Role of Environmental Factors in Asthma

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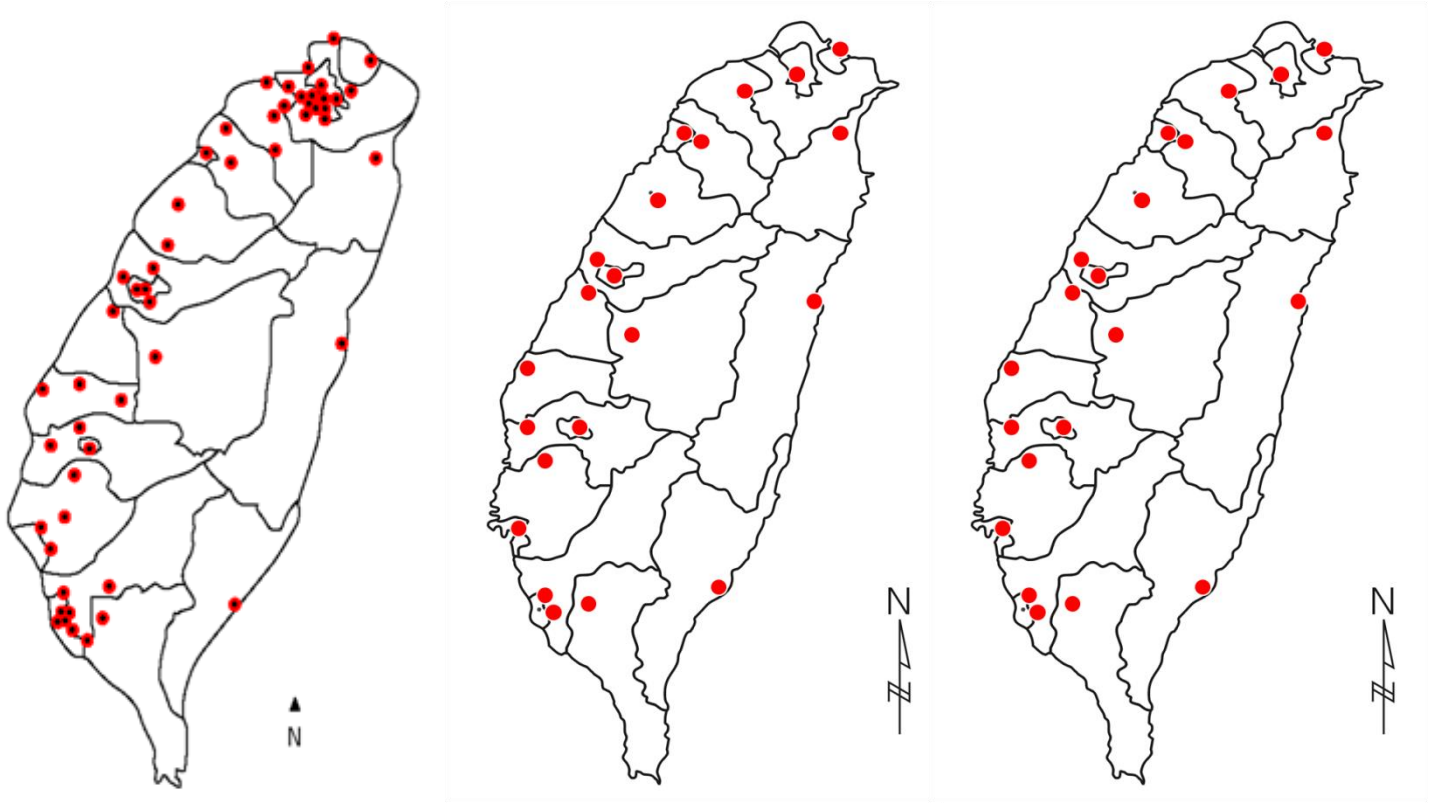
A true environmental example

Increased incidence of allergic rhinitis, bronchitis and asthma, in children living near a petrochemical complex with SO_2 pollution

- **The petrochemical complex increased nearby SO_2 pollution at the communities.**
- **Allergic rhinitis was increased for children aged 0–12**
- **Bronchitis was increased for children aged 0–4**
- **Asthma was increased for children aged 0–4 living in these communities**
- **台西、麥寮跟東勢鄉**

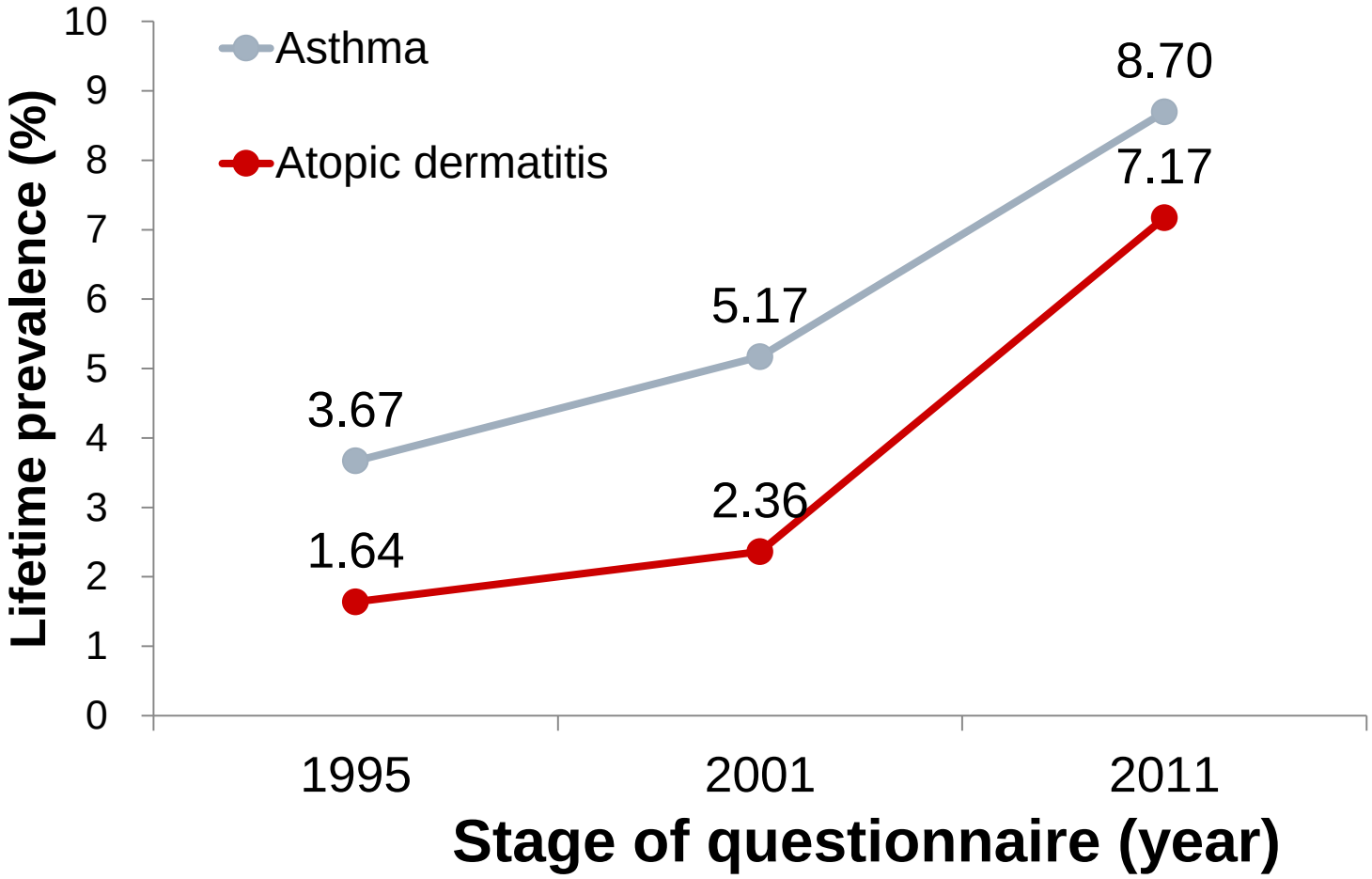
(Chiang, …, Chan, Env Int 2016)

topic disease Surveys in Taiwan

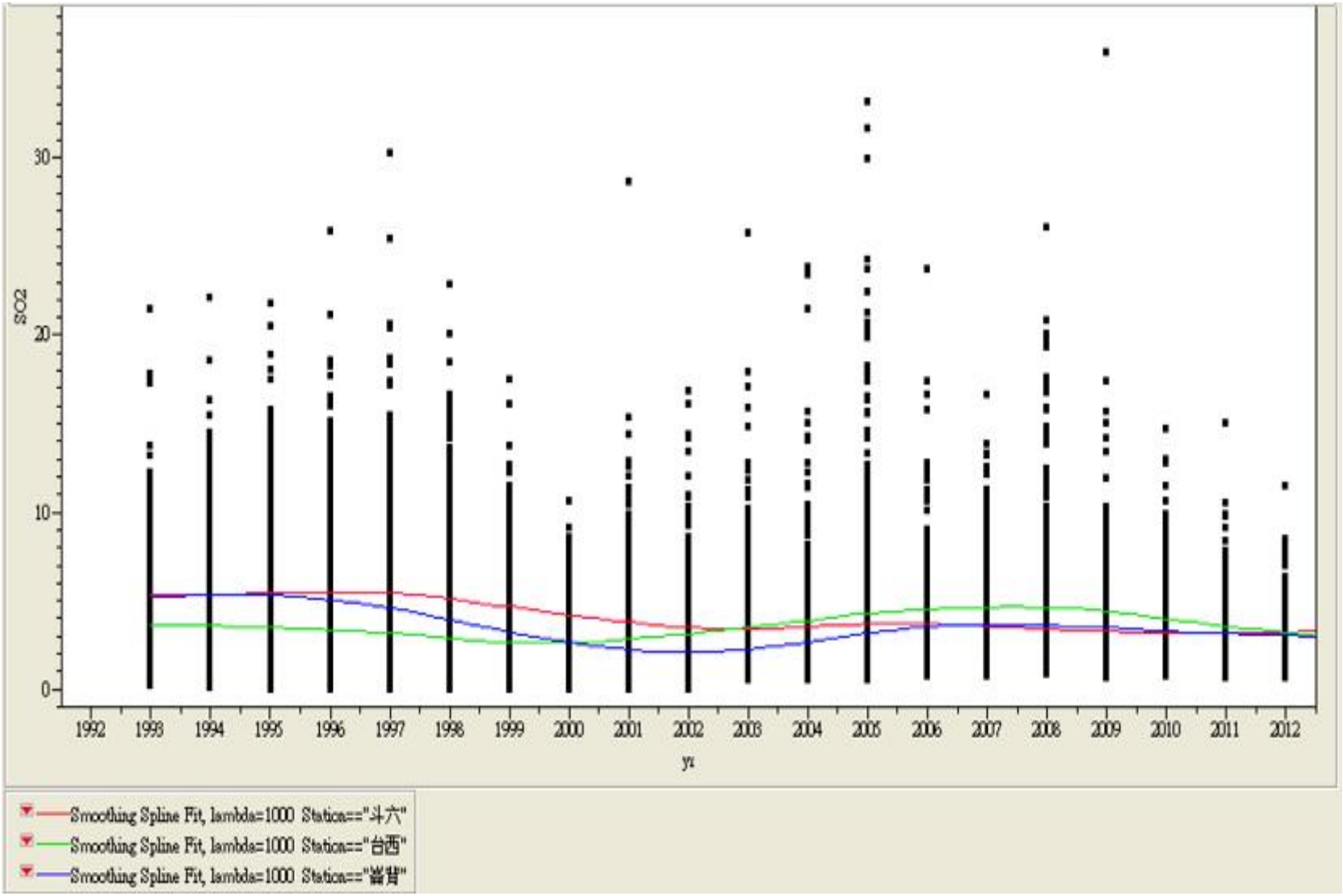


Atopic diseases: asthma, atopic dermatitis, allergic rhinitis in children's parents

Life-time prevalence of asthma and atopic dermatitis in middle school children

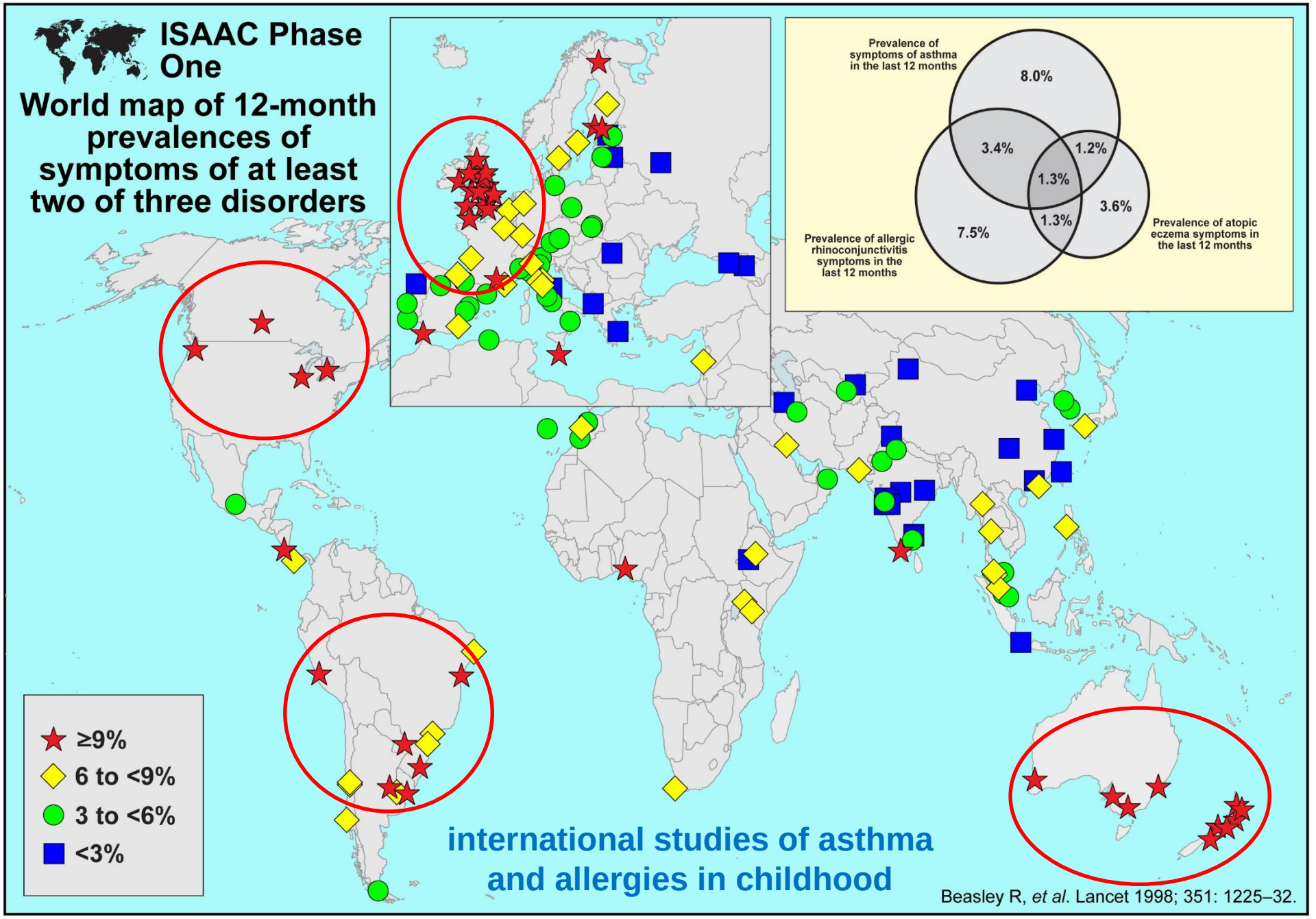


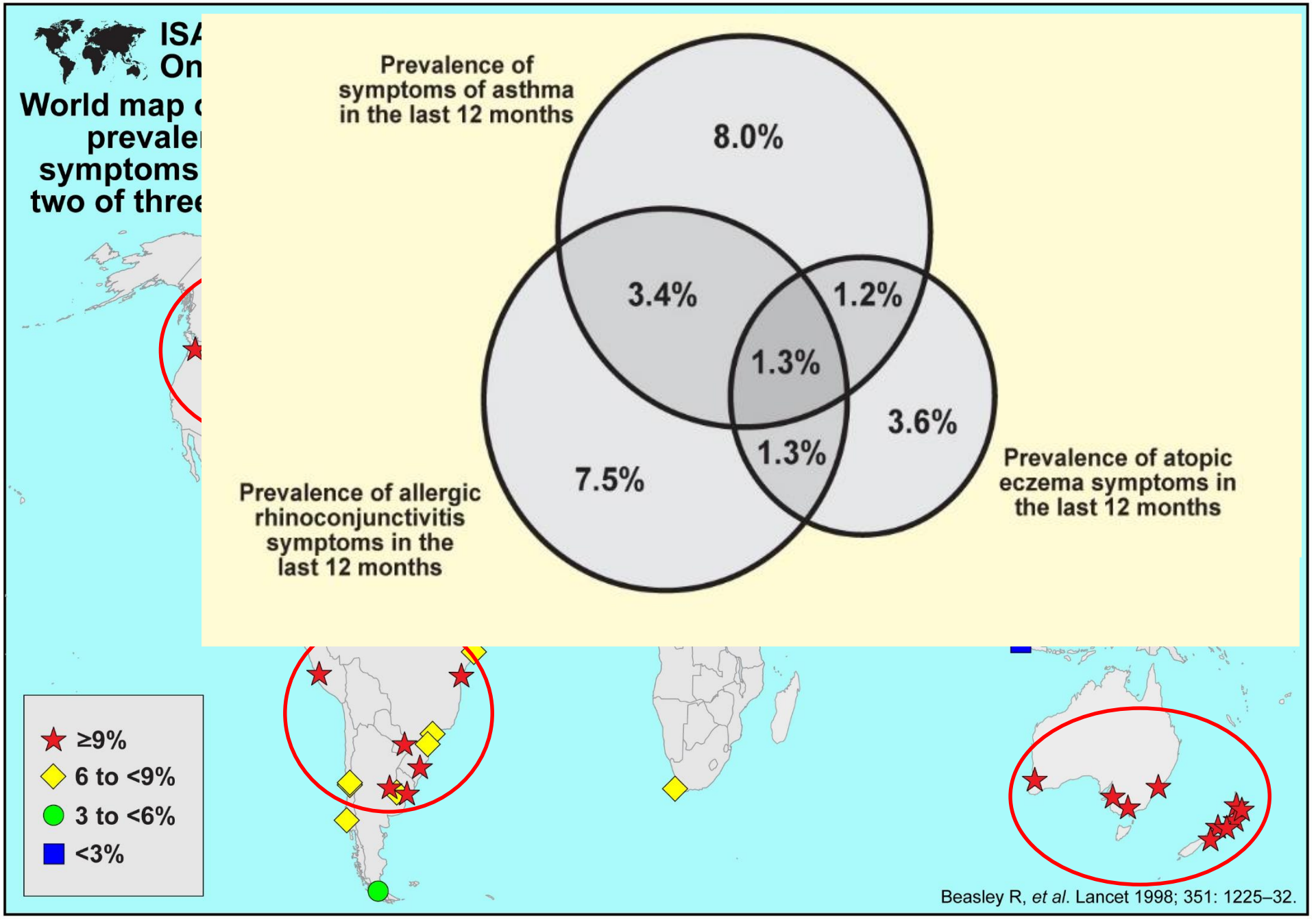
SO2 yearly average



Possibilities

- **Coincidence**
  - **↑ allergic diseases**
  - **↑SO2**
- **Emission truly induce allergic conditions**
- **Others**


ISAAC Phase One
World map of 12-month prevalences of symptoms of at least two of three disorders
Prevalence of symptoms of asthma in the last 12 months
8.0%
3.4%
1.2%
1.3%
3.6%
1.3%
7.5%
Prevalence of allergic rhinoconjunctivitis symptoms in the last 12 months
Prevalence of atopic eczema symptoms in the last 12 months
≥9%
6 to <9%
3 to <6%
<3%
international studies of asthma and allergies in childhood
Beasley R, et al. Lancet 1998; 351: 1225–32.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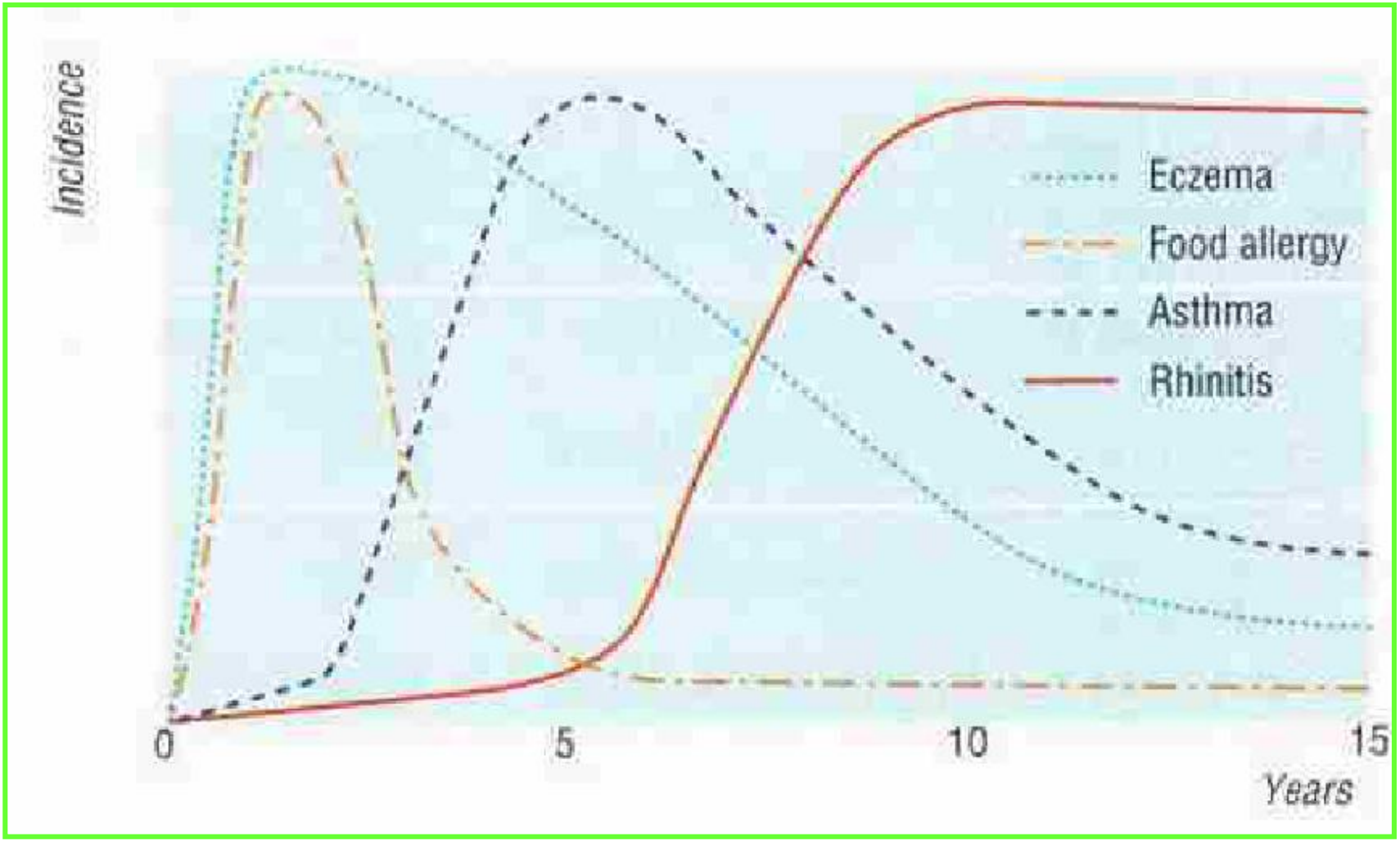
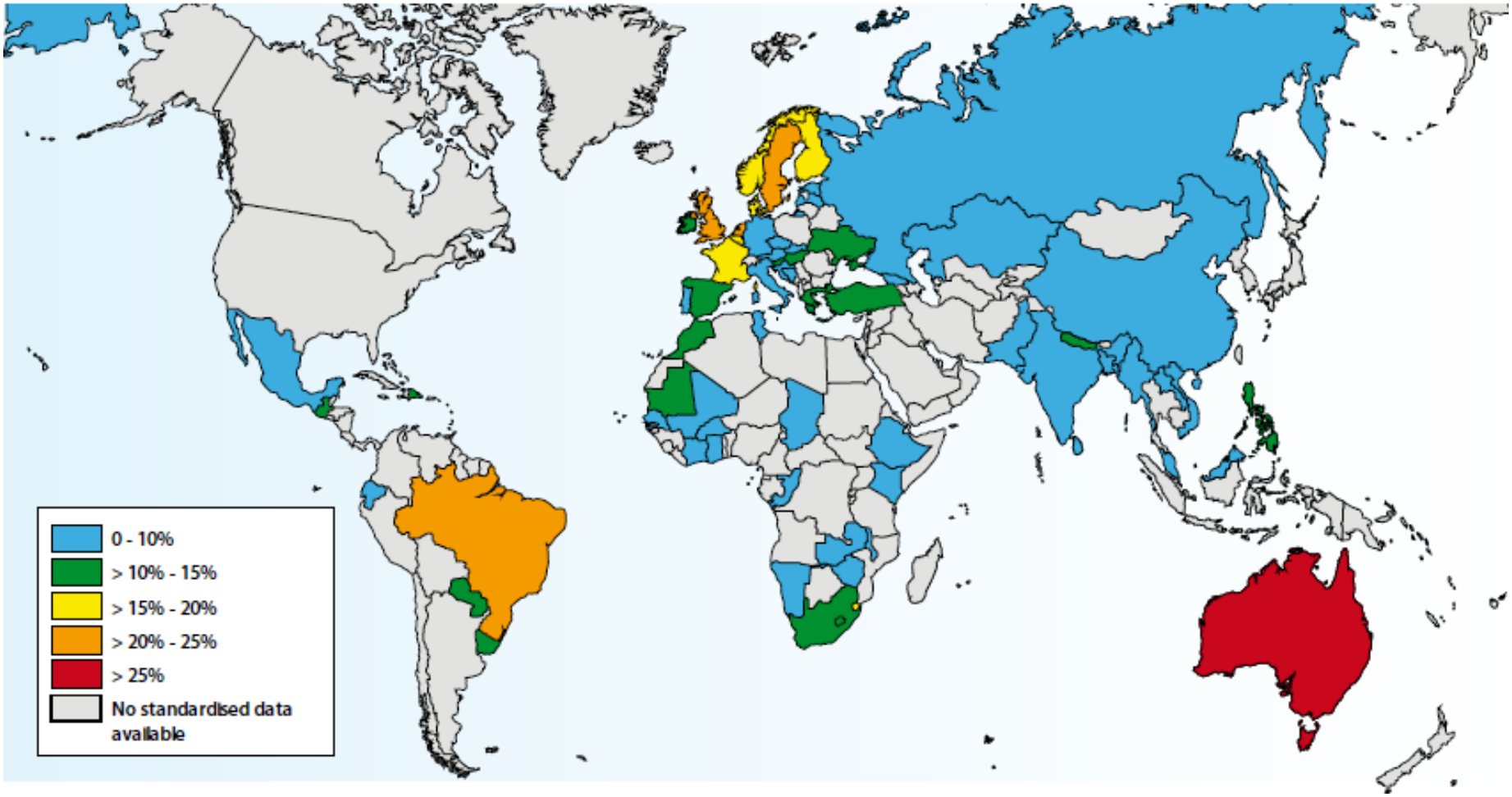
The Atopic March



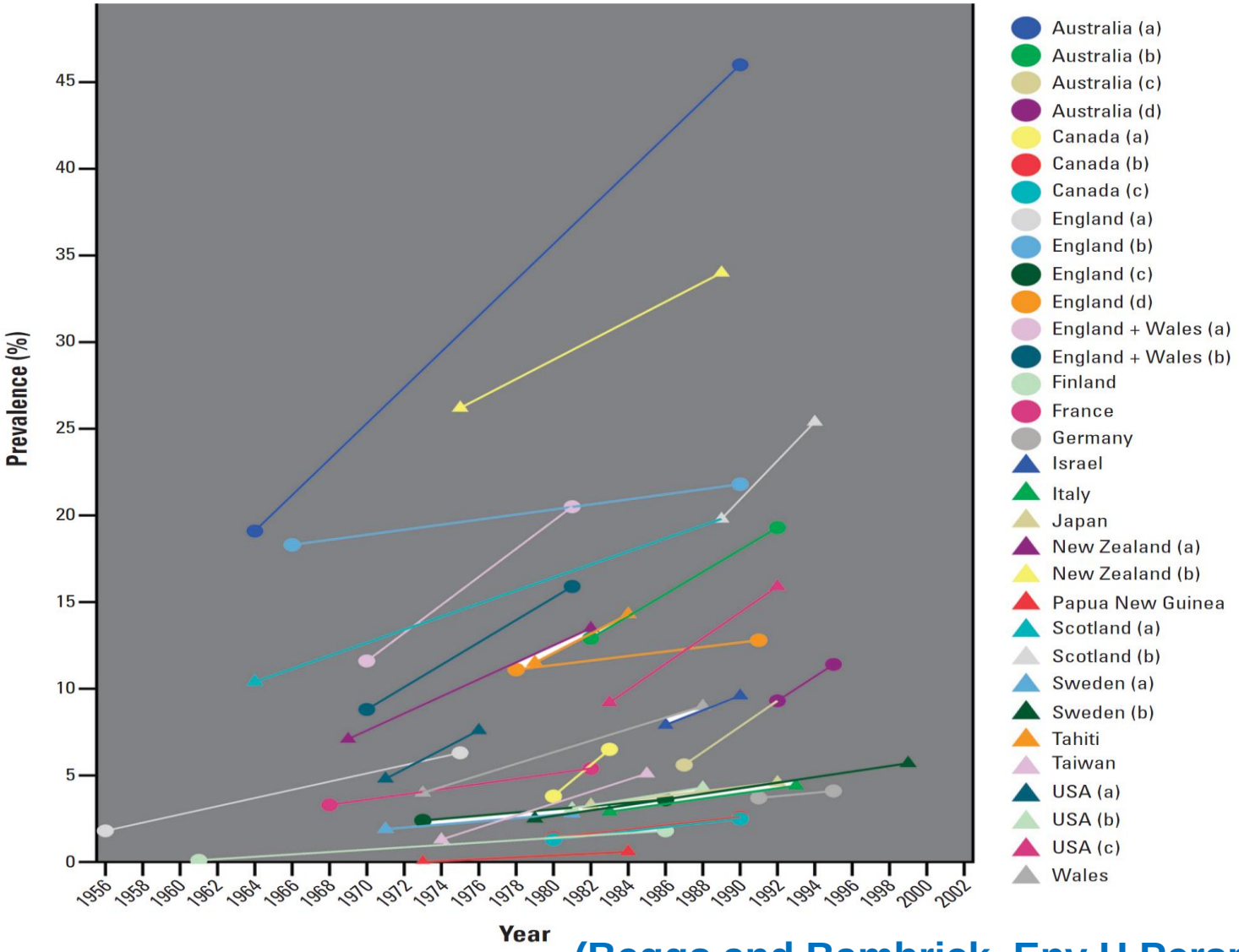
Prevalence of asthma symptoms in 18 to 45 year olds (WHO) 2002-2003



It's possible to catch asthma after childhood!

(Courtesy of Global Asthma Network)

Asthma Prevalence by countries



(Beggs and Bambrick, Env H Persp 2005)

Sources of air pollution

- **Human sources**
  - **Stationary sources**
    - **Point sources: smokestacks**
    - **Fugitive sources: dirt roads, farmland, construction site, burning for agricultural purposes.**
    - **Area sources: industrial or agricultural areas.**
  - **Mobile sources**

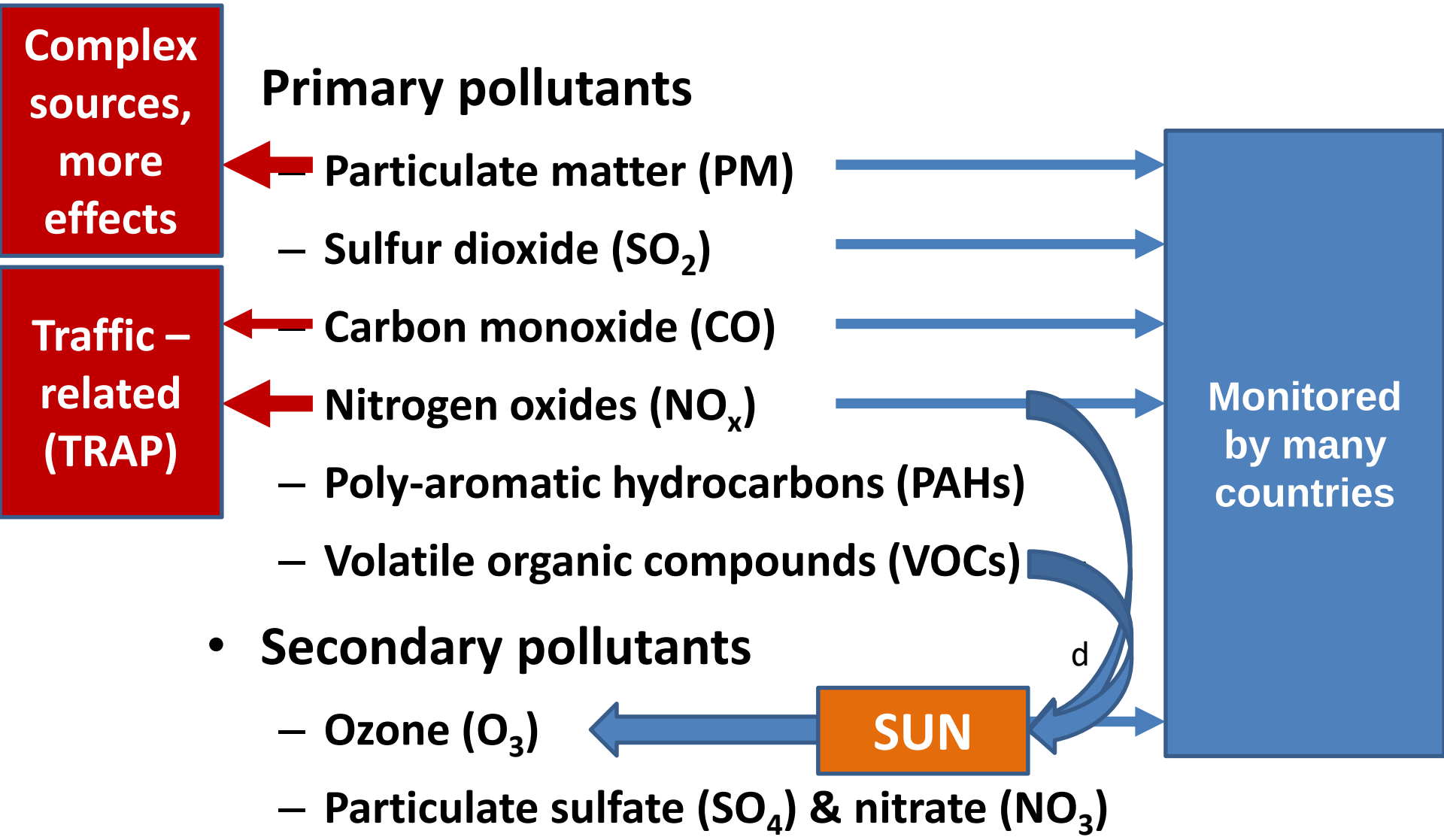
- **Nature sources**
  - **Volcanic eruptions, geysers, hot springs, bogs, wildfires, windstorm, thunderstorms.**

Environmental factors for atopic diseases

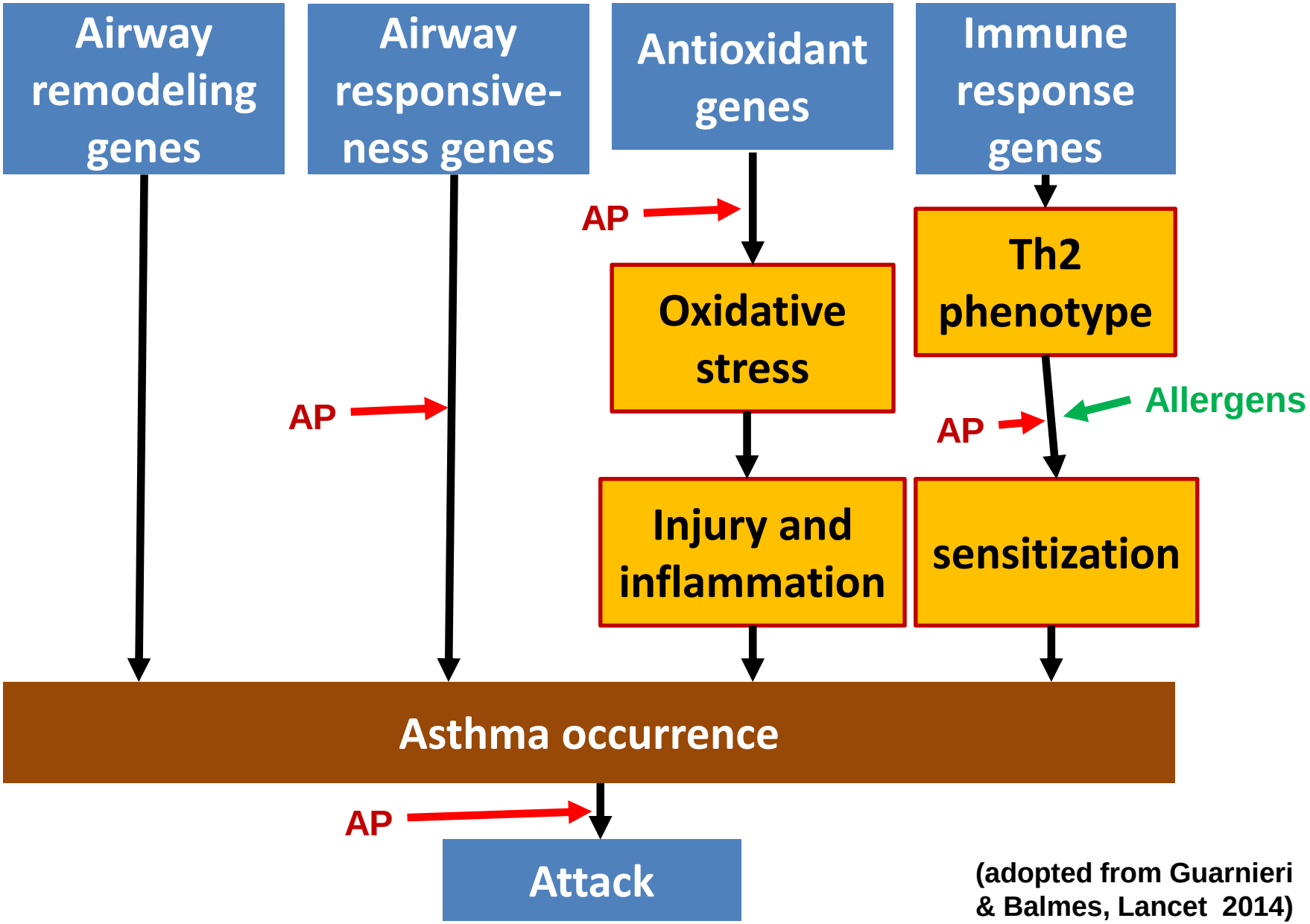
- **Allergen**
  - Indoor: domestic mites, furred animals (e.g. dogs, cats, mice), cockroaches, molds, yeasts
  - Outdoor: pollen, molds
  - Occupational: high or low molecular weight sensitizers
- **Non-allergen**
  - Viral infections
  - Bacteria
  - Tobacco smoke
  - Irritants
  - Outdoor or indoor air pollution
  - Diet
  - Medication (acetaminophen)
  - Stress

(GINA 2015, modified Box A2-1)

Air pollutants from human sources



Air pollution (AP) effects on asthma



(adopted from Guarnieri & Balmes, Lancet 2014)

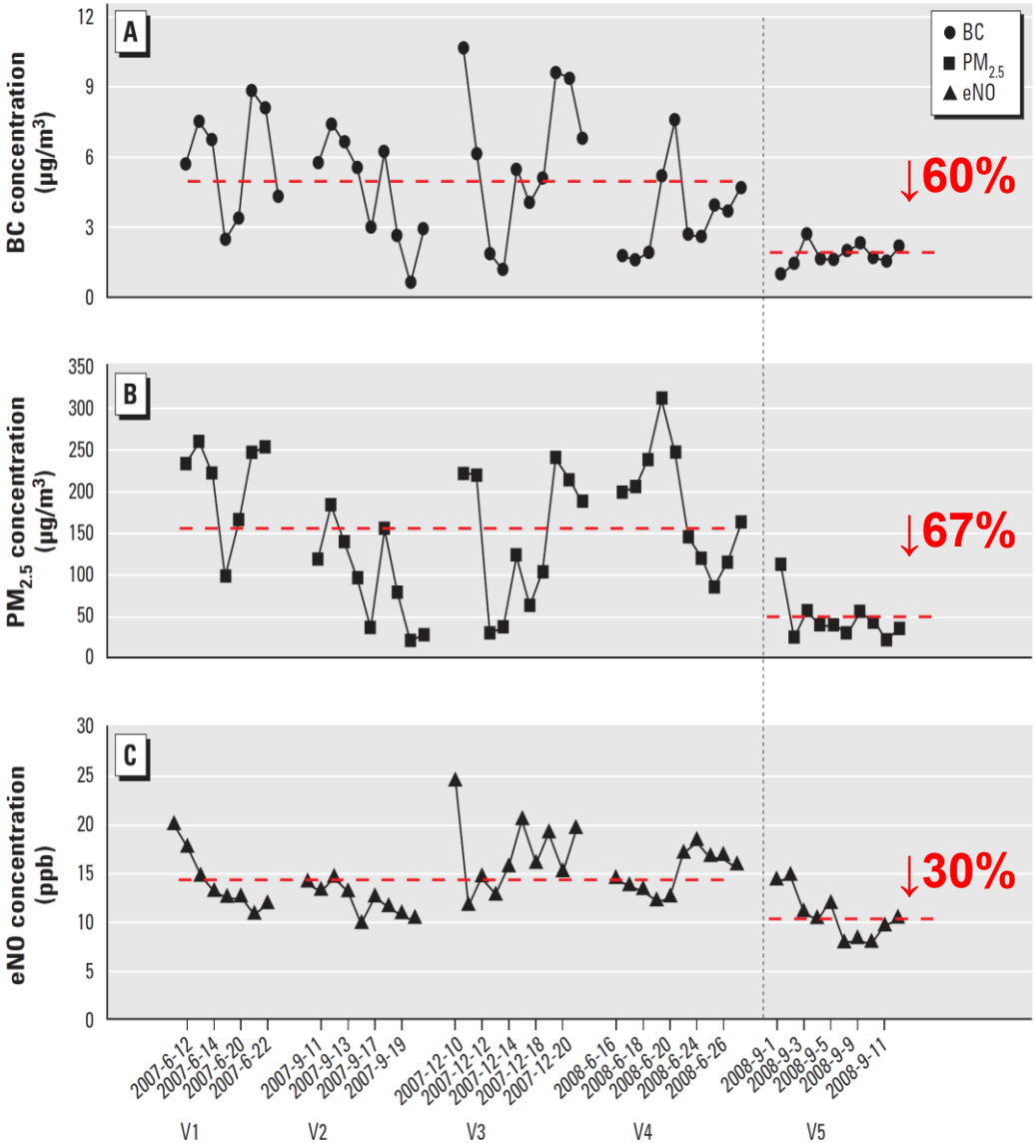
Effects on attacks in people having asthma?

Beijing Olympics, 2008

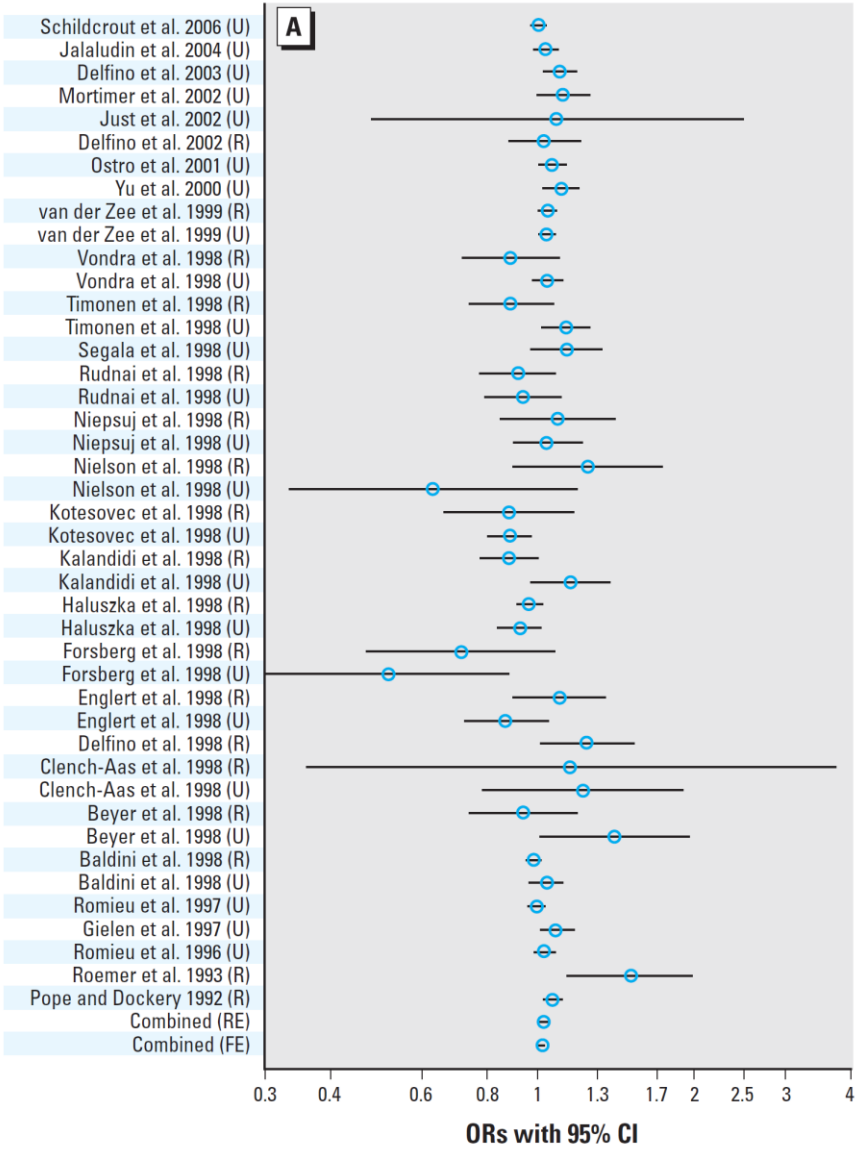
- 38 children, mean age 10.6 y
- Exhaled nitric oxide (eNO) as an acute respiratory inflammation biomarker
- BC: black carbon

(Lin et al., Env H Persp 2011)

46% reduction of asthma outpatient visits
(Li et al., Sci Total Env 2010)



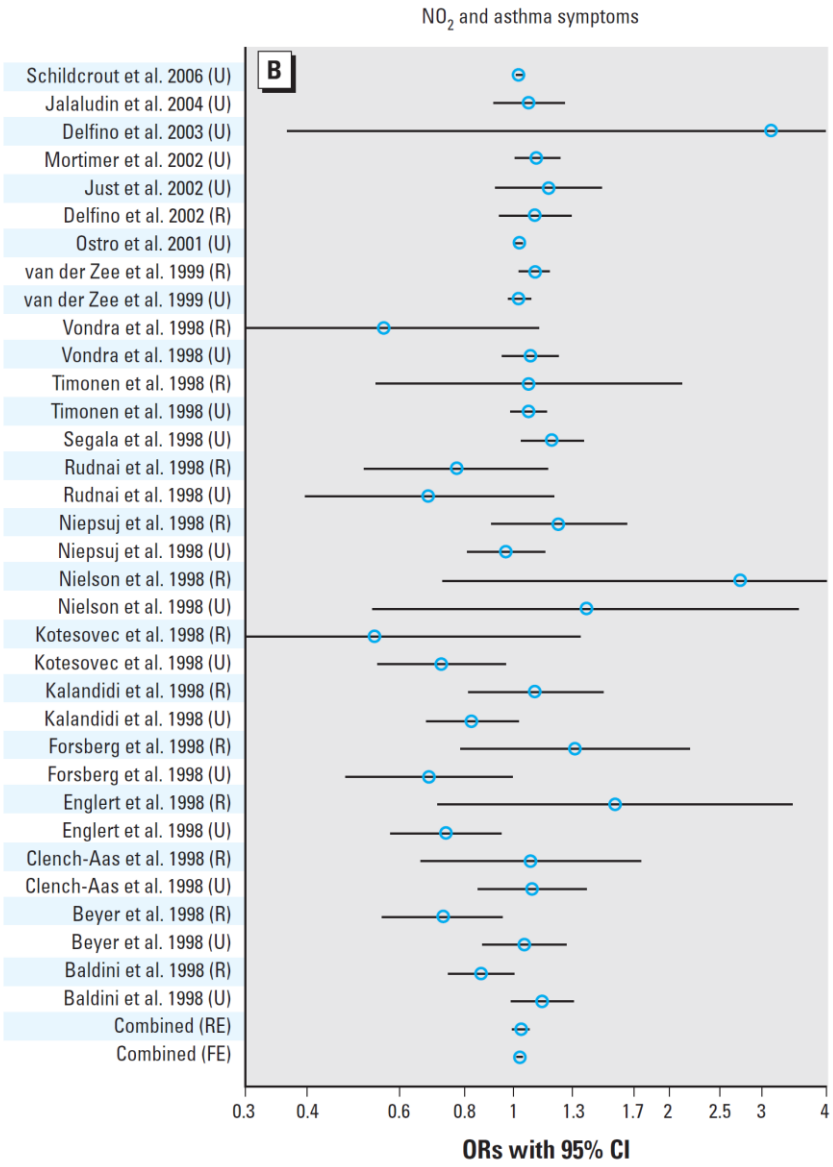
Short-term effects of PM_{10} on asthmatic children: Meta-analysis of 36 studies



- PM_{10}, 10 µg/M^3 ↑
  - ↑ 2.8% in asthma attack
  - (↑) 1.2% in cough
  - (↓) 0.082 L/min in Peak Expiratory Flow (PEF)

(Weinmayr et al., Env H Persp 2010)

Short-term effects of NO_2 on asthmatic children: Meta-analysis of 36 studies



- NO_2, 10 µg/M^3 (5 ppb)↑
  - ↑ 3.1% in asthma attack

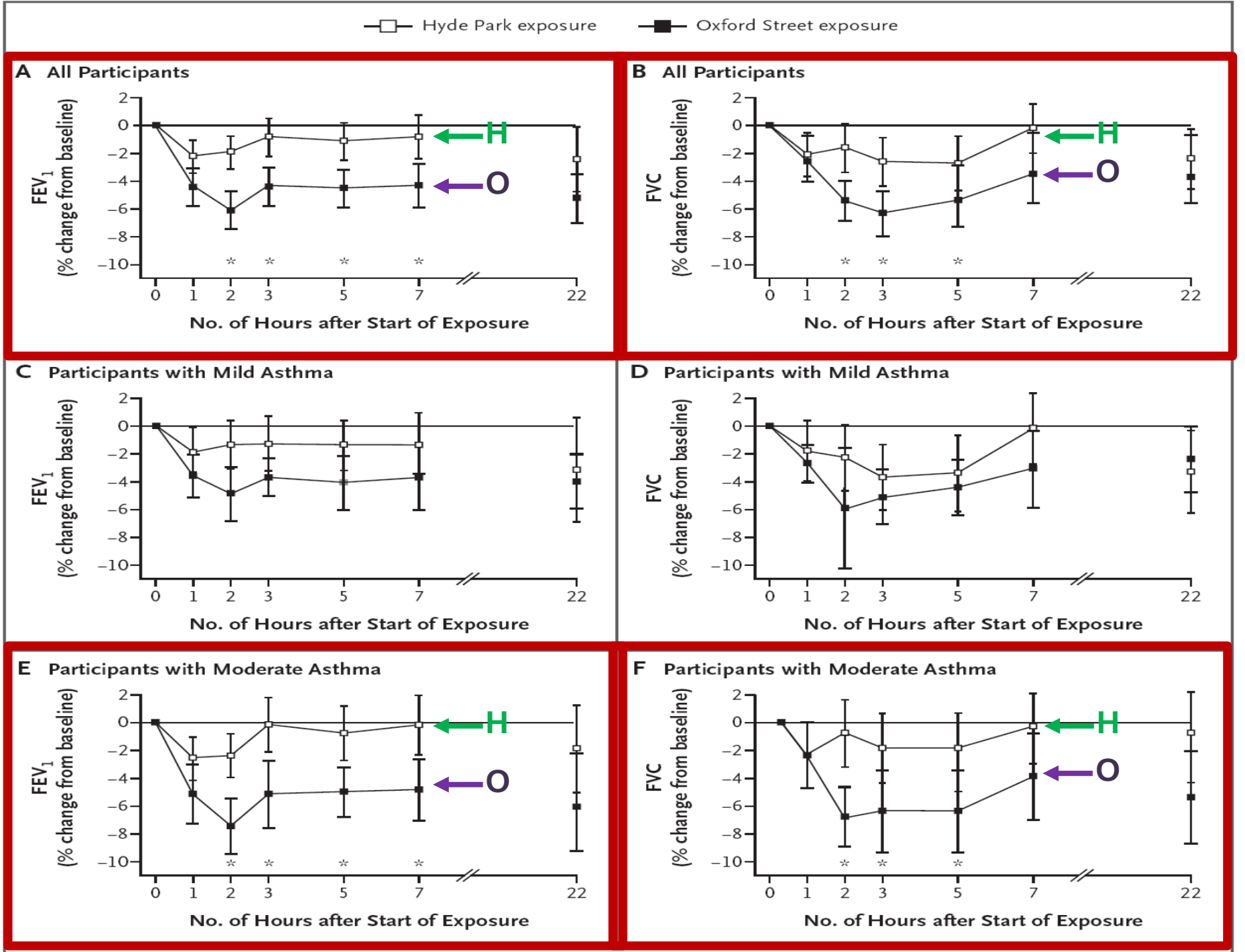
(Weinmayr et al., Env H Persp 2010)

Air pollutants on lung function - acute

- 60 adults with either mild or moderate asthma
- Randomized, crossover study
- Walked for 2 hours along a London street (Oxford Street) and, on a separate occasion, through a nearby park (Hyde Park).

- Higher exposures to $PM_{2.5}$, ultrafine particles, elemental carbon, and NO_2 on Oxford Street than in Hyde Park.

(McCreanor et al., NEJM 2007)


Hyde Park exposure
Oxford Street exposure
A All Participants
B All Participants
C Participants with Mild Asthma
D Participants with Mild Asthma
E Participants with Moderate Asthma
F Participants with Moderate Asthma
FEV1 (% change from baseline)
FVC (% change from baseline)
H
O
2
0
−2
−4
−6
−8
−10
0
1
2
3
5
7
22
*
No. of Hours after Start of Exposure

Air Quality Index

- **Similar indices exist for many countries, differing in the pollutants considered and recommendations offered.**
- **UK Daily Air Quality Index is based on concentrations of NO_2, SO_2, O_3, $PM_{2.5}$, and PM_{10}.**

Tuesday
1 September 2015
9 - 10 pm (AEST)
Previous | Next | Select
Show data readings

Pollutants		Ozone O3	Ozone O3	Nitrogen dioxide NO2	Visibility NEPH	Carbon monoxide CO	Sulfur dioxide SO2	Particles PM10	Particles PM2.5	Site AQI	Regional AQI
Averaging Periods		1-hour average	rolling 4-hour average	1-hour average	1-hour average	rolling 8-hour average	1-hour average	rolling 24-hour average	rolling 24-hour average	highest level at the site	highest level for the region
Sydney East	Randwick	2	12	20	17		0	30		30	37
	Rozelle	1	3	28	20	5	0	32	30	32	
	Lindfield	1	6	23	24		0	29		29	
	Chullora	1	3	28	27	5	1	37	33	37	
	Earlwood	2	4	19	27			30	23	30	
Sydney North-west	Richmond	3	7	15	16		0	25	45	45	45
	St Marys	4	8	8	13			20		20	
	Vineyard	3	19	23	28		0	32		32	
	Prospect	2	5	30	24	2	1	35	37	37	
Sydney South-west	Bargo	10	18	14	10		0	18		18	40
	Bringelly	5	13	8	13		0	25		25	
	Camden	8	17	7	17	1		23	27	27	
	Campbelltown West	1	2	21	11	4	0	25		25	
	Liverpool	1	3	25	20	3		36	40	40	
	Oakdale	26	33	1	3			15		33	
Illawarra	Wollongong	2	2	19	10	4	0	26	28	28	37
	Kembla Grange	1	4	11	11			27	37	37	
	Albion Park Sth	4	11	9	10		0	24	26	26	
Lower Hunter	Wallsend	1	3	20	23		0	27	24	27	44
	Newcastle	1	8	25	22	6	1	35	30	35	
	Beresfield	4	4	21	21		1	44	31	44	
Central Coast	Wyong	2	6	14	11	2	0	22	21	22	22
Central Tablelands	Bathurst							21		21	21
North-west Slopes	Tamworth							25		25	25
South-west Slopes	Albury							31		31	31

- **Traditional AQI**
  - **The maximum of the Individual AQIs**
  - **Does not taken into account the multiple pollutant situation**
- **AQHI**
  - **Sum of the Individual pollutants Augmented risk (IAR).**
  - **If both ozone (O_3) and particule matter ($PM_{2.5}$) levels are high, then the risk for health is likely twice as big as if only particule matter level was be high.**

- **Traditional AQI = max [*IAQI* ($PM_{2.5}$), *IAQI* (PM_{10}), *IAQI* (O_3), *IAQI* (NO_2), *IAQI* (SO_2)]**
- **AQHI Augmented Risk = *IAR* (NO_2) + *IAR* (SO_2) + *IAR* (O_3) + max[*IAR* ($PM_{2.5}$), *IAR* (PM_{10})]**

UK health message based on daily Air Quality Index

	AQI	Lung problems	Asthma
Low	1–3	Enjoy usual outdoor activities	
Moderate	4–6	Symptomatics: consider reducing strenuous physical activity, particularly outdoors	
High	7–9	Reduce strenuous physical exertion, particularly outdoors	Might need to use reliever inhaler more
Very high	10	Avoid strenuous physical activity	Might need to use reliever inhaler more

UK health message based on daily Air Quality Index

	AQI	Adults with heart problems	Older
Low	1–3	Enjoy usual outdoor activities	
Moderate	4–6	Symptomatics: consider reducing strenuous physical activity, particularly outdoors	
High	7–9	Reduce strenuous physical exertion, particularly outdoors	Reduce physical exertion
Very high	10	Avoid strenuous physical activity	Avoid strenuous physical activity

Do air pollution increase risk of developing asthma?

National survey of asthma in middle school children

Locations of the 55 air monitoring stations in Taiwan - 1994

Totally, 326,562 children were included whose schools were located within 2 km of the stations, 1995-6

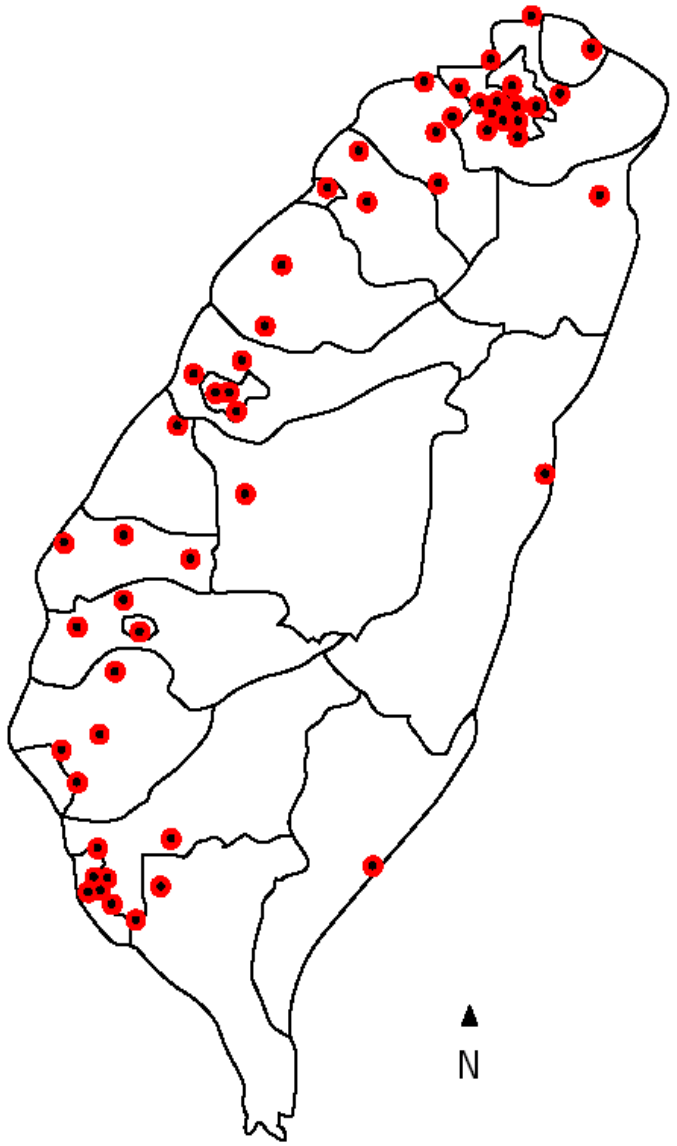
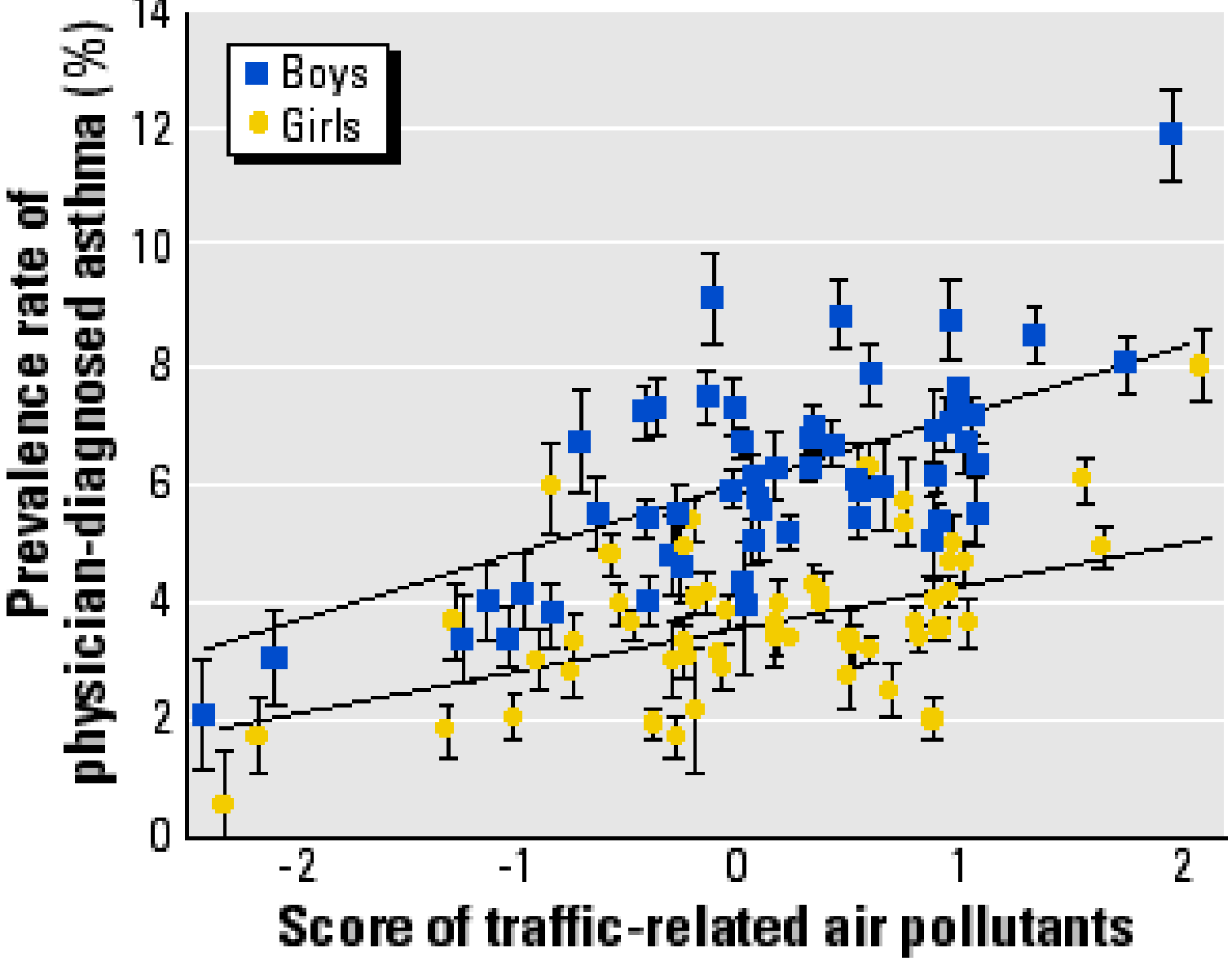


Figure 1. The 55 air pollution monitoring stations in this study and their 2-km catchment areas in Taiwan, 1994.

(Guo et al., Env H Persp, 1999)

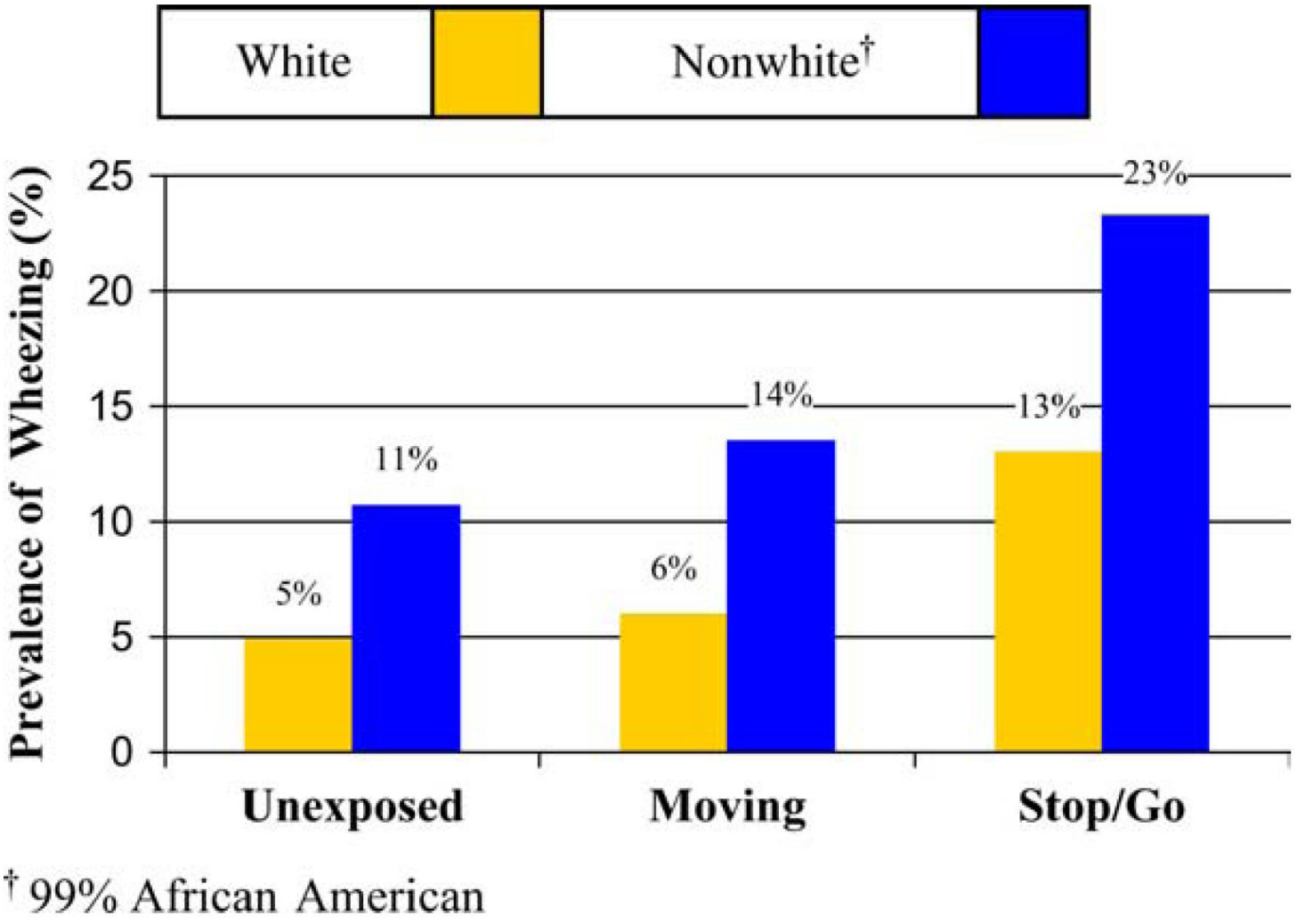


NO2 median=22 ppb
IQR: 17 – 28
==25% ↑ asthma

~2% ↑ asthma for 1 ppb ↑ in NO2

(Guo et al., Env Health Persp, 1999)

Prevalence of wheeze (without cold) among infants stratified by race



(Ryan et al., JACI 2005)

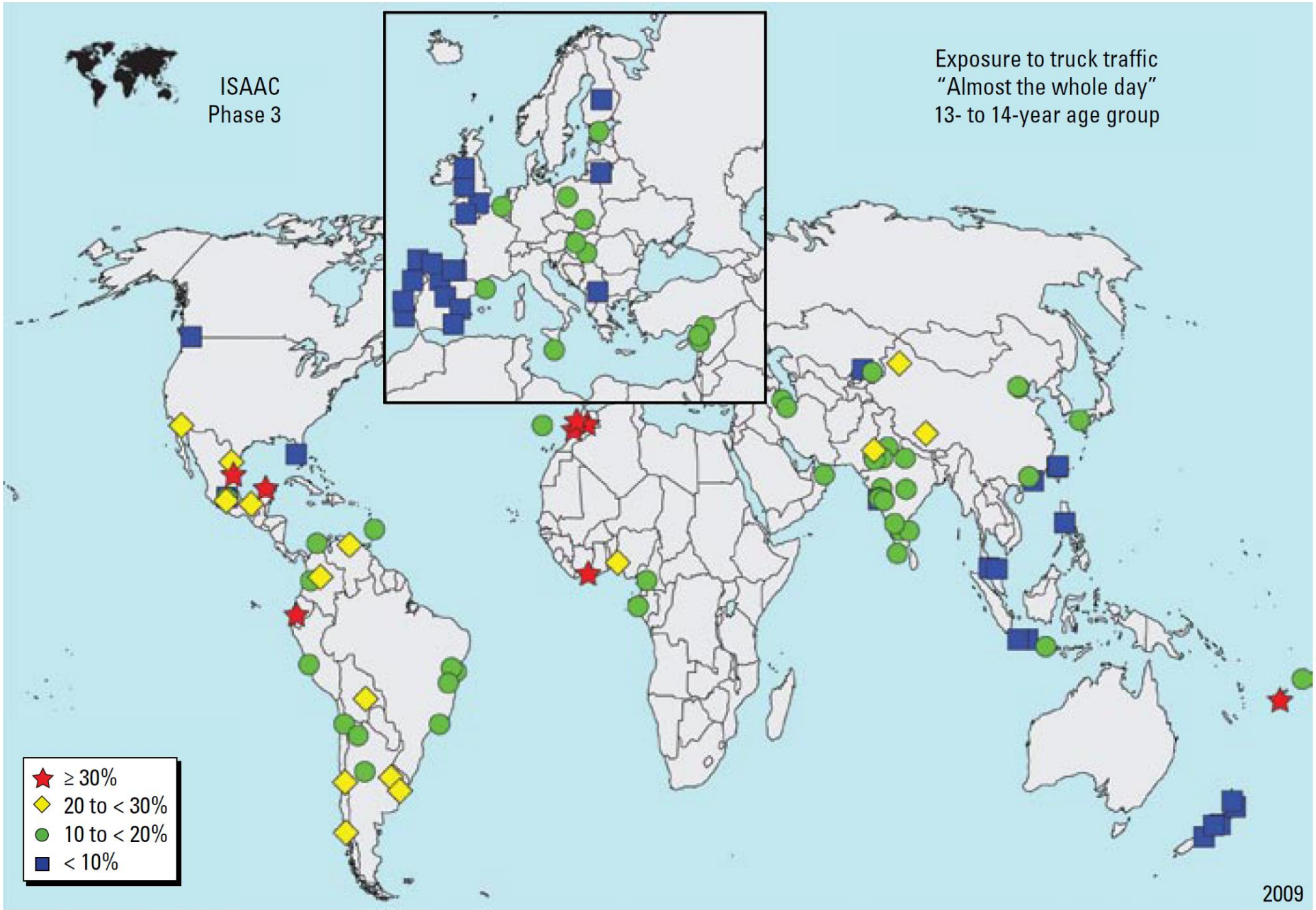
Traffic-related air pollutants (TRAP) & asthma onset, 8 year follow-up

- 217 children in Southern California Children's Health Study
- Prospective cohort
- New asthma in 8 years of follow-up (incidence)
- NO_2 monitors

- Incident asthma HR: 1.29 [CI 1.07–1.56] across interquartile range of 6.2 ppb NO_2

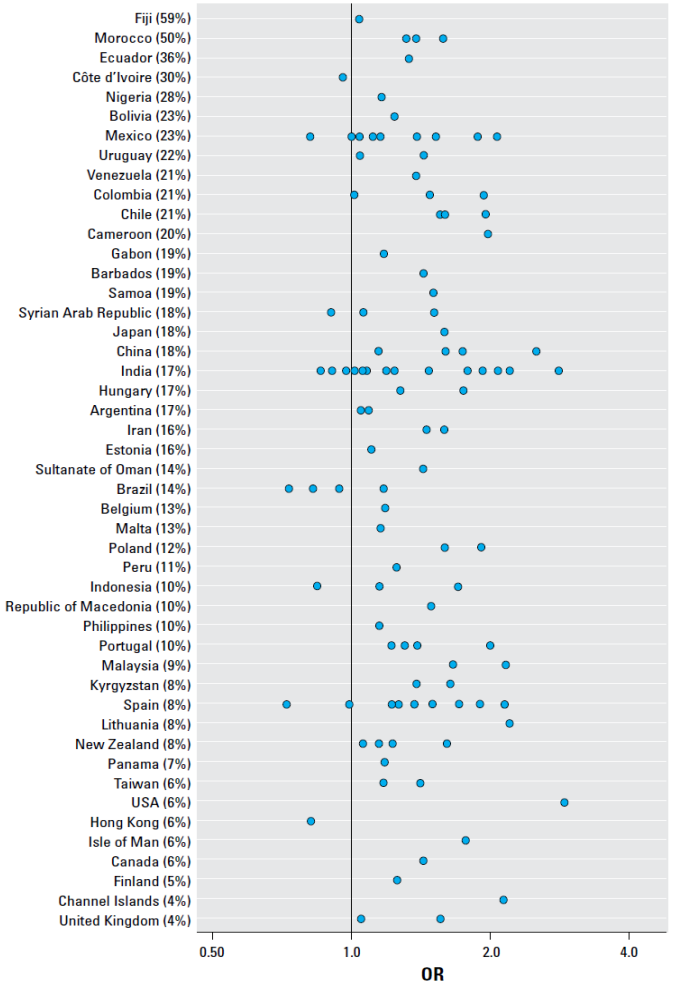
(Jerrett et al., Env H Persp 2008)

Global survey ISSAC III, on truck traffic

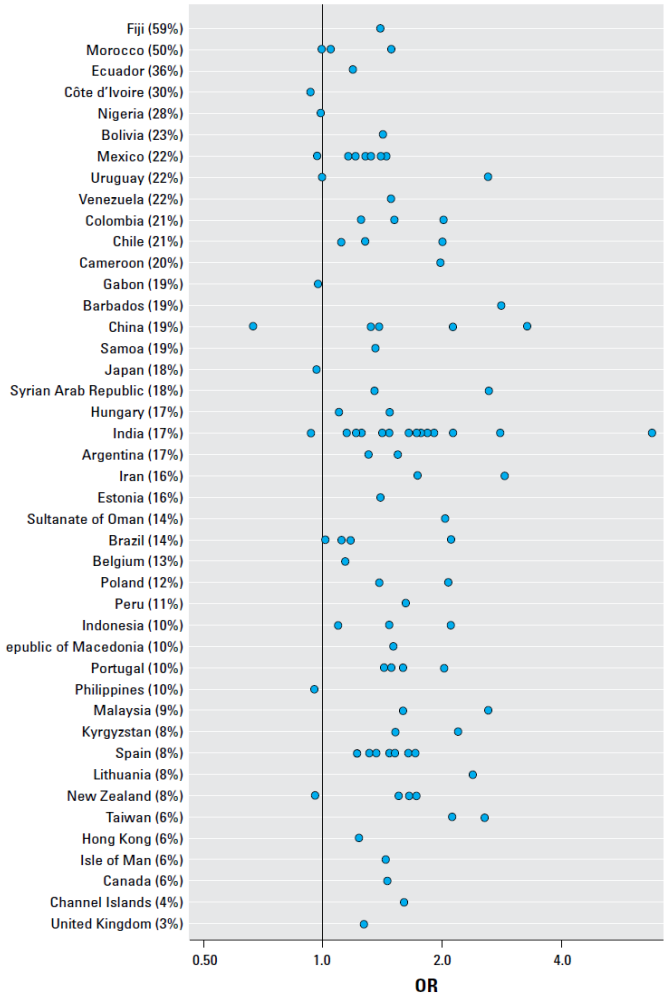


ORs for “almost the whole day” truck traffic vs. “never,” 13- to 14-year-olds

wheeze



rhinoconjunctivitis



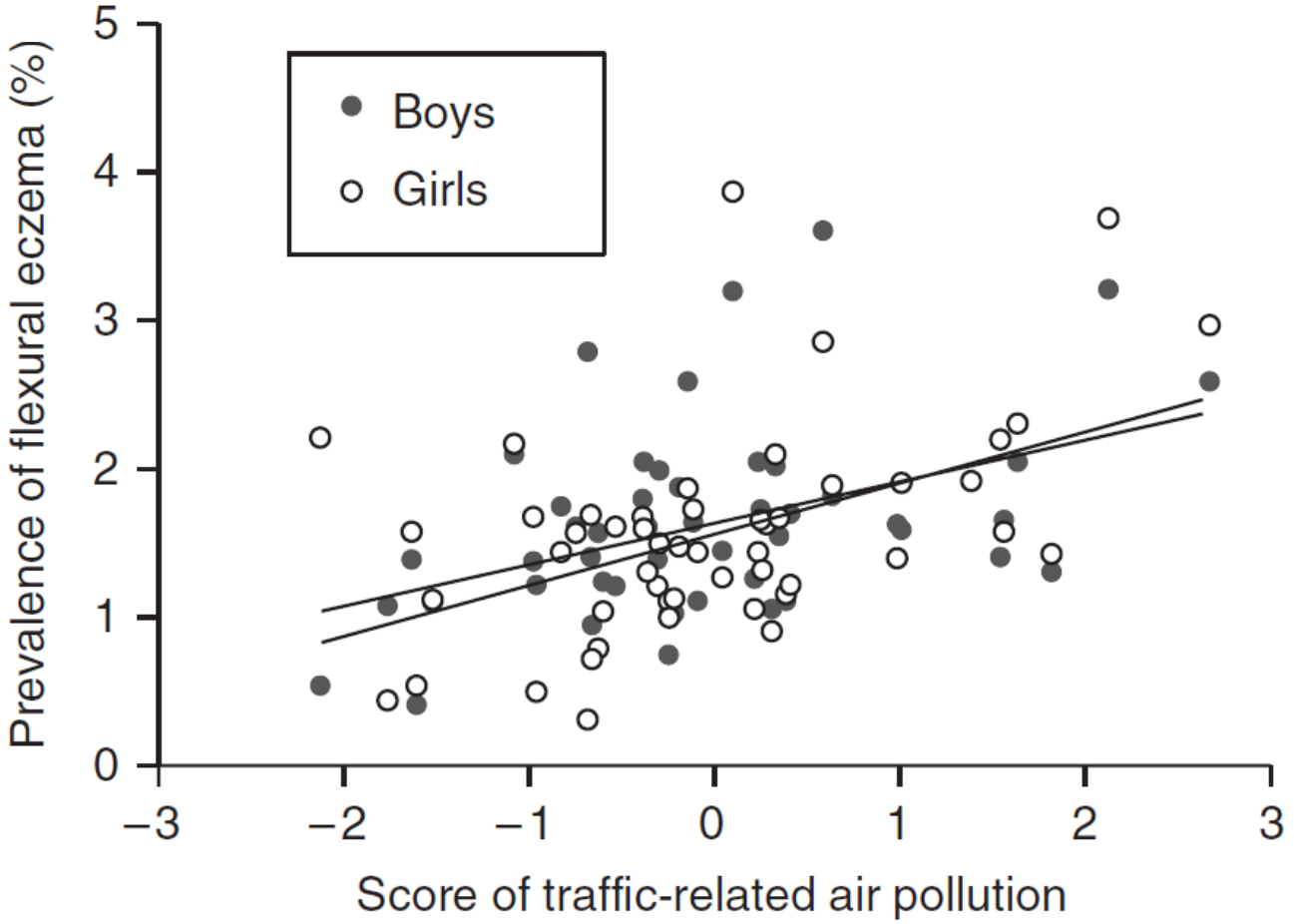
(Brunekreef et al. EHP 2009)

ORs for “almost the whole day” truck traffic vs. “never,” 13- to 14-year-olds

eczema

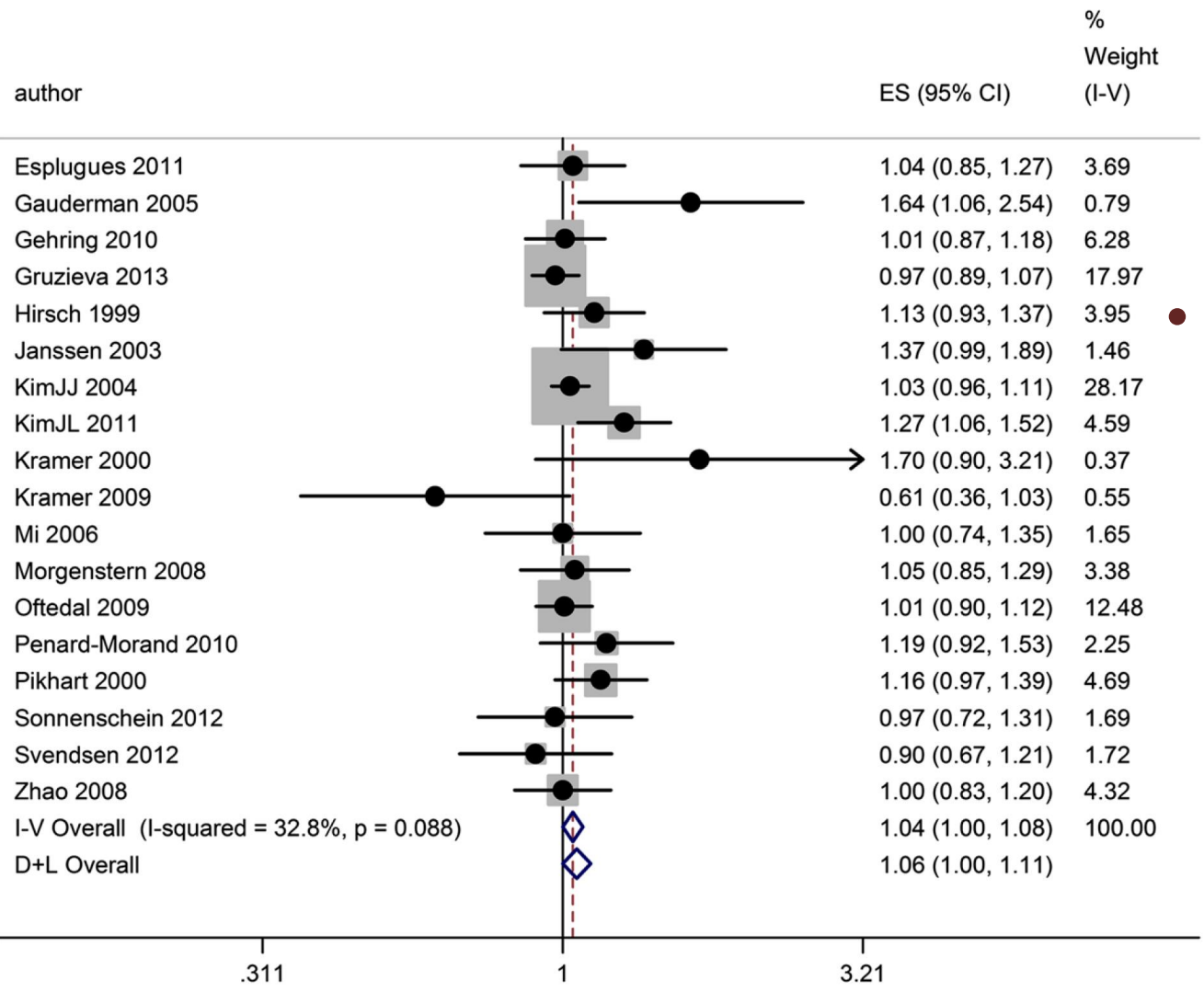
(Brunekreef et al. EHP 2009)

Traffic-related air pollution and prevalence rates of eczema



(Lee et al., J Invest Dermatol 2008)

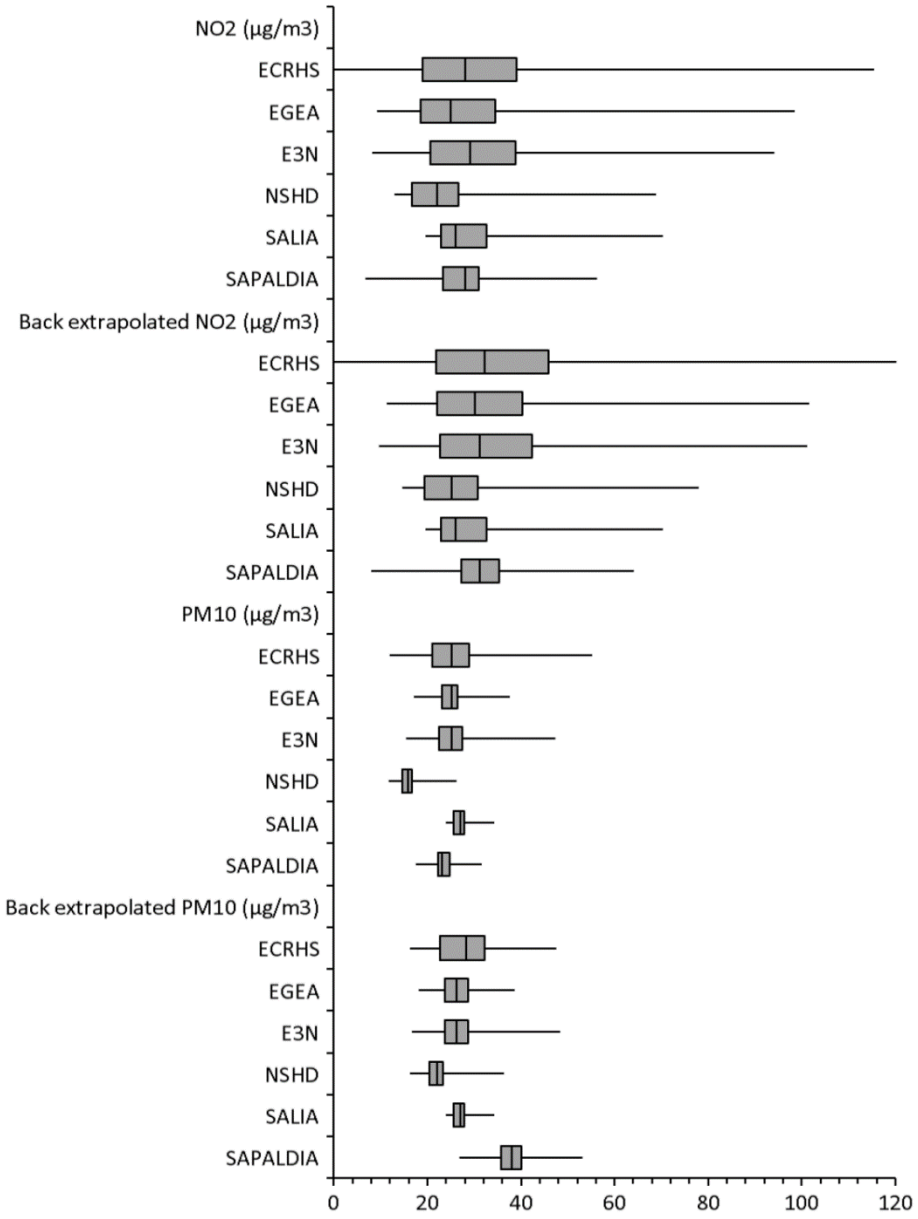
NO_2 and current asthma prevalence in children: meta-analysis



- **NO_2, 10 µg/m³ (5 ppb)↑**
  - **↑ 6.0% in current asthma prevalence**

(Favarato et al., Air Qual Atmos Health 2014)

Air pollution and adult asthma incidence by follow-up



6 prospective cohorts from 24 areas in 8 countries, f/u over 10-year period, total population of 23,704 (ESCAPE)

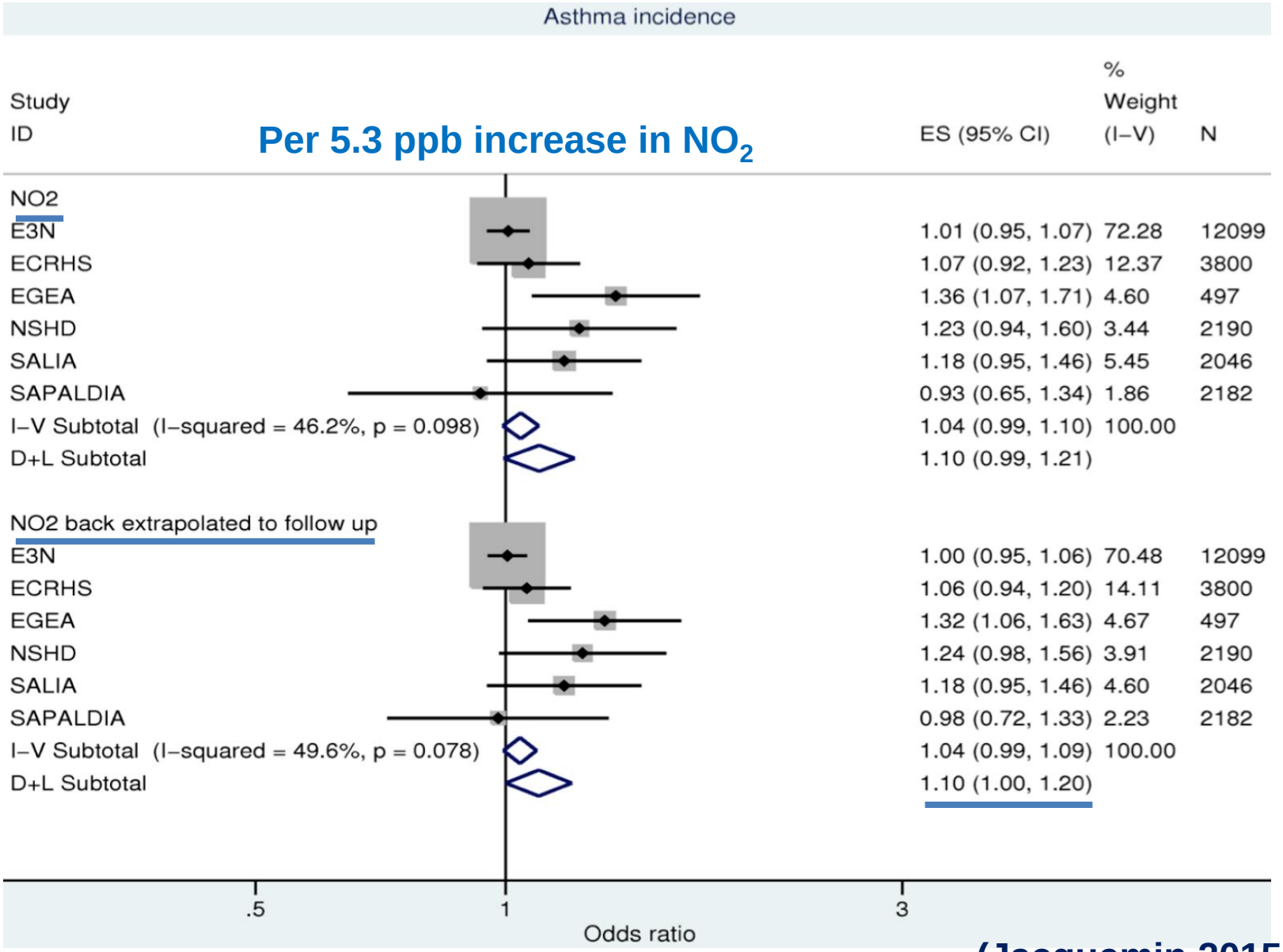
Age at baseline about 35~55 y

No asthma at baseline, Objective assessment of asthma

1257 incident case of asthma

(Jacquemin Env H Persp 2015)

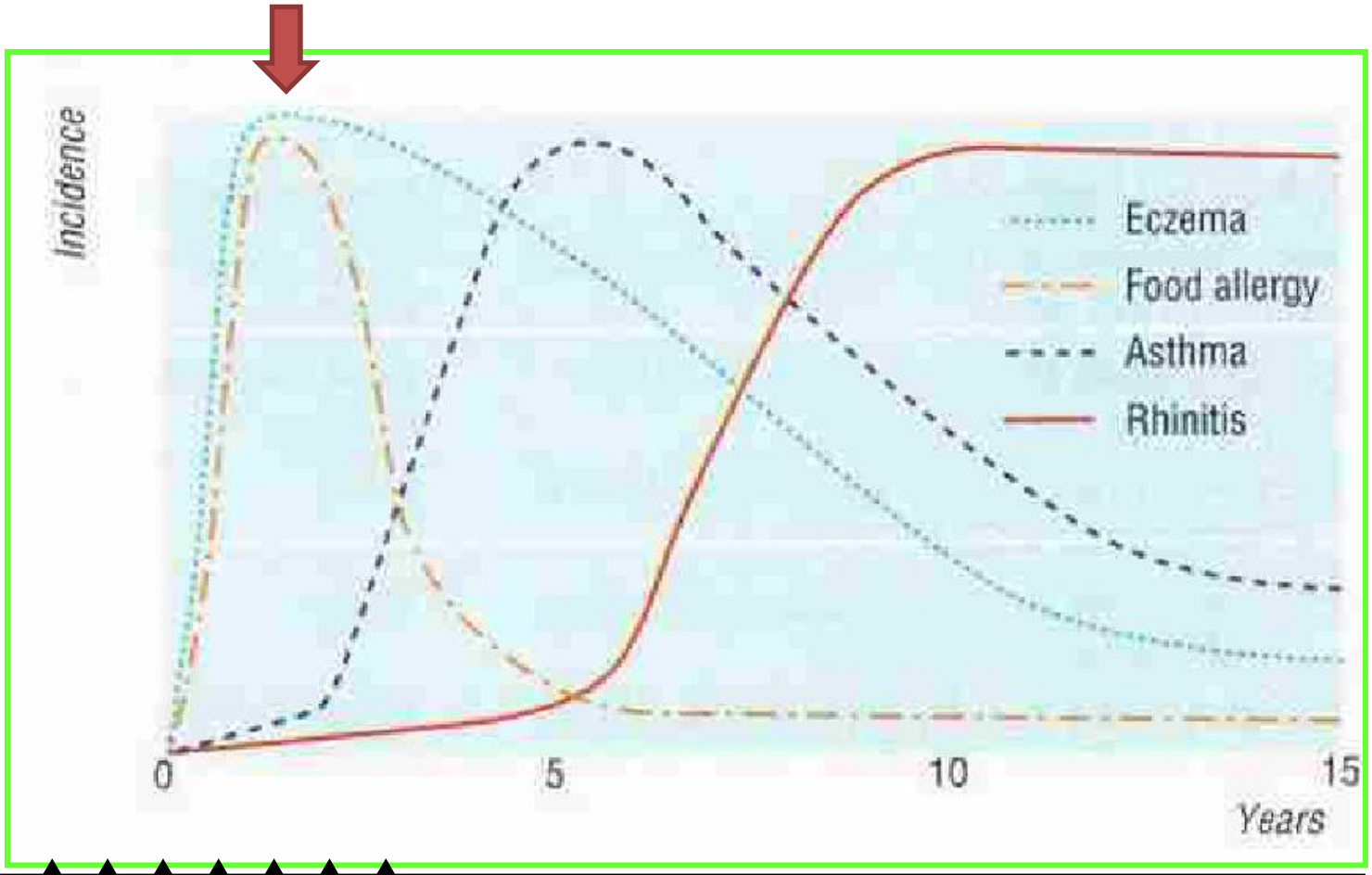
Air pollution and adult asthma incidence



(Jacquemin 2015 EHP)

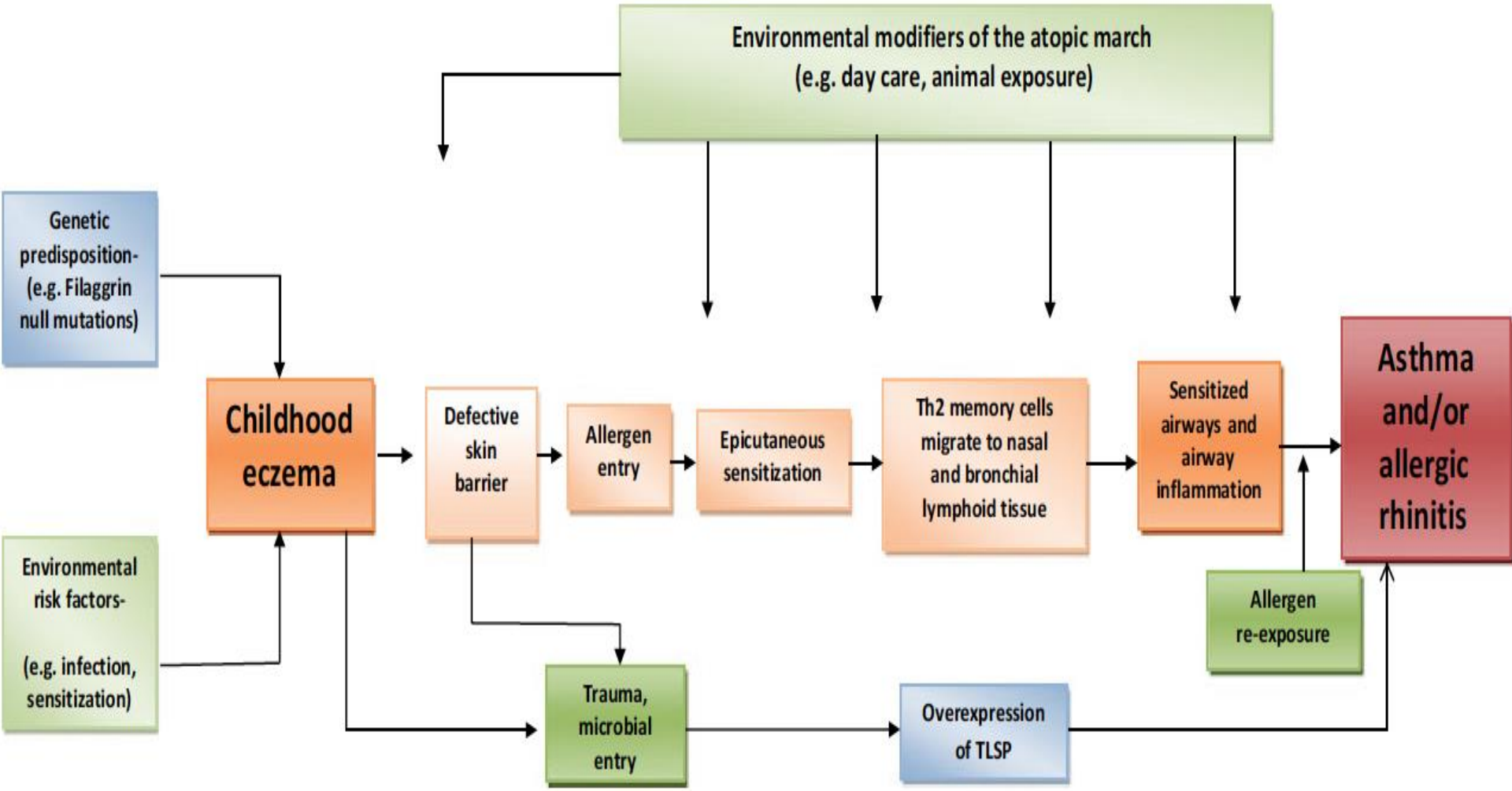
The Atopic March – early life exposure

Genetic factors



Environment

A proposed pathway of atopic march



Allergy 2014;69:17–27.

Meta-analysis of birth cohorts

Early childhood TRAP exposure to atopic outcomes

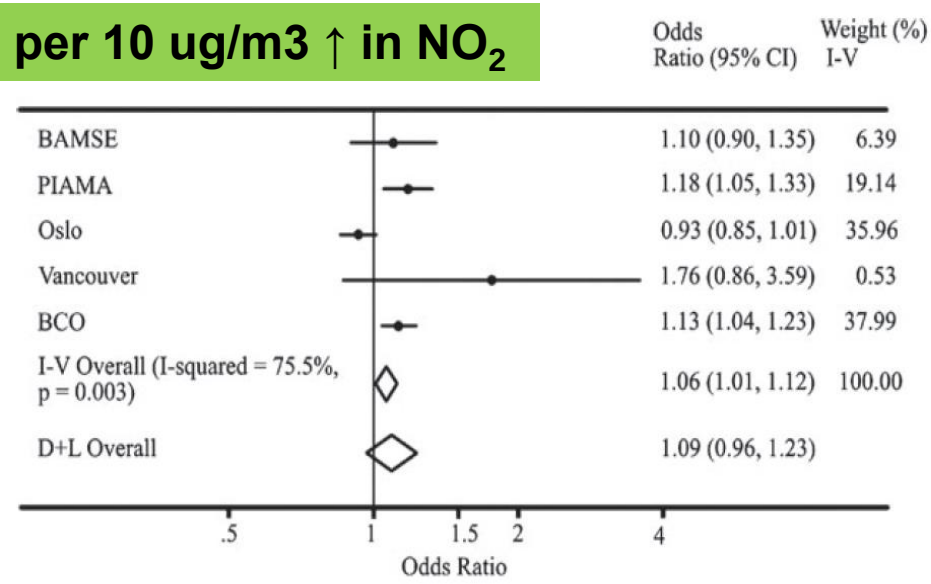
- **Exposure: Particles (PM10, PM2.5, black carbon), gases (NO2, NO, NOX) and proximity to roads.**
- **Outcomes: asthma, wheeze, eczema, hay fever and sensitization to allergens.**

- **INCLUDED:**
- **BAMSE, Barn Allergi Miljo¨ Stockholm Epidemiologi**
- **BCO, British Columbia birth cohort**
- **CCAAPS, Cincinnati childhood allergy and air pollution study**
- **CCCEH, Columbia centre for children's environmental health**
- **COPSAC, Copenhagen prospective study on asthma in childhood**
- **GINI & LISA, German infant nutrition intervention programme & lifestyle related factors on the human immune system and development of allergies in children**
- **GINI plus & LISA plus, German infant nutrition intervention programme plus & lifestyle related factors on the human immune system and development of allergies in children plus**
- **INMA, Infancia y Medio Ambiente**
- **Oslo, Oslo birth cohort**
- **PIAMA, prevention and incidence of asthma and mite allergy**
- **Vancouver, Vancouver birth cohort.**

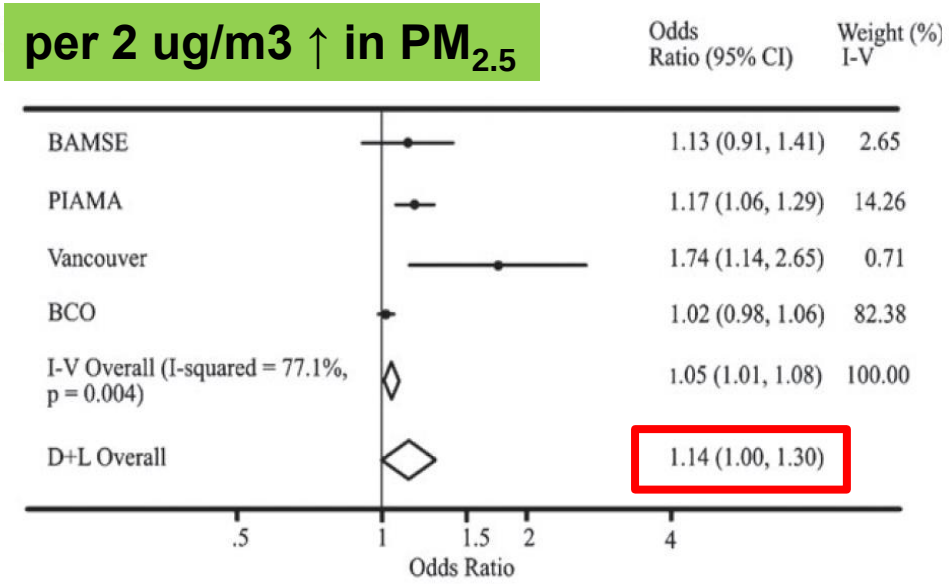
(Bowatte et al., Allergy 2015)

Early childhood TRAP exposure to asthma

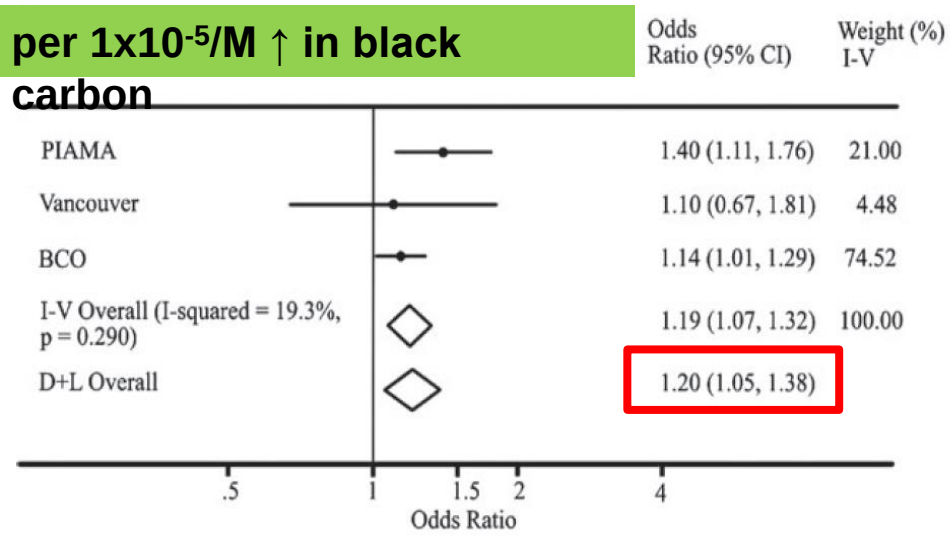
per 10 ug/m3 ↑ in NO_2



per 2 ug/m3 ↑ in $PM_{2.5}$



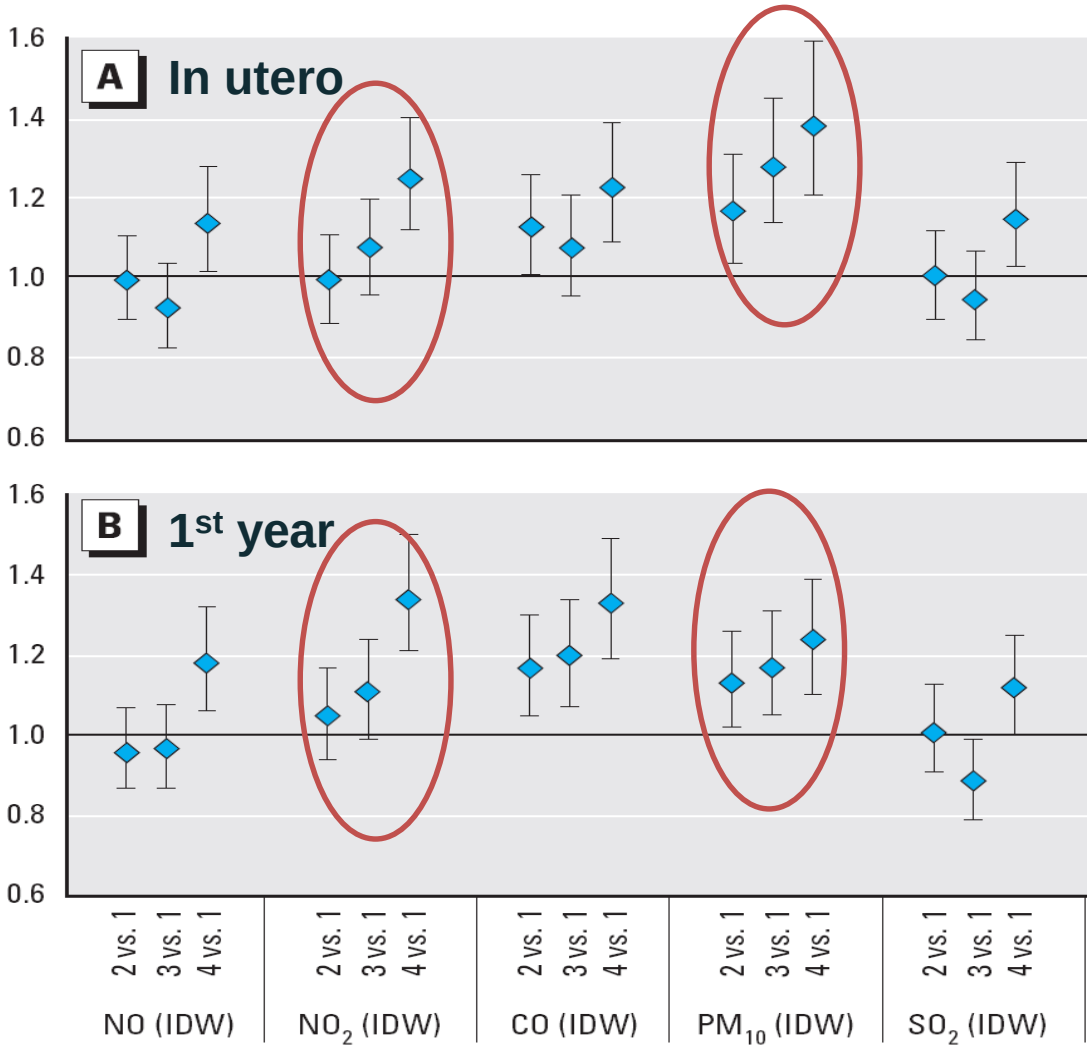
per 1x10^{-5}/M ↑ in black carbon



↑ exposure to $PM_{2.5}$ → ↑ sensitization to both aero- and food allergens.

(Bowatte et al., Allergy 2015)

Risk of asthma and exposure to air pollutants during early life

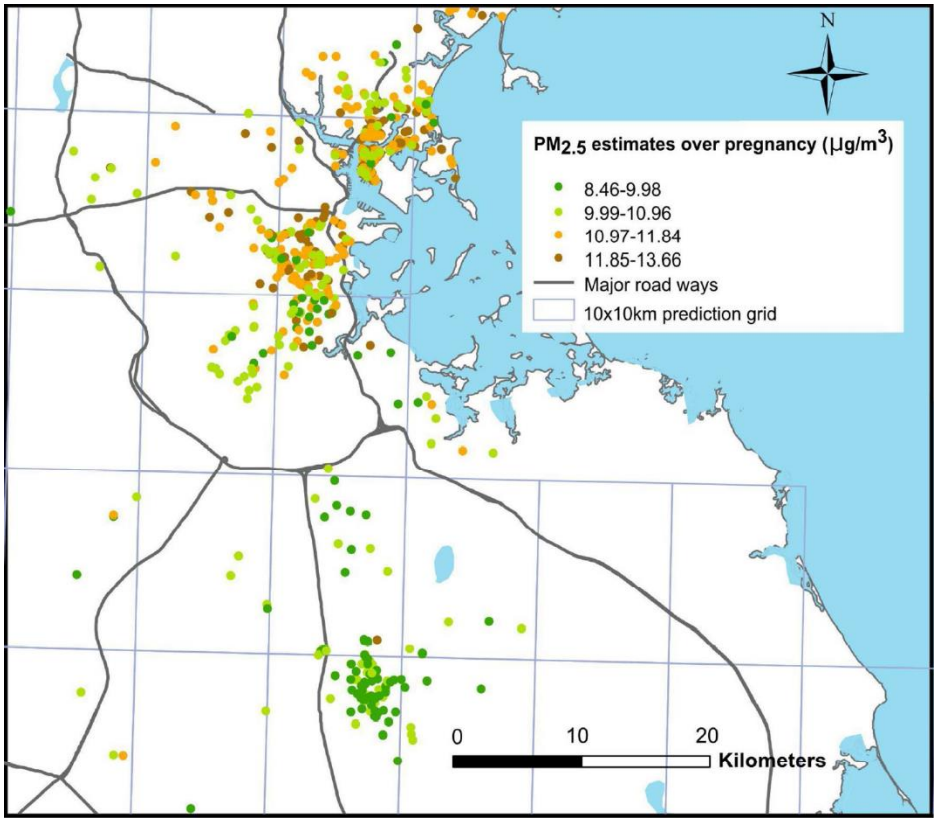


(Clark et al., EHP 2010)

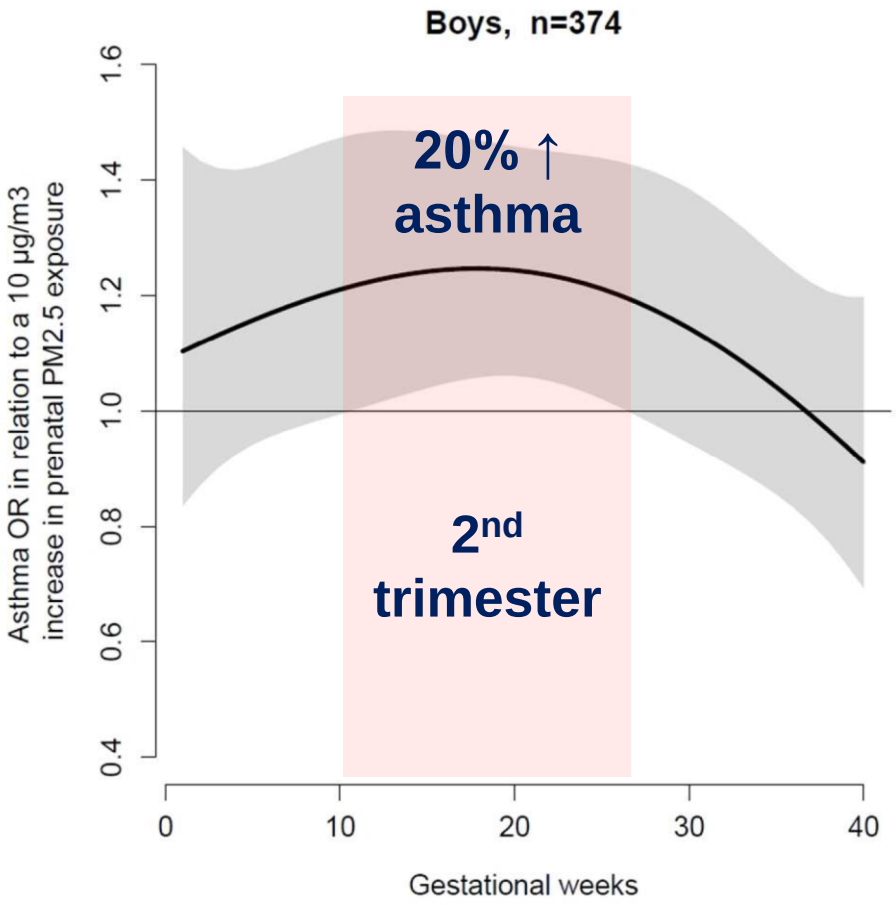
Window during gestation?

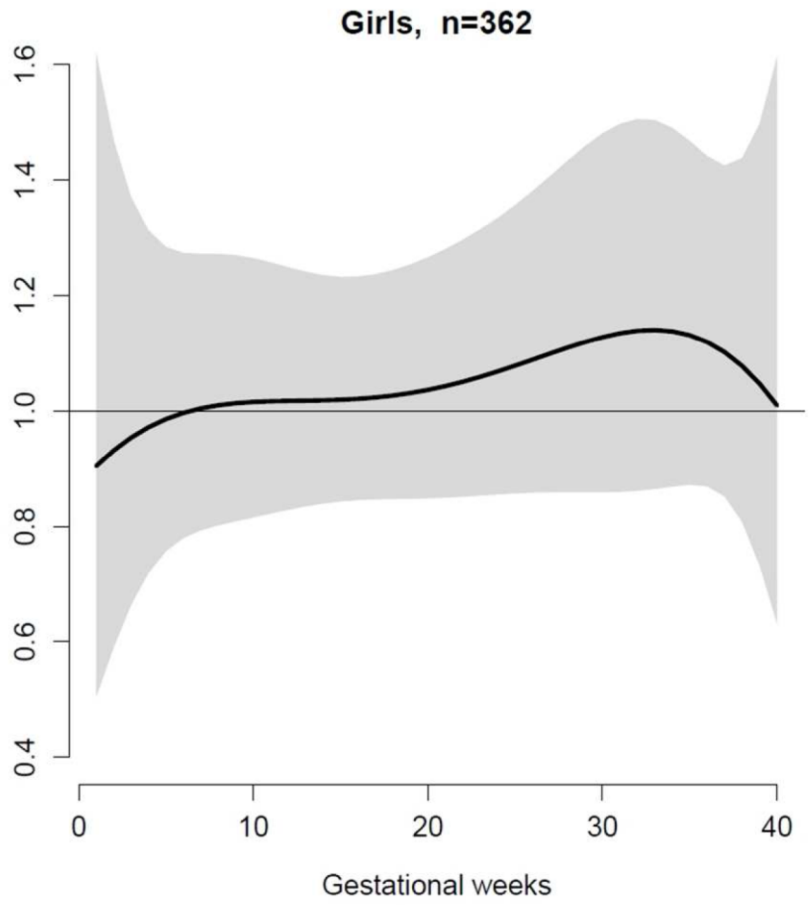
- 736 full-term (≥37 weeks) children, New England Area
- Mother's daily $PM_{2.5}$ exposure estimated over gestation by a validated satellite-based spatio-temporal resolved model, using distributed lag modeling (DLMs)
- Exposure: Weekly averaged $PM_{2.5}$ levels over pregnancy
- Outcome: Physician-diagnosed asthma in children by age 6 years
- Effect modification by sex was also examined.

(Hsu et al., AJRCCM 2015)



Weekly $PM_{2.5}$ levels (per 10 ug/M^3 ↑) and asthma onset



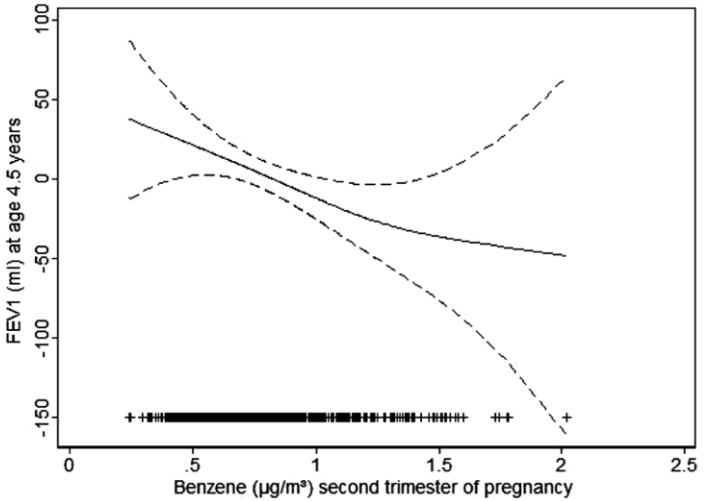


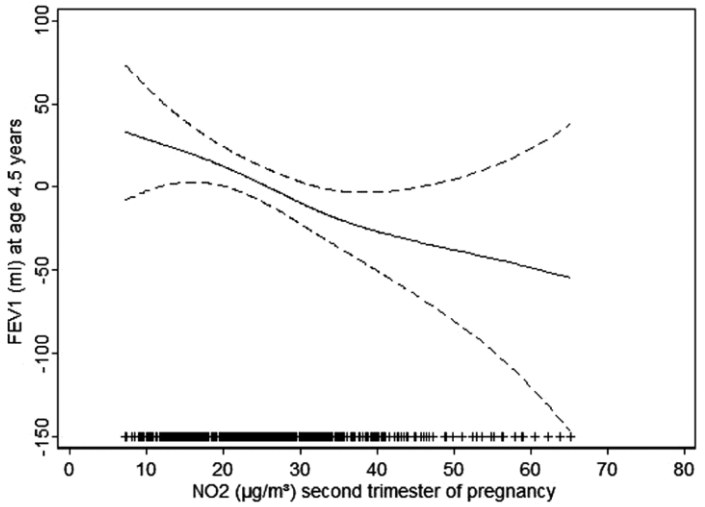
(Hsu et al., AJRCCM 2015)

Air pollution exposure during 2nd trimester and lung function

- **Spirometry in 620 children (4.5 y) (n=620)**
- **Land use regression (LUR) to estimate individual residential exposures to benzene and NO_2 during specific trimesters of pregnancy and the first year of life.**

- **GAM, adjusted for area of study, child's sex & age, height and weight, ethnic background, birth weight, maternal social class & education, maternal/paternal smoking in pregnancy, ETS 0–14 months, and lower respiratory tract infections 0–14 months.**

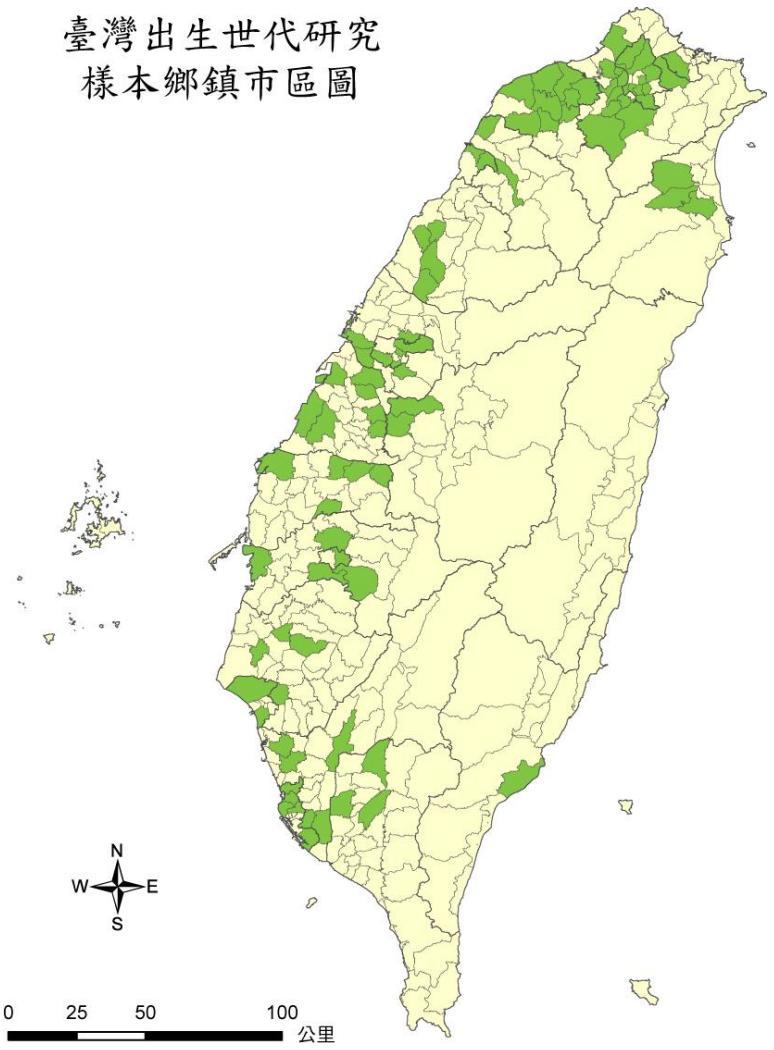




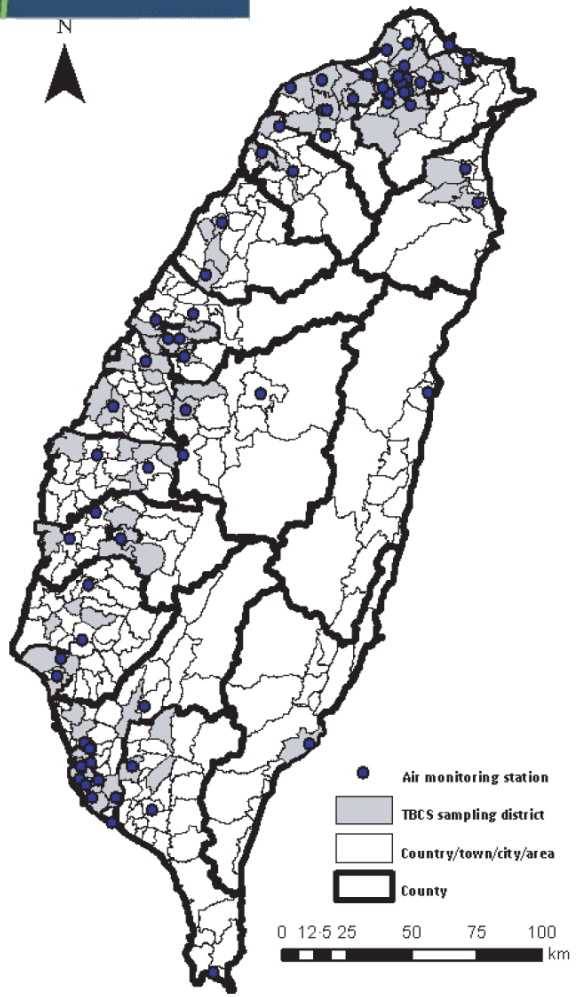
(Morales et al., Thorax 2015)

Taiwan Birth Cohort Study: perinatal air pollution and atopic eczema

- Systematic sampling for 85 townships and random sampling for individual births
- Drawn from National Birth Report data 1.2005~12.2005
- Sampling rate≒12%
- Air pollution data by monitoring stations and kriging (monthly) extrapolation
- Physician diagnosed atopic eczema at 2 year of age



Perinatal air pollution and atopic eczema by age 2 years, Taiwan Birth Cohort Study (TBCS)



Period	CO (OR across IQR)
First trimester	1·51 (1·16–1·97)**
Second trimester	0·86 (0·65–1·15)
Third trimester	1·19 (0·87–1·64)
3 months after birth	0·87 (0·67–1·12)
Whole gestational period	1·37 (1·06–1·78)*
From conception to 3 months postnatal	1·16 (0·87–1·55)

CO median during the 1st trimester = 536, IQR = 220 ppb (410 → 630 ppb)

Other criteria pollutants not significant after adjustment

Adjusted for infant sex, maternal age, birthweight, parental atopy, birth order, recently immigrated mother, maternal ETS, maternal education, annual household income, mouldy walls, nearby factories, postnatal ETS, birth season and county of residence.

(Huang et al., Br J Dermatol 2015)

Known

- Traffic pollutants & particles triggers asthma attack
- Traffic pollutants & particles may induce asthma
  - Adulthood exposure
  - Childhood exposure
  - Prenatal exposure

Need to know

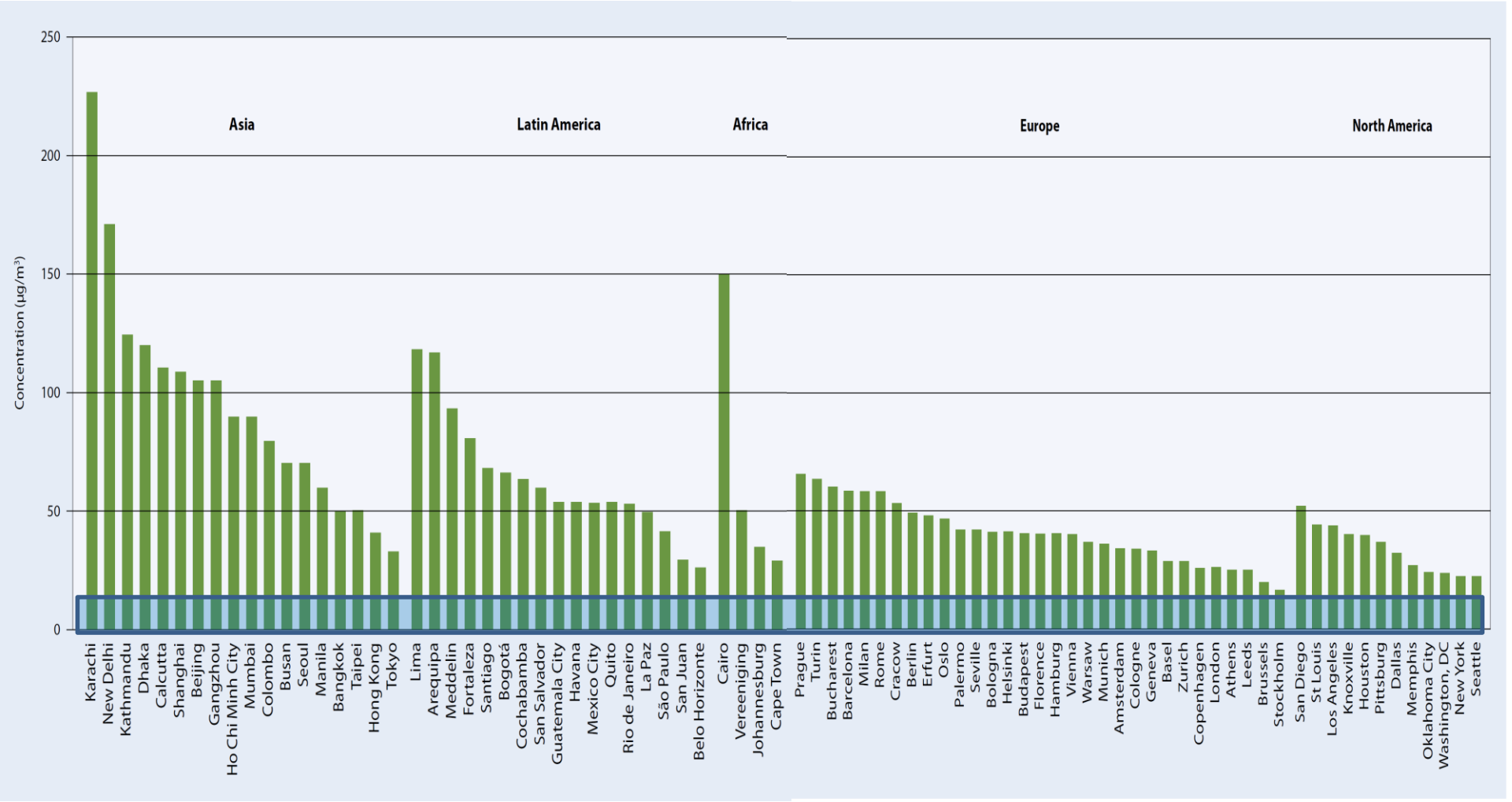
- Dose-response is probably not linear
- Critical window of exposure, including prenatal periods
- Air pollutants cannot be separated, thus some uncertainty exists in estimating each pollutant's effect
- Combined two or three pollutants may have different overall effect

Recommendation

- **Watch for AQI**
  - **Exercise outdoors**
- **Avoid living or working in a place with too high NO_2 or high $PM_{2.5}$**
  - **Adults**
  - **Children**
  - **Pregnant women**

- **When travel: Look for international data of air quality**

Annual average PM_{10} concentrations observed in selected cities worldwide



Source: WHO Air Quality Guidelines 2005

Thank You for Your Attention!