

# Impact of air pollution on human health



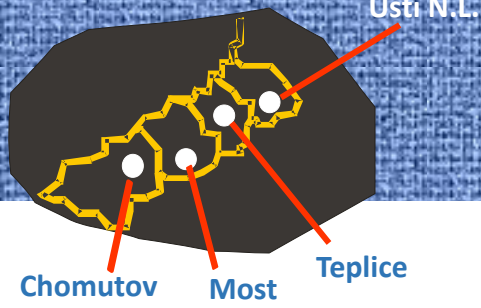
R. J. Sram

The Czech Academy of Sciences, Institute of Experimental Medicine, Prague, Czech Republic



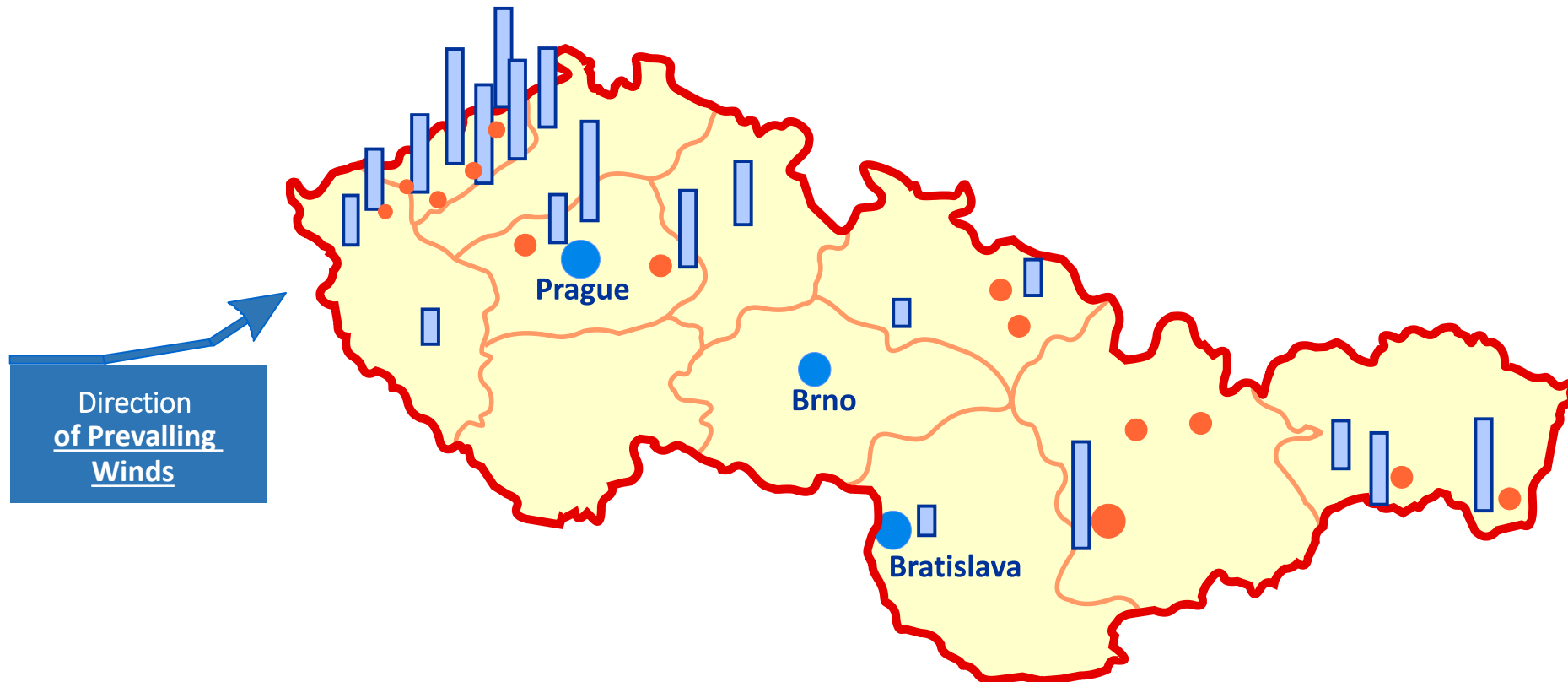
Conference „Fighting Air Pollution“, Ostrava, November 19, 2018

Mining Districts



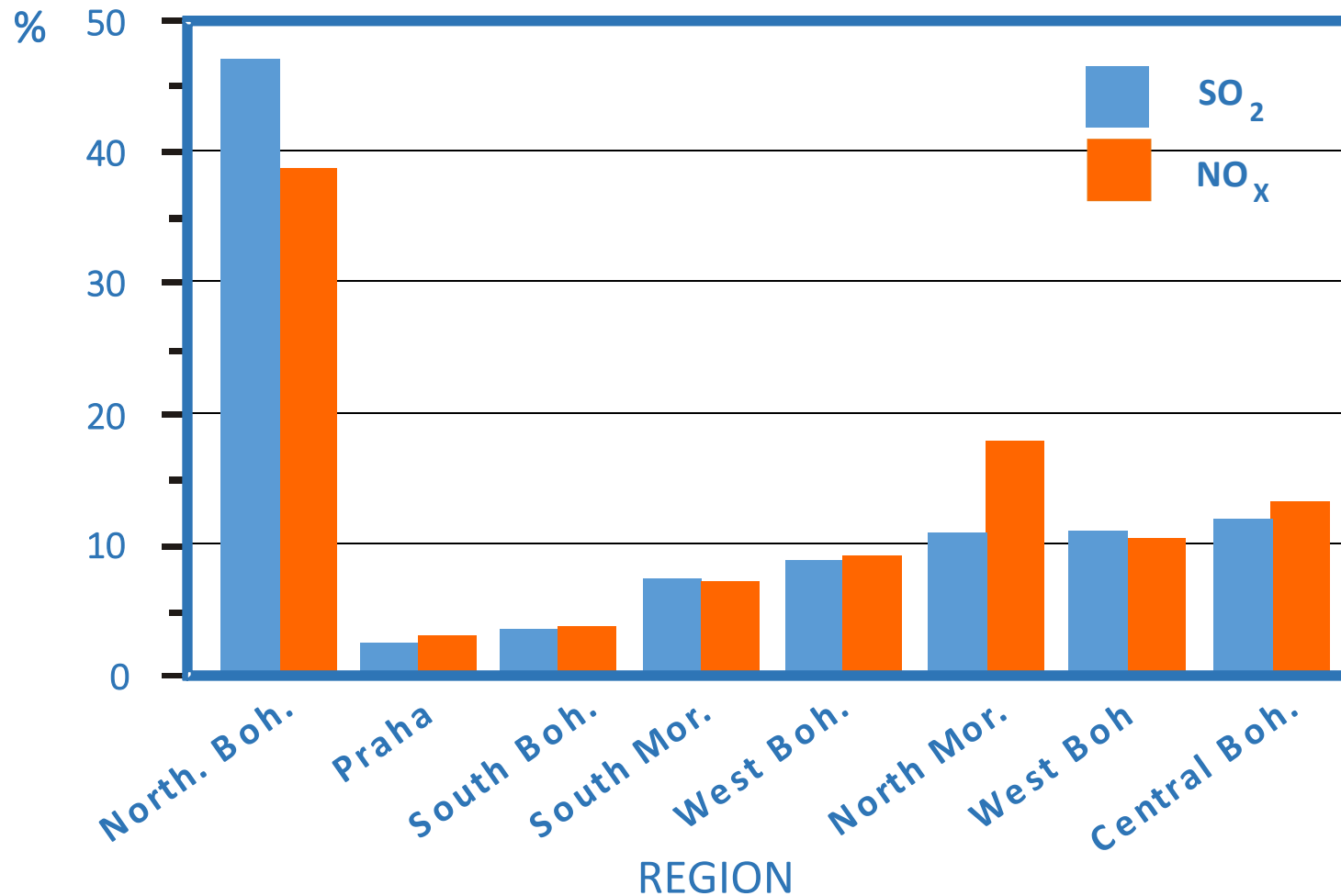
498,000 inhabitants

# DISTRIBUTION OF THE MAIN EMISSION CENTRES IN CZECHOSLOVAKIA

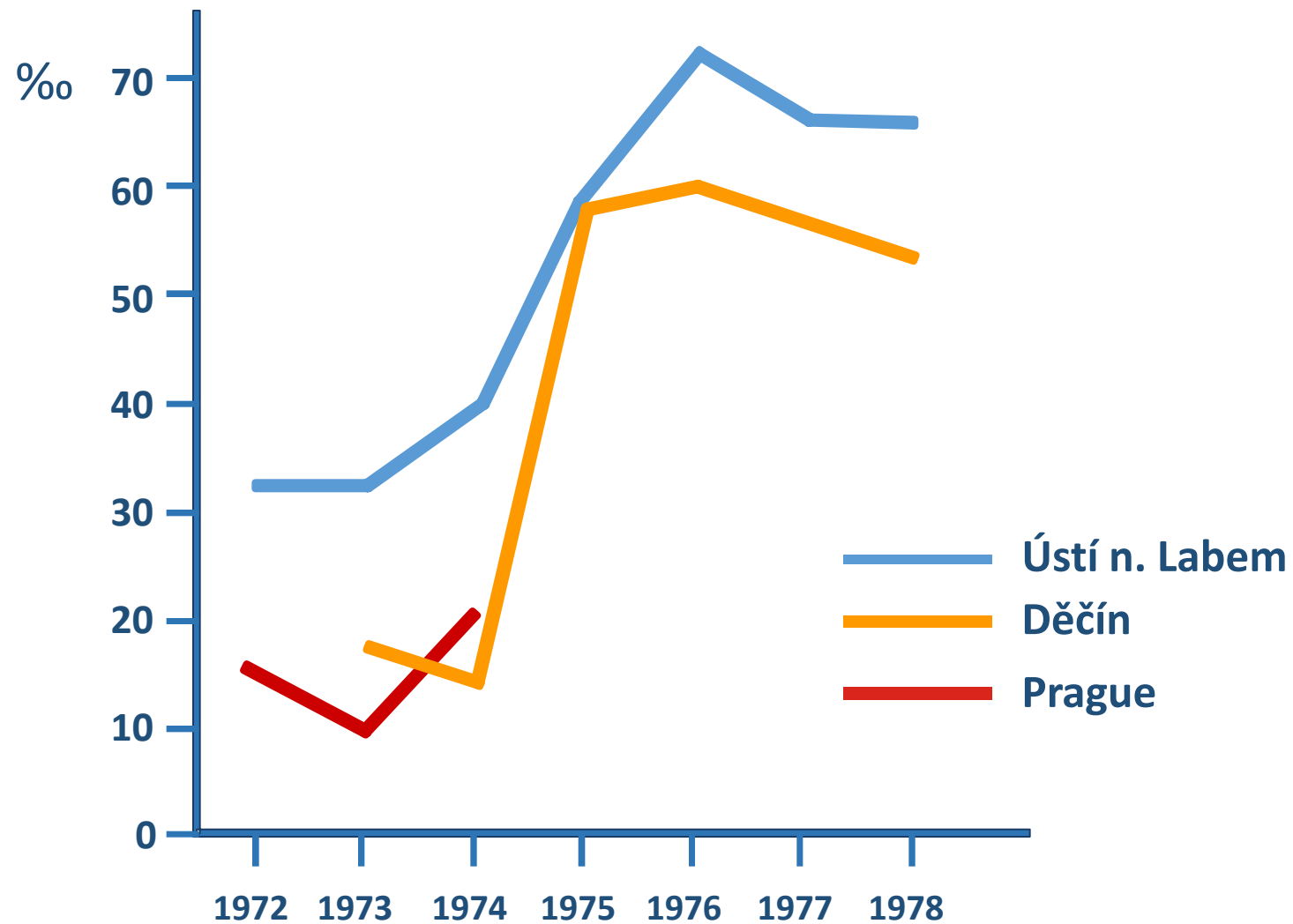


# RATIO OF ABSOLUTE EMISSION

## CZECH REPUBLIC 1988



# INCIDENCE OF BIRTH DEFFECTS



# THE FREQUENCY OF CHILDREN WITH DELIVERY WEIGHT LESS THAN 2500 G

Year	Teplice		Ústí n.L.		Jablonec	
	N	%	N	%	N	%
1882	1546	8.3	1591	8.1	1102	5.5
1983	1511	8.3	1551	8.4	1061	6.5
1984	1374	9.2	1460	7.7	1063	4.3
1985	1351	7.9	1510	7.5	--	--
1986	1408	6.5	1532	8.7	--	--

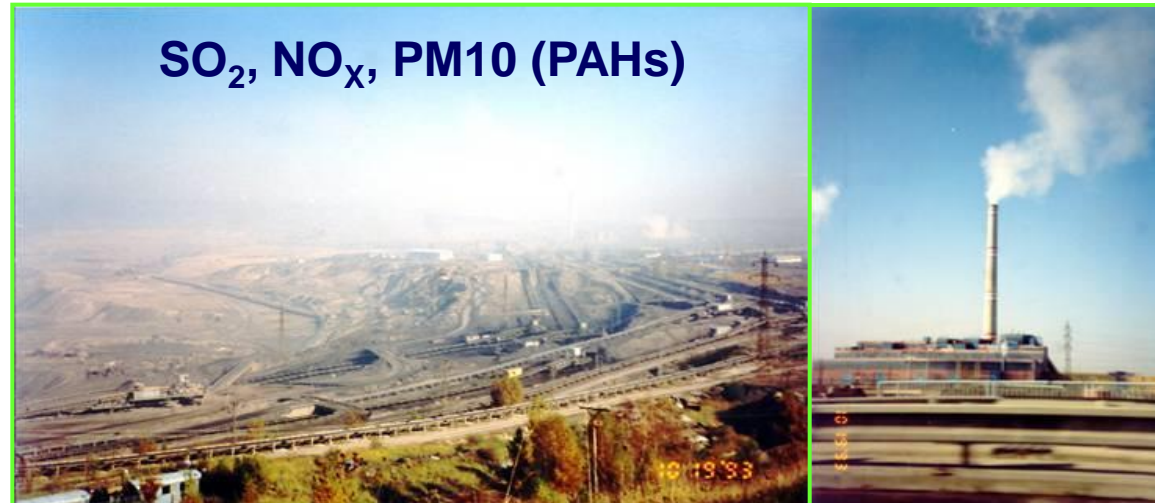
# MORBIDITY OF CHILDREN IN THE MINING DISTRICTS IN THE REGION OF NORTHERN BOHEMIA (1988)

Disease	Morbidity of Children No. of Cases/100	
	Czech Republic	Mining Districts
Urinary & Kidney (chronic)	0.89	1.12
Respiratory (unspecific)	0.54	<b>2.90</b>
Allergy	1.70	2.93
Mental illness	0.53	1.06
Skin	0.65	1.29
	(0-6 yrs. old)	
Urinary & Kidney (chronic)	1.42	1.68
Respiratory (unspecific)	0.45	<b>1.40</b>
Mental illness	2.00	4.09
Endocrine	1.17	1.54
Skin	0.73	1.09
Other Chronic	0.92	1.79
	(7-15 yrs. old)	

# Background



Air Pollution in the Teplice District, Czech Republic derives from the use of locally mined coal for industry and home heating, and is higher in winter than summer.



# TEPLICE PROGRAM

## IMPACT OF AIR POLLUTION ON HUMAN HEALTH

Model district

**TEPLICE**

(coal power plant  
open pit mines  
industry)

Control district

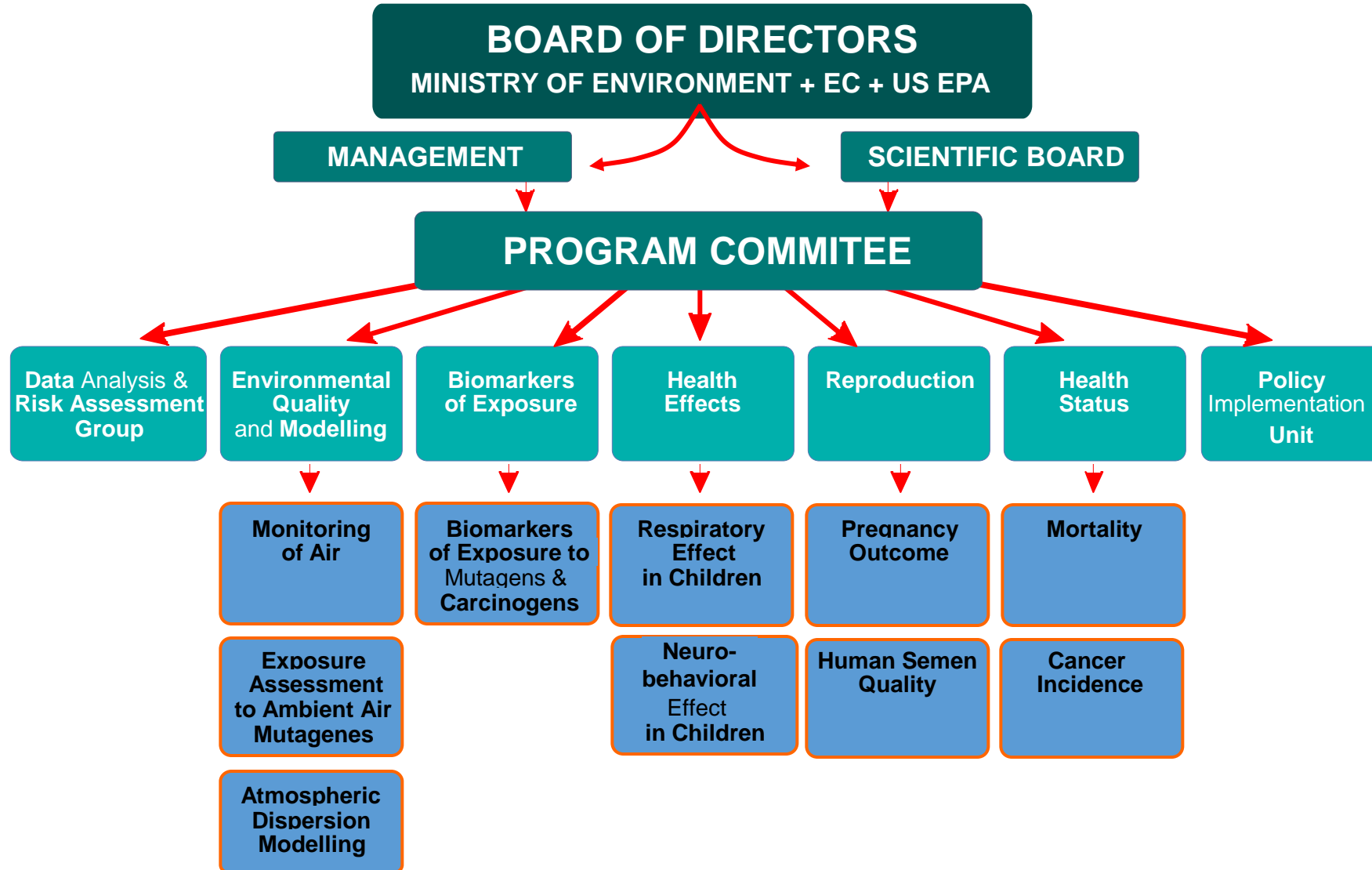
**PRACHATICE**

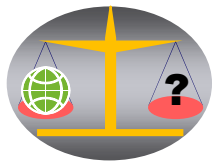
(agricultural  
area)





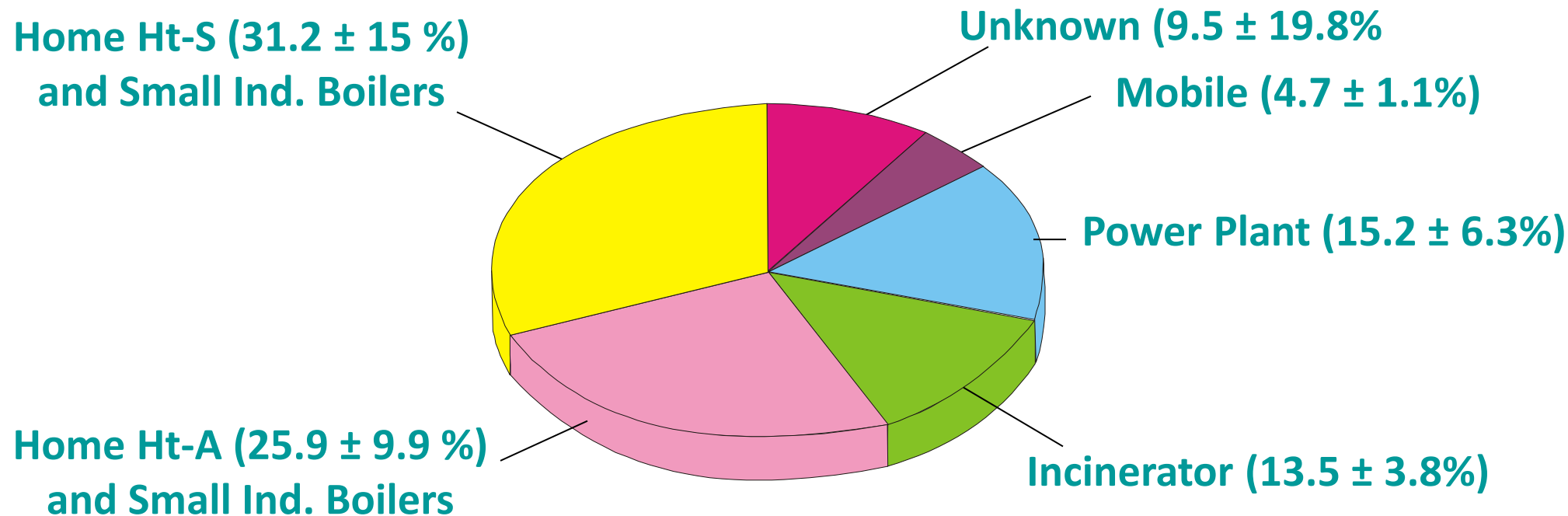
# TEPLICE PROGRAM





# APPORTIONMENT OF TEPLICE FINE MASS

January – February, 1994



Average Fine Mass Concentration =  $52.6 \mu\text{g}/\text{m}^3$

# GENOTOXICITY AND EMBRYOTOXICITY OF URBAN AIR PARTICULATE MATTER IN VITRO



**Characterization  
of biologically active pollutants**

# CONTRIBUTION OF THE MAJOR PAH-DNA ADDUCTS TO THE TOTAL DNA ADDUCTS LEVEL FROM URBAN SAMPLES

*(Binková et al. 1999)*

PAH-DNA  
adducts  
derived  
from



9-OH-B[a]P

anti - BPDE

B[b]F

B[k]F

B[j]F

CHRY

B[a]A

I[c,d]P

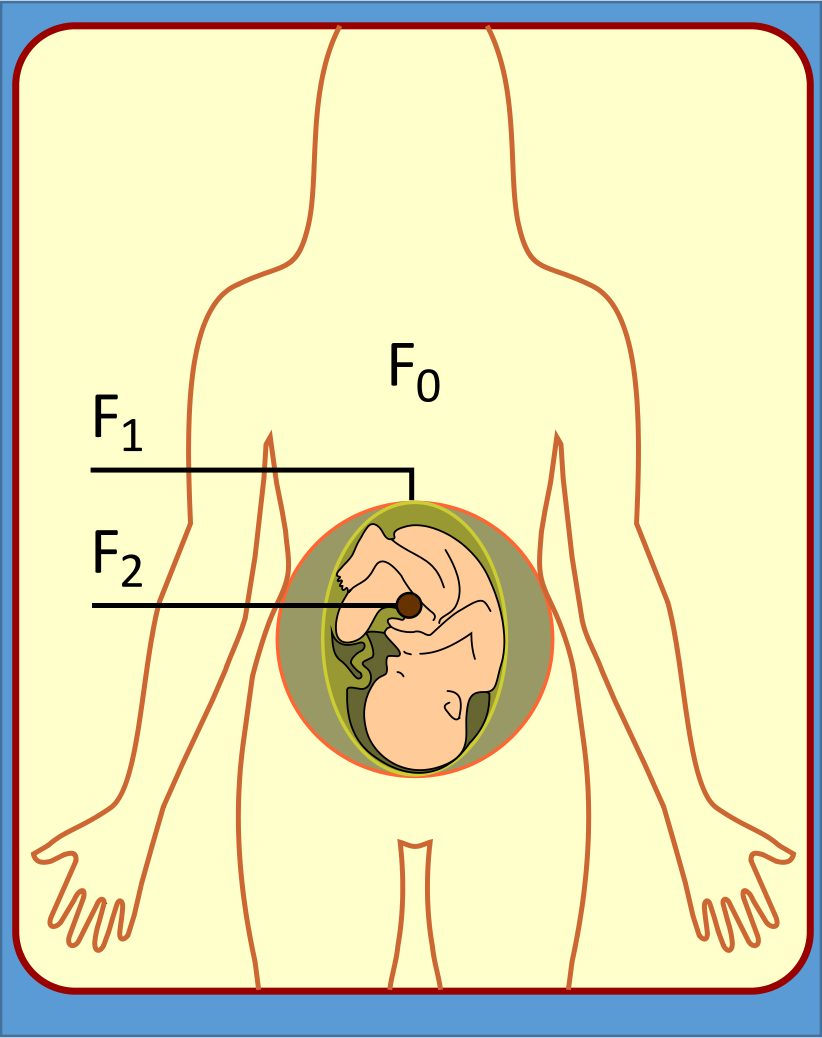
Total radioactivity from all DNA adducts detected approx. 50 %

AIR POLLUTION

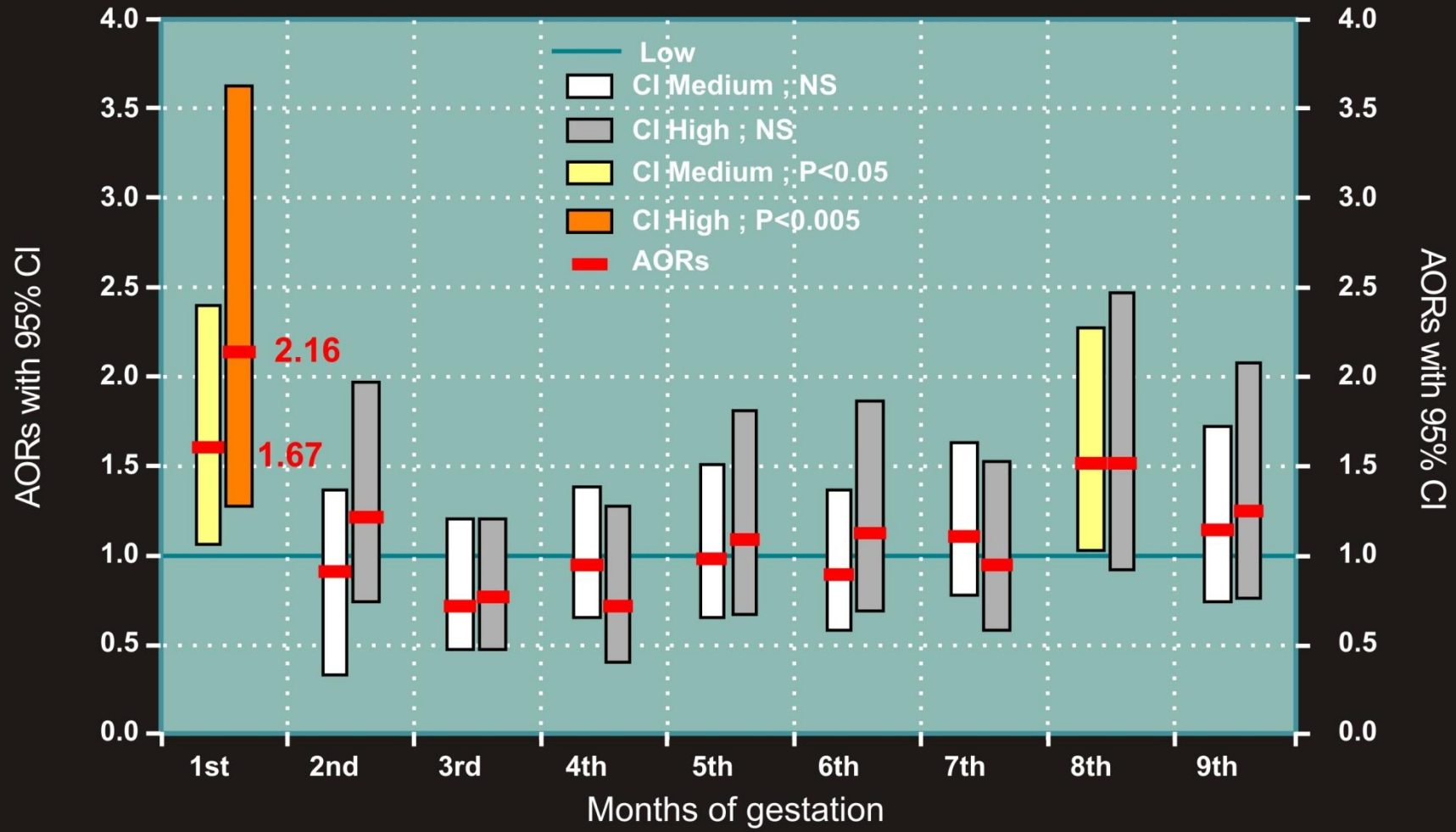
AIR POLLUTION



PREGNANCY  
OUTCOME



# CARCINOGENIC PAHs & IUGR IN TEPLICE





# PREGNANCY OUTCOME - RISK OF c-PAHs

**AMBIENT EXPOSURE**  
to 15 ng c-PAHs/m<sup>3</sup>/month  
(2.8 ng B[a]P/m<sup>3</sup>)



**INDOOR EXPOSURE (50-60%)**  
approximately to 9 ng c-PAHs/m<sup>3</sup>/month  
(1.7 ng B[a]P/m<sup>3</sup>)

# IMPACT OF IUGR

- **Child Mortality**
- **Child Morbidity**
- **Delayed Growth**
- **Non-Insulin Dependent Diabetes**
- **Hypertension**
- **Ischemic Heart Disease**

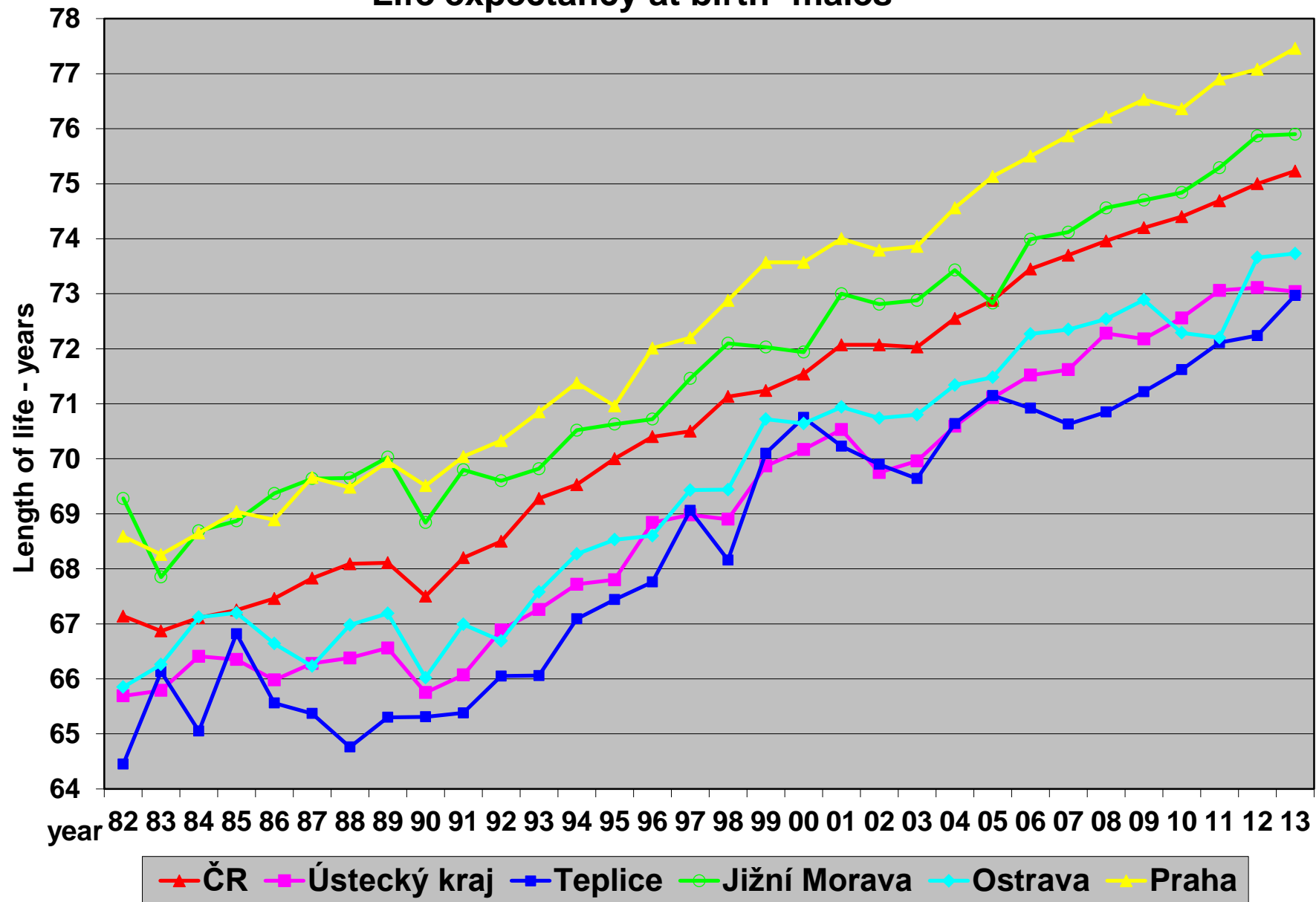
AIR POLLUTION

AIR POLLUTION

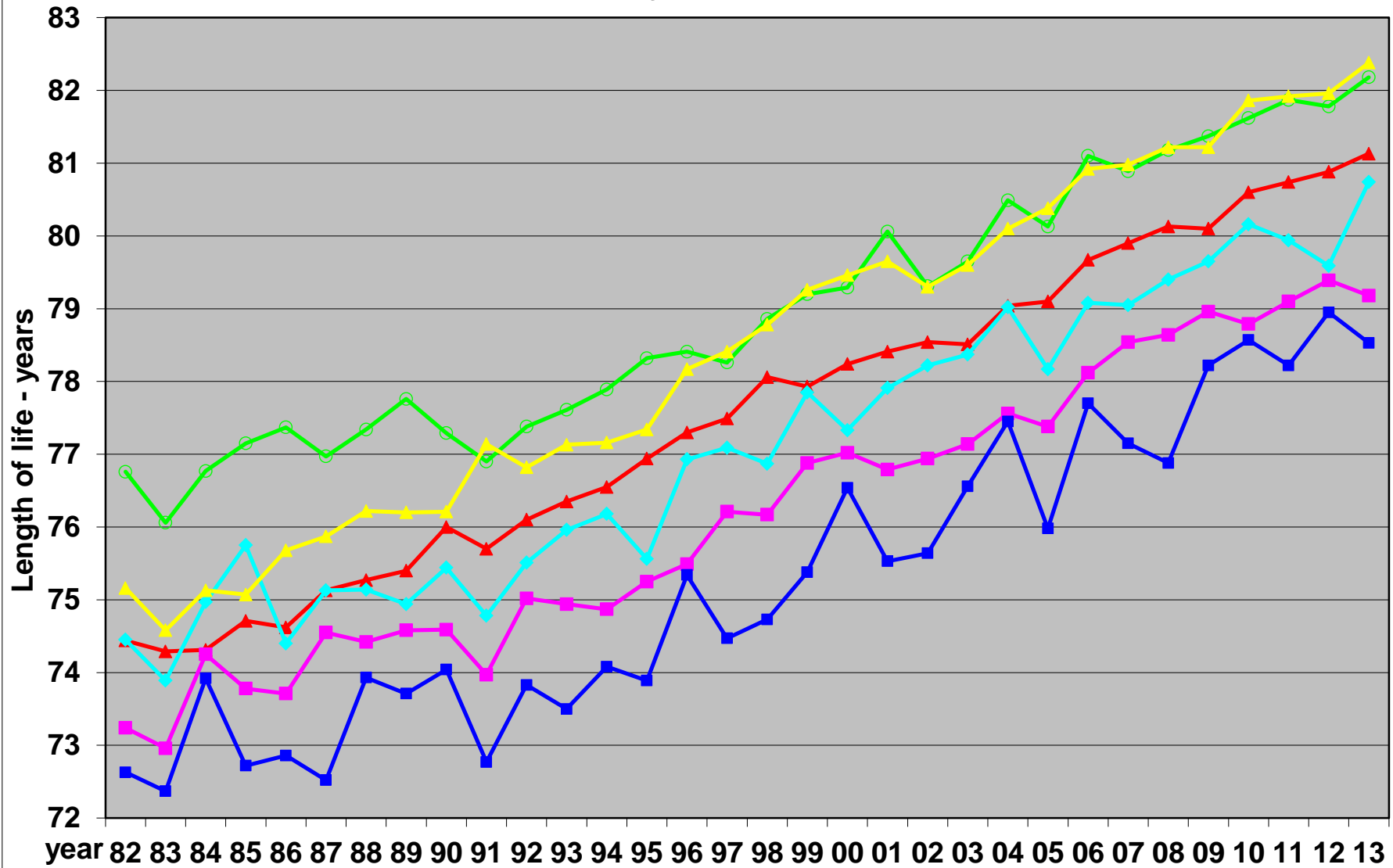


LIFE EXPECTANCY

### Life expectancy at birth- males



# Life expectancy at birth - females



ČR Ústecký kraj Teplice Jižní Morava Ostrava Praha

# EFFECT OF AIR POLLUTION TO POPULATION OF MINING DISTRICTS

- 1) Constantly decreased **life expectancy of males and females**
- 2) Constantly increased **mortality to cardiovascular diseases**
- 3) In children born in seventieth and eightieth we should expect in later adulthood the increased incidence of:  
**hypertension, ischemic heart disease, diabetes of 2<sup>nd</sup> grade, affected the sperm quality**
- 4) **Damage of genetic material(DNA) will unfavorably affect generations yet unborn**

**PM2.5**

# PM 2.5

<b>EU</b>	<b>25</b>	$\mu\text{g}/\text{m}^3$
<b>USA</b>	<b>12</b>	$\mu\text{g}/\text{m}^3$
<b>WHO</b>	<b>10</b>	$\mu\text{g}/\text{m}^3$

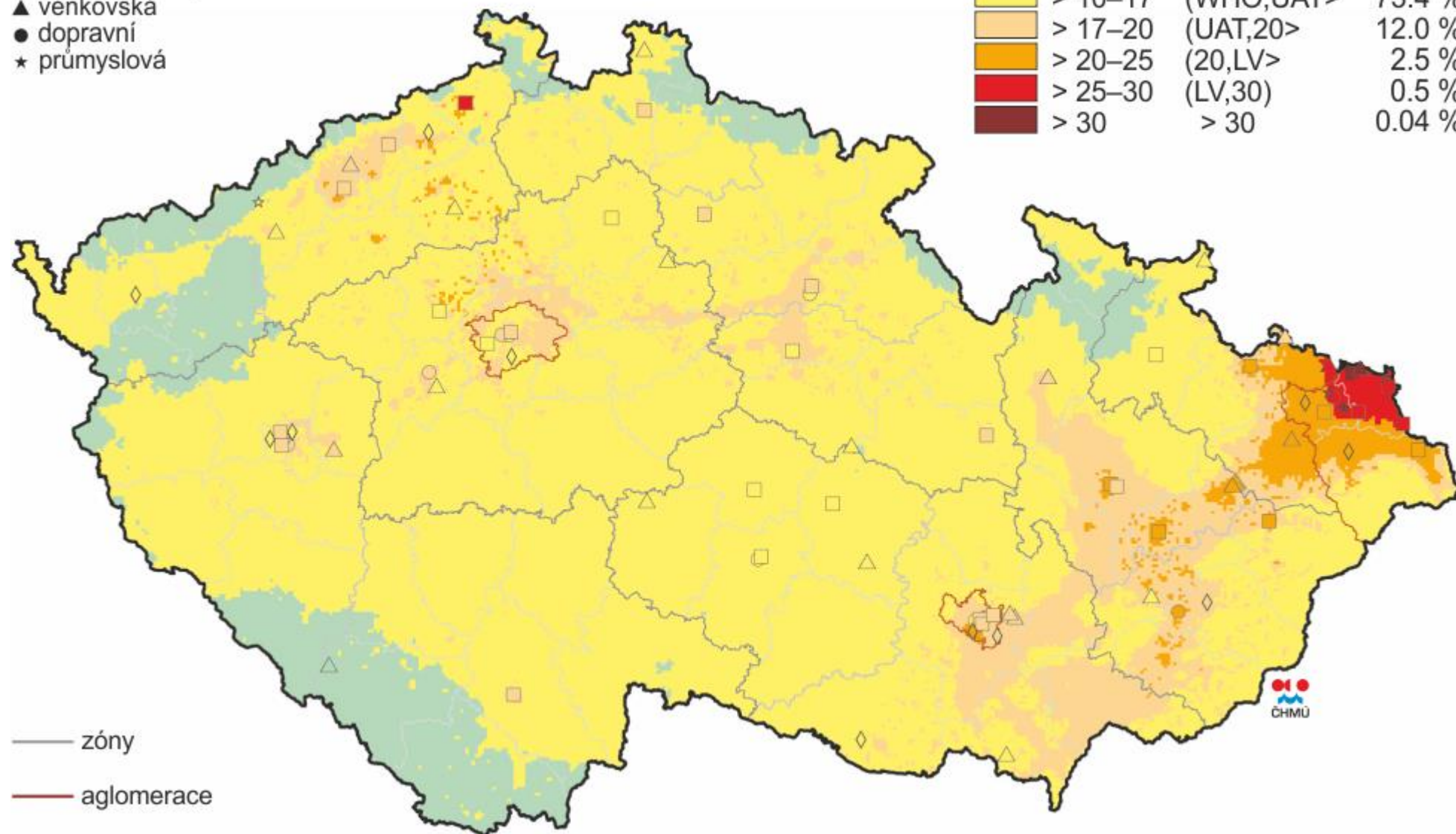


klasifikace stanic

- městská pozadová
- ◆ předměstská pozadová
- ▲ venkovská
- dopravní
- ★ průmyslová

koncentrace [ $\mu\text{g}\cdot\text{m}^{-3}$ ]

≤ 10	≤ WHO	11.6 %
> 10–17	(WHO,UAT>	73.4 %
> 17–20	(UAT,20>	12.0 %
> 20–25	(20,LV>	2.5 %
> 25–30	(LV,30)	0.5 %
> 30	> 30	0.04 %



Obr. IV.1.4 Pole roční průměrné koncentrace  $\text{PM}_{2,5}$ , 2016

**B[a]P**

## B[a]P

C.B.B. Guerreiro et al. “Benzo(a)pyrene in Europe: Ambient air concentrations, population exposure and health effects”,  
Environmental Pollution 214 (2016) 657-667

→ Acceptable risk level: 0.12 ng B[a]P/m<sup>3</sup>

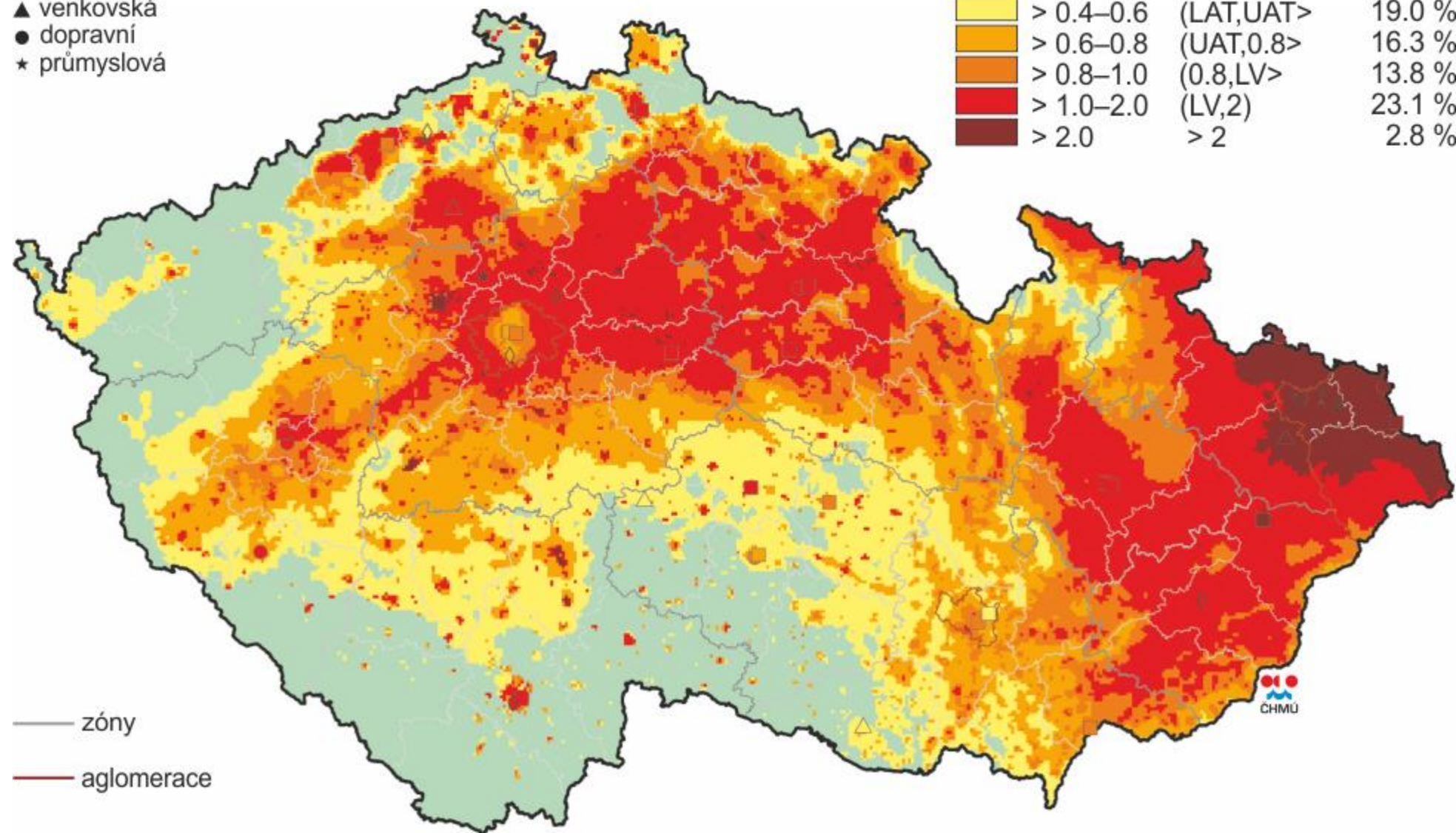
Increasing tendency in B[a]P emissions - implementation of climate mitigation policies promoting the use of biomass burning for domestic heating

klasifikace stanic

- městská pozadová
- ◆ předměstská pozadová
- ▲ venkovská
- dopravní
- ★ průmyslová

koncentrace [ $\text{ng}\cdot\text{m}^{-3}$ ]

≤ 0.4	≤ LAT	25.0 %
> 0.4–0.6	(LAT,UAT>	19.0 %
> 0.6–0.8	(UAT,0.8>	16.3 %
> 0.8–1.0	(0.8,LV>	13.8 %
> 1.0–2.0	(LV,2)	23.1 %
> 2.0	> 2	2.8 %



Obr. IV.2.1 Pole roční průměrné koncentrace benzo[a]pyrenu, 2016



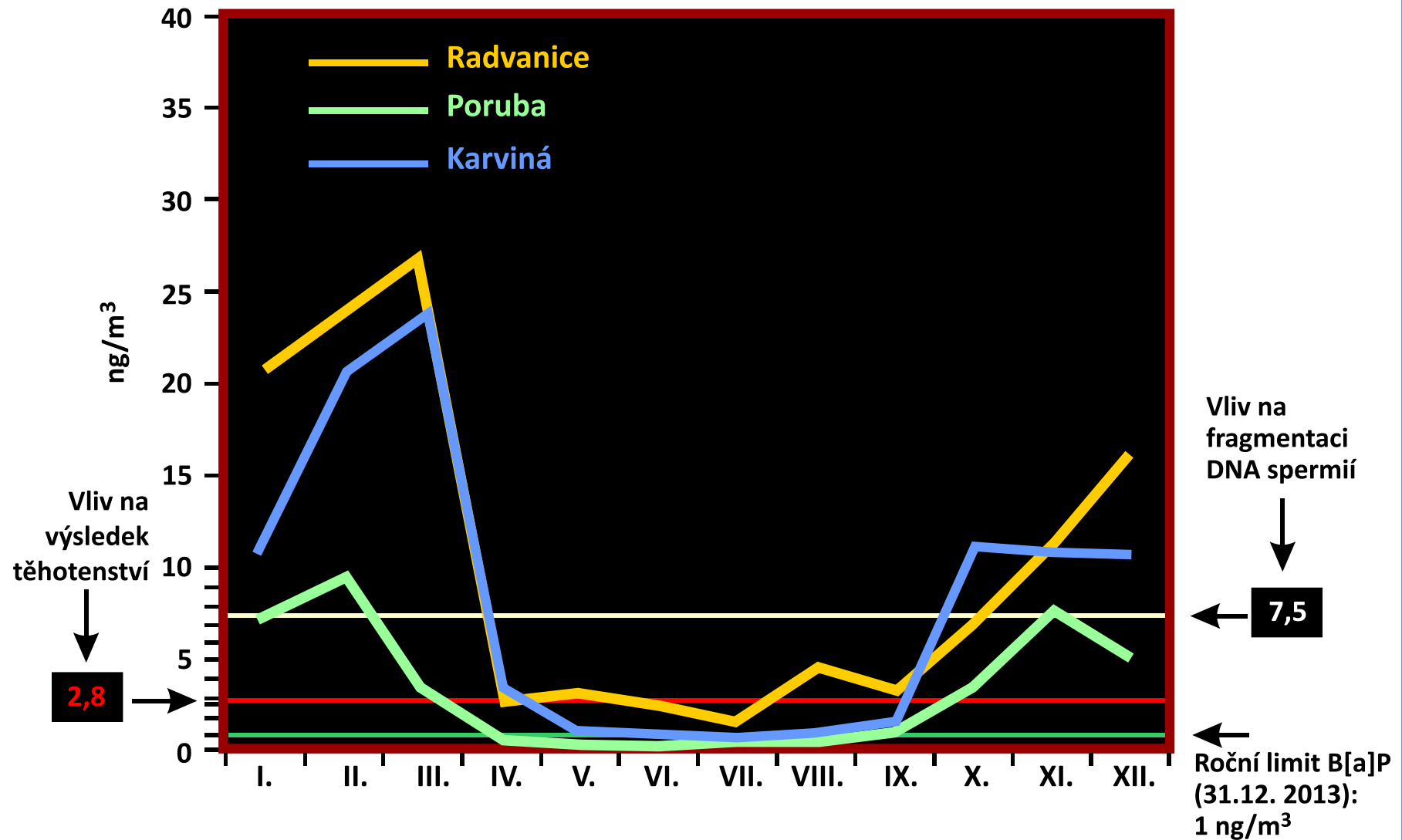
# AIR POLLUTION 2010 – 2017

(CHMI)

Locality	PM10 $\mu\text{g}/\text{m}^3$	PM2.5 $\mu\text{g}/\text{m}^3$	B[a]P $\text{ng}/\text{m}^3$
Ostrava-Poruba	39.9 $\pm$ 41.4 / <b>27.4 <math>\pm</math> 21.5</b>	32.2 $\pm$ 37.0 / <b>21.7 <math>\pm</math> 15.9</b>	3.8 $\pm$ 6.2 / <b>2.5 <math>\pm</math> 0.7</b>
Ostrava -Bartovice	61.7 $\pm$ 45.6 / <b>35.1 <math>\pm</math> 27.0</b>	46.7 $\pm$ 38.2 / <b>35.5 <math>\pm</math> 29.8</b>	7.2 $\pm$ 8.1 / <b>9.6 <math>\pm</math> 6.0</b>
Karvina	54.3 $\pm$ 50.0 / <b>35.3.8 <math>\pm</math> 26.8</b>	X / <b>27.0 <math>\pm</math> 19.2</b>	6.3 $\pm$ 8.8 / <b>3.9 <math>\pm</math> 1.4</b>
Prague-Smichov	37.9 $\pm$ 20.1 / <b>31.0 <math>\pm</math> 26.3</b>	21.1 $\pm$ 14.2 / <b>22.0 <math>\pm</math> 17.7</b>	X
Prague -Libus	27.4 $\pm$ 16.9 / <b>21.1 <math>\pm</math> 16.8</b>	20.3 $\pm$ 13.1 / <b>16.7 <math>\pm</math> 12.9</b>	0.9 $\pm$ 1.2 / <b>0.9 <math>\pm</math> 0.3</b>
Ceské Budejovice	25.2 $\pm$ 16.9 / <b>18.5 <math>\pm</math> 13.9</b>	X / <b>14.6 <math>\pm</math> 10.4</b>	1.5 $\pm$ 1.8 / <b>1.3 <math>\pm</math> 0.5</b>

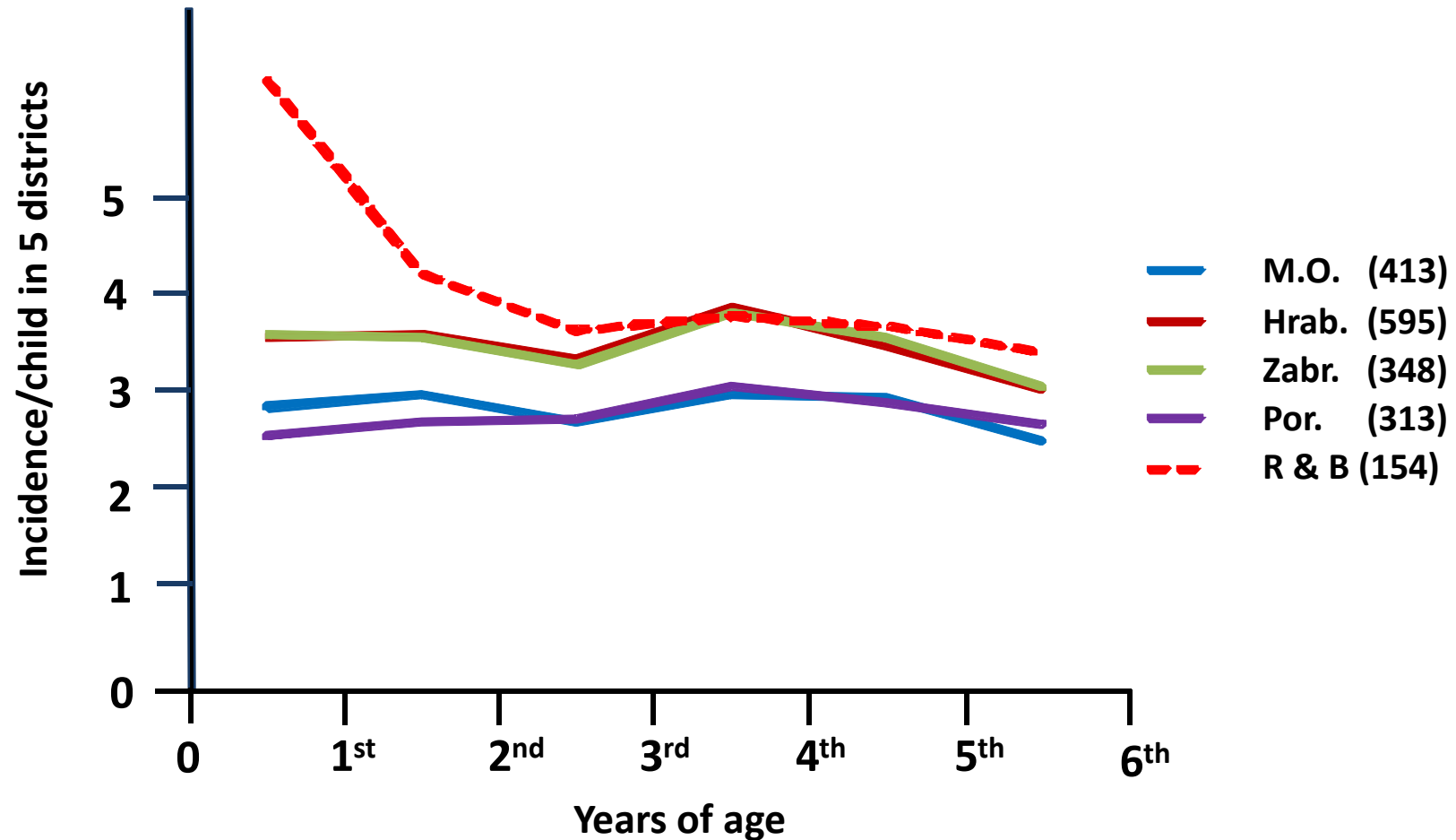
# OSTRAVA STUDY

# Měsíční koncentrace benzo[a]pyrenu (2012)



# CHILDREN RESPIRATORY MORBIDITY

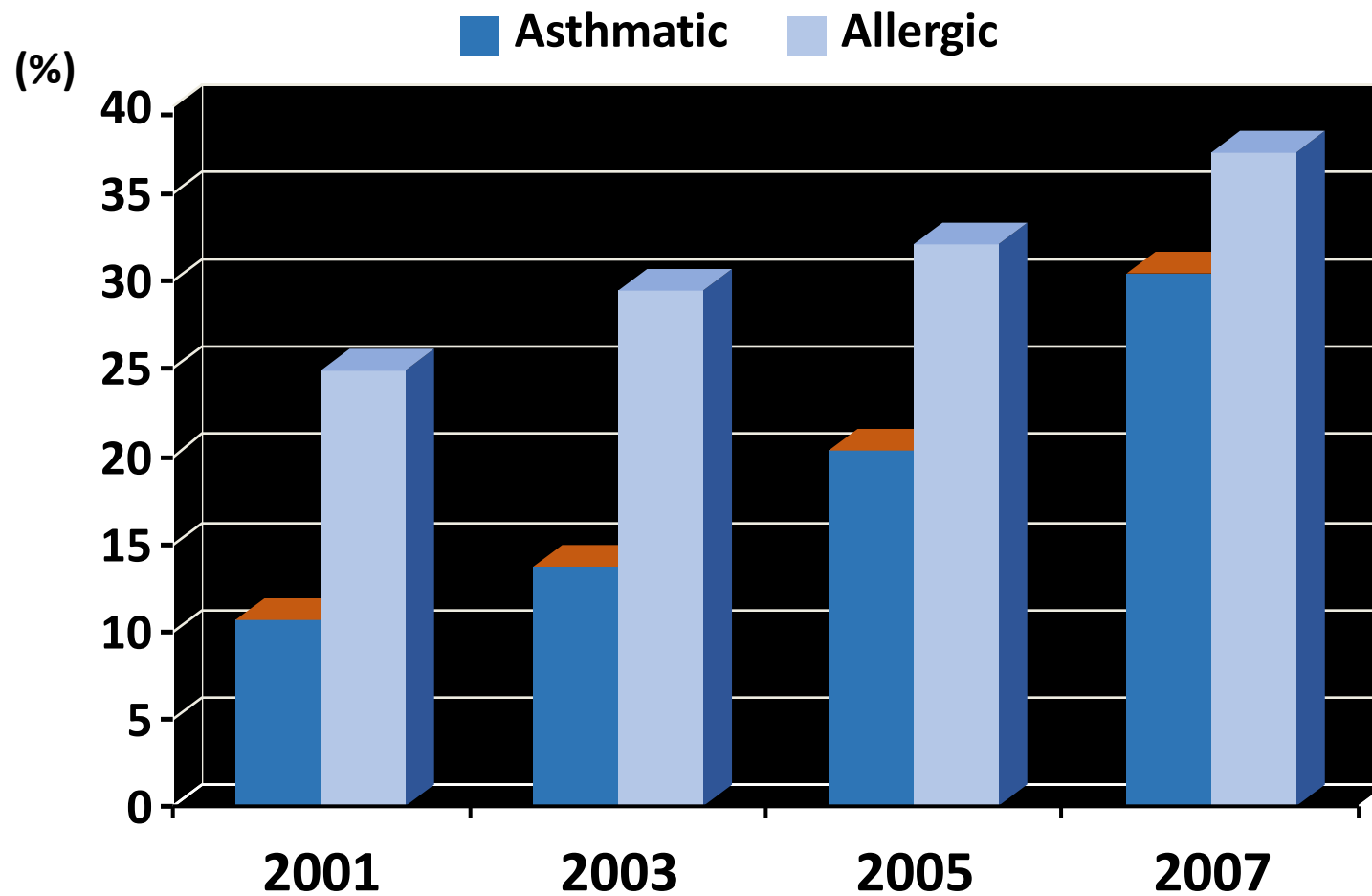
(URI + bronchitis + laryngitis + pneumonia + tonsillitis + otitis media)





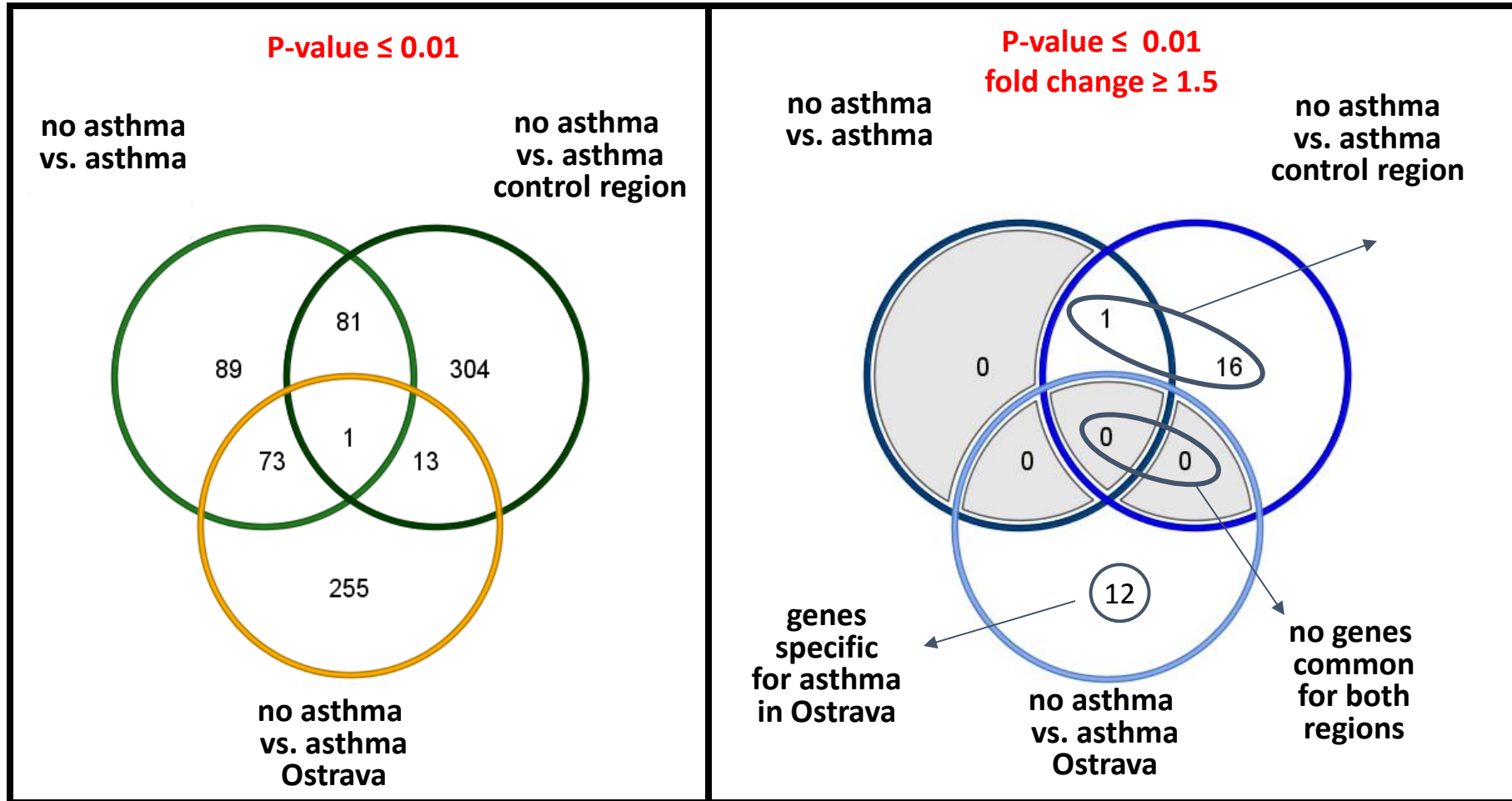
# ASTHMATIC AND ALLERGIC CHILDREN

OSTRAVA – BARTOVICE 2001 - 2007



# COMPARISON OF 'NO ASTHMA' VS. 'ASTHMA' T-TEST RESULTS

In the Venn diagrams shown below, the t-test results obtained using all experiments either with a p-value cutoff of 0.01 or a p-value cutoff of 0.01 and at least a 1.5 fold change are compared



# SUMMARY

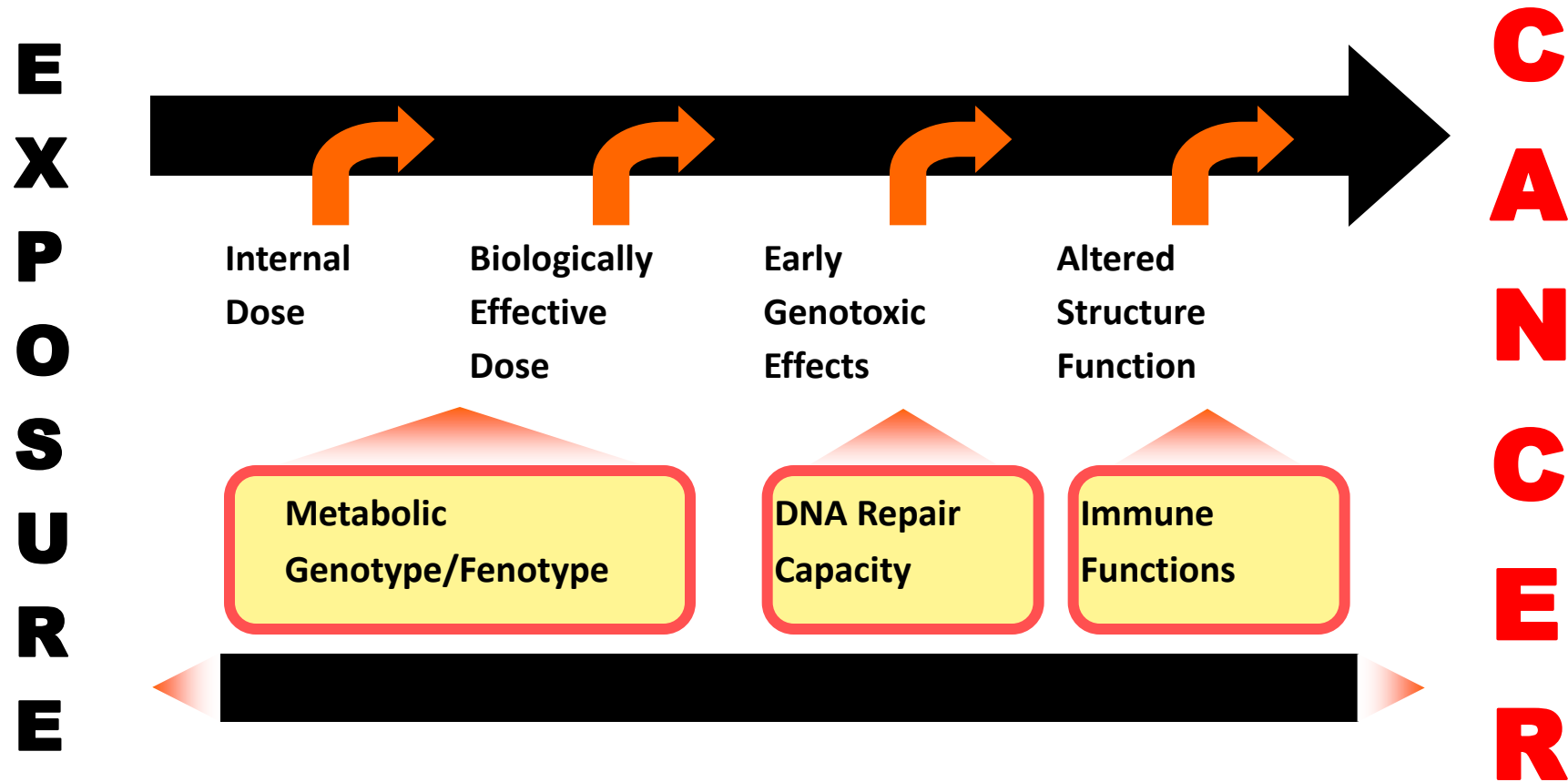
- **Results indicate disease specific and region-dependent gene expression profiles.**
- **Gene expression profiles for asthma children are different between the polluted and control regions.**
- **In each region were observed specific transcripts comparing asthma vs. no asthma, 17 transcripts in the control region, 12 transcripts in the polluted region.**
- **Comparing “no asthma” or “asthma” groups, a strong region effect was observed (57 and 92 transcripts with > 1.5 fold changes).**
- **Asthma bronchiale in Prachatice – the allergic type of asthma response to allergens.**
- **Asthma bronchiale in Ostrava - the nonallergic type of asthma induced by irritants as air pollution, ETS, viruses.**

# **BIOMARKERS**

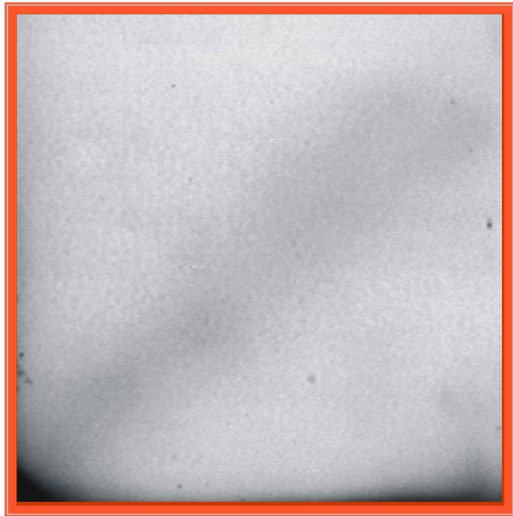
The word "BIOMARKERS" is centered in a bold, black, sans-serif font. Below the text, there are two large, stylized arrows. Each arrow is composed of a vertical bar on the left and a horizontal bar on the right, with a curved bottom edge. The color of the arrows is a gradient from light orange at the top to dark red at the bottom. The arrows point downwards and outwards from the center of the word.

# HUMAN BIOMARKERS

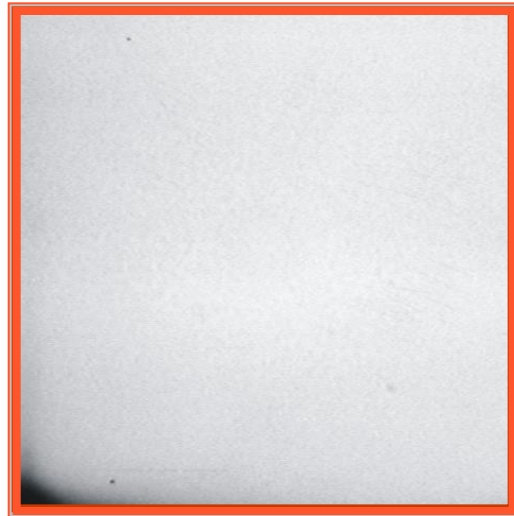
## Genetic/Carcinogenic Risks



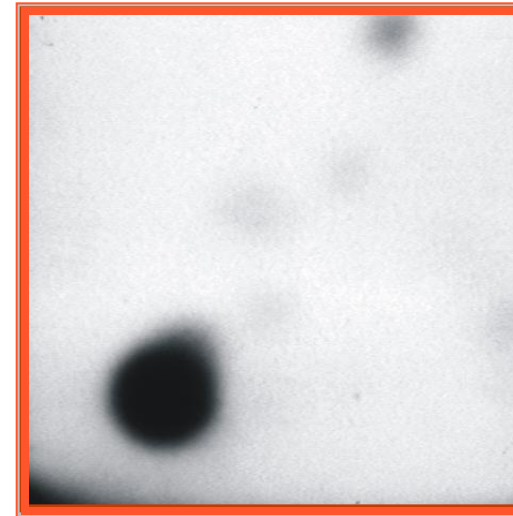
# Autoradiographs of thin layer chromatograms with DNA adduct pattern of:



DNA isolated from lymphocytes  
of subject sampled  
in January 2004  
(1st sampling period)



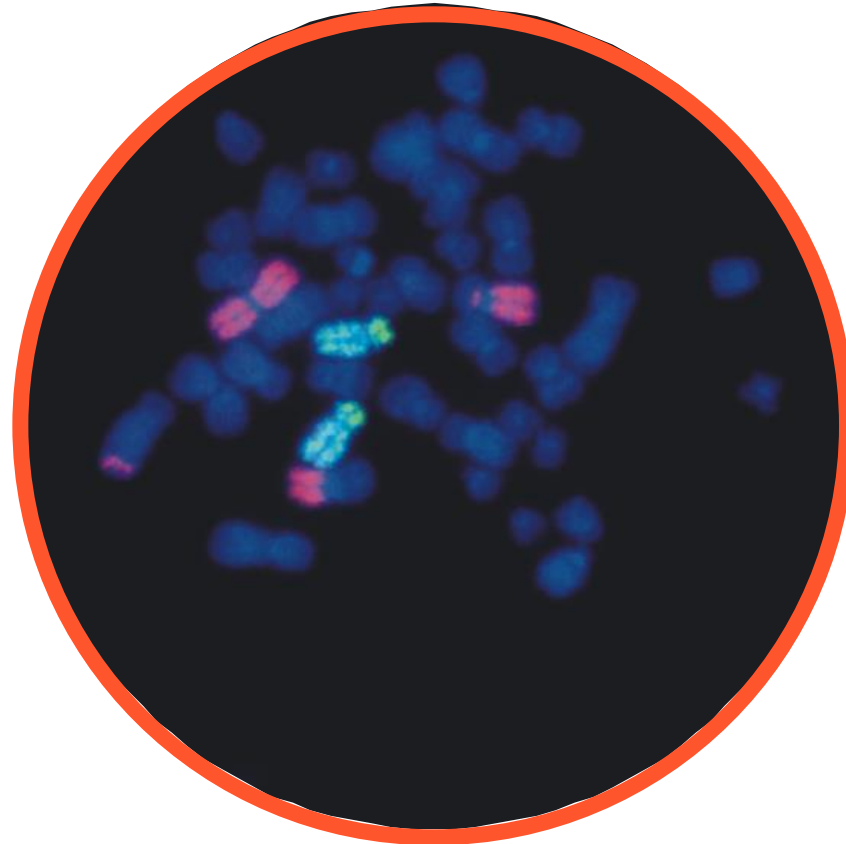
Water blank



Positive control (DNA isolated from  
the lung of rats intraperitoneally  
treated with 100 mgB[a]P/kg b.w.)

# CYTOGENETIC ANALYSIS

FISH analysis

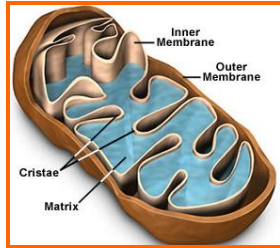


**t(Ab);t(Ab);t(Ba)**

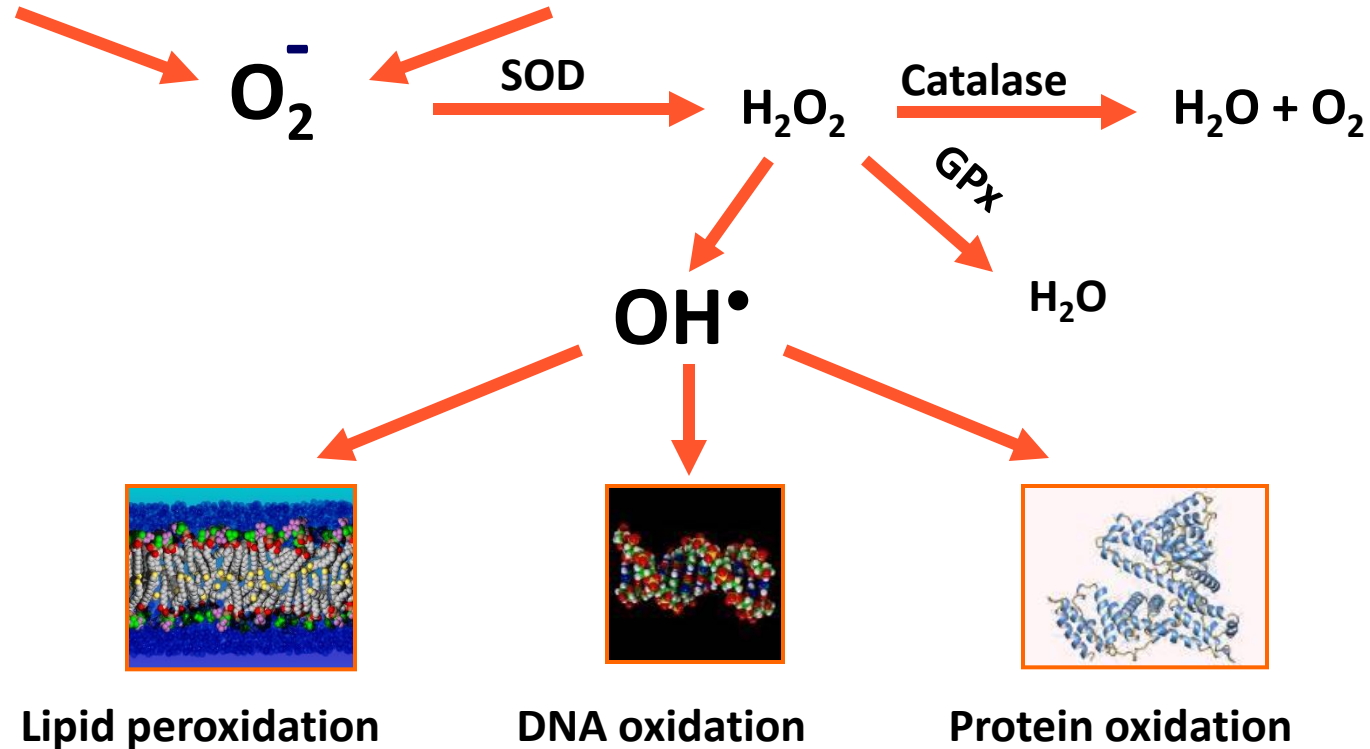
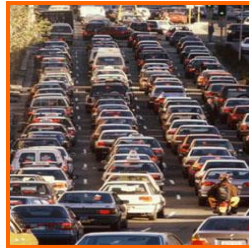
Three translocations  
between chromosome 1  
and unpainted chromosomes

# Reactive oxygen species

Endogenous sources



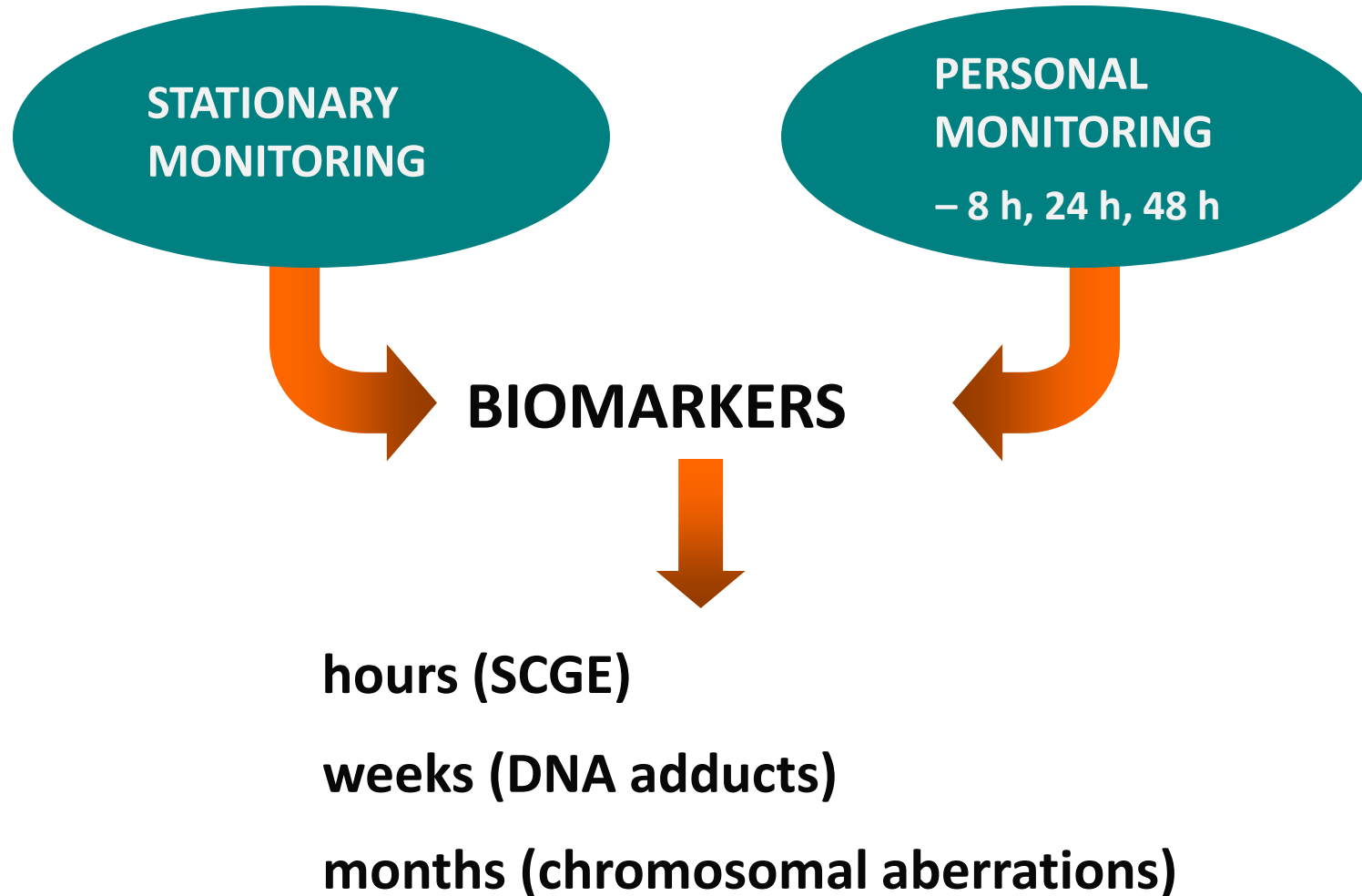
Exogenous sources





# EXPOSURE VS. BIOMARKERS

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# HUMAN STUDIES AND BIOMARKERS OF EXPOSURE, EFFECT AND SUSCEPTIBILITY

- ➔ PM2.5 Stationary monitoring
- ➔ c-PAHs Personal monitoring  
Stationary monitoring
- ➔ VOC Personal monitoring  
Stationary monitoring
- ➔ Cotinine
- ➔ Triglycerids, Total, HDL and LDL  
cholesterol
- ➔ Vitamins A, C, E
- ➔ DNA adducts by  $^{32}\text{P}$ -postlabeling
- ➔ Chromosomal aberrations  
conventional, FISH,  
micronuclei
- ➔ Oxidative damage  
8-oxodG, 15-F2T-isoP,  
proteins, SCGE
- ➔ Genetic polymorphisms
- ➔ Gene expression

# PERSONAL MONITORING IN PRAGUE



# PERSONAL SAMPLING OSTRAVA

January 11 – 28, 2010

**B[a]P**  **14.6 ng/m<sup>3</sup>**

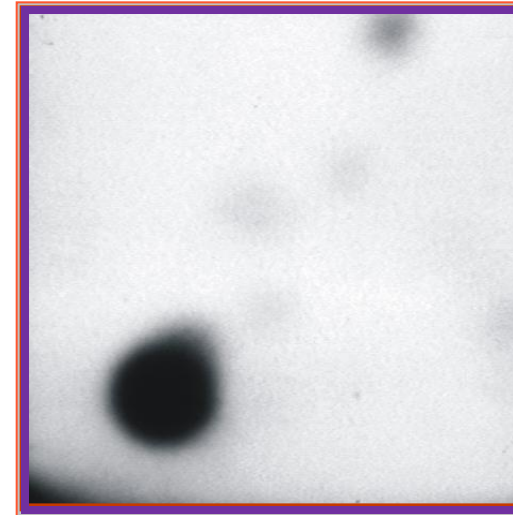
## **Autoradiographs of thin layer chromatograms with DNA adduct pattern of:**



**DNA isolated from lymphocytes  
of subject sampled  
in January 2004  
(1st sampling period)**



**Water blank**



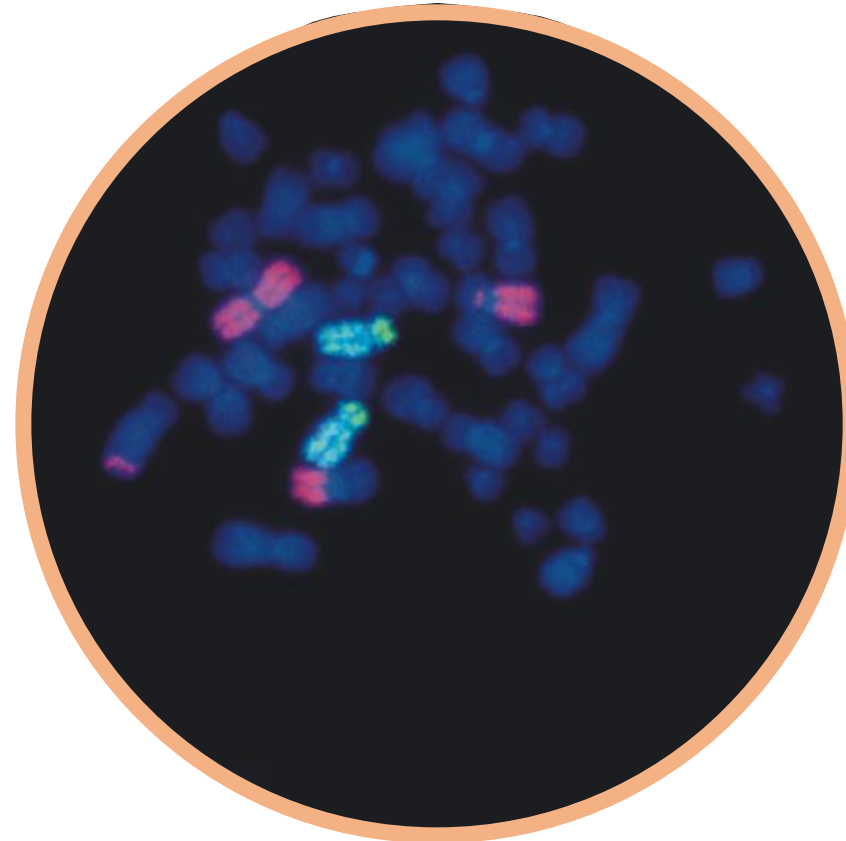
**Positive control  
(DNA isolated from the lung of rats  
intraperitoneally treated  
with 100 mgB[a]P/kg b.w.)**

# DNA adducts

	N	B[a]P ng/m <sup>3</sup>		B[a]P –“like“		Total	
		2009	2010	2009	2010	2009	2010
Prague	64	0.80 ± 0.55	2.86 ± 1.87	0.21 ± 0.06	0.25 ± 0.12	1.30 ± 0.41	1.37 ± 0.47
Ostrava	98	2.73 ± 2.60*	14.8 ± 13.3*	0.28 ± 0.08*	0.16 ± 0.06*	1.37 ± 0.37	1.03 ± 0.33*
Controls	42	0.80 ± 0.62		0.10 ± 0.03		0.76 ± 0.20	

# CYTOGENETIC ANALYSIS

FISH analysis



**t(Ab);t(Ab);t(Ba)**

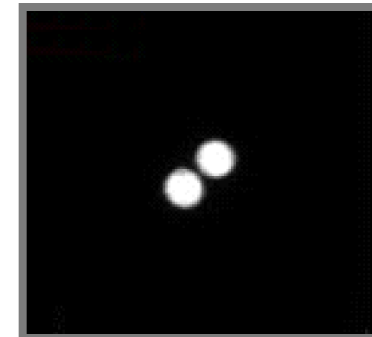
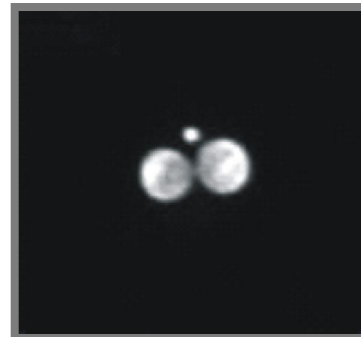
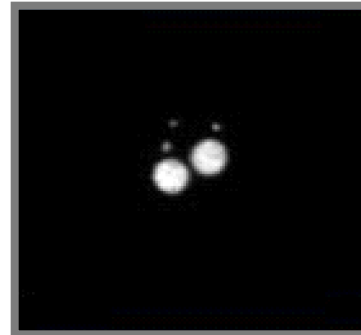
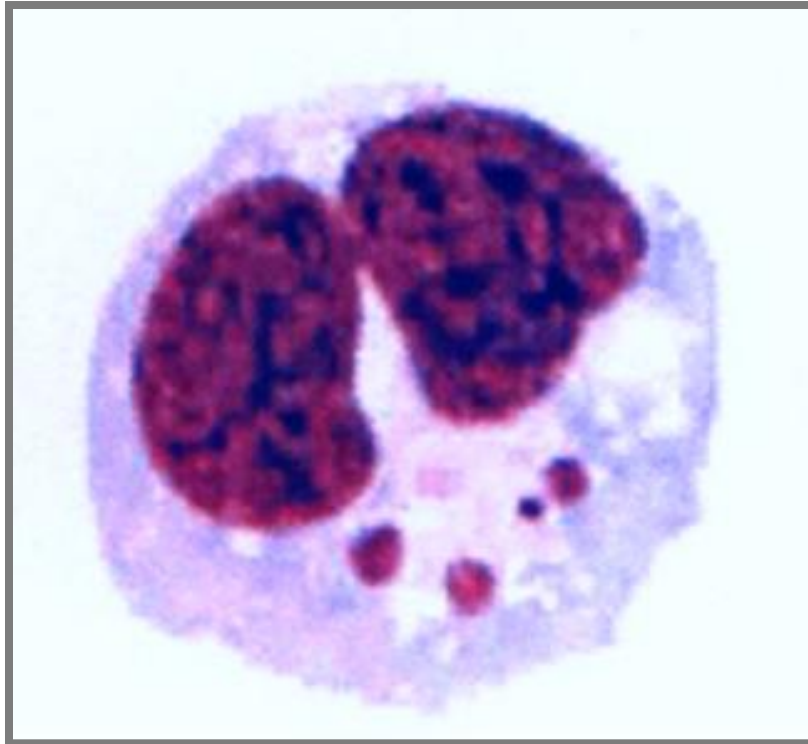
Three translocations  
between chromosome 1  
and unpainted chromosomes

# Genomic frequency of translocations (FISH)

	N	B[a]P ng/m <sup>3</sup>		% AB.C.		F <sub>G</sub> /100	
		2009	2010	2009	2010	2009	2010
Prague	60	0.80 ± 0.55	2.86 ± 1.87	0.27 ± 0.18	0.23 ± 0.15	1.43 ± 1.15	1.39 ± 1.03
Ostrava	98	2.73 ± 2.60	14.8 ± 13.3*	0.26 ± 0.19	0.22 ± 0.18	1.44 ± 1.23	1.25 ± 1.18
Controls	42	0.80 ± 0.62		0.21 ± 0.16		1.13 ± 1.01	



# MICRONUCLEI



# FREQUENCY OF MICRONUCLEI

(impact of 3-weeks stay in Ostrava region, January 2010)

<b>Groups</b>	<b>sampling</b>	<b>N</b> <b>(6000 b./person)</b>	<b>%</b> <b>AB.B. S MN</b>	<b>MN/1000</b>
<b>controls</b>	<b>I.</b>	<b>4</b>	<b>0.81 ± 0.15</b>	<b>8.32 ± 1.63</b>
	<b>II.</b>	<b>4</b>	<b>0.80 ± 0.14</b>	<b>8.47 ± 1.55</b>
<b>exposed</b>	<b>I.</b>	<b>4</b>	<b>0.74 ± 0.43</b>	<b>7.96 ± 4.92</b>
	<b>II.</b>	<b>4</b>	<b>1.14 ± 0.55</b>	<b>12.91 ± 6.49 *</b>

\*  $p < 0.05$

# Oxidative stress (in winter) 15-F2t-isoprostane (pg/ml)

	N	B[a]P ng/m <sup>3</sup>		15-2Ft-IsoP	
		2009	2010	2009	2010
Prague	60	0.80 ± 0.55	2.86 ± 1.87	165.9 ± 41.7	256.5 ± 104.7*
Ostrava	98	2.73 ± 2.60*	14.8 ± 13.3*	279.3 ± 303.6*	279.5 ± 124.5

\* p < 0.05

# QUESTIONS



**Dose-effect relationship?**

**Possible adaptive response ?**

# PROJECT G-NEW

- 1)**
  - 100 mothers
  - 100 newborns
  - Summer 2013
  - Karvina (exposed)
  - Ceske Budejovice (control)
  
  - 100 mothers
  - 100 newborns
  - Winter 2014
  - Karvina (exposed)
  - Ceske Budejovice (control)
  
- 2)**
  - Impact of diet
  - 10 mothers – diet for 7 days
  - Each season & location

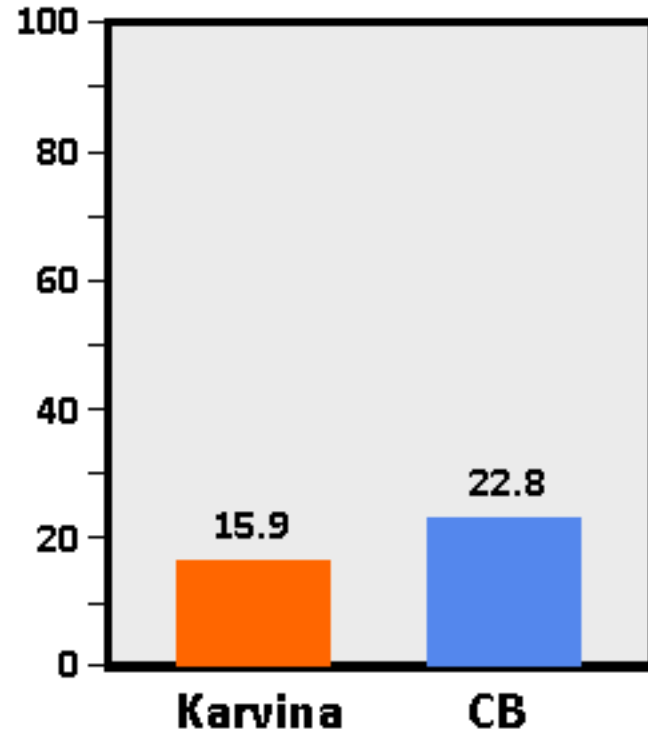
# PROJECT G-NEW

- ➔ **PM2.5Hi-Vol monitoring**
- ➔ **c-PAHs Hi-Vol monitoring**
- ➔ **Mothers**
- ➔ **Urine 8-oxodG, PAHs**
- ➔ **Plasma 15-F2T-isoP, cotinine, metabolomics**
- ➔ **Milk PAHs**
- ➔ **Diet PAHs, questionnaires**
- ➔ **Newborns**
- ➔ **DNA adducts by <sup>32</sup>P-postlabeling**
- ➔ **Gene expression**
- ➔ **Plasma 15-F2T-isoP, metabolomics**
- ➔ **Urine 8-oxodG, PAHs**

# NUTRITIONAL QUALITY OF DIET

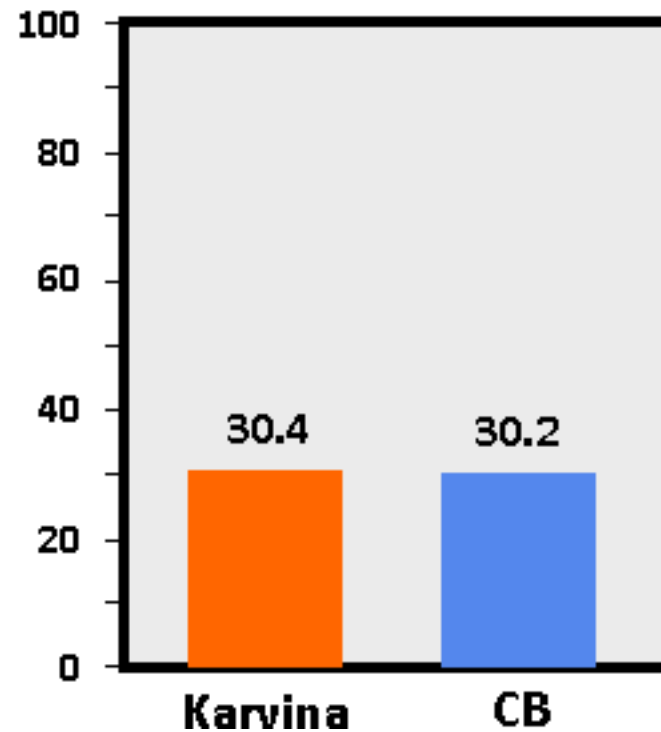
## VEGETABLES

% days with RDI 300 g/day



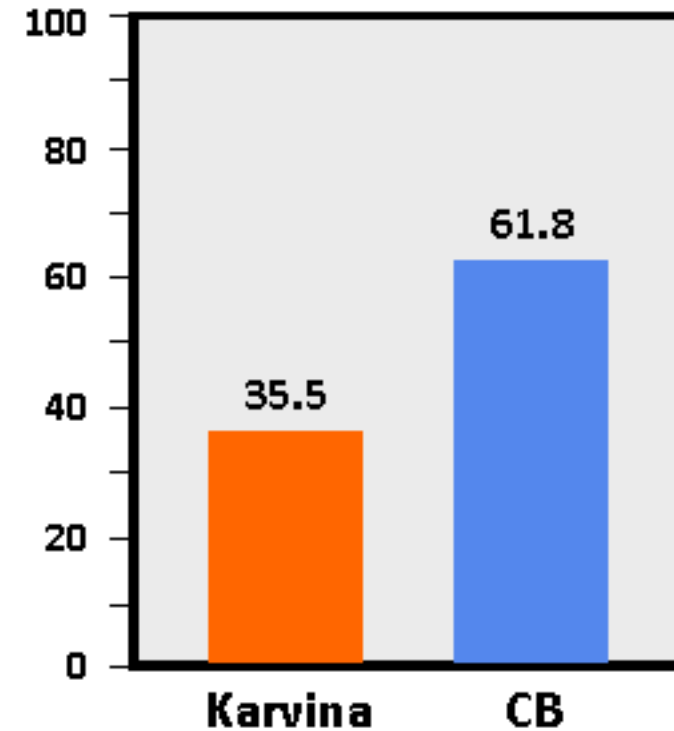
## MILK, DIARY PRODUCTS

% days with RDI servings

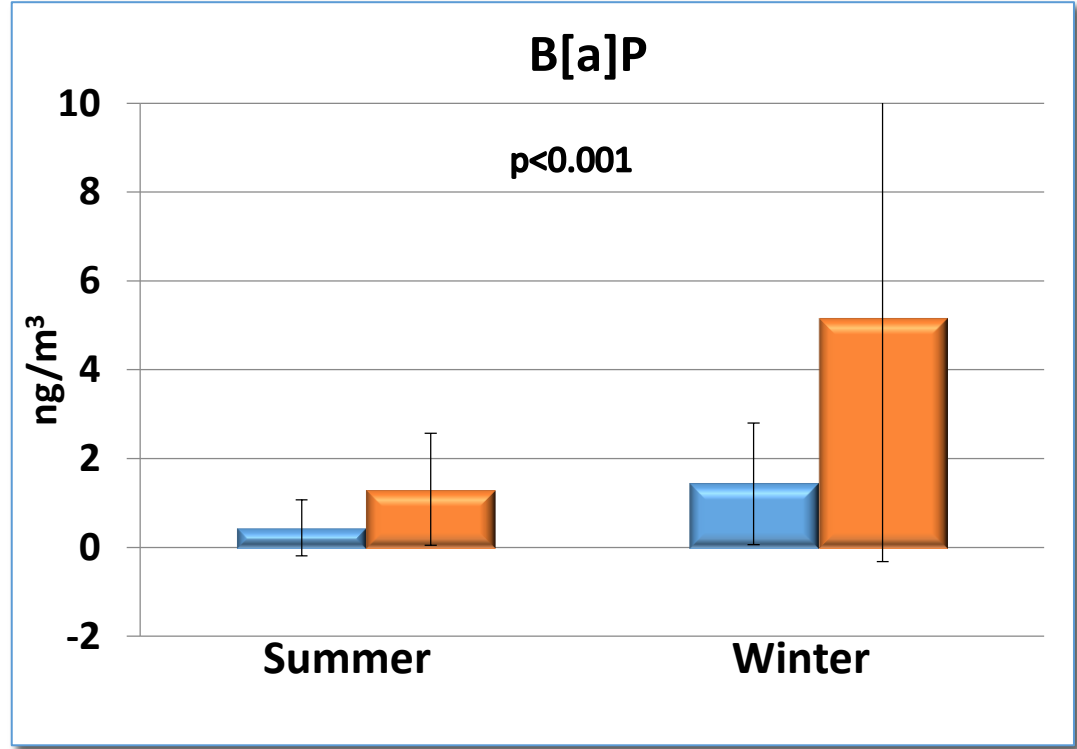
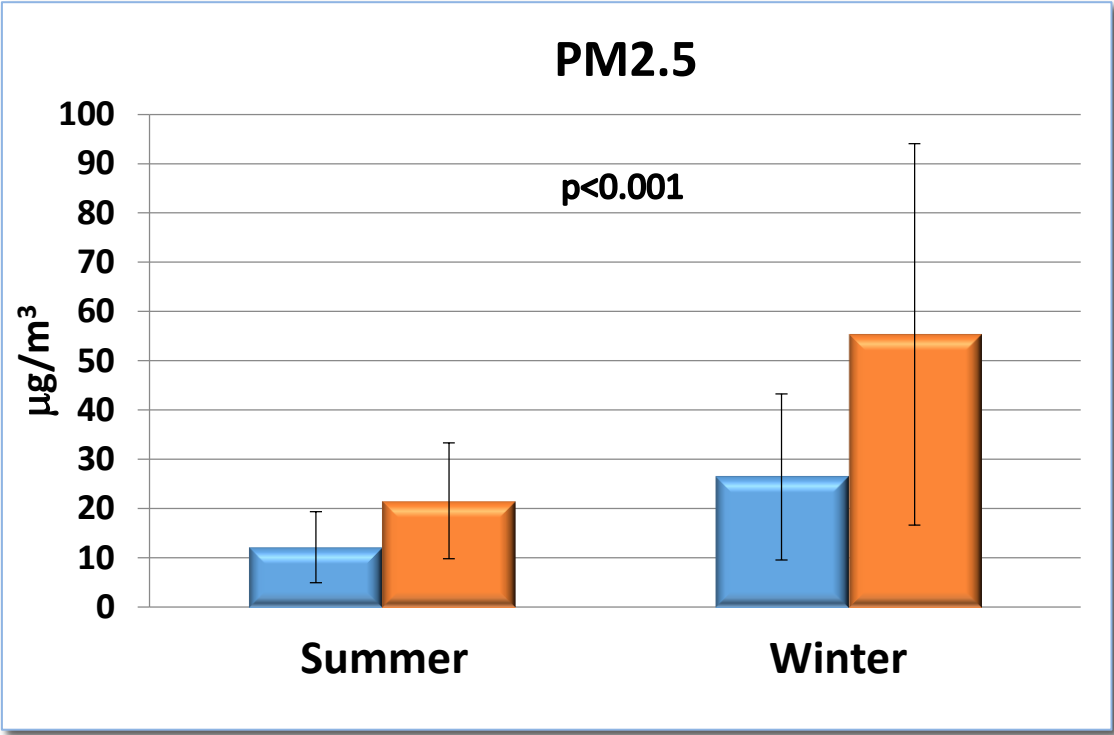


## FRUITS

% days with RDI servings



# EXPOSURE TO PM 2.5 AND B[a]P



 Ceske Budejovice

 Karvina



# PAHs IN DIET – CHEMICAL ANALYSIS

- ¼ of consumed diet
- Daily intake : 1.58 kg



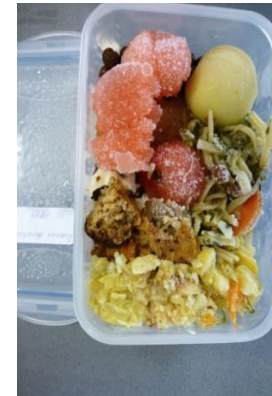
C90 – 30.8.2013



C90 – 31.8.2013



C90 – 1.9.2013



C90 – 2.9.2013



C90 – 3.9.2013

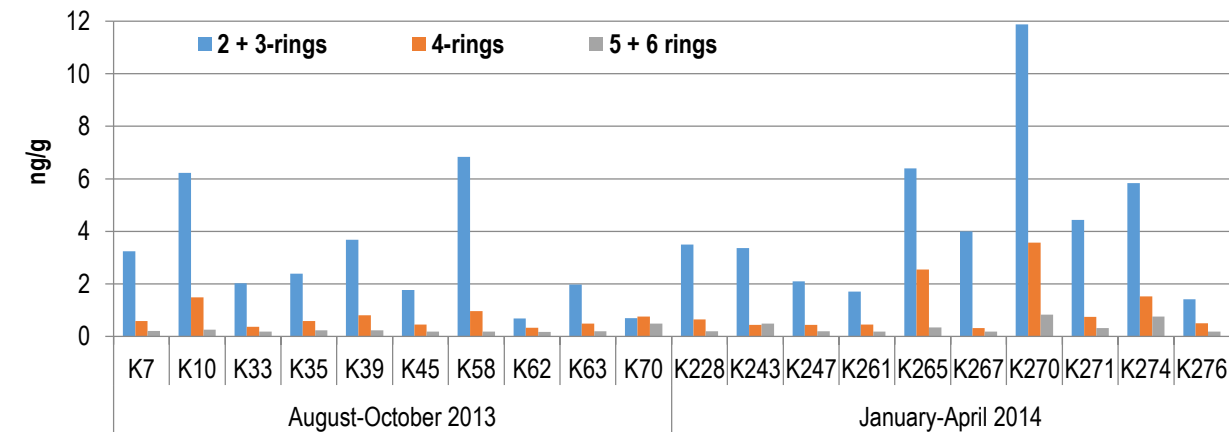
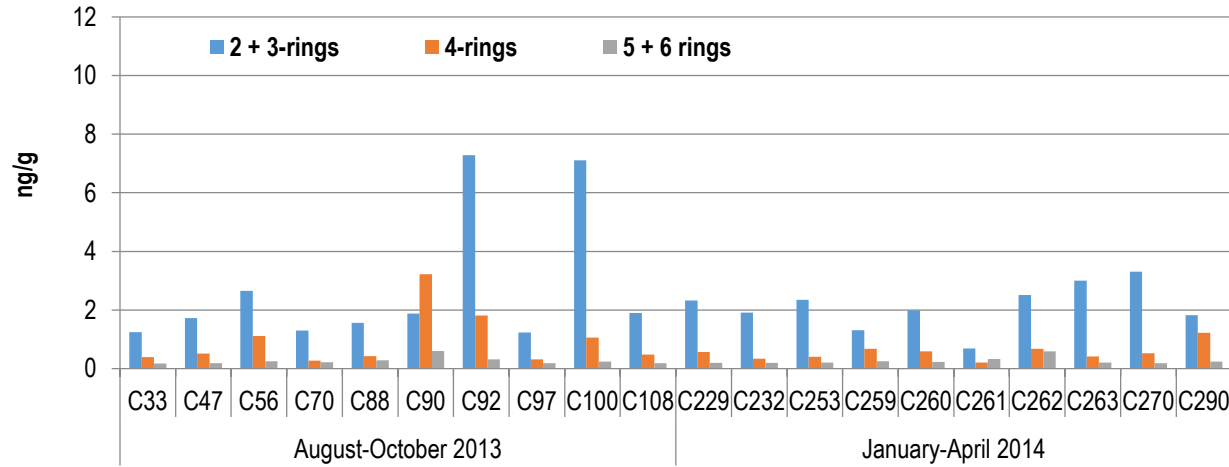


C90 – 4.9.2013

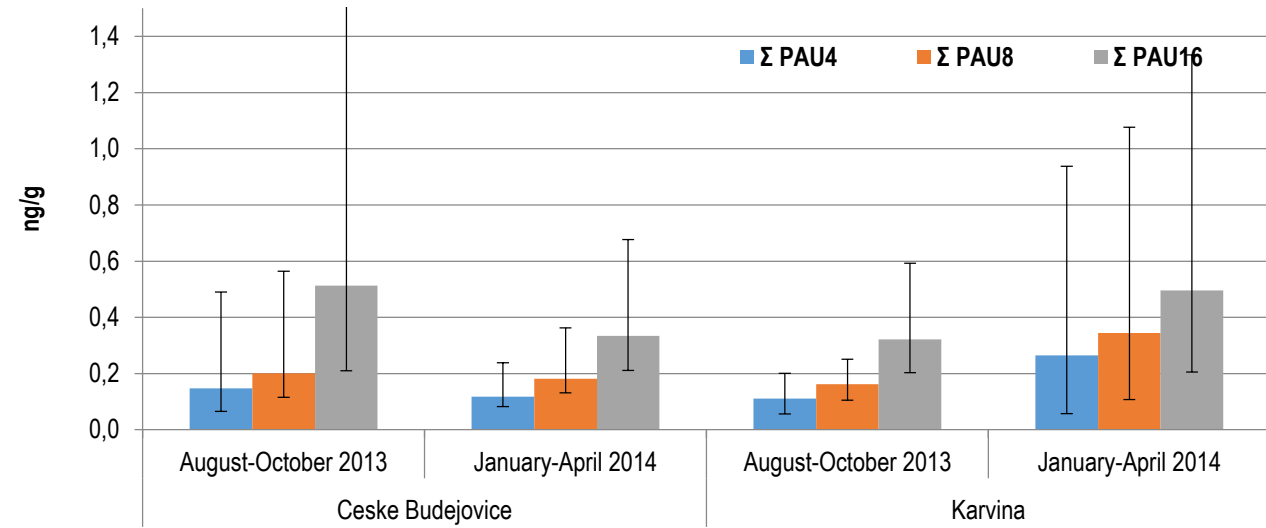


C90 – 5.9.2013

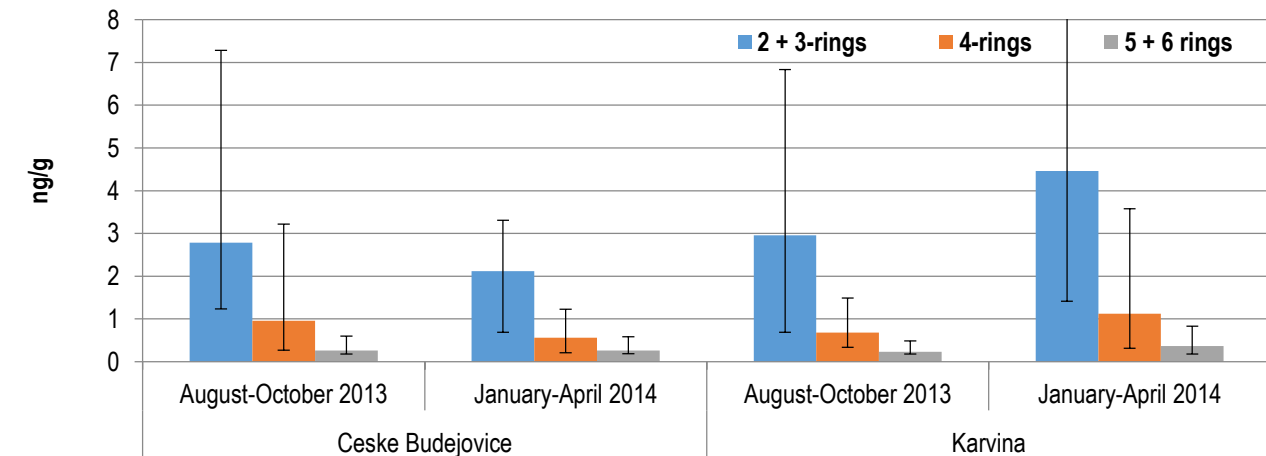
# PAHs in diet



Σ PAH4: BaP, CHR, BaA, BbF  
 Σ PAH8: PAH4, BkFA, BghiP, DBahA, IP



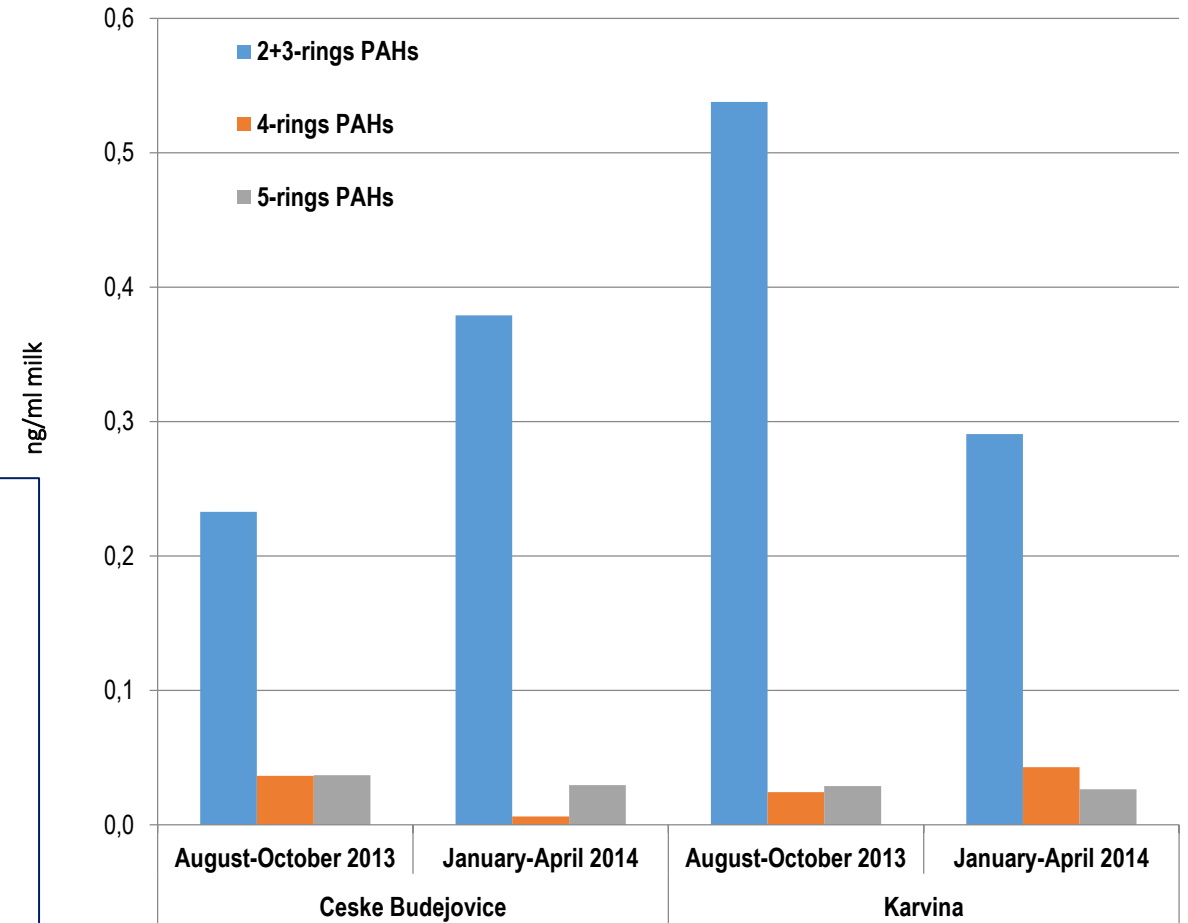
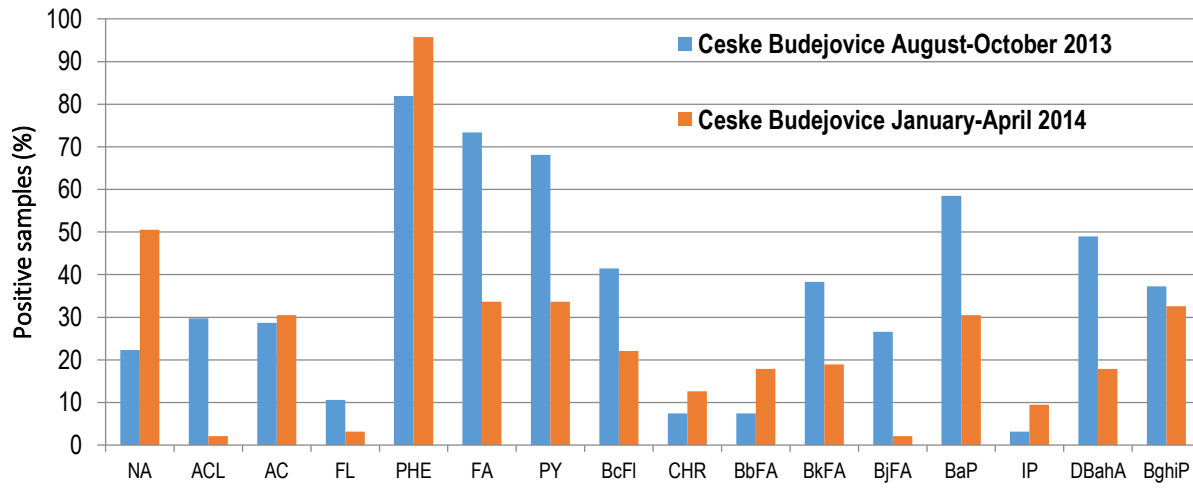
2 + 3-rings PAHs: NA, AC, ACL, FL, PHE, AN  
 4-rings PAHs: FA, PY, BaA, CHR, BcF, 5MC  
 5 + 6-rings PAHs: BbFA, BkFA, BjFA, BaP, DBahA, IP, BghiP, CPP, DBaIP, DBaeP, DBaiP, DBahP



\* Error bars indicate minimum and maximum concentration

# PAHs in human breast milk

2 + 3-rings PAHs: NA, AC, ACL, FL, PHE, AN  
 4-rings PAHs: FA, PY, BaA, CHR, BcF, 5MC  
 5 + 6-rings PAHs: BbFA, BkFA, BjFA, BaP, DBahA, IP, BghiP,  
 CPP, DBalP, DBaeP, DBaiP, DBahP



Science of the Total Environment 562 (2016) 640–647



Contents lists available at ScienceDirect

Science of the Total Environment

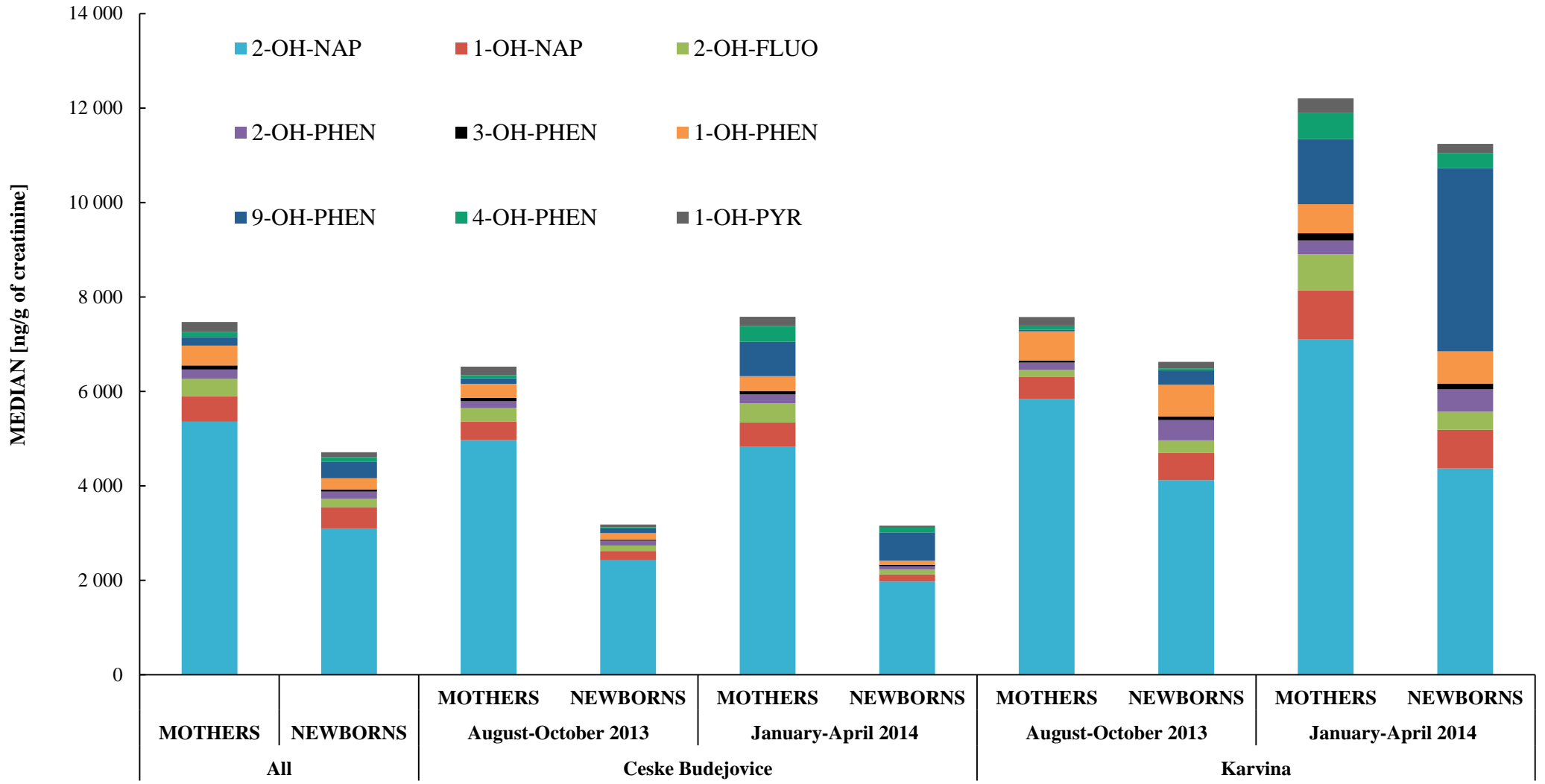
journal homepage: [www.elsevier.com/locate/scitotenv](http://www.elsevier.com/locate/scitotenv)



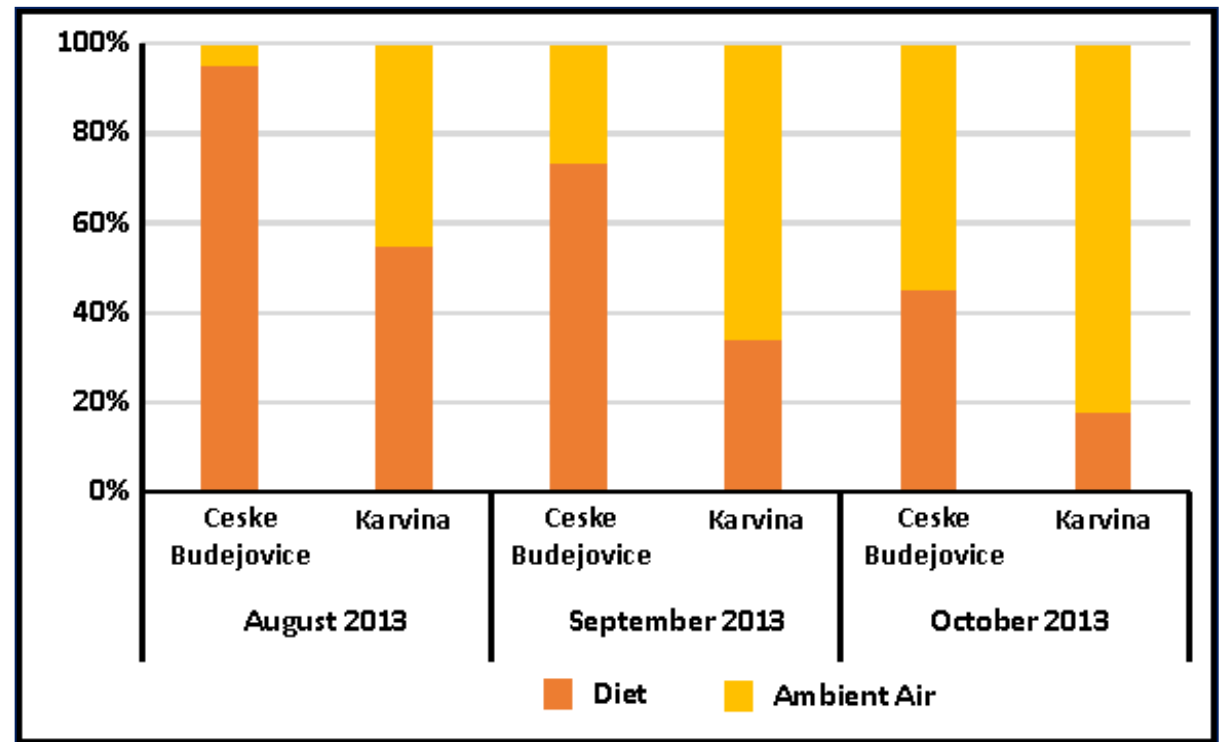
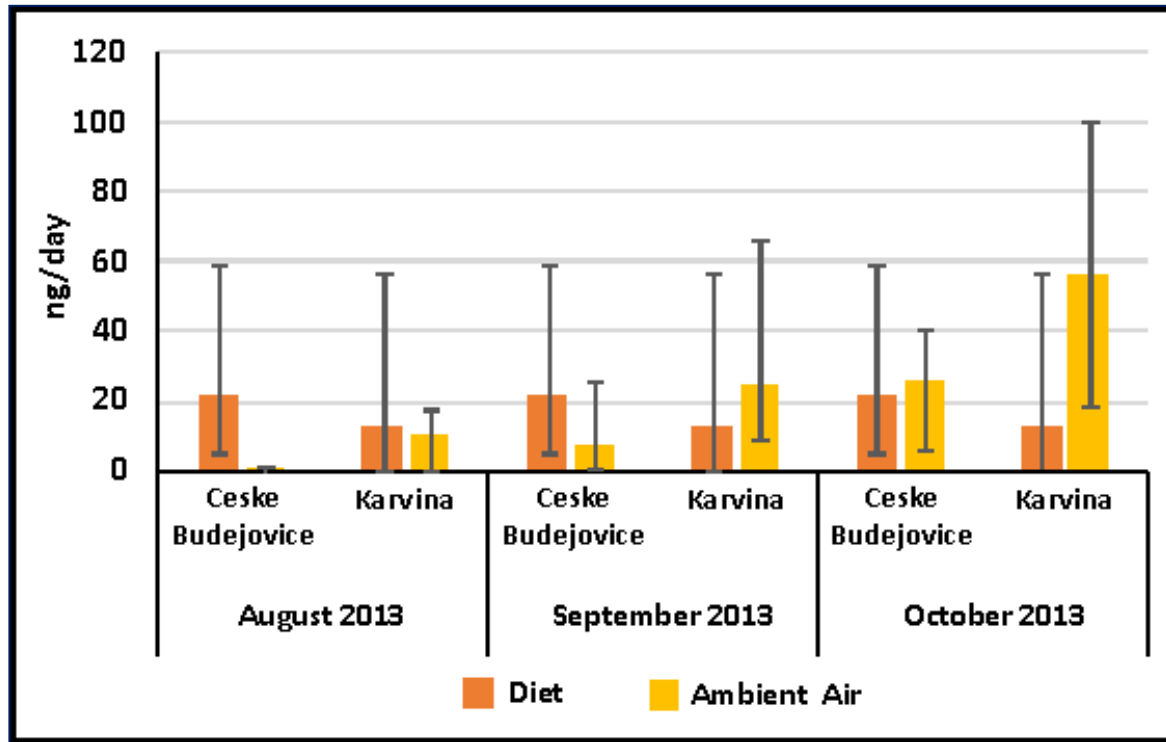
Relationship between atmospheric pollution in the residential area and concentrations of polycyclic aromatic hydrocarbons (PAHs) in human breast milk

Jana Pulkrabova<sup>a,\*</sup>, Michal Stupak<sup>a</sup>, Andrea Svarcova<sup>a</sup>, Pavel Rossner<sup>b</sup>, Andrea Rossnerova<sup>b</sup>, Antonin Ambroz<sup>b</sup>, Radim Sram<sup>b</sup>, Jana Hajslova<sup>a</sup>

<sup>a</sup> University of Chemistry and Technology, Prague, Faculty of Food and Biochemical Technology, Department of Food Analysis and Nutrition, Technicka 3, 166 28 Prague 6, Czech Republic



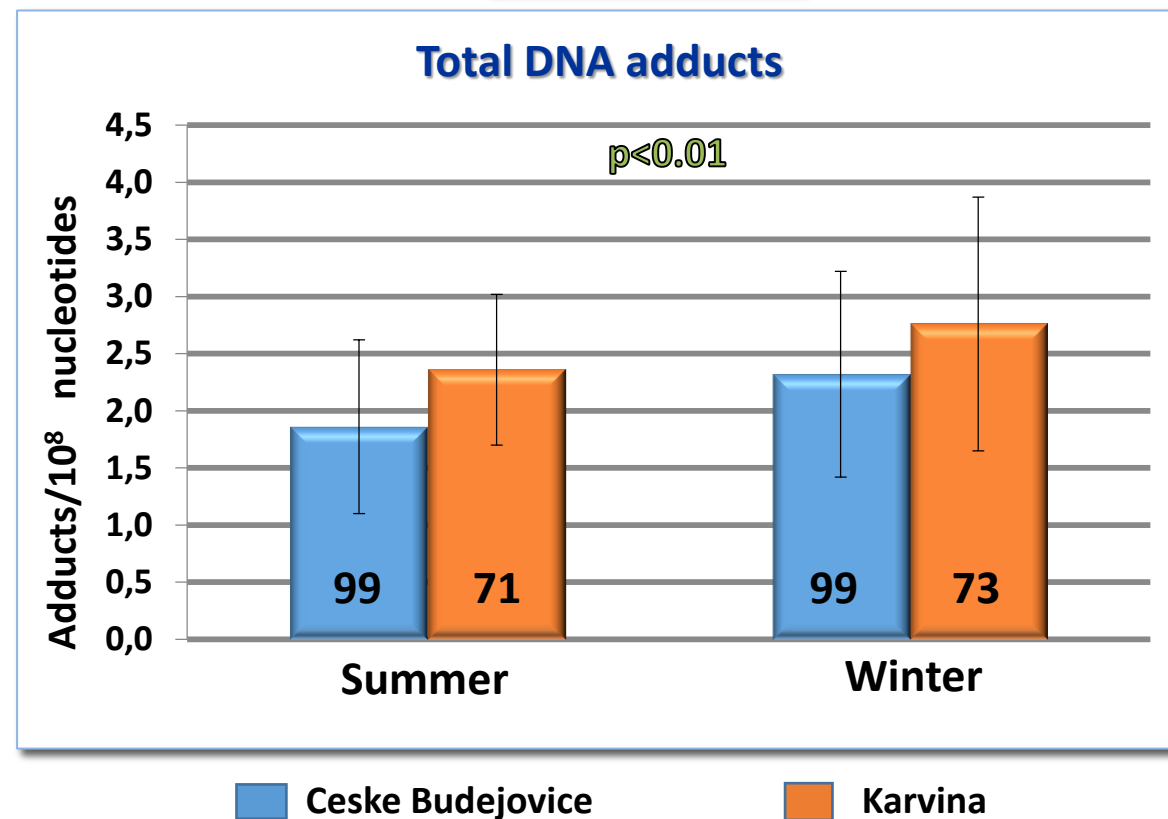
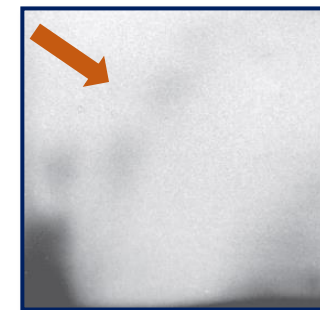
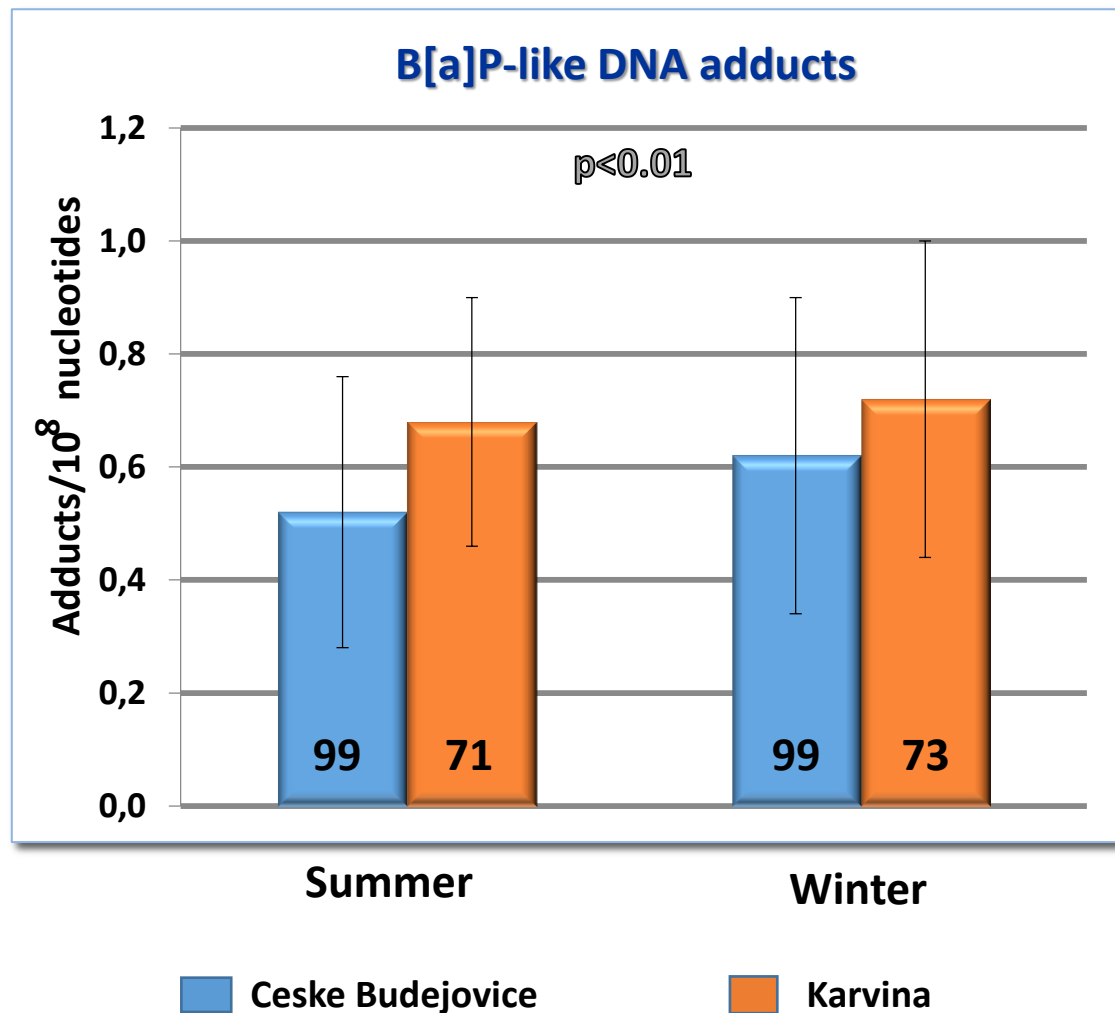
# INTAKE OF B[a]P FROM AMBIENT AIR AND DIET



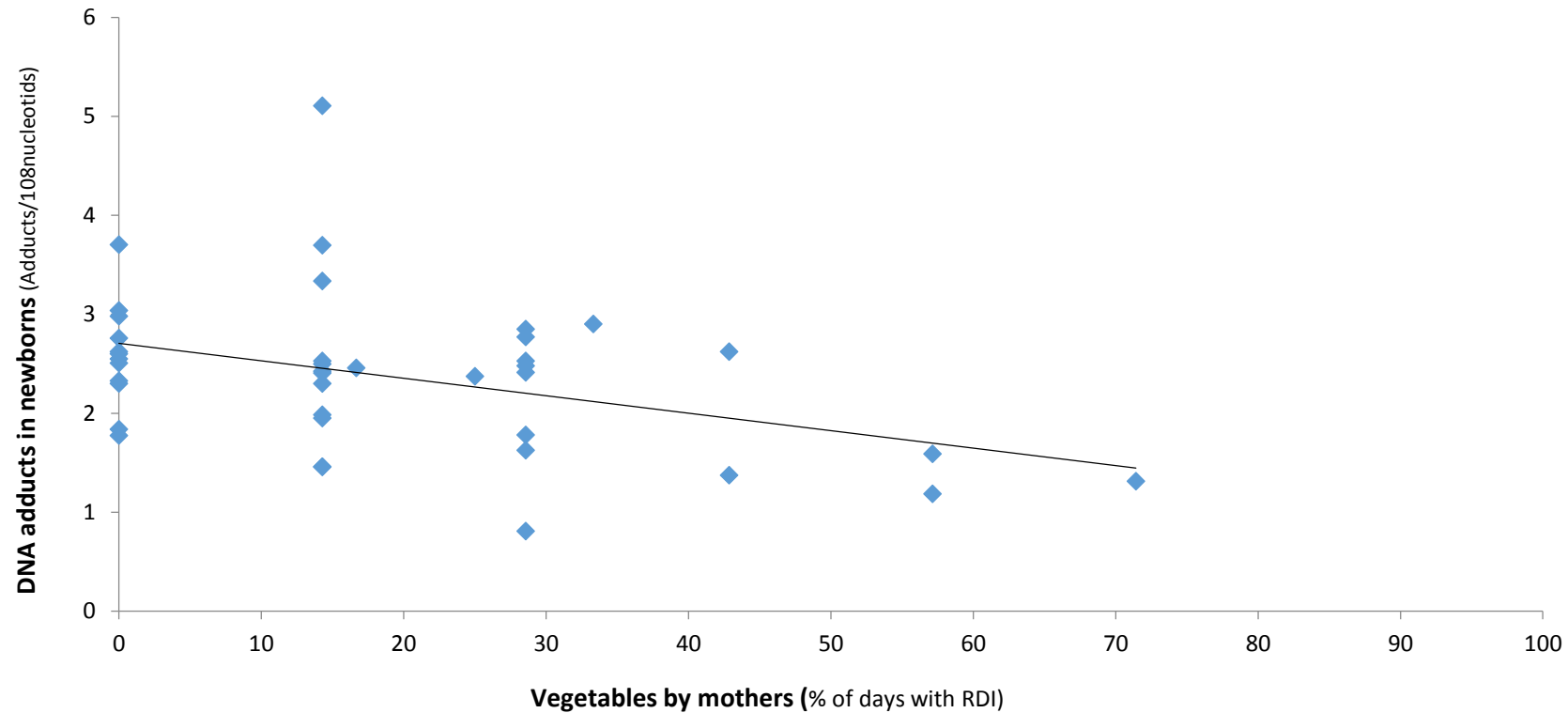
# CONCLUSIONS

- The first such complex study on the assessment of human exposure to PAHs in the Czech Republic
- The first data on the levels of OH-PAHs in urine of the Czech population
  - Approximately 2x higher median  $\Sigma$ OH-PAHs in urine from winter period in Karvina compared to Ceske Budejovice
- **HUMAN EXPOSURE**
  - The importance to monitor both the dietary intake together with exposure via inhalation was documented
  - In summer period the major part of exposure (60 – 90%) is via diet while in winter more than 60% is via inhalation
  - Newborns – milk contribute by about 20 – 50% of the total exposure depending on the season

# DNA ADDUCTS IN NEWBORNS



# DNA adducts in newborns vs. vegetables intake by mothers



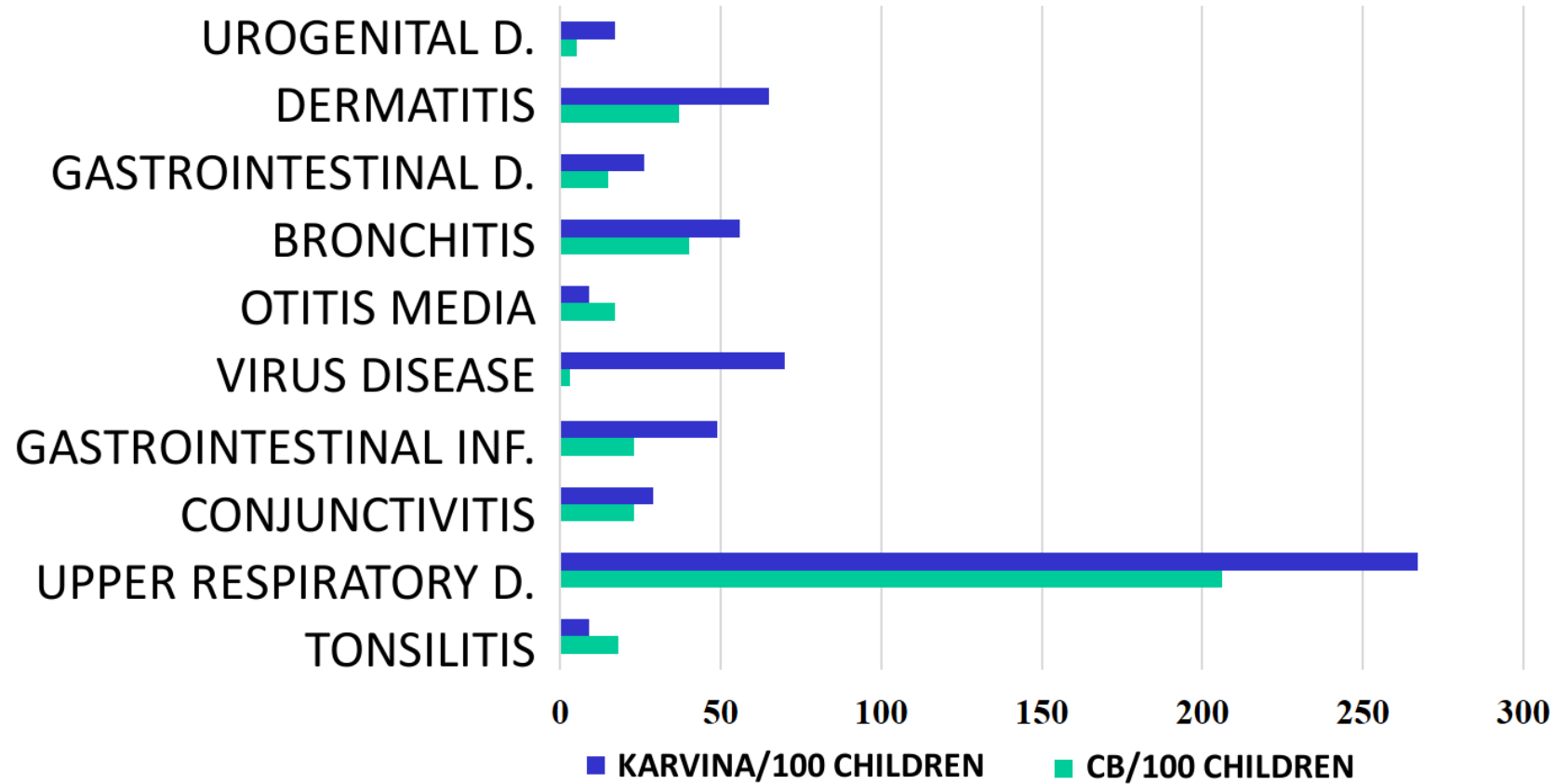


# OXIDATIVE STRESS IN NEWBORNS

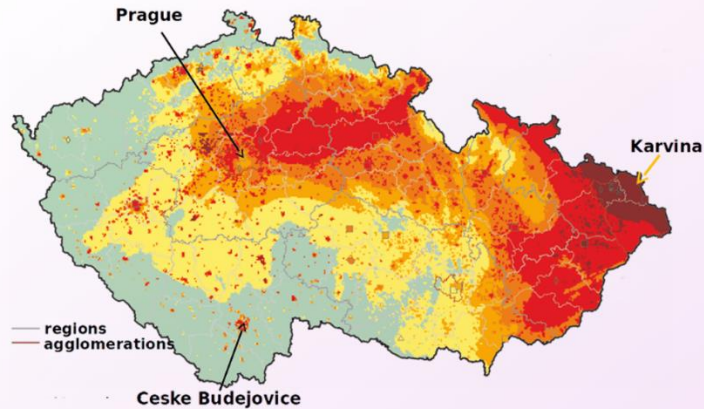
			8- oxodG mmol/mmol creatinine
SUMMER	Ceske Budejovice	N 99	4.7 ± 1.4
	Karvina	71	4.7 ± 2.4
WINTER	Ceske Budejovice	99	4.2 ± 1.5
	Karvina	73	5.7 ± 2.9 ***

\*\*\* p<0.001

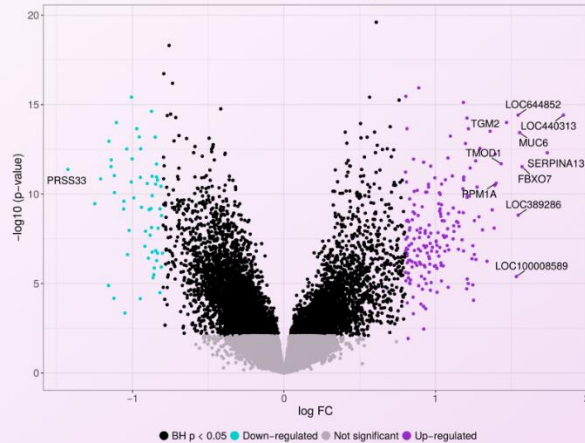
# MORBIDITY OF CHILDREN AT 2 YS OF AGE



# Comparison of locality and season



## Karvina winter genes



*MUC6* ↑  
inflammatory  
immune response

*SERPINA13* ↑  
blood coagulation  
inflammation  
Parkinson disease

*FBOX7* ↑  
oxidative stress in  
neuron  
Parkinson disease

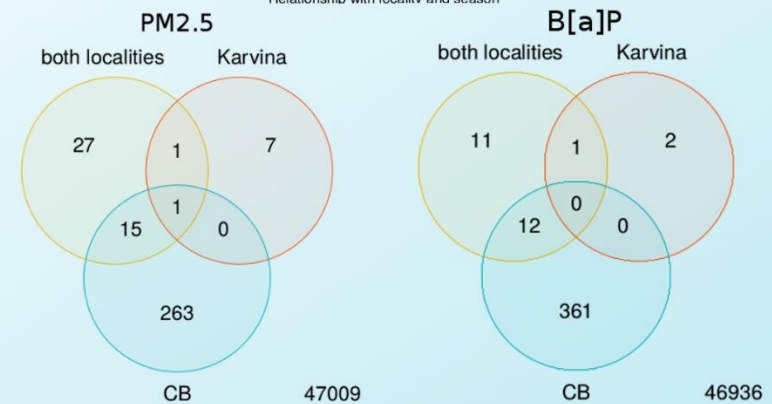
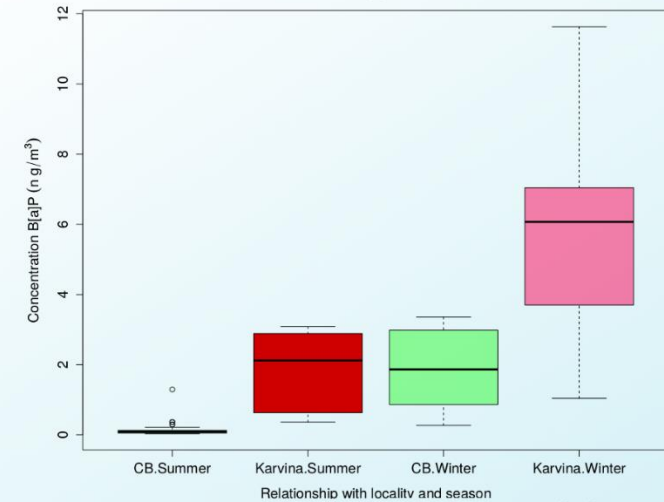
## Karvina winter pathways

*porphyrin and chlorophyll metabolism*  
heme synthesis, transportation, and metabolism

*NRF2 pathway*  
cellular defense against oxidative stress

*Neurotrophin signaling pathway*  
brain development processes

# Influence of B[a]P and PM2.5



## Karvina

*TAF15* neurological disease (B[a]P)  
*FBXO41* immune system (PM2.5)

## CB

The most of genes were correlated in control locality.

# CONCLUSIONS

- 1) Exposure to B[a]P represents a significant health risk for the population of the Czech Republic (62 % living in regions with the exposure > 1 ng/m<sup>3</sup>/year)**
- 2) PM<sub>2.5</sub> and B[a]P concentrations were higher in Karvina in both seasons**
- 3) DNA adducts were significantly higher in newborns from Karvina in both seasons**
- 4) DNA oxidative damage in newborns was higher in Karvina during winter**
- 5) Increased concentrations of PAHs metabolites in children urine were associated with decreased birth length, birth weight and head circumference**
- 6) Diet may be a significant source of PAHs exposure, especially when their concentrations in ambient air are lower**
- 7) Morbidity of children at 2 ys of age was higher in a more polluted district**

## CONCLUSIONS

**DUE TO A HIGH AIR POLLUTION CZECH REPUBLIC  
SEEMS TO BE A PARADISE TO STUDY THE IMPACT  
OF PM<sub>2.5</sub> AND PAH<sub>s</sub> EXPOSURE TO HUMAN HEALTH,  
ESPECIALLY TO CHILD DEVELOPMENT**

# ACKNOWLEDGEMENT

J. Hajslova

J. Pulkrabova

V. Kotek

K. Urbancova

A. Milcova

A. Pastorkova

A. Ambroz

M. Dostal

J. Pavlikova

P. Rossner, Jr.

A. Rossnerova

I. Solansky

V. Svecova

J. Topinka

M. Veleminsky, Jr.

**Thank you for your attention**

# ACKNOWLEDGEMENT

Supported by the grant  
of the Czech Academy of Sciences,  
Strategy AV21, Qualitas  
and  
EU Horizon 2020 HBM4EU

**QUALITAS**

Kvalitní život  
ve zdraví i nemoci

 Akademie věd  
České republiky

**Strategie AV21**  
Špičkový výzkum ve veřejném zájmu



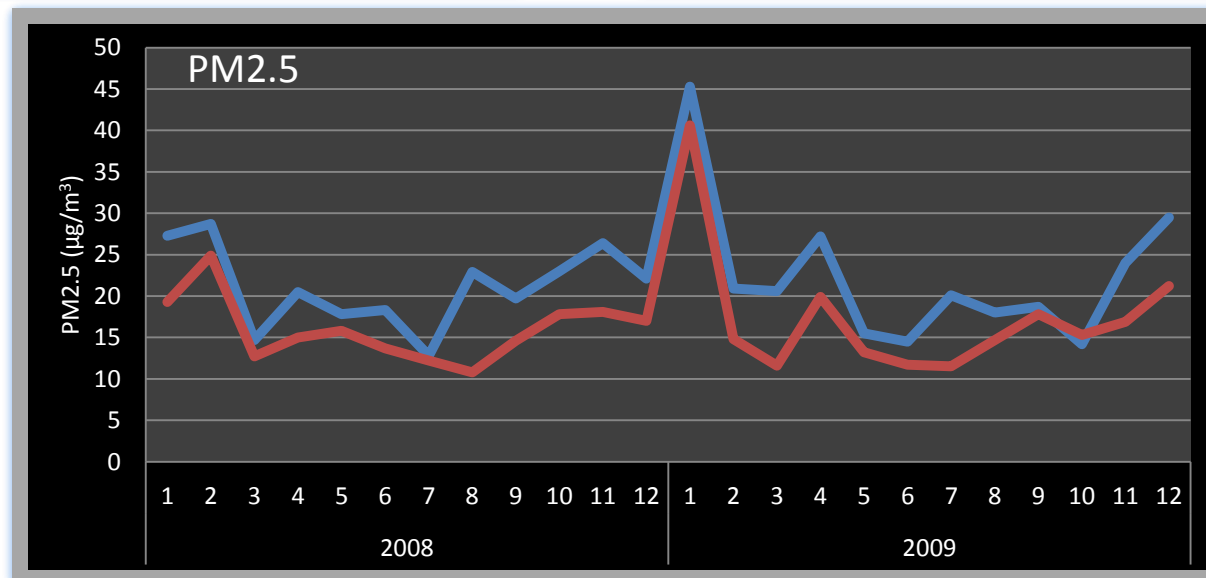
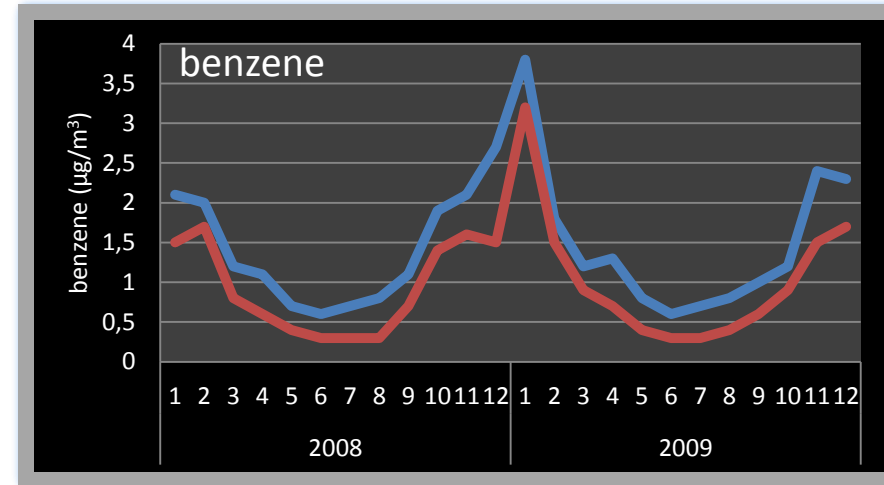
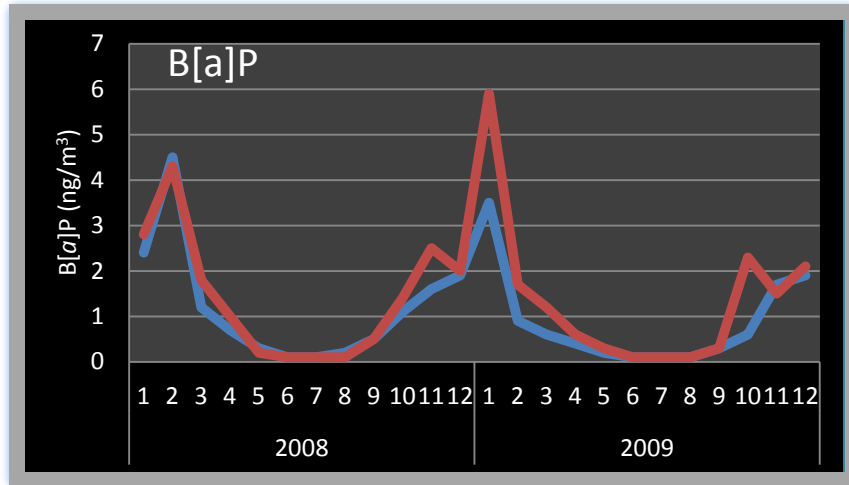


**CHANGES  
IN THE TRANSCRIPTOME  
OF PREGNANT MOTHERS**

# CONCENTRATIONS OF POLLUTANTS (months)

— Prague

— Ceske Budejovice



# DNA ADDUCTS IN MOTHERS AND NEWBORNS (<sup>32</sup>P-postlabeling)

(Prague vs. Ceske Budejovice)

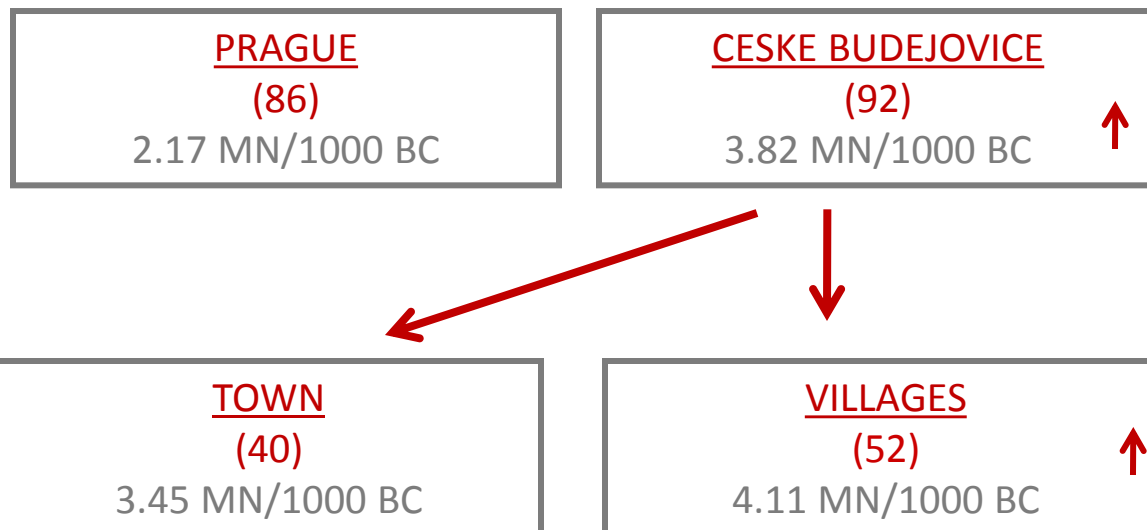
Adducts/10 <sup>8</sup> nucl.	N	Peripheral blood mothers		Cord blood		Placenta	
		Average ± S.D.		Average ± S.D.		Average ± S.D.	
		B[a]P-like	Total	B[a]P-like	Total	B[a]P-like	Total
Prague	80	0.24±0.18	1.23±1.09	0.23±0.18	0.98±0.89	0.24±0.18	1.15±1.06
Ces. Budejovice	76	0.44*±0.39	1.59*±1.46	0.41*±0.41	1.40*±1.31	0.54*±0.48	1.94* #±1.46

# OXIDATIVE DAMAGE

Lipid peroxidation (15-F<sub>2t</sub>-isoprostane)

		<i>Peripheral blood mothers</i>	<i>Cord blood</i>
pg/ml of plasma	<i>N</i>	mean ± S.D.	mean ± S.D.
Prague	80	192.9 ± 121.4	304.7 ± 211.9
Ceske Budejovice	76	129.8 ± 118.7	147.0 ± 125.0*

# MICRONUCLEI IN NEWBORNS



# DEREGULATION OF GENES

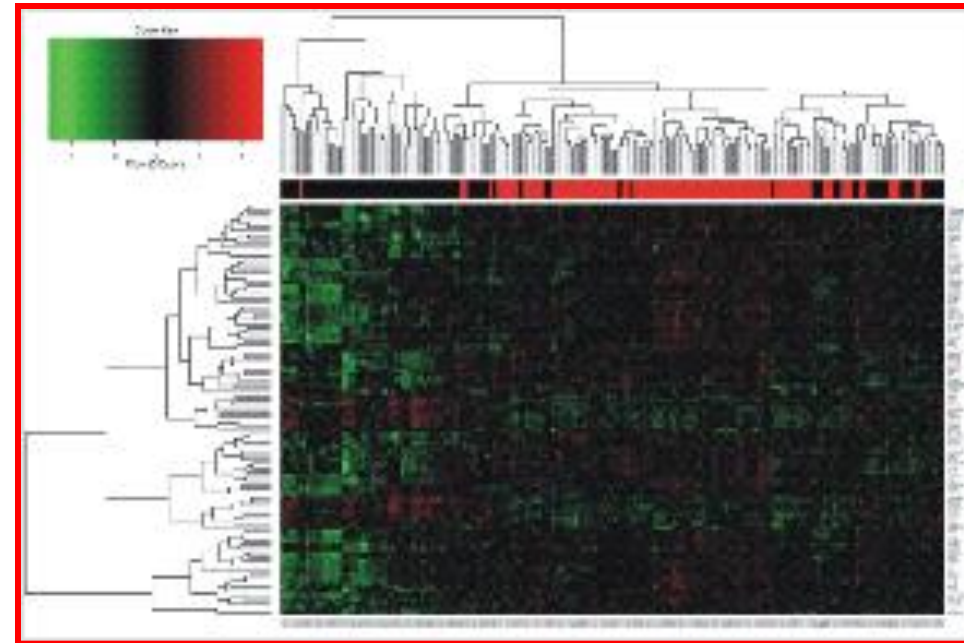
## Cord blood

Change: **104** genes

37 ↑

67 ↓

CB



**Increased** expression in CB:  
genes related to metabolism  
of xenobiotics

**Decreased** expression in CB  
genes related to immune response  
and autoimmune diseases

# CONCLUSIONS

- ➔ Studies of transcriptome indicate a new knowledge about a possible effect of air pollution to children health
- ➔ Surprisingly, the monthly exposure to B[a]P > 2.8 ng/m<sup>3</sup> increased IUGR as well as the deregulation of genes in newborns
- ➔ We should try to learn what is the impact of those data for the child development, specifically the effect of c-PAHs and PM2.5 exposures to respiratory morbidity

AIR POLLUTION

AIR POLLUTION



**CNS**



N.D. Saenen et al.

***In Utero* Fine Particle Air Pollution and Placental Expression of Genes  
in the Brain-Derived Neurotrophic Factor Signaling Pathway:  
An ENVIRONAGE Birth Cohort Study EHP 123:834-840 (2015)**



PM<sub>2.5</sub> 15-19  $\mu\text{g}/\text{m}^3$

deregulation of genes *BDNF* and *SYN1* in placenta

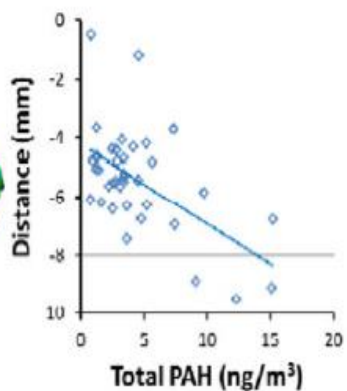
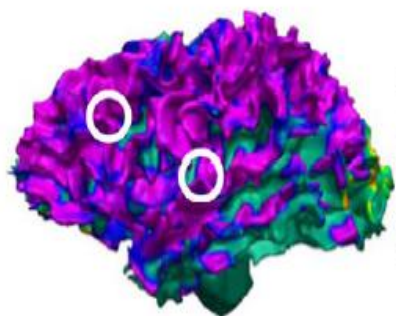
# PAHs & BDNF

D. Tang et al. Molecular and neurodevelopmental benefits to children of closure of a coal burning power plant in China. PLOS One 9(2014)e91966

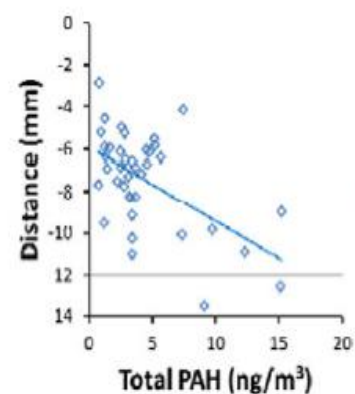
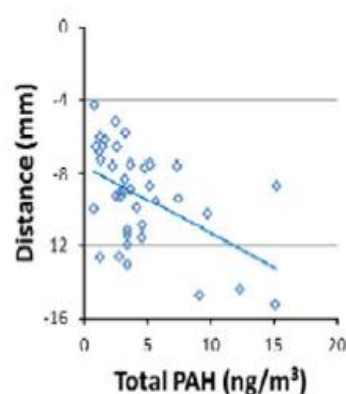
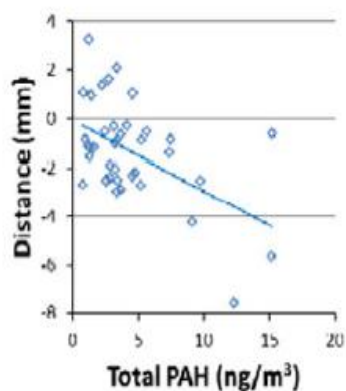
	2002(N=110)	2005(N=107)
PAH-DNA adducts	0.324±0.139	0.204±0.081*
BDNF, ug/dL	752.9±463.1	1266.6±619.8*
Gesell Scores Average	99.4±10.7	100.3±7.2
Motor	97.5±11.5	97.8±7.8
Adaptive	98.7±14.9	101.2±11.0
Language	102.1±12.8	100.5±9.8*
Social	99.4±11.8	101.8±6.8

\*p < 0.05

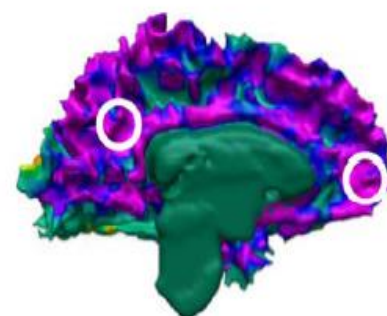
left lateral



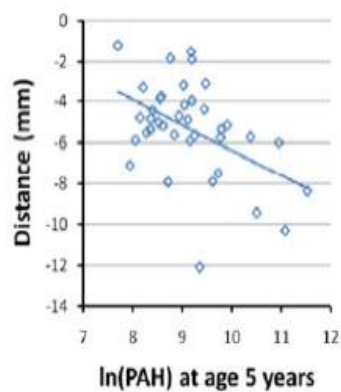
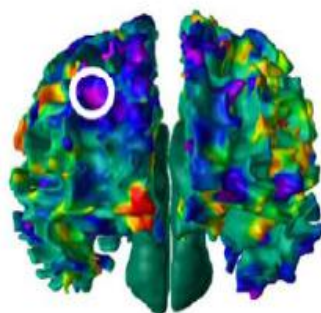
## Correlations with Prenatal PAH Level



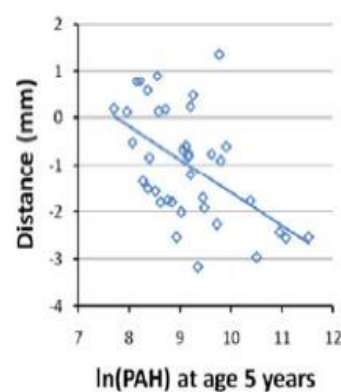
left mesial



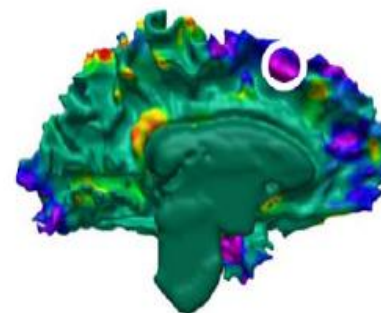
anterior



## Correlations with Postnatal PAH Levels



left mesial



# MMR study

- 1) Increased prenatal exposure to PAHs reduced left hemisphere white matter
- 2) Reduced white matter measures of the left hemisphere were associated with significantly higher scores for externalizing problems of the CBCL (child behavior checklist), as well as externalizing symptoms that included ADHD symptoms and conduct disorder problems.
- 3) Higher prenatal PAH exposure was associated with reduced processing speed during intelligence testing

# PAHs and cognitive functions

W.A.Jedrychowski et al. Prenatal exposure to polycyclic aromatic hydrocarbons and cognitive dysfunction in children. Environ Sci Pollut Res 22 (2015) 3631-3639

- 170 children in Cracow
- Exposure: PAH-DNA adducts, prenatal PAHs  $43.0 \pm 55.3$  ng/m<sup>3</sup>
- At age 7 ys Wechsler Intelligence Scale for Children
- Depressed verbal IQ index, cord blood adducts RR=3.0 (95%CI: 1.3, 6.8)
- Breast feeding 6 months – protective effect RR=0.3 (95%CI: 0.1, 0.9)
- Conclusion: PAHs are harmful to the developing fetal brain

# CONCLUSIONS

**Zvýšené koncentrace PM2.5 zvyšují výskyt:**  
**autismu**  
**poruch kognitivních funkcí u dětí**  
**onemocnění depresí**  
**incidence demence**  
**Parkinsonovy choroby**  
**ovlivňují koncentraci proteinu BDNF**

# ZÁVĚRY

**Zvýšené koncentrace PAHs :**

**ovlivňují hladinu BDNF**

**redukují bílou hmotu mozku**

**snižují kognitivní funkce u dětí**

**zvyšují výskyt ADHD**

# CONCLUSIONS

**DUE TO A HIGH AIR POLLUTION CZECH REPUBLIC  
SEEMS TO BE A PARADISE TO STUDY THE IMPACT  
OF PM<sub>2.5</sub> AND PAH<sub>s</sub> EXPOSURE TO HUMAN HEALTH**

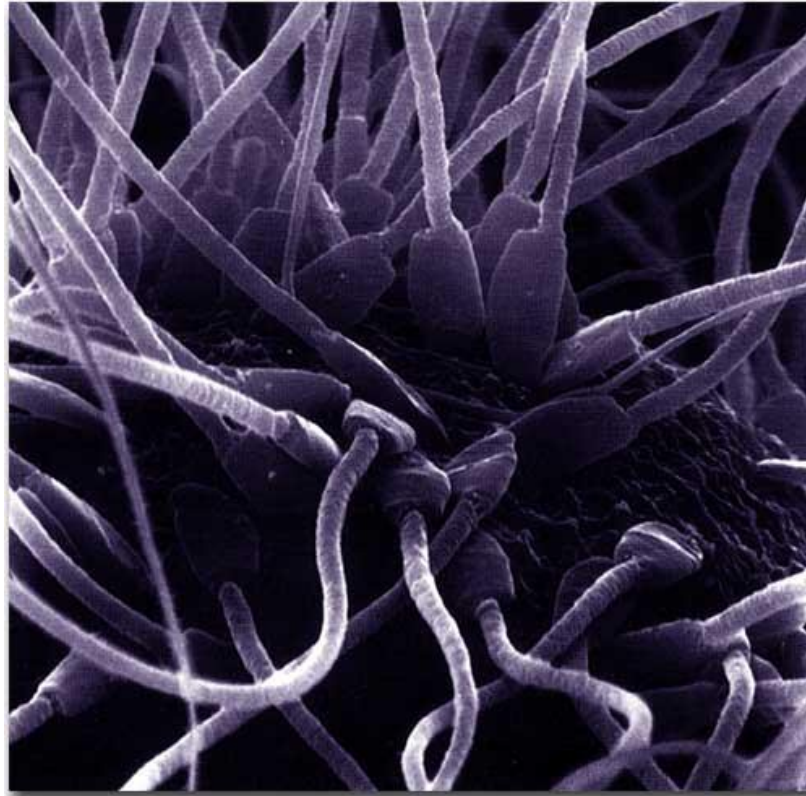
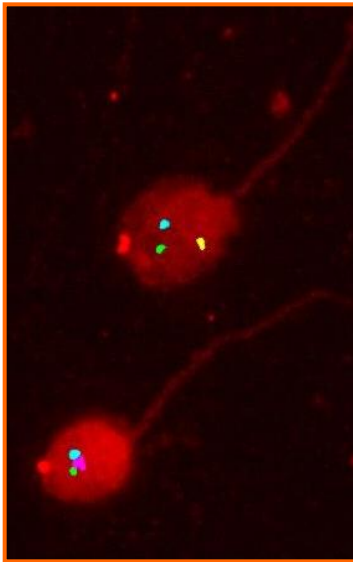




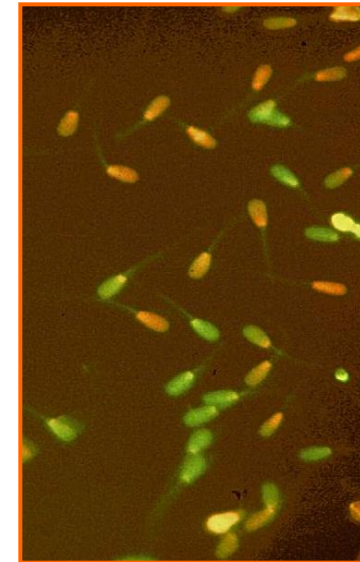
# DNA adducts

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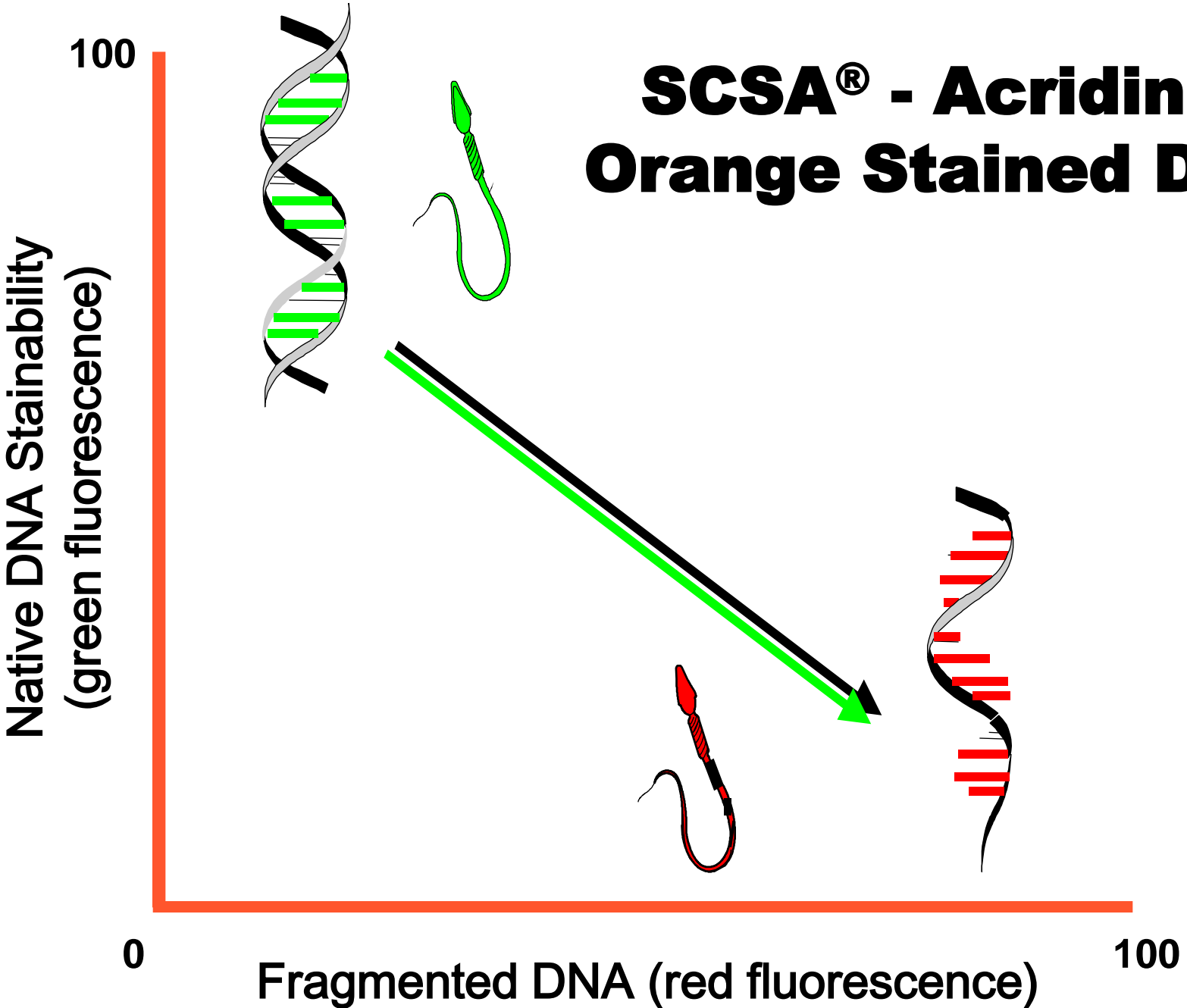
**chromosomes**



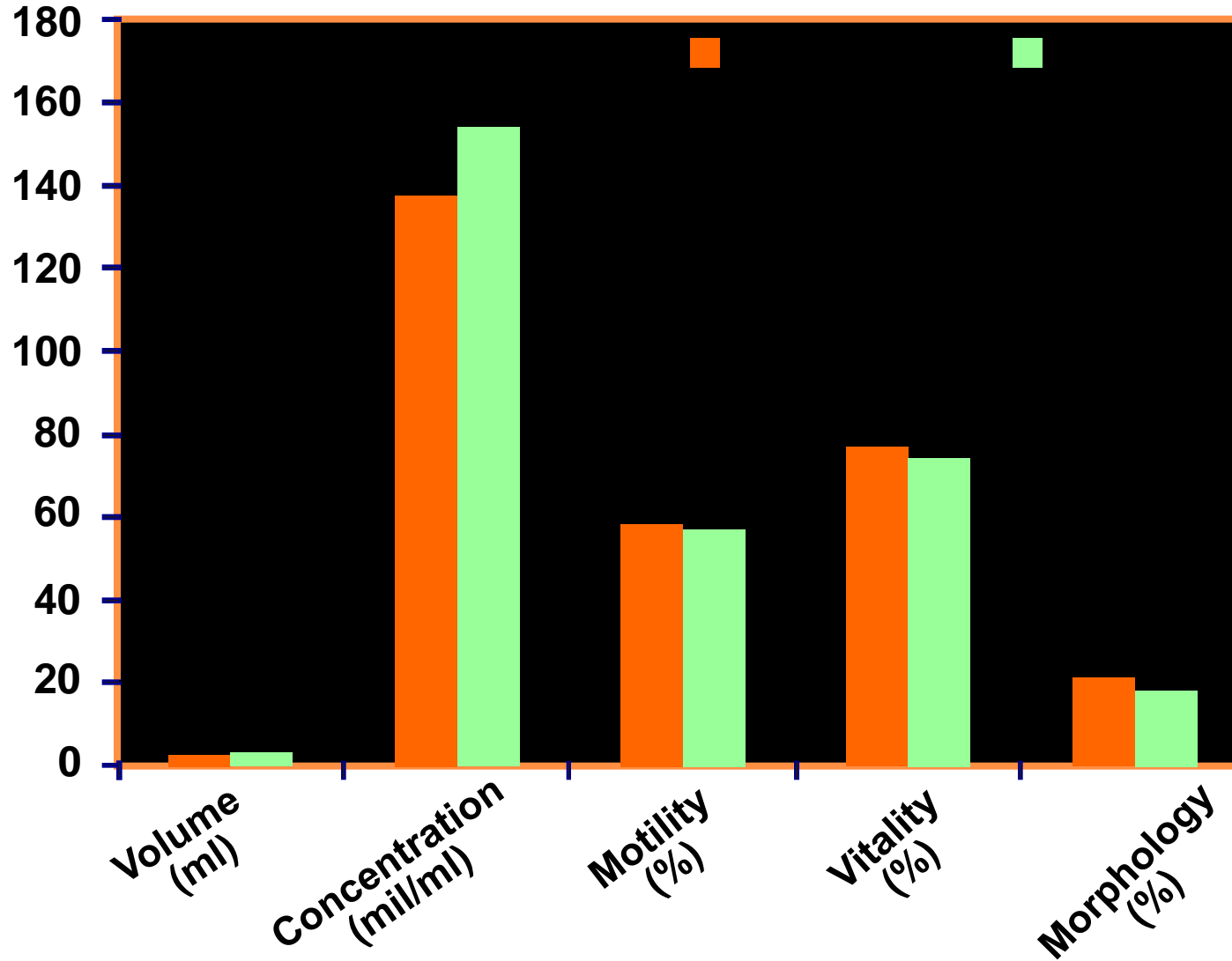
**chromatine**



# SCSA<sup>®</sup> - Acridine Orange Stained DNA



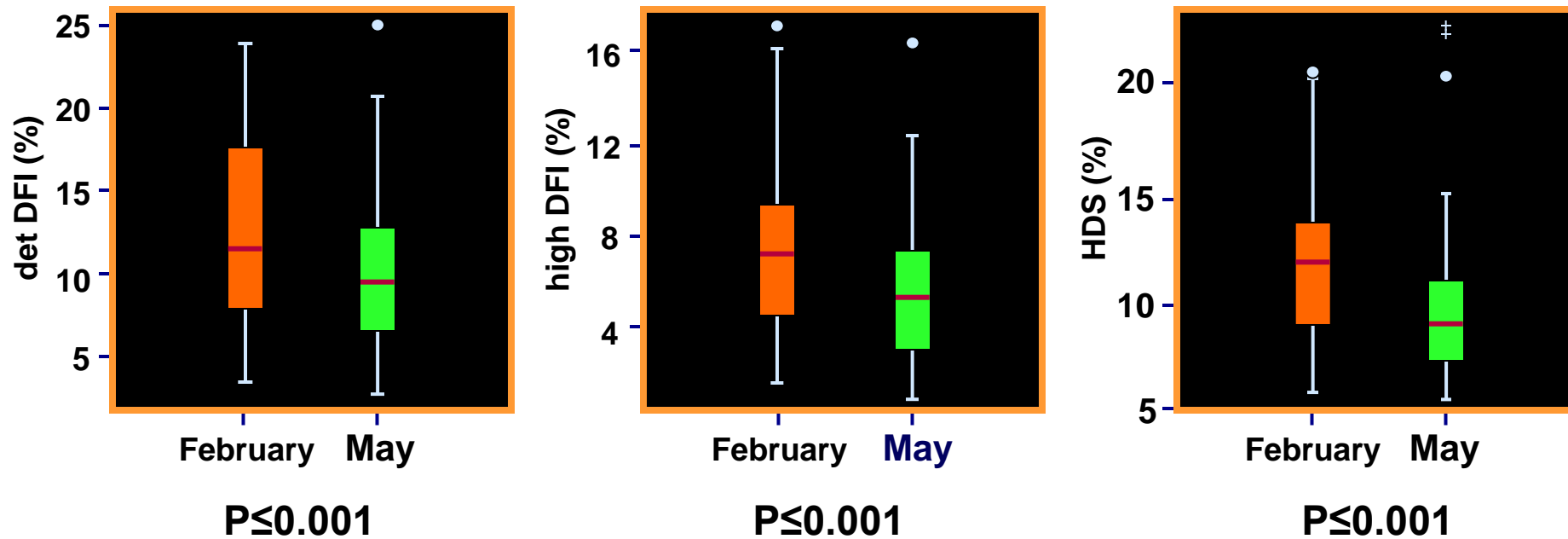
# Sperm analysis



# Policemen patrolling the streets in Prague centre with heavy traffic

The level of air pollution will be assessed on the basis of information from two source:

- data from stationary measuring stations AIM Prague
- for 48 h using personal sampling devices (URG Corp, USA)



**N=46**

dDFI < 15%	Feb 30	May 42
dDFI 15 – 30%	Feb 16	May 4
dDFI >30%	Feb 2	May 2
HDS >15%	Feb 10	May 4