

Respiratory health of 5 years followed-up Flemish infants in relation to perinatal exposure to traffic-related air pollutants

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Asthma - Allergy



- » Asthma epidemic during past decades despite air quality improvement -> however traffic related emissions have substituted for pollutants of industrial /heating origine (*Zmirou et al., 2004*)
- » Worldwide variance and increasing trends, stabilizing in some regions
- » 13-14 years old children ISAAC study, phase III (The Netherlands, 2002):

N= 6896	% ever	% last 12m
asthma	13	-
wheeze	23	12
itchy rash	21	13
eczeme	35	8
night cough	-	25

- » For most cases, **initial symptoms** already in first years of life

Risk factors allergic diseases



Predisposing factors

- » atopy (!) and gender

Causal factors

- » Indoor/outdoor exposure : e.g. house dust mite, pets, pollen
- » Work-related sensitizing agents ~ occupational asthma

Stimulating factors

- » respiratory infections, small length at birth, food, **air pollution**, smoking

Triggering factors

- » allergens, respiratory infections, physical exercise, climate, food

Does air pollution induce allergic diseases and asthma?



- » **WHO 2004:** “little evidence for childhood asthma prevalence/incidence and air pollution in general, but there is **suggestive evidence for causal association with living in close proximity to traffic**”Traffic related air pollutants may trigger exacerbations in already existing asthma and allergic responses are enhanced by exposure.
- » Particulate matter, DEP, NO₂, ozone: **potent oxidants**
 - » direct effects on lipids, proteins or indirect through activation of intracellular oxidant pathways
 - » children’s antioxidants enzyme activity reach adult level at 6m
- » Association asthma **incidence** with air pollution **can only be investigated by prospective cohort studies**

11 birth cohorts on air pollution – asthma/allergy

(Koppen et al., in press)

Study	N	Follow-up	exposure	Association with allergic/respiratory responses:
CCCEH, USA	303	6,12,24m	PAH ,EC, PM _{2.5}	Wheeze, cough, infections
CCCEH, Poland	>333	12,24m	PAH, PM _{2.5}	Wheeze, cough
CCAAPS, USA	570	12,24m	EC	wheeze
CzECH, Czech Rep	1133	3-4.5y	PAH, PM _{2.5} , PM ₁₀ , SO ₂ , NO _x	bronchitis
GINI/LISA, Germany (TRAPCA)	3066 + 3390	12,24m 6y	PM _{2.5} , NO ₂ , distance road	Cough, sneezing, runny/ stuffed nose, bronchitis At 6y: eczema, hay fever, pollen allergy
PIAMA, The Netherlands (TRAPCA)	3538	24m 4y	PM _{2.5} , NO ₂	Infections, wheeze Allergy (IgE total and food)
BAMSE, Sweden (TRAPCA)	3515	4y	PM ₁₀ , NO _x	Wheeze, allergy (IgE inhalant allergens)
Oslo cohort, Norway	2244	9-10y	PM _{2.5} , NO ₂ , NO	allergy house dust mite (SPT)
Copenhagen Prospective	205	3y	PM ₁₀ , NO ₂ , NO _x , CO	wheeze
Bern, Switzerland	241	5 wks	PM ₁₀ , NO ₂ , O ₃	Lung function, eNO
FLEHS, Belgium	159	5y	PM ₁₀ , NO ₂	Cough, itchy rash, allergy at 3y (SPT, pollen+house dust mite)

FLEHS Study population/area

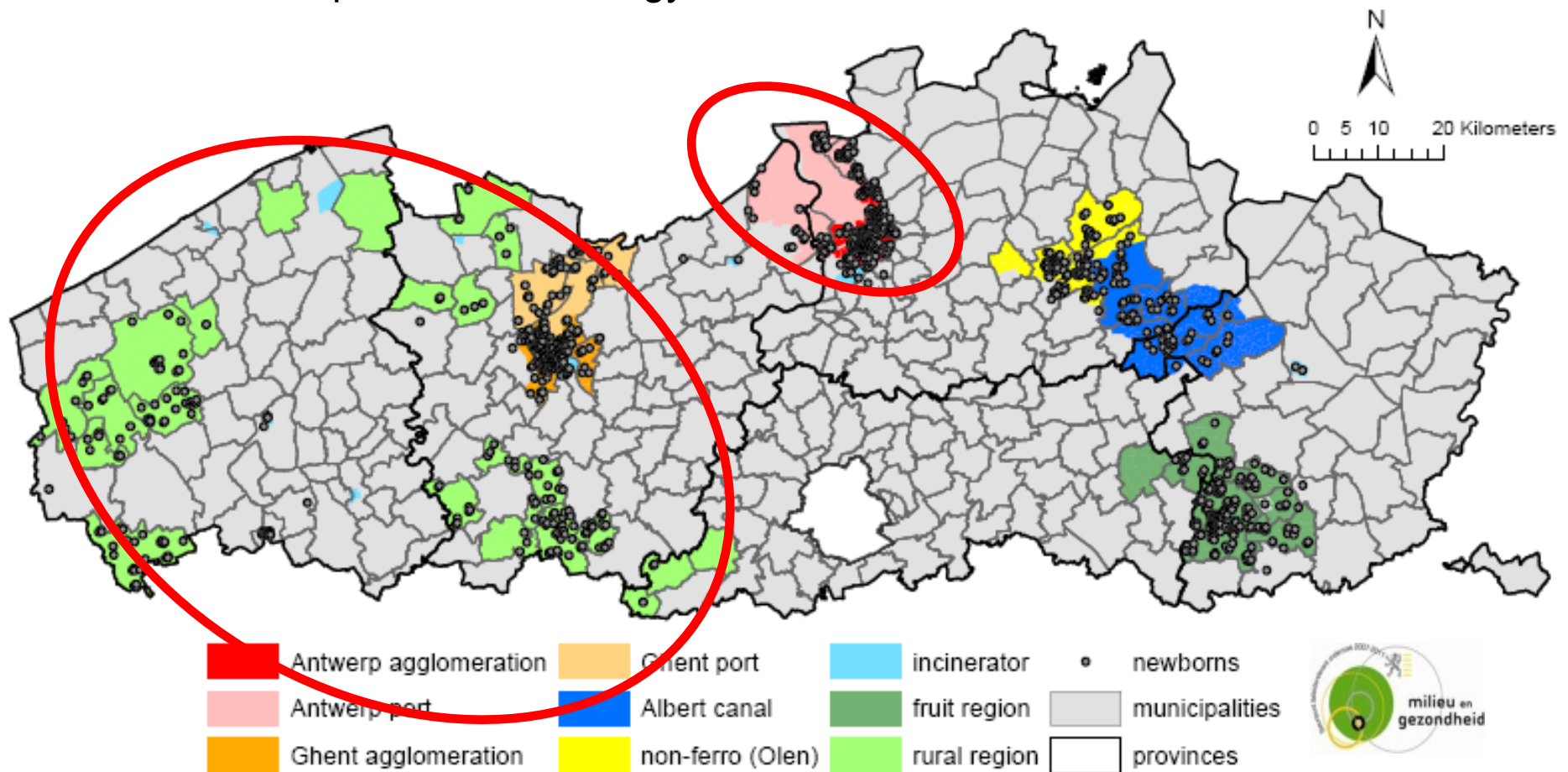


Birth cohort Flanders Environment & Health Survey (FLEHS I)

1196 newborns

25 maternities, 2 stem cell banks (2002-2004)

N=159 followed up for asthma/allergy

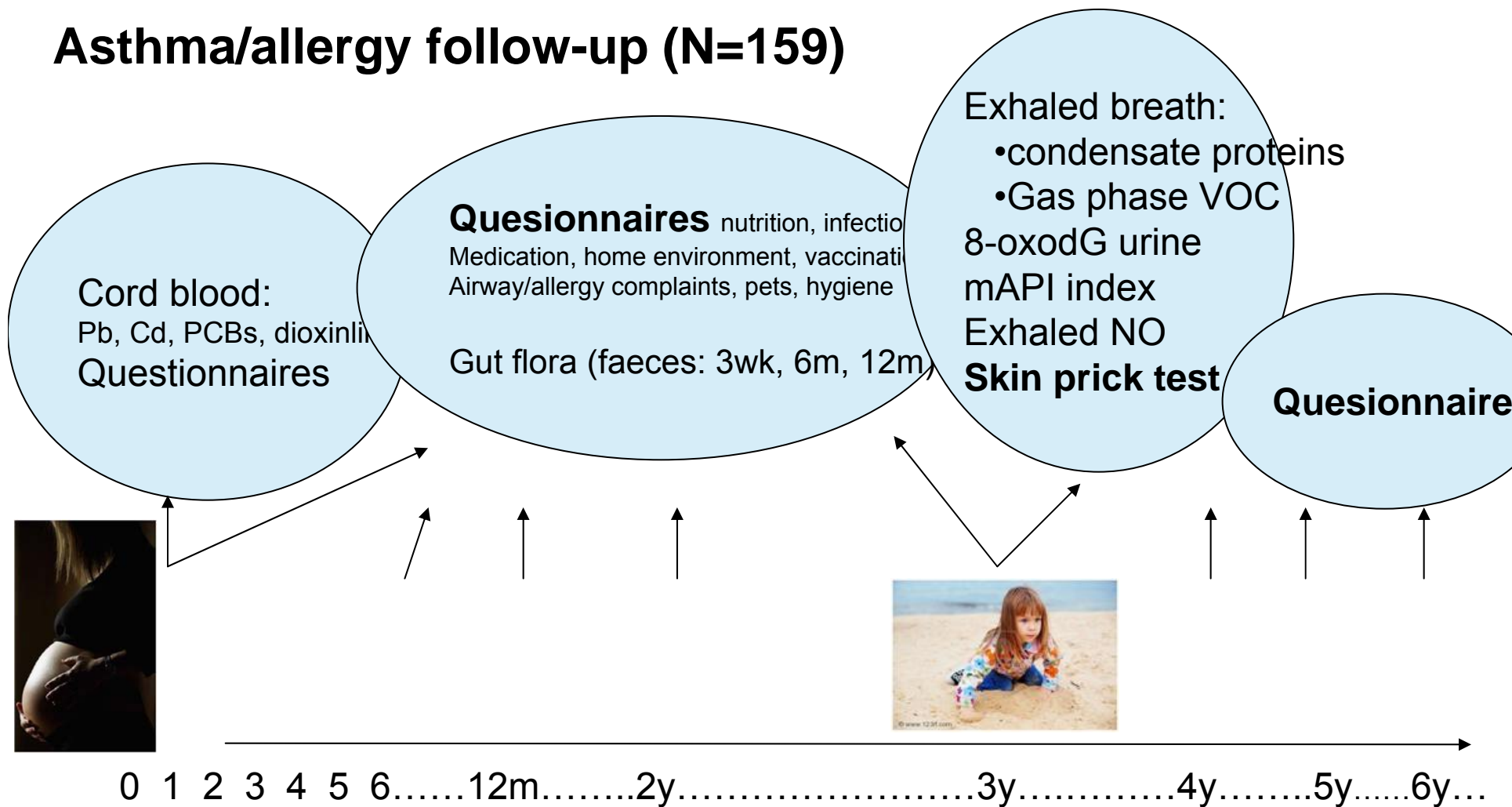


Outdoor air pollutant concentrations per region



Outdoor component	Urban (n=81)	Rural (n=51)
Distance to major road (km)	0,3 (0,2-0,5)	0,5 (0,2-0,7)
Interpolated concentrations		
NO₂ (µg/m³)		
1 th trimester pregnancy	42,4 (37,5-46,5)	17,0 (14,5-21,0)
2 th trimester pregnancy	45,1 (39,6-48,1)	17,2 (13,1-20,4)
3 th trimester pregnancy	46,7 (40,9-49,9)	18,2 (16,2-22,4)
First 3m	47,2 (41,1-50,1)	20,2 (17,2-21,8)
First year	46,7 (44,8-47,7)	17,7 (16,7-20,1)
PM₁₀ (µg/m³)		
1 th trimester pregnancy	34,1 (31,9-36,7)	33,0 (30,5-37,6)
2 th trimester pregnancy	35,9 (33,3-39,8)	31,4 (29,3-36,2)
3 th trimester pregnancy	38,4 (35,3-42,8)	32,5 (30,6-36,0)
First 3m	39,6 (37,6-42,8)	34,3 (30,8-37,2)
First year	38,3 (36,6-40,8)	32,9 (31,1-35,1)

Asthma/allergy follow-up (N=159)



**Interpolated conc. NO₂, PM₁₀ (4x4 km, home address, IRCEL):
3 trim pregnancy, 3m, 1y**

Research question: relation perinatal/postnatal exposure to outdoor air pollutants and allergy/respiratory health

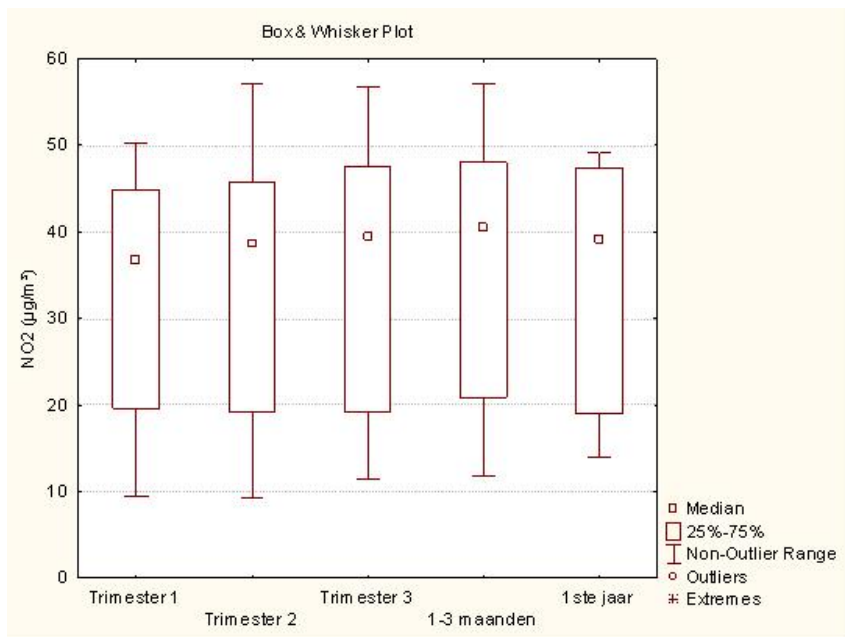
Follow-up study → longitudinal data

Statistical analysis per binary health effect (0/1)

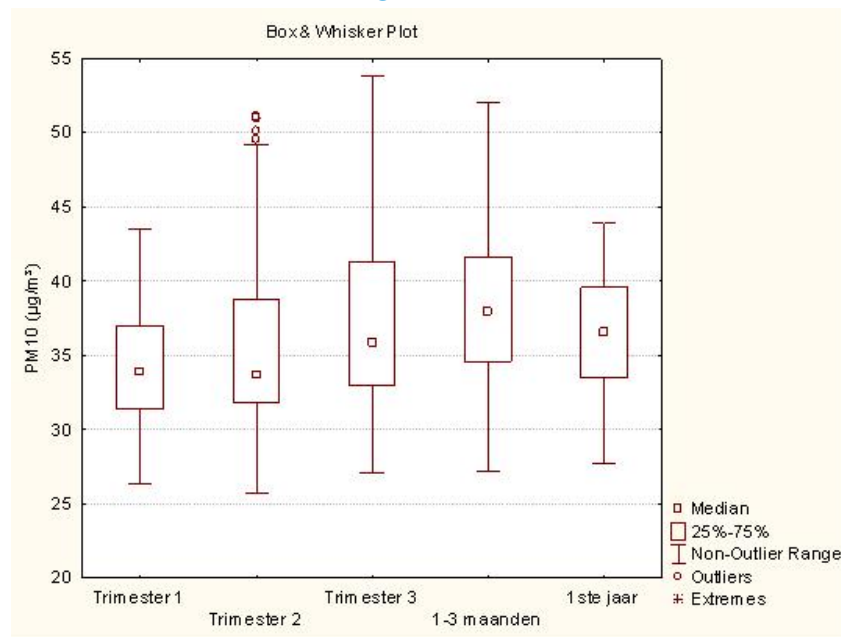
- **On one time point:** Multiple logistic regression
- **Over time:** health effect within individual correlated over different time points → Mixed model analysis with evaluation of intra-individual correlation matrix: e.g. Generalized Estimating Equations (GEE)

Analysis: single pollutant models

NO₂ (µg/m³)



PM₁₀ (µg/m³)



separate models for each pollutant and for each time point of exposure to this pollutant

Possible factors of influence aside from outdoor pollutants (questionnaire data)

- Gender
- Age mother at delivery
- Season delivery
- Birth weight
- Education mother
- Number of family members
- Smoking during pregnancy
- Alcohol during pregnancy
- Breastfeeding at 3 weeks and 6 months
- Familial asthma
- Individual asthma
- Hay fever
- Food allergy
- Skin allergy
- Animal allergy
- Contact with farm animals
- Nursery



Results: Skin prick test at age 3y



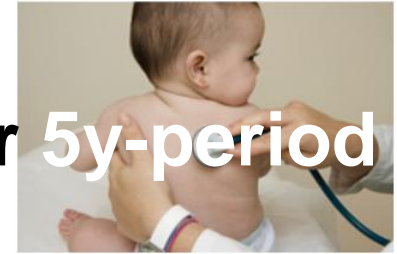
Skin prick test at age of 3 years:
11% positive for house dust mite and/or pollen

multiple logistic regression

Positive skin prick on age 3y	OR (95% CI)	p-value
NO ₂ averaged over first 3m (µg/m ³) for ↑10 µg/m ³	1.97 (1.01-3.71)	0,04
Consumption fish fats mother during pregnancy (g fat/day)	1,16 (1,03-1,31)	0,016
Consumption Bifidus products	2,04 (1,15-3,63)	0,013

NO₂ 1-3 months of life ~ NO₂ trim 1, 2, 3; ~ NO₂, PM₁₀, NO_x, benzene: 1st year of life

Results: Allergy/respiratory effects over 5y-period



Prevalence health effect on the time points of follow-up

Health effect	Time point questionnaire								
	3 w	6 m	12 m	18 m	24 m	30 m	36 m	4 y	5 y
Wheezing	18 /152	26 /139	33 /137	19 /138	19 /133	20 /112	18 /127	11 /108	6 /66
Airway infection	2 /151	30 /138	41 /134	70 /134	27 /131	23 /112	25 /127	19 /108	13 /96
Coughing day	41 /152	92 /139	100 /136	91 /138	74 /133	70 /111	86 /126		
Coughing night	9 /151	65 /139	86 /137	81 /138	72 /132	68 /111	85 /127		
Coughing medication								52 /108	41 /96
Itchy rash			24 /135		20 /134		24 /125	18 /107	17 /96
Eczema								10 /17	8 /17

Results: longitudinal analysis

» Autoregressive correlation matrix

➡ the correlation between 'measurements' collected close in time is higher than those taken farther in time

» Selected confounders

- Airway infection, wheezing en coughing
 - gender, season birth, individual asthma, age mother, number of family members and breastfeeding at 3 weeks (only for coughing)
- Eczema en itchy rash
 - gender
- For all outcomes
 - age child

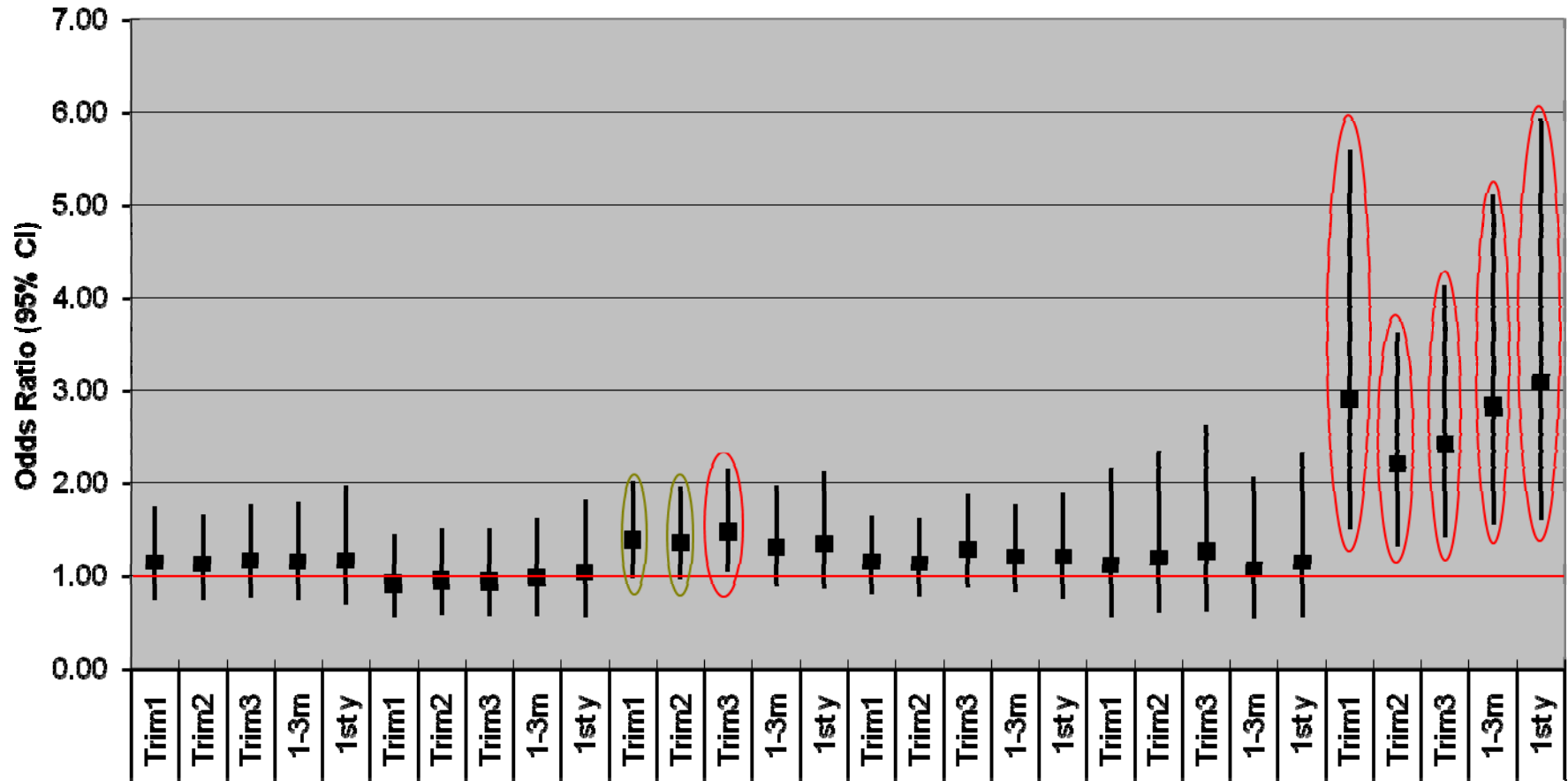


Results longitudinal analysis

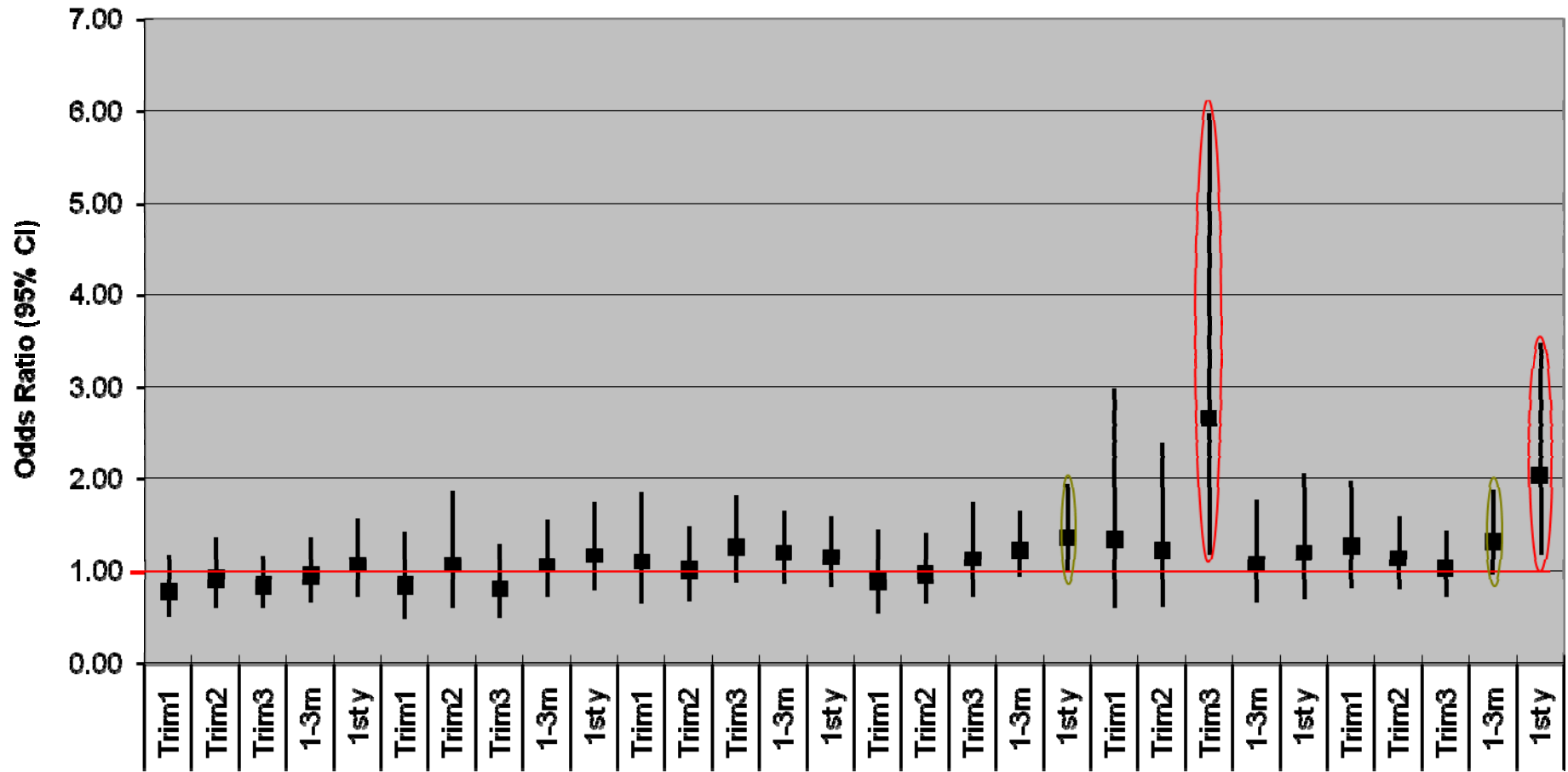
- » Association (odds ratio) between an increase in interquartile range (IR) in the pollutant concentration and health effect, after correction for selected confounders
- » Interquartile ranges

	NO₂ (µg/m³)	PM₁₀ (µg/m³)
Trimester 1	25.3	5.6
Trimester 2	26.5	7.0
Trimester 3	28.2	8.35
1-3 months	27.1	7.05
1st year	28.4	6.05

Results NO₂ vs. health effects



Results PM₁₀ vs. health effects



Conclusion

In current FLEHS follow-up from 0-5y

- » Wheezing: 12-19%,
- » Itchy rash: 15-19%
- » Positive skin prick test for pollen/ house dust mite at 3y: 11%



Most important associations between **traffic pollutants** and **allergy**:

- » NO₂ - skin prick test at 3y
- » NO₂ - itchy rash over 5y follow-up

-> Results small-scaled cohort in accordance with other atopic disease follow-up birth cohorts (*Brauer et al., 2007; Morgenstern et al., 2008; Nordling et al., 2008; Krämer et al., 2009*)

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Relation allergic sensitisation and traffic pollutants?



- » DEP enhance symptoms in already allergic subjects (Nordenhäll et al., 2001)
- » Unknown wheater traffic-related exposure can induce sensitization to a neoantigen -> conflicting studies (*cf. Oftedal et al., 2007*)
- » Mechanisms
 - » Interaction of pollen with air pollutants increasing allergenicity (PM on pollen) (*Wyller et al., 2000*)
 - » DEP at higher conc and with short exposure time enhances immunological responses to allergens (observed in human intervention studies, animals, *in vitro*)



Conclusion

- » Findings of our follow-up study conform the suggestive evidence of relation between **atopic diseases** and **living/growing up in proximity of traffic**
- » 2 final remarks to taken in mind
 - » Exposure parameters associated with other traffic-related parameters e.g. noise, EC, UFP, urban environment
 - » Prenatal exposure of influence (*Miller et al., 2004; Jedrychowski et al., 2009; Latzin et al, 2009; Koppen et al., in press*) -> BUT: **not clear-cut to assign observed effect mainly to perinatal exposure** -> may be strongly correlated to levels later in life!



Study partners

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