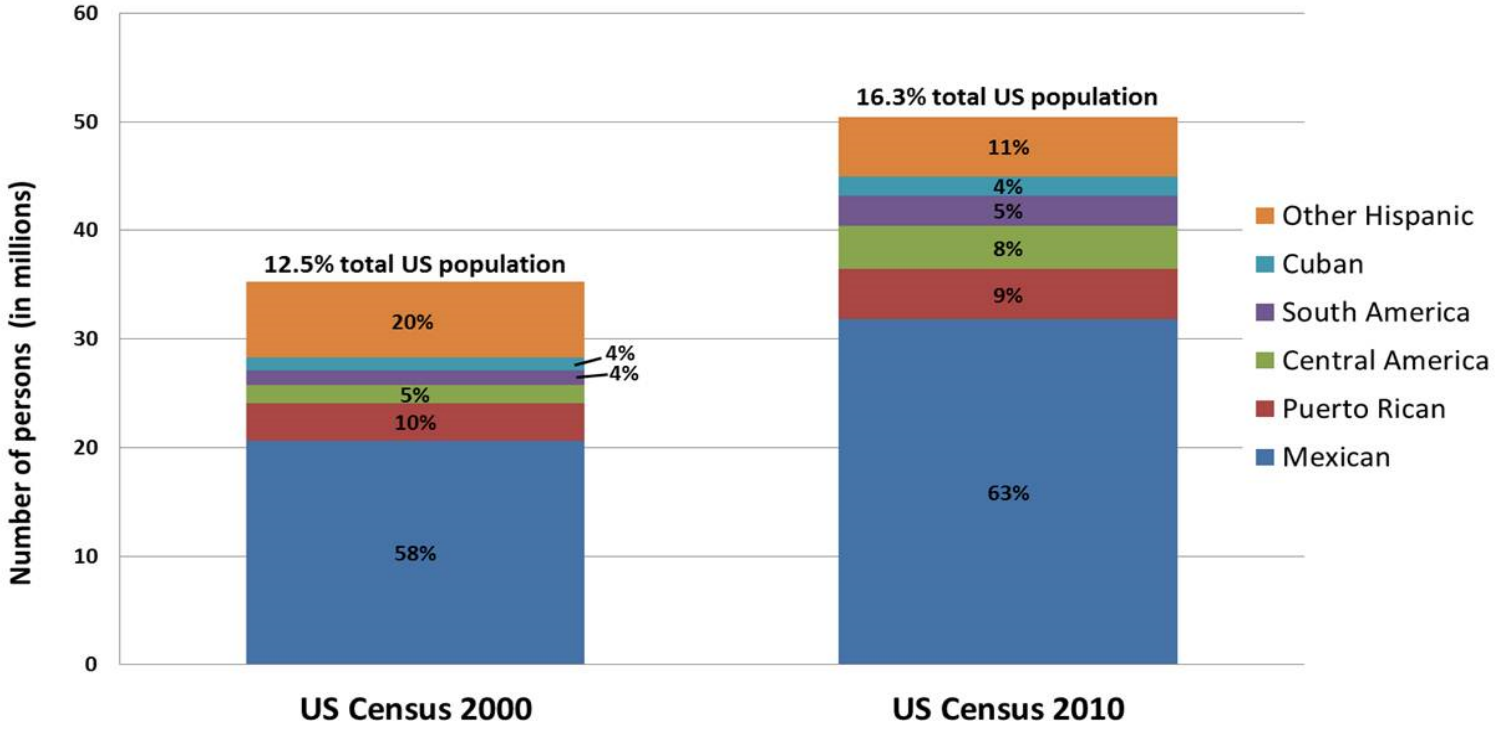
University of Pittsburgh
Division Chief, Pulmonary Medicine
UPMC Children's Hospital of Pittsburgh
Past President, American Thoracic Society (2020-2021)

University of Pittsburgh

Disclosure of Conflicts of Interest

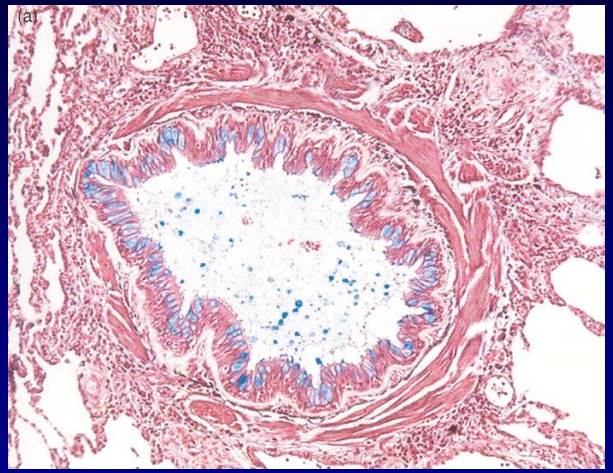
- I received research materials (inhaled steroids) from Merck, in order to provide medications free of cost to participants in an NIH-funded study, unrelated to this presentation

- I do not intend to discuss unapproved/investigative use of commercial product(s)/device(s) in my presentation

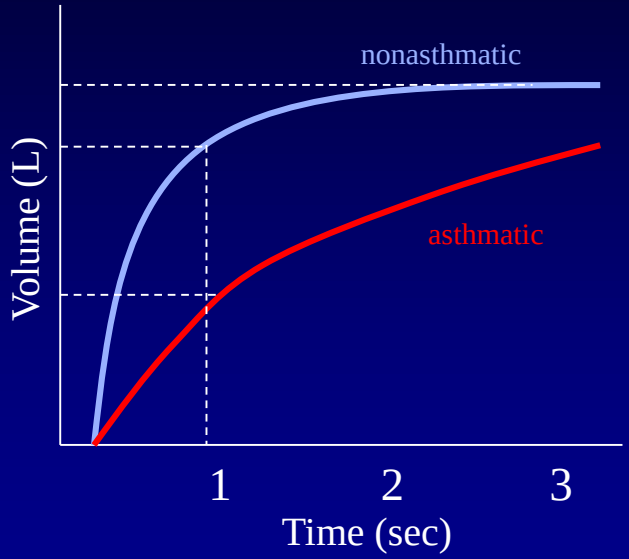

Number of persons (in millions)
60
50
40
30
20
10
0
12.5% total US population
20%
4%
4%
5%
10%
58%
16.3% total US population
11%
4%
5%
8%
9%
63%
US Census 2000
US Census 2010
Other Hispanic
Cuban
South America
Central America
Puerto Rican
Mexican

Asthma

- Affects >300 million people worldwide, including ~19 million adults in the U.S.
- Costs : ~$81 billion per year in the U.S

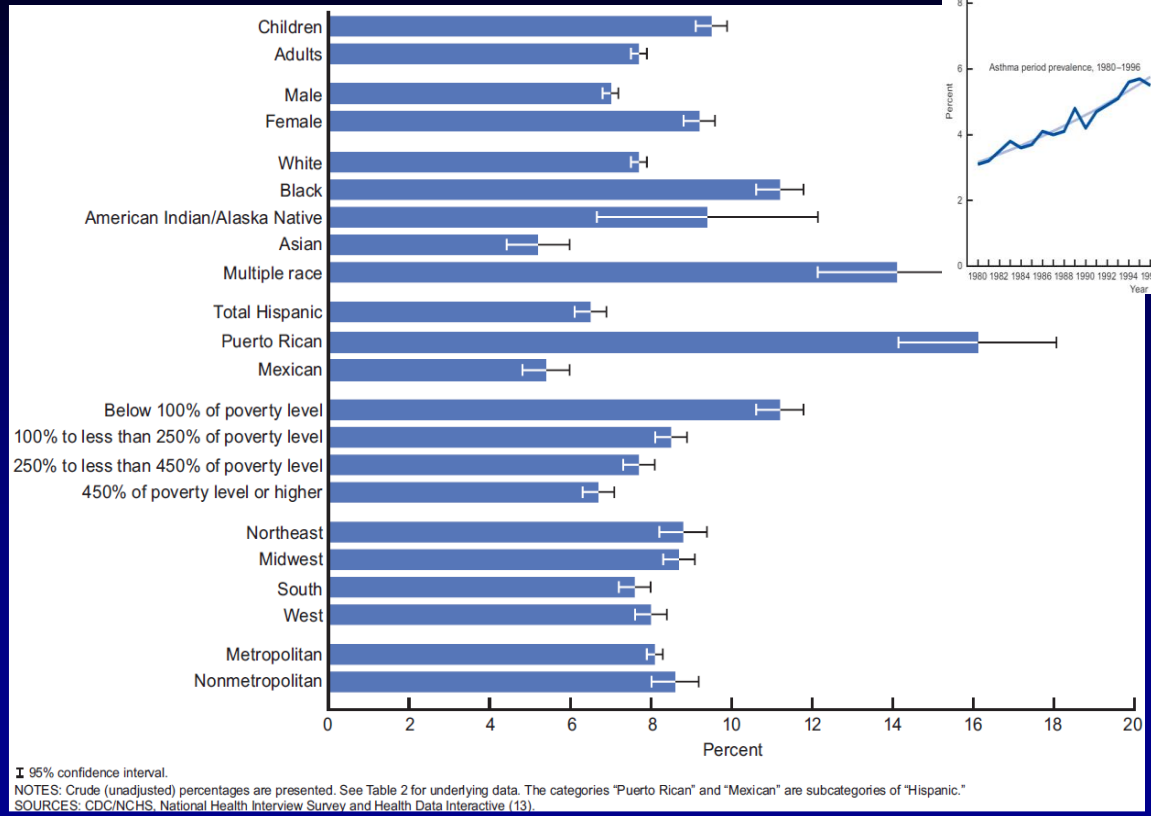


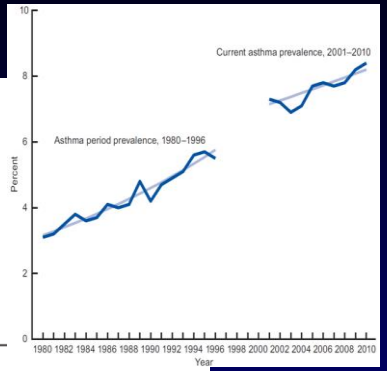
- Airway Inflammation
- Airway Remodeling
- Airway Hyperreactivity
- Airflow Obstruction



FEV_1 = Forced Expiratory Volume at 1 Second

National Surveillance of Asthma: United States, 2001–2010



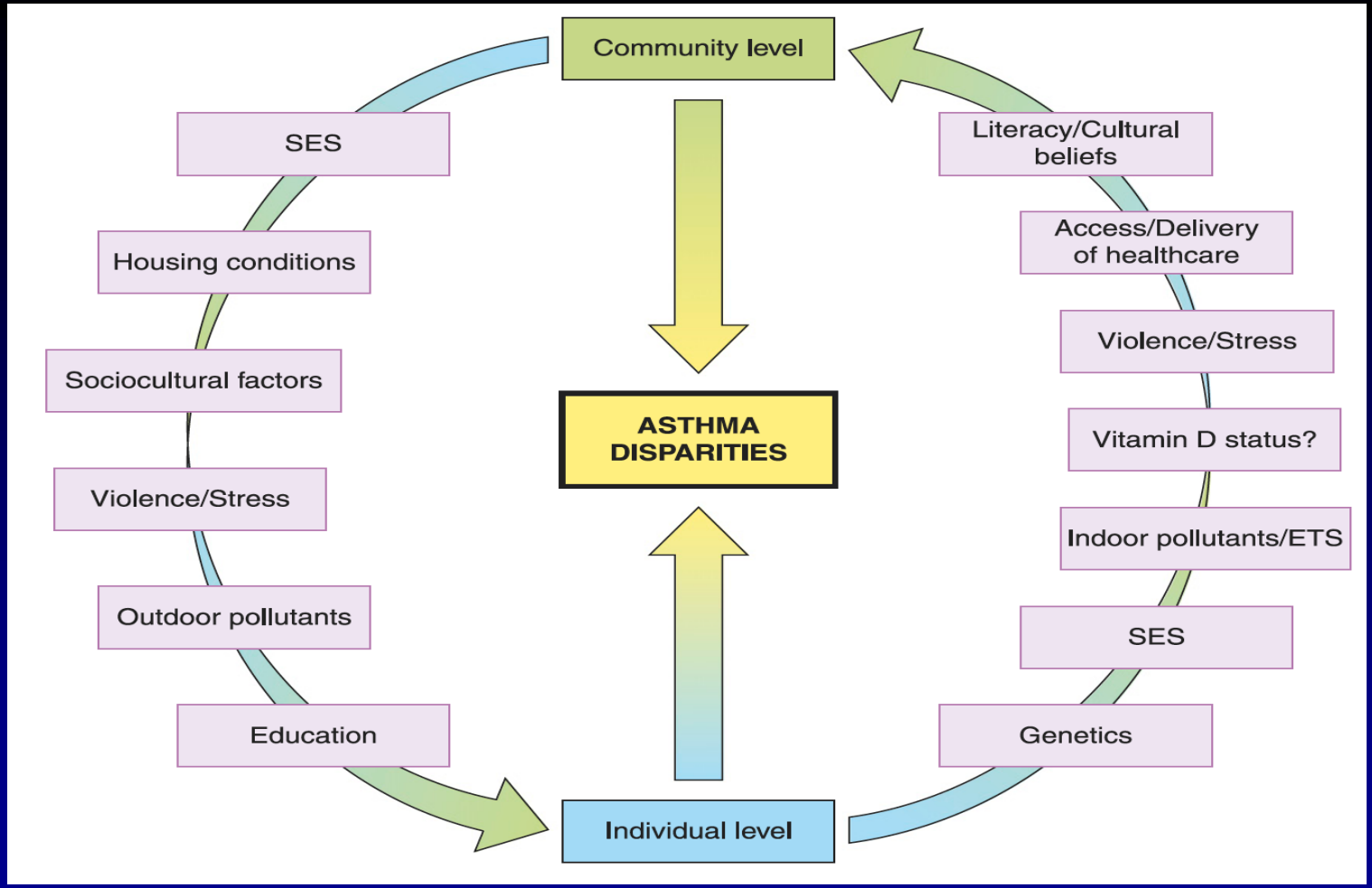


I 95% confidence interval.

NOTES: Crude (unadjusted) percentages are presented. See Table 2 for underlying data. The categories "Puerto Rican" and "Mexican" are subcategories of "Hispanic."

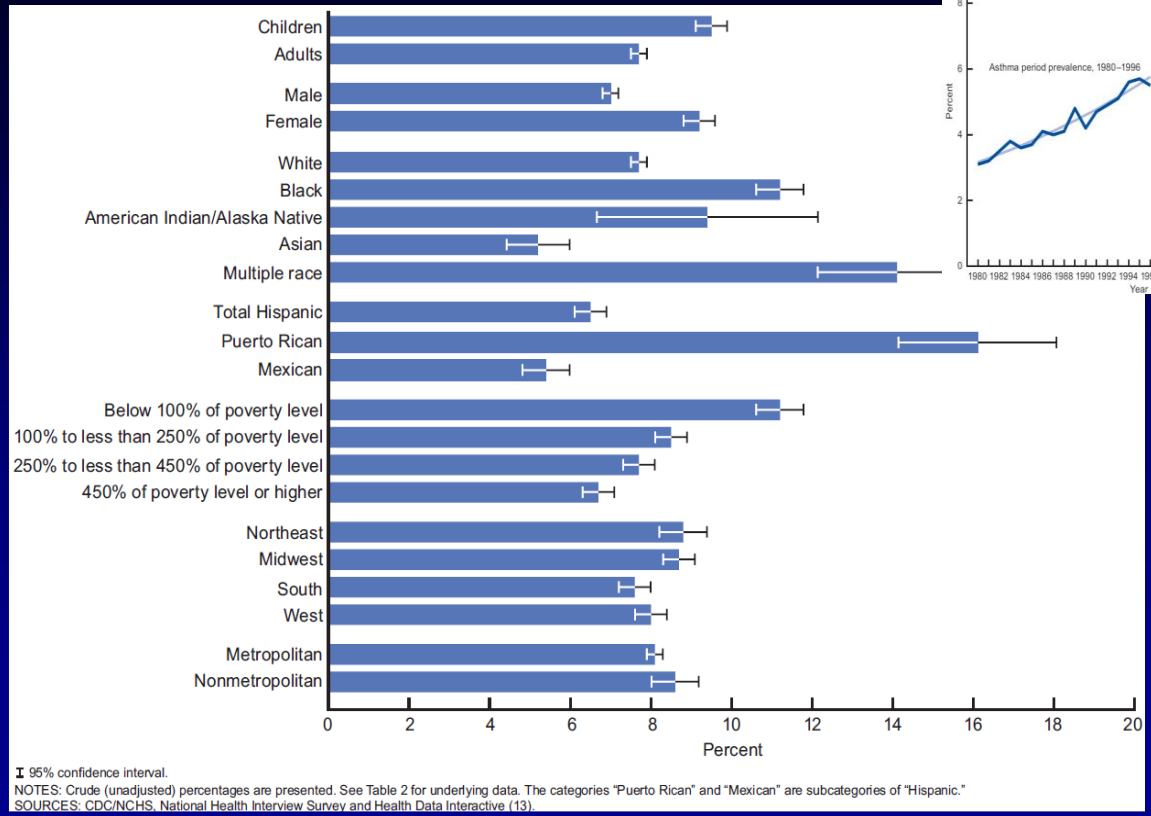
SOURCES: CDC/NCHS, National Health Interview Survey and Health Data Interactive (13).

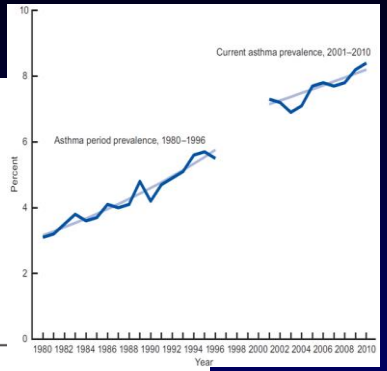
CDC Monitoring the Nation's Health



Forno E, Celedón JC. Am J Respir Crit Care Med 2012; 185:1033-5.

National Surveillance of Asthma: United States, 2001–2010





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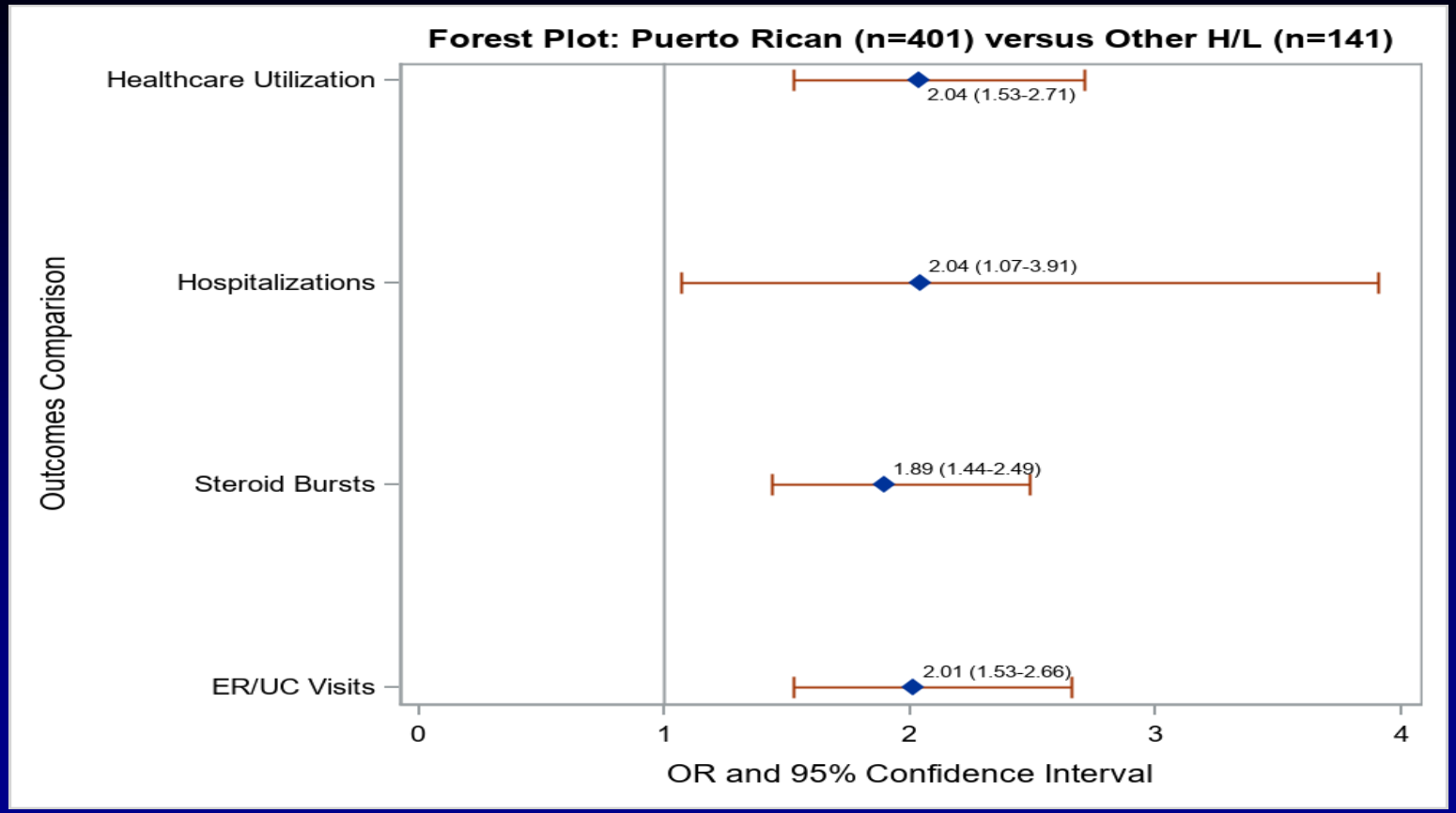
SOURCES: CDC/NCHS, National Health Interview Survey and Health Data Interactive (13).

CDC Monitoring the Nation's Health

Adjusted* estimates of the prevalence of current physician-diagnosed asthma in U.S. Hispanics

Subgroup	Prevalence (95% CI)
Puerto Ricans	15.3% (13.2%–17.6%)
Cubans	8.6% (7.1%–10.4%)
Dominicans	6.7% (5.3%–8.5%)
Mexicans	3.4% (2.7%–4.1%)

*For age, sex, education, age at immigration, time in the U.S., smoking, BMI, and health insurance. *Barr RG et al. Am J Respir Crit Care 2016; 193(4):386-95.*

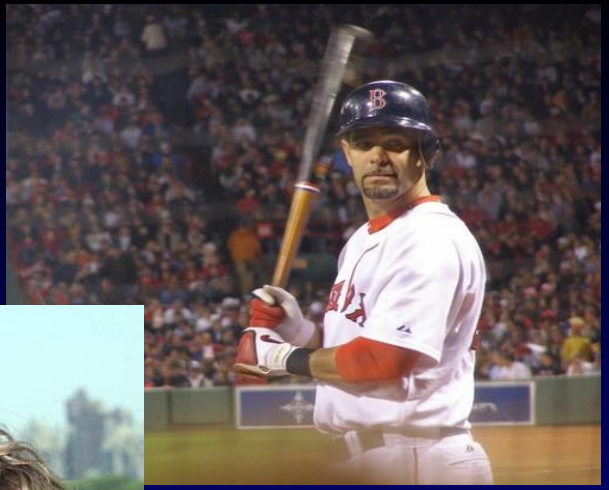


Cardet JC et al. J Allergy Clin Immunol 2022 Jun 30 (Epub ahead of print)

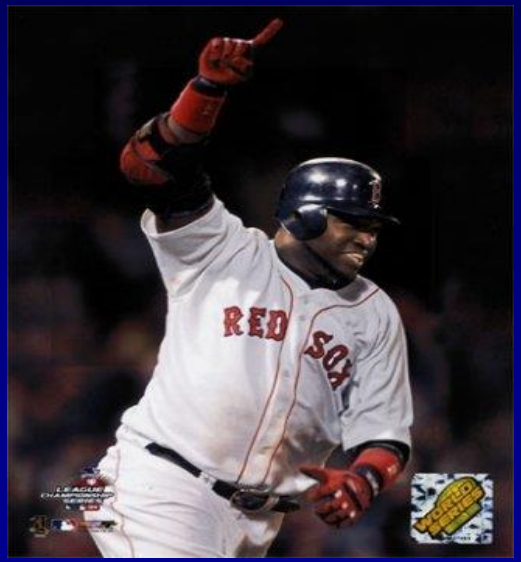
The “Hispanic Paradox”

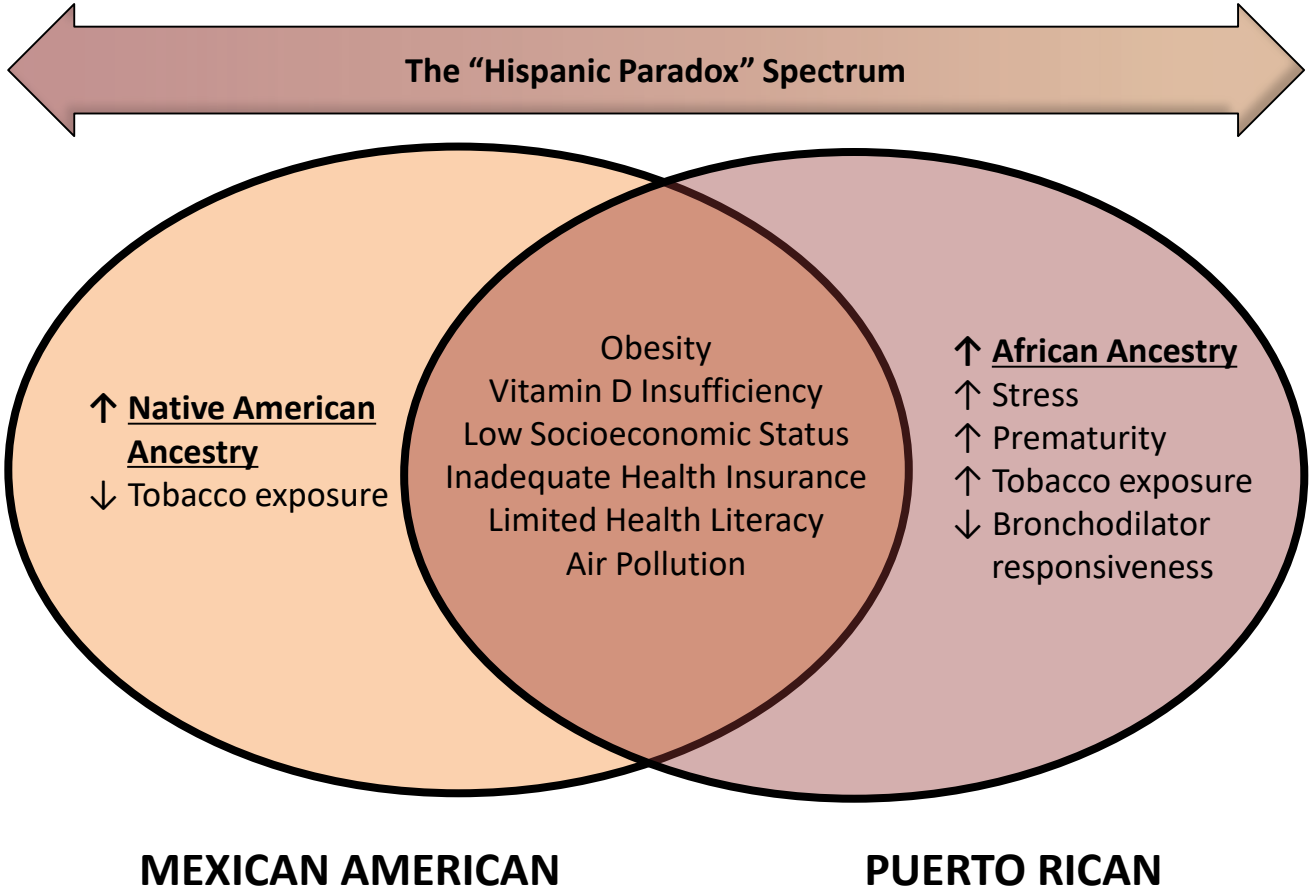
- Puerto Ricans have the highest prevalence, morbidity and mortality from asthma of all major ethnic groups in the United States
- Mexican Americans have the lowest burden of asthma of all ethnic groups in the United States

- Hunninghake G et al. Am J Respir Crit Care Med 2006; 173:143-163.
- Forno E, Celedón JC. Curr Opin Allergy Clin Immunol. 2009 ;9:154-160.
- Forno E, Celedón JC. Am J Respir Crit Care Med 2012; 185:1033-1035.
- Rosser F, Forno E, Celedón JC. Am J Respir Crit Care Med 2014; 189:1316-1327.
- Szentpetery S,…, Celedón JC. J Allergy Clin Immunol 2016;138:1556-1558.




Patrick Cooper / Retna Ltd.

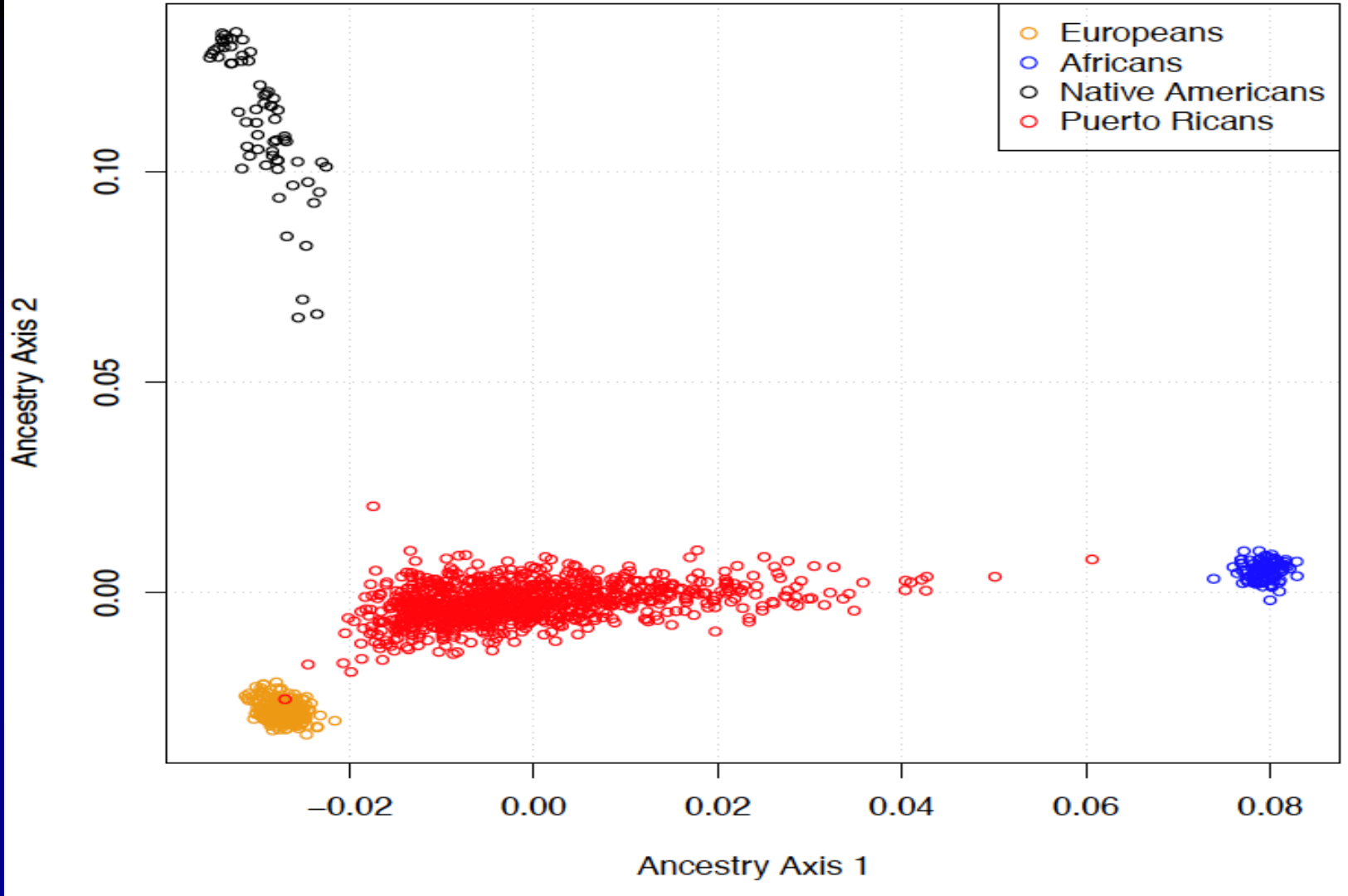

RED SOX



Rosser F, Forno E, Celedón JC. Am J Respir Crit Care Med 2014; 189:1316-1327.

1.

Racial Ancestry

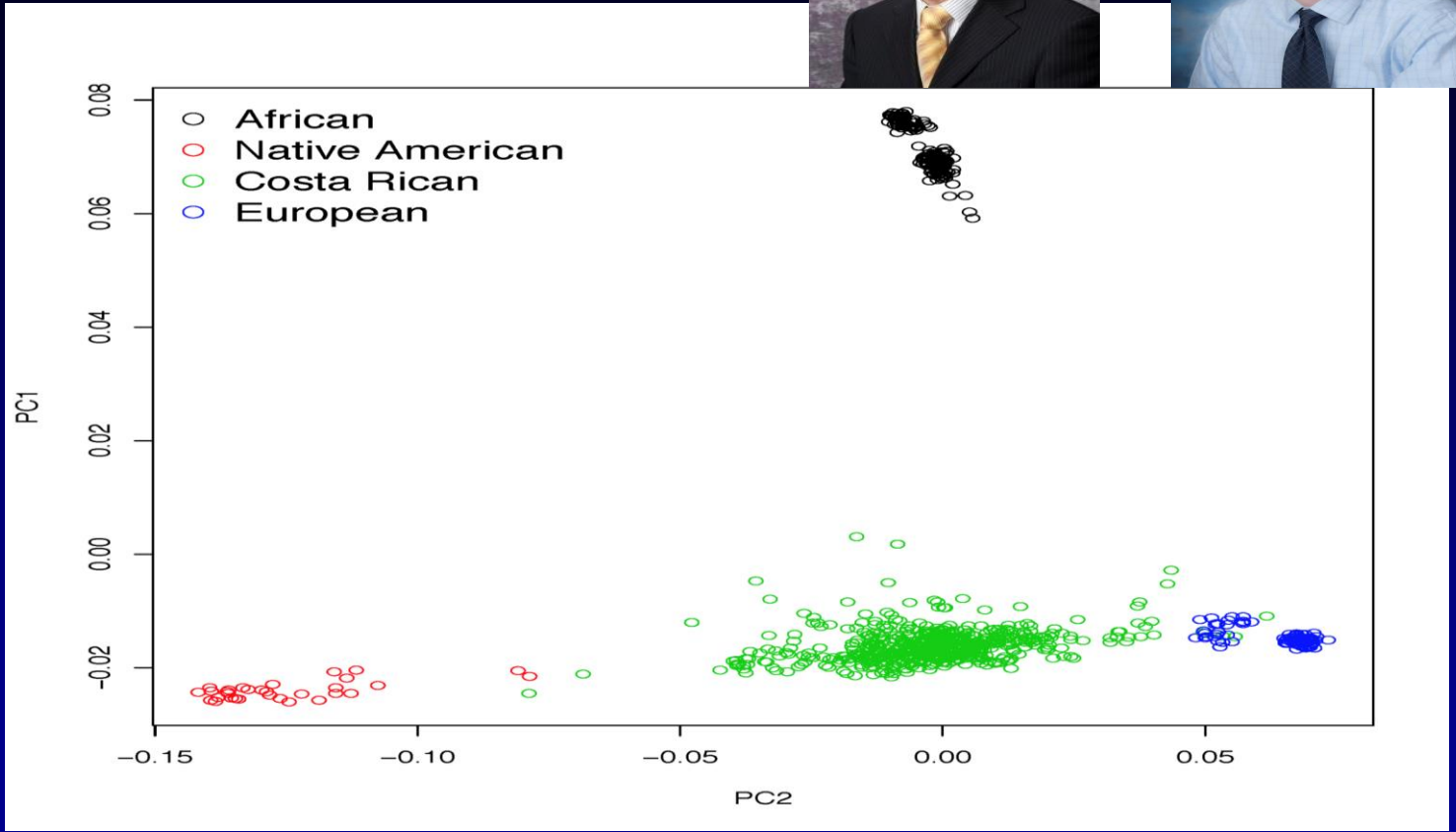

Europeans
Africans
Native Americans
Puerto Ricans
Ancestry Axis 2
0.10
0.05
0.00
−0.02
0.00
0.02
0.04
0.06
0.08
Ancestry Axis 1

African Ancestry and Lung Function in Puerto Rican youth with asthma (Combined Cohort)

	Beta coefficient (95% CI) , P value
Outcomes	**Adjusted***
Pre-BD FEV1 (ml)	-105 (-159 to -51), <0.001
Pre-BD FVC (ml)	-133 (-197 to -69, <0.001
Post-BD FEV1 (ml)	-152 (-210 to -94), <0.001
Post-BD FVC (ml)	-145 (-211 to -79), <0.001

*For age, gender, income, ICS use, study site, height, height squared and body mass index. **Per each 20% increment in African ancestry. Brehm J et al. J Allergy Clin Immunol 2014.


NICARAGUA
PANAMA
OCEANO PACIFICO
MAR CARIBE
PROVINCIA DE GUANACASTE
PROVINCIA DE ALAJUELA
PROVINCIA DE HEREDIA
PROVINCIA DE LIMON
PROVINCIA DE PUNTARENAS
PROVINCIA DE SAN JOSE
PROVINCIA DE CARTAGO
CORDILLERA DE GUANACASTE
CORDILLERA CENTRAL
CORDILLERA DE TALAMANCA
PENINSULA DE NICOYA
PENINSULA DE OSA
ISLA DEL COCO
LIBERIA
PUNTARENAS
ALAJUELA
HEREDIA
SAN JOSE
CARTAGO
LIMON
ESCALA 1: 300 000
0 20 40 60 Km.
ESCALA: 1:1 900 000
SIGNOS CONVENCIONALES
LUGARES POBLADOS
Capital de la República
Capital de Provincia
Otras Poblaciones
Límite Provincial
Límite Internacional
ABREVIATURAS
B. Bahía
C. Cerro
I. Isla
N. Norte
Pen. Península
Pta. Punta
Pto. Puerto
R. Río
S. San, Santo, Santa
V. Volcán
Autorizado por el Instituto Geográfico Nacional
Fuente: Mapas Oficiales IGN.
7 441040 499011
Elaborado por:
Oliman Fernandez C. &
Carlos Hidalgo V.
Edición 1996



Chen W, Brehm J et al. Chest 2014; 145(4):704-10.

Native American Ancestry, Lung Function and COPD in Costa Ricans (n=506)

Outcomes	Beta coefficient (95% CI) , P value Adjusted*
Pre-BD FEV1 (ml)	109 (33.6 to 184), 0.005
Pre-BD FVC (ml)	112 (22.2 to 202), 0.02
Pre-BD FEV1/FVC (%)	0.87 (-0.03 to 1.8), 0.06

*For age, gender, height, education, current smoking, pack-years of smoking and case-control status. **Per each 10% increment in Native American ancestry

Racial ancestry and asthma in Hispanics (GALA and CHS)

Ancestry	Group	Mean ancestry cases	Mean ancestry controls	OR (95% CI)*	*P* value
Native American	Meta-analysis†	—	—	0.72 (0.66-0.78)	**1.5×10^{-15}**
African	Meta-analysis‡	—	—	1.40 (1.14-1.72)	**.001**
European	Meta-analysis**	—	—	1.13 (0.89-1.45)	NS

Pino-Yanes M et al. J Allergy Clin Immunol 2015;135(1):228-35

Racial Ancestry and the Hispanic Paradox

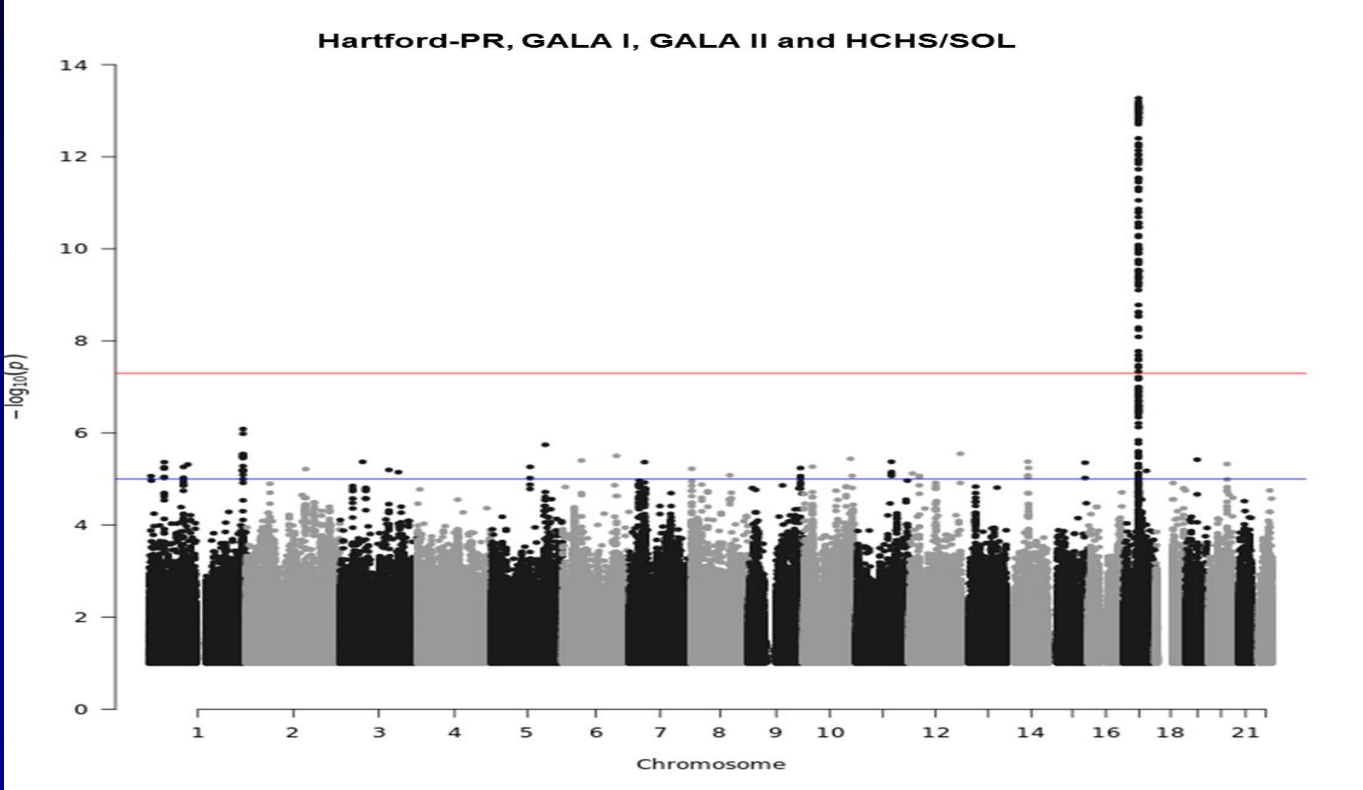
- Our findings (in PR children, CR adults, and NM adults), together with those in African American adults and Hispanics in GALA/CHS, strongly suggest that discrepancies in the burden of obstructive airway diseases (asthma and COPD) between Puerto Ricans and Mexican Americans are at least partly due to differences in underlying racial ancestry
- Ancestry is a marker of SDOH-related environmental and behavioral factors, in addition to genetic variation

2. Genomics and epigenetics

A GWAS of Asthma in Puerto Ricans

Study	PR-GOAL (n=948)	GALA I (n=437)	GALA II (n=1,786)	SOL (n=1,866)
Age (years)	10 (2.7)	18 (9)	13 (3)	48 (14)
Gender (male)	495 (52%)	187 (43%)	907 (51%)	784 (42%)
Asthma	523 (55%)	251 (57%)	892 (50%)	478 (26%)
Study sites	Hartford (CT)/San Juan (PR)	Puerto Rico and New York	Four U.S. cities and Puerto Rico	Four U.S. cities
Genotyping platform	Illumina 2.5 M	Affymetrix 6.0 Gene Chip	Axiom LATI Array (Affymetrix)	Illumina SOL custom array

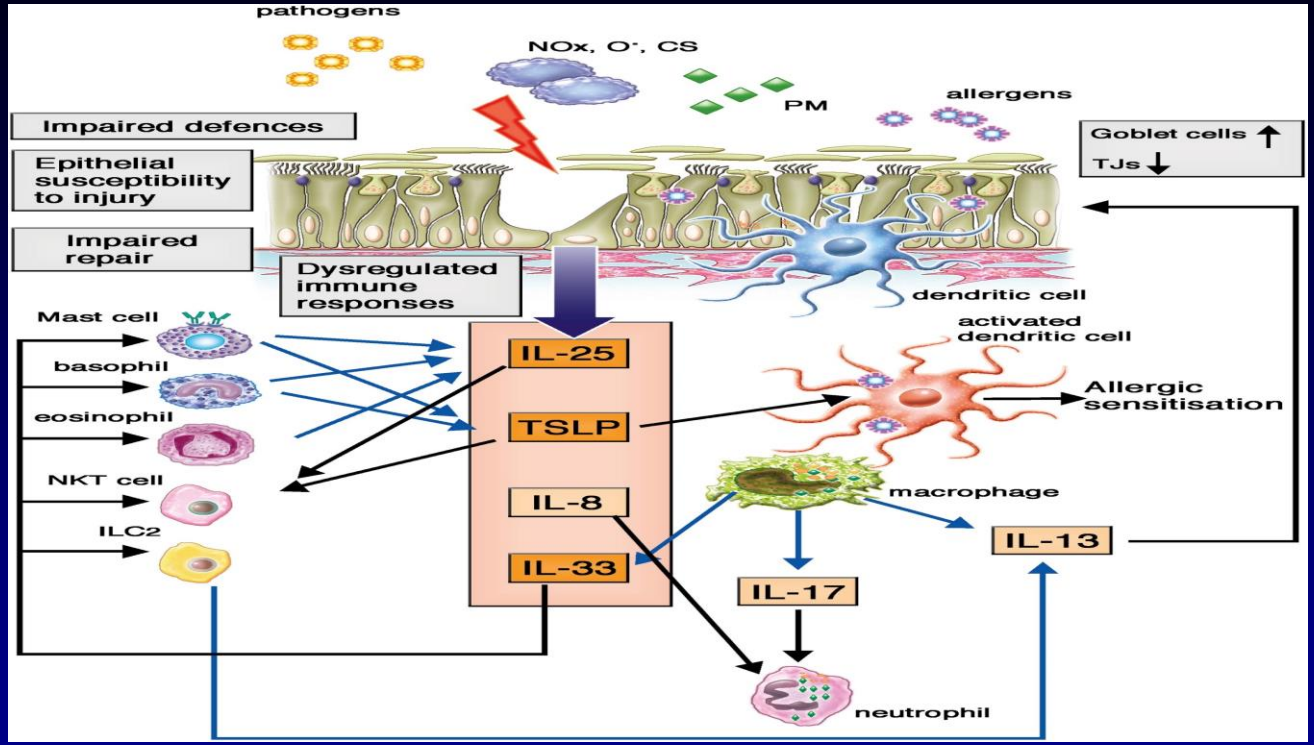
A GWAS of Asthma in Puerto Ricans (n=5,054)



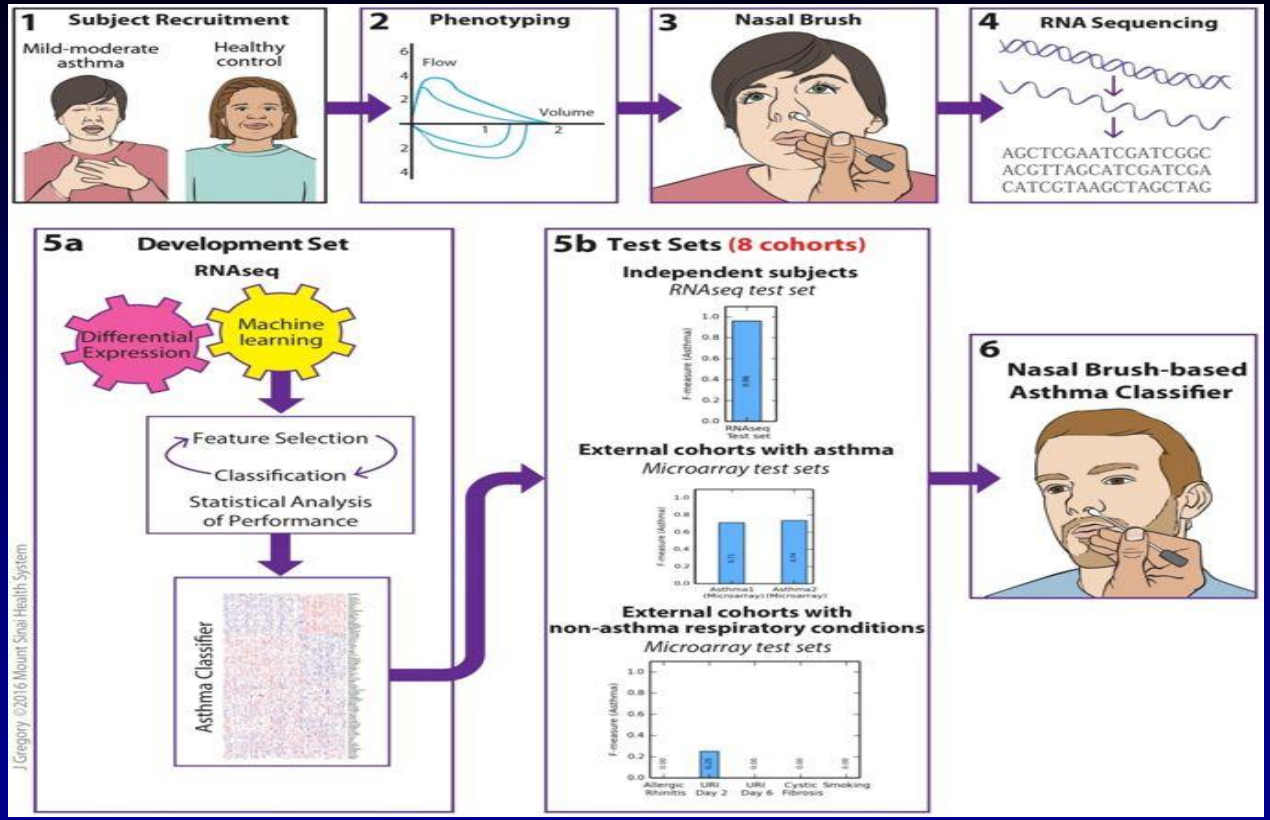
A GWAS of Asthma in Puerto Ricans

- Our findings in 5,054 Puerto Ricans participating in four studies (PR-GOAL, SOL, GALA I and II) confirm and emphasize the importance of the chr. 17q21 locus as a susceptibility gene for asthma
- We also replicated prior findings for SNPs in *IL1RL1* and *TSLP*, but not for *IL33*
- Next step is to conduct analyses of gene-by-environment interactions on chromosome 17q21

Yan Q et al. Eur Respir J 2017; 49(5):1601505.

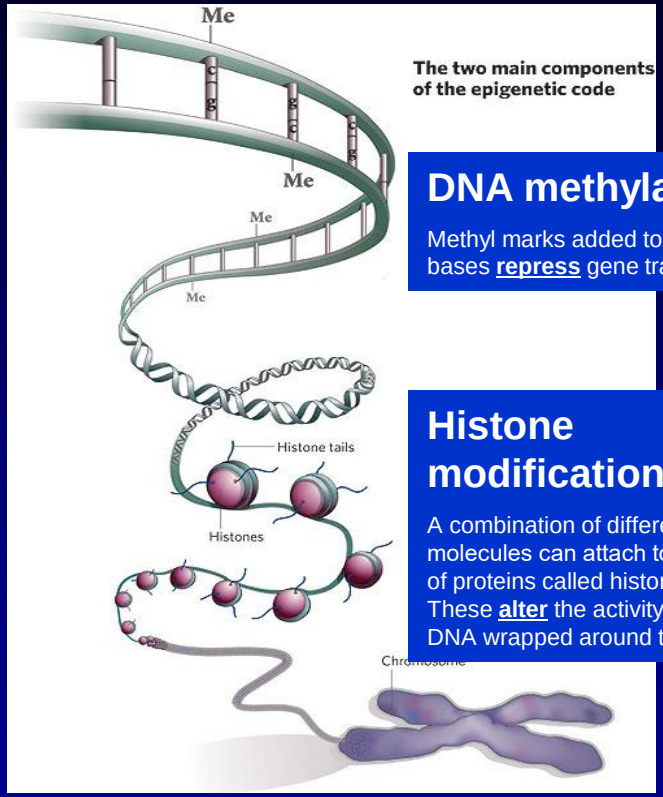


Journal of Allergy and Clinical Immunology 2017; 139, 1736-1751DOI: (10.1016/j.jaci.2017.04.005).



Pandey G et al. Sci Rep 2018 Jun 11;8(1):8826.

Epigenetic Marks

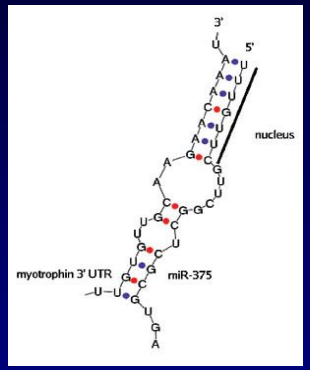


DNA methylation

Methyl marks added to certain DNA bases **repress** gene transcription

Histone modifications

A combination of different molecules can attach to the 'tails' of proteins called histones. These **alter** the activity of the DNA wrapped around them



MicroRNAs

Small non-coding RNAs that **block translation** of messenger RNAs into proteins

THE LANCET
Respiratory Medicine

DNA methylation in nasal epithelium, atopy, and atopic asthma in children: a genome-wide study

Erick Forno, MD [*] • Ting Wang, PhD [*] • Cancan Qi, MsC [*] • Qi Yan, PhD • Cheng-Jian Xu, PhD • Nadia Boutaoui, PhD • Yueh-Ying Han, PhD • Prof Daniel E Weeks, PhD • Yale Jiang • Franziska Rosser, MD • Judith M Vonk, PhD • Sharon Brouwer, BSc • Edna Acosta-Perez, PhD • Angel Colón-Semidey, MD • María Alvarez, MD • Prof Glorisa Canino, PhD • Prof Gerard H Koppelman, MD [†] • Wei Chen, PhD [†] • Prof Juan C Celedón, MD [†]

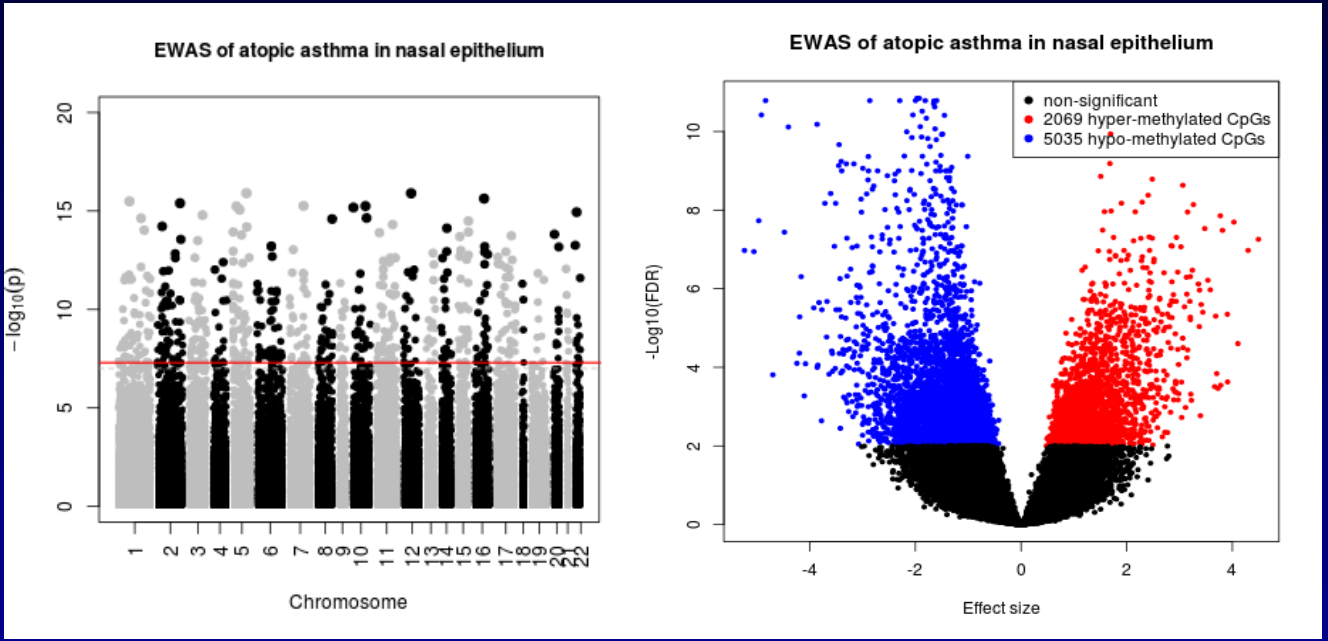
Table 1 –Characteristics of study participants in the discovery and replication cohorts

	Puerto Rico (discovery cohort)				Yang et al.		PIAMA	
	Atopy	No atopy	Atopic asthma	Non-atopic controls	Atopic asthma	Non-atopic controls	Atopy	No atopy
N (%)	312 (64·6%)	171 (35·4%)	169 (61·9%)	104 (38·1%)	36 (50%)	36 (50%)	207 (47·9%)	225 (52·1%)
Age (years)	15 (3)	15 (3)	15 (3)	16 (3)	11·1 (0·8)	10·9 (0·9)	16·4 (0·2)	16·3 (0·2)
Female sex, n (%)	140 (44·9%)	93 (54·4%)	66 (39·1%)*	61 (58·7%)	17 (47·2%)	19 (52·8%)	92 (44·4%)	127 (56·4%)
Race/ethnicity								
• Hispanic/Latino	100%				13·9%[a]		0%	
• African American	0				91·7%		0%	
• Non-Hispanic White	0				6·9%		97·1%	
• Other/missing	0				4·2%		2·9%	
Asthma, n (%)	169 (54·2%)*	67 (39·2%)	169 (100%)*	0 (0%)	36 (100%)*	0 (0%)	27 (13·0%)	6 (2·7%)
Total IgE (IU/mL)	409 [207-816]*	43 [22-93]	386 [214-806]*	42 [21-78]	366 [185-785]	29 [16·5-49·5]	140 [55-140]	20 [10-55]
Number of positive allergen-specific IgEs+	2 [1-3]*	0	2 [1-3]*	0	n/a	0	2 [1-3]*	0

The Puerto Rico cohort (EVA-PR) is a case-control study of asthma. Yang et al. is a case-control study of atopic asthma. PIAMA is a birth cohort, unselected for either atopy or asthma. Numbers represent number of participants (%) for categorical variables and mean (SD) or median [interquartile range] for continuous variables. *P<0·05 for atopy vs. no atopy, or asthma vs. no asthma within each cohort. n/a: not available in public dataset. [a]Does not add up to 100% because participants could report more than one race/ethnicity.

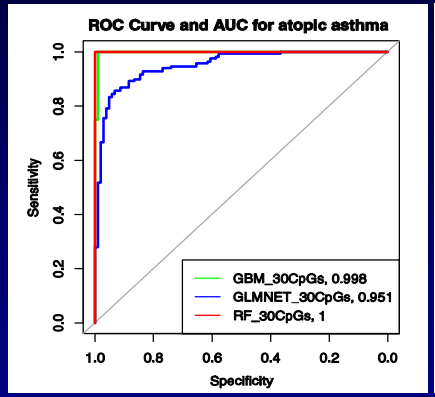
Forno E et al. Lancet Respiratory Medicine 2019 Apr; 7(4):336-346.

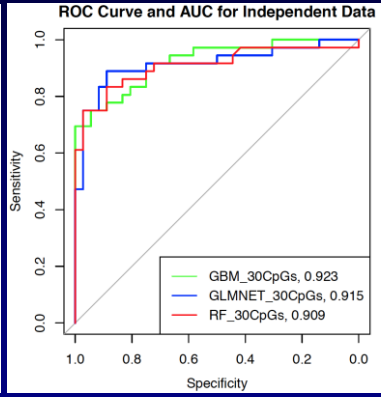
Epigenome-wide association study of atopic asthma in Puerto Rican children (n=273)

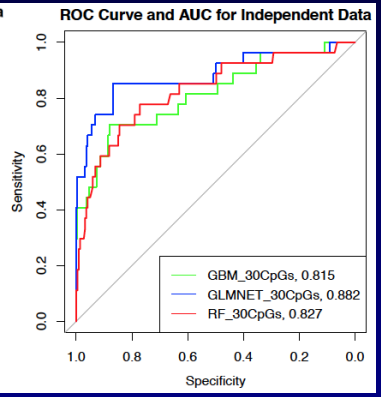


Yang et al.

PIAMA







Accuracy = 88%

Accuracy = 82%

Accuracy = 87%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3. Psychosocial stressors, mental health, and asthma

Exposure to Violence, Stress and Asthma in Puerto Ricans

- Puerto Ricans have the highest prevalence, morbidity and mortality from asthma of all ethnic groups in the US
- Puerto Ricans are both exposed to high levels of violence and highly susceptible to stress

  -Martinez-Taboas A et al. J Trauma Stress 2006; 19:439-48.

  -Vermeiren R et al. Pediatrics 2003; 111:535-40.

  -Rosser F et al. Am J Respir Crit Care Med 2014; 189(11):1316-27.
- Stress and violence have been linked to asthma and asthma morbidity
  - Rosenberg S, … Celedón JC. J Allergy Clin Immunol 2014;134:1009-15.
  - Landeo-Gutierrez J, Celedón JC. Am J Respir Crit Care Med 2020; 201: 917-22.

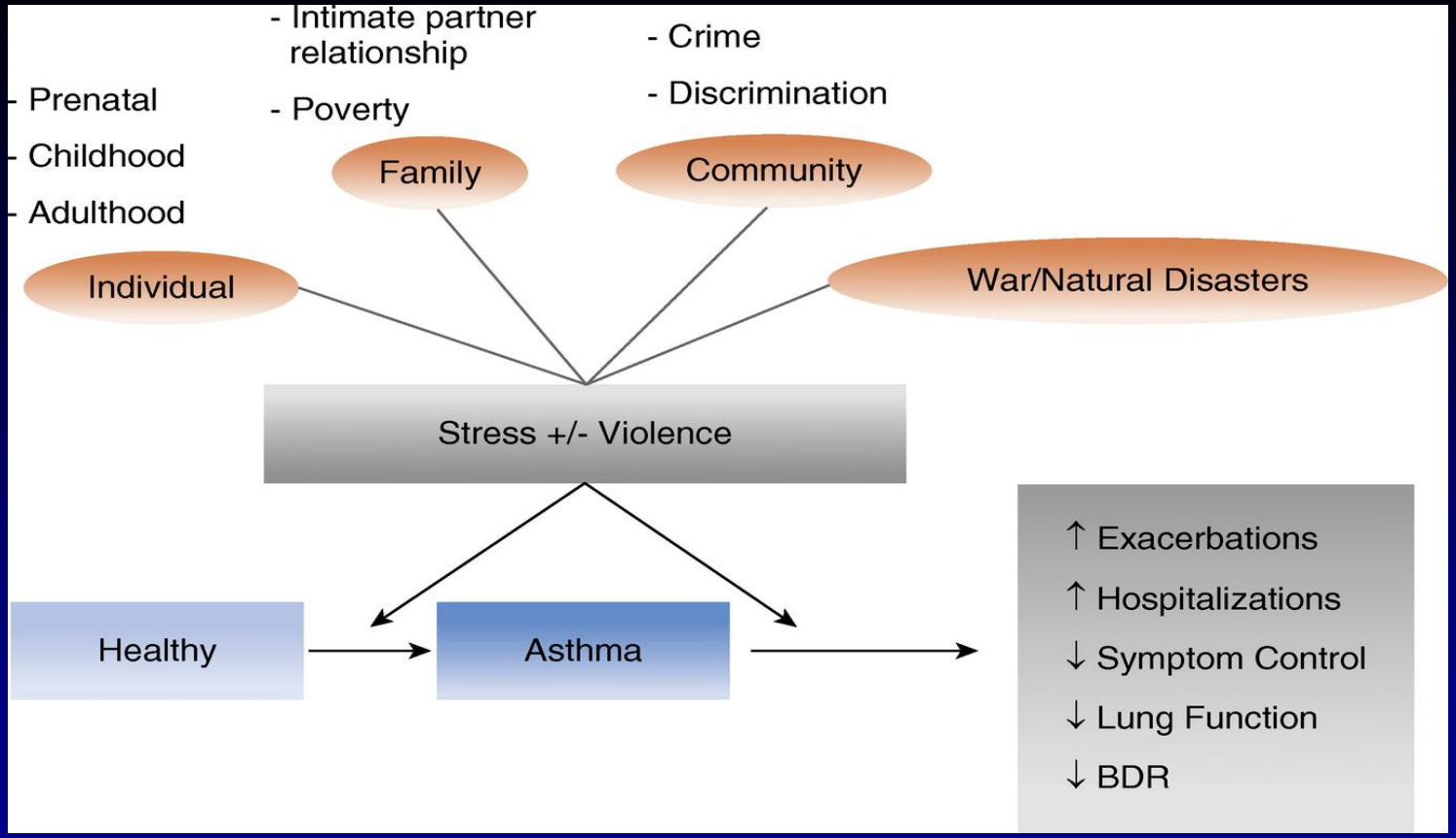
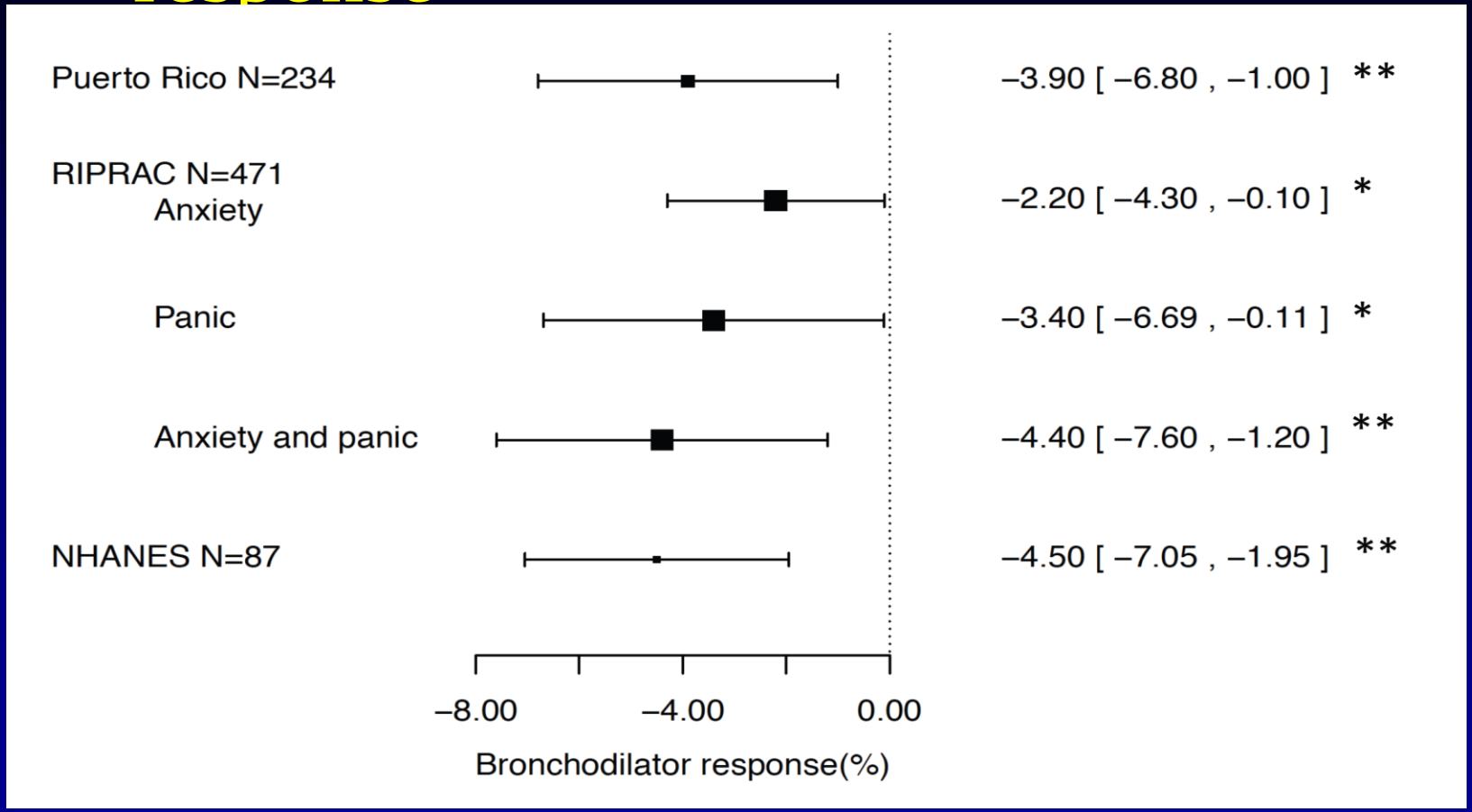


Figure 1. Exposure to violence, chronic stress, and asthma. Landeo-Gutierrez J, Forno E, Miller G, Celedón JC. *Am J Respir Crit Care Med* 2020; 201(8):917-922.

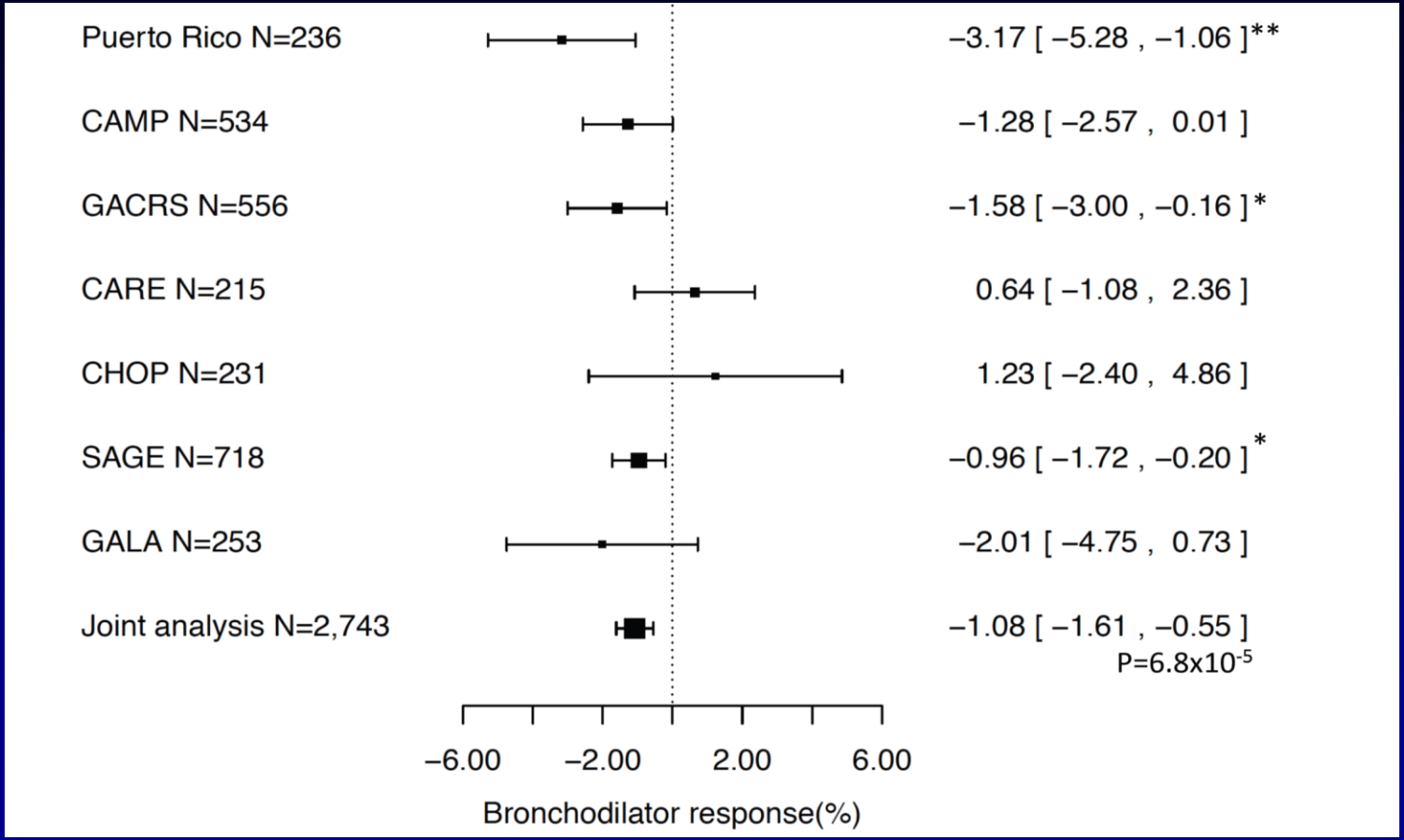
Violence-related distress and bronchodilator response

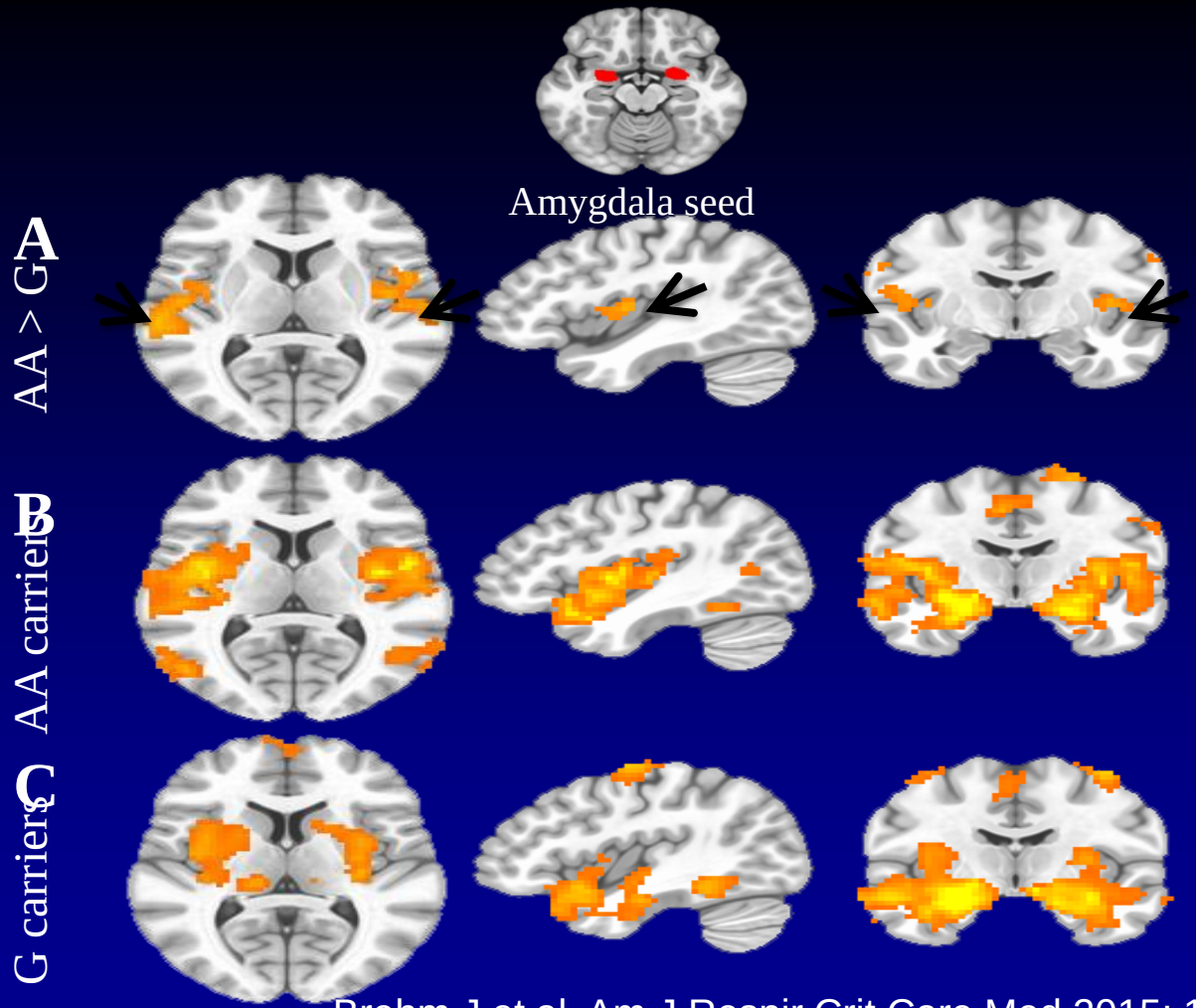
- Puerto Ricans have lower response to short-acting bronchodilators (BDR) than members of other ethnic groups
  - This has been partly attributed to ethnic-specific variation in the frequency of SNPs in *ADRB2*
- Chronic stress (alone or accompanied by acute stress) has been associated with reduced expression of *ADRB2* in leukocytes of subjects with asthma
  - Miller GE, Chen E. *Proc Natl Acad Sci U S A* 2006;103:5496-5501.
- We hypothesized that violence-related distress and chronic stress causes reduced BDR in Puerto Ricans and others

Stress and bronchodilator response



ADCYAP1R1 and BDR



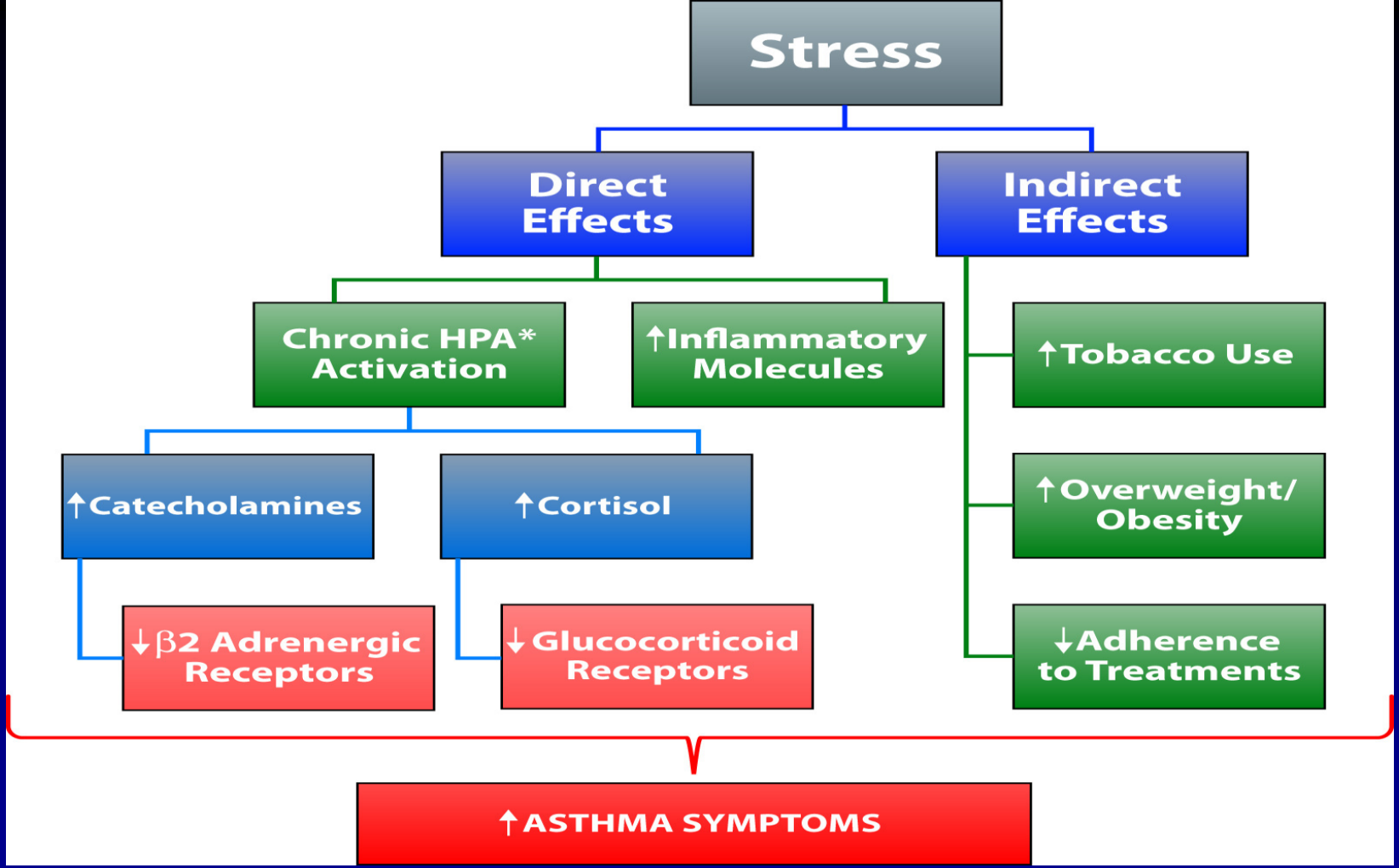


Brehm J et al. Am J Respir Crit Care Med 2015; 192:47-56.

ADCYAP1R1 and BDR

- Both stress and an *ADCYAP1R1* SNP are associated with reduced BDR in children with or at risk for asthma
  - This SNP is also associated with reduced expression of *ADRB2* in CD4+ T lymphocytes of subjects with asthma
- Our findings are consistent with a negative effect of SNP rs34548976 on BDR through neuro-hormonal mechanisms (e.g persistently high catecholamine levels) leading to down-regulation of *ADRB2* in highly stressed children
- Our results provide potential mechanisms for stress-induced morbidity in other cardiopulmonary diseases

Brehm J et al. Am J Respir Crit Care Med 2015; 192(1):47-56.



Landeo-Gutierrez J, Celedón JC. Annals Asthma Allergy Immunol 2020; 125 (4): 393-8.

ETV, depression, and asthma in Puerto Rican adults

- In 3,049 Puerto Rican adults ages 18 to 64 years: who lived in Puerto Rico:
  - Lifetime exposure to violence and suicidal ideations were significantly associated with increased odds of asthma, even after accounting for obesity, smoking status, and other confounders
  - Similar results were found for ETV, suicidal ideations, and asthma-COPD overlap, a more severe condition

Han Y et al. J Asthma 2019; 56: 663-661.

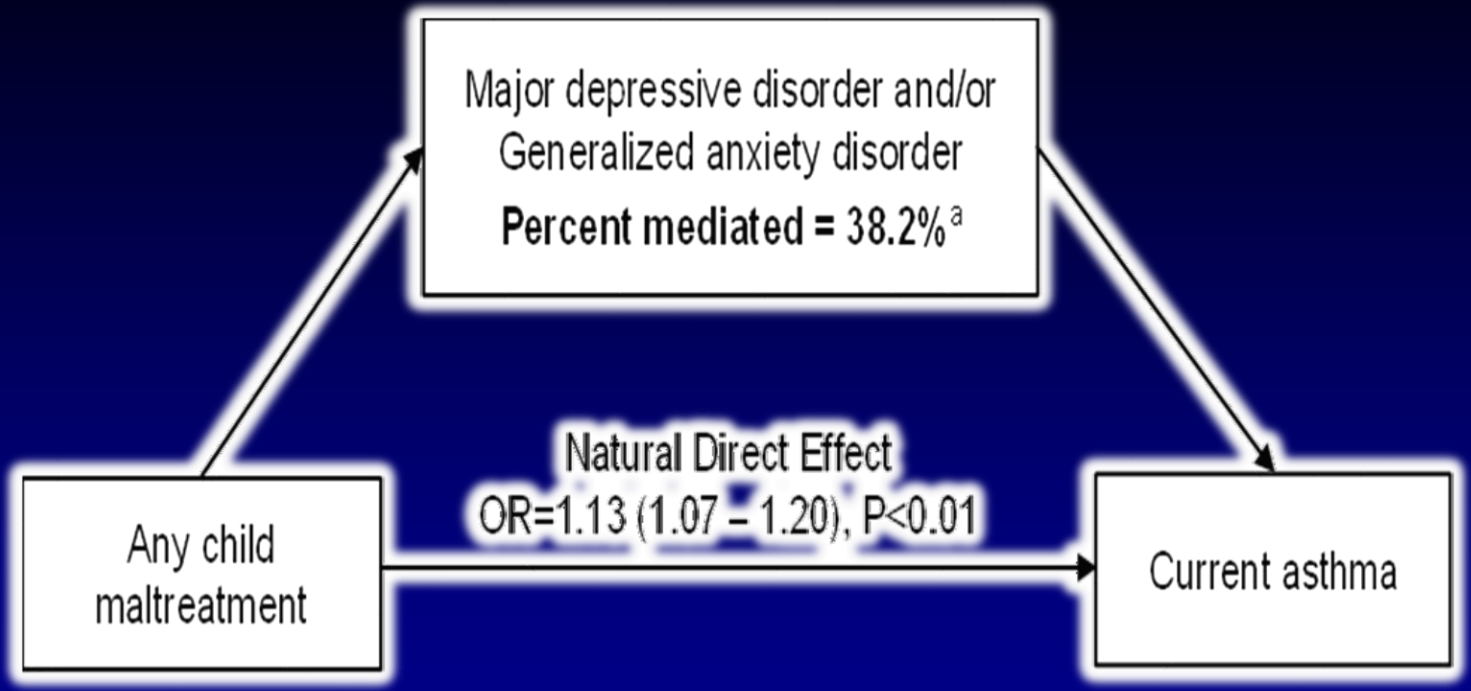
Child Maltreatment + Asthma in Adults

- Child maltreatment has been linked to major depressive disorder (MDD) and generalized anxiety disorder (GAD) among adults in PR and elsewhere
- MDD and GAD have been associated with asthma in adults in large prospective studies (e.g., CARDIA)
- We examined whether an association between child maltreatment and current asthma is mediated by MDD or GAD in a study of ~121,000 British adults 40 years and older in the UK Biobank

Child maltreatment and current asthma in the UK Biobank

Variable	Odds Ratio, 95% confidence interval, P value
Any child maltreatment	1.22 (1.15 to 1.28), <0.01
# of child maltreatment types	
None	1.0 (reference)
One	1.07 (1.01 to 1.15), <0.05
Two	1.30 (1.19 to 1.43), <0.01
Three or more	1.73 (1.56 to 1.92), <0.01

Models adjusted for age, sex, race, educational attainment, income, body mass index, smoking status, pack-years of smoking, and serum CRP level.

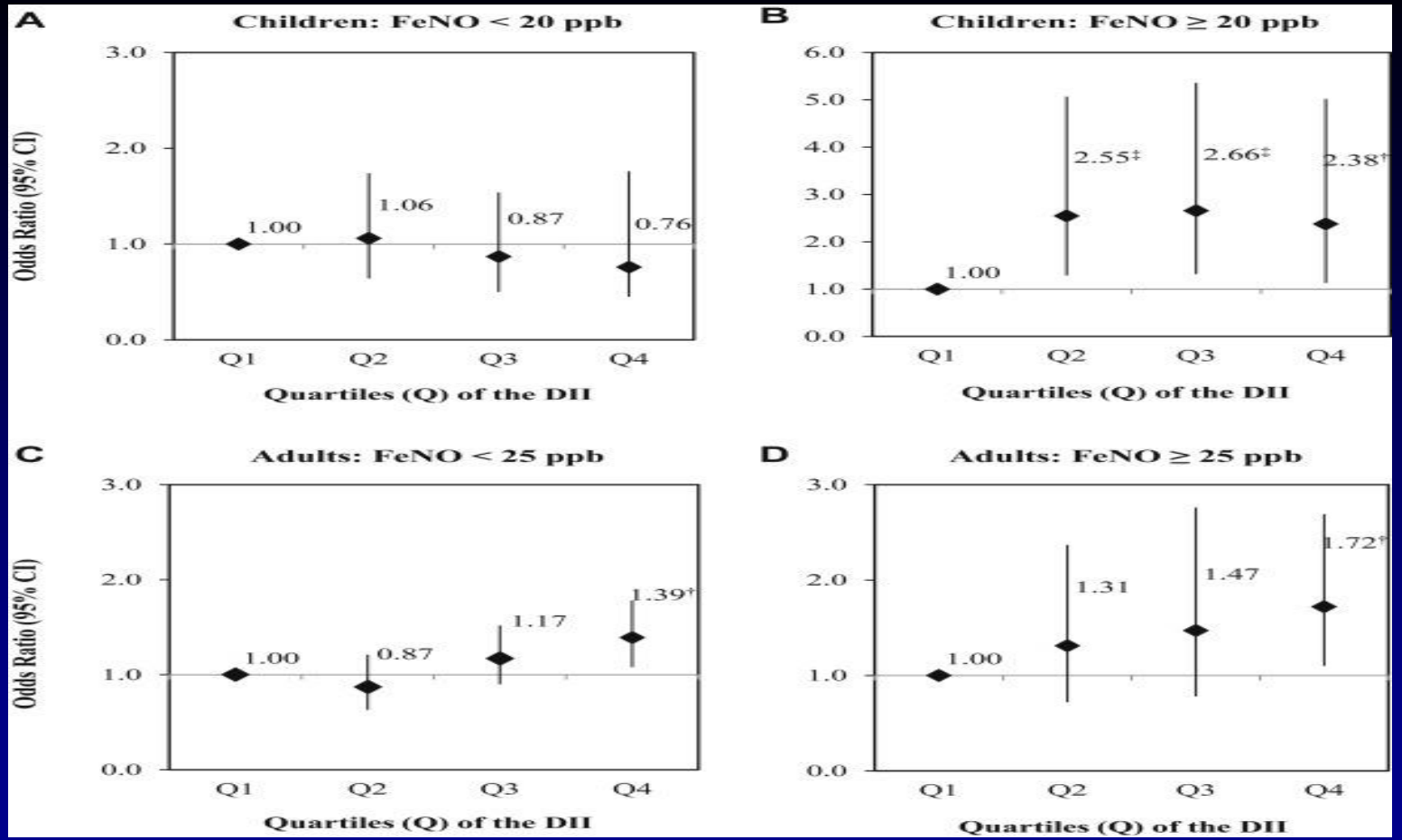


All models adjusted for age, sex, race, education, household income, body mass index, smoking status, pack-years of smoking, and serum CRP level

Child Maltreatment and Asthma in Adults

- Our findings suggest that major depressive disorder (MDD) and generalized anxiety disorder (GAD) mediate some of the estimated effects of child maltreatment on asthma in adults, independently of cigarette smoking
- Clinicians should be aware of concurrent MDD and GAD in adults with asthma, particularly in those who experienced child maltreatment
  - Han YY et al. Eur Respir J 2022 Mar 17 [Epub ahead of print].

4. Diet



Han Y, et al. J Allergy Clin Immunol Pract. 2018 May-Jun;6(3):834-841.

Multivariable analysis of the E-DII or the AHEI-2010 and current asthma and current asthma symptoms among adults in HCHS/SOL

Predictors	Current asthma (n=962)	Current asthma symptoms (n=2,085)
	Odds Ratio (95% CI)	
E-DII		
Quartile 1	1.0 (ref.)	1.0 (ref.)
Quartile 2	1.08 (0.76, 1.52)	**1.32 (1.03, 1.69)**
Quartile 3	1.33 (0.97, 1.82)	**1.37 (1.10, 1.71)**
Quartile 4	1.35 (0.97, 1.90)*	**1.42 (1.12, 1.81)***
Hispanic/Latino background		
Cuban	1.0 (ref.)	1.0 (ref.)
Mexican	**0.49 (0.28, 0.86)**	0.74 (0.51, 1.08)
Puerto Rican	**1.72 (1.01, 2.92)**	1.02 (0.74, 1.43)
Others	**0.61 (0.40, 0.92)**	0.90 (0.68, 1.19)
AHEI-2010		
Quartile 1	1.0 (ref.)	1.0 (ref.)
Quartile 2	1.11 (0.84, 1.48)	0.96 (0.75, 1.23)
Quartile 3	0.90 (0.64, 1.28)	0.85 (0.62, 1.16)
Quartile 4	0.94 (0.61, 1.43)	0.88 (0.63, 1.21)
Hispanic/Latino background		
Cuban	1.0 (ref.)	1.0 (ref.)
Mexican	**0.49 (0.27, 0.89)**	0.76 (0.52, 1.11)
Puerto Rican	**1.74 (1.02, 2.94)**	1.02 (0.72, 1.42)
Others	**0.61 (0.40, 0.92)**	0.91 (0.68, 1.21)

Han Y et al. Ann Am Thorac Soc. 2020 Mar;17(3):293-301.

Multivariable analysis of the E-DII or the AHEI-2010 scores and lung function measures among adult participants in HCHS/SOL

Lung function measures	E-DII	AHEI-2010
	β (95% CI)	
All Participants (n=11,817)		
%predicted FEV_1	**-0.75 (-1.07, -0.42)**	**0.76 (0.31, 1.20)**
%predicted FVC	**-0.58 (-0.87, -0.29)**	**0.55 (0.16, 0.94)**
%predicted FEV_1/FVC	-0.18 (-0.42, 0.06)	0.23 (-0.05, 0.51)
Participants without asthma (n=10,948)		
%predicted FEV_1	**-0.71 (-1.02, -0.41)**	**0.77 (0.40, 1.14)**
%predicted FVC	**-0.58 (-0.88, -0.29)**	**0.55 (0.17, 0.92)**
%predicted FEV_1/FVC	-0.11 (-0.30, 0.08)	0.21 (-0.01, 0.43)
Participants with asthma (n=869)		
%predicted FEV_1	-0.80 (-2.73, 1.14)	-0.24 (-2.52, 2.05)
%predicted FVC	-0.12 (-1.52, 1.29)	-0.43 (-2.00, 1.15)
%predicted FEV_1/FVC	-1.05 (-2.53, 0.44)	0.56 (-1.26, 2.37)

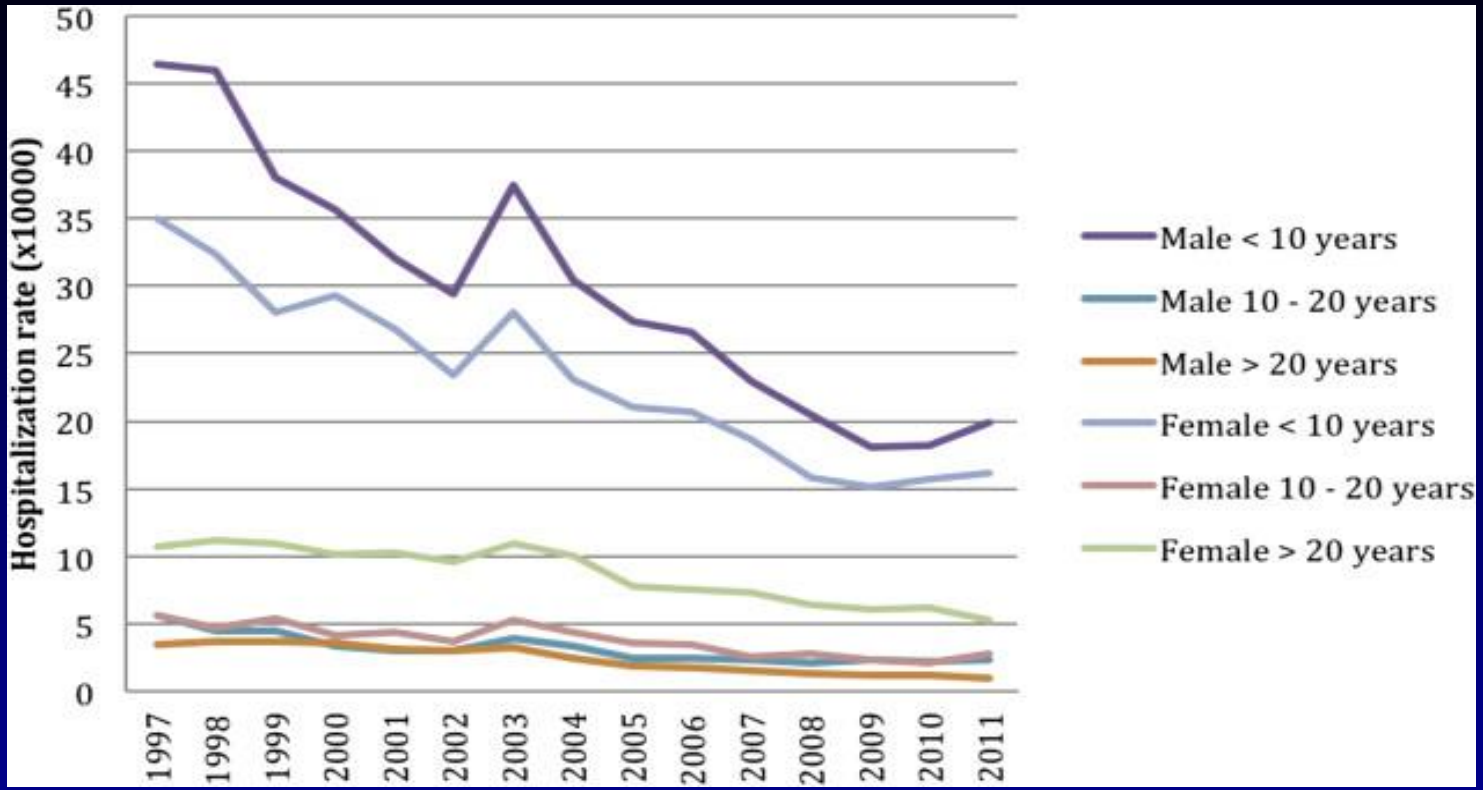
Han Y et al. Ann Am Thorac Soc. 2020 Mar;17(3):293-301.

Diet and asthma

- Current evidence suggests that dietary patterns (i.e. a “Mediterranean diet”) are more important than individual nutrients or vitamins
  - High consumption of fruits and vegetables
  - Low consumption of saturated and trans fats, coupled with consumption of unsaturated fats (e.g., olive oil)
- A healthy diet and exercise are needed to prevent and manage obesity, a major risk factor for asthma and worse asthma outcomes

5.

Improving Asthma Care



Soto-Martinez M et al. J Allergy Clin Immunol Pract 2014; 2(1):85-90.

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Treatment	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years				
	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6■
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA▲	Daily and PRN combination low-dose ICS-formoterol▲	Daily and PRN combination medium-dose ICS-formoterol▲	Daily medium-high dose ICS-LABA + LAMA and PRN SABA▲	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium-dose ICS and PRN SABA or Daily low-dose ICS-LABA; or daily low-dose ICS + LAMA,▲ or daily low-dose ICS + LTRA,* and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium-dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA▲ or Daily medium-dose ICS + LTRA,* or daily medium-dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2–4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Assess Control

- First check adherence, inhaler technique, environmental factors,▲ and comorbid conditions.
- **Step up** if needed; reassess in 2–6 weeks
- **Step down** if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta$_2$-agonist; LAMA, long-acting muscarinic antagonist; LTRA, leukotriene receptor antagonist; SABA, inhaled short-acting beta$_2$-agonist

▲ Updated based on the 2020 guidelines.

* Cromolyn, Nedocromil, LTRAs including Zileuton and montelukast, and Theophylline were not considered for this update, and/or have limited availability for use in the United States, and/or have an increased risk of adverse consequences and need for monitoring that make their use less desirable. The FDA issued a Boxed Warning for montelukast in March 2020.

** The AHRQ systematic reviews that informed this report did not include studies that examined the role of asthma biologics (e.g. anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13). Thus, this report does not contain specific recommendations for the use of biologics in asthma in Steps 5 and 6.

■ Data on the use of LAMA therapy in individuals with severe persistent asthma (Step 6) were not included in the AHRQ systematic review and thus no recommendation is made.

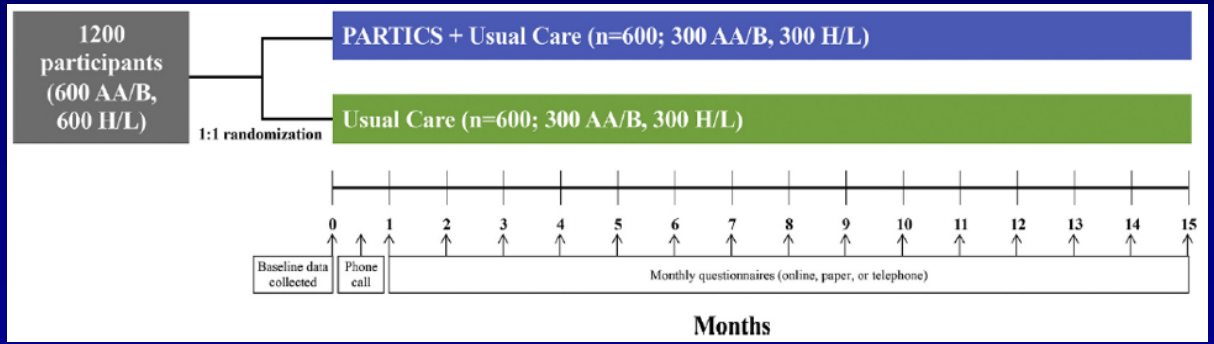
December 2020

PCORI-PREPARE study

- PeRson EmPowered Asthma RElief (PREPARE)
- Randomized, open-label, pragmatic clinical trial
- 1,201 Black and Latinx adults with moderate to severe persistent asthma.
- Intervention:

PARTICS (**P**atient-**A**ctivated, **R**eliever-**T**riggered **I**nhaled **C**ortico**S**teroids)
1 puff QVAR: 1 puff rescue inhaler
and 5 puffs QVAR:
1 rescue nebulization

University of Illinois Chicago, Chicago, IL
University of South Florida, Tampa, FL



PARTICS trial results

- 1,201 adult participants (603 NH Black and 598 Hispanic)
- Instructions at baseline visit + 15 months of follow up
- The annualized rate of severe asthma exacerbations was 0.69 (95% CI, 0.61 to 0.78) in the intervention group and 0.82 (95% CI, 0.73 to 0.92) in the usual-care group (hazard ratio, 0.85; 95% CI, 0.72 to 0.99; P<0.05). ACT scores increased by 3.4 points (95% CI, 3.1-3.6) in the intervention group and by 2.5 points (95% CI, 2.3 to 2.8) in the usual-care group (difference, 0.9; 95% CI, 0.5 to 1.2)

Israel E et al. N Eng J Med 2022; 386:1505-1518

•. 2017 Sep 7;377(10):965-976.

Severe asthma

- Asthma requiring treatment with high dose ICS + a second controller and/or systemic corticosteroids to prevent it from becoming “uncontrolled” or that remains “uncontrolled” despite this therapy (3%-10% of adults with asthma.
  - Must be differentiated from difficult to treat asthma by excluding or treating:
    - Alternative diagnoses (e.g., vocal cord dysfunction, upper airway obstruction, CHF, COPD)
    - Poor adherence with treatment (*very common*)
    - Co-morbidities (e.g., GERD, obesity) and triggers (allergens, smoking, and stressors)

- Severe asthma is a heterogenous syndrome comprising several phenotypes and endotypes (e.g., T2-high vs. T2-low asthma)

  Israel E, Reddel HK. N Eng J Med 2017; 377(10):965-976.

-

Table 1. Biologic Agents Approved by the Food and Drug Administration for the Treatment of Severe Asthma.*

Biologic Agent (Therapeutic Target and Mechanism of Action)	Route of Administration and Dose†	Forms	Indication	Patient Yr of Age†	Efficacy	Safety Concerns
Benralizumab (interleukin-5Rα; antibody binds to interleukin-5Rα on eosinophils and basophils, depleting them through antibody-dependent, cell-mediated cytotoxicity)	SC; 30 mg every 4 wk (first 3 doses), followed by 30 mg every 8 wk	Prefilled syringe, autoinjector pen	Severe eosinophilic asthma	≥12	Reduced exacerbations, reduced symptoms, small or moderate effect on FEV_1; decrease or withdrawal of OGs if blood eosinophils >150/μl; improved quality of life	Helminthic infections, hypersensitivity reactions, abrupt discontinuation of OGs
Dupilumab (interleukin-4Rα; antibody binds to interleukin-4Rα, inhibiting interleukin-4 and interleukin-13 signaling in hematopoietic cells [e.g., B cells, CD4+ helper T cells, and eosinophils], epithelial cells, and airway smooth-muscle cells)	Adults and adolescents: SC; initial dose of 400 mg, followed by 200 mg every 2 wk; for glucocorticoid-dependent patients or patients with concomitant moderate-to-severe atopic dermatitis, initial dose of 600 mg, followed by 300 mg every 2 wk Children, ages 6–11 yr: SC; dose depends on body weight‡	Prefilled syringe, autoinjector pen	Severe eosinophilic asthma (FDA), severe type 2 asthma (EMA), OG-dependent asthma; other indications: CRS with nasal polyposis, moderate-to-severe atopic dermatitis	≥6	Reduced exacerbations, reduced symptoms, improved lung function; decrease or withdrawal of OGs, irrespective of blood eosinophil count at baseline; improved quality of life	Helminthic infections, hypersensitivity reactions, abrupt discontinuation of OGs, hypereosinophilic conditions (e.g., EGPA), conjunctivitis
Mepolizumab (interleukin-5; antibody binds to circulating interleukin-5)	Adults and adolescents: SC; 100 mg every 4 wk Children, ages 6–11 yr: SC; 40 mg every 4 wk	Prefilled syringe, autoinjector pen	Severe eosinophilic asthma; other indications: EGPA, hypereosinophilic syndrome	≥6	Reduced exacerbations, reduced symptoms, small or moderate effect on FEV_1; reduction or withdrawal of OGs if blood eosinophils >150/μl; improved quality of life	Helminthic infections, hypersensitivity reactions, abrupt discontinuation of OGs, herpes zoster infections (rare)
Omalizumab (IgE; antibody binds to Fc part of free IgE, inhibiting binding of IgE to FcεRI on mast cells and basophils and FcεRII on dendritic cells and eosinophils)	SC; 75 to 375 mg every 2 to 4 wk according to body weight and pretreatment level of serum total IgE	Prefilled syringe	Severe allergic asthma; other indication: chronic idiopathic urticaria	≥6	Reduced exacerbations, reduced symptoms, small effect on FEV_1; improved quality of life	Serum sickness, hypereosinophilic conditions (e.g., EGPA), abrupt discontinuation of OGs; black-box warning for anaphylaxis (occurring in ±0.2% of patients)
Reslizumab (interleukin-5; antibody binds to circulating interleukin-5)	IV; 3 mg/kg every 4 wk	IV infusion	Severe eosinophilic asthma	≥18	Reduced exacerbations, reduced symptoms, small or moderate effect on FEV_1; improved quality of life	Helminthic infections, abrupt discontinuation of OGs; black-box warning for anaphylaxis (occurring in ±0.3% of patients)
Tezepelumab (TSLP)	SC; 210 mg every 4 wk	Prefilled syringe	Severe asthma	≥12	Reduced exacerbations, reduced symptoms, improved lung function; improved quality of life	Pharyngitis, arthralgia, back pain

* CRS denotes chronic rhinosinusitis, EGPA eosinophilic granulomatosis with polyangiitis, EMA European Medicines Agency, FcεRI high-affinity receptor for the Fc region of IgE, FcεRII low-affinity receptor for the Fc region of IgE, FDA Food and Drug Administration, FEV_1 forced expiratory volume in 1 second, interleukin-4Rα interleukin-4 receptor α, interleukin-5Rα interleukin-5 receptor α, IV intravenous, OGs oral glucocorticoids, SC subcutaneous, and TSLP thymic stromal lymphopoietin.
† Information on dose and age is for patients with severe asthma as the main indication.
‡ For pediatric patients, ages 6 to 11 yr, with a body weight of 15 kg to less than 30 kg, the recommended dose of dupilumab is 100 mg every 2 wk or 300 mg every 4 wk; for children with a body weight of 30 kg or more, the dose is 200 mg every 2 wk.

Bruselle G and Koppelman G. N Eng J Med 2022; 386:157-171

6. Root Causes of Disparities

Key Environmental Risk Factors for Health Disparities in Asthma in the U.S.

Risk Factor	Impact
Tobacco smoke	**SHS in utero causes asthma in children. Smoking worsens asthma in all.**
Air pollution	**Causes asthma in children and worsens asthma in children and adults**
Occupational hazards	**Cause and worsen asthma in adults.**
Infectious agents	**Viruses are the main cause of severe asthma exacerbations across lifespan.**
Obesity	**May cause asthma and does worsen asthma in children and adults.**

Modified from Celedón JC et al. Annals Am Thorac Soc 2014; 11:473-479.

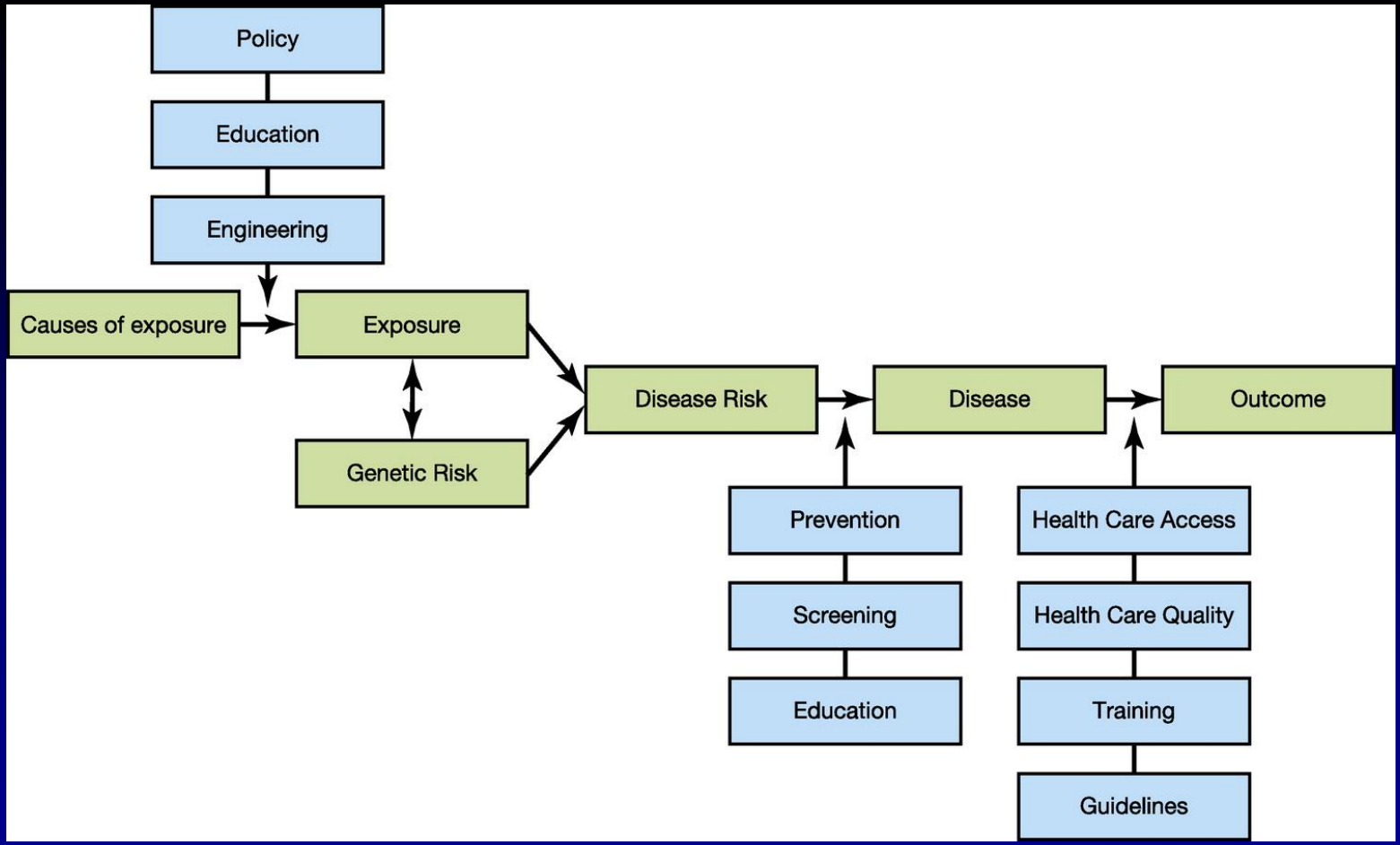
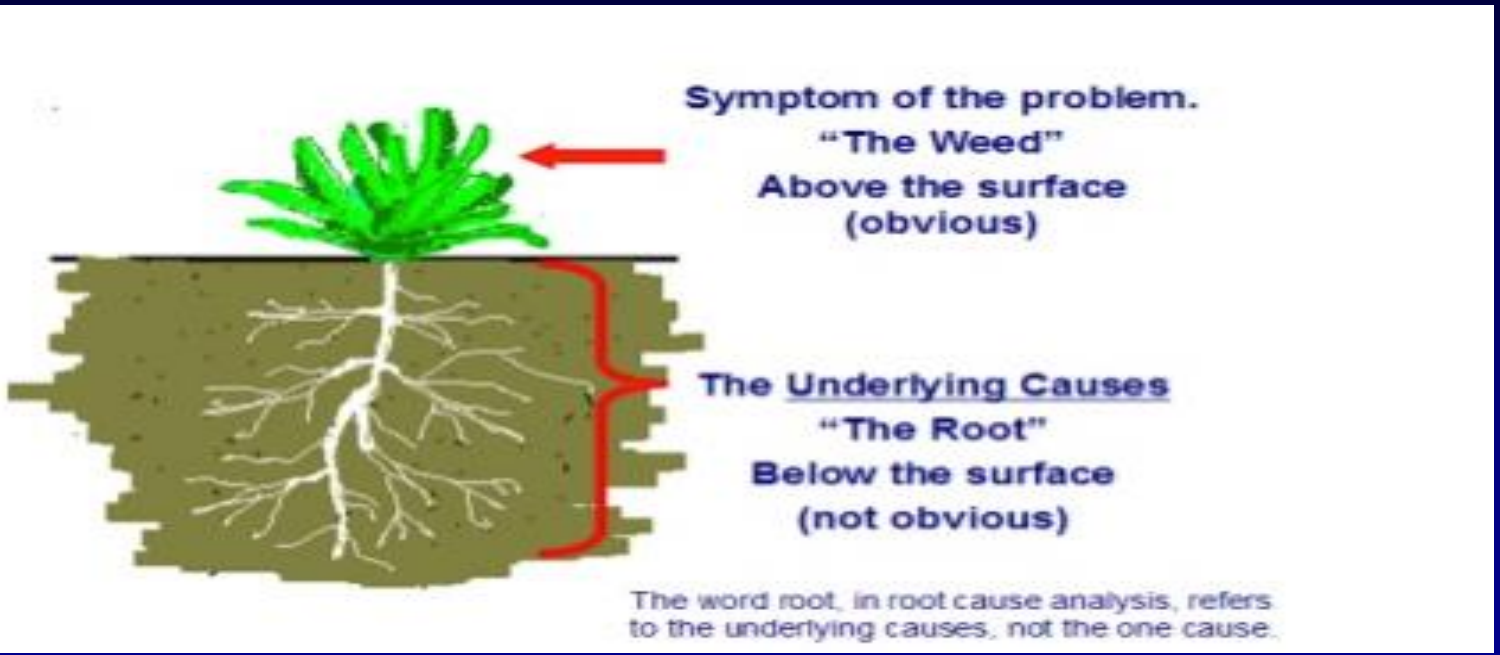
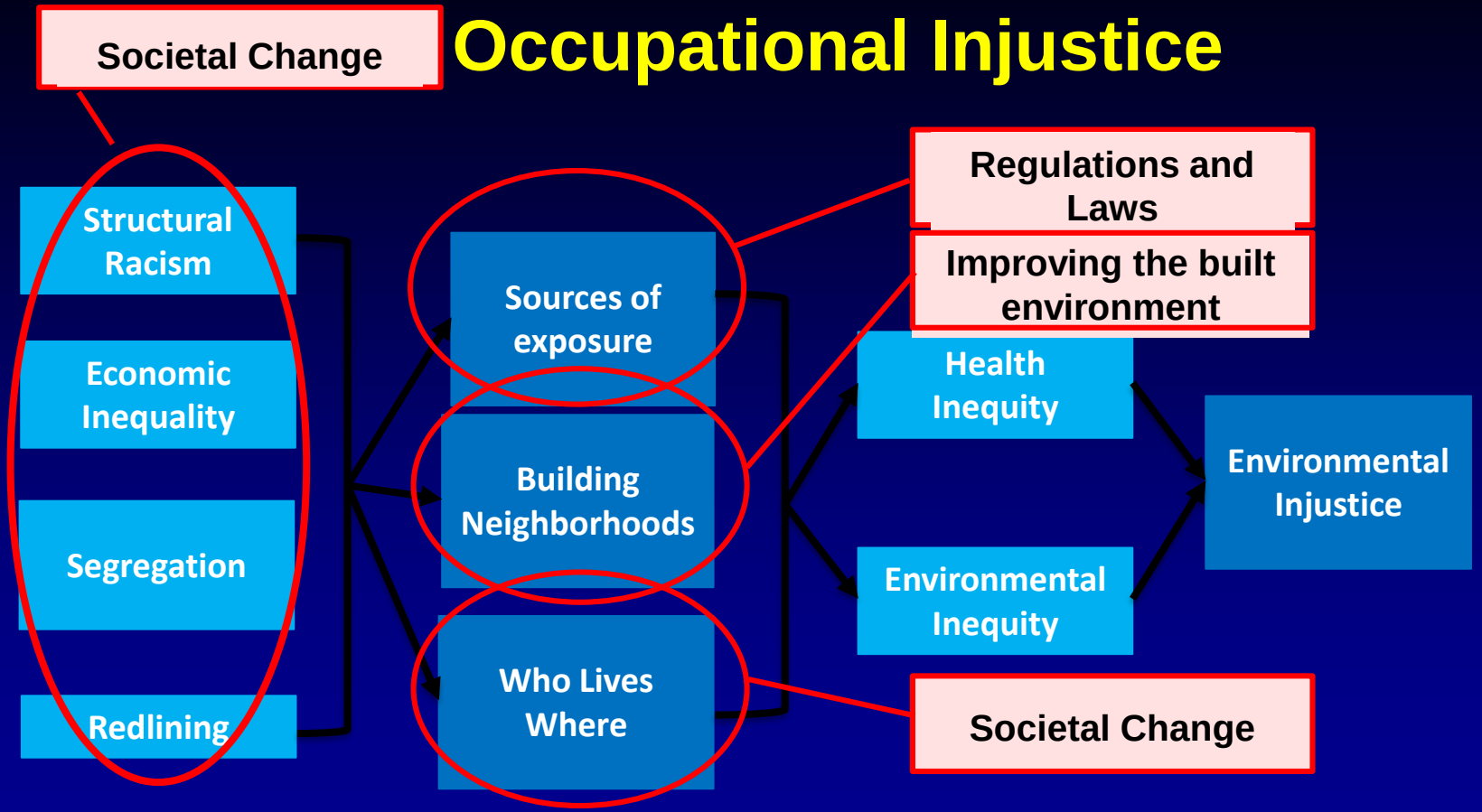


Figure 1. Conceptual framework for disease causation. Group differences at any stage in this pathway can result in respiratory health disparities. Adapted by permission from: Juan C. Celedón; Jesse Roman; Dean E. Schraufnagel; Alvin Thomas; Jonathan Samet; *Annals ATS* 11, 473-479.
DOI: 10.1513/AnnalsATS.201402-059PS

Adress the root causes



Dismantling Environmental + Occupational Injustice



The Affordable Care Act 2010: towards universal health care through Medicaid Expansion

- Expansion of Medicaid for adults up to 138% of the FPL
- From 2010 to 2016
  - 20 million people gained health insurance via ACA
  - Uninsured rate fell from ~17.8% to 10%

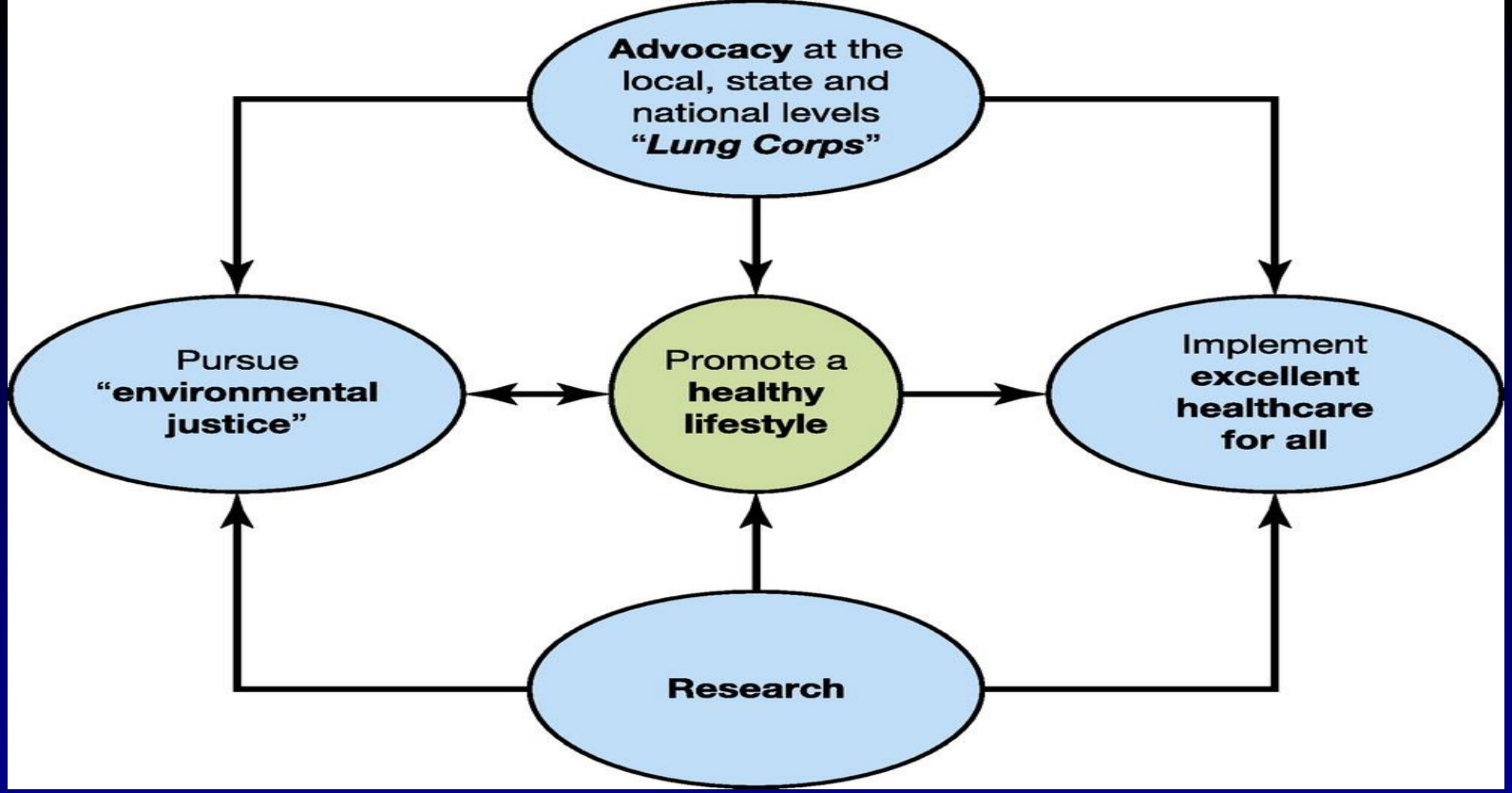


Figure 2. Overview of the approach of the ATS to help eliminate respiratory health disparities

Published in: Juan C. Celedón; Jesse Roman; Dean E. Schraufnagel; Alvin Thomas; Jonathan Samet; *Annals ATS* 11, 473-479.

7. Summary

Conclusions

- Asthma is a major public health problem in Hispanic adults with marked variability in disease burden across Hispanic subgroups

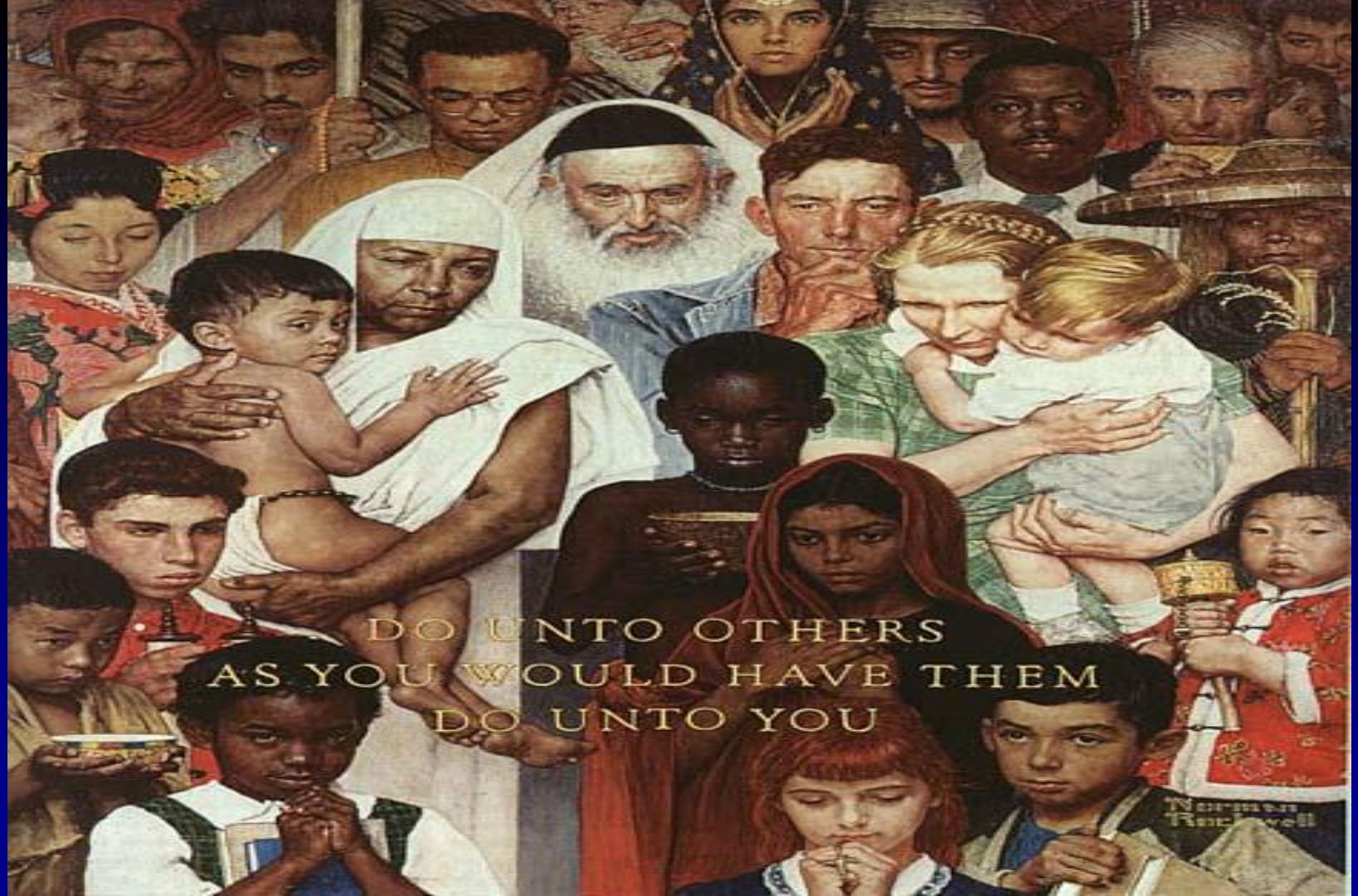
- The “Hispanic paradox” is likely multifactorial and due to differences in ancestry-correlated environmental and behavioral factors, including tobacco use, diet, and psychosocial stress.

Conclusions

- Asthma management includes addressing environmental triggers (e.g., tobacco use) and lifestyle (e.g., diet, exercise) and co-morbidities such as obesity
- Barriers to care must be addressed when implementing current asthma guidelines in Hispanic populations
- Health disparities are best addressed using a multipronged approach involving all key stakeholder

Collaborators

- *University of Pittsburgh:* J. Brehm, Y. Han, W. Chen, E. Forno, Q. Yan
- *Carnegie Mellon U. (Pittsburgh, PA):* B. Klei, K. Roeder
- *University of Puerto Rico (San Juan, PR):* E. Acosta, G. Canino
- *Harvard University (Boston, MA):* B. Raby, E. Israel
- *Brown University (Providence, RI):* Elizabeth McQuaid
- *Emory University (Atlanta, GA):* Kerry Ressler
- *U. of California at San Francisco (San Francisco, CA):* E. Burchard
- *University of Pennsylvania (Philadelphia, PA):* H. Hakonarson
- *U. of South Florida (Tampa, FL):* J.C. Cardet
- *U. of Groningen (The Netherlands):* G. Koppelman
- *Albert Einstein College of Medicine (Bronx, NY):* R. Kaplan


DO UNTO OTHERS
AS YOU WOULD HAVE THEM
DO UNTO YOU

Audience Q & A

AMGEN

NHMA
National Hispanic Medical Association

NHMA Upcoming Events

- **COVID-19 Virtual Briefing Series Session 18: Long COVID and the Future of Vaccines**
  - Wednesday, October 26th, 2022 – 7:00 – 8:15 PM ET
  - Register: https://bit.ly/NHMACOVIDBriefing
- **NHMA 26th Annual Conference:** Chicago, IL – April 27 – April 30th, 2023: Hyatt Regency Chicago
- **NHMA VaccinateForAll Campaign**
  - New websites launched – HispanicHealth.info & Vaccinateforall.org
  - Register for FREE to join over 200+ individuals and organizations the champions today!

If you have any questions about our programs or events, please email vgearity@nhmamd.org or jhernandez@nhmamd.org

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