

# TÓXICOS AMBIENTALES, REPRODUCCIÓN Y COMPLICACIONES OBSTÉTRICAS

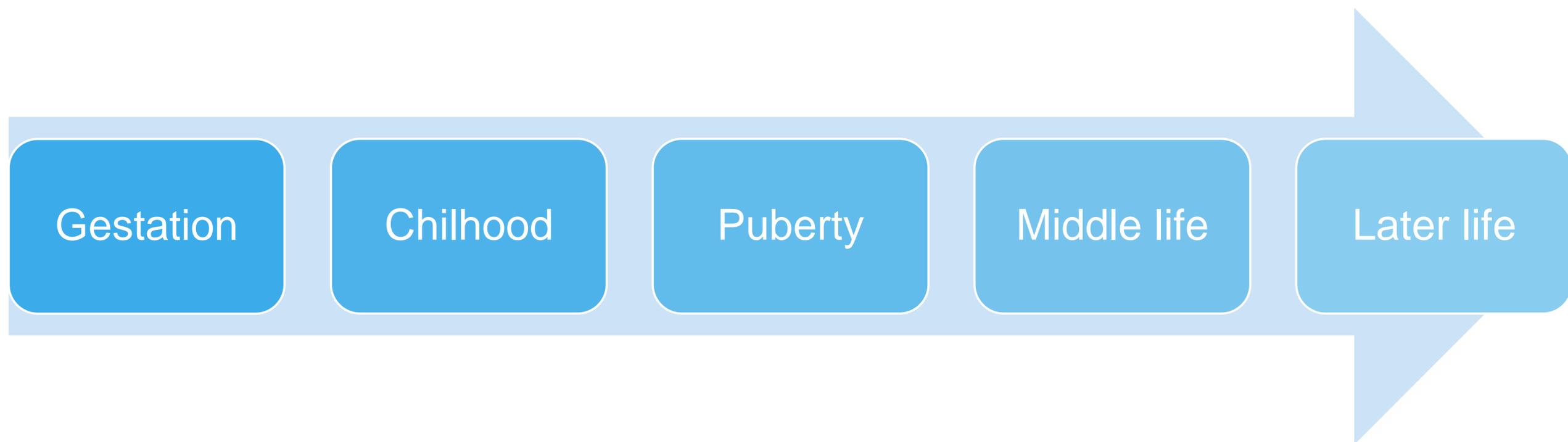
**BCNatal** | Centre Medicina Maternofetal i Neonatal de  
Barcelona

Hospital Sant Joan de Déu - Hospital Clínic  
Universitat de Barcelona

# Contaminantes ambientales

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La exposición preconcepcional y prenatal: influencia en la salud a lo largo de la vida



# Influencia ambiental

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## Gestación

Fertilidad

Pérdidas fetales

Anomalías congénitas

Parto pretérmino

Crecimiento fetal

## Infancia

Respiratorio

Neurodesarrollo

Salud reproductiva

Cáncer

Stillerman KP. *Reprod Sci* 2008

Windham G. *Fertil Steril* 2008

Slama R. Cambridge University Press; 2010

# Parto pretérmino

## REVIEW



### What contributes to disparities in the preterm birth rate in European countries?

*Marie Delnord, Béatrice Blondel, and Jennifer Zeitlin*

#### KEY POINTS

- Medical practices and policies related to subfertility treatments and indicated preterm deliveries have a clear impact on country-level preterm birth rates and trends.
- Recent studies confirmed the role of many potentially modifiable population factors – BMI, smoking, and environmental exposures – in determining preterm birth risk.
- It is important to rule out gestational age measurement artifacts.



European Commission's revised proposal limits ability to protect public from endocrine-disrupting chemicals

**INTERNATIONAL FEDERATION OF GYNECOLOGY & OBSTETRICS**  
**Recommendations for Preventing Exposure to Toxic Chemicals**

Advocate for policies to prevent exposure to toxic environmental chemicals

Work to ensure a healthy food system for all

Make environmental health part of health care

Champion environmental justice

**World Health Organization** **UNEP**  
 United Nations Environment Programme

State of the Science of  
**Endocrine Disrupting Chemicals**  
 2012

Summary for Decision-Makers

Edited by  
 Ake Bergman  
 Jerrold J. Heindel  
 Susan Jobling  
 Kai R. T.

**HEALTH COSTS IN THE EUROPEAN UNION**  
 HOW MUCH IS RELATED TO EDCS?

**HEAL**  
 Health Economics and Environmental Assessment of Endocrine-Disrupting Chemicals

**AUTISM**  
**DIABETES**  
**BREAST CANCER**  
**OBSESITY**  
**PROSTATE CANCER**  
**INFERTILITY**

Phthalates  
 BPA  
 Non-stick coatings  
 Parabens  
 Pesticides



**AIM DECLARATION ON ENDOCRINE DISRUPTING COMPOUNDS**

Time to grab the chance to protect European citizens' health from EDCs

Contents lists available at ScienceDirect

**International Journal of Gynecology and Obstetrics**

www.igo.org journal homepage: www.elsevier.com/locate/ijgo

SPECIAL COMMUNICATION

International Federation of Gynecology and Obstetrics opinion on reproductive health impacts of exposure to toxic environmental chemicals☆

Gian Carlo Di Renzo<sup>a</sup>, Jeanne A. Conry<sup>b</sup>, Jennifer Blake<sup>c</sup>, Mark S. DeFrancesco<sup>b</sup>, Nathaniel DeNicola<sup>b</sup>, James N. Martin Jr.<sup>b</sup>, Kelly A. McCue<sup>b</sup>, David Richmond<sup>d</sup>, Abid Shah<sup>d</sup>, Patrice Sutton<sup>e</sup>, Tracey J. Woodruff<sup>e,\*</sup>, Sheryl Ziemer van der Poel<sup>f</sup>, Linda C. Giudice<sup>g</sup>



- Profesionales de la salud
- Salud ambiental /salud publica



# SUSTANCIAS QUÍMICAS



# Químicos y metales pesados

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Pueden pasar a formar parte del **ambiente fetal**



La exposición fetal es **difícil de medir** directamente



Se pueden **bioacumular en el feto**



**Variabilidad genética**

# S. Químicas

## Neurodesarrollo

LBW/FGR

Reproductivo, tiroides, PE

Malformaciones congénitas



<b>PCBs</b>	Decreased semen quality
	Low birth weight
	Development of attention deficit– hyperactivity disorder– associated behavior
	Reduced intelligence quotient
<b>PFAS</b>	Pregnancy-induced hypertension and preeclampsia
	Reduced birthweight
	Reduced fetal growth
	Increased risk for thyroid disease in children
<b>PBDEs</b>	Impaired neurodevelopment
	Reduction in sustained attention and fine manipulative abilities
<b>Phenols</b>	Female reproductive toxicity (e.g., recurrent miscarriage)
	Aggression and hyperactivity in female children
	Impaired behavioral regulation (anxious, depressive, and hyperactive behaviors) in girls aged 3 y
	Reduced neonatal thyroid-stimulating hormone in boys
	Decreased thyroxine concentrationsa
<b>Phthalates</b>	Shortened gestational age
	Male reproductive tract development (reduced anogenital distance)
	Impaired neurodevelopment
	Reduction in executive function at age 4–9 y
<b>Perchlorate</b>	Altered thyroid function in newborns
	Wang. Environmental
<b>Pesticides</b>	Impaired fetal growth
	Impaired neurodevelopment: increased risk of pervasive developmental disorder at age 2 y, increase in attention problems and attention deficit hyperactivity disorder behaviors at age 3 y, and reduction in working memory capabilities and intelligence quotient at age 7 y
	Increased susceptibility to testicular cancer
	Childhood cancers (leukemia and brain tumor)
<b>Solvents</b>	Spontaneous abortion and fetal loss
	Decreased fetal and birthweight
	Congenital malformations

# Metales pesados



The American College of  
Obstetricians and Gynecologists  
WOMEN'S HEALTH CARE PHYSICIANS

## COMMITTEE OPINION

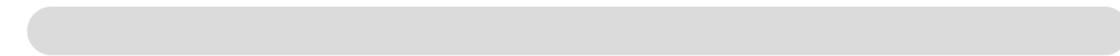
### Neurodesarrollo



LBW/FGR



Reproductivo, tiroides, PE



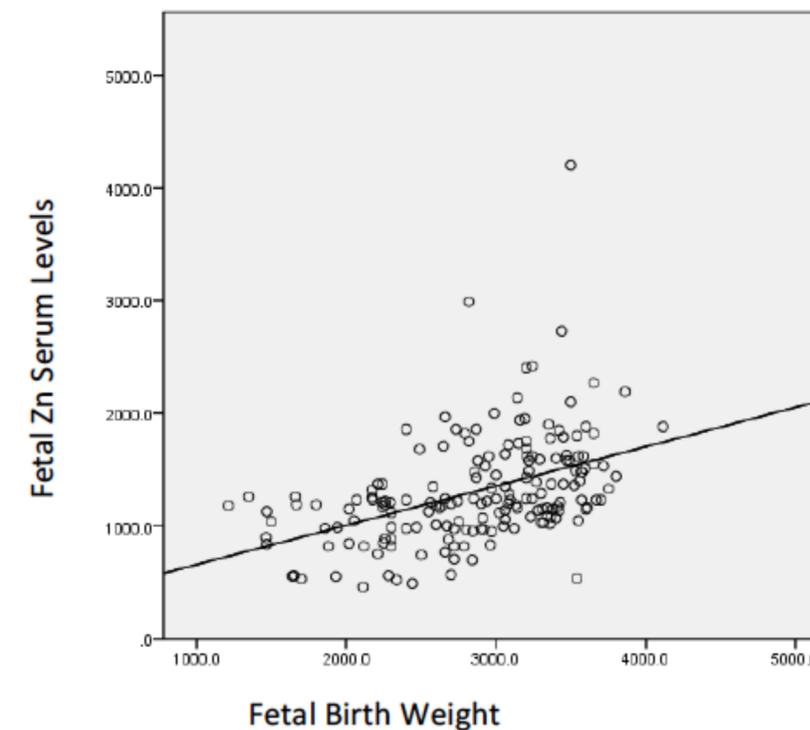
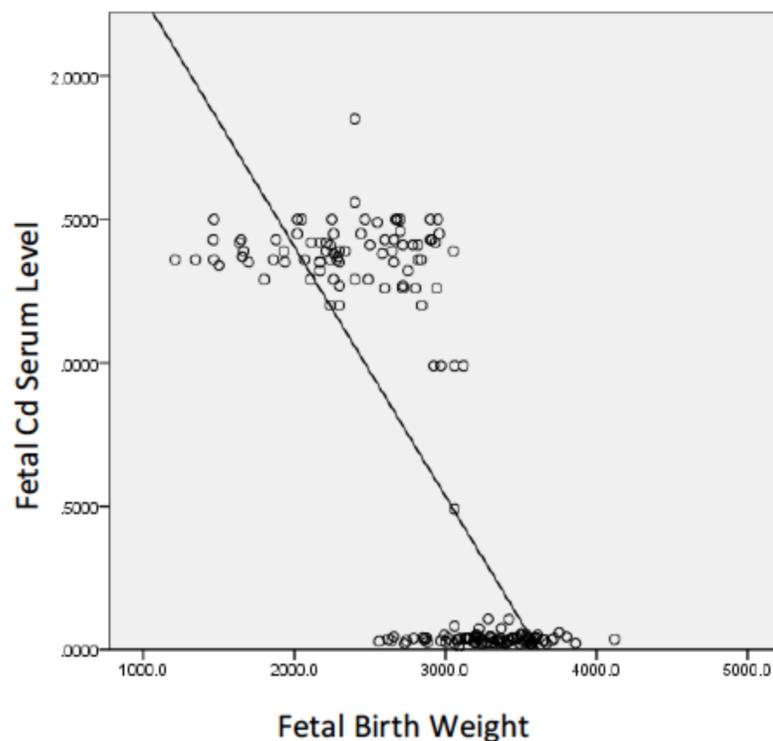
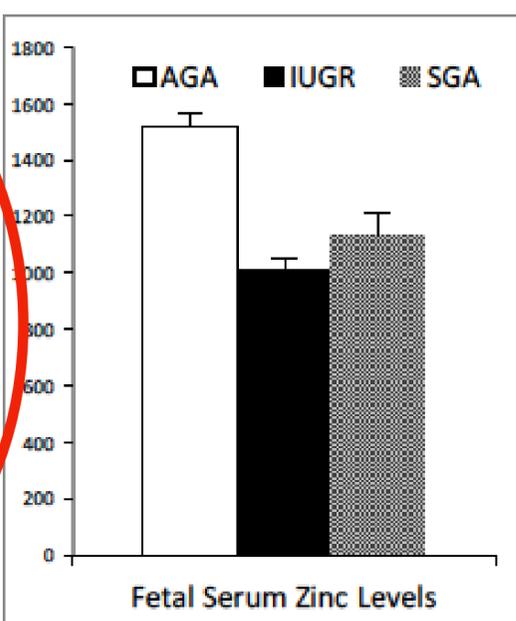
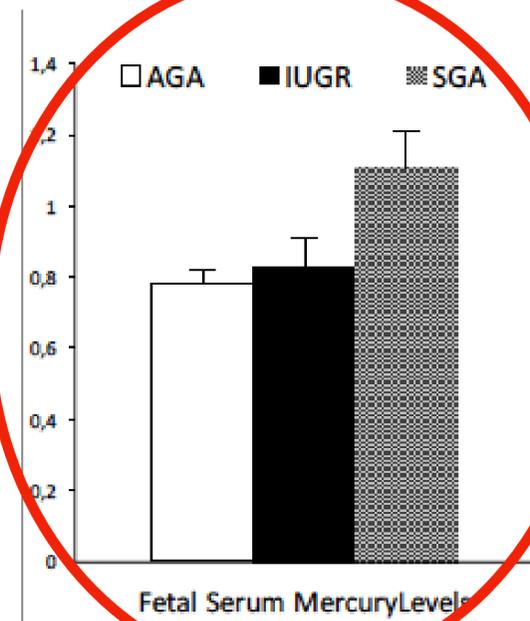
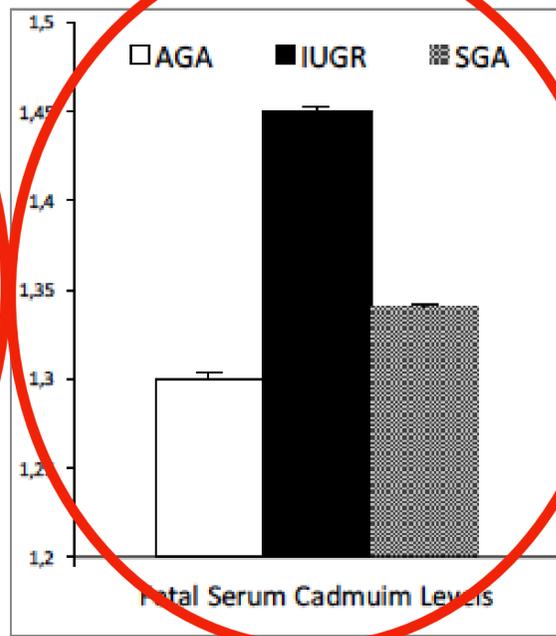
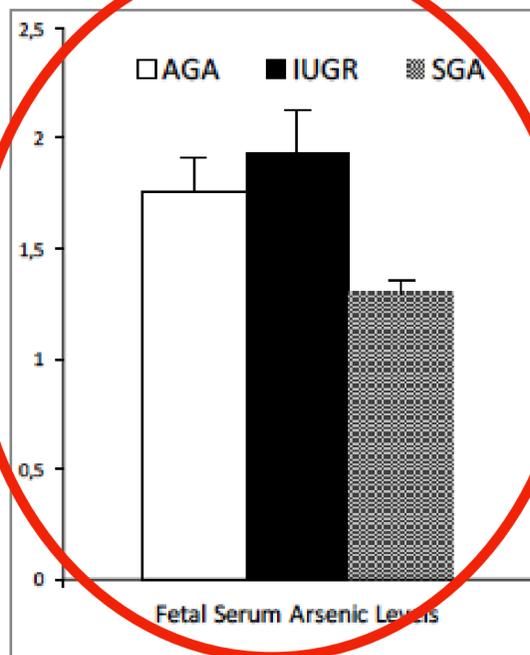
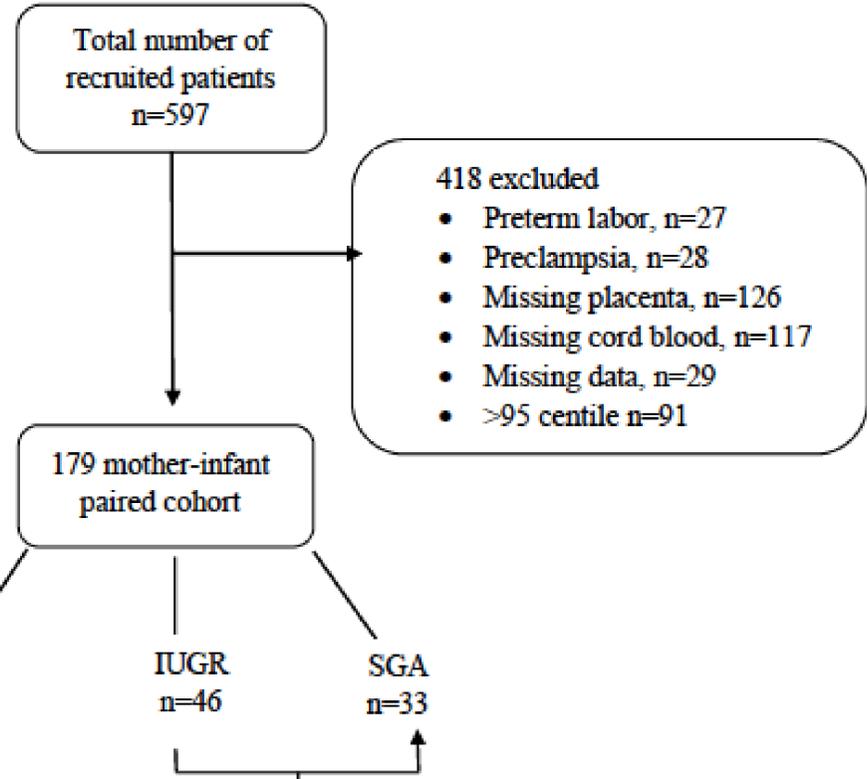
Malformaciones congénitas



#### Heavy metals

<b>Cadmium</b>	Alterations of epigenetic signatures in the DNA (DNA methylation) of the placenta and of the newborns
	Reduced intelligence quotient
	Increased risk of emotional problems in 7- to 8-year-old boys
<b>Lead</b>	Alterations in genomic methylation
	Impaired neurodevelopment (decrease in cognitive function, decreased intelligence quotient, increased incidence of attention-related behaviors and antisocial behavior problems, and decreased hearing measured in children, reduced intellectual development)
<b>Mercury</b>	Reduced cognitive performance
	Impaired neurodevelopment
	Reduced psychomotor outcomes
	Neurobehavioral deficits

# Químicos. Metales pesados





# POLUCIÓN AMBIENTAL



# Polución ambiental



## EHE



## Air pollution exposure in early pregnancy and adverse pregnancy outcomes: a register-based cohort study

David Olsson,<sup>1</sup> Ingrid Mogren,<sup>2</sup> Bertil Forsberg<sup>1</sup>

Swedish Medical Birth Register  
1998 to 2006  
n=120,755.

- ✓ Elevados niveles **O3** en **1er tr.** Aumenta el riesgo de **PE** y PPT
- ✓ PPT asociado a la exposición de O3 es más frecuente entre madres asmáticas



## RCF



A Section 508–conformant HTML version of this article is available at <http://dx.doi.org/10.1289/ehp.1409423>.

Research | Children's Health

### Prenatal Exposure to NO<sub>2</sub> and Ultrasound Measures of Fetal Growth in the Spanish INMA Cohort

*Carmen Itigues,<sup>1,2</sup> Ana Esplugues,<sup>1,2</sup> Jordi Sunyer,<sup>2,3,4,5</sup> Mikel Basterrechea,<sup>2,6,7</sup> Ana Fernández-Somoano,<sup>2,8</sup> Olga Costa,<sup>1</sup> Marisa Estarlich,<sup>1,2</sup> Inmaculada Aguilera,<sup>9,10</sup> Aitana Lertxundi,<sup>6,11</sup> Adonina Tardón,<sup>2,8</sup> Mònica Guxens,<sup>2,3,4,5,12</sup> Mario Murcia,<sup>1,2</sup> Maria-Jose Lopez-Espinosa,<sup>1,2</sup> and Ferran Ballester,<sup>1,2</sup> on behalf of the INMA Project*

Spanish INMA Study

2003 to 2008

n=2,415.

- ✓ Impacto del **NO<sub>2</sub>** en el crecimiento fetal
- ✓ Asociación con RCF (biometrías US) y peso al nacimiento



## Neurodesarrollo



### A Review of Epidemiological Research on Adverse Neurological Effects of Exposure to Ambient Air Pollution

Xiaohui Xu<sup>1\*</sup>, Sandie Uyen Ha<sup>2</sup> and Rakshya Basnet<sup>1</sup>

<sup>1</sup>Department of Epidemiology and Biostatistics, School of Public Health, Texas A&M Health Science Center, College Station, TX, USA, <sup>2</sup>College of Public Health and Health Professions, University of Florida, Gainesville, FL, USA

✓ Efectos adversos en la función neuroconductual en niños y adultos

✓ **Traffic-related air pollution (TRAP):**

- Disminuyen habilidades neurocognitivas
- Secuelas en sistema nervioso (fatiga, cefalea, dificultad de concentración)
- Enfermedades neurológicas (Alzheimer, Parkinson, y autismo)

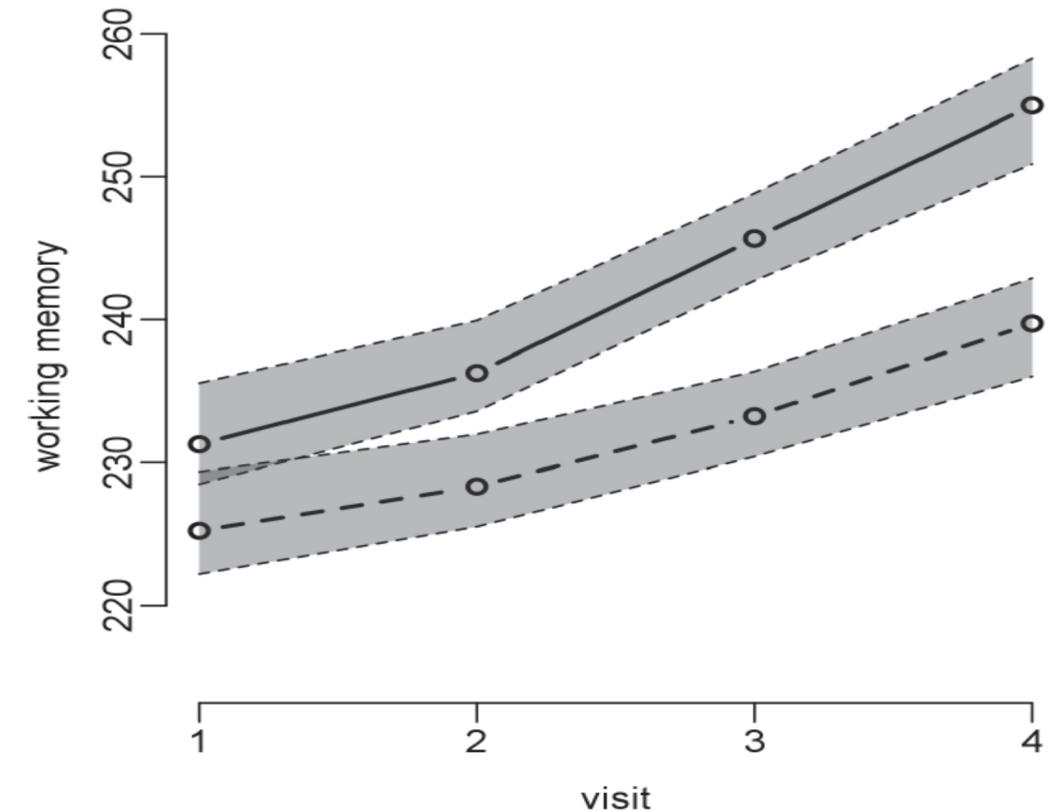
# Polución ambiental



## Neurodesarrollo



- ✓ Niños en escuelas con altos niveles de TRAP muestran menores avances en el desarrollo cognitivo



**Fig 2. Working memory development by high- or low-traffic-air-pollution school.** Dashed line = high traffic air pollution; continuous line = low traffic air pollution; gray shading indicates 95% CIs. Adjusted for age, sex, maternal education, residential neighborhood socioeconomic status, and air pollution exposure at home; school and individual as nested random effects in 2,715 children and 10,112 tests from 39 schools.

Barcelona, Spanish Study

Aged 7 to 10, 39 schools

n=2,715.

Sunyer et al. 2015



# CONTAMINACION DEL AGUA



# Contaminantes del agua



Pueden pasar de la madre al feto



Pueden influenciar en el peso fetal y duración gestación



DBPs: > 600  
THMs: chloroform, bromodichloromethane, dibromochloromethane, and bromoform

Windham and Fenster 2008  
Danielsson et al. 1986; Dowty et al. 1976  
Richardson et al. 2007; Ashley et al. 2005



DBPs pueden causar enfermedades tras largos periodos de exposición



Diferentes rutas de exposición

# Contaminantes del agua

## RCF



Table 3  
Low<sup>a</sup> and very low<sup>b</sup> birth weight

Citation	Exposure	Adjusted OR (95% CI)
<i>Low birth weight: Total THM</i>		
Källén and Robert (2000)	Chlorine dioxide vs no chlorination	0.93 (0.84–1.03)
	Sodium hypochlorite vs no chlorination	<u>1.15 (1.05–1.26)</u>
Jaakkola et al. (2001)	No chlorination/high color vs no chlorination/low color	<u>1.02 (0.91–1.14)</u>
	Chlorination/low color vs no chlorination/low color	0.99 (0.90–1.09)
	Chlorination/high color vs no chlorination/low color	0.97 (0.89–1.06)
Toledano et al. (2005)	Overall: high TTHM (>60 µg/L) vs low TTHM (<30 µg/L)	<u>1.09 (0.93–1.27)</u>
	United utilities: high TTHM (>60 µg/L) vs low TTHM (<30 µg/L)	<u>1.19 (1.14–1.24)</u>
<i>Very low birth weight: Total THM</i>		
Källén and Robert (2000)	Chlorine dioxide vs no chlorination	0.84 (0.65–1.09)
	Sodium hypochlorite vs no chlorination	<u>1.11 (0.90–1.36)</u>
Toledano et al. (2005)	Overall: high TTHM (>60 µg/L) vs low TTHM (<30 µg/L)	<u>1.05 (0.82–1.34)</u>
	United utilities: high TTHM (>60 µg/L) vs low TTHM (<30 µg/L)	<u>1.20 (1.07–1.34)</u>

<sup>a</sup> Less than 2500 g.

<sup>b</sup> Less than 1500 g.

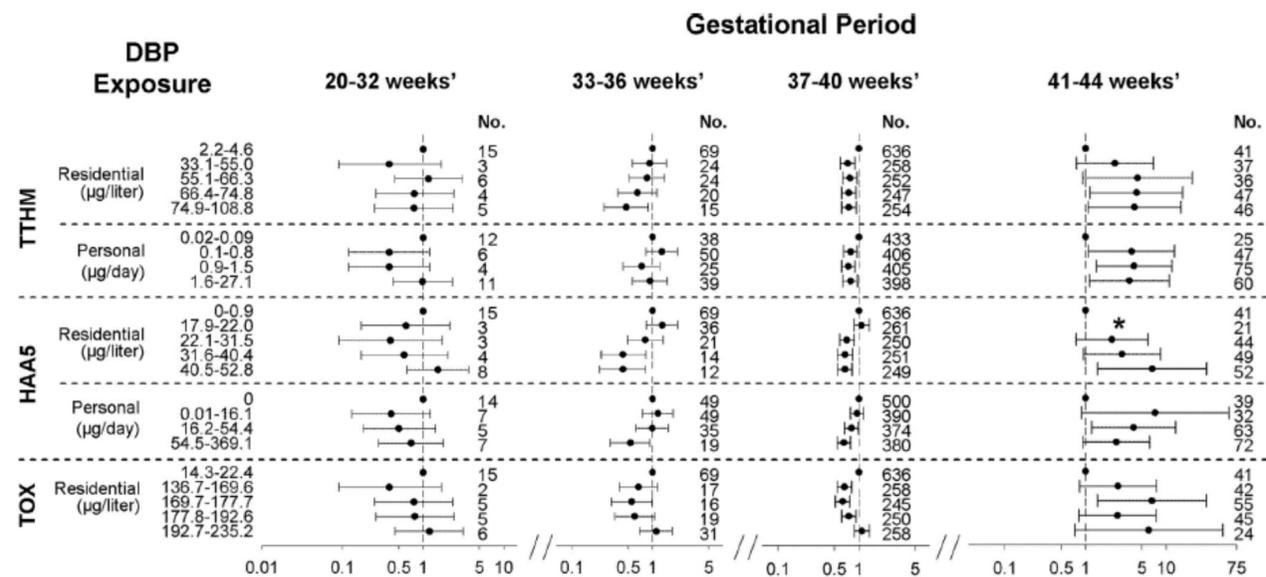
✓ IUGR, SGA, y LBW son las complicaciones obstétricas más fr. asociadas a la exposición de DBP durante el embarazo

# Contaminantes del agua

## PPT



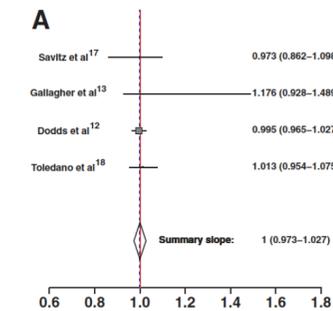
Evidencia de los efectos en la reducción de la duración del tiempo gestacional (PPT) es inconsistente



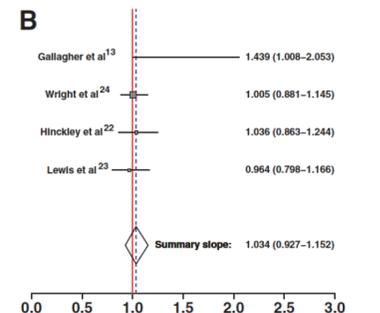
Hoffman et al. 2008; Lewis et al. 2007; Wright et al. 2004

OR per 10µg TTHM/L

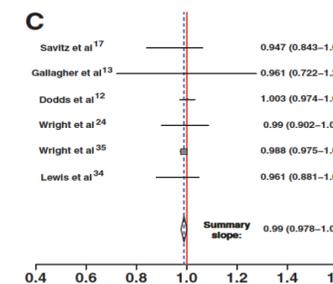
### LBW



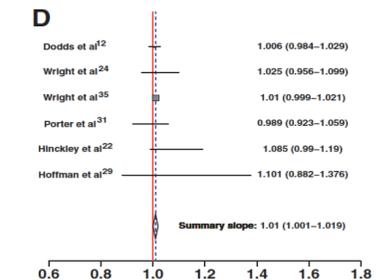
### Term LBW



### Preterm delivery

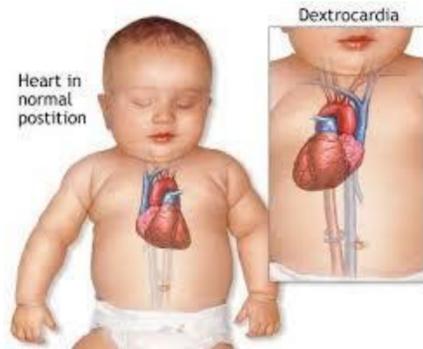


### SGA



Grellier et al. 2010

## Anomalías congénitas



- ✓ Pueden asociarse a algunos químicos usados en agricultura:  
**Nitratos, atrazina, y arsenico**

## Efecto carcinógeno



- ✓ **Arsenico**
- ✓ No hay información suficiente referente a otras sust. químicas



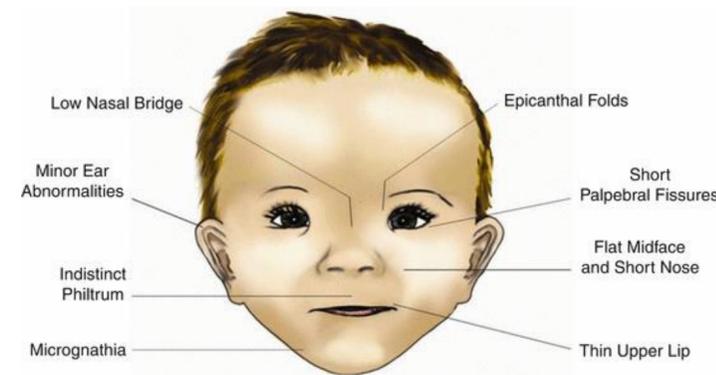
# TABACO Y ALCOHOL



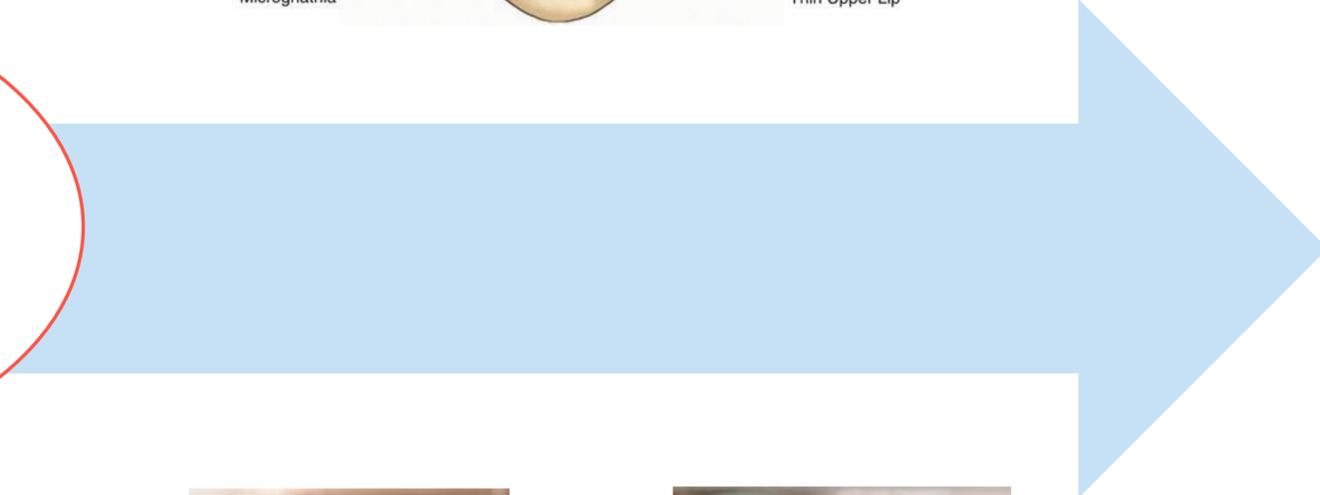
# Tabaco y alcohol

## Smoking-Induced Changes in the Maternal Immune, Endocrine, and Metabolic Pathways and Their Impact on Fetal Growth: A Topical Review

Sally Sabra<sup>a</sup> Eduard Gratacós<sup>a,b</sup> Maria Dolores Gómez Roig<sup>a,c</sup>



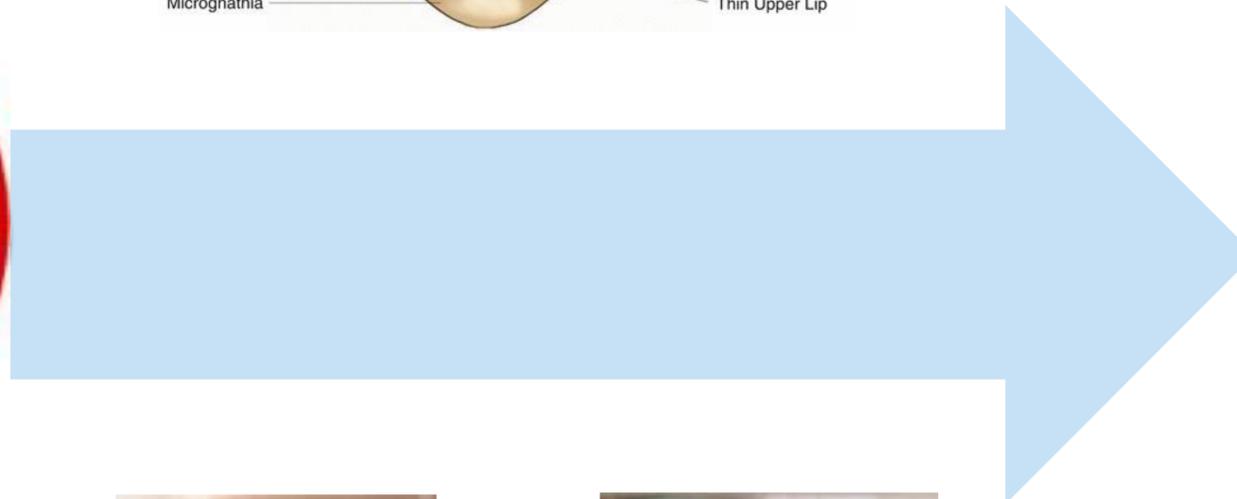
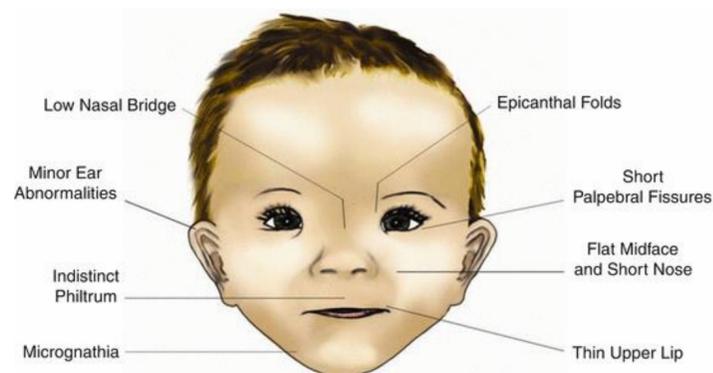
TABACO  
ALCOHOL



# Tabaco y alcohol

## Smoking-Induced Changes in the Maternal Immune, Endocrine, and Metabolic Pathways and Their Impact on Fetal Growth: A Topical Review

Sally Sabra<sup>a</sup> Eduard Gratacós<sup>a,b</sup> Maria Dolores Gómez Roig<sup>a,c</sup>





RoyalCollegeObsGyn @RCObsGyn · Apr 12

"Heavy drinking can cause fetal alcohol spectrum disorders and it's also been linked with #miscarriage" - @iregan7



**Brit women worst in Europe for boozing while pregnant**

BRITISH women are the most likely in Europe to drink alcohol while pregnant, a study suggests. Nearly one in three continue drinking, despite...

[thesun.co.uk](http://thesun.co.uk)

## GIN SLIP MUMS Brit women worst in Europe for boozing while pregnant with one in three ignoring advice to quit booze

Just four per cent of Norwegian mums-to-be kept boozing, while the average figure was 16 per cent across 11 other countries

By Nick McDermott, Health Editor

11th April 2017, 9:04 pm | Updated: 12th April 2017, 9:36 pm



6 COMMENTS

**BRITISH women are the most likely in Europe to drink alcohol while pregnant, a study suggests.**

Nearly one in three continue drinking, despite official advice to avoid **booze**.

Researchers from the Norwegian Institute of Public Health surveyed 7,905 women from 11 European countries.

They found 29 per cent of UK women admitted drinking when pregnant.

In contrast, just four per cent of Norwegian mums-to-be kept boozing, while the average figure was 16 per cent across the nations.

Alcohol can seriously affect the development of an unborn baby, increasing the risk of miscarriage, premature birth, low birth weight, learning difficulties and behavioural problems.

More than 6,000 babies are born in Britain with foetal alcohol spectrum disorder each year.

Among women who confessed to drinking while expecting, 39 per cent consumed at least one unit of alcohol per month.

That is the equivalent of a single measure of spirits, half a pint of beer, or half a small glass of wine. After the UK, the countries with the largest proportion of women drinking when pregnant were Russia on 27 per cent and Switzerland with 21 per cent.

Women from Croatia, Finland, France, Italy, Norway, Poland, Russia, Serbia, Sweden, Switzerland and the UK took part in the study, published in the journal Women And Birth.



**Coordinator: L. Gómez**

	UNDERSTANDING	PREDICTING	REVERTING
<p><b>CLINICAL PROJECTS</b></p> <p><i>Team Leader:</i> L. Gómez</p>	<p><b>Chemicals</b> S. Sabras</p> <p><b>Air</b> M. Cahuana</p> <p><b>Water</b> C. Molinet</p> <p><b>Anxiolytics and antidepressants</b> L. Cortés</p> <p><b>Microbiome</b> S. Fernández</p>		<p><b>OH</b> <b>Repeated motivational intervention</b> C. Molinet</p>
<p><b>BASIC RES. PROJECTS</b></p> <p><i>Team Leader:</i> L. Gómez</p>	<p><b>Alcoholic model: FAS/ IUGR</b> L. Almeida, J. Parra</p>		<p><b>Alcoholic model: Antioxidant therapies in FAS/ IUGR</b> L. Almeida, J. Parra</p>

