



# Asthma Research in Peru

**Karina Romero MD, MSc**

Research Associate, A.B. PRISMA

Fogarty Global Health Fellow 2012-2013

[kromero@prisma.org.pe](mailto:kromero@prisma.org.pe)

# Collaborative alliances



THE UNIVERSITY  
of NORTH CAROLINA  
at CHAPEL HILL



# The Peru Urban versus Rural Asthma (PURA) Study: methods and baseline quality control data from a cross-sectional investigation into the prevalence, severity, genetics, immunology and environmental factors affecting asthma in adolescence in Peru

Colin L Robinson,<sup>1</sup> Lauren M Baumann,<sup>1</sup> Robert H Gilman,<sup>2,3,4</sup> Karina Romero,<sup>3</sup> Juan Manuel Combe,<sup>3</sup> Lilia Cabrera,<sup>3</sup> Nadia N Hansel,<sup>1,5</sup> Kathleen Barnes,<sup>6</sup> Guillermo Gonzalez,<sup>4</sup> Robert A Wise,<sup>1,5</sup> Patrick N Breyse,<sup>5</sup> William Checkley<sup>1,2,3,4</sup>



## Effects of distance from a heavily transited avenue on asthma and atopy in a periurban shantytown in Lima, Peru

Lauren M. Baumann, MHS,<sup>a,b</sup> Colin L. Robinson, BA,<sup>a,b</sup> Juan M. Combe, MD,<sup>b</sup> Alfonso Gomez, MD,<sup>b</sup> Karina Romero, MD,<sup>b</sup> Robert H. Gilman, MD,<sup>b,c,d</sup> Lilia Cabrera, RN,<sup>b</sup> Nadia N. Hansel, MD, MPH,<sup>a,e,f</sup> Robert A. Wise, MD,<sup>a,f</sup> Patrick N. Breyse, PhD, MHS,<sup>f</sup> Kathleen Barnes, PhD,<sup>a,e</sup> Juan E. Hernandez, PhD,<sup>g</sup> and William Checkley, MD, PhD<sup>a,b,d</sup> *Baltimore, Md, Lima, Peru, and Cuernavaca, Mexico*



FIG 1. Distribution of the 725 study households in Pampas de San Juan around the main avenue of Lima, Peru. The thick black line represents the main avenue (Avenida Miguel Iglesias) that intersects our study community. The black circles represent households in our study. The thin white lines represent distances from the avenue in 100-meter intervals.

# Asthma cohorts

**Genetic Susceptibility to asthma and indoor pollution in Peru.**

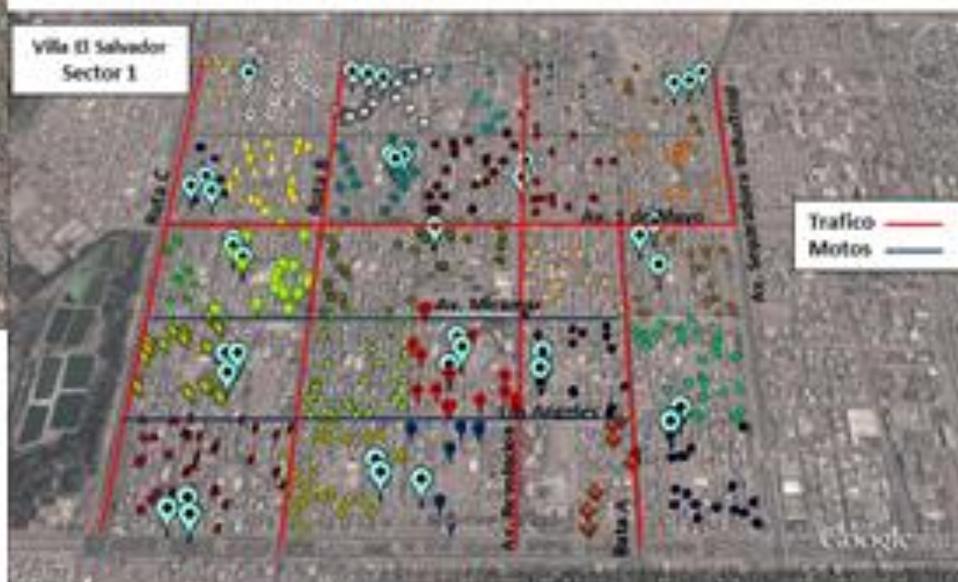
- Gene by Environment Interaction study
- 1,200 participants
- 600 asthmatics, 600 controls
- Twice weekly visits for symptom assessment, spirometry q3 months & PM<sub>2.5</sub>/NO<sub>2</sub> monitoring
- Longitudinal follow-up 6-9 months

# Subgrupos Ambientales

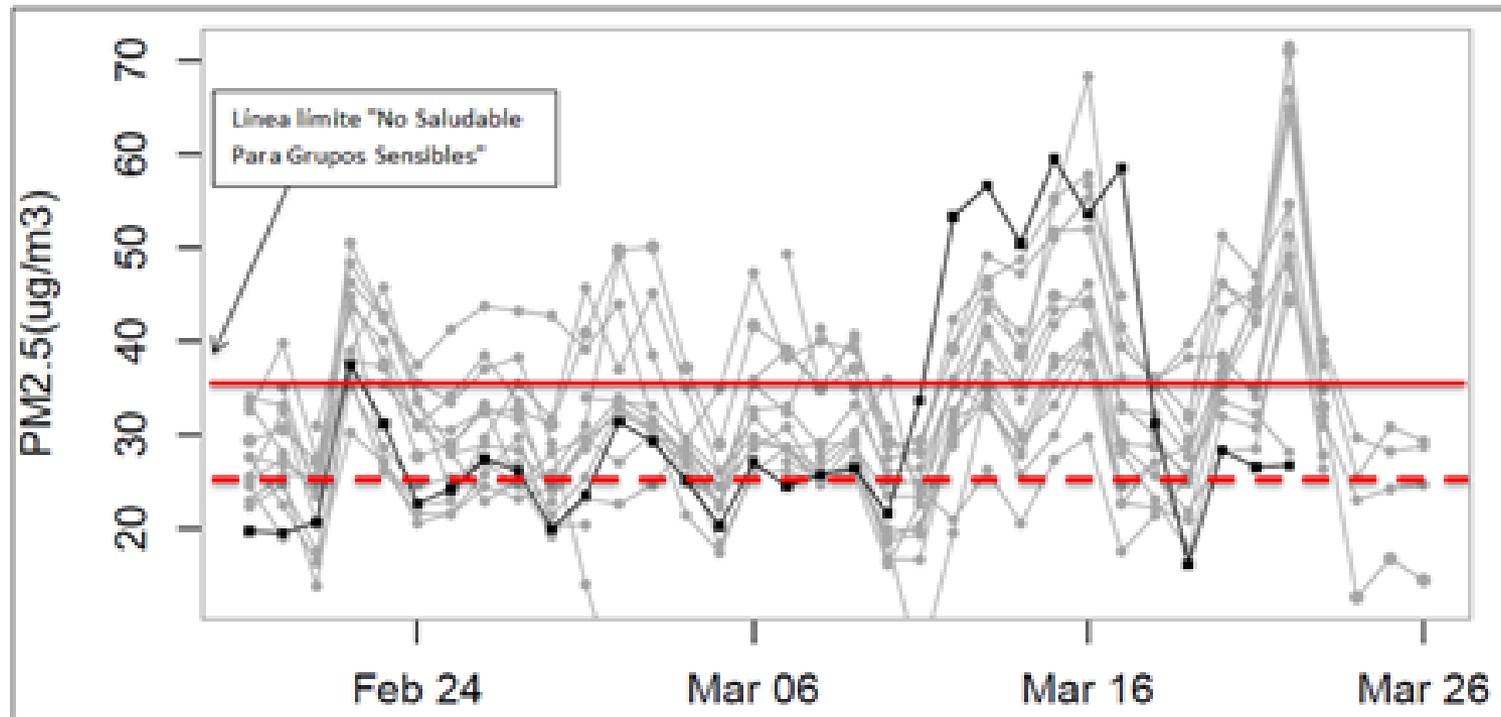
## Pampas de San Juan de Miraflores



## Villa El Salvador- Sector 1



## RESUMEN DE MEDICIONES AMBIENTALES: PSJM (FEB-MARZO 2013)



- ▶ Límite "No Saludable para Grupos Sensibles" (asmáticos), (según Agencia de Protección del Ambiente, EEUU)
- ▶ Límite permitido por la OMS para 24 horas

# Preliminary results

CLASSIFICATION OF ASTHMA BY SEVERITY				
Severity	%	B2 use (%)	Oral steroid (%)	ICS (%)
PREVIOUS	23.9	0	8.0	0
MILD INTERMITTENT	13.4	35.0	14.6	0
MILD PERSISTENT	34.6	45.2	18.7	<b>4.4</b>
MODERATE PERSISTENT	<b>14.9</b>	47.6	20.9	2.3
SEVERE PERSISTENT	<b>13.1</b>	58.8	<b>32.4</b>	2.9



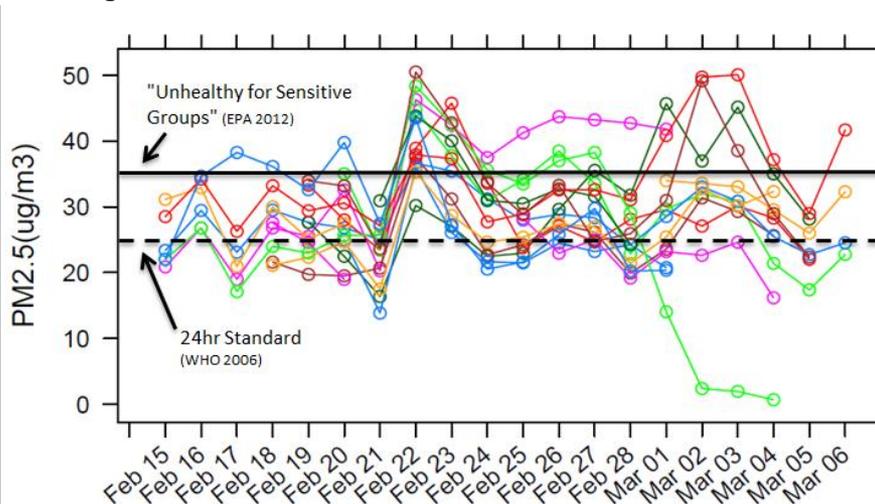
# Preliminary results

## Predictors of Asthma control:

- % predict FEV1 (AUC= 68%)
- Exhaled Nitric Oxide (AUC= 64%)
- ACT questionnaire (AUC= 89%)
- ICS intake



## Exposure: Indoor Pollution



Diet/ P. Activity??

## Overweight:

Asthmatics = **17.4%**

Controls = 13.4%

(PM2.5 according with local reporte must be lower than:  
**15 ug/m3**)

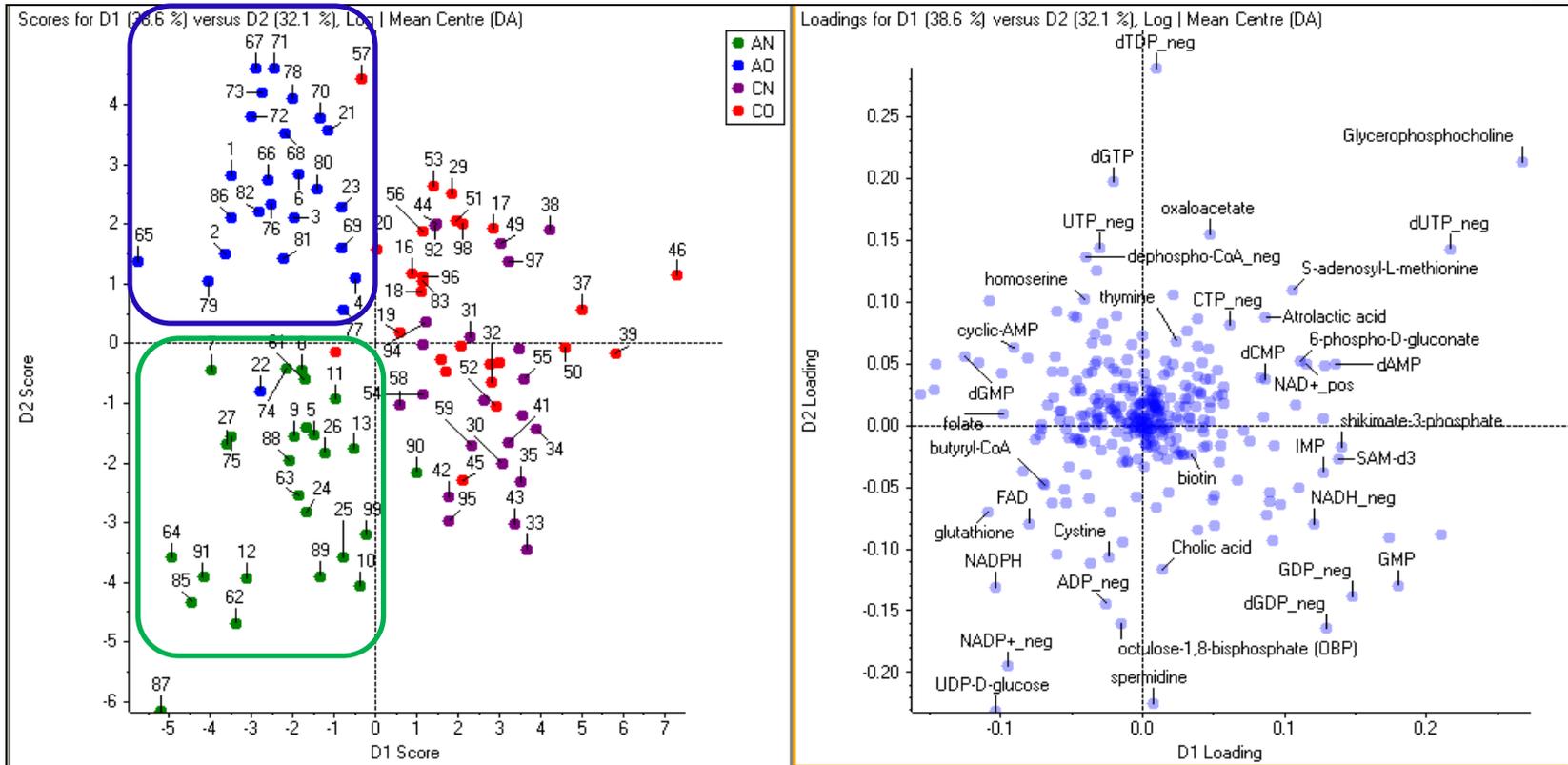
# Training research on Asthma cohort in Peru

- **Area of interest:** Obesity-Asthma Link In Children
- **Suggestion:** Design a research project that can be incorporated into research that is ongoing at the research site. Easier to work on an **ongoing project** given the logistics of obtaining IRB approval.  
GASP Cohort: 600 children asthmatics & 600 controls.
- **Objectives:**
  - To analyze the Metabolic Profiling of serum Samples from Asthmatic and Overweight Subjects.
  - To evaluate the Body Composition Measurements Associated With Current Asthma



# Metabolic Profiling Analysis of serum samples from Asthmatic and Overweight children.

## Principal Component Analysis and Discriminant Analysis PCA-DA



HPLC-MS based metabolomic profiling approach revealed some novel statistically highly significantly changed metabolites that differentiate between asthmatic patients and control subjects. The biochemistry behind these changes in metabolite concentrations need to be further investigated..

# Obesity-Asthma Link In Children: Body Composition Measurements Associated With Current Asthma

K. Romero<sup>1,2</sup>, N.N. Hansel<sup>3</sup>, S.L. Pollard<sup>4</sup>, J.J. Lima<sup>5</sup>, C.M. Johnson<sup>3</sup>, P.N. Breyse<sup>4</sup>, D.L. Williams<sup>4</sup>, W. Checkley<sup>2,4</sup>

<sup>1</sup>AB Prisma - Lima/PE, <sup>2</sup>Center of Excellence in Chronic Diseases/PE, <sup>3</sup>Johns Hopkins University - Baltimore/US, <sup>4</sup>Johns Hopkins Bloomberg School of Public Health, Baltimore – Baltimore/US, <sup>5</sup>Center for Pharmacogenomics & Translational Research at Nemours Children's Clinic.

## INTRODUCTION

- Adiposity may be an important risk factor for asthma risk and severity, but the nature of this association remains unclear, also longitudinal studies points that high body weight would precede asthma symptoms.<sup>1</sup>
- Currently, there is still not consensus over how to adjust for body size, when using adiposity as a proxy for cardiovascular/respiratory risks, specially during childhood which could have implications for the interpretation of indices of adiposity.<sup>2</sup>
- Most studies have limited the analysis of adiposity to body mass index (BMI) or waist circumference; however, some adiposity and body composition phenotypes may be more strongly associated with asthma than others.<sup>1,3</sup>
- Our objective was to explore the association between several measurements of body composition and asthma in children in a low-resource, peri-urban setting in Lima, Peru.

## METHODS

- We included data from 446 children in Peru (225 healthy controls without asthma and 221 children with asthma) aged 9 to 19 years.
- Cases were defined as having physician-defined asthma based on symptoms, spirometry and use of asthma medications as per National Asthma Education and Prevention Program guidelines.
- We also collected demographic information including age, sex, self-reported smoking, second-hand smoke exposure and maternal education, and assessed atopy by Phadiatop.
- We assessed adiposity with the following measurements of body composition: BMI, waist circumference, hip circumference and bioimpedance to calculate body fat, fat mass, lean mass, fat mass index(FMI), lean mass index (LMI) and skeletal muscle index (SMI).
- We used multiple logistic regression to analyze associations between each body composition measure and asthma, adjusted for age, sex, atopy, maternal education, height, and self-reported history of tobacco smoking.

## ACKNOWLEDGEMENTS

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## RESULTS

- Of 221 asthmatics, 24 (8.3%) had severe persistent asthma and 26 (11.1%) had uncontrolled asthma.
- In single variable analysis, we found that both BMI (mean 22.6 vs. 21.9 kg/m<sup>2</sup>; p=0.06) and LM (mean 39.0 vs. 36.8 kg; p=0.004) were greater in asthmatics than in healthy controls whereas body fat, fat mass, FMI, SMI, waist circumference and hip circumference were not.
- In multiple variable logistic regression we found that only lean mass and LMI were directly associated with an increased odds of asthma (OR 1.11, p<0.01 and OR 1.30, p<0.01 respectively).

**Table1. Multiple variable logistic regression of asthma as a function of adiposity and body composition measure.**

Adiposity/body composition measurement	Odds ratio	95% CI	p-value
Body mass index per kg/m <sup>2</sup>	1.04	(0.98 - 1.11)	0.16
Body fat, per 1%	0.99	(0.96 - 1.01)	0.30
Fat mass, per 1 kg	0.99	(0.96 - 1.03)	0.72
Fat mass index, per 1 kg of muscle mass/m <sup>2</sup>	0.99	(0.92 - 1.06)	0.74
Lean mass, per 1 kg	1.11	(1.05 - 1.18)	<0.01
Lean mass index, per 1 kg of muscle mass/m <sup>2</sup>	1.30	(1.13 - 1.51)	<0.01
Skeletal muscle index, per 1 kg of muscle mass/m <sup>2</sup>	0.91	(0.71 - 1.18)	0.49
Waist circumference, per cm	0.99	(0.97 - 1.03)	0.96
Hip circumference per cm	1.03	(0.99 - 1.06)	0.08

## CONCLUSIONS

- The relationship between adiposity and current asthma varied depending on the body composition measurement. It is still unclear, however, what is the adiposity phenotype most strongly correlated with asthma.
- Our analysis indicates that body composition measures like lean mass and lean mass index should be considered for use in future studies.

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- Wells J, Cole T. Height, adiposity and hormonal cardiovascular risk markers in childhood: how to partition the associations? *Int J Obes* 2014, online March 2014; doi:10.1038/ijo.2014.24.
- Jensen M, Gibson P, Collins C, Wood L. Lean mass, not fat mass, is associated with lung function in male and female children with asthma. *Pediatric Res* 2014; 75(1-1): 93-8.



# Association Between Vitamin D Serum Concentrations And Asthma In A Low-Resource, Peri-Urban Setting In Peru: A Case-Control Analysis



S.L. Pollard, MSPH<sup>1</sup>, N.N. Hansel, MD, MPH<sup>2</sup>, J.J. Lima, PharmD<sup>3</sup>, K.M. Romero, MD<sup>4</sup>, K. Tomaino, RD<sup>2</sup>, G. Malpartida-Guzmán, BS<sup>4</sup>, P.N. Breyse, PhD MHS<sup>1</sup>, D.L. Williams, DrPH<sup>1</sup>, E. Mougey, PhD<sup>3</sup>, C.M. Johnson, BSPH<sup>2</sup>, W. Checkley, MD, PhD<sup>2</sup>

<sup>1</sup>Johns Hopkins Bloomberg School of Public Health, Baltimore, <sup>2</sup>Johns Hopkins School of Medicine, Baltimore, <sup>3</sup>Nemours Children's Center, Jacksonville, <sup>4</sup>A.B. PRISMA, Lima, Perú

## INTRODUCTION

- Vitamin D deficiency has been implicated in the increased incidence of asthma globally.
- Peru has one of the highest asthma burdens worldwide. An estimated 12% of adolescents in our study community have asthma.
- While studies have shown a relationship between vitamin D levels and asthma risk, other studies have shown no effect.
- Few studies have examined this relationship in low- and middle-income countries.
- Our objective was to determine the association between monohydroxy vitamin D<sub>3</sub> [25(OH)D<sub>3</sub>] serum concentrations and asthma risk in a low-resource setting in Peru.

## METHODS

### Overall Study

- Case-control study of 919 children (557 asthma, 362 controls) 9 to 19 years of age in two peri-urban communities of Lima
- Follow-up of children with asthma for six months following end of case-control study

### Study Population

- Sub-sample of 339 children (170 asthma, 169 controls) 9 to 19 years of age in a peri-urban community of Lima
- Case definition:
  - Wheezing in the last 12 months
  - Use of asthma medications in the last 12 months
  - Physician diagnosis of asthma.

### Measurements

- Demographic information including age and sex, anthropometric measurements, history of smoking, and second-hand smoke exposure.
- Serum samples collected in the spring (September – December) of 2012
- We measured 25(OH)D<sub>3</sub> and 25(OH)D<sub>2</sub> concentrations in serum using liquid chromatography-mass spectrometry (LC-MS-MS).

### Statistical analyses

- Multiple linear regression adjusting for confounders.
- We did not include overweight or atopy in regression models because they are likely on the causal pathway of interest.
- Instead we stratified analyses to study effect modification of atopy on the association between 25(OH)D<sub>3</sub> and asthma.

## RESULTS

### Monohydroxy D<sub>3</sub> concentrations in children with and without asthma.

- In Table 1, we display the demographic characteristics between children with and without asthma in the study population.
- In Figure 1, we display the vitamin D concentrations in children with and without asthma.
- Mean 25(OH)D<sub>3</sub> concentrations were 31.0 ng/ml for asthmatics and 36.0 ng/ml for controls (p=0.003).
- All 25(OH)D<sub>2</sub> concentrations were below the limit of detection.
- Percentage deficiency ( $\leq 20$  ng/ml) in 25(OH)D<sub>3</sub> was 9.4% versus 4.7% in asthma versus children without asthma (p=0.09).

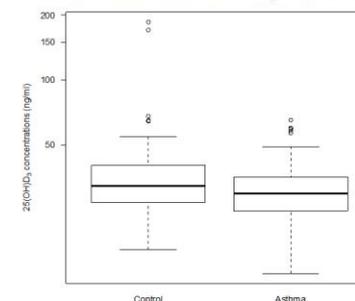
### Multiple logistic regression modeling

- In multiple logistic regression, adjusted odds of asthma increased by 45% for a 10 ng/ml decrease in 25(OH)D<sub>3</sub> levels (OR=1.45, 95% CI 1.14–1.85).
- Adjusted odds of 25(OH)D<sub>3</sub> deficiency was 2.4-fold higher in asthmatics versus controls (OR=2.37, 95% CI 0.96–5.89).
- Decreased vitamin D levels were associated with increased odds of asthma among those with atopy (OR=1.48 per 10 ng/ml decrease, 95% CI 1.12–2.01, p=0.008), but not in those without atopy (OR=1.35, 95% CI: 0.83–2.19, p=0.23).

Table 1. Characteristics of cases and controls

	Cases	Controls	p-value
Age, years	14.0	14.4	0.21
% female	46%	62%	0.003
% with history of smoking	13%	8.4%	0.18
% living with smoker	17%	24%	0.10
% overweight	19%	13%	0.19
% deficient in 25(OH)D <sub>3</sub>	9.4%	4.7%	0.09

Figure 1. 25(OH)D<sub>3</sub> concentrations in children with asthma versus healthy controls



## CONCLUSIONS

- Asthma was inversely associated with 25(OH)D<sub>3</sub> levels, and this effect appears to be limited to those with atopy.
- Future studies should investigate this association prospectively and through randomized trials to provide further evidence for supplementation for asthma prevention and treatment.

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# NUTRITIONAL COMPONENT

(Prepared by Carla Tarazona RD)

- Obtain information about **Dietary Patterns** Intake in children.
- Assessment of **Household Food Security** and relationship with asthma status.
- Development a nutritional software.
- Development & Validation of a Food Frequency Questionnaire.
- HFIAS – Household Food Insecurity Access Scale\* (USAID 2007)

# Preliminary outcomes

- Food Items that hint a protective characteristic

Kiwicha

Maca

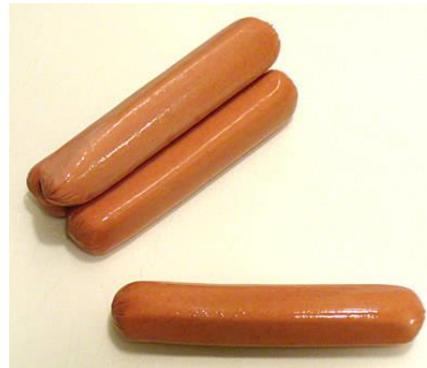
Soy



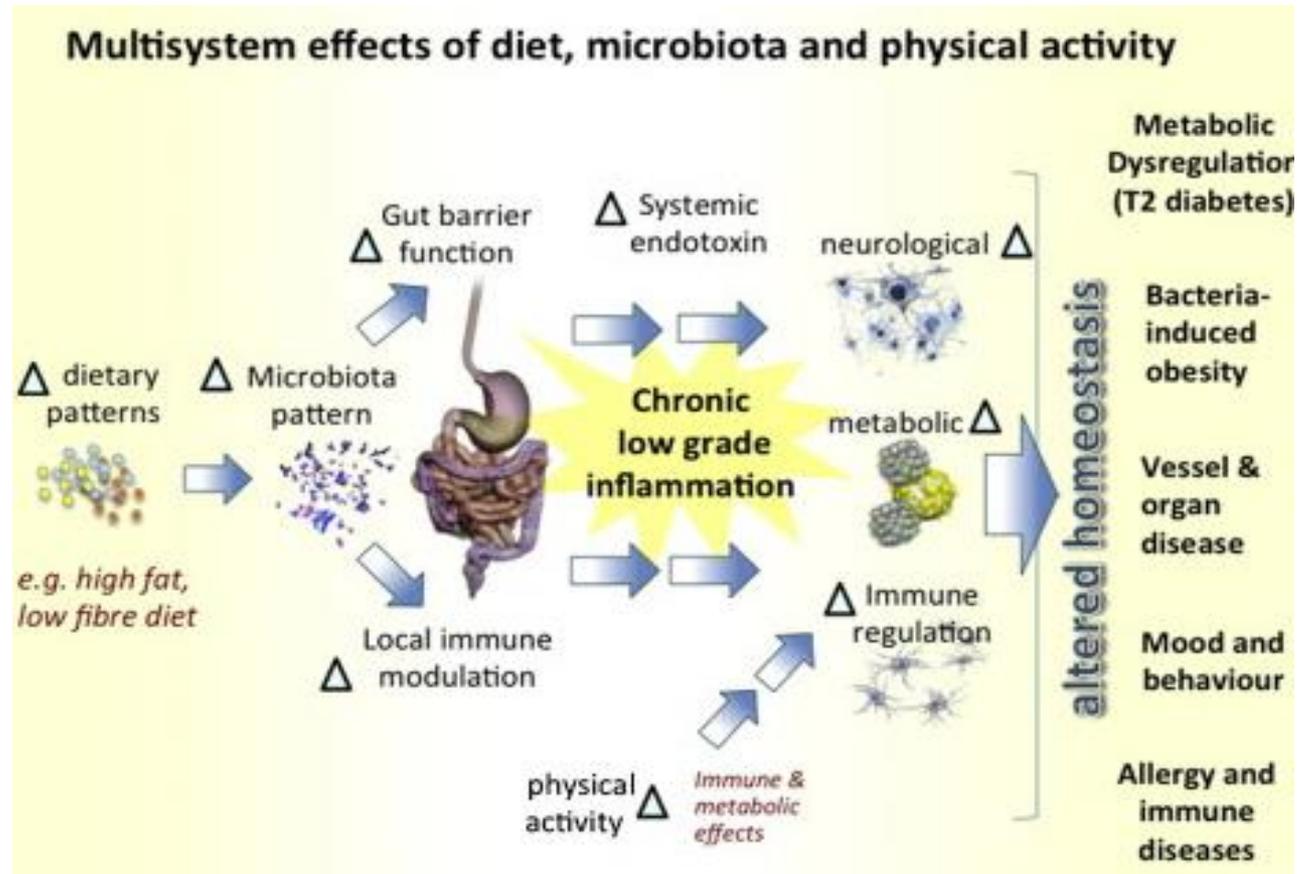
- Food items that hint a characteristic of exacerbation

- Hot dog

- Chips and snacks



# Future directions



-“**Interdisciplinary approach** to assess and promote **immune health** should be an integral part of **NCD prevention**, with a greater focus **early in the life course** before disease processes are established. (Prescott, JACI 2013).

-**Translational research** to avoid gap between basic science and implementation.

# Future directions

- **Metabolomics:** Approach well-suited to study environmental factors on asthma.  
Investigate biochemical profile of asthma-obese phenotype?
- Gut/lung Human **Microbiome: crosstalk?**  
Relationship with allergic diseases?  
Interventions & Longitudinal studies.
- Micronutrients- **Vitamin D** add-on asthma therapy in vitamin-D deficient children receiving ICS

# Future directions & Innovations

*Integrated and effective global health solutions will be realized through synergistic, transdisciplinary and evidence-based research.*

Innovative care constellations that build on patient/community engagement as well as public-private partnerships.



**Drawn by José A ( 9yrs), SJM, 2013**

# Future studies & Innovation

- Qualitative research (in-depth interviews, focus groups) with families affected by asthma, understand perceptions/barriers to treatment. Interview doctors who treat patients in these areas. Medication adherence in asthmatics.
- Cost-effectiveness analysis of asthma treatment.
- Speed up the discovery of new treatments
- Improve self-management
- Identifying key gaps in asthma knowledge (ACT questionnaire)/rapid dissemination of project results/ improve quality of life for people with asthma and Peruvian healthcare systems
- Develop gene-environment interaction research responsive to health disparities, using asthma as a case study.

# Thanks!

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- Patrick Breysse PhD
- Robert Hamilton MD, PhD
- Robert H. Gilman MD, DTM&H



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