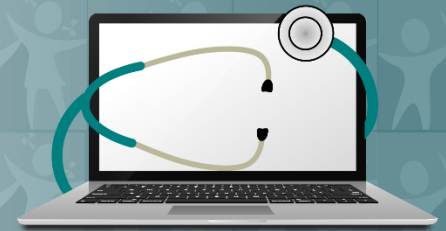




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Pediatric Environmental Health Specialty Units



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Mold, Lead, Mercury



# New findings on air pollution and pregnancy

(Airing differences)

- **Gary Loy, MD MPH Maternal-Fetal Medicine, Rush University Medical College**
- 

## **Full Disclosure of Faculty Financial Interests or Relationships**

I declare no financial interest or other relationship with any manufacturers of any commercial products that may be discussed during this presentation.

- I participated in development of two web-based educational not-for-profit CME offerings “Fresh Air for Mom” and “Healthy Fish Choices”
- I am Obstetrical Advisor to the Pediatric Environmental Health Surveillance Unit (PEHSU - Region V)

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## Objectives

- List the **air pollutants** known to increase risk for adverse pregnancy outcomes
- Describe the *uncertainties* related to the studies on environmental exposures and pregnancy outcomes
- Be able to **counsel** pregnant and pre-conception patients on reducing risk due to air pollutants

# Air Pollution Exposure During Pregnancy

## Outline of A Strategy To Reach The Objectives Of This Webinar

**Background** – possible causes and effects and mechanisms

**Paper review** – preterm birth is not associated with air pollution

**Paper review** – preterm birth is associated with air pollution

Discussion of potential error

**Paper review** – Autism is caused by air pollution

**Paper review** – No it's not

Discussion of potential error

**Paper review** - Disparities in outcomes

Discussion of clinical and public health implications

Conclusions and Recommendations.

## Background: What environmental threats?

### The Faroes Statement: Human Health Effects of Developmental Exposure to Chemicals in Our Environment - 2007

“The periods of embryonic, fetal and infant development are remarkably susceptible to environmental hazards. **Toxic exposures to chemical pollutants during these windows of increased susceptibility can cause disease and disability** in infants, children and across the human lifespan.

Among the effects of toxic exposures recognized in the past have been **spontaneous abortion, congenital malformations, lowered birthweight** and other adverse effects.”

2007 Nordic Pharmacological Society

*Basic & Clinical Pharmacology & Toxicology* **102**73–75

## **Importance of establishing biologic plausibility**

Mechanism identification may suggest likelihood of clinical significance and suggest potential for prevention



## Biologic Plausibility (example...)

Exposures to airborne particulate matter and adverse perinatal outcomes: a biologically plausible mechanistic framework

*Environmental Health Perspectives* 114:1636–1642 (2006). doi:10.1289/ehp.9081 available via <http://dx.doi.org/> [Online 17 August 2006]

*posed framework. The literature indicates that the effects of PM on LBW, PTD, and IUGR may manifest through the cardiovascular mechanisms of oxidative stress, inflammation, coagulation, endothelial function, and hemodynamic responses.*

## Biologic Plausibility and mechanism of fundamental heritable change through fetal environmental exposures

Ross, Michael G., and Mina Desai. Gestational programming: population survival effects of drought and famine during pregnancy. *Am J Physiol Regul Integr Comp Physiol* 288: R25–R33, 2005; doi:10.1152/ajpregu.00418.2004.—The process whereby a stimulus or stress at a critical or sensitive period of development has long-term effects is termed “programming.” Studies in humans and animals convincingly demonstrate that environmental perturbations in utero may permanently change organ structure and metabolism and/or alter homeostatic regulatory mechanisms among the offspring. These programmed changes may be the origins of adult diseases, including cardiovascular disease, obesity, and diabetes. Through-

In summary, gestational programming appears to have contributed to species adaptation and population survival. These developmental responses and processes are still functional in humans and have likely contributed to the current epidemic of hypertension, obesity, and diabetes. A concerted scientific

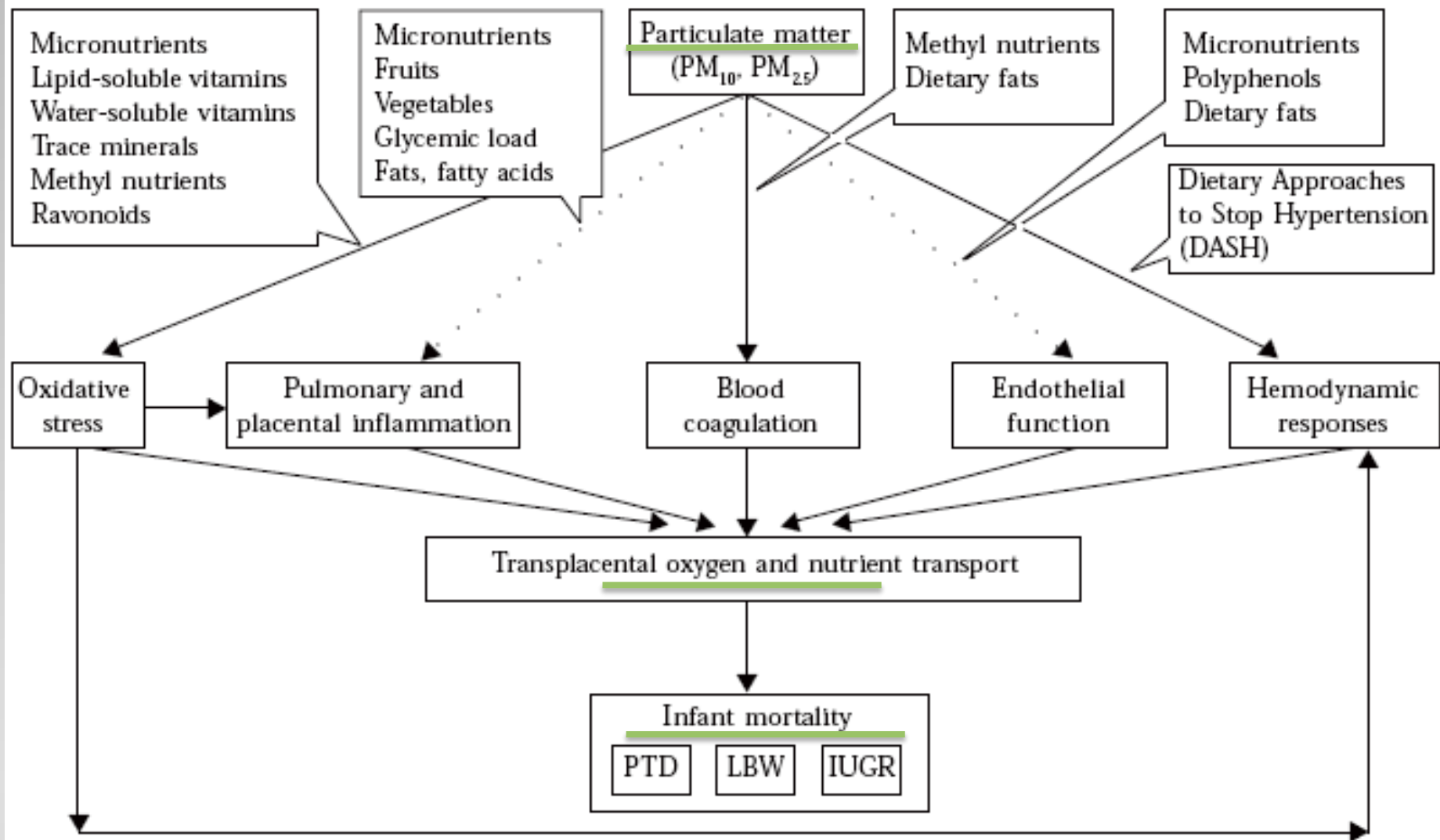
# Air Pollution

Pregnant women exposed to high levels of nitrogen dioxide, carbon monoxide and particulate matter are at an increased risk of experiencing restricted fetal growth and low birthweight. (Preidt 2009)



- An association between air pollution and birth defects and **altered fetal growth and altered parturition is biologically plausible.**
- BUT.... Remember that other environmental and risk factors must be considered and are difficult to rule out during research studies. Some of these may include smoking, maternal health as well as behaviors and other exposures that may be encountered at work and/or during extracurricular activities.

**Figure 1.** Proposed biologic framework for exploring possible effect modification of PM–birth outcomes by maternal nutrition.

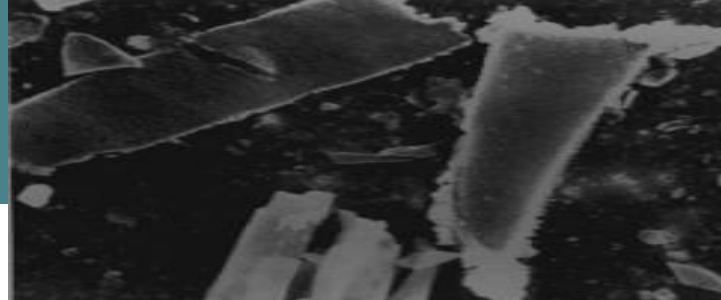


# Exposures and Risk Factors (Air Pollution)

## 4 Common Air Pollutants

- **Carbon monoxide** – found in car exhaust and industrial emissions, as well as in cigarette smoke. It interferes with the blood's ability to absorb and transport oxygen.
- **Ozone** – a byproduct created when other pollutants react in sunny conditions.
- **Nitrogen dioxide** – forms when automobile and industrial emissions combine with oxygen.
- **Particulate matter** – created by combustion from automobiles and industry as well as mechanical processes, such as tire wear.

## Recall particulate matter?



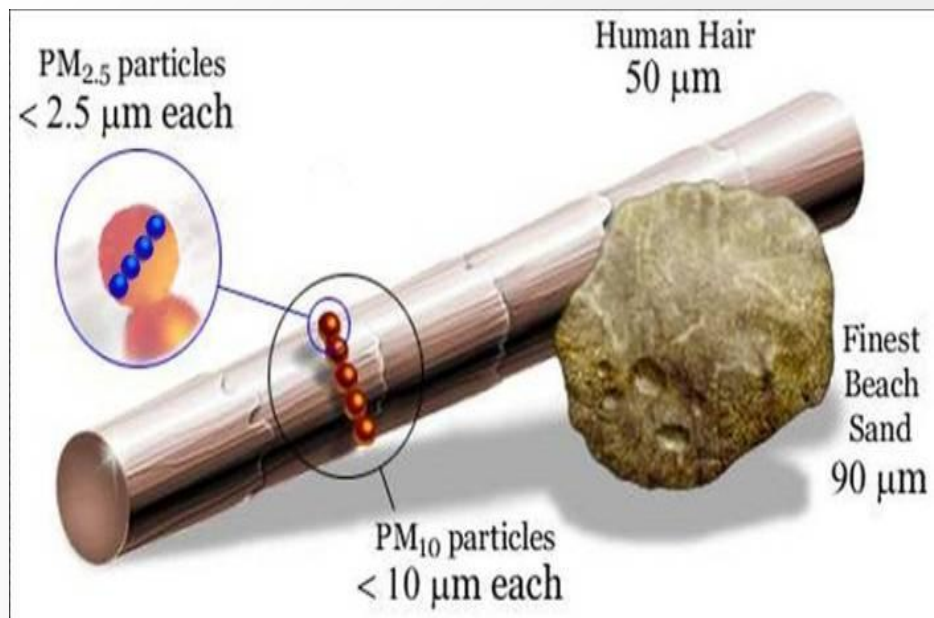
Particulate matter, also known as **particle pollution or PM**, is a complex mixture of extremely small particles and liquid droplets. Particle pollution is made up of a number of components, including acids (such as **nitrates and sulfates**), **organic chemicals**, **metals**, and soil or dust particles (<http://www.epa.gov/pm/>).

PM is characterized according to size largely due to the variation of health effects associated with particles of different diameters.

**Fine particles (PM<sub>2.5</sub>)** are less than 2.5 microns ( $\mu\text{m}$ ) in diameter and are found in smoke haze.

**Coarse particles are (PM<sub>10</sub>)**

<http://www.epa.gov/ne/airquality/pm-what-is.html>



# Particulate Matter

**Sources** of indoor and outdoor particulate matter are derived from both anthropogenic and natural activities.

- **Major sources of PM 2.5 are**: exhaust from cars and trucks (especially those with diesel engines); open burning; wildfires; tobacco smoke; fireplaces and woodstoves; cooking; dust from roads and construction; agricultural operations; and coal and oil-burning boilers, power plants and some industrial processes, including oil refining and pulp and paper production

*(<http://www.epa.gov/ne/airquality/pm-what-is.html>)*

## Background and Context

### What are the most commonly reported Fetal effects from air pollutant exposure?



#### *Decreased placental size and quality*

- Animal studies have suggested that volumes of placental compartments and the calibers of maternal blood spaces were reduced (*Veras 2008*).

#### *Fetal growth delay*

- Studies using ultrasound measurements of fetal growth found strong associations between fetal growth delay and maternal PM exposure during mid-pregnancy (*Hansen 2008*).

#### *Small for Gestational Age (SGA)*

- Fine particulate matter exposure, PM 2.5, is associated with low birthweight, preterm birth, and SGA births (*Shah 2011*).
- Coarse particulate matter exposure, PM10, is associated with SGA births (*Shah 2011*).



### *Low birthweight – preterm birth*

- Exposures of pregnant women to higher levels of certain PM<sub>2.5</sub> chemical constituents originating from sources such as oil combustion and road dust are associated with lower birth weight (*Glinianaia 2004*)

### *Stillbirth*

- Air pollution in Ohio associated with stillbirth, a geospatial cohort study – effect of PM 2.5 (*Defranco 2015*)

### *Patent ductus arteriosus and major defects*

- Recent evidence illustrates a statistically significant association between coarse particulate matter and patent ductus arteriosus (*Strickland 2009, Ritz B 2002*). Various major defects (*Stingone J, et al. Environmental Health Perspectives. volume 122 number 8, August 2014*)

# Major Cardiac Defects

- In a study done by the UCLA School of Public Health using CBDMP [Registry](#) data, it was found that the risk of **birth defects increased** among women exposed to elevated amounts of ozone and carbon monoxide in the second month of pregnancy.
- The second month of pregnancy is when significant heart and organ development occurs. Therefore, it is not surprising to find that women who are exposed to high levels of these two pollutants may have an increased risk of having a child born with a [heart defect](#).
- The study found that some of these heart defects were [conotruncal heart defect](#), [pulmonary artery/valve defect](#) and [aortic artery/valve defect](#). The study did not take into account other prenatal exposures such as smoking, vitamin use and maternal health.

# Error or Potential Errors in Studies on Air Pollution Exposure During Pregnancy

Particulates grossly classified as  $PM_{2.5}$  and grossly measured as a “mass” exposure quantity in  $ug/m^3$  carry along different exposure substances in differing ratios in different regions or countries that vary across time.

Classifying exposure at a specific site does not assure the location of the individual exposed pregnant person for any particular period of time (even if known home address – people do work)

Individuals and cohorts in particular environmental, social and medical contexts differ in their acquired as well as genetic susceptibility to the effect of the exposure

Actual amount of air with a particular toxin level breathed by individuals across pregnancy is hardest to measure. In particular in global studies – indoor air pollution varies widely and by family role.

The definition of or identification of the outcome varies in studies and is inexactly measured (eg. In autism in preterm birth studies) – Even when meticulously measured, the condition that is measured and compared in frequency of occurrence may be measured with variety of different tools.

Study designs vary from population based cohorts (suited to look at multiple outcomes) to case-control studies (best suited to look at multiple exposures), and from prospective to retrospective.

Estimation of  $PM_{2.5}$  has ranged from local monitoring stations data with the assumption of (various) proximity limited inclusion of pregnant subjects, to remote distance assessment and modeling of potential exposure on the ground.

.....Outcome of Preterm Birth

## Preterm Birth Not Associated

### Outdoor Air Pollution, Preterm Birth, and Low Birth Weight: Analysis of the World Health Organization Global Survey on Maternal and Perinatal Health

*Nancy L. Fleischer,<sup>1</sup> Mario Merialdi,<sup>2</sup> Aaron van Donkelaar,<sup>3</sup> Felipe Vadillo-Ortega,<sup>4,5</sup> Randall V. Martin,<sup>3,6</sup> Ana Pilar Betran,<sup>2</sup> João Paulo Souza,<sup>2</sup> and Marie S. O'Neill<sup>7</sup>*

Reference: *Environmental Health Perspectives* • volume 122 | number 4 | April 2014

# Preterm Birth Not Associated

- Study Purpose: We examined whether outdoor PM<sub>2.5</sub> was associated with adverse birth outcomes among 22 countries in the World Health Organization Global Survey on Maternal and Perinatal Health from 2004 through 2008.
- Methodology: Long-term average (2001–2006) estimates of outdoor PM<sub>2.5</sub> were assigned to 50-km-radius circular buffers around each health clinic where births occurred. We used generalized estimating equations to determine associations between clinic-level PM<sub>2.5</sub> levels and preterm birth and low birth weight at the individual level, adjusting for seasonality and potential confounders at individual, clinic, and country levels. Country-specific associations were also investigated. 2004 through 2008.

## Preterm Birth Not Associated

- Key Results: Across all countries, adjusting for seasonality, PM<sub>2.5</sub> was not associated with preterm birth, but was associated with low birth weight [odds ratio (OR) = 1.22; 95% CI: 1.07, 1.39 for fourth quartile of PM<sub>2.5</sub> (> 20.2 µg/m<sup>3</sup>) compared with the first quartile (< 6.3 µg/m<sup>3</sup>)].

**Table 2.** Adjusted ORs (95% CI) for preterm birth and LBW associated with a 10-µg/m<sup>3</sup> increase in PM<sub>2.5</sub> and with quartiles of PM<sub>2.5</sub> (relative to the lowest quartile) after adjusting exposure estimates to account for seasonality, WHO Global Survey on Maternal and Perinatal Health, 2004–2008.

Outcome	Model 1	Model 2
Preterm birth		
PM <sub>2.5</sub> (10 µg/m <sup>3</sup> )	0.96 (0.91, 1.02)	0.96 (0.90, 1.02)
< 6.35	1.0 (Reference)	1.0 (Reference)
6.35 to < 12.32	1.08 (0.95, 1.22)	1.08 (0.95, 1.24)
12.32 to < 22.20	1.05 (0.90, 1.23)	1.06 (0.90, 1.25)
≥ 22.20	0.96 (0.79, 1.17)	0.96 (0.79, 1.18)

All models are GEE models with a logit link. All models were adjusted for mother's age, education, parity, prenatal care, and infant's sex. Model 2 also adjusted for country-level variables GDP per capita, urbanicity, health care expenditure per capita, and Gini coefficient. Models for 10 µg/m<sup>3</sup> PM<sub>2.5</sub> and quartiles of PM<sub>2.5</sub> were run separately. PM<sub>2.5</sub> levels were seasonally adjusted.

## Preterm Birth Not Associated

- Conclusions/Significance: Outdoor PM<sub>2.5</sub> concentrations were associated with low birth weight but not preterm birth. In rapidly developing countries, such as China, the highest levels of air pollution may be of concern for both outcomes.



## Preterm Birth Associated

Exposure to airborne particulate matter during pregnancy is associated with preterm birth: a population-based cohort study

Emily DeFranco<sup>1,2\*</sup>, William Moravec<sup>2</sup>, Fan Xu<sup>3</sup>, Eric Hall<sup>1</sup>, Monir Hossain<sup>4</sup>, Erin N. Haynes<sup>3</sup>, Louis Muglia<sup>1,2</sup> and Aimin Chen<sup>3</sup>

Reference: *DeFranco et al. Environmental Health (2016) 15:6*

# Preterm Birth Associated

- Study Purpose: Test the hypothesis that exposure to fine particulate matter in the air (PM<sub>2.5</sub>) is associated with increased risk of preterm birth (PTB).
- Methodology: Geo-spatial population-based cohort study, using live birth records from Ohio (2007–2010) linked to average daily measures of PM<sub>2.5</sub>, recorded by 57 EPA network monitoring stations across the state. Geographic coordinates of the home residence for births were linked to the nearest monitoring station using ArcGIS. Association between PTB and high PM<sub>2.5</sub> levels (above the EPA annual standard of 15 µg/m<sup>3</sup>) was estimated using GEE, with adjustment for age, race, education, parity, insurance, tobacco, birth season and year, and infant gender.

## Preterm Birth Associated

- Key Results: Pregnancies with high PM<sub>2.5</sub> exposure through pregnancy had increased PTB risk even after adjustment for coexisting risk factors, adjOR 1.19 (95 % CI 1.09–1.30). Assessed per trimester, high 3rd trimester PM<sub>2.5</sub> exposure resulted in the highest PTB risk, adjOR 1.28 (95 % CI 1.20–1.37).

**Table 3** Preterm birth rate by PM<sub>2.5</sub> levels in Ohio 2007 – 2010 and trimester of exposure in pregnancy

	PM <sub>2.5</sub> < 15 µg/m <sup>3</sup>		PM <sub>2.5</sub> ≥ 15 µg/m <sup>3</sup>		p-value
	n	% Preterm	n	% Preterm	
First trimester	175,649	8.34	49,272	8.87	<0.001
Second trimester	185,883	8.47	39,038	8.43	0.835
Third trimester	181,665	8.08	43,256	10.05	<0.001
Entire pregnancy	200,259	8.27	24,662	9.99	<0.001

% preterm represents the rate of birth <37 weeks of gestational age among the study cohort of singleton non-anomalous live births

## Preterm Birth Associated

Conclusions/Significance: Exposure to high levels of particulate air pollution, PM2.5, in pregnancy is associated with a 19 % increased risk of PTB; with greatest risk with high 3rd trimester exposure. Although the risk increase associated with high PM2.5 levels is modest, the potential impact on overall PTB rates is robust as all pregnant women are potentially at risk.

# Error or Potential Error - Differences in the Studies On Preterm Birth

*Key study differences and comparisons:*

Defranco\_”yes” study – on ground monitoring station exposure estimates, vs the remote sensing data observation and modeling and retro-time fitting information in the Fleischer global population “no” study.

Potential next steps: just believe the local monitoring and birth address data.

.....Outcome of Autism

## Autism Associated

### Autism Spectrum Disorder and Particulate Matter Air Pollution before, during, and after Pregnancy: A Nested Case–Control Analysis within the Nurses' Health Study II Cohort

Raanan Raz,<sup>1</sup> Andrea L. Roberts,<sup>2</sup> Kristen Lyall,<sup>3,4</sup> Jaime E. Hart,<sup>1,5</sup> Allan C. Just,<sup>1</sup> Francine Laden,<sup>1,5,6</sup> and Marc G. Weisskopf<sup>1,6</sup>

Reference: *Environmental Health Perspectives* • volume 123 | number 3 | March 2015

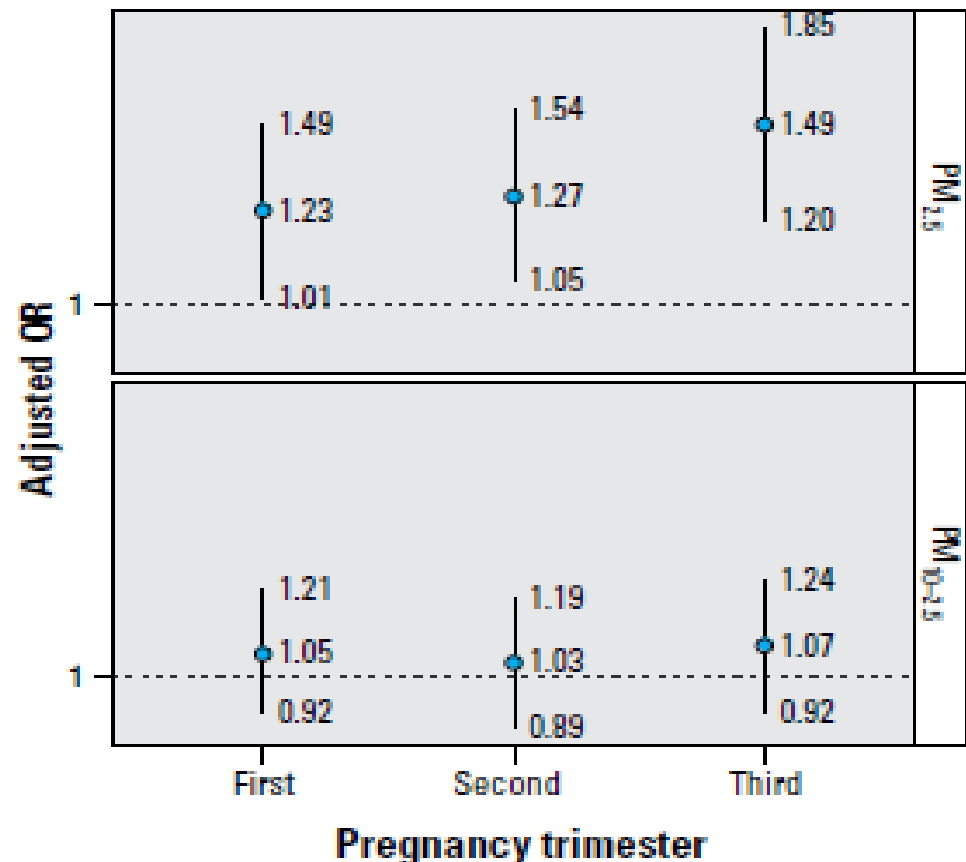
# Autism Associated

- Study Purpose: We explored the association between maternal exposure to particulate matter (PM) air pollution and odds of ASD in her child.
- Methodology: We conducted a nested case–control study of participants in the Nurses' Health Study II (NHS II), a prospective cohort of 116,430 U.S. female nurses recruited in 1989, followed by biennial mailed questionnaires. Subjects were NHS II participants' children born 1990–2002 with ASD (n = 245), and children without ASD (n = 1,522) randomly selected using frequency matching for birth years. Diagnosis of ASD was based on maternal report. Exposures: Monthly averages of PM with diameters  $\leq 2.5 \mu\text{m}$  (PM<sub>2.5</sub>) and 2.5–10  $\mu\text{m}$  (PM<sub>10–2.5</sub>) were predicted from a spatiotemporal model for the continental United States and linked to residential addresses.



## Autism Associated

- Key Results: PM<sub>2.5</sub> exposure during pregnancy was associated with increased odds of ASD, with an adjusted odds ratio (OR) for ASD per interquartile range (IQR) higher PM<sub>2.5</sub> (4.42  $\mu\text{g}/\text{m}^3$ ) of 1.57 (95% CI: 1.22, 2.03) among women with the same address before and after pregnancy (160 cases, 986 controls).



**Figure 2.** ORs for ASD with exposure to particulate matter during pregnancy trimesters. ORs are adjusted for child sex, year of birth, month of birth, maternal age at birth, paternal age at birth, and census income. The analyses are limited to nonmovers only (i.e., those for whom prepregnancy and postpregnancy addresses were the same). Cases,  $n = 160$ , controls  $n = 986$ .

## Autism Associated

- Conclusions/Significance: Higher maternal exposure to PM<sub>2.5</sub> during pregnancy, particularly the third trimester, was associated with greater odds of a child having ASD.

# Autism Not Associated

## Air Pollution Exposure during Pregnancy and Childhood Autistic Traits in Four European Population-Based Cohort Studies: The ESCAPE Project

*Mònica Guxens,<sup>1,2,3,4</sup> Akhgar Ghassabian,<sup>4,5</sup> Tong Gong,<sup>6</sup> Raquel Garcia-Esteban,<sup>1,2,3</sup> Daniela Porta,<sup>7</sup> Lise Giorgis-Allemand,<sup>8,9</sup> Catarina Almqvist,<sup>6</sup> Aritz Aranbarri,<sup>10,11</sup> Rob Beelen,<sup>12</sup> Chiara Badaloni,<sup>7</sup> Giulia Cesaroni,<sup>7</sup> Audrey de Nazelle,<sup>1,2,3,13</sup> Marisa Estarlich,<sup>3,14</sup> Francesco Forastiere,<sup>7</sup> Joan Forns,<sup>1,2,3,15</sup> Ulrike Gehring,<sup>12</sup> Jesús Ibarluzea,<sup>3,11,16</sup> Vincent W.V. Jaddoe,<sup>5,17,18</sup> Michal Korek,<sup>19</sup> Paul Lichtenstein,<sup>6</sup> Mark J. Nieuwenhuijsen,<sup>1,2,3</sup> Marisa Rebagliato,<sup>3,14,20</sup> Rémy Slama,<sup>8,9</sup> Henning Tiemeier,<sup>4,18,21</sup> Frank C. Verhulst,<sup>4</sup> Heather E. Volk,<sup>22,23,24</sup> Göran Pershagen,<sup>19</sup> Bert Brunekreef,<sup>12,25</sup> and Jordi Sunyer<sup>1,2,3,26</sup>*

Reference: *Environmental Health Perspectives* • volume 124 | number 1 | January 2016

# Autism Not Associated

- Study Purpose: We aimed to assess whether prenatal air pollution exposure is associated with childhood autistic traits in the general population.
- Methodology: Ours was a collaborative study of four European population-based birth/child cohorts— CATSS (Sweden), Generation R (the Netherlands), GASPII (Italy), and INMA (Spain). Nitrogen oxides (NO<sub>2</sub>, NO<sub>x</sub>) and particulate matter (PM) with diameters of  $\leq 2.5 \mu\text{m}$  (PM<sub>2.5</sub>),  $\leq 10 \mu\text{m}$  (PM<sub>10</sub>), and between 2.5 and 10  $\mu\text{m}$  (PM<sub>coarse</sub>), were estimated for birth addresses by land-use regression models based on monitoring campaigns performed between 2008 and 2011. Levels were extrapolated back in time to exact pregnancy periods. [Outcome measure] - We quantitatively assessed autistic traits when the child was between 4 and 10 years of age. Children were classified with autistic traits within the borderline/clinical range and within the clinical range using validated cut-offs.

## Autism Not Associated

- Key Results: A total of 8,079 children were included. Prenatal air pollution exposure was not associated with autistic traits within the borderline/clinical range (odds ratio = 0.94; 95% CI: 0.81, 1.10 per each 10- $\mu\text{g}/\text{m}^3$  increase in  $\text{NO}_2$  pregnancy levels).

**Table 3.** Fully adjusted combined associations<sup>a</sup> between air pollution during pregnancy<sup>b</sup> and autistic traits within the borderline/clinical range.

Pollutant	Autistic traits within the borderline/clinical range				Autistic traits within the clinical range			
	<i>n</i> <sup>c</sup>	OR (95% CI)	<i>p</i> -Heter	<i>I</i> <sup>2</sup>	<i>n</i> <sup>c</sup>	OR (95% CI)	<i>p</i> -Heter	<i>I</i> <sup>2</sup>
$\text{NO}_2$ (per $\Delta 10 \mu\text{g}/\text{m}^3$ )	6	0.95 (0.81, 1.10)	0.431	0.00%	4	0.87 (0.67, 1.14)	0.955	0.00%
$\text{NO}_x$ (per $\Delta 20 \mu\text{g}/\text{m}^3$ )	6	0.98 (0.88, 1.09)	0.438	0.00%	4	0.93 (0.78, 1.11)	0.640	0.00%
$\text{PM}_{10}$ (per $\Delta 10 \mu\text{g}/\text{m}^3$ )	4	0.90 (0.68, 1.19)	0.419	0.00%	3	0.92 (0.55, 1.54)	0.368	0.00%
$\text{PM}_{2.5}$ (per $\Delta 5 \mu\text{g}/\text{m}^3$ )	4	0.71 (0.37, 1.37)	0.052	61.24%	3	1.01 (0.63, 1.63)	0.472	0.00%
$\text{PM}_{\text{coarse}}$ (per $\Delta 5 \mu\text{g}/\text{m}^3$ )	4	0.96 (0.72, 1.28)	0.300	18.16%	3	0.87 (0.55, 1.38)	0.320	12.33%
$\text{PM}_{2.5}$ absorbance (per $\Delta 10^{-5} \text{m}^{-1}$ )	4	0.82 (0.57, 1.18)	0.244	27.95%	3	0.70 (0.44, 1.12)	0.899	0.00%
Traffic intensity on the nearest road (per $\Delta 5,000 \text{ mv}/\text{day}$ )	3	1.00 (0.92, 1.09)	0.721	0.00%	3	0.98 (0.85, 1.14)	0.508	0.00%
Total traffic load on all major roads within 100-m buffer (per $\Delta 4,000,000 \text{ mv}/\text{day} \times \text{m}$ )	5	1.02 (0.89, 1.16)	0.752	0.00%	3	0.90 (0.70, 1.16)	0.691	0.00%

## Autism Not Associated

- Conclusions/Significance: Prenatal exposure to NO<sub>2</sub> and PM was not associated with autistic traits in children from 4 to 10 years of age in four European population-based birth/child cohort studies.

# Error or Potential Error- Differences in the Studies On Autism

*Key study differences and comparisons:*

Outcome measures may be identifying a different condition; also exposure methodology assessments different (because the ASD was classified as yes at a particular score – the study inundated with borderline cases). The “yes” study identified autism as a diagnosis – probably more severely affected group . The level of exposure in the “no” study was less than in the “yes” study.

Potential next steps: *Quoted from EHP ( Environmental Health Perspectives • volume 124 | number 1 | January 2016 )* Mònica Guxens, [author of the “no” study] is an assistant research professor at the Centre for Research in Environmental Epidemiology in Barcelona.

“I do not think that ASDs are different in Europe than in the U.S., but the best way to check what is going on here is to try to replicate the U.S. studies in Europe following a similar study design.”

*Loy editorial – sure this is a good idea, but really the studies measured something different using different methodology.*

# Mechanism Investigation Through Epi

Time to air another difference – that of disparity

Utility: Study of differential influence of PM by Race/Ethnicity may elucidate mechanisms, may be hypothesis generating.



## Disparity in Physiological Effect

# Ambient Air Pollution and Newborn Size and Adiposity at Birth: Differences by Maternal Ethnicity (the Born in Bradford Study Cohort)

Anna Schembari, Kees de Hoogh, Marie Pedersen, Payam Dadvand, David Martinez, Gerard Hoek, Emily S. Petherick, John Wright, and Mark J. Nieuwenhuijsen

Reference: *Environ Health Perspect* doi: 10.1289/ehp.1408675

# Disparity in Physiological Effect

## Introduction

In order to investigate **ethnic differences in the association between ambient air pollution and newborn's size**, pregnancy women were recruited, n=9,067 divided between 4,189 White (46%) and 4,878 Pakistani (54%).

2007-2010, Bradford cohort study in England

# Disparity in Physiological Effect

## Method – outcomes

Multivariate linear regression models:

- Effect modification by maternal ethnicity (white British vs Pakistani origin) on the associations of air pollution and birthweight, head circ., skin fold thickness.

(covariates included self reported ethnicity, pregnancy, morphologic, demographic components, maternal glucose tolerance. Interaction term included between ethnicity and air pollution in the models, also stratified by period of exposure during pregnancy)

# Disparity in Physiological Effect

**Results** - relating to 1.BIRTHWEIGHT and 2. ADIPOSITY

Ambient air pollution and BIRTHWEIGHT

**A 5 ug/m<sup>3</sup> increase in mean 3<sup>rd</sup> trimester PM<sub>2.5</sub> was associated with significantly lower birthweight and smaller head circumference .....**

In children of White British mothers

-43g; [95% CI -76;-10] Birthweight,

**Not in children of Pakistani origin**

9g; [95% CI -17;35] Birthweight

# Disparity in Physiological Effect

## Results

HOWEVER.....

Associations of the outcomes with  $\text{NO}_2$  and  $\text{NO}_x$  were mostly non-significant in both ethnic groups. And note that British White mothers were more likely to have a BMI over  $25\text{kg/m}^2$

# Disparity in Physiological Effect

## Discussion – Significance

**Importance:** Low birthweight impacts on neonatal and long term physical and intellectual morbidities

Adiposity impacts on obesity and occurrence of insulin resistance, diabetes, and cardiovascular disease

Ethnic variation to similar exposures suggests **differential impact on potentially vulnerable populations**

**Speculation:** Exposure may be preventable .

# Implications for Practice (and for ACTION)

- **Detect** environmental threats in the lives/households of your patients  
Suggestions for screening? THEN WHAT ????
- **Educate** patients regarding potential threats – resources include  
EPA publications – make available in the office  
Community/ patient population awareness – web info at every fingertip
- Who to ask for Resources – questions – **ask PEHSU** your friendly neighborhood  
(Region V) PEHSU. THEN WHAT ???????
- **Mitigate impact** of exposures through recommendation of behavioral changes, patient level action.
- **Protect the immediate environment** – improve air quality - individual action.....

## OFFICE based ACTION - Preconception Visit

- Environmental Exposure Questionnaire

*Huffling, K (Adapted from Davis 2007).*

- Discuss interventions
- Consult as necessary  
Pediatric Environmental Health Specialty Units  
( PEHSU's )

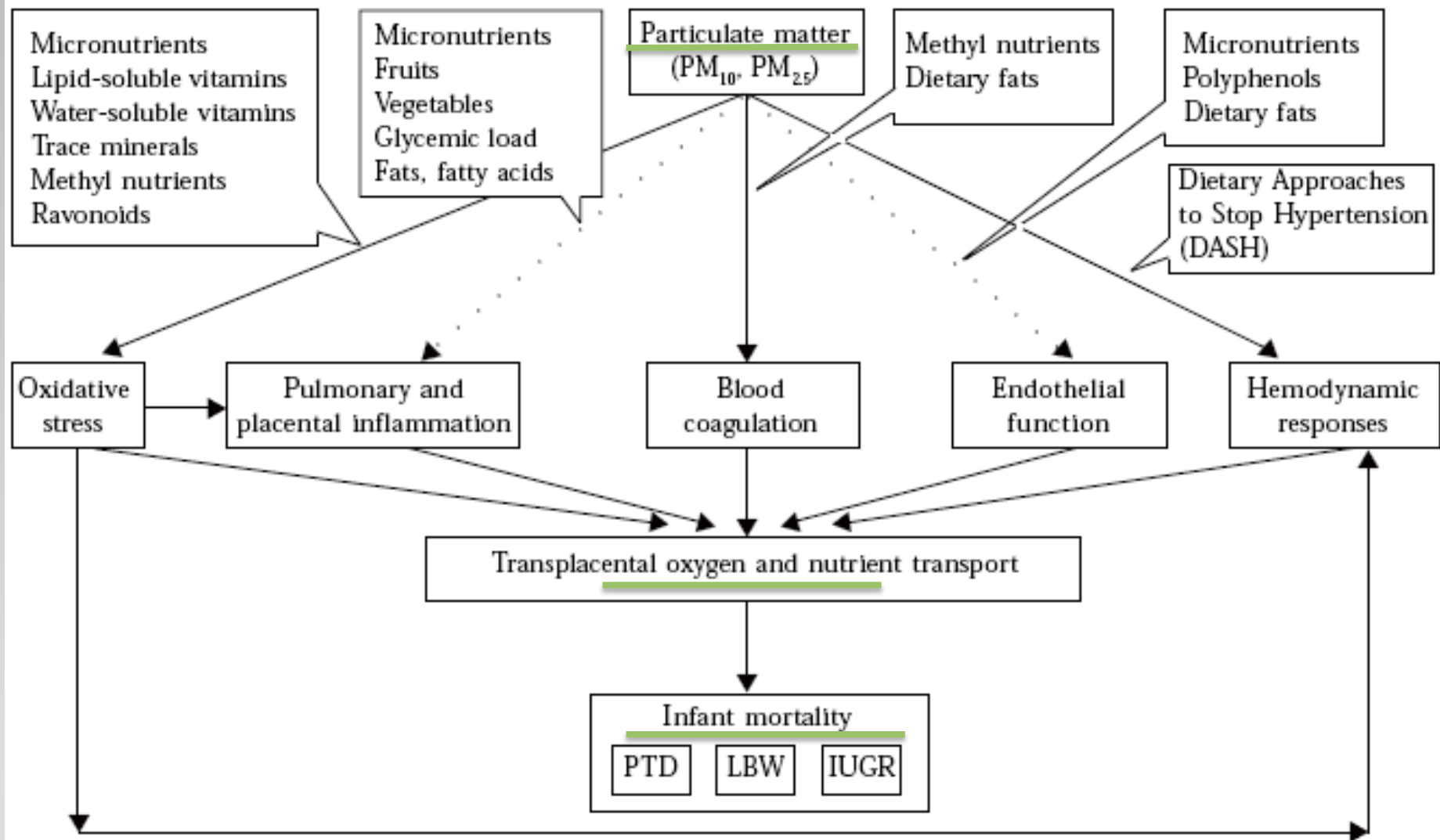


## Implications for Practice (and for ACTION) - INDIVIDUAL DEFENSE – a mechanistic framework

Recall the slide of the onslaught of PM 2.5 and multiple effect pathways

Specific individual dietary behavioral advice is reasonable

**Figure 1.** Proposed biologic framework for exploring possible effect modification of PM–birth outcomes by maternal nutrition.



## Implications for Practice

### (and for ACTION) - INDIVIDUAL DEFENSE – a mechanistic framework

***Reasonable Specific individual dietary behavioral advice based on most consistently proposed and supported mechanism of biological effect of PM – oxidative stress, inflammatory subcellular and tissue inflammation:***

- Assure vitamin pre-conceptional supplementation - “fat-soluble carotenoids and vitamin E, water-soluble vitamin C80, and methyl nutrients including the B vitamins pyridoxine (B6), cyanocobalamin (B12), and folate. Carotenoids may protect against oxidant damage.”
- Assure adequate folate through supplementation – coagulation balance support as well as mechanisms as yet certainly determined to reduce fetal anomaly.
- Dietary awareness and counsel – Food diary and cultural assessment - Reduce trans- and - saturated fatty acids and increasing omega-3 fatty acids ( choose healthy Fish) are also associated with a reduced inflammatory status.
- Support endothelial function through Micronutrient antioxidants - representing  $\beta$ -carotene subfractions derived from vegetables and fruits – a balanced, portioned diet.

*quotes from : Ciência & Saúde Coletiva, 12(6):1591-1602, 2007*

## Implications for Practice

### (and for ACTION) - INDIVIDUAL DEFENSE – a mechanistic framework

- Encourage a DASH diet – “The favorable effects of fruits and vegetables, low-fat dairy products, and reduced sodium suggested by Dietary Approaches to Stop Hypertension (DASH) indicate the possible role for micronutrients in reducing the risk for pre-pregnancy hypertension. Several mechanisms of polyphenols have been researched, including their antioxidant functions.”
- Eat more fruits and vegetables: “Fruits and vegetables contain a myriad of different components of varying antioxidant capacity, thus offering a range of possibilities for altering PM induced oxidative effects. Based on the NHANES III findings, grain consumption is inversely associated with an elevated CRP concentration.
- And finally, keep encouraging use of olive oil, mushrooms, cruciferous vegetables, and nuts - “ associated with a favorable homocysteine profile. Adding vegetables may reverse the PM induced increases inflammatory response. High intakes of refined grains, and processed meat and low consumption of cruciferous and yellow vegetables may exacerbate the inflammatory processes. “

*quotes from : Ciência & Saúde Coletiva, 12(6):1591-1602, 2007*

# How to reduce exposure from PM pollution?

*Considering that we have limited or expensive options to choose our air or change it, these are less optimal or universally applicable interventions*

- The American Lung Association recommends three steps to protect yourself indoors: Use a heat recovery ventilator or an energy recovery ventilator to quietly provide the fresh filtered air you need while quietly removing stale polluted air.
- Seal leaks in the building shell to block entry of unfiltered outdoor air during the heating and air conditioning seasons. NOTE: Sealing leaks also blocks entry of dust and insects.
- Use space and water heating systems that cannot put combustion gasses into the building interior. AND JUST STAY IN on bad days
- Individuals can contribute to cleaner air by personal choices - choosing cleaner sources of energy and using energy more efficiently. For instance, carpooling or taking public transportation, maintaining automobile emissions controls on one's cars, walking or biking to work or school can make a difference. Limiting the use of fireplaces (use seasoned wood) or wood and coal burning stoves, and seeking out more efficient heating and cooling systems can also contribute to cleaner air.
- What about WHOLE COMMUNITIES at risk???

## ACTION we can take as a group – potentially affecting over-exposed cohorts

- Advocacy – patient level through screening practices in your institutions and offices:  
Develop simple, efficient, patient-centered process to understand your patients' environmental threats (self-report/survey/waiting room activities)
- Advocacy- community level through capacity building within interested groups of patients and community leaders  
Determine “who cares” in your patients' communities  
Partner with concerned community organizations (Little Village Environmental Justice Organization in Pilsen here in Chicago)
- Advocacy – policy level through support of ACOG SMFM initiatives to respond to environmental threats
- Continue at policy level to support recent efforts to add obstetricians to the working panels of docs in the federally supported regional PEHSU's

# Call to ACTION

- Participate – through projects and collaborations, build new knowledge of level of effects and successes of interventions
- Join the ACOG / SMFM interest groups/ communities – create new ideas
- Get involved in local community-based initiatives that foster patient level, community institutional level cooperation to gather information, interpret results and plan for action
- Take the opportunity to Learn More – EPA/CREHM web-based education
- Recognize that different environments, different populations, present different problems, and combine to create disparity in health outcomes.

## Parting Thoughts:

“An important outcome of pregnancy is no longer just a healthy newborn but a human being biologically predisposed to be healthy from birth to old age.”

On Exposure to Toxic Environmental Agents  
ACOG/ASRM



Thank you



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Toxic environmental chemicals: the role of the reproductive health professional

[http://prhe.ucsf.edu/prhe/clinical\\_resources.html](http://prhe.ucsf.edu/prhe/clinical_resources.html)

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