Asthma in Schools and Social Determinants of Health

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March 23, 2022 3:05-3:40

Severe Asthma Update

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HARVARD MEDICAL SCHOOL

Disclosures

- ABAI Board of Directors, Secretary, and CAP-Co-Chair and MOC Co-Chair
- AAAAI Board of Directors
- Consulting GSK, Genentech, Novartis, Sanofi, Regeneron, Teva, Astra Zeneca- asthma therapies
- NIH funding

Objective

1. To understand the relevance of school exposures in asthma as a Source of Disparities and Social Determinants of Health
2. To identify interventions targeting the environment and supporting policies and change in support of schools
3. To take what we learned in schools to personalized strategies for difficult to control asthma

Case

- 7-year old Puerto Rican boy with severe persistent asthma Comes to Clinic 1 week after 3rd ICU admission for status asthmaticus triggered by viral illness.
- Referred to A/I/P specialist but has “no showed” to these two scheduled visits.
- Parents are divorced and mother immigrated 18 months ago
- PE: BMI 35, Boggy nasal turbinates- mouth breather
- Flovent 110mcg 2puffs twice daily – not using a spacer
- Allergen skin testing demonstrates positives to mouse allergen and dust mite
- He attends an urban school and notices his asthma symptoms are more pronounced at school

What are some Social Determinants of Health to consider in this scenario?

- Social determinants of health (SDOH) defined by WHO as "conditions in which people are born, grow up, live, work and age.
- Influence health, risk of illness and life expectancy.
- Social inequities in health–the unfair and avoidable differences in health status across groups in society– due to uneven distribution of social determinants.

Davis et al JACI 2021, https://health.gov/healthypeople/objectives-and-data/social-determinants-health, https://www.cdc.gov/healthyyouth/disparities/index.htm

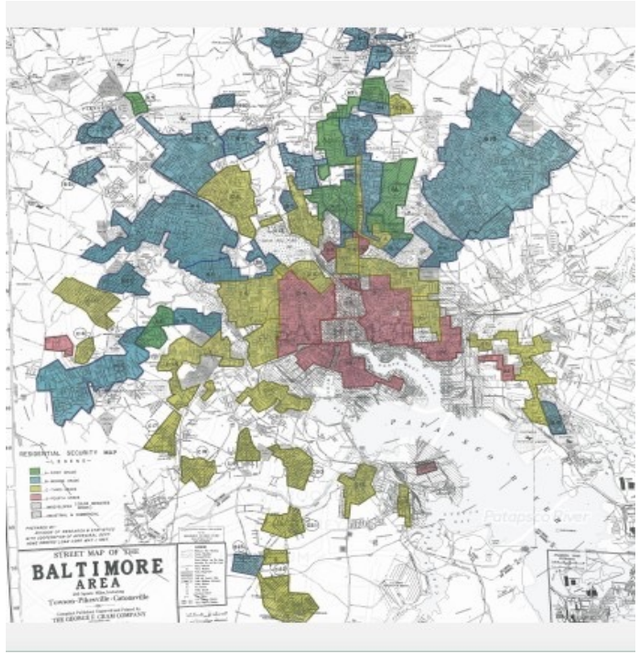
What do we know social determinants of health disparities in urban asthma?

"Best"

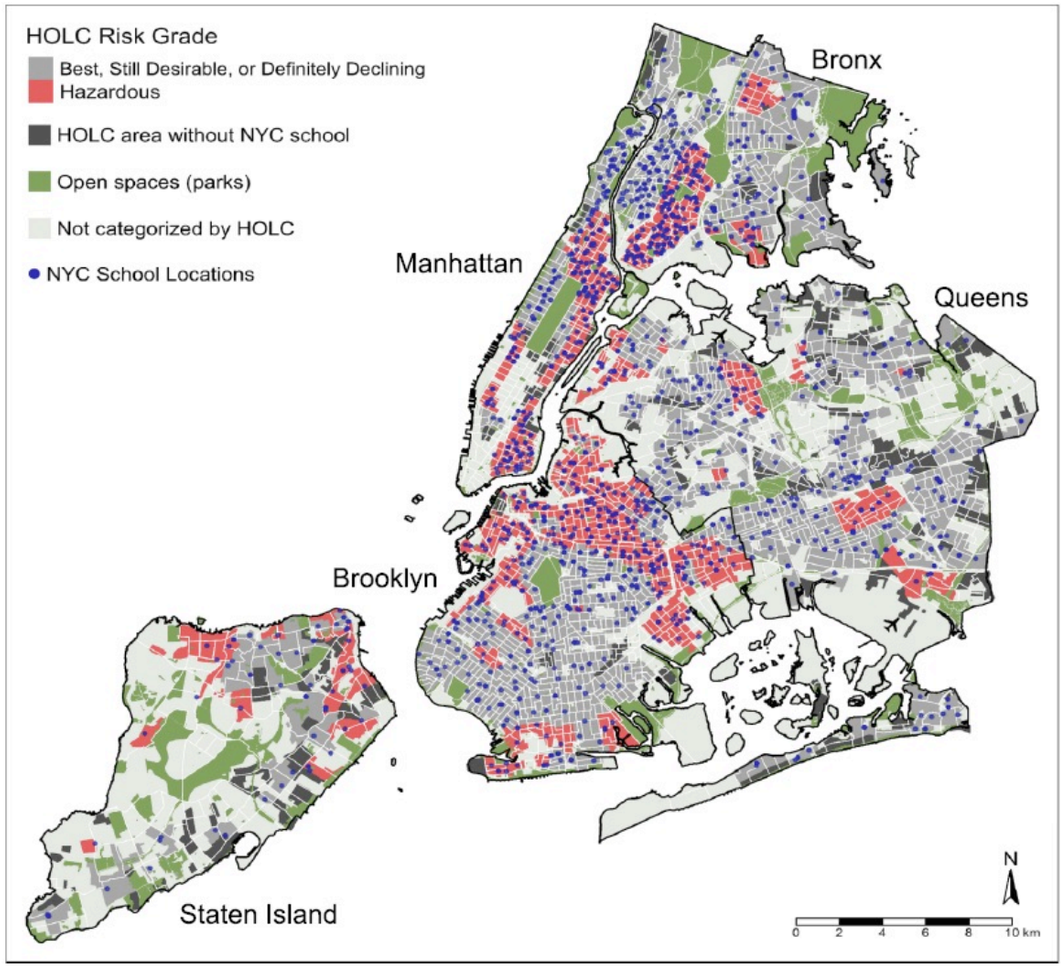
"Still Desirable"

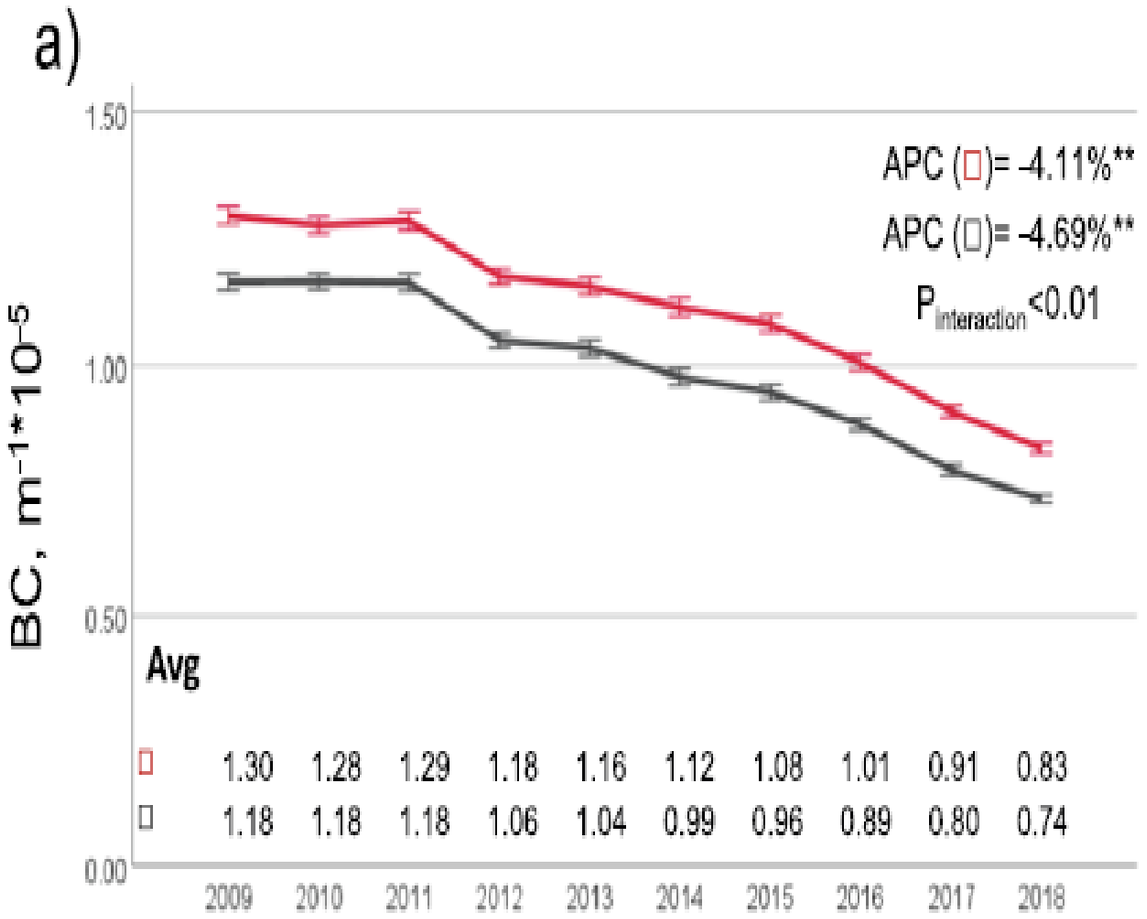
"Definitely Declining"

"Hazardous"



Residential Redlining in NYC Schools and Air Pollution Trends





Wa-Jung K, et al Environmental International 2022

Addressing inequities in asthma by focusing on children's environments

For the past 20 Dr. Wanda Phipatanakul has been asking why asthma hits so hard in urban and lower-income areas. (Image: AdobeStock/Illustration: Sebastian Stankiewicz, Boston Children's Hospital)

https://answers.childrenshospital.org/asthma-inequities/

Economic Policy Institute

BROADER, BOLDER APPROACH TO EDUCATION

Education inequalities at the school starting gate

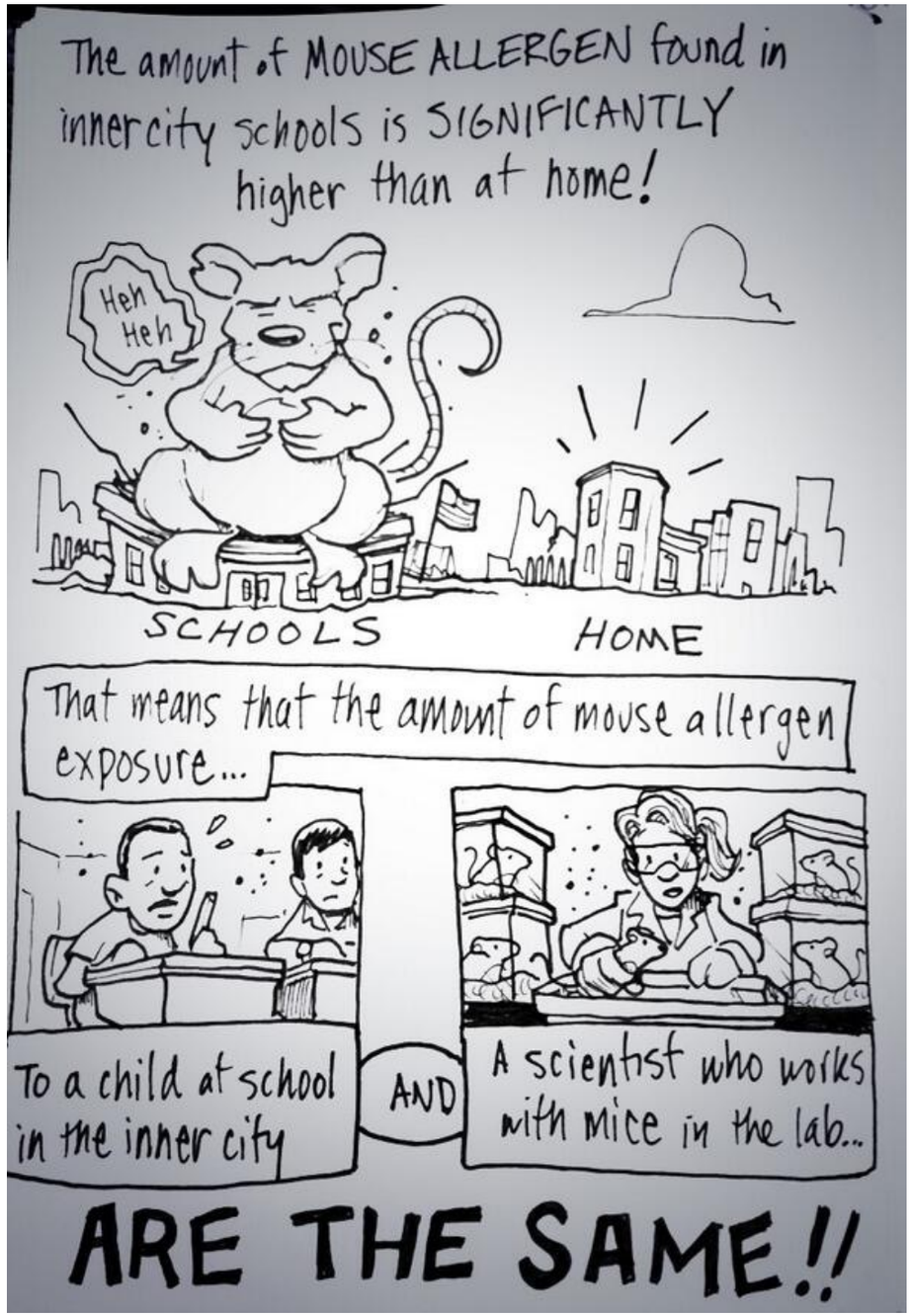
Gaps, trends, and strategies to address them

Report • By Emma García and Elaine Weiss • September 27, 2017

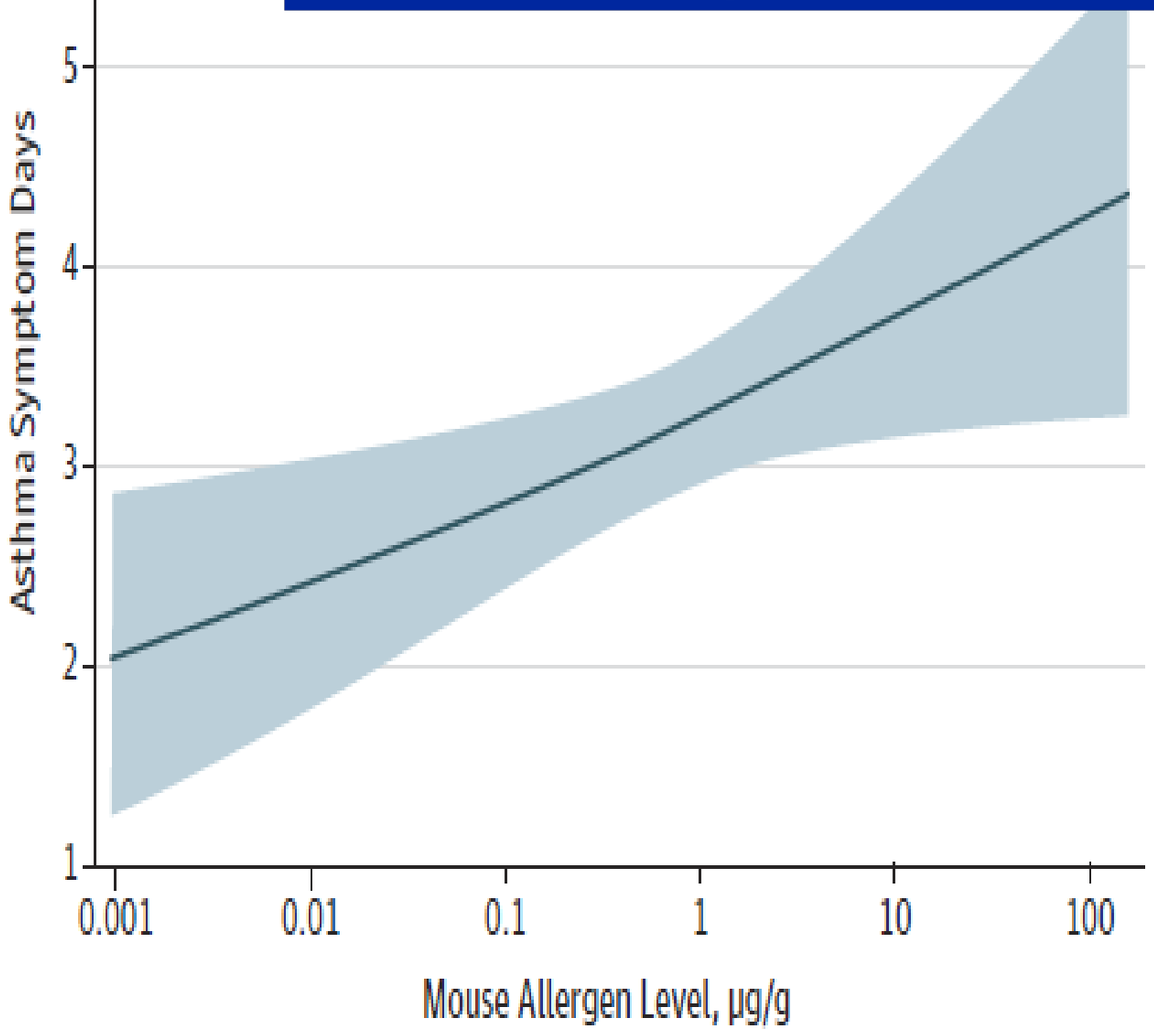
What do we know about exposures in schools?

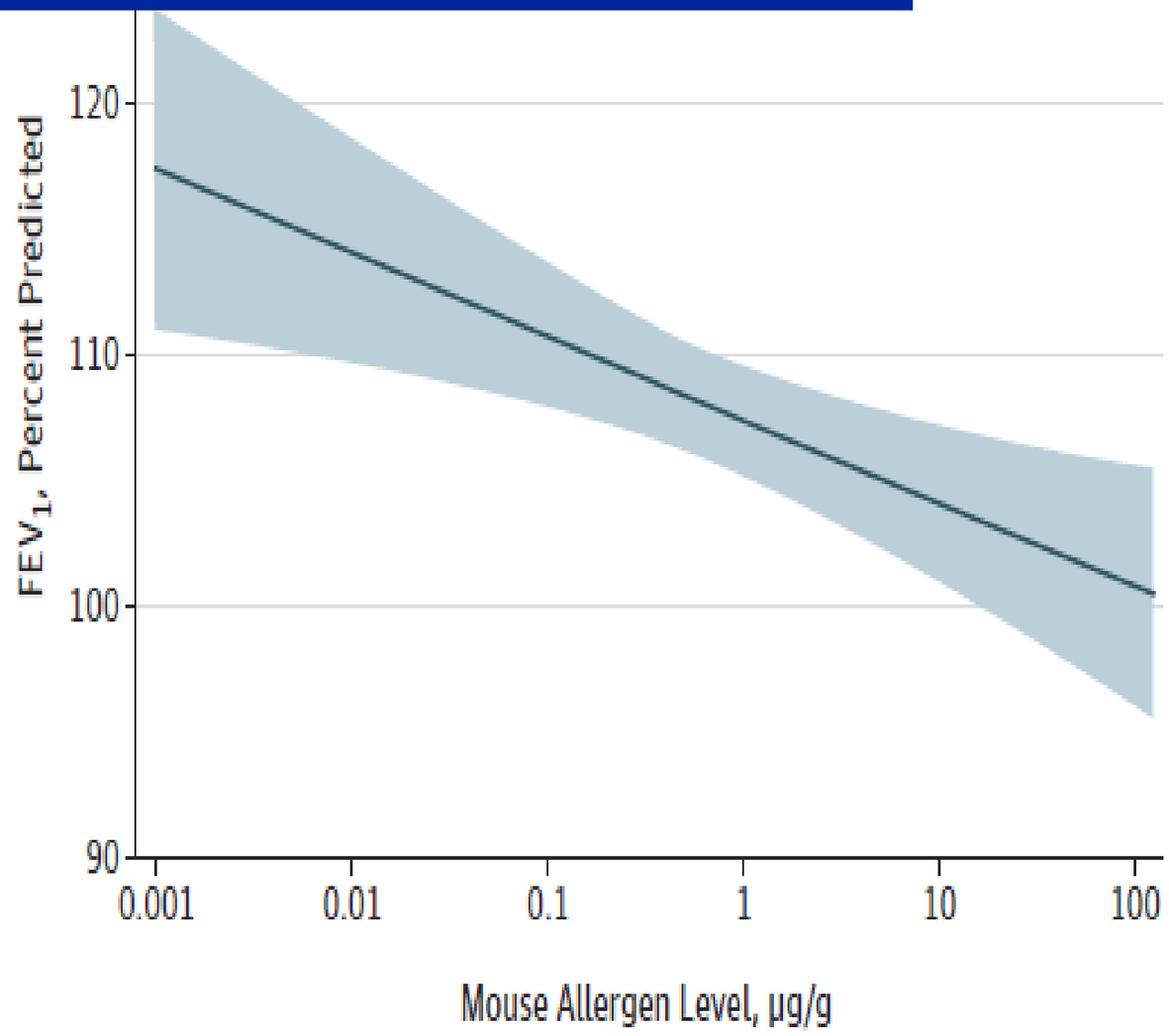
Twitter:
Booster Shot Comics
@BoosterShotCmx

What did Dr. Phipatanakul find in her study on inner city schools? Spoiler: its totally mice #AAAAI #graphicmedicine



Classroom Mouse Allergen Exposure and Asthma Symptoms and Lung Function





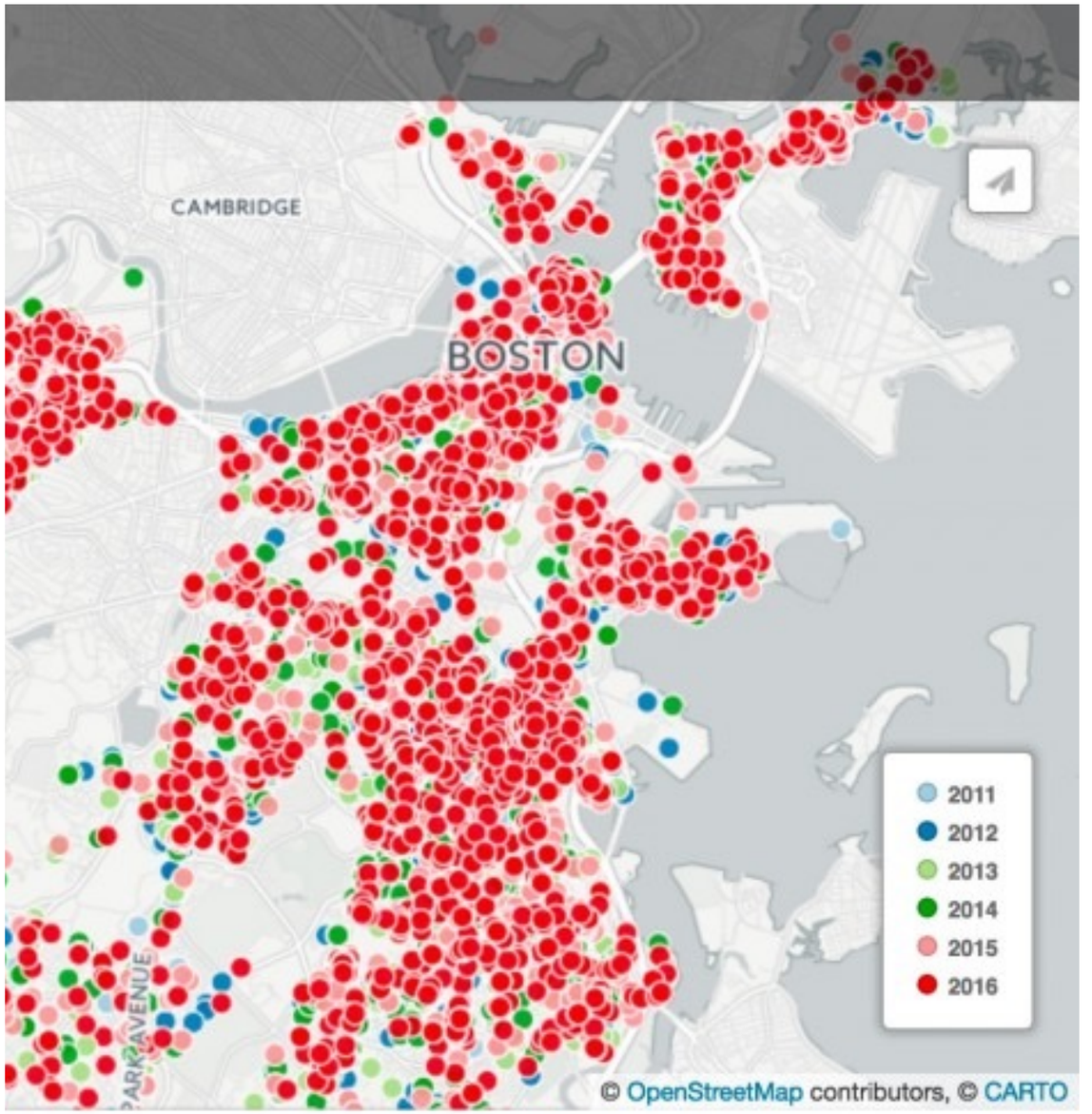
Sheehan WJ, et al JAMA Peds 2017

America Is on the Verge of Ratpocalypse

Warmer weather is fueling a rodent surge, straining public health systems and the economy. It's time for the federal government to step in.

By **EMILY ATKIN** | August 23, 2017

Bobby Corrigan is the rat master. Some call him the rat czar. To others, he is simply a rodentologist, or as NBC recently described him, "one of the nation's leading experts on rats." Call him what you want; he is mostly alarmed. "I travel all over the world with this animal, and the amount of complaints and feedback and questions I hear



Photograph: Shutterstock

NYC is hiring a 'rat czar' that'll be paid up to $170,000 a year

You'll need a "killer instinct" to get the job.

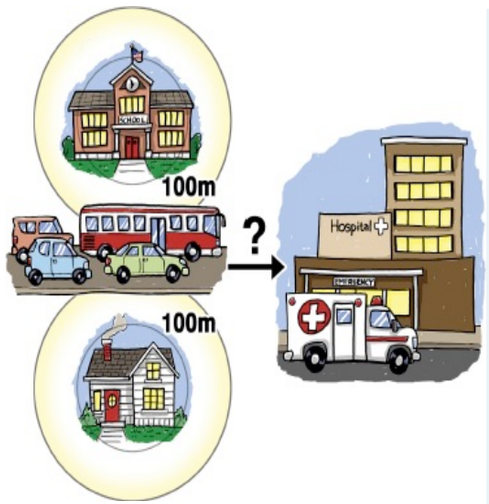
The Washington Post
Democracy Dies in Darkness

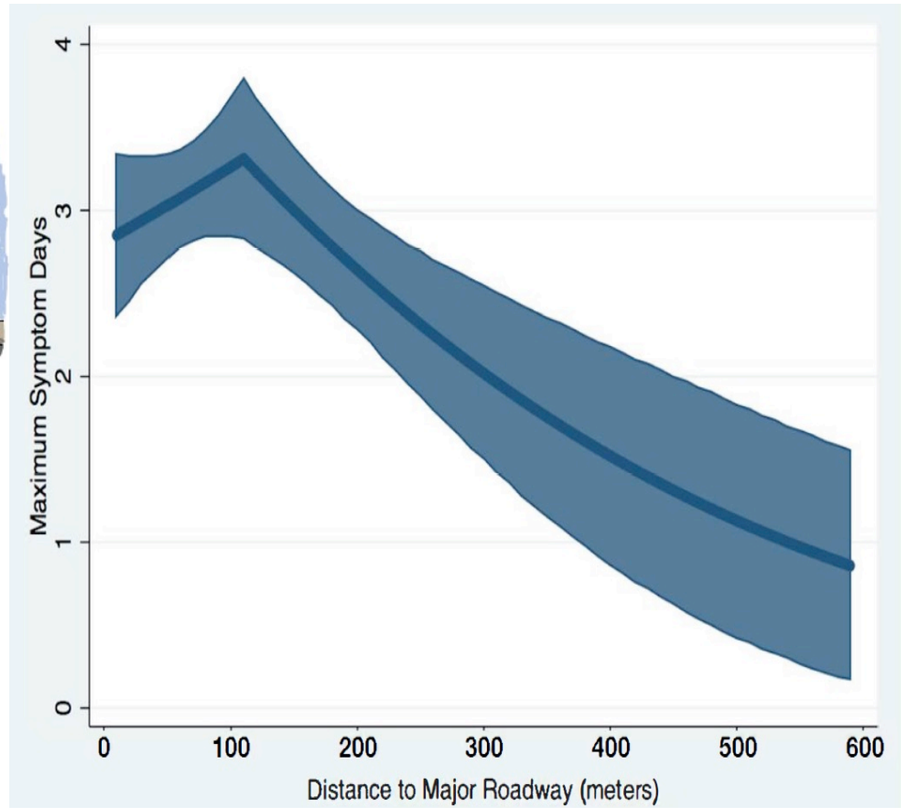
MORNING MIX

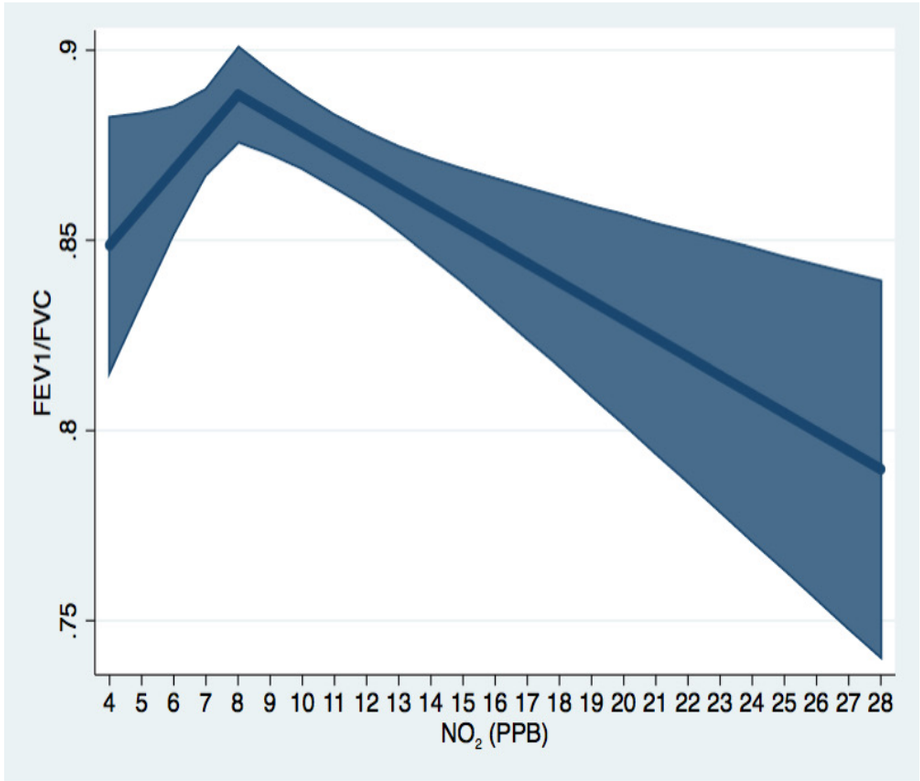
NYC waged a war on rodents. Now it's searching for a new 'rat czar.'

'The ideal candidate is highly motivated and somewhat bloodthirsty,' the job posting says

Urban schools, traffic and distance to roadways, air pollution and asthma morbidity





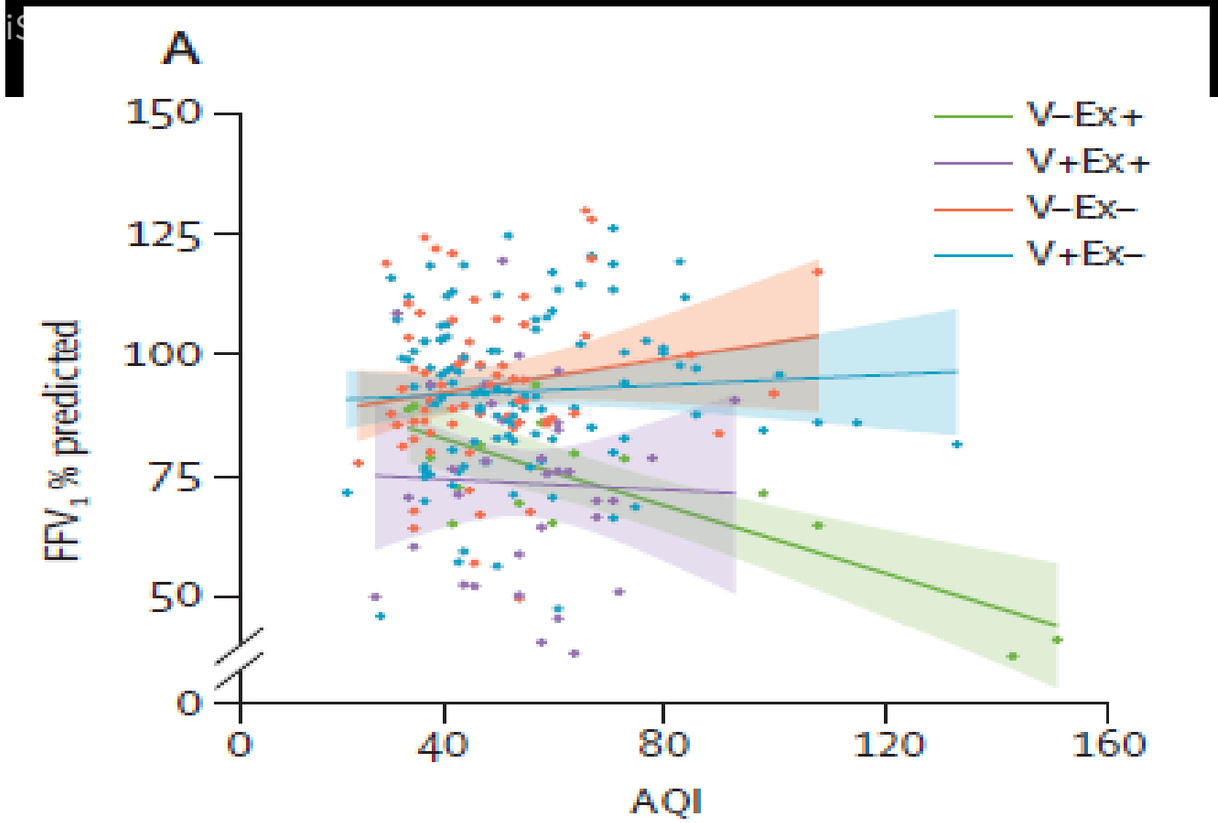


Gaffin, JM, et al JACI 2018 and Hauptman, et al JACI 2020

Air pollutants in low-income urban areas linked with youth asthma attacks: study

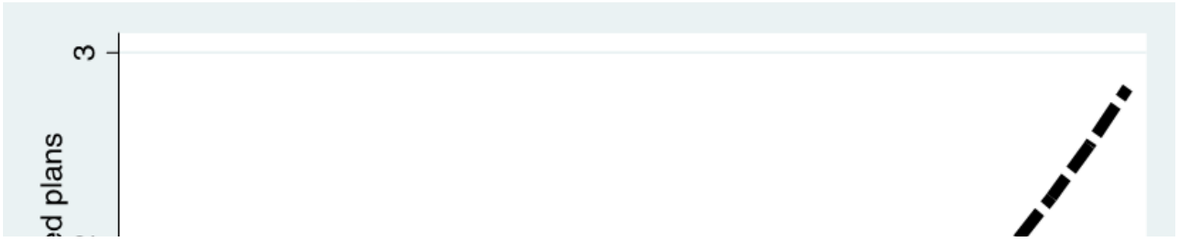
Researchers were able to connect individual pollutants with certain changes in airway functions and gene expression during the attacks.

By Gianna Melillo | Jan. 05, 2023 Changing America

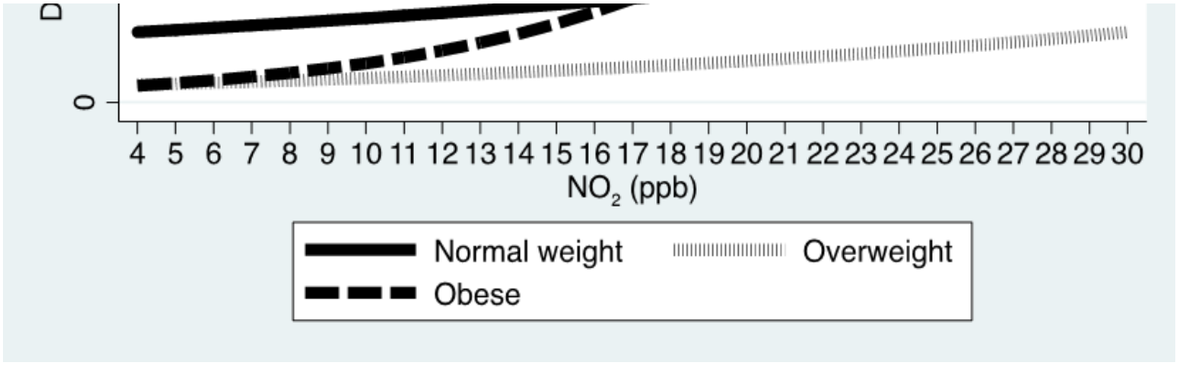


- Data from children living in low-income urban areas across the country show ozone and fine particulate matter are associated with asthma attacks.
- Nonviral attacks among urban children were also more common compared with those living in rural regions, research showed.
- EPA newly lowered annual standard PM 2.5 from 12 µg/m^3 to 9 – 10 µg/m^3

How does BMI interact with school pollution exposure and asthma?



Strategies to normalize BMI (diet and exercise) and improve school environment is critical

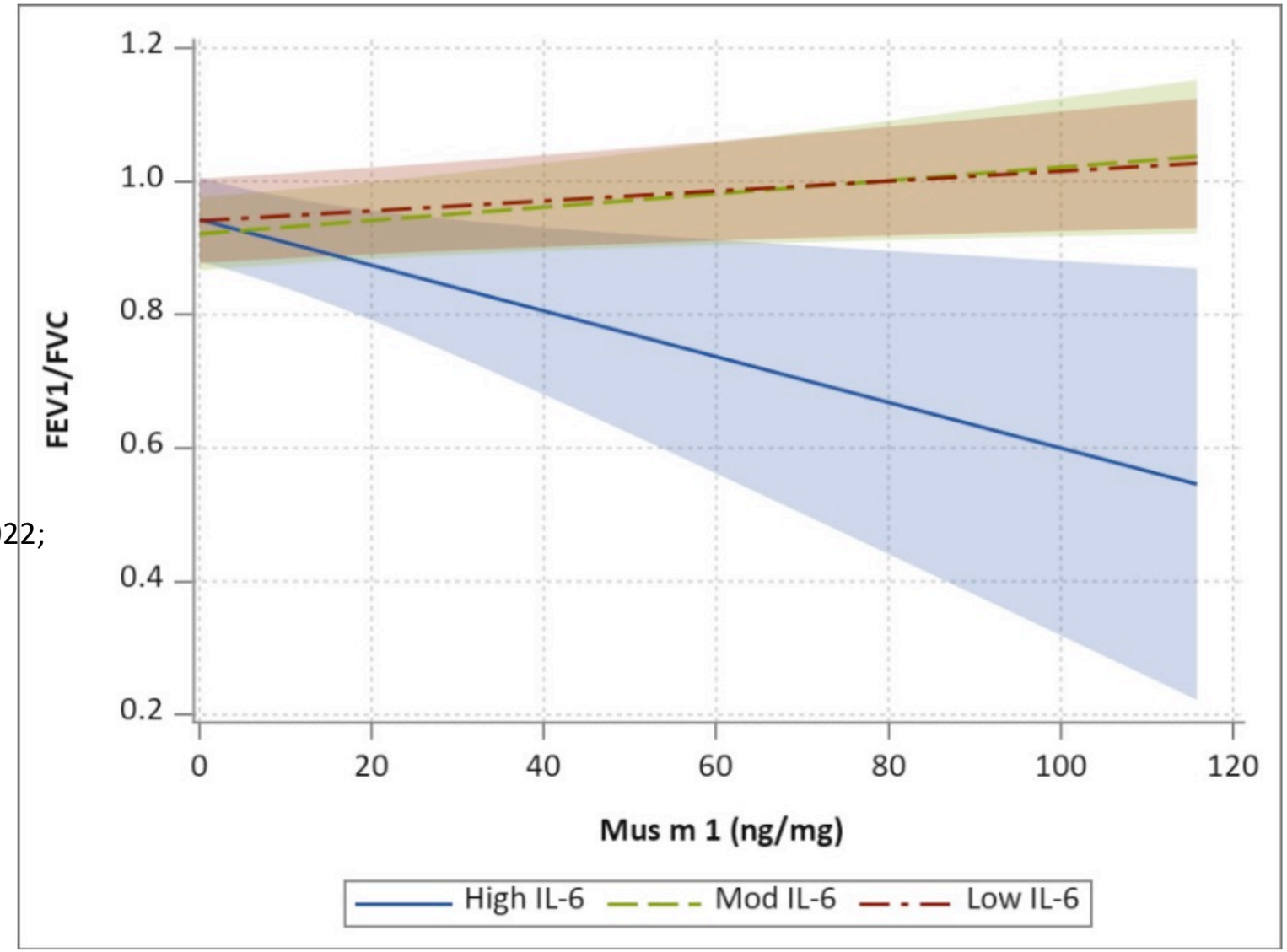


Permaul P, et al JACI Oct 2020

Relationships further modified by cytokines such as IL6

Permaul P, Peters MC, et al JACI In Practice 2021- Severe Asthma Research Program

High Plasma IL-6 Levels May Enhance the Adverse Effects of Mouse Allergen Exposure in Urban Schools on Asthma Morbidity in Children

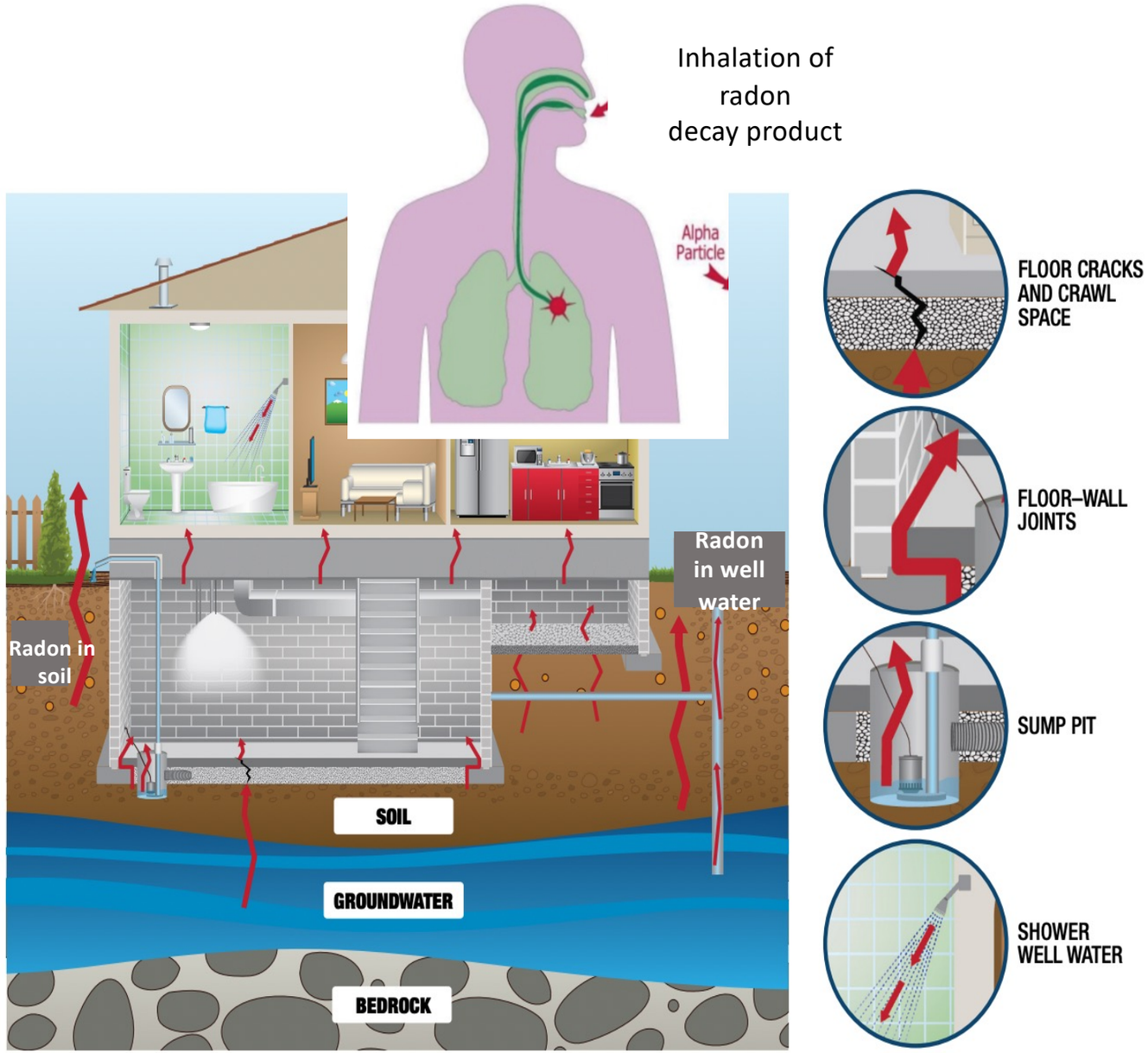


AAAAI 2022
Featured abstract
Permaul P, et al JACI 2022;
149 (2) AB156

UNPUBLISHED
confidential
DO NOT CITE

- Radon is a naturally radioactive gas
  - formed by the decay of uranium radionuclides naturally present in rocks in the earth's crust
  - well-known for carcinogenic effects (lung cancer)
  - oxidative stress in cell culture
  - associated with COPD mortality
- Asthma is well known to be triggered by environmental inhalants

- No studies to date on radon and asthma morbidity



CRCPD Publication No. E-18-2

Long-term exposure to Radon is associated with asthma diagnosis in urban youth

Radon exposure (moving avg)	Asthma diagnosis	
	Home	School
1 month	1.2 (0.7-1.92)	**1.18 (1.62-6.5)[b]**
5 month	1.07 (0.67-1.69)	**1.48 (2.15-9.06)[b]**
7 month	1.26 (0.77-2.04)	**5.19 (2.33-11.5)[b]**
12 month	1.41 (0.84-2.34)	
24 month	1.61 (0.93-2.79)	
36 month	**2.01 (1.09-3.69)[a]**	
48 month	**2.15 (1.10-4.17)[a]**	
60 month	**2.25 (1.11-4.54)[a]**	

Greater effect size with longer exposure window

Short-term exposure to Radon is associated with respiratory symptoms in urban youth

Radon exposure (moving avg)	Wheezing		Nighttime difficulty breathing		Nocturnal cough		Missed school days	
	Home	School	Home	School	Home	School	Home	School
1 month	1.05 (0.65-1.67)	1.76 (0.89-3.48)	0.79 (0.39-1.62)	2.18 (0.88-5.42)	1.21 (0.77-1.89)	1.55 (0.82-2.95)	1.18 (0.64-2.19)	**5.27 (2.09-13.2)[b]**
5 month	1.03 (0.65-1.62)	**2.68 (1.34-5.38)[b]**	0.80 (0.40-1.61)	**3.53 (1.38-9.04)[b]**	1.20 (0.78-1.85)	**2.36 (1.23-4.53)[b]**	1.12 (0.61-2.04)	**7.63 (2.91-20)[b]**
7 month	1.16 (0.71-1.89)	**2.91 (1.34-6.33)[b]**	0.98 (0.48-1.99)	**4.46 (1.58-12.54)[b]**	1.37 (0.86-2.19)	**2.5 (1.21-5.18)[a]**	1.24 (0.66-2.33)	**8.98 (3.12-25)[b]**

Long-term exposure to Radon is associated with respiratory symptoms in urban youth

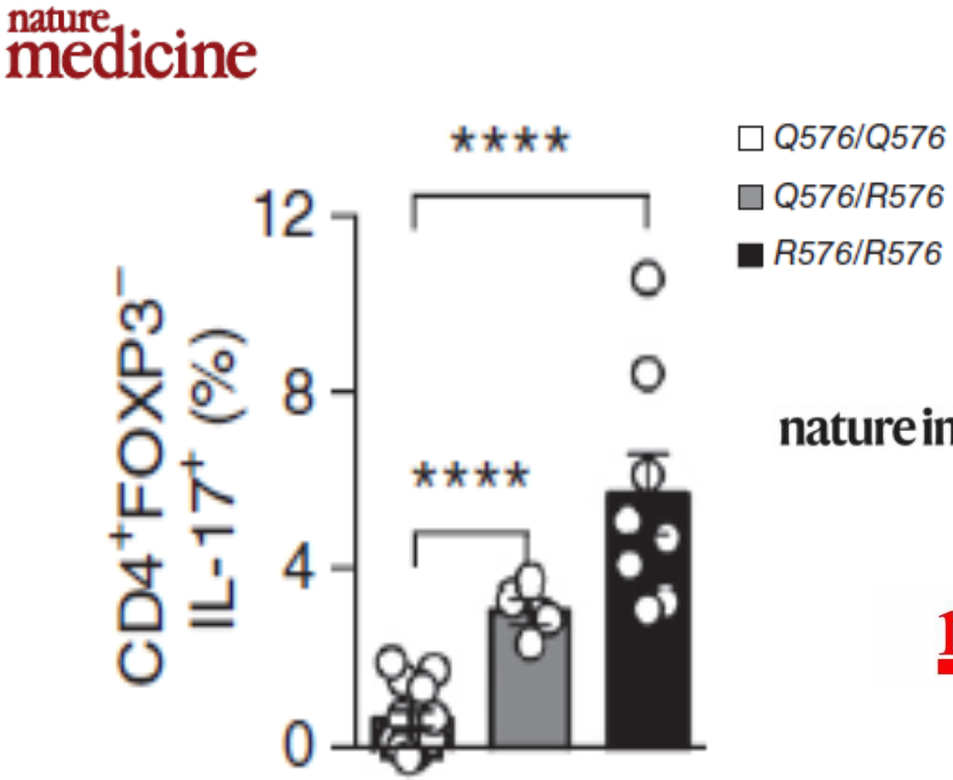
12 month	**1.2 (0.71-2.01)**		**1.08 (0.52-2.23)**		**1.50 (0.91-2.46)**		**1.36 (0.71-2.61)**	
24 month	1.34 (0.77-2.33)		1.15 (0.52-2.52)		**1.76 (1.03-3)[a]**		1.48 (0.74-2.98)	
36 month	1.55 (0.84-2.84)		1.27 (0.54-2.96)		**2 (1.11-3.62)[a]**			
48 month	1.67 (0.86-3.22)		1.31 (0.52-3.31)		**2.24 (1.17-4.25)[a]**		1.83 (0.79-4.22)	
60 month	1.75 (0.87-3.51)		1.31 (0.49-3.48)		**2.43 (1.23-4.78)[b]**		1.98 (0.81-4.8)	

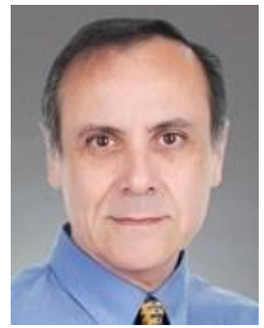
Mukharesh L, …Phipatanakul W, and Gaffin JM. Peds Pulmonology 2022

Taking what we learned in schools to Precision Medicine

An asthma associated IL4R polymorphism Increases Airway Inflammation by Conversion of regulatory T cells to Th_{17}-like Cells

- IL-4Rα-Q576R polymorphism- (glutamine (Q) to arginine R substitution at position 576 of the IL-4Rα)
  - R allele frequency 68% (blacks/hispanics); 20% (whites)
  - R allele associated with severe asthma
  - Unique among *IL4R* polymorphisms, directly drives T_H2 to T_H17 inflammatory response in the airways
  - Dose response relation with severity
  - Augmented by obesity



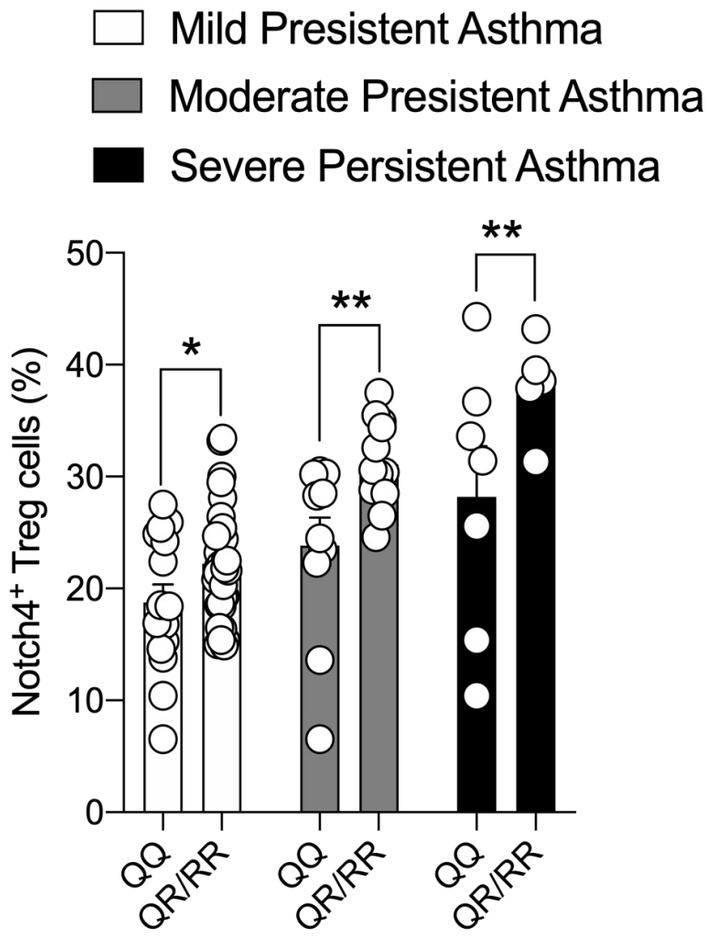


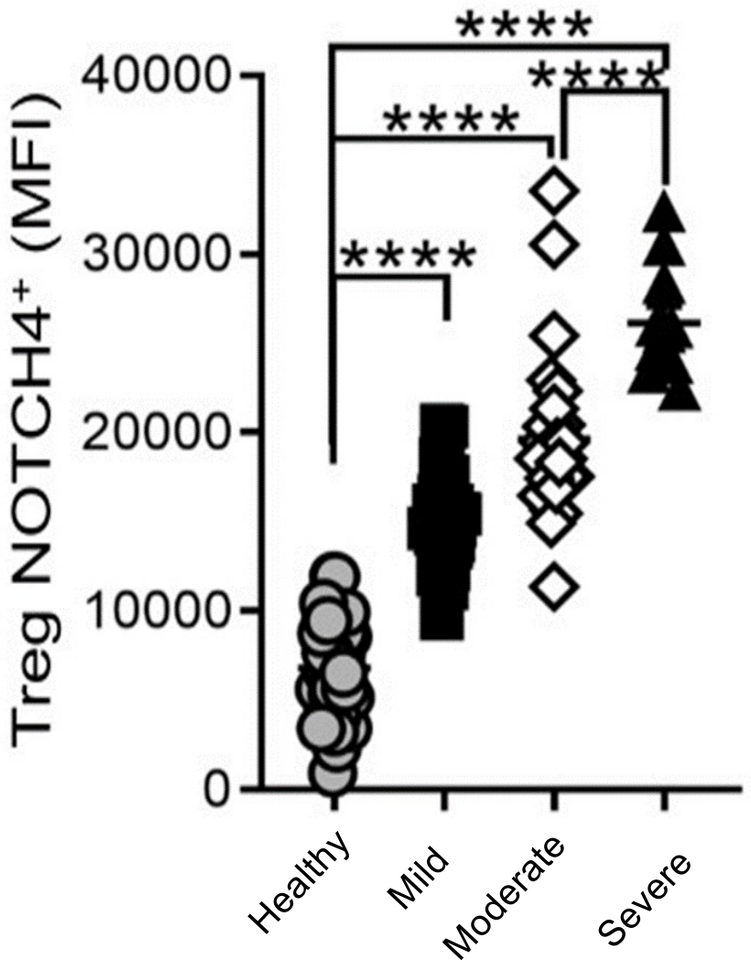
Massoud et al, Nat Med 2016; 22(9):1013-22

Hani H, et al Nature Immunol November, 2020

Babat, S, et al Nature March 2021

IL-4RαR576 impacts % circulating NOTCH4⁺ Tregs and asthma severity



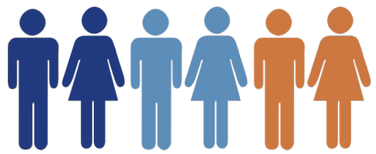


Hani H, et al … Phipatanakul W, and Chatila T, Nature Immunol November, 2020

Persistent Asthma

Cohort

IL4R$^{Q576/Q576}$
IL4R$^{Q576/R576}$
IL4R$^{R576/R576}$



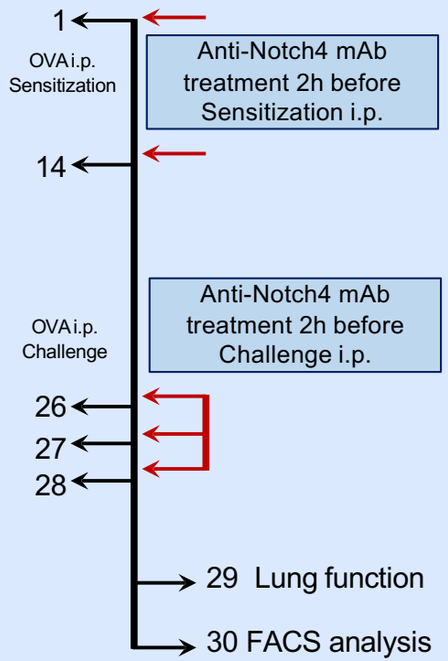
Il4ra^{R576} *Foxp3*^{YFPCre}
Il4ra^{R576} *Foxp3*^{YFPCre} *Notch4* $^{\Delta/\Delta}$
Il4ra^{R576} *Foxp3*^{YFPCre} *Grb2* $^{\Delta/\Delta}$
Il4ra^{R576} *Foxp3*^{YFPCre} *Il6ra* $^{\Delta/\Delta}$

Study design

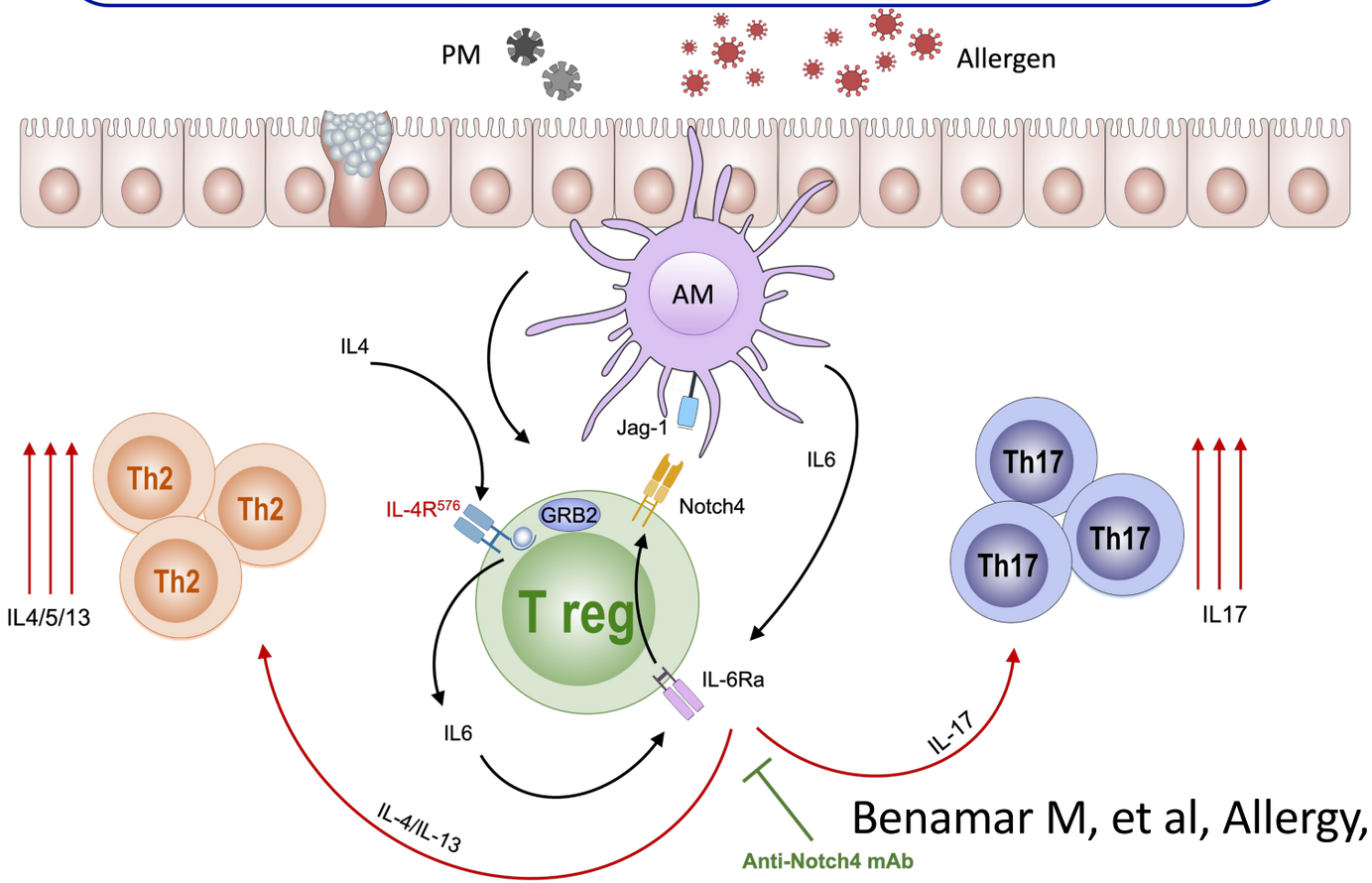
Lung function analysis

FACS analysis

Therapy



The IL4-Ra-R576 variant exacerbates asthmatic inflammation via a T_{reg} Cell GRB2-IL-6-Notch4 Circuit

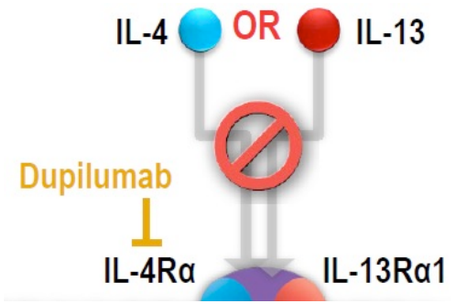


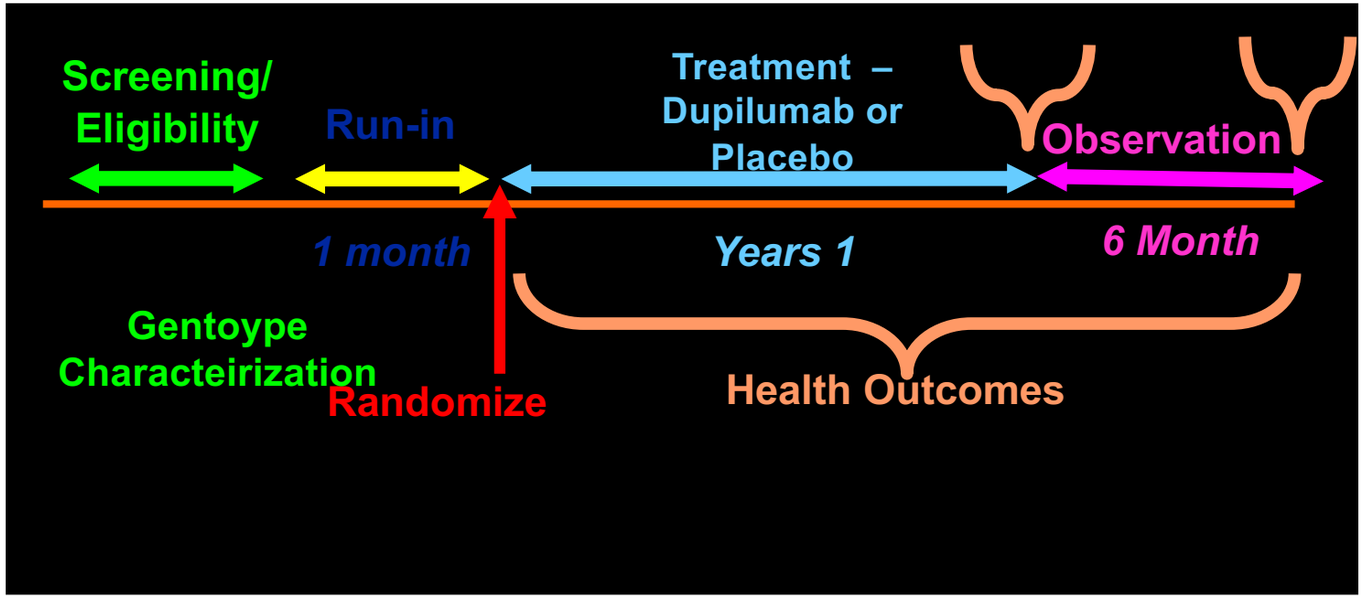
Benamar M, et al, Allergy, 2022

Investigating Dupilumab's Effect in Asthma by Genotype IDEA Trial
https://ideaasthma.org

Boston- Phipatanakul/Israel
New Jersey- Oppenheimer
Michigan- Kim/Zoratti
Cleveland-Kaleb
NY-Montefiore- Sjariwal
U Penn- Bamarjee

NIH U01 AI143514 – Phipatanakul/Chatila
3 Groups by Genotype 1: 1 Dupilumab vs. Placebo



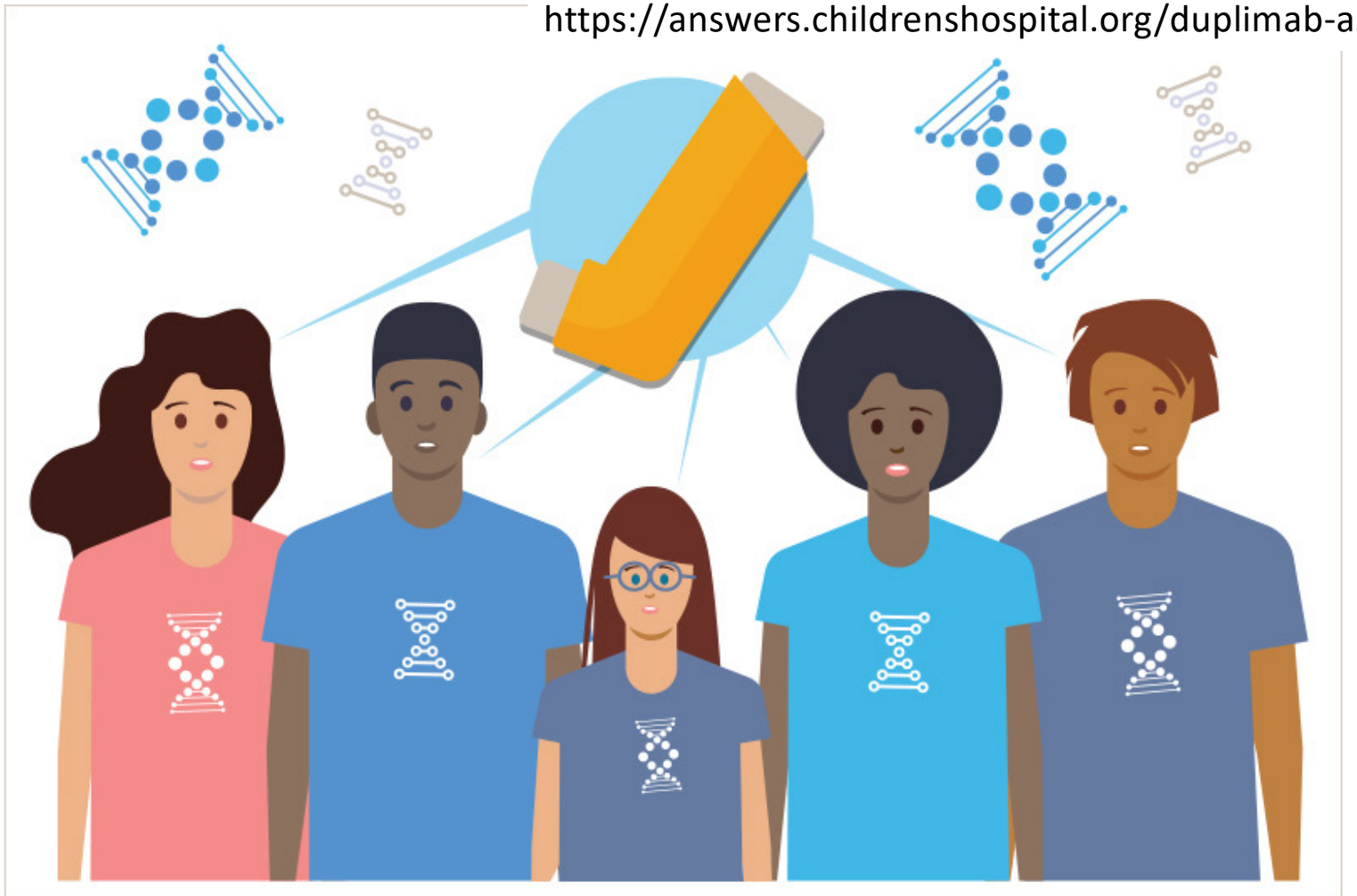


Will investigate genotype driven (personalized) response to therapy and study preliminary mechanisms in disease modification

Trial for severe asthma targets a mutation common in children of color

Posted on September 7, 2021 by Nancy Fliesler | Clinical, Research
Tags: asthma, clinical trials, genetics and genomics, precision medicine

https://answers.childrenshospital.org/duplimab-asthma/



Some lessons learned so far..

- School environment is important in asthma disparities even after adjusting for home (particularly, mouse/mold allergen, pollutants) and other risk factors (obesity, sleep issues, inflammatory markers) augment this risk
- What can be done about this?

JAMA | Original Investigation

Effect of School Integrated Pest Management or Classroom Air Filter Purifiers on Asthma Symptoms in Students With Active Asthma A Randomized Clinical Trial

Wanda Phipatanakul, MD, MS; Petros Koutrakis, PhD; Brent A. Coull, MD, PhD; Carter R. Petty, MA; Jonathan M. Gaffin, MD, MMSc; William J. Sheehan, MD; Peggy S. Lai, MD, MPH; Lisa M. Bartnikas, MD; Choong-Min Kang, PhD; Jack M. Wolfson, PhD; Mihail Samnaliev, PhD; Amparito Cunningham, MD, MPH; Sachin N. Baxi, MD; Perdita Permaul, MD; Marissa Hauptman, MD, MPH; Michelle Trivedi, MD, MPH; Margee Louisias, MD, MPH; Liming Liang, PhD; Peter S. Thorne, PhD, MS; Nervana Metwali, PhD; Gary Adamkiewicz, PhD, MPH; Elliot Israel, MD; Andrea A. Baccarelli, MD, ScD; Diane R. Gold, MD, MPH; for the School Inner-City Asthma Intervention study team

IMPORTANCE School and classroom allergens and particles are associated with asthma morbidity, but the benefit of environmental remediation is not known.

OBJECTIVE To determine whether use of a school-wide integrated pest management (IPM) program or high-efficiency particulate air (HEPA) filter purifiers in the classrooms improve asthma symptoms in students with active asthma.

DESIGN, SETTING, AND PARTICIPANTS Factorial randomized clinical trial of a school-wide IPM program and HEPA filter purifiers in the classrooms was conducted from 2015 to 2020 (School Inner-City Asthma Intervention Study). There were 236 students with active asthma attending 41 participating urban elementary schools located in the Northeastern US who were randomized to IPM by school and HEPA filter purifiers by classroom. The date of final follow-up was June 20, 2020.

INTERVENTIONS The school-wide IPM program consisted of application of rodenticide, sealing entry points, trap placement, targeted cleaning, and brief educational handouts for school staff. Infestation was assessed every 3 months, with additional treatments as needed. Control schools received no IPM, cleaning, or education. Classroom portable HEPA filter purifiers were deployed and the filters were changed every 3 months. Control classrooms received sham HEPA filters that looked and sounded like active HEPA filter purifiers. Randomization was done independently (split-plot design), with matching by the number of enrolled students to ensure a nearly exact 1:1 student ratio for each intervention with 118 students randomized to each group. Participants, investigators, and those assessing outcomes were blinded to the interventions.

MAIN OUTCOMES AND MEASURES The primary outcome was the number of symptom-days with asthma during a 2-week period. Symptom-days were assessed every 2 months during the 10 months after randomization.

RESULTS Among the 236 students who were randomized (mean age, 8.1 [SD, 2.0] years; 113 [48%] female), all completed the trial. At baseline, the 2-week mean was 2.2 (SD, 3.9) symptom-days with asthma and 98% of the classrooms had detectable levels of mouse allergen. The results were pooled because there was no statistically significant difference between the 2 interventions ($P = .18$ for interaction). During a 2-week period, the mean was 1.5 symptom-days with asthma after use of the school-wide IPM program vs 1.9 symptom-days after no IPM across the school year (incidence rate ratio, 0.71 [95% CI, 0.38-1.33]), which was not statistically significantly different. During a 2-week period, the mean was 1.6 symptom-days with asthma after use of HEPA filter purifiers in the classrooms vs 1.8 symptom-days after use of sham HEPA filter purifiers across the school year (incidence rate ratio, 1.47 [95% CI, 0.79-2.75]), which was not statistically significantly different. There were no intervention-related adverse events.

CONCLUSIONS AND RELEVANCE Among children with active asthma, use of a school-wide IPM program or classroom HEPA filter purifiers did not significantly reduce symptom-days with asthma. However, interpretation of the study findings may need to consider allergen levels, particle exposures, and asthma symptoms at baseline.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT02291302

JAMA. 2021;326(9):839-850. doi:10.1001/jama.2021.11559

Editorial page 816

Supplemental content

CME Quiz at jamacmelookup.com

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The members of the School Inner-City Asthma Intervention study team appear in Supplement 3.

Corresponding Author: Wanda Phipatanakul, MD, MS, Boston Children's Hospital, Harvard Medical School, 300 Longwood Ave, Boston, MA 02115 (wanda.phipatanakul@childrens.harvard.edu).

The JAMA Network

JAMA Journal of the American Medical Association

W Phipatanakul, et al , JAMA, Sept 7 2021

Effect of an Integrated Pest Management on Classroom Air Filter Purifiers on Asthma Symptoms in Students with Active Asthma: A Randomized Clinical Trial

Available at jama.com and on The JAMA Network Reader at mobile.jamanetwork.com

Screen Recruit

Randomization* Intervention Starts

Intervention* Ends

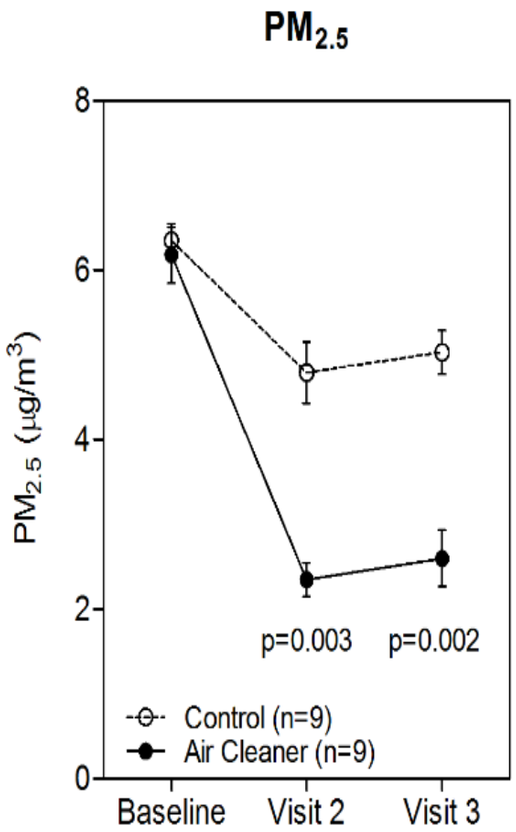
Season	spring	summer	fall	winter	spring	summer
		Clinic visit	Phone Survey	Phone Survey	Phone Survey	Phone Survey
Clinical Trial		Baseline Exposure		PFT/FeNO School/Home Exposure		PFT/FeNO School/Home Exposure

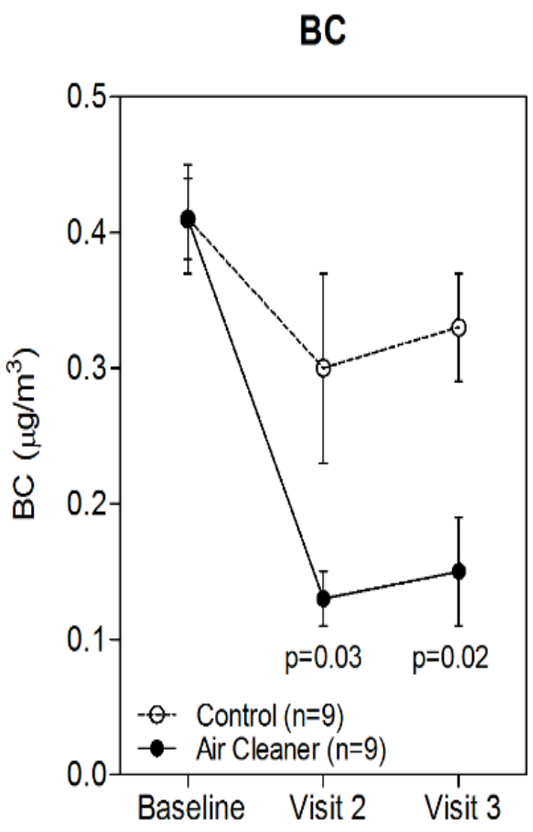
50 students/Year , 6-10 schools
250 students, 40 schools 5 years

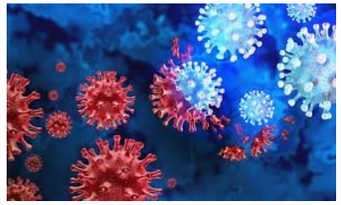
***Classroom Air Filter Versus Sham Control**

***Cafeteria/Classroom School Integrated Pest Management/Control**

Classroom HEPA Filters Reduce Particulate Pollutants and Airbone Allergens Compared to Sham





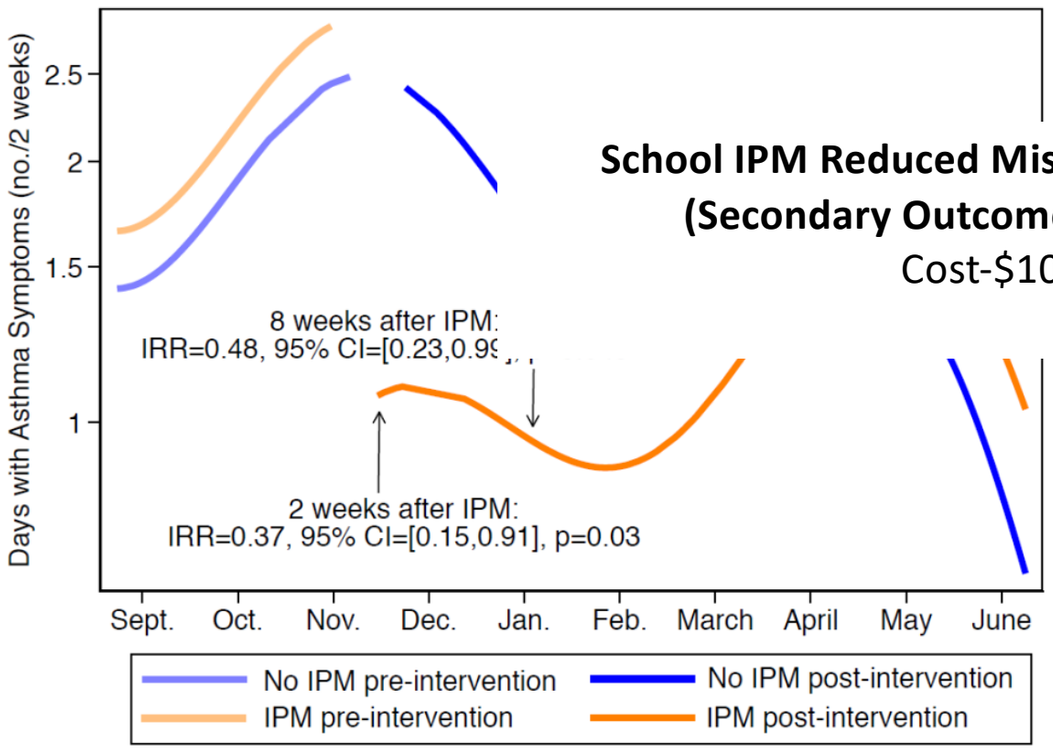


Lai PS R21 NIAID Molecular epidemiology of viruses in Schools
NIEHS R21
HEPA filters role on viruses in schools

Jhun, Phipatanakul, JACI in Practice 2017; 5(1):154-159

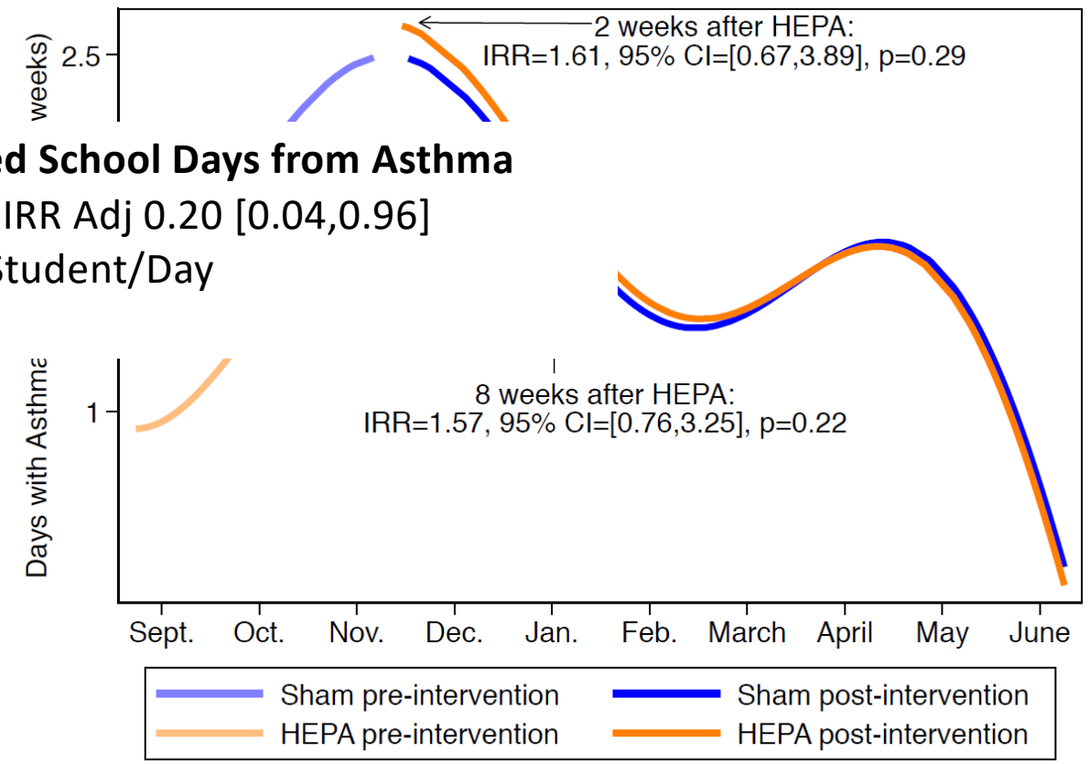
Phipatanakul, W, et al JAMA Sept 2021

Time Effect of the School IPM and Classroom HEPA on Health Effects



School IPM Reduced Missed School Days from Asthma (Secondary Outcome) IRR Adj 0.20 [0.04,0.96]

Cost-$10/Student/Day



Phipatanakul, W, et al JAMA Sept 2021

EDITORIAL

JAMA

School Classrooms as Targets to Reduce Allergens and Improve Asthma

William W. Busse, MD; Daniel J. Jackson, MD

…" implementing allergen avoidance with targeted environments and in selected patients may improve the likelihood of success…."

"Childhood asthma often is a lifelong disease"

"Early life efforts to improve asthma control that are safe and effective may diminish consequences and need for systemic corticosteroids…"

"Allergen avoidance for asthma is safe, rational, and remains worthy of continued consideration and study"

JAMA Sept 2021

Classroom HEPA filtration in Students Exposed to Higher Indoor Classroom Mold than at Home

	HEPA (N=43)	Sham (N=38)	P
Group 1 (indoor mold)	-5.44	-3.30	0.025
Group 2 (outdoor mold)	-4.15	-3.93	0.330
Environmental Relative Mold Index (ERMI)	-1.29	+0.63	0.026
FEV1% increase	4.69	0.47	0.034

Vesper, S, et al 2022 J Asthma

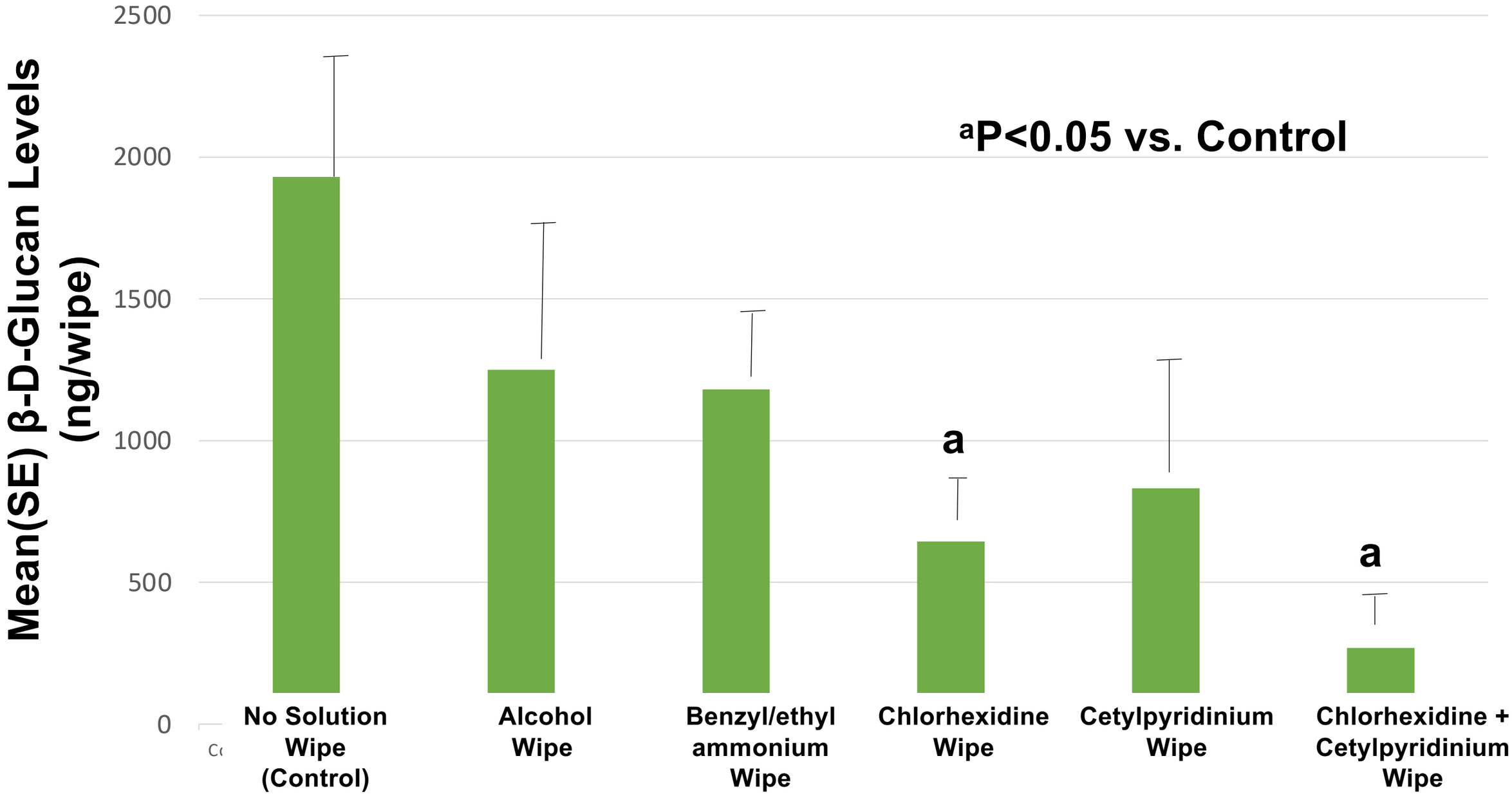
Are You Allergic to Your Smartphone? Study Suggests It's Covered in Allergens

By Michelle Pugle on November 10, 2022 — Fact checked by Dana K. Cassell

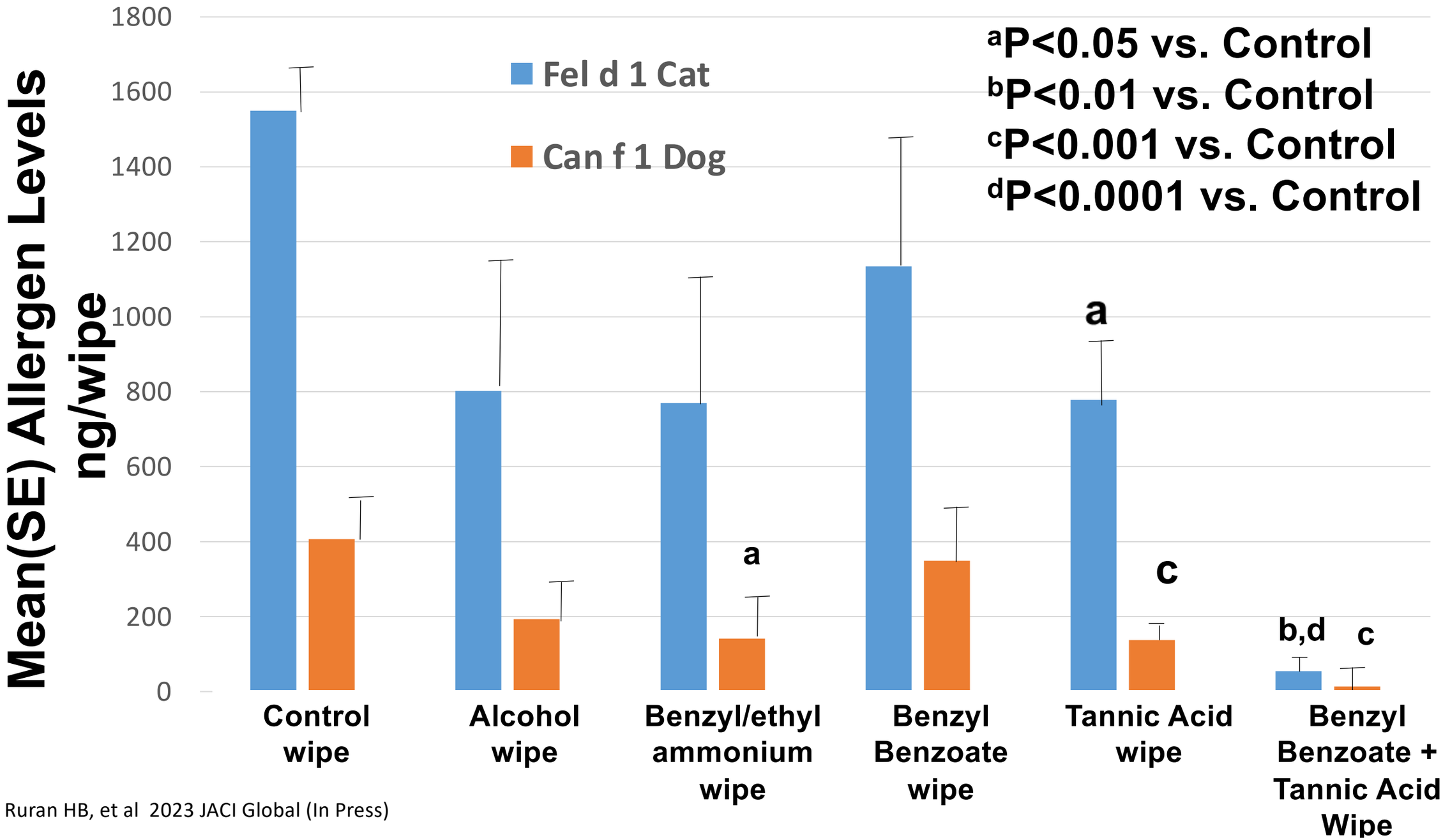
A new study suggests that smartphones harbor environmental hazards such as allergens and should be cleaned regularly. Eldad Carin/Stocksy

- **A new study suggests that smartphones are hosts for allergens like pet dander and fungus.**
- **The researchers say that people with allergies or asthma should clean their phones regularly to minimize their risk of a severe reaction.**
- **The researchers also noted some effective ways to clean your smartphone.**

Ruran HB, et al 2023 JACI Global (In Press)
https://www.jaci-global.org/article/S2772-8293(22)00094-7/fulltext



Ruran HB, et al 2023 JACI Global (In Press)



Ruran HB, et al 2023 JACI Global (In Press)

In Summary…

- Environmental Interventions work when target exposures are reduced
- Multi-faceted approaches have been the standard approach and recommended by NAEPP, but there is rising evidence in the role of single-faceted, particularly among pests (mouse/cockroach) which may have more practicality in public policy interventions and targeted in underserved populations
- We can intervene on relevant community exposures through school specific interventions- but more sustained measures are needed to have lasting benefit on health- Benefit may be on more select populations (severity, exposure risk factors)
- Interventions in school can impact a community as opposed to individuals at home
- Important to incorporate future strategies to provide healthy environments for kids in school, particularly thinking of policies for fair and equitable resource allocation in underserved populations.
- Consideration of other vectors of exposure- smartphones? Other items?
- Really important to think about with ongoing challenges in the pandemic

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- Community Schools and Families

NIH National Institute of Allergy and Infectious Diseases