OR 29/2010

INTARESE

Workshop Report on Integrated Monitoring

Alena Bartonova and Hai-Ying Liu (eds)

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Norwegian Institute for Air Research

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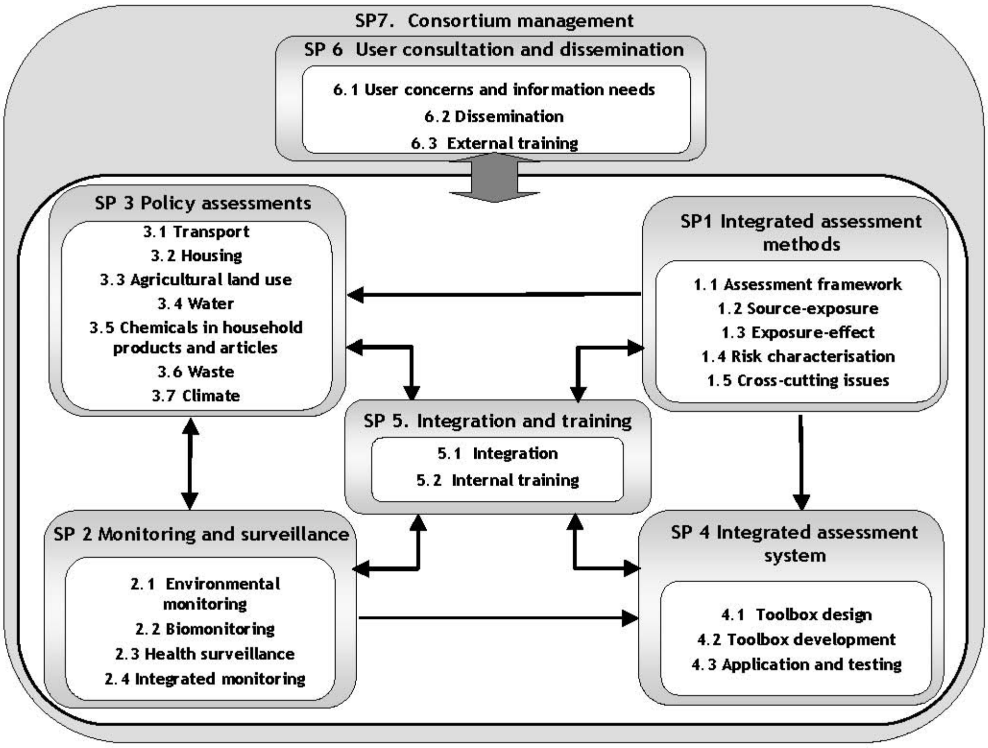
Preface

This report is a deliverable of a project INTARESE (Integrated assessment of health risks of environmental stressors in Europe). INTARESE is funded under the EU 6th Framework Programme Priority 6.3 Global Change and Ecosystems, Contract No. 018385. The purpose of INTARESE is to support implementation of the European Environment and Health Action plan, by providing the methods and tools needed for integrated assessment of health risks from environmental stressors (e.g. air and water pollution, climate change).

The project INTARESE involves leading scientists and practitioners from 33 institutions in Europe, as listed below.

Institution	**Acronym**	**Country**
Imperial College London	IC	UK
London School of Hygiene and Tropical Medicine	LSHTM	UK
National Institute for Public Health and the Environment	RIVM	Netherlands
Utrecht University	UU	Netherlands
Agence Francaise de Securite Sanitaire Environnmentale	AFSSE	France
Kansanterveyslaitos (National Public Health Institute)	KTL	Finland
Norsk Institutt for Luftforskning	NILU	Norway
ASL Rome	ASL	Italy
National and Kapodistrian University of Athens	NKUA	Greece
Forschungszentrum fur Umwelt und Gesundheit GmbH	GSF	Germany
Netherlands Organisation for Applied Scientific Research	TNO	Netherlands
Karolinska Institutet	KI	Sweden
Consejo Superior de Investigaciones Cientificas	CSIC	Spain
World Health Organisation, Rome	WHO	Italy
Université Catholique Louvain	UCL	Belgium
Fundació IMIM (Municipal Institute of Medical Research)	FIMIM	Spain
University of Maastricht	UM-ICIS	Netherlands
Health Protection Agency, UK	HPA	UK
Institute of Experimental Medicine AS CR	IEM	Czech Republic
Vlaamse Instelling voor technologisch onderzoek NV	VITO	Belgium
Czech National Institute of Public Health	CNIPH	Czech Republic
Vinca Institute of Nuclear Sciences, Serbia and Montenegro	IV	Serbia
Slovak Medical University -Institute of Preventive and Clinical Medicine	RB-SMU	Slovakia
University of Stuttgart	USTUTT	Germany
Institut de Veille Sanitaire	INVS	France
Institut National de l'Environnement Industriel et des Risques	INERIS	France
Department of Civil Protection - Italy	DCP	Italy
Centre for Research and Technology Hellas	CERTH	Greece
European Chemical Industry Council	CEFIC	Belgium
CSTB	CSTB	France
Barcelona Science Park (Parc Científic de Barcelona)	BSP	Spain
IC Consultants Ltd	ICON	UK

The project INTARESE has been arranged within six technical 'sub-projects', supported through a seventh dealing with project coordination, as structured below.



This report is one of SP 2 tasks-integrated monitoring. SP2–monitoring and surveillance is included to review and develop the monitoring tools and data sources in the way to support implementation of integrated environment and health assessment methodology. WP2.4 integrated monitoring is to explore the ways of linking and enhance various sources and technologies in order to provide a more integrated (e.g. EU-wide, multi-agent, multi-pathway, multi-media/receptor) approach to monitoring in the EU.

The key contents within this report are:

- Integrated monitoring: the way forward
- Approaches to integrate monitoring for environment and health impact assessment;
- Biomonitoring in the INTARESE concept of interated risk assessment
- Exposure-Dose-Response integration: looking for a common currency
- Case study on Pb in blood-Europe
- Environment and health information system in France
- Eco-toxicology–use for investigating interaction of stressors for integrated risk assessment -Spain

- Environmental Exposure and Ecosurveillance
- Monitoring of organohalogens body burdens of the Czech population
- Exposure to c-PAHs case studies
- Environmental data and human biomonitoring in France
- The concept of integrated monitoring in the Flemish Environmental Health Survey (FLESH)
- Integrated monitoring – vision or reality?
- The impact of air pollution to human health-Czech Experience
- Occupational exposure monitoring-approach used in FIBRETOX
- INTARESE toolbox guidance

For more information, please visit INTARESE website at http://www.intarese.org or contact Dr. Hai-Ying Liu, E-mail: hyl@nilu.no.

Reference

INTARESE (Integrated assessment of health risks of environmental stressors in Europe), available at: http//www.intarese.org (accessed on 1 November 2005).

Project No. 018385
INTARESE
Integrated Assessment of Health Risks of Environmental Stressors in Europe

Integrated Project
Thematic Priority

Deliverable 64: Workshop report on Integrated Monitoring (WP 2.4)

Due date of deliverable: 12/2008
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Organisation name of lead contractor for this deliverable: NILU	Revision: Final version

Project co-funded by the European Commission with the Sixth Framework Programme (2002-2006)		
Dissemination Level		
PU	Public	
PP	Restricted to other programme participants (including the Commission Services)	X
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services	

Contents

INTARESE Subproject SP 2 “Monitoring and Surveillance”

Meeting and training workshop

Aim

The aim of the meeting is to address the issues of monitoring for the purposes of integrated environmental health impact assessment, to provide basis for further INTARESE project work towards the objective to give guidance on integrated monitoring. The two specific objectives are:

- To identify the commonly experienced methodological and practical issues encountered in integrated environmental health impact assessment
- To specify activities to be performed in SP2 and WP2.4 that would lead to providing the guidance.

Agenda

June 2, 14:00-18:00	WP2.2 meeting: introduction and discussion • Greet Schoeters: WP 2.2 progress and work plan • Miguel Borras: Eco-toxicology–use for investigating interaction of stressors for integrated risk assessment -Spain • Milena Jovasevic-Stojnovic: Lead case study-Belgrade. • Milena Cerma: Lead case studies-Czech Republic • Nadine Frery: Lead study-France • Roel Smolders: Case study on Pb in blood-Europe • Radim Sram: Case study on PAHs-Czech Republic
June 2, 19:00-21:00	Trip on the fjord
June 3, 09:00-12:30	Integrated monitoring: introduction and invited speakers • Alena Bartonova: Introduction; the INTARESE methods • Hai-Ying Liu: Integrated monitoring • Lars-Otto Reiersen: The AMAP program • Nadine Frery: Experience from France • Greet Schoeters: Integrated Monitoring Approaches in Flanders

	• Miquel Borras: Environmental exposure and ecosurveillance-Spain
June 3, 12:30-13:30	Lunch
June 3, 13:30-18:00	• Milena Cerna: EHMP-The Czech Environmental Health Monitoring Program • Radim Sram: The Teplice program • Maria Dusinska: Integrating information: the Fibretox project • Roel Smolders: Exposure-Dose-Response integration: looking for common currency • Tek-Ang Lim: Environment and Health information system in France • Clive Sabel: INTARESE toolbox guidance
June 3, 20:00-22:00	Conference dinner
June 4, 09:00-12:00	Common session: Brainstorming- integrated monitoring: definition, goals, criteria Presentation of Eric Lebret: integrated monitoring
June 4, 12:30-18:00	WPs 2.1-2.4 summary and planning Tek-Ang Lim: WP 2.3 Health surveillance Roel Smolders: WP 2.2 Biomonitoring Jan Duyzer: WP 2.1 Environmental monitoring Alena Bartonova: WP 2.4 Integrated monitoring
June 5, 10:30-12:00	Common session: Implications for WP2.4 – research questions and definition of case studies
June 5. 12:00-13:00	Meeting closed

Related materials

- D 51: Draft review on integrated monitoring
- WP 2.4-presentation of integrated monitoring
- Presentations from invited speakers

Discussion points

- Main integrated health and environment monitoring programs
- The common issues encountered in integrated monitoring
- Definition of monitoring

- Aims, goals, objectives and framework of integrated monitoring
- Case studies of WPs 2.1-2.4
- Actions towards providing guidance for integrated monitoring
- Publications

Summary

WP 2.2 Bio-monitoring

- Three case studies: Lead (VITO), PCBs (SMU), PAHs (IEM)
- Improve cooperation with WPs 2.1, 2.3 and 2.4
- Continue interaction with SP4 on HBM fact sheets
- Deliverables and publications (one published, one submitted, two drafts)
    - Overview of biomarkers, submitted
    - Publication on applicability of new technologies “omics” in human biomonitoring, draft
    - Publication on the applicability of non- invasive matrices for human biomonitoring, draft
    - Quality criteria for biomarkers and biomarker databases, is processing.

- Discussed the background and data availability regarding the lead studies in Spain, France, Czech Republic and Serbia:

    - Miguel Borras: Eco-toxicology–use for investigating interaction of stressors for integrated risk assessment-Spain

        - The use of eco-toxicology in Spain
          -Investigating interaction of stressors
          -Identify new hazards, refining exposure calculations.
          -Integrate in case study (eco surveillance)

    - Milena Jovasevic-Stojnovic

        - Belgrade–Lead case study. Blood from preschool children exposure to car industry. It is unclear if she can get data.

    - Nadine Frery

        - Background: Old study 10 years ago, 3500 children (lead level in blood); new study included environmental data. Since pilot study will be initiated in Sept, 2008, so data is not available. But so far they have data on adults.
        - Problems: Translating data, transferring data and standard format are very important. Furthermore, ethical aspects are rather important.
        - Questions: Is there anybody handling this issue? Is the responsibility of use of the data transferred after use of data? What about transboundary use?
        - What are minimum requirements for a database? Do we really need personalized human biomonitoring data?

- Roel Smolders-Case study Pb in blood around Europe

  - Identification of projects: HBM database (www.hbm-inventory.org); ESBIO + INTARESE Members, Peer-reviewed publications (web of knowledge), Screening for relevance (Europe, survey) and E-mail address available.
  - Questions and discussion
    - Is analytical quality a problem?
    - From received data so far, can you come up with minimum requirements? Must dig deeper; must focus on the aim: that will give the requirements. What can we solve with the collected data and what not?
    - Miguel Borras is willing to look at getting Spanish data. Roel Smolders needs to inform Miguel who he has contacted.
    - Make a common letter – in order to collect data from different countries. What will we do? How do we use it? How to publish? How to make it easier to obtain data? Maybe it is too late to do it? Roel Smolders wants to start analyzing the data.

- Radim Sram: case study on PAHs

  - Questions and discussion
    - Is it possible to make toxic-kinetic model with input and output, without doing all the individual steps? Answer: all steps are needed to make a risk assessment; it is difficult to give clear answer.
    - What data can be used for public health? They are trying to interpret the data for public health.
    - Pregnancy outcome, hearing (earlier PAH was only known to be carcinogenic)

WP 2.4 Integrated monitoring

Presentation and deliverable 51 from WP 2.4 as the basic materials to trigger further discussion about integrated monitoring. The definition, goals, objectives and criteria for integrated monitoring were discussed after invited speakers and Eric Lebret’s presentation: the goal-oriented definition of integrated monitoring.

Framework

- Why do we divide monitoring systems into natural, man-made and eco systems? It targets to distinguish regarding the policy interventions.
- Framework need to be developed further to make clear that we include policy indicators.

The definition of monitoring

- Monitoring (RIVM): Monitoring is the systematic and repeated determination, analysis and interpretation of environmental quality and environment-related health status.
- Risk monitoring (IPCS): a process of following up the decisions or actions in risk management, in order to ascertain that risk containment or reduction with respect of a particular hazard is assured. Risk monitoring is an element of risk management.
- Monitoring (USEPA): monitoring is a periodic or continuous surveillance or testing.
- Monitoring (WHO): monitoring is the continuous oversight of an activity to assist in its supervision and to see that it proceeds according to plan. Monitoring involves the specification of methods to measure activity, use of resources, and response to services against agreed criteria.
- INTARESE: Integrated monitoring is the systematic (pre-concieved, standardized, methodological, orderly, and organized) and repeated (in time, across space) determination, analysis and interpretation of environmental quality and environment-related health status. Added value of information – the increased weight of evidence - is provided by reducing uncertainty in assessment by the integration of different elements of the causal chain.

Goal-oriented definition of "integrated" monitoring-the goal defines the integration.

Identify the added value of, and methods for, integration in:

- Compliance monitoring
    - (REACH): human bio-monitoring may provide additional information in the compliance dossier
    - Other legal frameworks (see INTARESE policy areas) (e.g. air quality, water quality, and soil quality): providing new information to allow revisions of the norms.
    - Compatibility of norms with the goal of achieving the policy targets.
    - Use of compliance monitoring generated data for other purposes than compliance. Example: assessment of environmental radiation exposure using data generated in the National network for monitoring of radioactivity in the environment.

- Alerts monitoring
    - Quick response to a specified threat. E.g., smoke alert, heat alert, predictions of threshold exceedance (pollution). Defined actions on defined levels, the actions may be better targeted.
    - E.g., heat alert is "integrated"– simultaneous forecast based on simultaneous evaluation of meteorology, air pollution, emergency hospital visits, mortality. Allows focusing actions properly.

- "Finger on the pulse" monitoring
    - Identification of a threat, e.g., cancer clusters, based on analysis of existing monitoring data.
    - Early warning: building an alert system that allows identification of (new) threats. E.g., observation of an exponential increase of body burden with

contaminants will lead then source identification, then action to forbid/regulate sources.
  - Use of indicator organisms to allow the identification of (new) threats.

- Accountability monitoring

  - Integration of information will allow demonstration of effectiveness of previously used measures, and thus allows accountability. Questions: are investments in environmental quality worthwhile? Do they pay off? (E.g. Health Effect Institute series of expert meetings can provide accountability to environmental regulations). Integration provides a better view of the causal chain.

- Trends monitoring (AMAP, www.amap.no)
- (after) Disaster monitoring (Gulf war, Chernobyl, Seveso, Bhopal, other accidents) – assess damage, mitigation options and future preventive measures. It will demonstrate preparedness.

Summary: Integrative approach will support the validity of the causal relationship. Biomarkers could represent one of the tools that support the connection between external exposure and health effect, and could provide additional early warning information. Monitoring networks often combine several monitoring goals in one network.

Relationships between monitoring and modeling:

- modeling is an integrated method within a monitoring system
- connecting information from different sources through models

Case studies

- To integrate environmental monitoring, biomonitoring and health surveillance

  - PCBs-exposure biomarker-health effects (e.g. diabetes)-Czech Republic and Slovakia
  - PAHs-pregnancy outcomes in Czech Republic
  - PM2.5 - Cardiovascular Disease/Mortality/Morbidity. It is important but it is a challenge.
  - What about Arsenic (As)?
  - What about combined effects: PCB + PAH?

- Integrated monitoring by combined exposure, effects and health outcomes

  - Exposure, effects, health outcomes
    -Go to health registers to get relevant data
    - Eurostat – national levels (birth weight, length, and months of pregnancy)
    -Challenge: find other health endpoints that can be interesting in the future; another challenge is the time lag: e.g. environmental data from 40 years ago and health endpoints discovered today.
  - Different stressors: e.g. chemical and heat
  - Trends – monitoring to set thresholds – work on timeframe – baseline

    - Environmental burden of disease, this tackles the combined exposure/agent (Ex PCBs + PAHs), it is possible to attribute it to the specific pollutant.
- Integrated monitoring by including other tools and other data such as modeling and GIS, socio-economic aspects
    - It might be possible to have a case study which integrates all kinds of available monitoring data, not just e.g. environmental data and health data.
    - Integrate data through a model
- To connect and use different monitoring (environmental monitoring and biomonitoring) in same space or time
- Questions: What kind of implications do these case studies make for our work? What if the data is not there? Do we start a survey?
- Summary: stick to PCBs and PAHs. Difficult to link the HBM to the environmental monitoring. Could collaborate with SMU, and expand it into the health.

WPs next step tasks

SP 2 Monitoring and surveillance

Format a data request letter

Regarding the data request to data providers, INTARESE SP 2 needs to format a common letter:

- Why do we need data?
- How do we use data?
- What are publications rules with data?

Publications and INTARESE website

Everybody needs to check on the INTARESE publication strategy, both for procedures around submission of abstracts and of articles, and for acknowledgement.

Everybody is encouraged to check on the INTARESE website periodically in order to know what is going on.

WP 2.1 Environmental monitoring

Air pollution (PM10)

- Air pollution in the Netherlands
    - Involved partners: TNO, IC, NILU and WP 3.1-traffic
      -Concentrations calculation over land use-IC
      -Remote sensing-CERCH
      -Monitoring stations, collection data between different sources, map to show monitoring stations and its influence area (TNO).
      -Simple methods: exposure calculation and uncertainty analysis (NILU)
      - TNO has started it in Rijnmond area (2 million populations): PM 10 and PM 2.5
- Get air pollution data from Barcelona is processing

Noise

- Exposure to noise will start from Netherlands use simple method, at the end, it could be completed around the whole Europe

PAHs in Prague

- Need to check with IEM; would involve TNO, NILU, possibly CSIC in modeling.
    - Exposure through full chain
    - Biomarkers through whole chain

Lead

Lead protocol is in progress (IV Milena Jovasevic-Stojnovic). First step is to review existing data in Serbia, next is modeling data.

Publications

The group has considered publications and will make the publication plan available.

Susane Lopez-Aparicio from NILU (sla@nilu.no) is involved WP 2.1

WP 2.2 Bio-monitoring

Tasks

- Task 1: Development and testing of new methods to apply biomonitoring data in the context of integrated risk assessment: development of case studies
- Task 2: Improve cooperation with WP2.1 and WP2.3 particularly in the context of anticipated activities in WP2.4
- Task 3: Continue interaction with SP4 on HBM fact sheets
- Task 4: Continue and finalise the work as was agreed at the Copenhagen meeting

Deliverables:

- Mth 30 Draft: overview of case studies
- Mth 36: Draft: linking biomonitoring data to environment and health data
- Mth 42: final report on case studies

WP 2.3 Health surveillance

Tasks

- Task 1: how to deal with the lack of local health data? The focus of this task is to work on how to tackle the lack of health data at the local level when doing a Health Impact Assessment at the local level.
    - A case study will be developed on PM 10 effects on human health in three countries (France, Italy and Norway) and maybe the UK depending on data availability.
    - Discussion has been launched about including the Netherlands in the study and as such linking this case study to the Rijmond case study developed in

WP 2.1. WP leader from both WP 2.1 and 2.3 agreed on linking the case studies for this task.

- Task 2: lung cancer projection, this work will deal with how to obtain relevant information on lung cancer mortality in the next 10 or so years. This work will be of interest for SP3 when comparing the outcomes of their policy case studies. Lung cancer projection work will be carried for hopefully 4 countries (France, Italy, Norway and UK) depending on data vailability.

WP 2.4 Integrated monitoring

- Send review template to Greet Schoeters for Flanders project review
- Request Mathilde to review the French heat warming monitoring system.
- Revise the D51-define a clear goal, develop the framework further to include policy implementation, define the indicators within framework based upon the INTARESE full chain.
- Finalize manuscript “approaches to integrate monitoring for integrated environment and health impact assessment”.
- Need to add one chapter “protocol and assessment for integrated monitoring” in next scoping report to increase the weight of evidence.
  - Distill specific objectives (categorize) of true examples of monitoring (add periodicity in description of examples)
  - Define to what degree and across which dimensions integration took place
  - Describe what is needed to translate to impact indicators
  - Write this in background document for toolbox
  - Draw up specific recommendations for goal-oriented integration in future monitoring

AOB

Send mail to Miranda Loh and Vlasta Svecova regarding the PAHs data in ENVIRISK

Clive Sabel, Scott Randall, Susana Lopez-Aparicio and Hai-Ying Liu briefly met on June 4, and Clive will be in contact with them regarding the use of GIS in environmental health.

List of participants

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Appendix

1. Alena Bartonova: Workshop: Integrated monitoring The way forward
2. Hai-Ying Liu: WP 2.4-Integrated monitoring
3. Greet Schoeters: WP 2.2-Biomonitoring in the INTARESE concept of interated risk assessment
4. Roel Smolders: WP 2.2-Exposure-Dose-Response integration: looking for a common currency
5. Roel Smolders: WP 2.2-Case study on Pb in blood-Europe
6. Tek-Ang Lim: WP 2.3-Environment and Health information system in France
7. Miguel Borras: Eco-toxicology–use for investigating interaction of stressors for integrated risk assessment -Spain
8. Miguel Borras:Environmental Exposure and Ecosurveillance
9. Milena Cerma: Monitoring of organohalogens body burdens of the Czech population
10. Radim Sram: Exposure to c-PAHs case studies
11. Nadine Frery: Environmental data and Human biomonitoring in France
12. Greet Schoeters: The concept of integrated monitoring in the Flemish Environmental Health Survey (FLESH) 2002 – 2006 - 2011
13. Milena Cerna: Integrated monitoring – vision or reality?
14. Radim Sram: The impact of air pollution to human health-Czech Experience
15. Maria Dusinska: Occupational exposure monitoring; Approach used in FIBRETOX
16. Clive Sabel: WP 4.2-INTARESE toolbox guidance

INTARESE Project:
SP2 Tromsø 2.-5.6.2008

Workshop: Integrated monitoring

The way forward

Alena Bartonova
NILU

Outline

1. Intarese Method
   - Frameworks
2. Integrated Monitoring
   - Aims
3. This workshop

INTARESE

The INTARESE Challenge

The aim:

- To develop, test and apply a methodology for integrated health and environment impact assessment, in order to support policy in the EU (assesments for policy, of policy)

The challenge:

- Dealing with complexity
- Dealing with uncertainty
- Lack of monitoring data
- Research and knowledge gaps
- Lack of consistent and effective tools and methods
- Inadequate or poorly specified indicators

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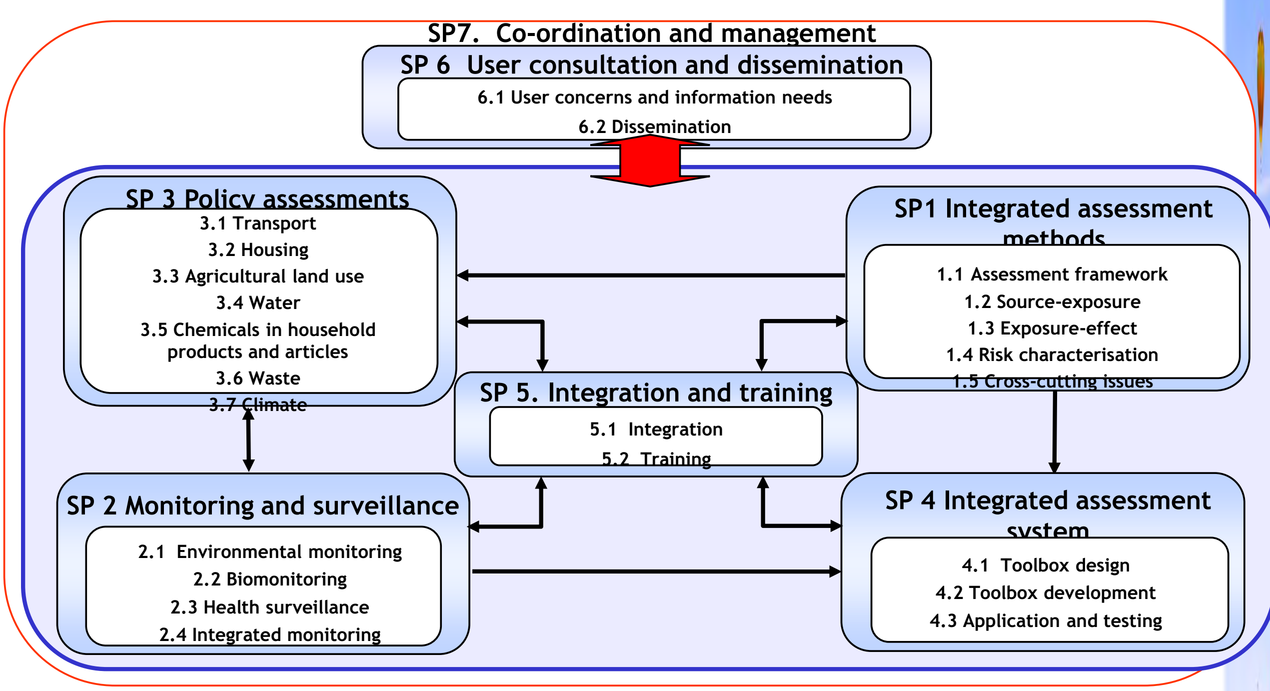
Sub-projects and Work Packages



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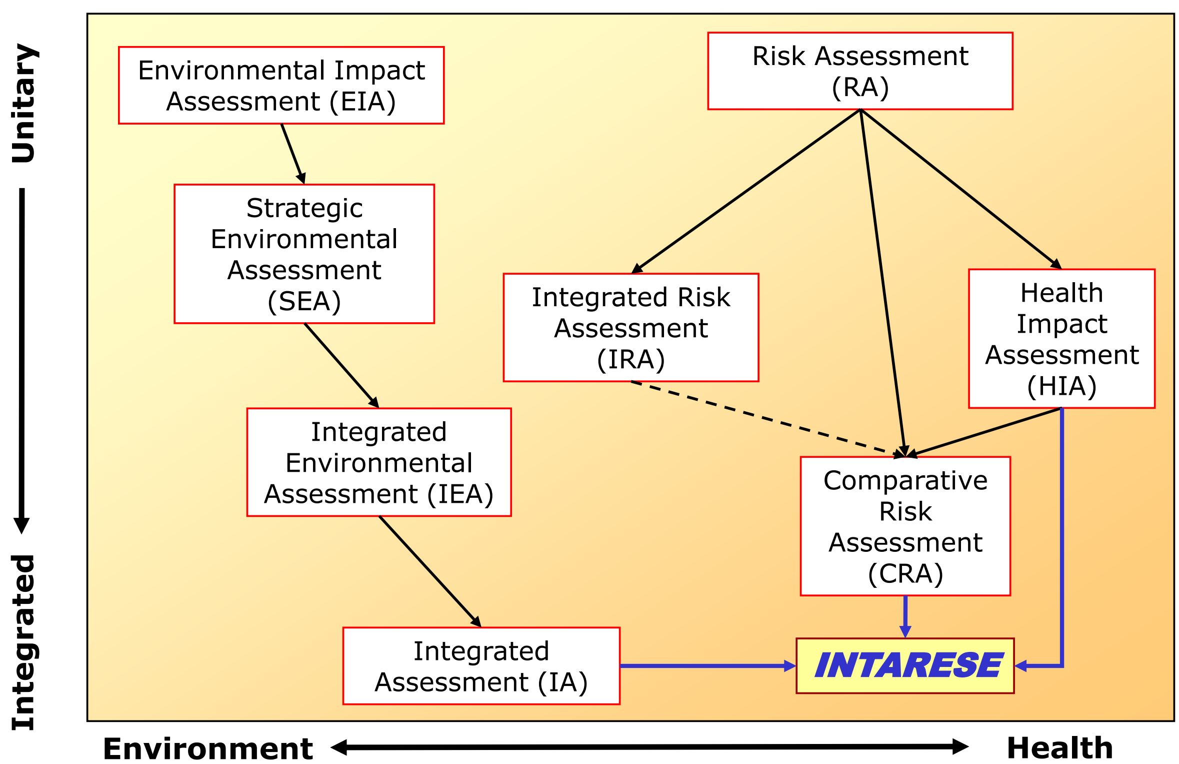
Implications for assessment

1. Complexity
   - Long chains of causality
   - Many-to-many relationships
2. Open systems
   - Poorly defined boundaries
   - Contextualised – including living/social environments
3. Scale-transcendent
   - Local – regional – inter-regional - global
   - Acute – chronic – lifelong – intergenerational

INTARESE

What type of assessment?

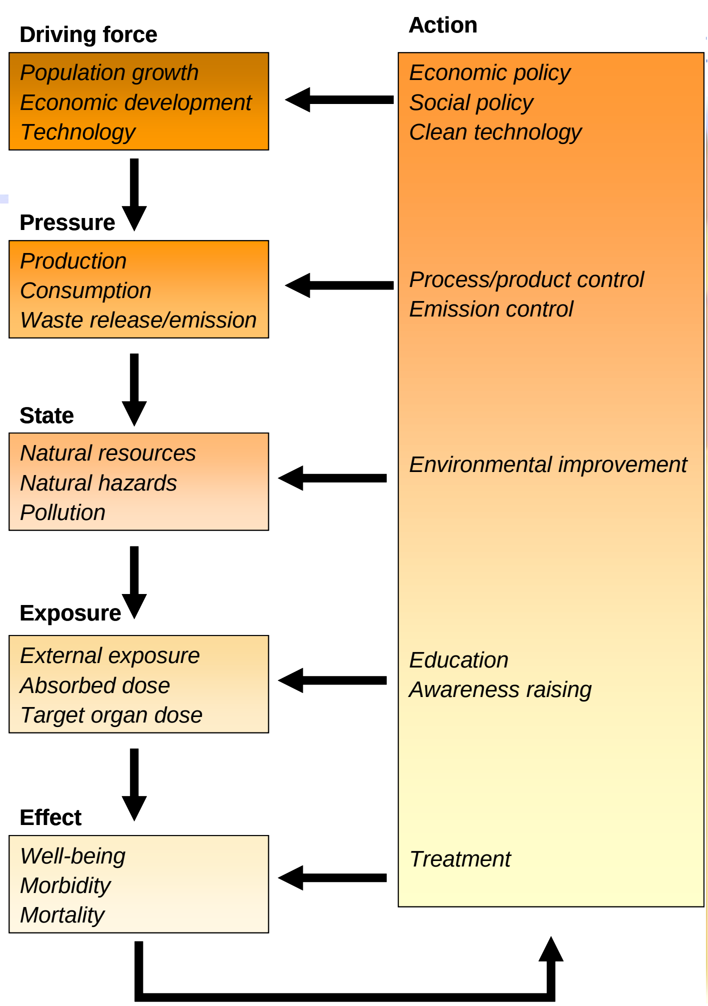
3. The genealogy of INTARESE



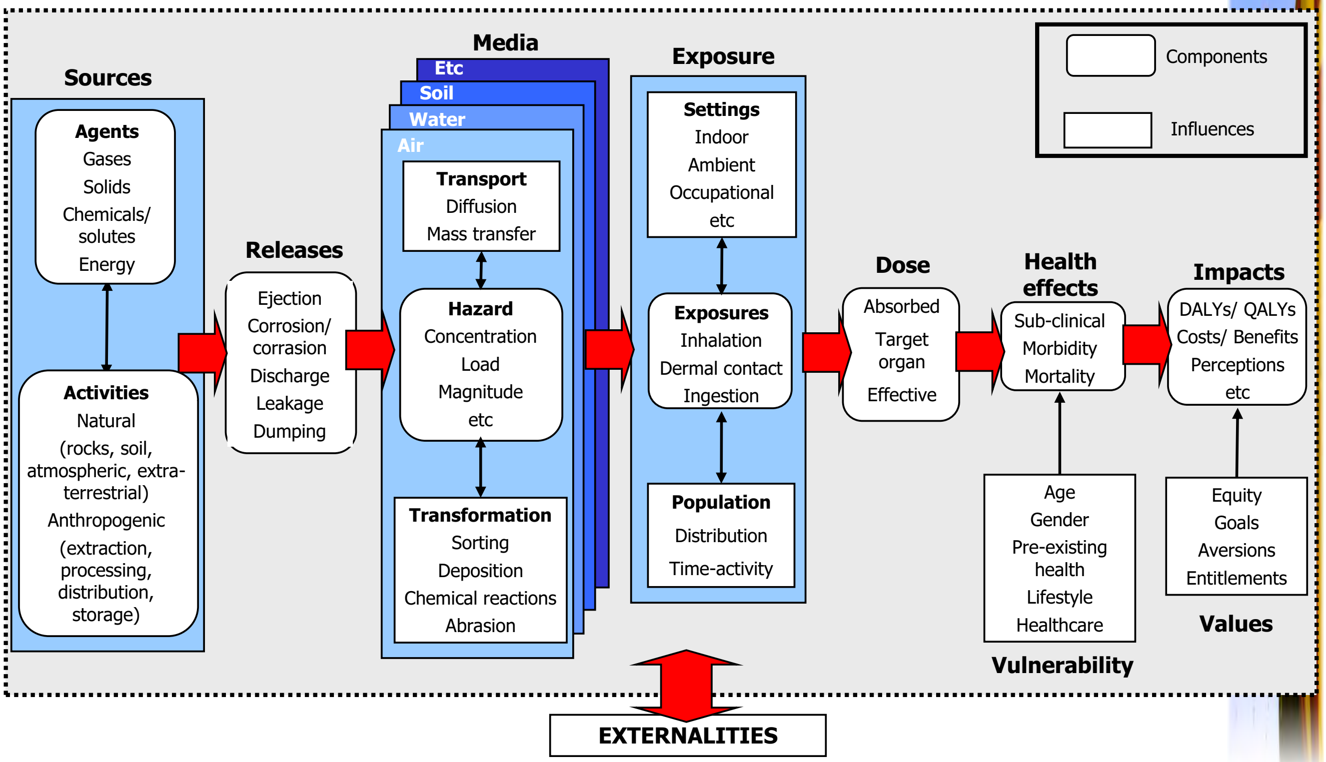
Conceptual framework

1. Why do we need a framework?
   - To reduce the limitations and ambiguity of words
   - To provide a visual means of representation
   - To emphasise the systemic nature of assessment
2. Key characteristics
   - Clarity – simple and understandable
   - Comprehensive – does not omit important factors
   - Flexibility – equally applicable to different issues
   - Balanced – does not bias assessments towards specific type of problem or specific interests
   - Realistic – reflects real-world structures and relationships

The DPSEEA framework

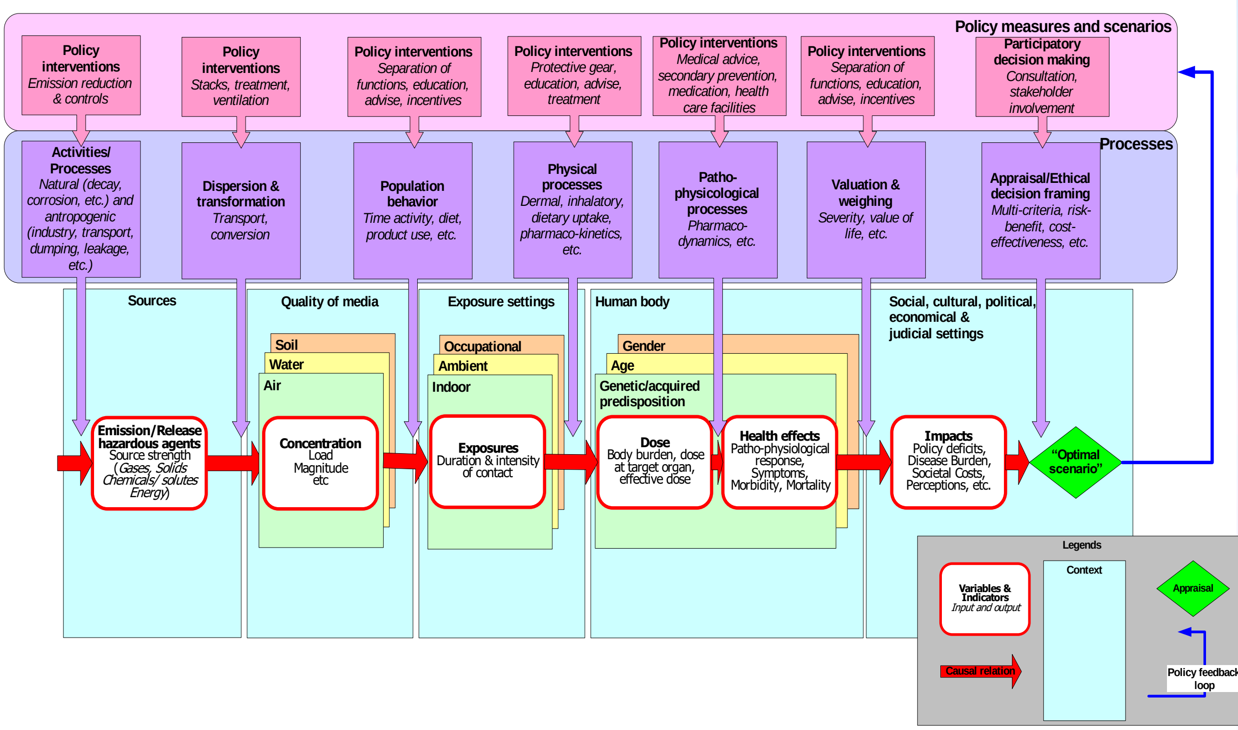


The conceptual framework: mark 1

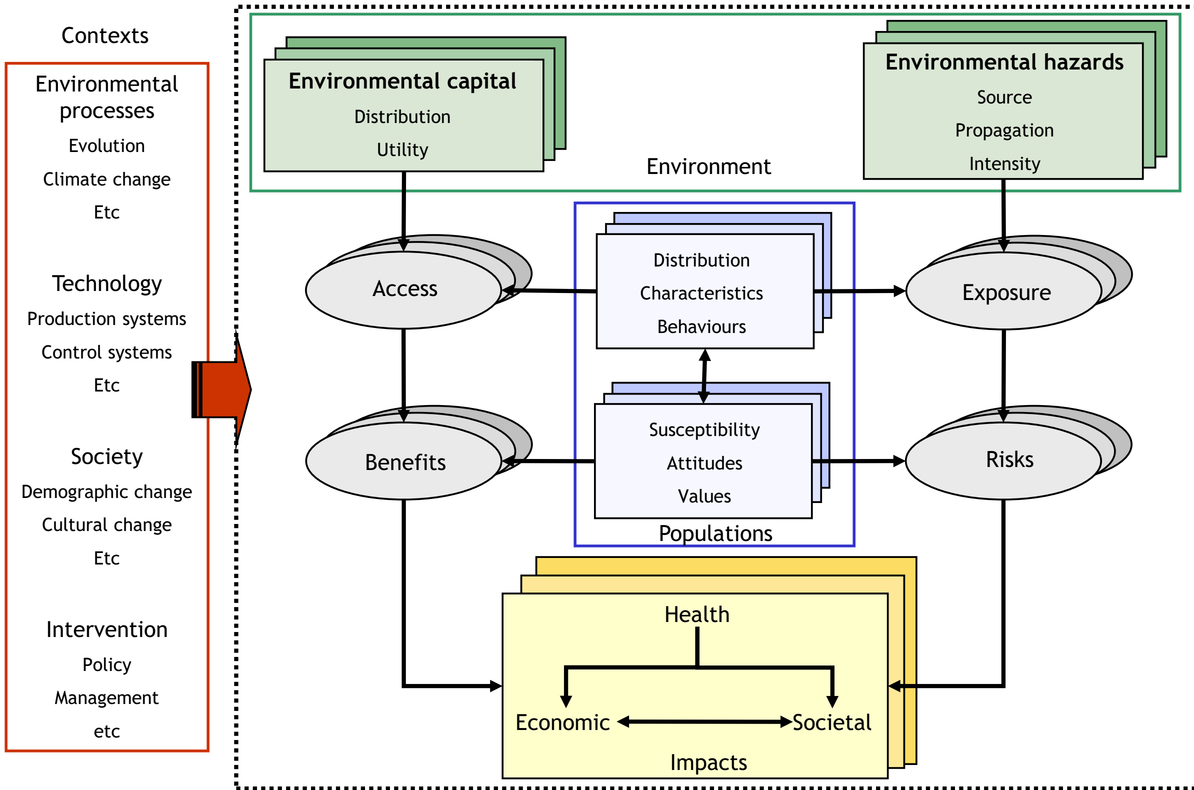


INTARESE

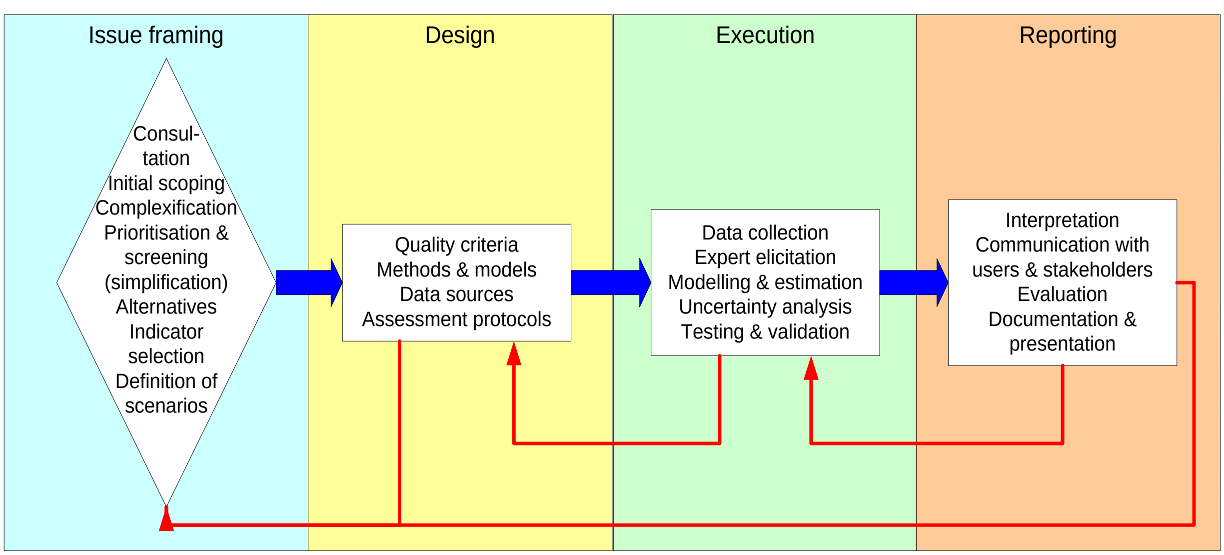
The conceptual framework: mark 2



The conceptual framework: mark 3



The analytical framework



Integrated monitoring
Specific objective 10

INTARESE

Aim: To assess the capability, and where appropriate develop methods, to combine various monitoring and analysis systems into an integrated monitoring system, covering different envrionmental, agents, media and pathways, and different population groups

Tasks:

- Define and develop tools needed to improve links between, and the balance and onteroperability of, existing monitoring systems in order to add value to the data they provide
- Expolore opportunities to establish ingtegrated monitoring systemns
- and to demonstrate capability in a range of specific areas

Integrated monitoring
Plan M25-42

INTARESE

1. Review of existing E&H monitoring systems (M30, D51)
2. Analysis of SP2&SP3 results (M36)
3. Identification of development needs for IM (M42)
4. Worskop (M33) and report (D64 –M36)
5. Preparation of scoping document for Integrated Environment and Health Monitoring for IEHAM (M42, D64.1)

Workshop aims

To address the issues of monitoring for the purposes of integrated environmental health impact assessment, to provide basis for further INTARESE project work towards the objective to give guidance on integrated monitoring.

Specifically, we would like to

- Identify the commonly experienced methodological and practical issues encountered in integrated environmental HIA
- Specify activities to be performed in SP2 and WP2.4 that would lead to providing the guidance.

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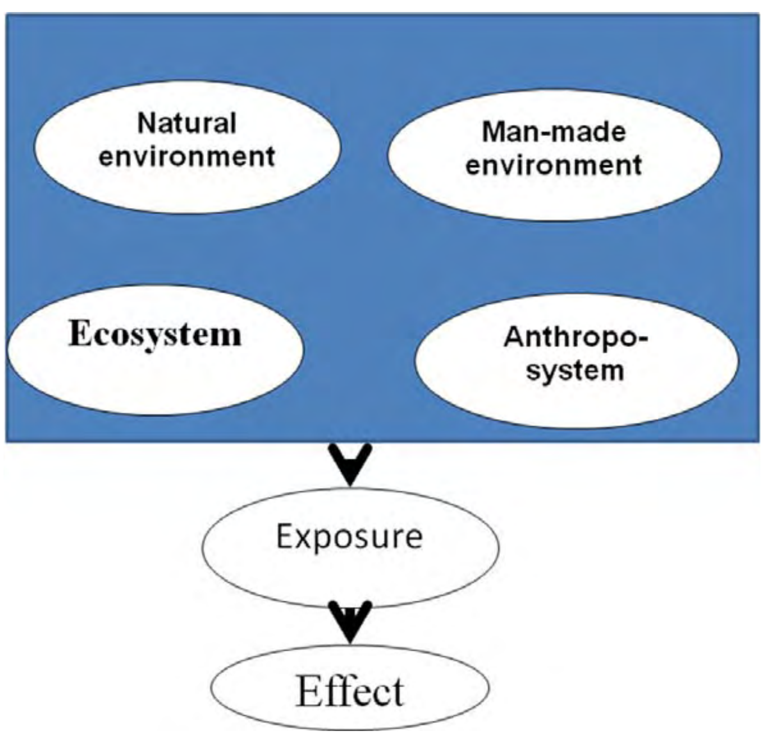
Integrated monitoring



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Information needs exposure

Scoping items

1. Associated health effect
2. Exposure metrics for health impact assessment
3. Time scale and step
4. Geographical scale and resolution
5. Population

Agent-related items

1. Agent
2. Source/activity
3. Release media
4. Route of exposure
5. Contact media
6. Contact duration/frequency

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Presentations

1. Hai-Ying Liu: Integrated monitoring
2. Lars-Otto Reiersen: The AMAP program (to be confirmed)
3. Nadine Frery: Experience from France
4. Greet Schoeters: Integrated Monitoring Approaches in Flanders
5. Miquel Borras: Environmental exposure and ecosurveillance
6. Milena Cerna: The Czech Environmental Health Monitoring Program
7. Radim Sram: The Teplice program
8. Maria Dusinska: Integrating information: the Fibretox project
9. Roel Smolders: Exposure-Dose-Response integration: looking for common currency
10. Tek-Ang Lim: Environment and Health information system in France
11. Clive Sabel: INTARESE toolbox

INTARESE

Workshop sessions

1. Presentations
2. Break out sessions I:
   - Definition (frameworks), criteria, methods
3. Break out sessions II:
   - Criteria, methods, the role of case studies
4. Plan for WP2.4: Now and M36-52
5. WP2.1-2.3 planning meetings
6. PSG meeting

INTARESE

Thank you for your attention!

Enjoy the workshop!

WP 2.4 Integrated Monitoring

Hai-Ying Liu, Alena Bartonova & Maria Dusinska

Norwegian Institute for Air Research - NILU
3 June 2008

Outline

- Report summary
- Framework
- Work plan

What is integrated monitoring?

- No clear definition
- In INTARESE, integrated monitoring for E & H impact assessment:
  - Develop definition
  - Review, develop and test methods
  - Recommendations

What is integrated monitoring (cont.)?

- In INTARESE,
  - the simultaneous measurement of physical, chemical and biological properties
  - of natural-man made environments, ecosystem and human system
  - across matrices from exposure to effect on human health
  - over both time and spatial scales
- Aim to provide a comprehensive, long term and systematic approach.

Why is integrated monitoring needed?

- Forms the backbone of integrated assessment.
- Enables the best use of monitoring and surveillance data for integrated environmental health assessment.
- Brings together different sources of existing information and information systems regarding a certain issue.
- Helps generate synergy between information and data.

How to do integrated monitoring?

- Review existing and planned integrated E & H monitoring programs
- Assessment of structure/design currently used in existing and planned integrated E & H monitoring programs
- Analysis of results of SP 1 (integrated assessment methods), SP 2 (monitoring and surveillance) and SP 3 (policy assessment) to date
- Identification of development needs
  - Key gaps in existing monitoring databases
  - Key gaps in existing monitoring and analytical capacities

How to do integrated monitoring (cont.)?

- State of art methods
  - GIS
  - Appropriate statistical methodologies
  - Mechanistic exposure-dose-response relationships
  - …
- Case studies (based on WP 2.1-2.3, additional)

  Test an "optimal" system considering the key gaps identified previously for monitoring and modeling in case studies.
  - Prague
  - Spain
  - …

Tentative results (I)

- Reviewed and assessed seven existing and planned integrated E & H monitoring programs
  - AMAP-Arctic Monitoring and Assessment Programme
  - ENHIS–European Environment and Health Information System
  - EHMSCR–The Environmental Health Monitoring System in the Czech Republic
  - GerES–German Environmental Survey
  - KiGGS–The German Health Interview and Examination Survey for Children and Adolescents
  - ONERC National Observatory of Climate Change Impact
  - PCB Monitoring and Assessment Projects in Slovakia
- Other integrated monitoring programs ?
  - INSPIRE-Infrastructure for Spatial Information in Europe
  - GEOSS-The Global Earth Observation System of Systems

Tentative results (II)

- Assessed three frameworks/strategies currently used in existing and planned integrated monitoring programs
  - DPSIR (Driving Force - Pressure - State - Impact - Response Framework) - EEA
  - DPSEEA (Driving Force - Pressure - State - Exposure – Effects – Action) -WHO
  - INTARESE full chain approach

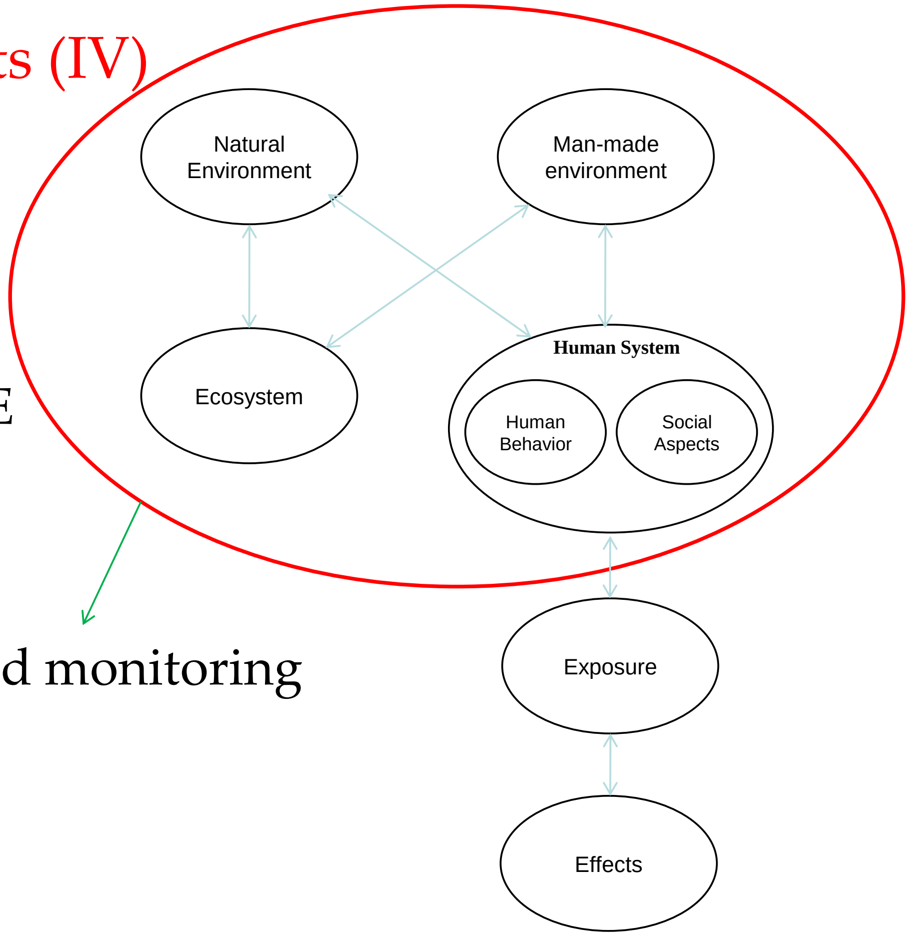
- Are there other frameworks?

Tentative results (III)

- Defined several gaps in existing monitoring programs
  - Narrow focus
  - Short-term
  - Different measurement protocols and sampling designs
  - Integration of monitoring indicators
  - Methods for control and qualification of uncertainties
  - GIS and statistical modeling techniques

Tentative results (IV)

- Possible integrated monitoring framework in E & H impact assessment



Tentative results (IV, cont.) What will be monitored?

- Not a single component, but a spatial-temporal process from sources to exposure to health effects (eco-anthropo-system)
- Pollution (e.g. source, process, concentration level etc.)
  - Terrestrial
  - Aquatic
  - Atmospheric
- Exposure – contact between an agent and a target
  - Exposure pathways – the course an agent takes from the sources to the targets (e.g. via air, soil, water, food, consumer products, etc.)
  - Exposure routes – the way an agent enters a target after contact (e.g. by ingestion, inhalation, or dermal absorption)
  - Exposure factors (e.g. time-activity levels, population characteritics, social determinants)
- Human health
  - Human dose
  - Health effects mechanism

To be continued (2008)

- An initial scoping document for an integrated monitoring and surveillance approach. End of June
- Paper on WP 2.4 approaches to Integrated Monitoring for Environment and Health Impact Assessment. End of July
- Case studies. Month 38, end of December
- Draft input to the toolbox. Month 39, end of December/beginning of January 2009

Task	Task Item	Month																		Resources (%)
		25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	
1	Review of currently existing E&H monitoring systems																			0.6
2	Analysis of SP2&SP3 results to date																			0.6
3	Identification of development needs for integrated monitoring, overview																			1.2
4	Workshop on "Integrated monitoring"																			0.4
5	Preparation of scoping document for Integrated E&H monitoring for health impact assessment																			1.2

Discussion points

- Concept and definition (Slides 3 and 4, page 6)
- Framework (Slide 11, pages 11-12)
- Case studies (Slide 7, page 6)

Conclusions

- This is not so much a conclusive work, but rather as a starting point to trigger further discussion
- This may eventually lead to defining a structured research agenda for integrated monitoring in E & H impact assessment

➢ Any suggestion and question?

WP2.2 meeting
Biomonitoring in the INTARESE concept of interated risk assessment

Tromso

June 2, 2008

Plans for the next 18 mths

Mth 25-42

- Task 1: Development and testing of new methods to apply biomonitoring data in the context of integrated risk assessment: development of case studies-

Partners : IC-(5); GSF (4);UCL (4);IEM (2);VITO (4);RB-SMU (4.5);INvS(1);BSP(3)

- Task 2:Improve coôperation with WP2.1 and WP2.3 particularly in the context of anticipated activities in WP2.4

Partners: Nilu (2.5);

- Task 3:Continue interaction with SP4 on HBM fact sheets

Partners : VITO (3)

- Task 4: Continue and finalise the work as was agreed at the Copenagen meeting

Partners: KI (1);VITO (1)

Deliverables:

- Mth 24: Overview of biomarkers submitted
- Mth 28: publication on applicability of new technologies “omics” in human biomonitoring (IC, P. Vineis)
- Mth 28: publication on the applicability of non-invasive matrices for human biomonitoring (GSF. K.W. Schramm)- draft available
- Mth 30: Quality criteria for biomarkers and biomarker databases (IC: P. Vineis & UCL: A. Bernard)

Case studies - use of human biomonitoring for risk assessment

- Lead – VITO: R. Smolders & G. Schoeters
- PAHs - IEM : R. Sram
- PCBs-RB-SMU : T. Trovnec

Deliverables

- Mth 30 Draft : overview of case studies
- Mth 36: Draft: linking biomonitoring data to environment and health data
- Mth 42: final report on case studies

Milestones and expected results:

- Mth 30: collated data base for HBM data for PCbs, PAHs and lead
- Mth 36: Finalised reviews
- Mth 42: final report on case studies

Exposure-dose-response integration: looking for a common currency

Roel Smolders

Environmental Toxicology

VITO, Belgium

Exposure-dose-response

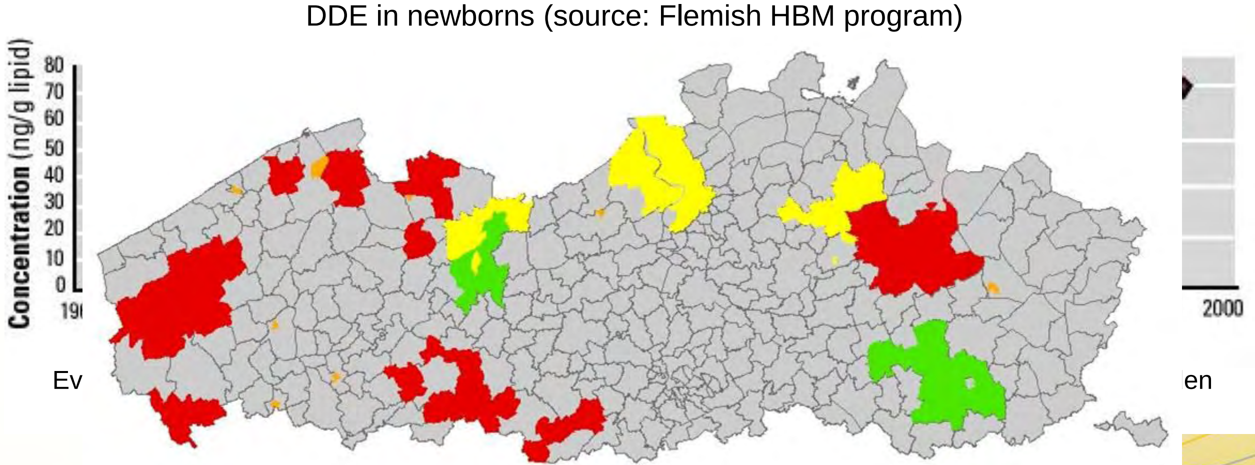
"The ability to generate new biomonitoring data often exceeds the ability to evaluate whether and how a chemical measured in an individual or population may cause a health risk or to evaluate its sources and pathways of exposure"

(NRC, 2006)

Exposure-dose-response

Changes in time/space

DDE in newborns (source: Flemish HBM program)

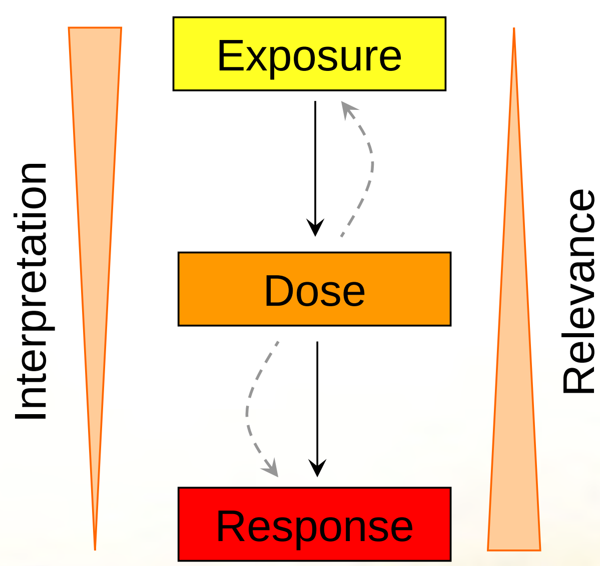


- More than 10% of population above reference P90
- Significantly higher than reference mean
- Not significantly different from reference mean
- Significantly lower than reference mean

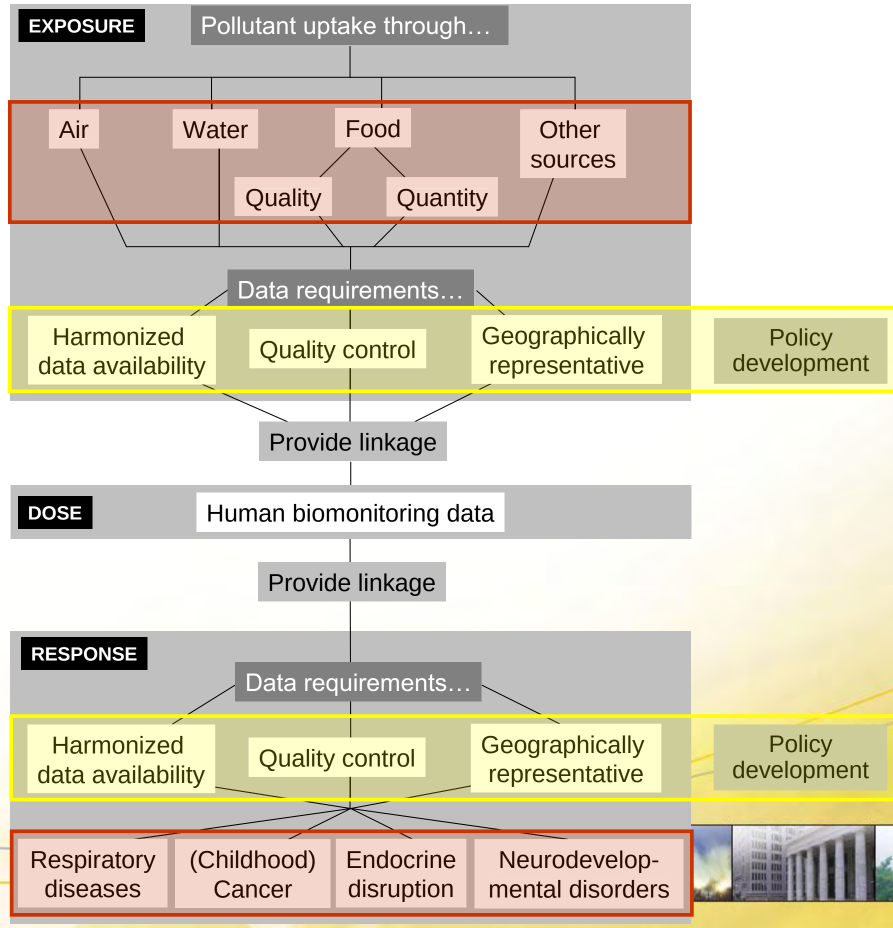
Exposure-dose-response

- Presence of a chemical ≠ risk
- Policy implementation
  - Identify sources
  - Health effects
  - Evaluate actions
- Integrated monitoring !!!

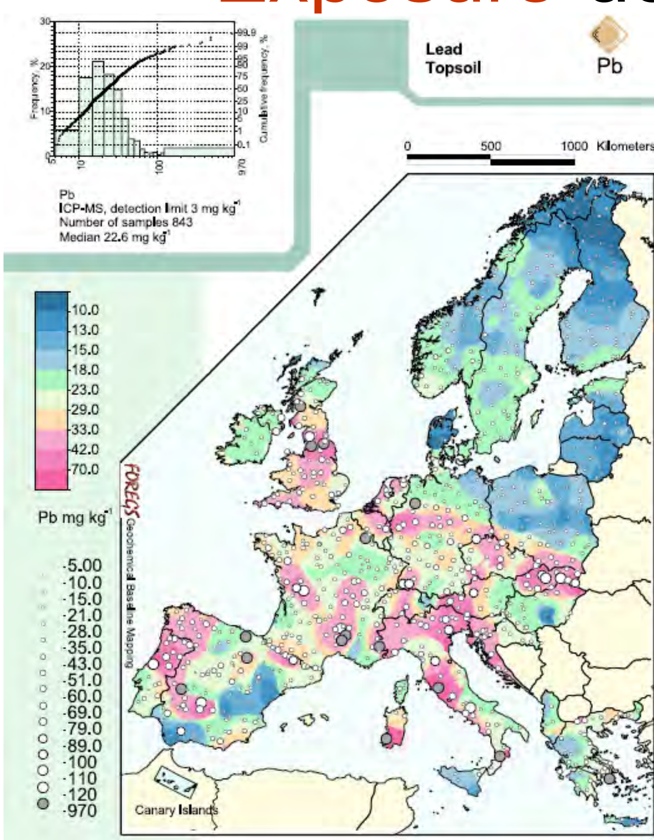
Exposure-dose-response

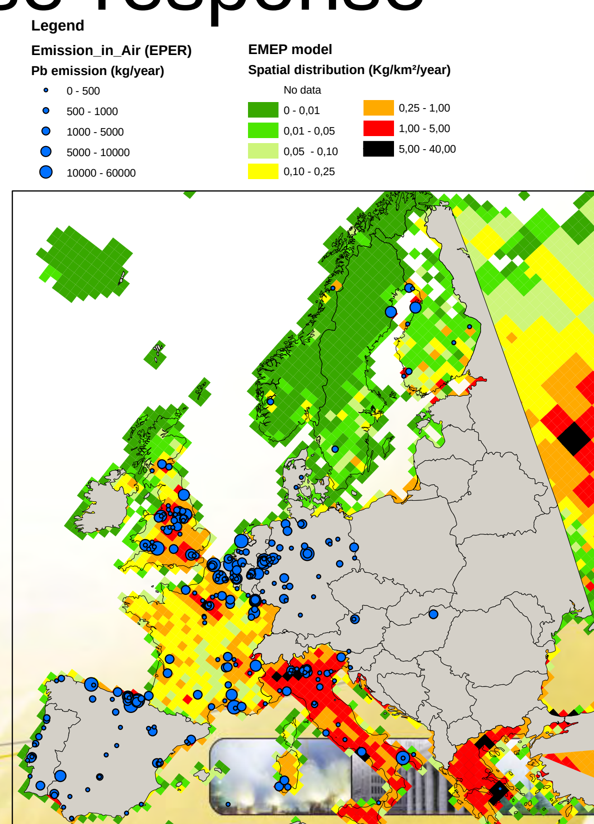


- Trade-off between ease-of-interpretation and relevance to human health issues
- Dose (biomonitoring data) is the central pivotal point
- Middle-out approach offers best possibilities for linking exposure-dose-response data
- Data availability in Europe ?



Exposure-dose-response





Exposure-dose-response

Information on routes of exposure

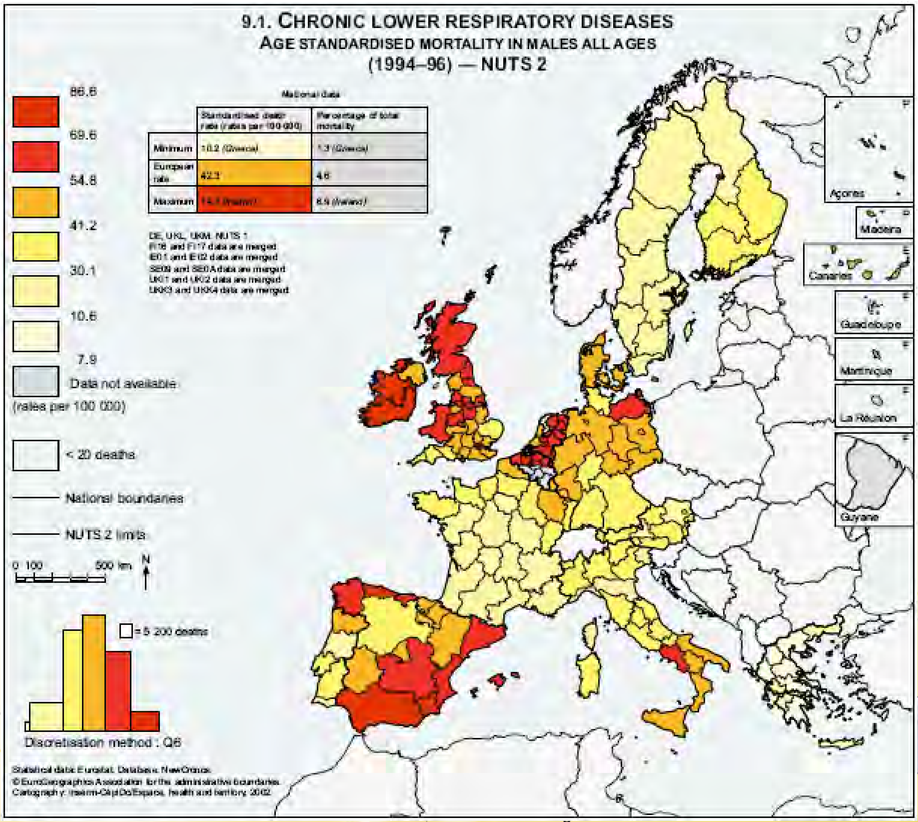
	Availability	Geographical context	Harmonization	Quality control	Policy developments
Air emission	☺	☺	☺	☺	☺
Air imission	☺	☺	☺	☺	☺
Water emission	☺	☺	☺	☺	☹
Water imission	😐	😐	😐	☺	☹
Food quality	😐	😐	☺	☺	😐
Food quantity	☺	☺	😐	😐	😐

Source: ESBIO Deliverable D3.1
(http://www.eu-humanbiomonitoring.org/doc/esbio_del_wp3.pdf)

Exposure-dose-response

- Already many activities ongoing
- Increased dynamics (E&H Action plan)
- European Pilot project on HBM
- INTARESE: case-studies on e.g. Pb

Exposure-dose-response



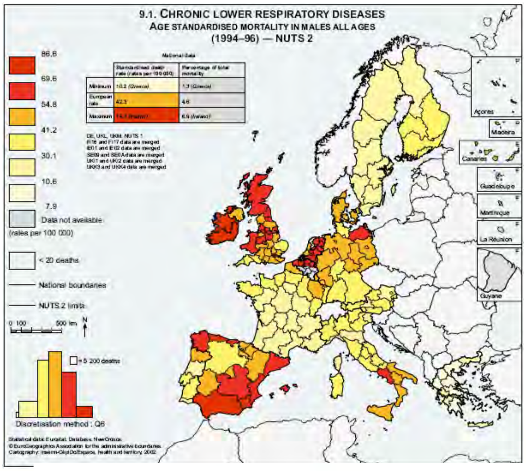
Exposure-dose-response

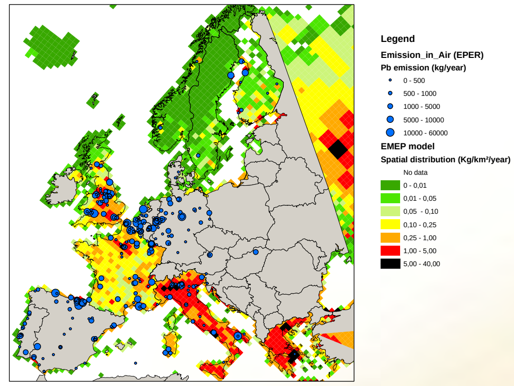
Information on health effects

	Availability	Geographical context	Harmonization	Quality control	Policy developments
Cancer (mortality)	☺	☺	☺	☺	☺
Cancer (incidence)	😐	😐	☺	😐	☺
Asthma	☺	😐	😐	☺	☺
Neurodevelopment	😐	☹	☹	☹	☺
Endocrine disruption	☹	☹	☹	☹	☺

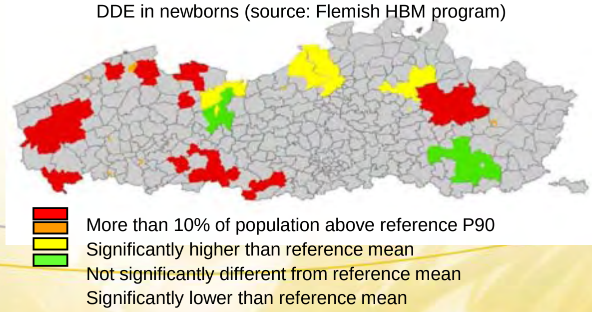
Source: ESBIO Deliverable D3.1
(http://www.eu-humanbiomonitoring.org/doc/esbio_del_wp3.pdf)

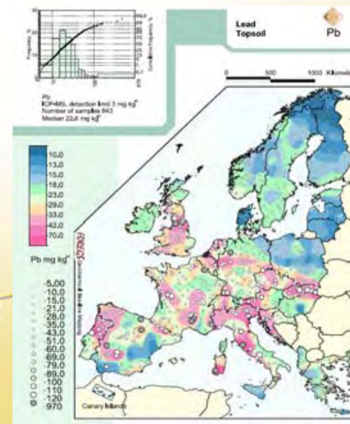
A common currency





DDE in newborns (source: Flemish HBM program)





A common currency

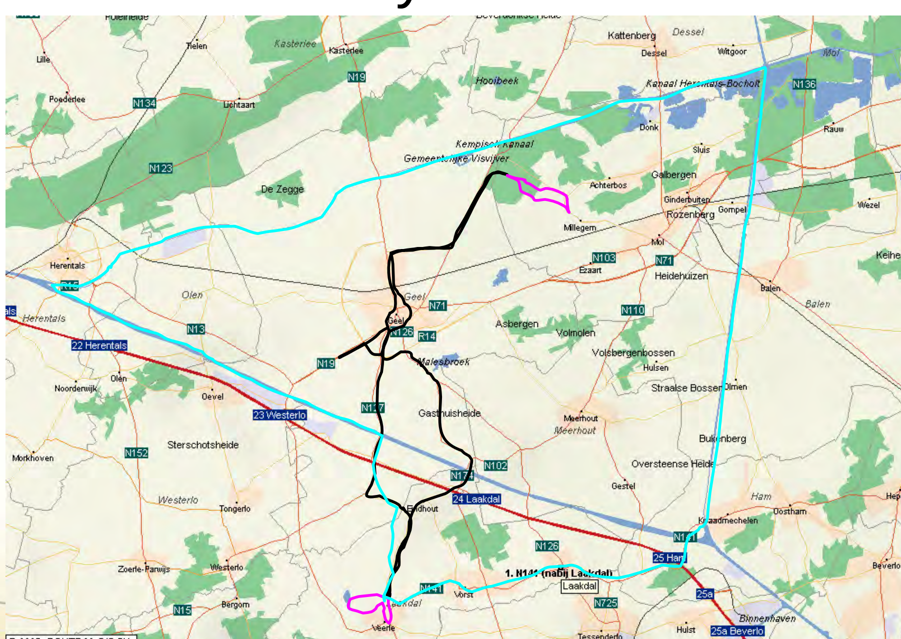
- GIS-based EDR platform
  - Opportunities for 'data-rich' substances
  - Incompatibilities among E&H databases require a degree of generalisation
  - Inter- and extrapolation
  - Spatial and temporal evolution
  - Links with research and policy making (INSPIRE directive)
  - Confounders of spatial analysis

Confounders for spatial analysis

- Micro-mobility
- Macro-mobility
- Non-spatial variability
- Privacy issues

Confounders for spatial analysis

- Micro-mobility



At home: 10 h
At work: 9 h
Outdoors: 4 h
Commuting: 1 h

Confounders for spatial analysis

- Micro-mobility

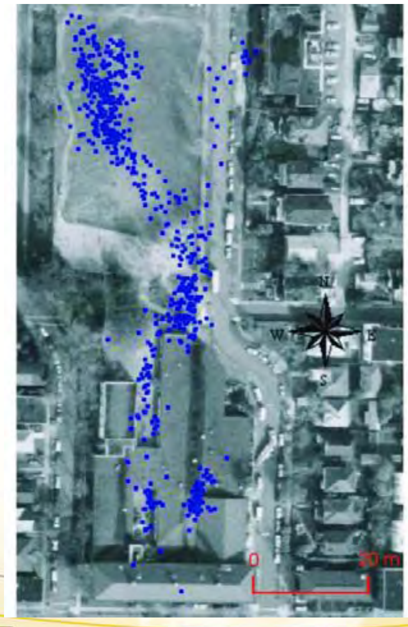


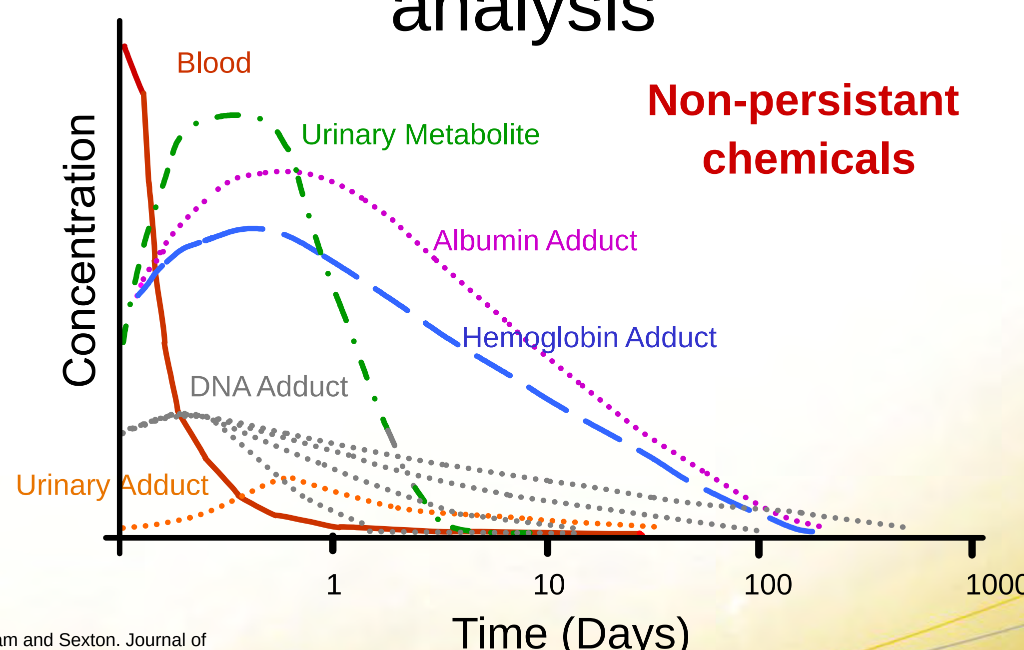
Table 6. Where children went: Fraction of monitored time (%) in each location and total monitored time for children wearing GPS-PAL units.

	Weekday		Weekend			
Location	Child 1	Child 2	Child 3	Child 4	Child 5	Child 6
Vehicle (inside)	4.8	15.0	9.7	21.4	19.0	0.0
School (inside)	52.7	80.4	0.0	0.0	0.0	0.0
Home (inside)[a]	5.8	4.6	52.5	0.0	0.0	83.4
Business (inside)[a]	0.0	0.0	37.8	78.6	81.0	0.0
Outdoors[b]	36.7	0.0	0.0	0.0	0.0	16.6
Monitored time (min)	513	480	468	416	387	700

[a]Stores, restaurants, cinemas, and other large buildings. [b]Parks, playgrounds, sidewalks, and yards.

Data taken from Elgethun et al 2003.
Environmental Health Perspectives 111:115-122

Confounders for spatial analysis

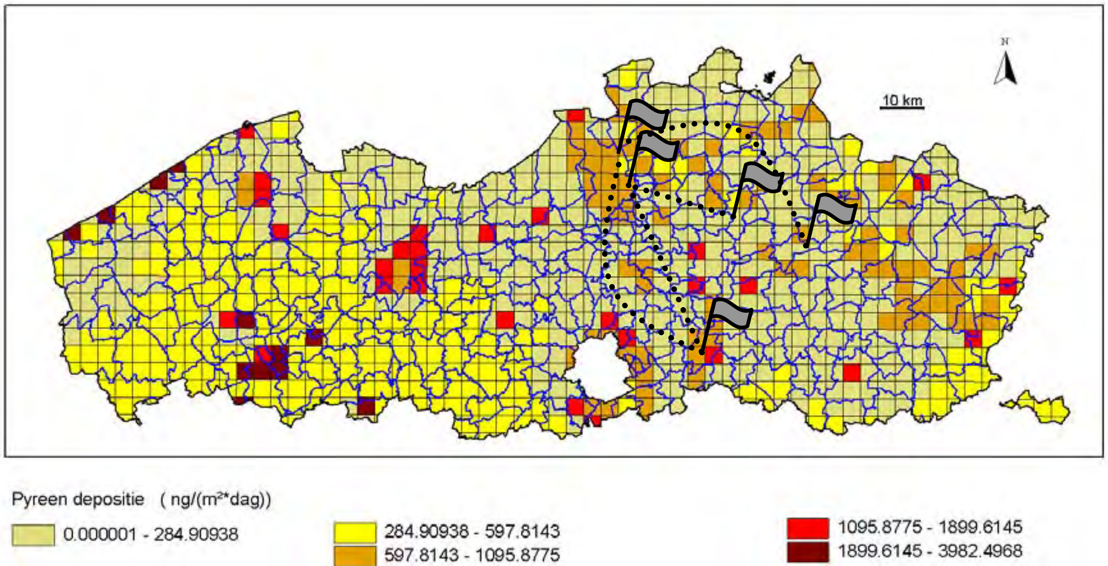


Non-persistant chemicals

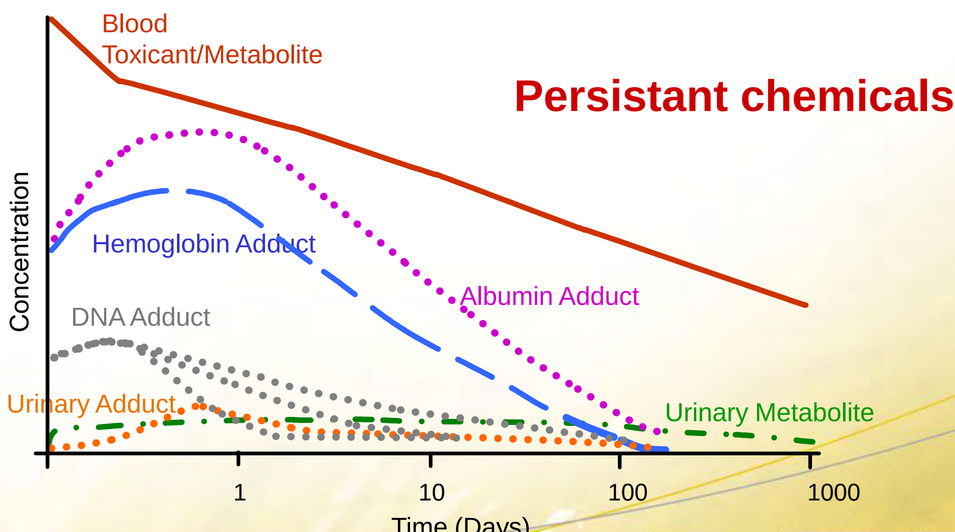
Needham and Sexton. Journal of Exposure Analysis and Environmental Epidemiology, 2000

Confounders for spatial analysis

- Macro-mobility



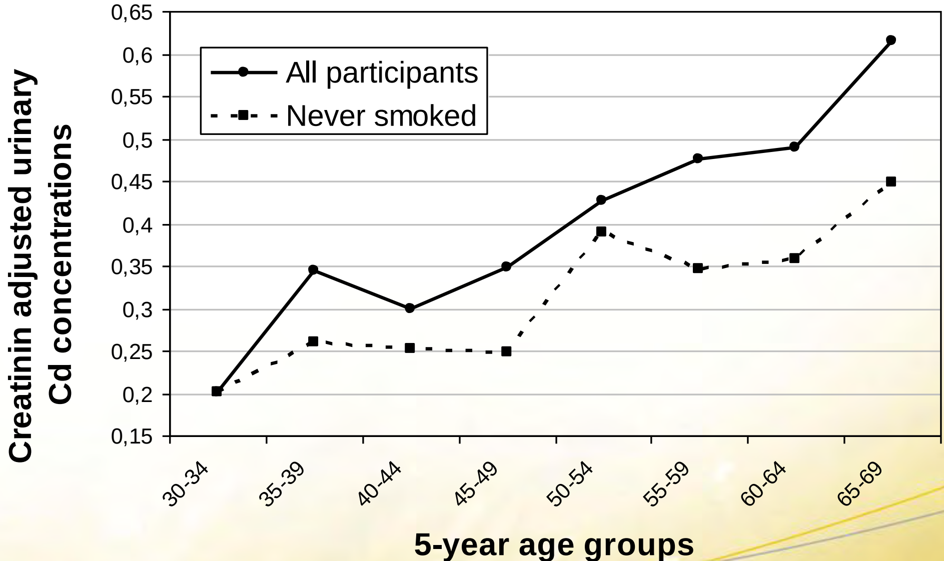
Confounders for spatial analysis



Needham and Sexton. Journal of Exposure Analysis and Environmental Epidemiology, 2000

Confounders for spatial analysis

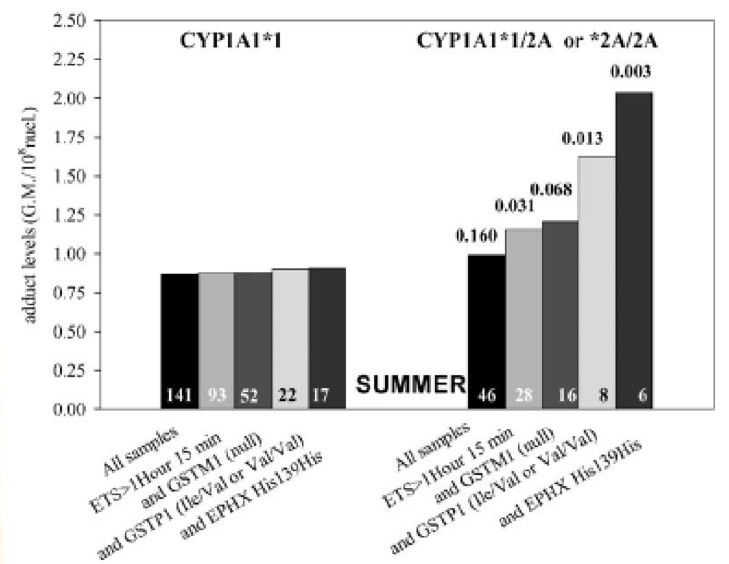
- Non-spatial variability



Redrawn from McEllroy et al. 2007
Science of the Total Environment 382: 214-223

Confounders for spatial analysis

- Non-spatial variability

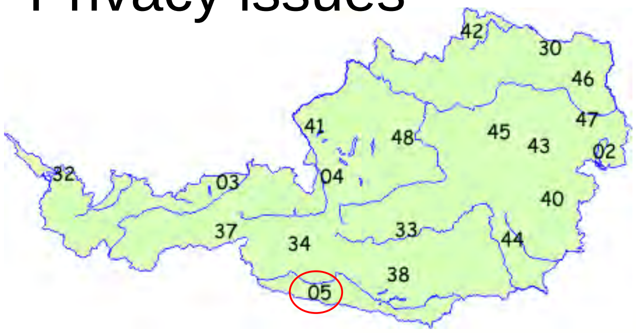


From Georgiadis et al. 2004
Toxicology Letters 149: 269-280

confidential – © 2006, VITO NV – all rights reserved

Confounders for spatial analysis

- Privacy issues



Measurement site:	**Vorhegg**	
Country:	Austria	
Code:	AT05	
Database code:	AT0005R	
Geographical coordinates:	46º 40'N, 12º 58'E	
EMEP coordinates (50 km):	109.75, 54.19	
Altitude above sea level:	1020	
In operation since:	January 1996	
Components	***Time res.***	***Period***
Air		
Ozone	1 h	1995->
SO_2, NO_2	24 h	1996->
Precipitation		
Precipitation amount	24 h	1997->
pH	24 h	1997->
SO_4, NO_3, NH_4, Cl	24 h	1997->
Na, K, Mg, Ca	24 h	1997->

Confounders for spatial analysis

- Privacy issues
  - No individual data
  - Some type of aggregation
    - Administrative (e.g. city, NUTS,…)
    - Topic related (e.g. distance from source)
    - Land-use (urban, semi-urban, rural)
    - …
  - Flexibility needed (≠ spatial scales)
  - Ecologic studies

Conclusions

- HBM benefits from integrated monitoring
  - (integrated) risk assessment
  - Policy implementation
  - Evaluation of actions
- HBM may be central pivotal point
- Common currency needed
- GIS-based EDR-platform
- Confounders need to be resolved

Case-study on Pb in blood

Roel Smolders, Greet Schoeters

WP2.2

INTARESE Project

Aim of the case study

- Feasibility to collect data around Europe
- Evaluate comparability
- Link with E&H data
  - At a generic European level
  - More in detail comparing Flanders with Serbia (cooperation with WP2.1)

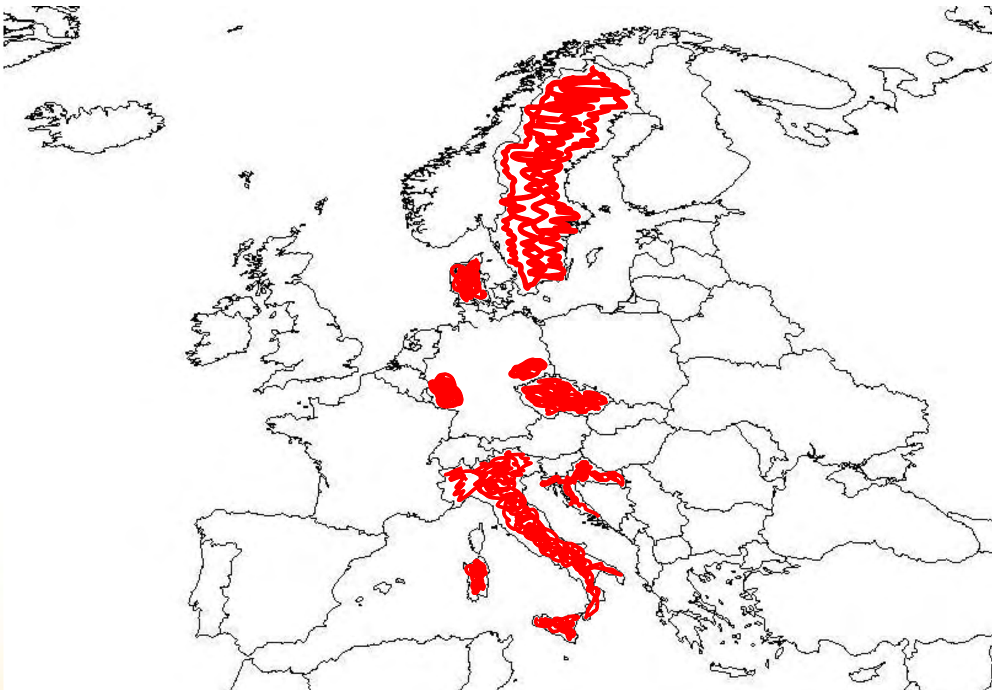
Identification of projects

- HBM database (www.hbm-inventory.org);
- ESBIO + INTARESE Members
- Peer-reviewed publications (web of knowledge)
  - Blood and biomonitoring and Pb (33 hits)
  - Blood and biomonitoring and lead (109 hits)
- Screening for relevance (Europe, survey,…)
- E-mail address available

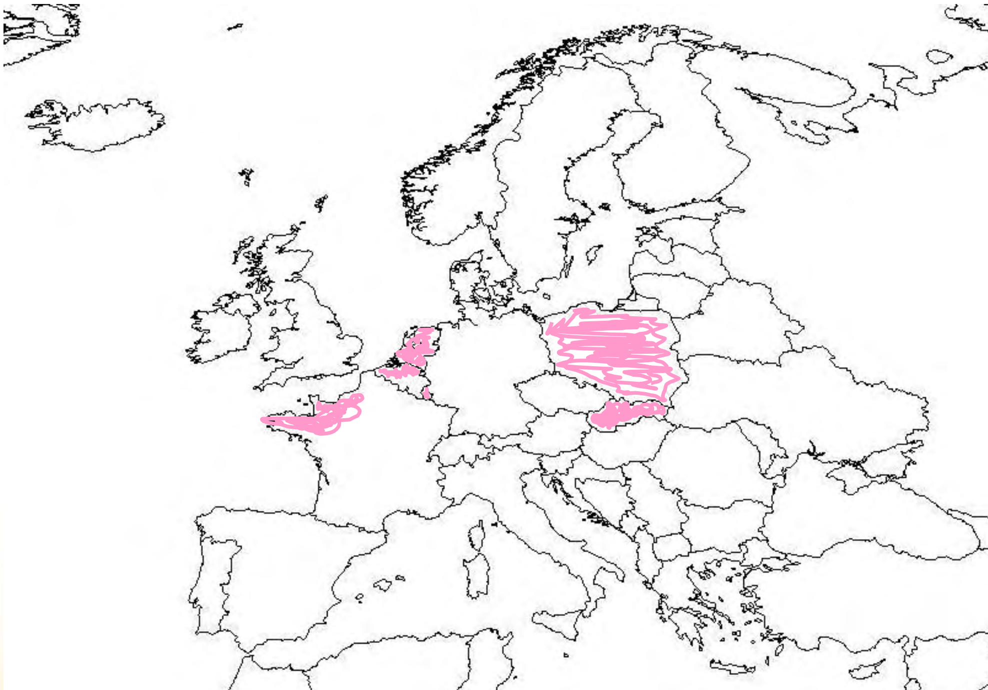
Data asked

- Raw data on lead in blood
- If unavailable, percentile data
- Limited meta-data
  - Age
  - Gender
  - Location of sampling
- All authors contacted twice, some more often

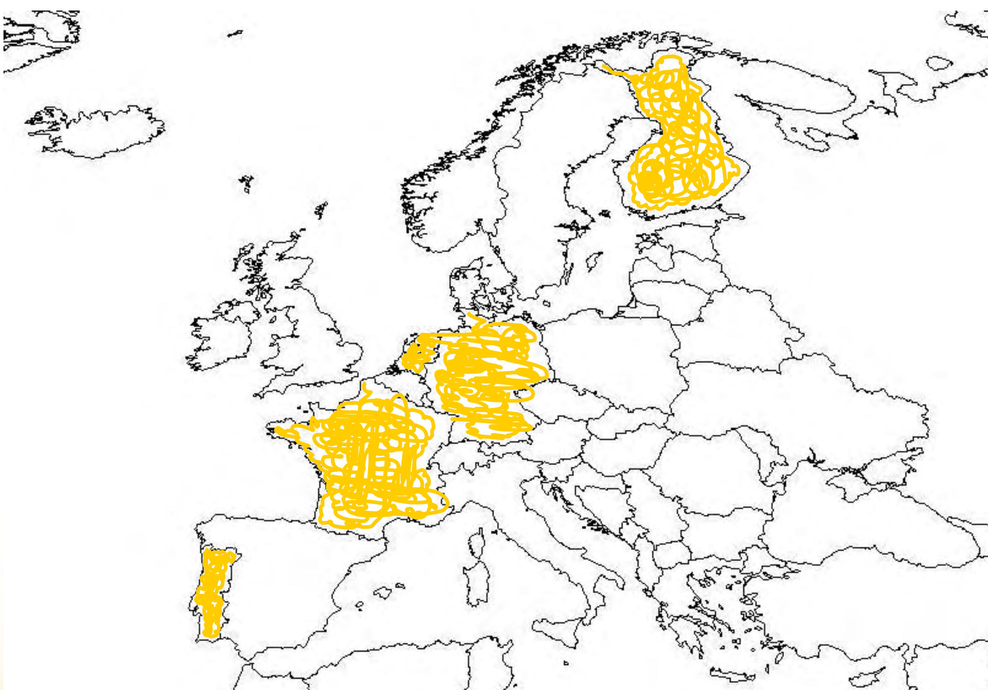
Results: Raw data received



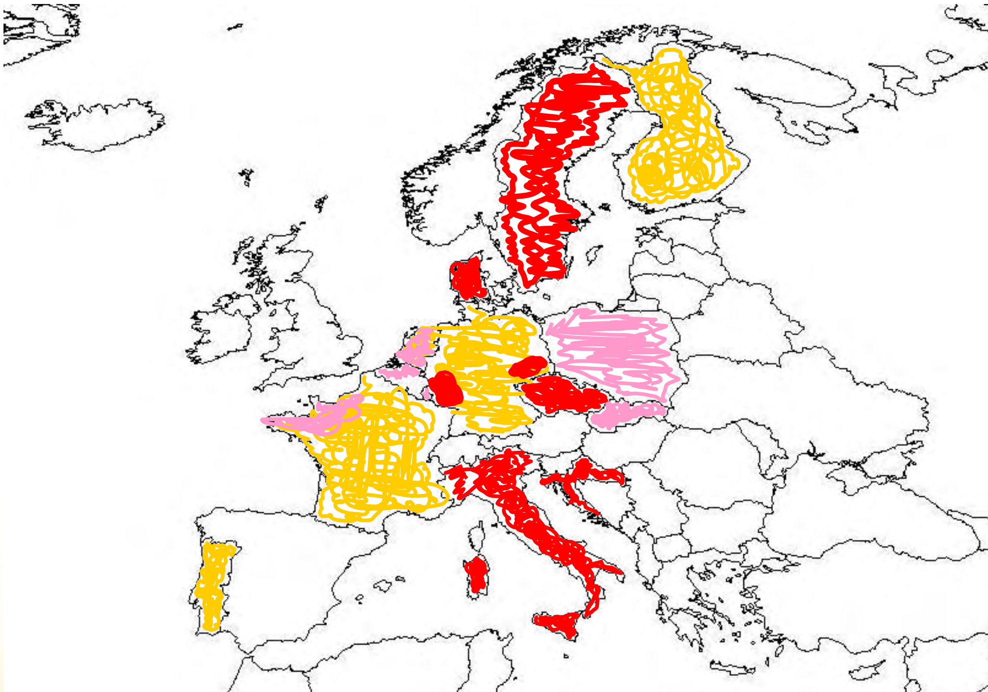
Results: (Raw) data expected



Results: Percentile data received



Results: Overall view



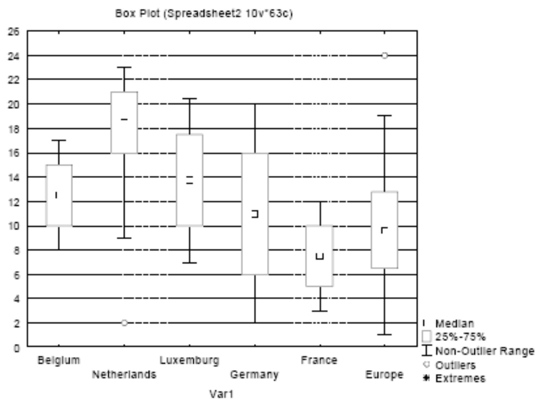
September 26, 2008

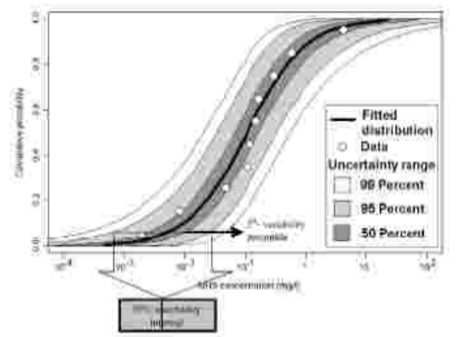
Results

Country	Gender	Sampling period	Age class	# data points
Croatia	Men	2002-2005	19-53	242
	Women	2004-2005	19-67	167
	Men	2004-2005	20-67	51
Sweden	Men	2003-2004	32-68	19
	Women	2003-2004	22-66	47
Czech Republic	Men	1996-2007	18-61	2837
	Women	1996-2007	18-58	1181
	Boys	1996-2007	6-13	905
	Girls	1996-2007	7-12	919
Italy	Men	2004	20-60	73
	Women	2004	25-58	36
Denmark	Men	1993-1994	31-77	103
	Women	1993-1994	30-75	86
Germany	Men	1987-1997		3332
	Women	1987-1997		7369

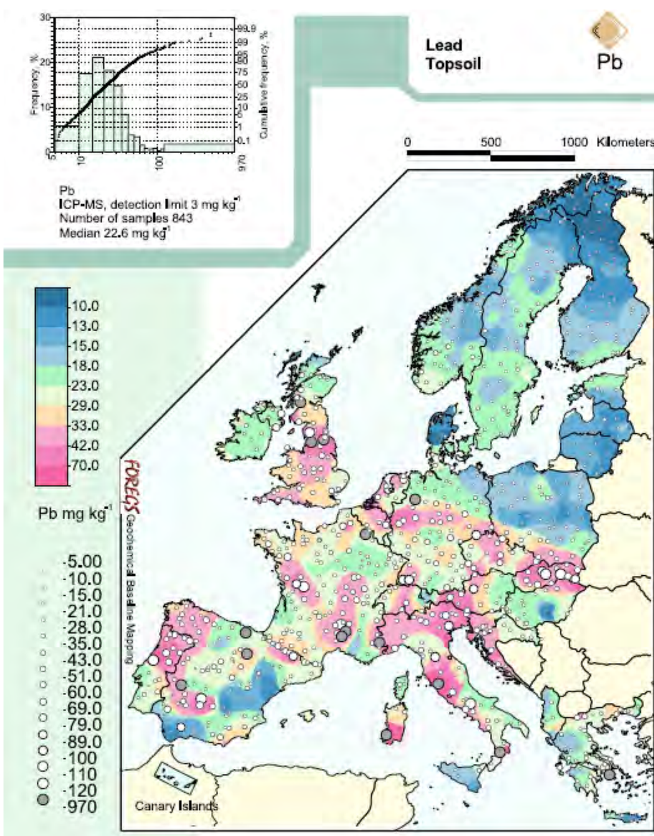
September 26, 2008

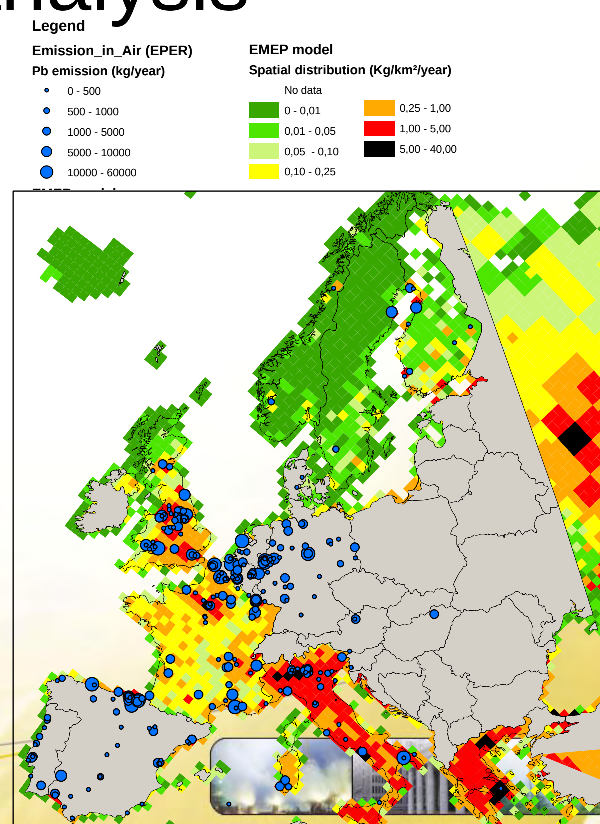
Future analysis





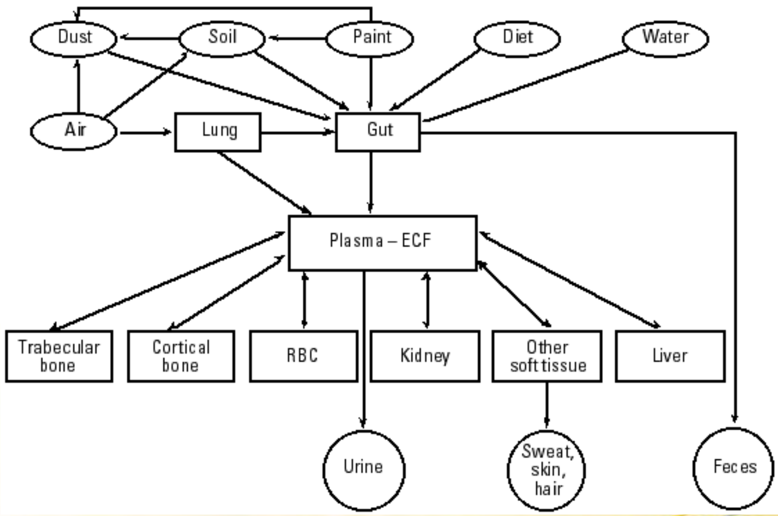
Future analysis





Future analysis

IEUBK Model: Integrated Exposure Uptake Biokinetic Model (?)



Environment & Health Information Systems in France

Tek-Ang LIM

SP2 Workshop
02-05 June 2008, Tromso Norway

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Environment & Health Information Systems in France

2004: Launching of the **French National Environment & Health Action Plan (PNSE)**

The PNSE includes **45 actions** aimed at achieving 3 major objectives**:**

- ✓ To ensure good quality for air and drinking water
- ✓ To prevent environmental exposure associated diseases, in particular cancers
- ✓To keep the population better informed and protect vulnerable groups (children and pregnant women)

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Priority Actions in order to Improve Sytems for Surveillance and Alert

- ✓ **Action 35 :** Improve the performance and integration of environmental health information systems.
  - ➢ current information might be inadequately used for the purpose of E&H risk assessments.

Work coordinated by AFSSET & IFEN

Contact: Jerome Lozach (AFSSET)

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Environment & Health Information Systems in France
PNSE Action 35 Description of works

Action 35 : Improve the performance and integration of environmental health information systems.

Works carried in two parts

- Inventory of Existing E&H datasets

- Surveys on linking data for the purpose of E&H risk assessments

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PNSE Action 35 Inventory of E&H datasets

Aim : provide a **clear idea** about **available data** and **improve information** to scientists and population

- Design of a questionnaire following the ISO 19115 standard on metadata

- Each questionnaire was filled and validated by the datasets manager

- Information on data collection, access, content of the DB, contact details, links to DB when possible

http://www.sante-environnement-travail.fr/liste.php3?id_mot=2886

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PNSE Action 35 Inventory of E&H datasets Results

- Too many DB in E&H (inventory not complete)
- Numerous actors gathering data in E&H
- Many information systems for the same environmental stressor (ex: water)
- Lack of metadata & geocoded data (esp health)
- Lack of quality indicators
- Limited access to health data (esp. at local level)

http://www.sante-environnement-travail.fr/liste.php3?id_mot=2886

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PNSE Action 35 Survey on Linking Data

Aim : Analyse feasibility of linking data from existing datasets on environment, health and population

- ✓ Data are commonly used for other purposes
- ✓ Essential tasks to process the data to meet our need for each study
- ✓ Very costly (time, money and work)

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Environment & Health Information Systems in France
PNSE Action 35 Survey on Linking Data Methodology

Survey carried by (face to face) **interviewing 19 research teams** who have (recently) performed **a HIA in E&H**

Their works were mainly about **assessing the health impacts** of an exposition **to environmental stressor at regional or local level**

- ✓ Identification and follow-up in time of individuals with medico-administrative DB
- ✓ Linkages of data from multiple sources

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PNSE Action 35 Survey on Linking Data Results

- ✓ Difficulty to identify main DB
- ✓ Difficulties commonly cited
  - lack of geocoded data & quality indicator
  - lack of metadata
  - lack of common identification in different DB
  - Disparities in time & geographical features

⇒ Important work carried before performing the analysis on the data (ad-hoc data building, harmonization of DB, assessment of missing data, etc.)

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Environment & Health Information Systems in France

PNSE Action 35 Survey on Linking Data Results

To overcome the difficulties

- ✓ Very strong assumptions
- ✓ Data extrapolation (time and geographical scale)
- ✓ Strong involvement of DB managers in the projects

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Environment & Health Information Systems in France

PNSE Action 35 Survey on Linking Data Recommendations

- ✓ Request for better identification of DB (definition of variables, track of changes in the variables, etc.)
- ✓ Need to capitalize work carried to process data (methodologies, new DB created from other sources of data, etc.)
- ✓ Better access to DB (very long and random administrative procedures)
- ✓ Adoption by DB managers of a minimum requirement in terms of time and geographical features to facilitate comparisons

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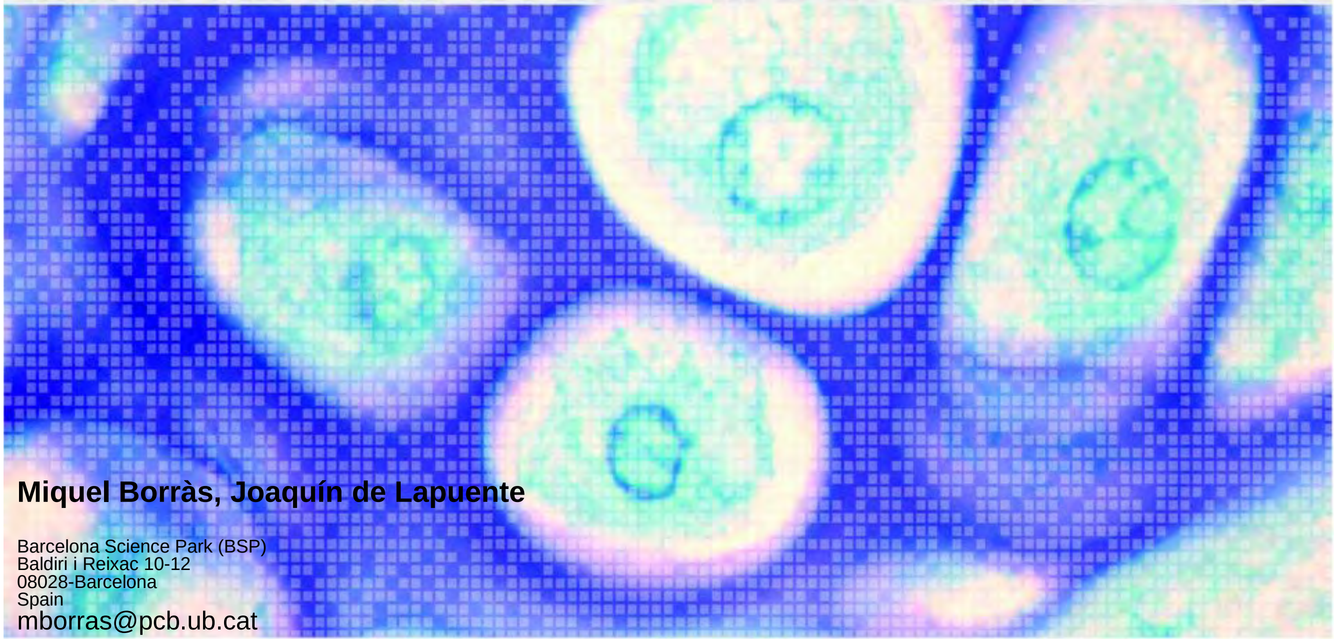
Centre de Recerca en Toxicologia

Eco-toxicology–use for investigating interaction of stressors for integrated risk assessment -Spain



Miquel Borràs, Joaquín de Lapuente

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Models

should be:
- ✓ comprehensive
- ✓ meaningful
- ✓ give insight on mechanisms

but, at the same time:
- ✓ quick
- ✓ cheap
- ✓ simple
- ✓ practical

realism + control = k

Models

- **quick answers to pressing questions**
  - laboratory tests
  - substitute species
  - conventional exposure

- **trying to be realistic**
  - field studies
  - native species
  - sentinels + biomarkers

Models

transactional approaches
- mesocosms
- lab animals in the wild
- wild animals in the lab

Animals as prospectors and integrators of environmental information

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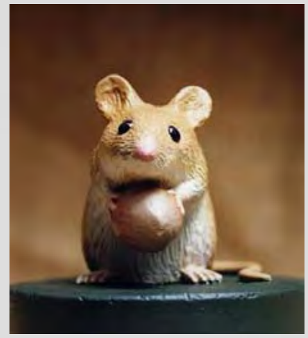
Animals

- prospect the environment
- take into account homeostasis
  (of the organism and of the environment)
- integrate information
  - ✓ spatial
  - ✓ temporal



Characteristics of Sentinel species:

- tolerate and accumulate pollutants
- ubiquitous
- frequent
- sedentary
- relatively long life span
- easy to capture and to manipulate

Risk assessment, general concepts

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factors:

- toxicity (*hazard assessment*)
- exposure

calculation:

- exposure / toxicity

related issues:

- *risk management*
- *risk communication*

Environmental Risk Assessment, general approaches

what is generally done:

- assess one compound
- in the lab

our aim:

- assess the risk of a complex situation
- in the field

Environmental Risk Assessment, regulatory approach

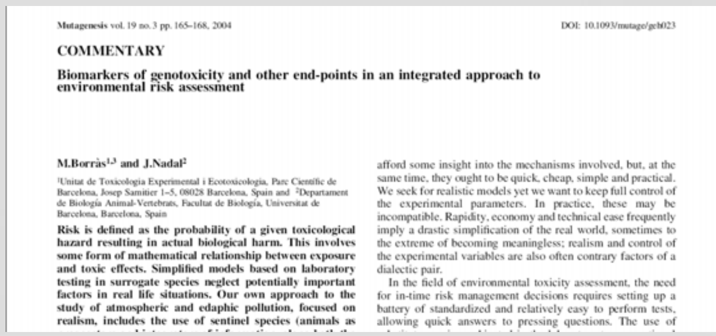
- **hazard assessment**: lab tests
  - *Daphnia magna* *(OECD 202)*
  - *Eisenia foetida* *(OECD 222)*
  - *Danio rerio* (zebra fish) (OECD 210)
  - *Scenedesmus subspicatus* and other algae (OECD 201)
  - *Vibrio fischerii* (Microtox, Mutatox)
- **exposure**
  - analysis of pollutants in the environment
- **calculation**
  - PEC / PNEC

Our model

steps

- **"actual harm" (rather than hazard) assessment (descriptive):**
  - for a real, concrete situation
  - based on actual effects

- **Risk Assessment (predictive):**
  - extrapolation to new situations
  - based on "internal" exposure (bioavailability)



Mutagenesis vol. 19 no. 3 pp. 165–168, 2004 DOI: 10.1093/mutage/geh023

COMMENTARY

Biomarkers of genotoxicity and other end-points in an integrated approach to environmental risk assessment

M.Borràs[1,3] and J.Nadal[2]

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Risk is defined as the probability of a given toxicological hazard resulting in actual biological harm. This involves some form of mathematical relationship between exposure and toxic effects. Simplified models based on laboratory testing in surrogate species neglect potentially important factors in real life situations. Our own approach to the study of atmospheric and edaphic pollution, focused on realism, includes the use of sentinel species (animals as

afford some insight into the mechanisms involved, but, at the same time, they ought to be quick, cheap, simple and practical. We seek for realistic models yet we want to keep full control of the experimental parameters. In practice, these may be incompatible. Rapidity, economy and technical ease frequently imply a drastic simplification of the real world, sometimes to the extreme of becoming meaningless; realism and control of the experimental variables are also often contrary factors of a dialectic pair.

In the field of environmental toxicity assessment, the need for in-time risk management decisions requires setting up a battery of standardized and relatively easy to perform tests, allowing quick answers to pressing questions. The use of

More...

Features

- consider pollution as a complex situation (not just "mixture")

- take into account homeostasis of the living organisms and of the environment itself

- polynomial expression of toxicity (cover the entire range of effects)

- all the measurements done in field conditions

And again...

Goals

- interpolate exposure data in a regression line to obtain a prediction of the biological harm to be expected

- assign the pairs "exposure, harm" to a conventional scale of risk

Assessment of the actual harm caused

"polynomial" toxicology

blocks of information		sentinel species	biomarkers
systemic effects		*Apodemus sylvaticus*	serum biochemistry
			histopathology
respiratory tract*		*Apodemus sylvaticus*	histopathology
reproduction	fertility	*Apodemus sylvaticus*	epidydimis cell count
	teratogeny	amphibian larvae	malformations
genotoxicity		*Apodemus sylvaticus*	Micronucleus Test
			Comet Test
populations		arthropods	abundance
			biodiversity

*Only in the case of atmospheric pollution; for soil assessment, respiratory tract may be considered together with other organs in the "systemic effects" block.

Assessment of the actual harm caused: calculations

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for each biomarker:

- severity score (comparing to controls) from 0 to 3, for each particular parameter
- sum of scores, divided by the number of parameters measured

within each block of information:

- sum of the values obtained for each biomarker, divided by the number of biomarkers considered

Integrated Toxicological Harm (ITH)

- sum of the values for each block, divided by the number of blocks

Envirnonmental Risk Assessment

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Toxicity

- ITH corresponding to, at least, three degrees of exposure (= distance to the focus)

Exposure

- bioavailable pollutants
  - edaphic: EROD, GST, MDA
  - atmospheric: immission gases (gaseous fraction) + “internal” metals (solid fraction)

Calculations

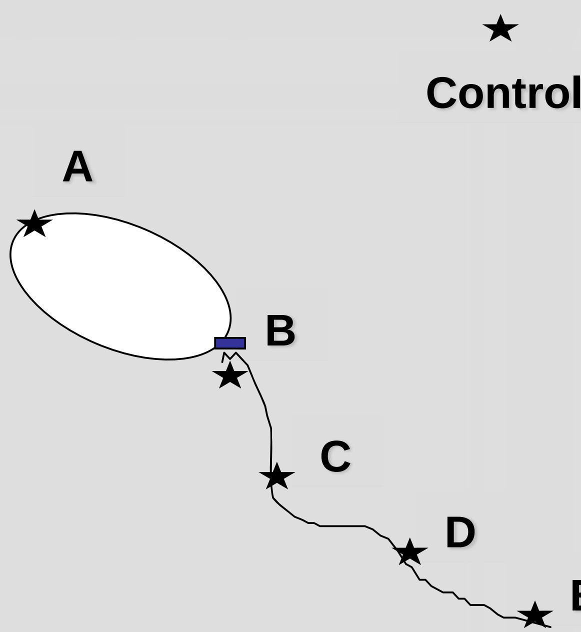
- regression line “ITH vs exposure”
  - allows to interpolate new exposure data
  - may be assigned to a conventional scale
  - assumes dose-dependence

An example: MSW landfills

Gavà
- Barcelona and metropolitan area
- > 3000000 inhabitants
- urban / industrial

Bellestar
- La Seu d'Urgell, rural area
- 11000 inhabitants
- urban / agricultural

Study areas in Garraf Landfil



Genotoxicity (Gavà landfil): study design

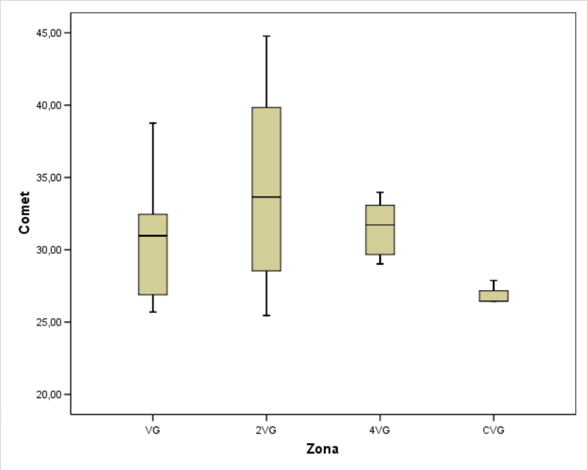
- capture of *Apodemus sylvaticus*, zones A, B, D and control (Shermann traps)
  - Micronucleus Test in circulating erythrocytes
  - Comet Test in circulating lymphocytes
- soil samples, zones A, B, C, D, E and control
  - Comet Test in coelomocytes of *Allolobophora caliginosa*

Genotoxic effects in limphocytes (*Apodemus sylvaticus*)

Year 1999

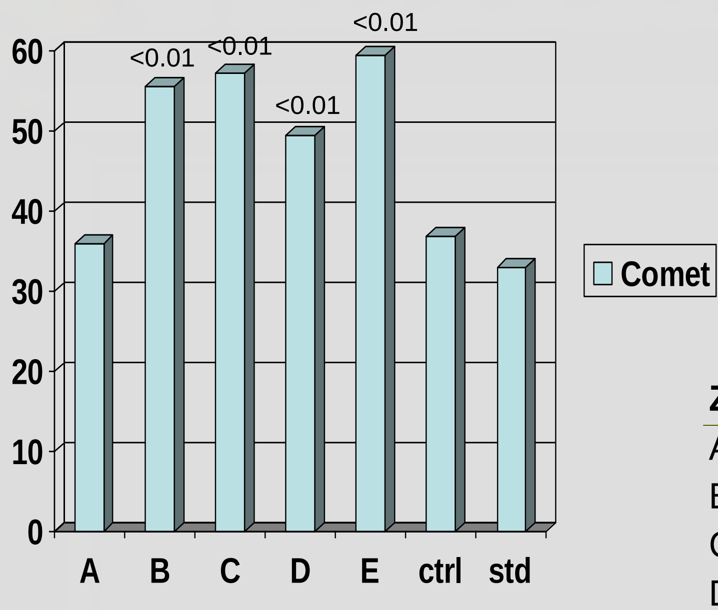
Zone	N	X ± SD
A	25	6.11 ± 3.2
B	15	8.83 ± 5.5
D	15	4.08 ± 3.7
Control	13	2.59 ± 1.7

(visual scoring)



Year 2004

Comet assay:Allollobophora



Zone	N	X ± SD
A	7	36 ± 5.4
B	8	55.5 ± 11.3
C	7	57.2 ± 3.8
D	9	49.3 ± 6.5
E	8	59.4 ± 11.7
Control	7	36.8 ± 5.6
Standard	8	32.9 ± 8.6

MNT- *Apodemus*

Zone	N	X ± SD
A	25	5 ± 2.7
B	24	6.37 ± 2.9
D	12	5.5 ± 1.9
Control	14	3.5 ± 1.7

Comparative Comet-MNT in *Apodemus sylv.*

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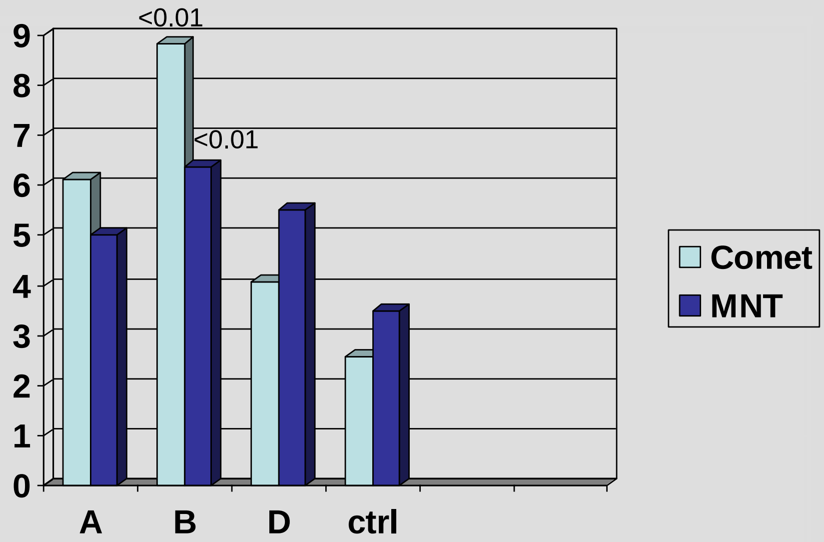

Arthropod biodiversity in Gava Landfil

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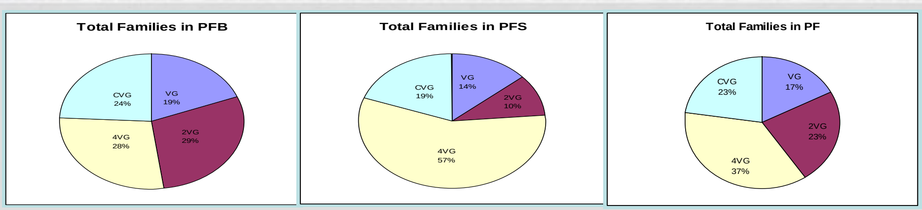


Percentage of families of arthropods captured

PFS	VG	2,528
	2VG	2,793
	4VG	2,775
	CVG	2,650
PFB	VG	3,027
	2VG	3,969
	4VG	3,605
	CVG	3,653
TOTAL	VG	3,683
	2VG	4,480
	4VG	4,038
	CVG	4,171

Margalef Index

		N0	*N1*	*N2*
PFS	VG	21	11,737	1,127
	2VG	21	23,315	1,071
	4VG	26	15,888	1,155
	CVG	20	17,035	1,104
PFB	VG	28	15,441	1,074
	2VG	39	21,014	1,094
	4VG	36	20,943	1,045
	CVG	36	14,281	1,066
TOTAL	VG	36	19,208	1,062
	2VG	45	26,424	1,076
	4VG	43	24,501	1,059
	CVG	42	17,031	1,067

Numbers of Hill obtained in studied sites. N0: Total number of families; N1: Number of abundant families; N2: Number of more abundant families

Modified Teratogenic Index of FETAX.

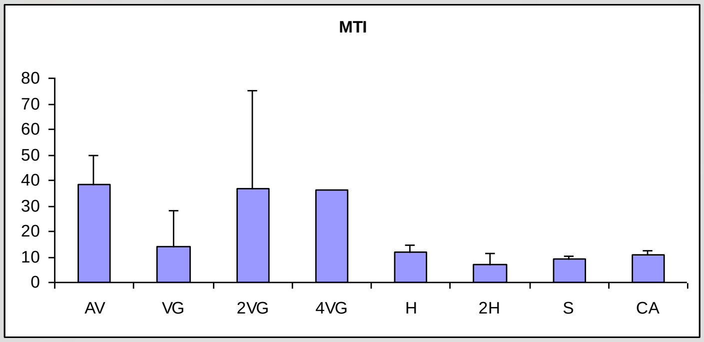
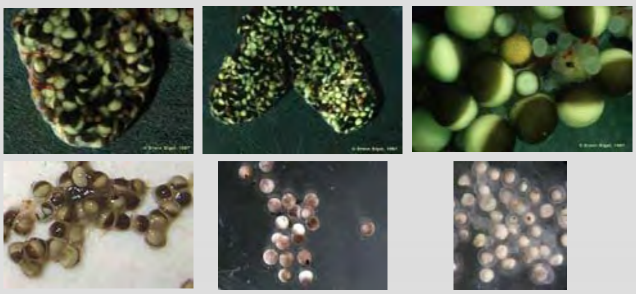
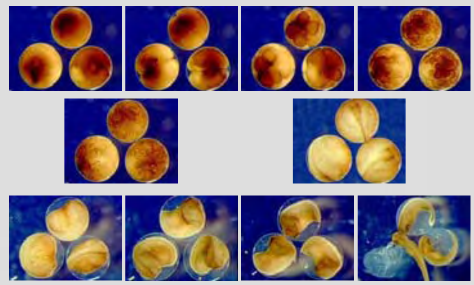


Figure 1.- MTI values obtained after exposure of embryos to surface water or soil extracts from the study zones. **AV**: surface water obtained next to the Garraf lixiviates pool; **VG**: extract of soil obtained next to the Garraf lixiviates pool; **2VG**: extract of soil obtained 2 kilometres downstream from Garraf lixiviates pool; **4VG**: extract of soil obtained 4 kilometres downstream from Garraf lixiviates pool; **H**: extract of soil immediate to Hostalets de Pierola lixiviates pool; **2H**: extract of soil 2 kilometres downstream from Hostalets de Pierola lixiviates pool); **S**: extract of soil immediate to Montferrer i Castellbó lixiviates pool; **CA**: extract of non contaminated soil.





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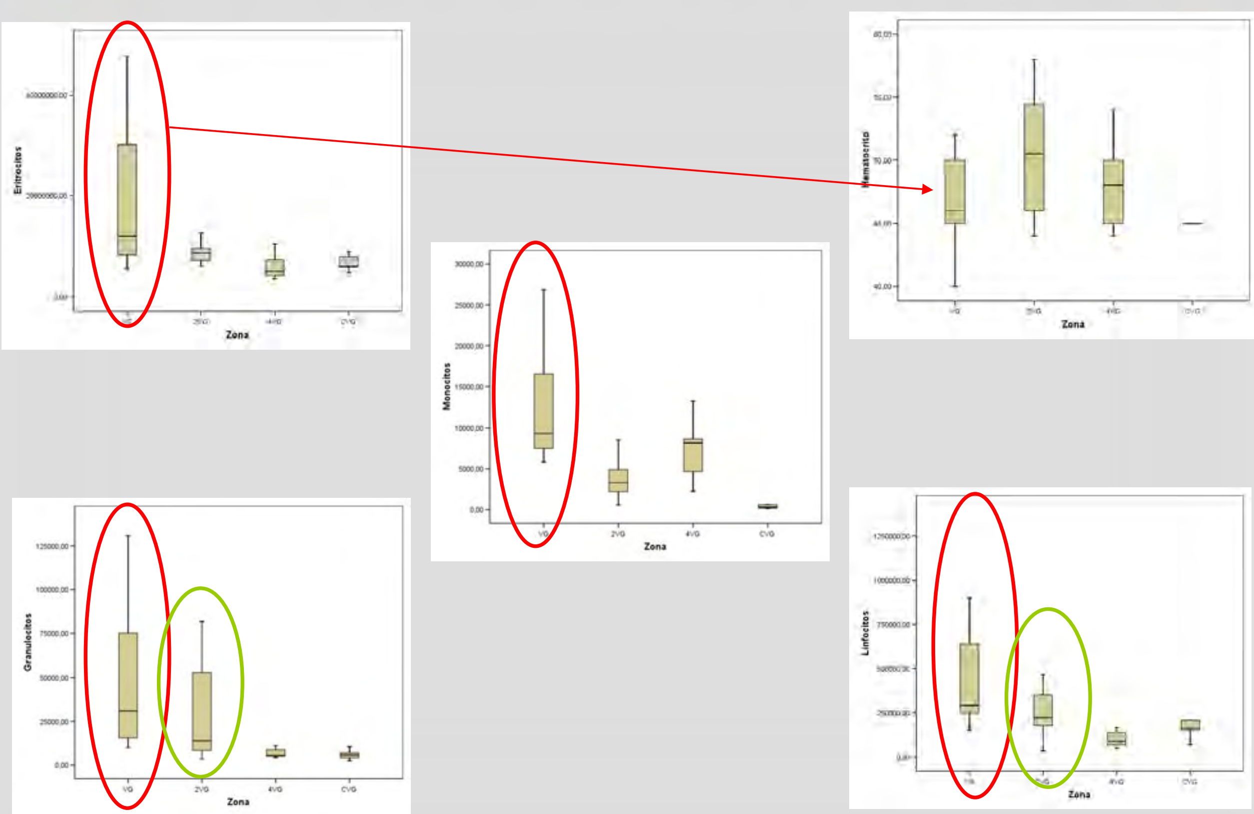
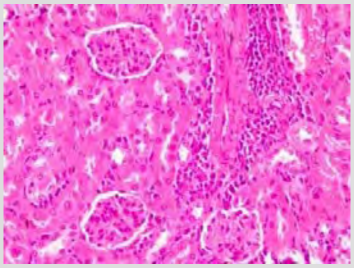
Haematology in wood mouse.



Histopathology in wood mouse.



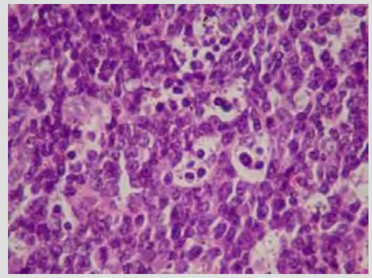
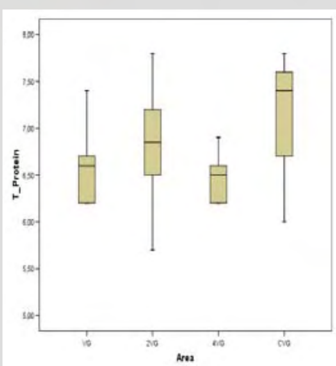
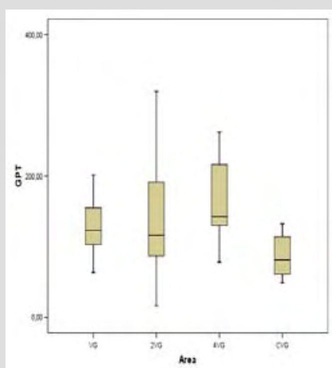


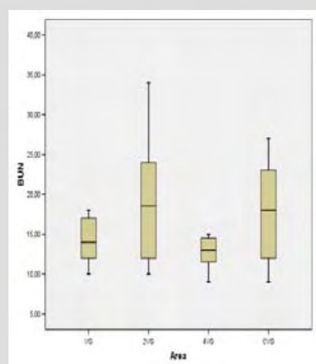
Table I.- Histopathological results. Mean scores are expressed as mean ± standard deviation. Statistical comparisons by Welch test.

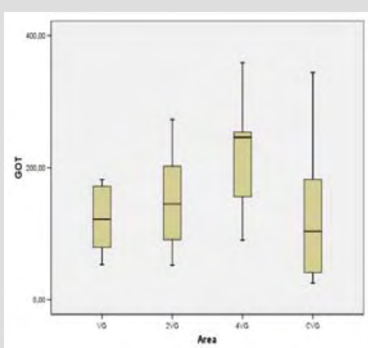
	Zone A (Bellestar)		Zone B (Collserola)		P (mean scores)
	Mean sc.	**% affected**	**Mean sc.**	**% affected**	
liver Kupffer cells	0 ± 0	0	0.81 ± 1.03	63	0.0019
liver inflamation/necrosis	1.54 ± 1.20	70	0.45 ± 0.91	20	0.0107
kidney interstitial nephritis	0.85 ± 1.07	54.5	0.11 ± 0.32	10	0.0304
lung several pathologies	0.69 ± 1.18	25	2.20 ± 2.26	75	0.0183
spleen several pathologies	1.36 ± 1.69	57	0.17 ± 0.41	10	0.0251

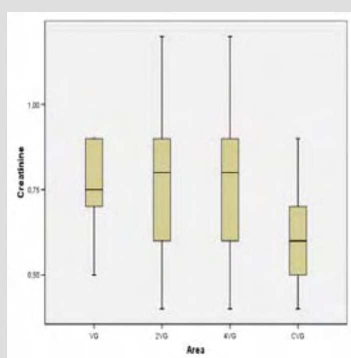
Serum Parameters in wood mouse.



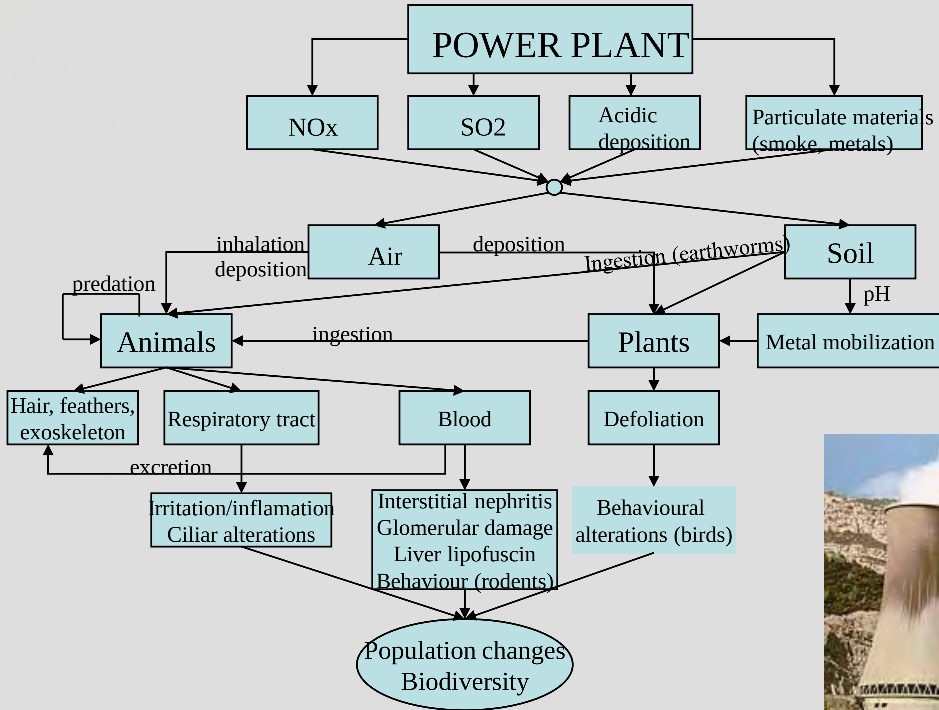




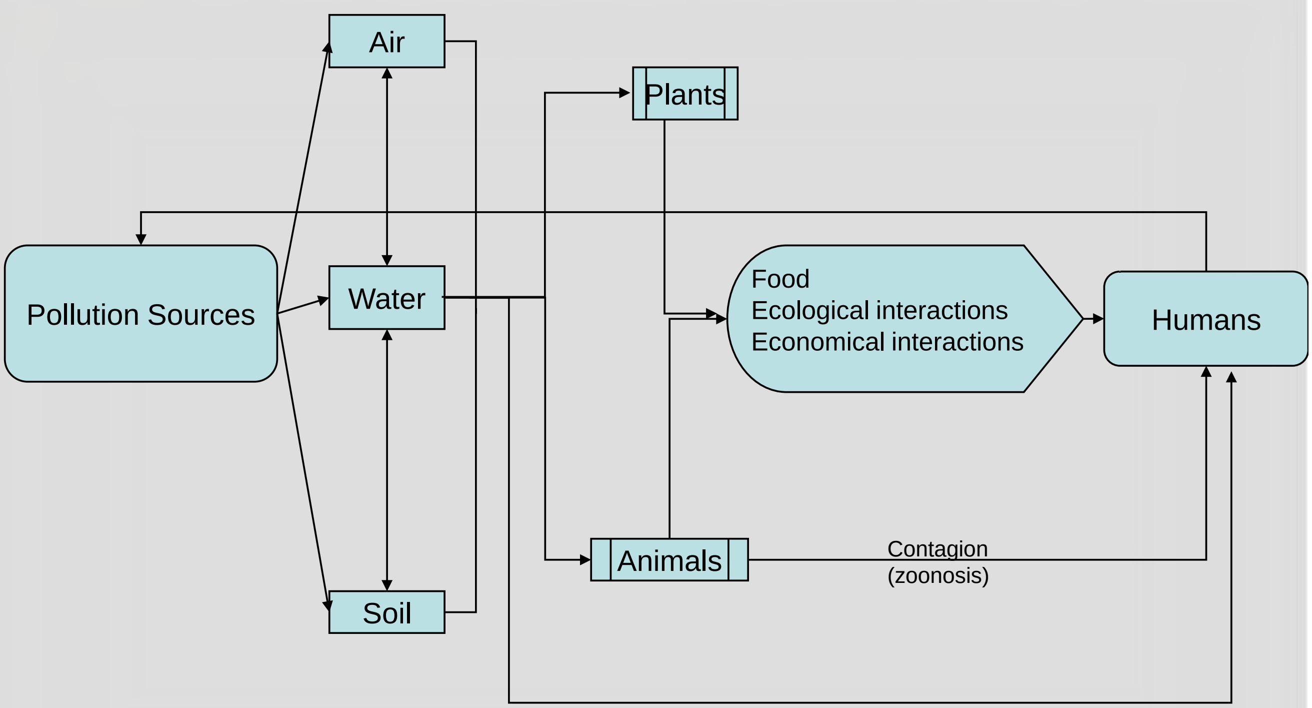




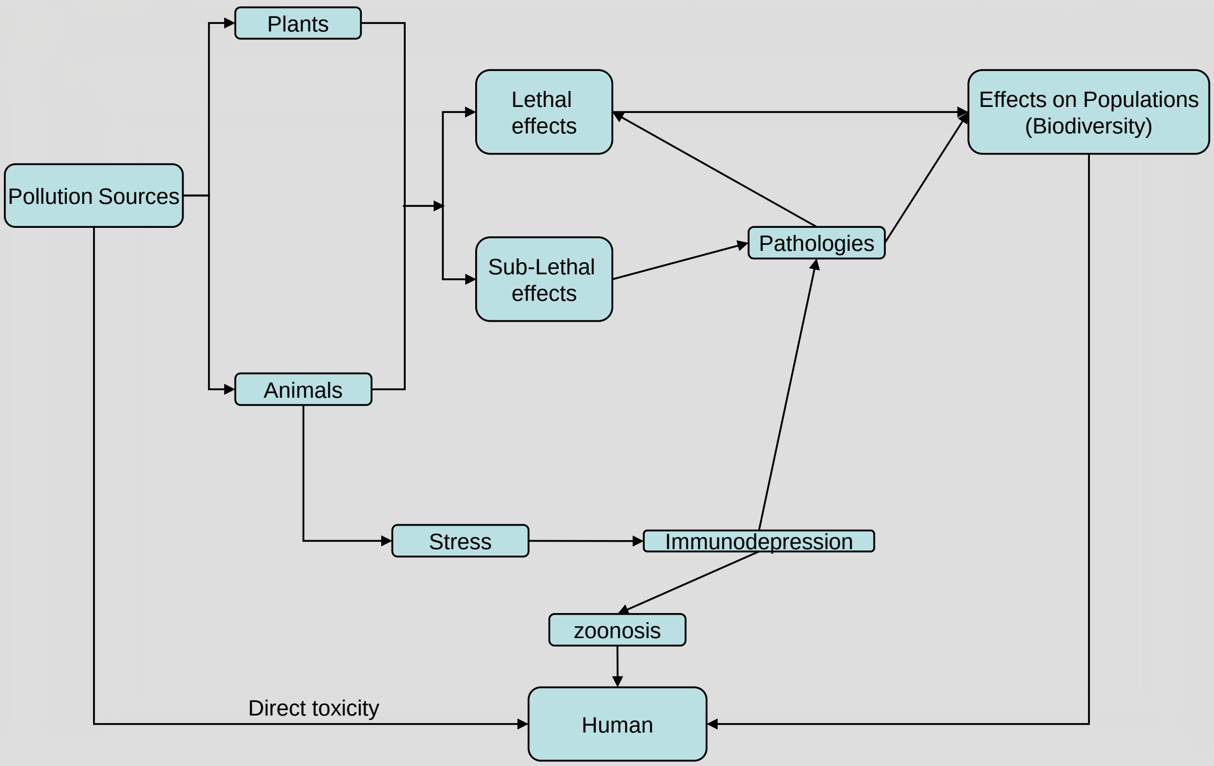
First attempts: Coal-Fired Power Plant



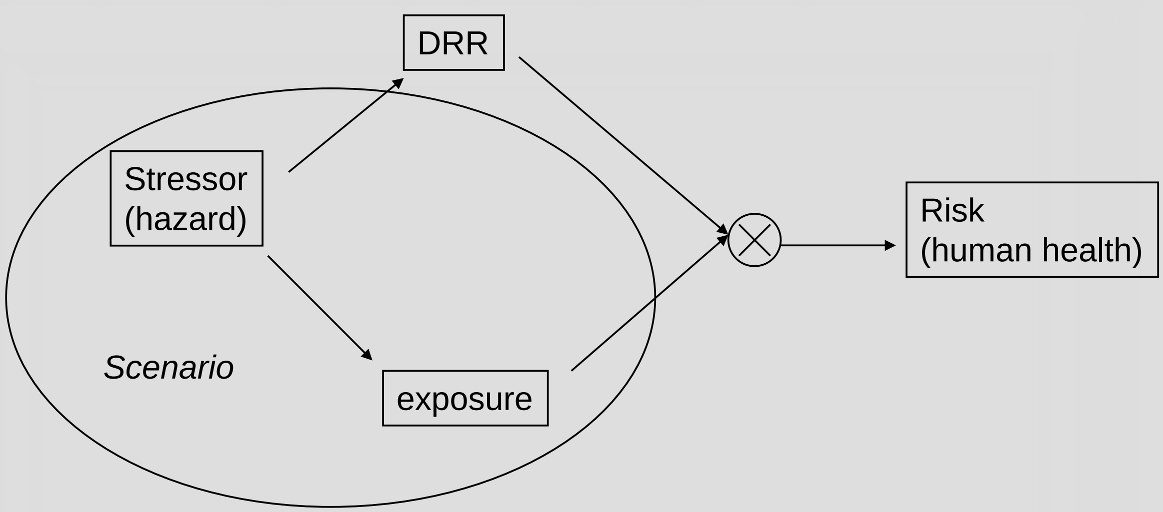
Exposure



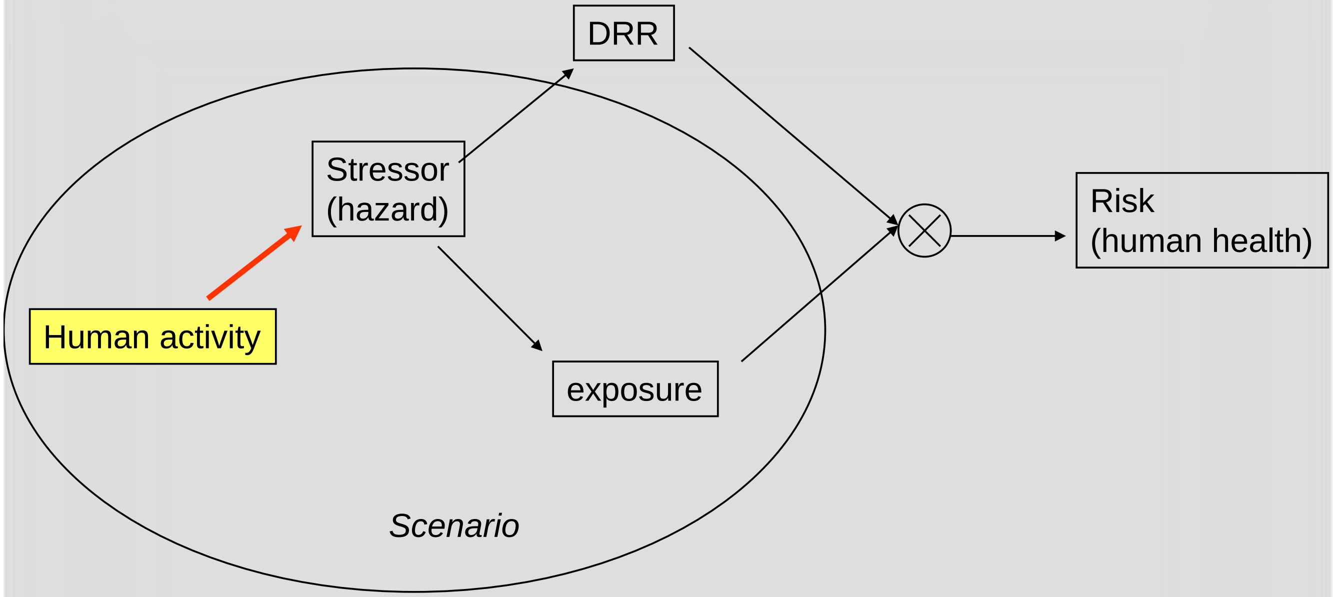
Effects



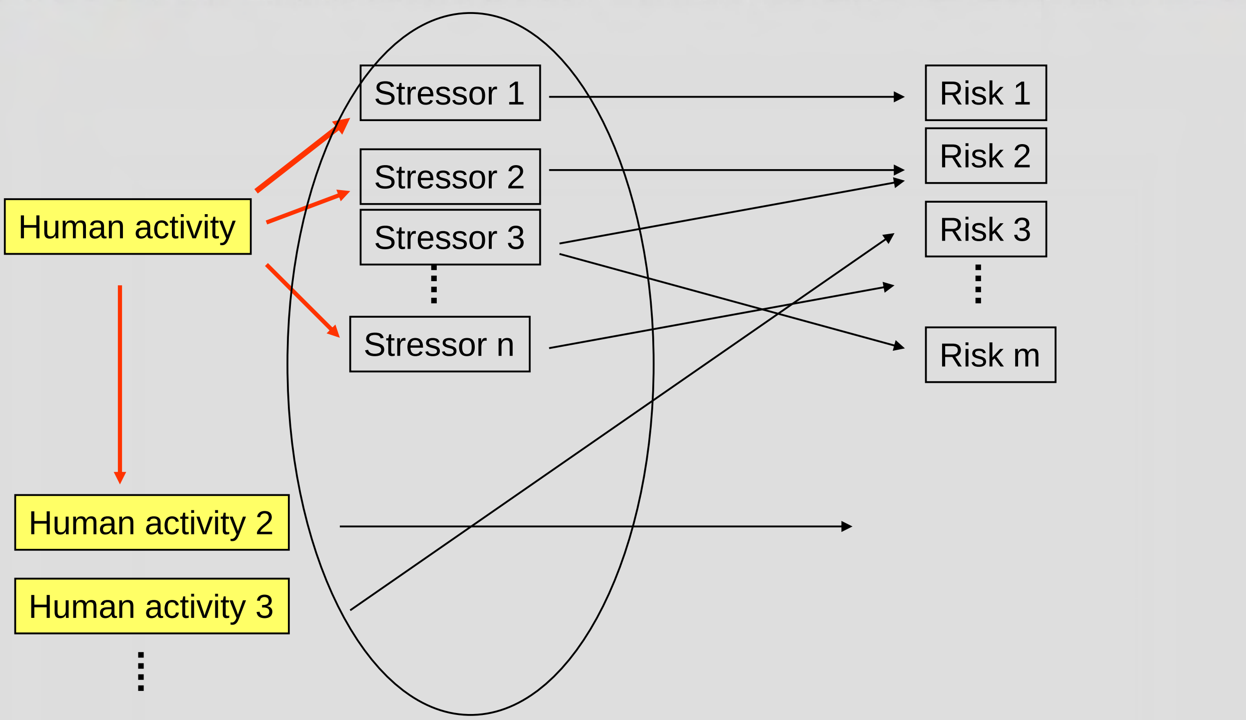
Risk assessment: naïf version



Risk assessment: not so easy I

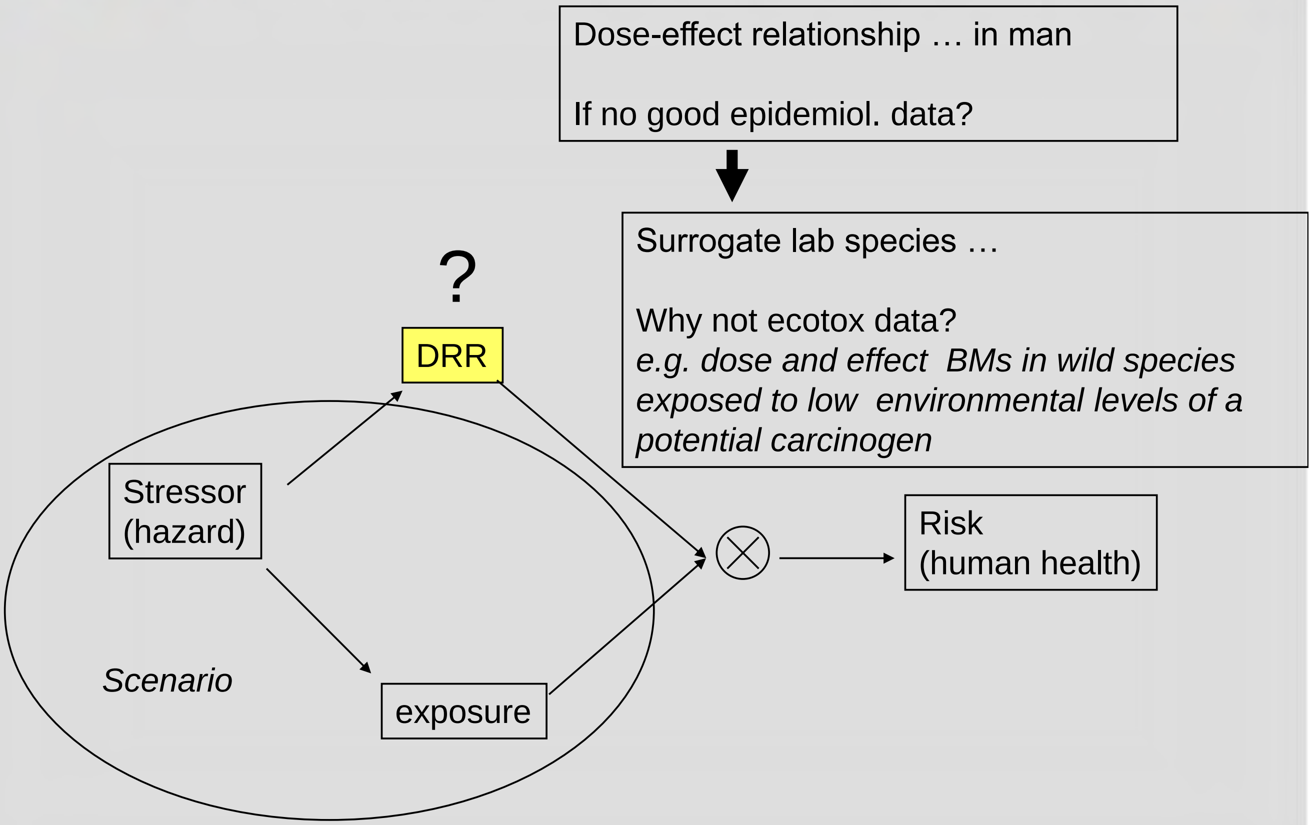


Risk assessment: not so easy I

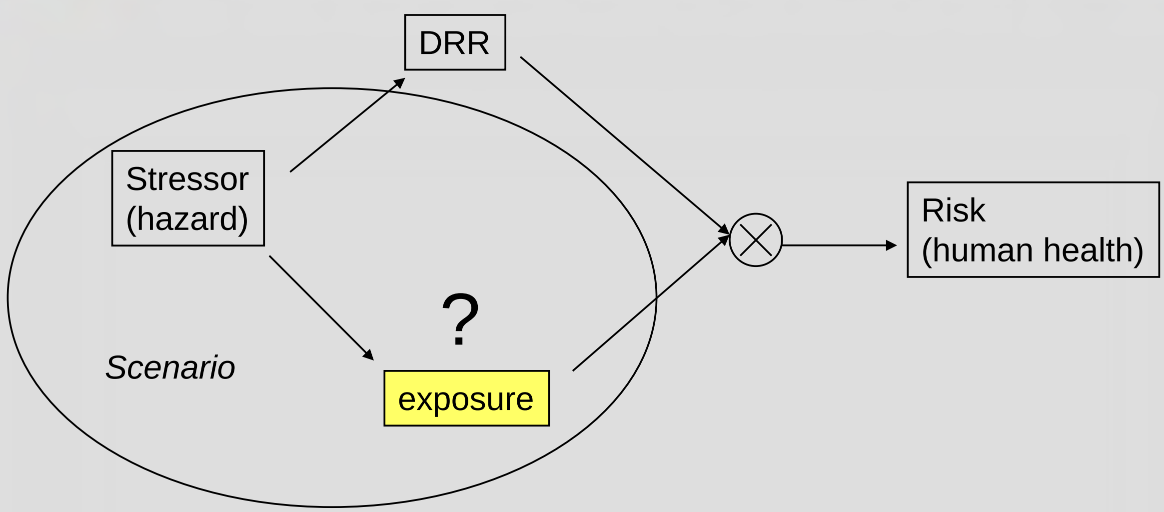


ecotox: integration of stressors? *e.g.: endocrine disruptors*

Risk assessment: not so easy II



Risk assessment: not so easy III



Exposure = Σ [stressor]$_{matrix}$ x intake rate x exposure duration

[stressor]$_{matrix}$ = f(x,y,t) ?

Monitoring: expensive
Modeling: uncertain

Risk assessment: not so easy III

Exposure = Σ [stressor]$_{matrix}$ x intake rate x exposure duration

[stressor]$_{matrix}$ = $f(x,y,t)$?

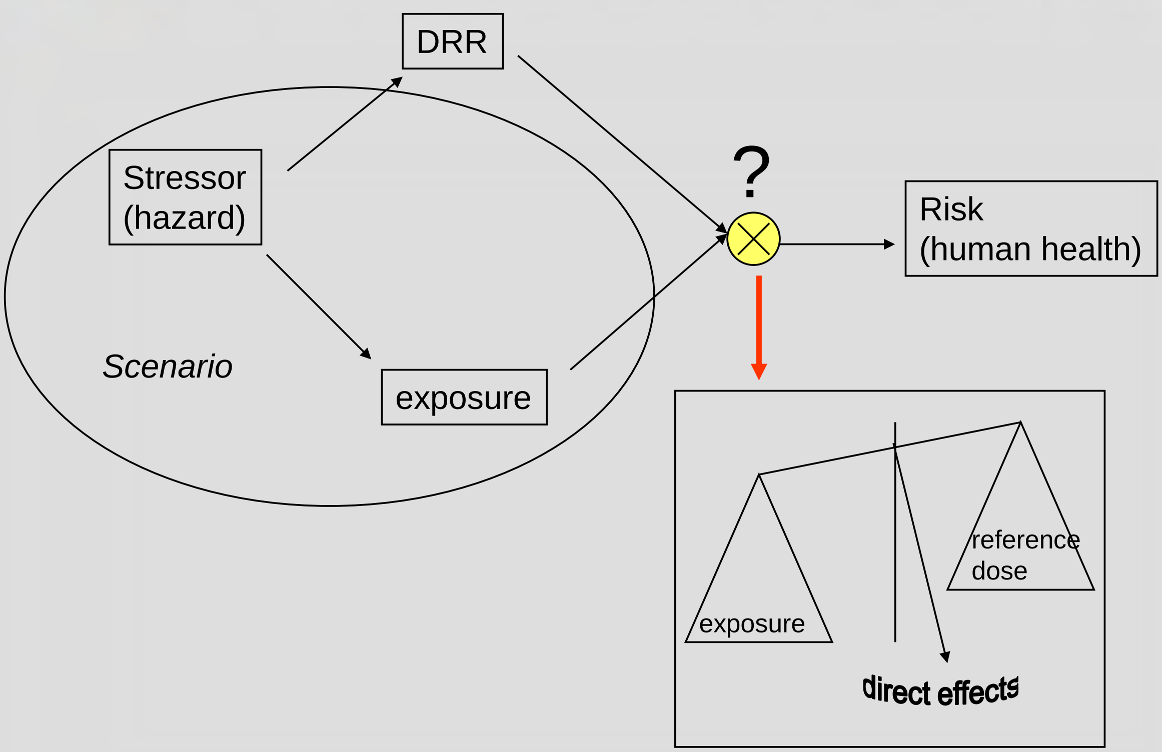
Monitoring: expensive
Modeling: uncertain

ERA: environmental BMs of exposure
matrix specific sentinels
….

minimize monitoring
improve exposure modeling
integrate long term exposures
…

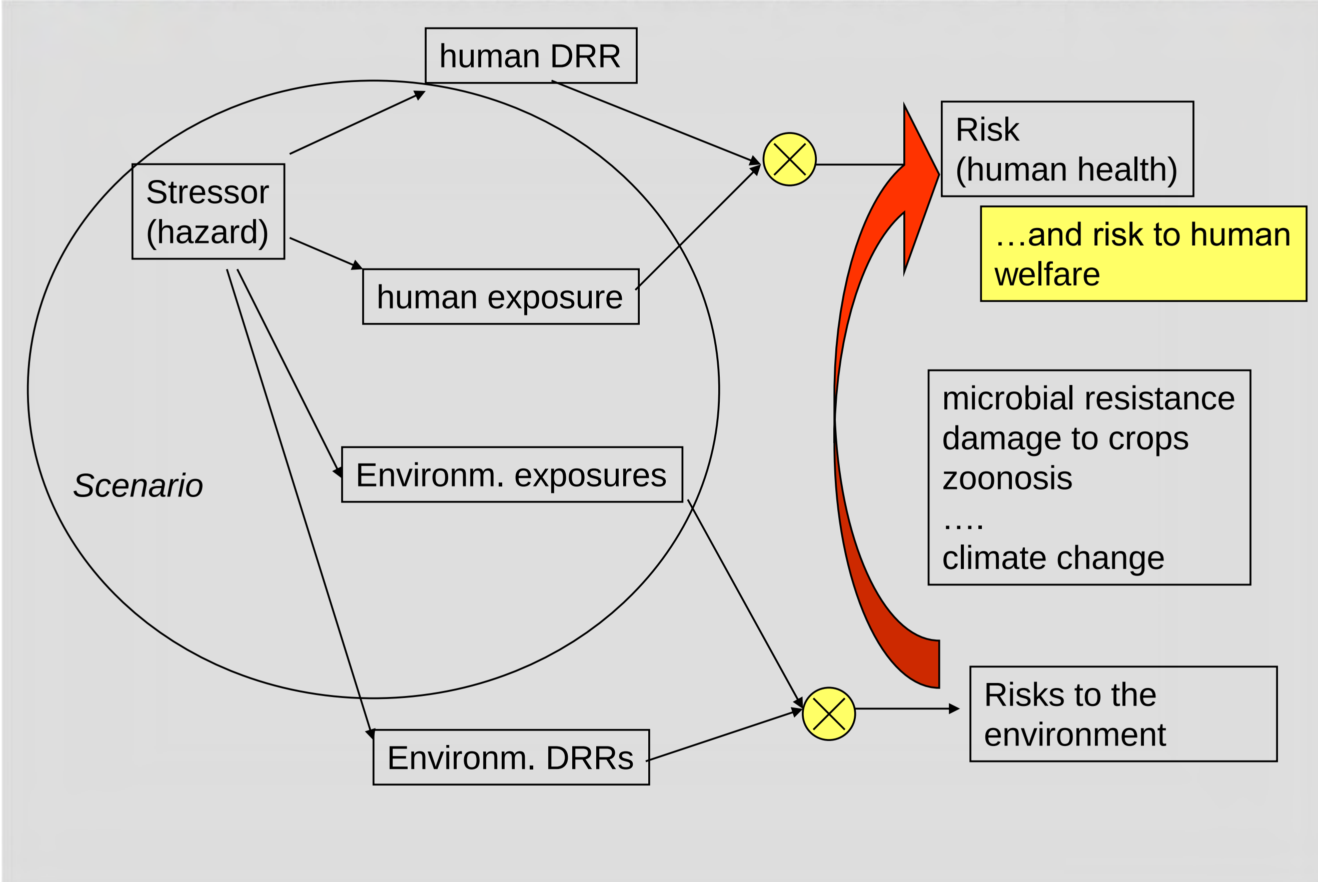
e.g. transfer along food chains

Risk assessment: not so easy IV

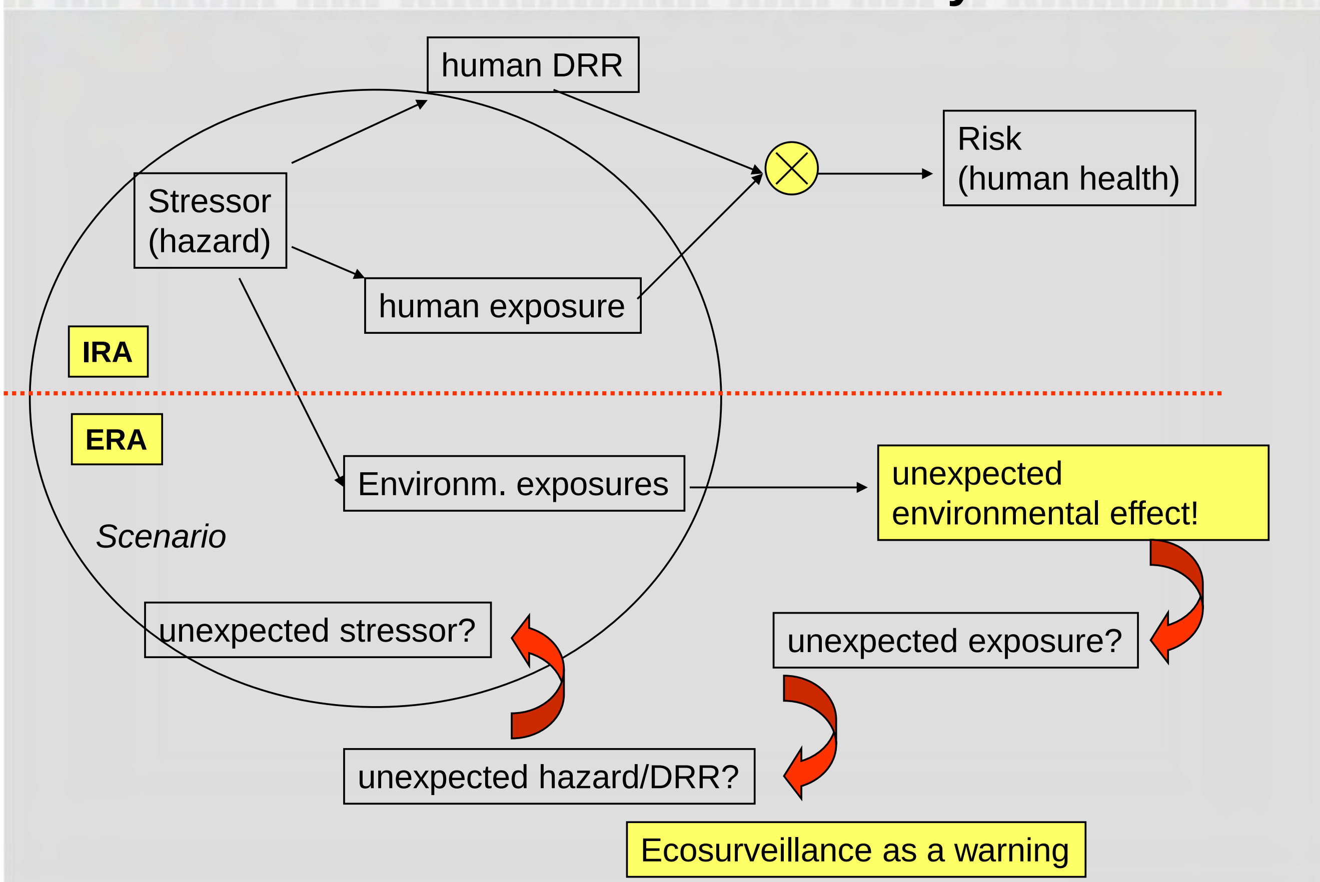


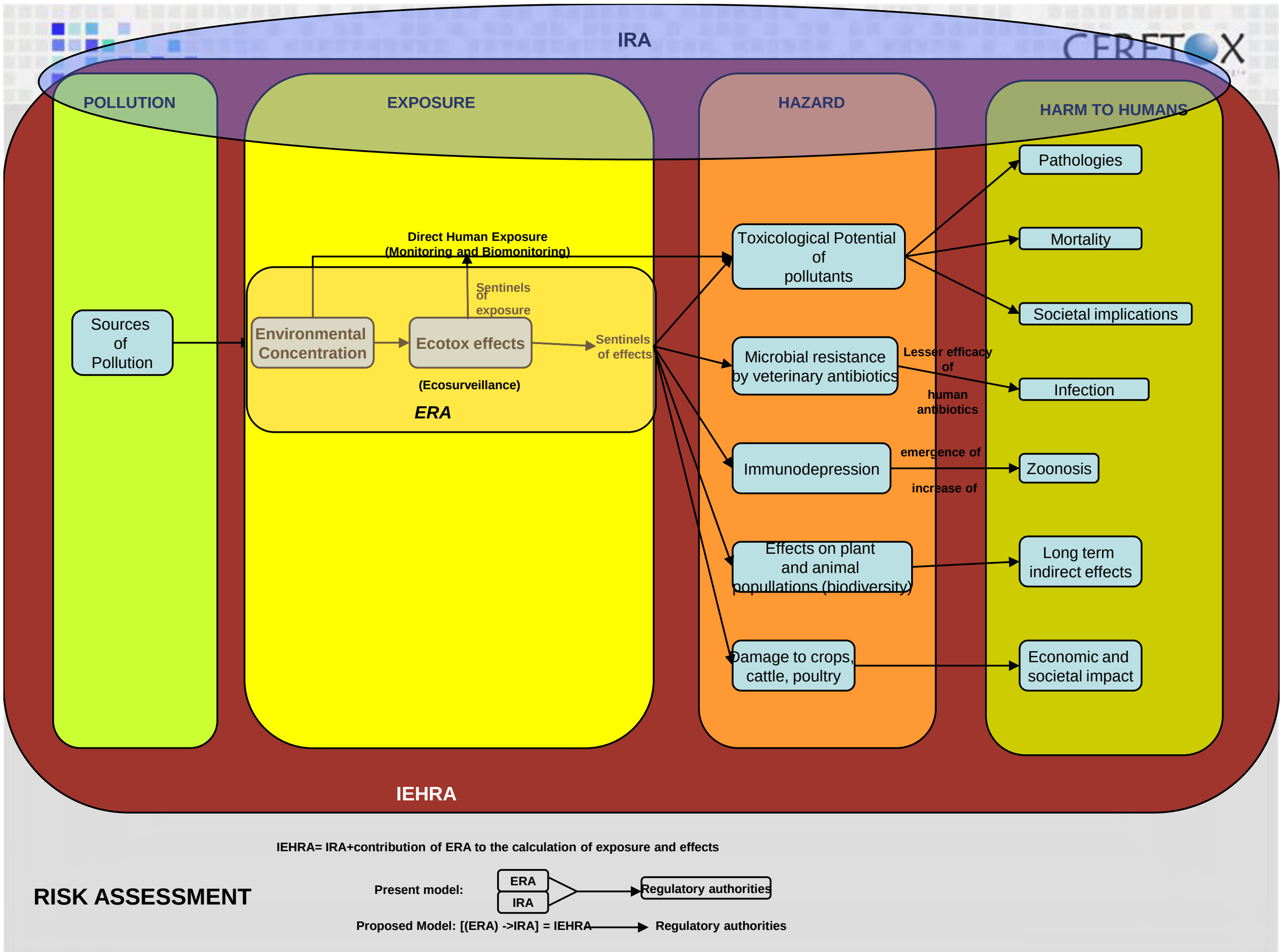
Indirect effects on human health?

Risk assessment: not so easy IV



Risk assessment: not so easy V





IEHRA

Epsilon:

Depend of stressors?

Depend of complex mixture?

Depend of quality of HBMs/EBMs?

Depend of climate characteristics?

Depend of time of exposure?

Depend of time of effects?

Depend of time of permanence in body?

Depend of distance to pollutant source?

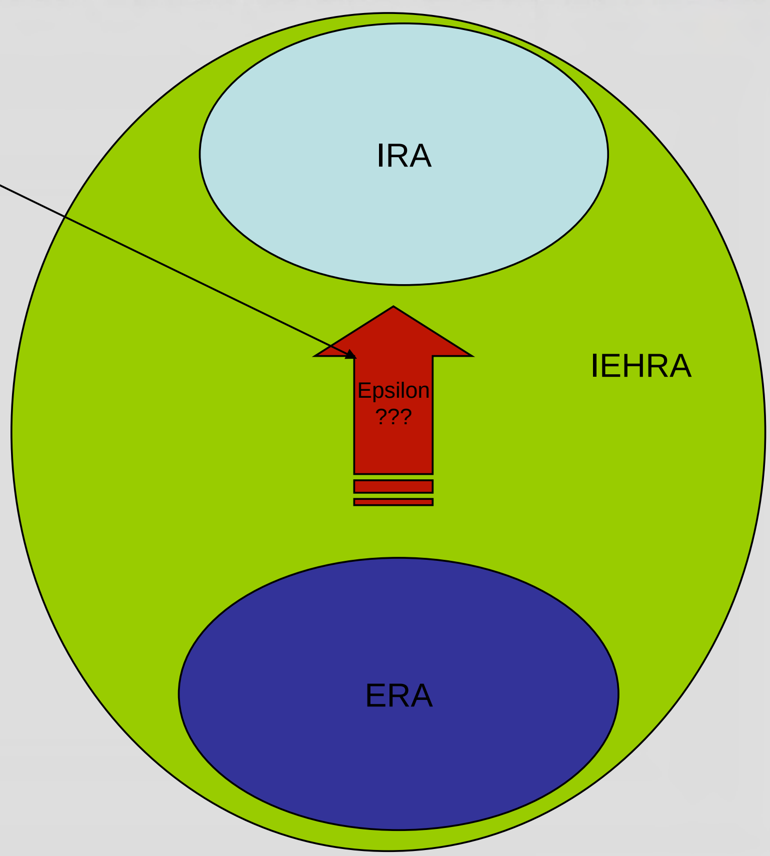
Depend of system/organ target?

Depend of susceptibility/genotype or phenotype?

Depend of data?

Depend of statistic model?

Depend of…?



How to proceed?

Use of "general" ecotox data (lab or field) to help in

- identifyng new hazards
  - exposure to complex situations
  - refinement of DRR
  - indirect effects on human welfare

- Use of existing Ecosurveillance data in the same or in a similar scenario

- "golden standard" for validation: studies carried out in parallel, previously designed

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Membre de: XIT XARXA DE CENTRES DE SUPORT A LA INNOVACIÓ TECNOLÒGICA CIDEM

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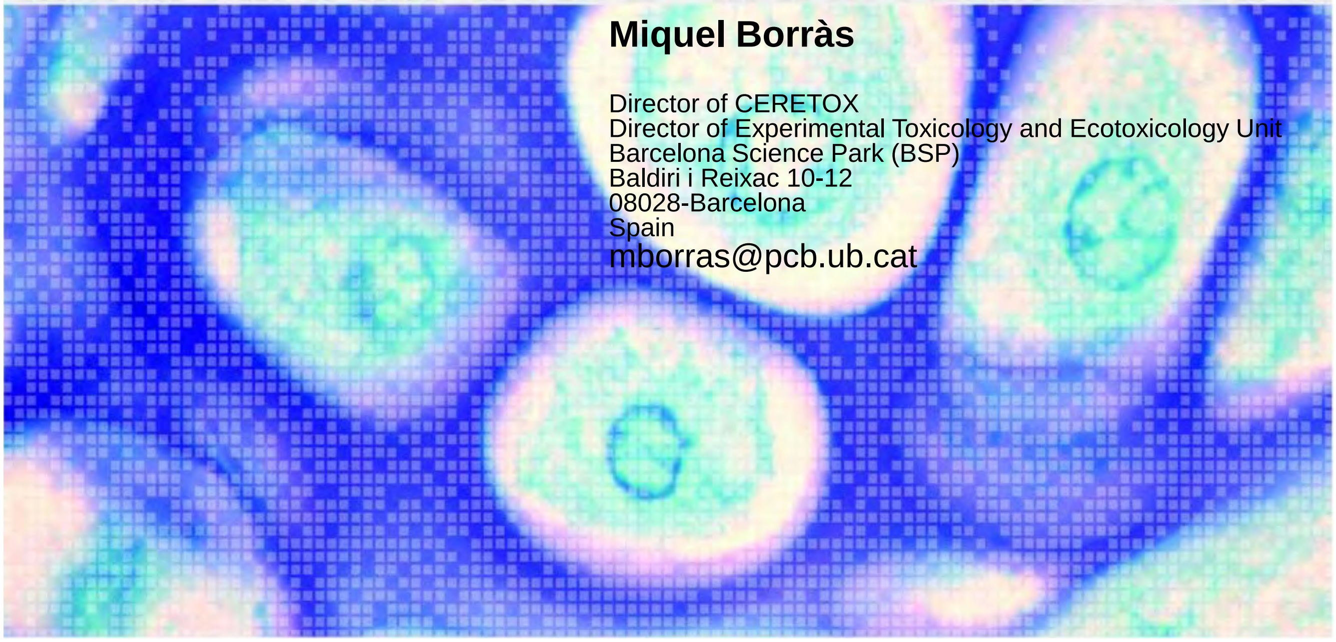
Environmental Exposure and Ecosurveillance



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Initial consideration of model

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should be:
✓ comprehensive
✓ meaningful
✓ give insight on mechanisms

but, at the same time:
✓ quick
✓ cheap
✓ simple
✓ practical

realism + control = k

Models

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- **quick answers to pressing questions**
  - laboratory tests
  - substitute species
  - conventional exposure

- **trying to be realistic**
  - field studies
  - native species
  - sentinels + biomarkers

Models

transactional approaches

- mesocosms
- lab animals in the wild
- wild animals in the lab

Animals as prospectors and integrators of environmental information

Animals

- prospect the environment
- take into account homeostasis
  (of the organism and of the environment)
- ntegrate information
  - ✓ spatial
  - ✓ temporal

Characteristics of Sentinel species:

- tolerate and accumulate pollutants
- ubiquitous
- frequent
- sedentary
- relatively long life span
- easy to capture and to manipulate

Risk assessment, general concepts

factors:

- toxicity (*hazard assessment*)
- exposure

calculation:

- exposure / toxicity

related issues:

- *risk management*
- *risk communication*

Environmental Risk Assessment, general approaches

what is generally done:

- assess one compound
- in the lab

our aim:

- assess the risk of a complex situation
- in the field

Environmental Risk Assessment, current approach

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- **hazard assessment**: lab tests
  - *Daphnia magna (OECD 202)*
  - *Eisenia foetida (OECD 222)*
  - zebra fish (OECD 210)
  - *Scenedesmus subspicatus* and other algae (OECD 201)
  - *Vibrio fischerii* (Microtox, Mutatox)
- **exposure**
  - analysis of pollutants in the environment
- **calculation**
  - PEC / PNEC

Our proposal

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steps

- **“actual harm” (rather than hazard) assessment (descriptive):**
  - for a real, concrete situation
  - based on actual effects
- **Risk Assessment (predictive):**
  - extrapolation to new situations
  - based on “internal” exposure (bioavailability)

More...

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Features

- consider pollution as a complex situation (not just "mixture")
- take into account homeostasis of the living organisms and of the environment itself
- polynomial expression of toxicity (cover the entire range of effects)
- all the measurements done in field conditions

And again...

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Goals

- interpolate exposure data in a regression line to obtain a prediction of the biological harm to be expected
- assign the pairs "exposure, harm" to a conventional scale of risk

Assessment of the actual harm caused

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"polynomial" toxicology

blocks of information		sentinel species	biomarkers
systemic effects		*Apodemus sylvaticus*	serum biochemistry
			histopathology
respiratory tract*		*Apodemus sylvaticus*	histopathology
reproduction	fertility	*Apodemus sylvaticus*	epidydimis cell count
	teratogeny	amphibian larvae	malformations
genotoxicity		*Apodemus sylvaticus*	Micronucleus Test
			Comet Test
populations		arthropods	abundance
			biodiversity

*Only in the case of atmospheric pollution; for soil assessment, respiratory tract may be considered together with other organs in the "systemic effects" block.

Assessment of the actual harm caused: calculations

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for each biomarker:

- severity score (comparing to controls) from 0 to 3, for each particular parameter
- sum of scores, divided by the number of parameters measured

within each block of information:

- sum of the values obtained for each biomarker, divided by the number of biomarkers considered

Integrated Toxicological Harm (ITH)

- sum of the values for each block, divided by the number of blocks

toxicity

- ITH corresponding to, at least, three degrees of esposure (= distance to the focus)

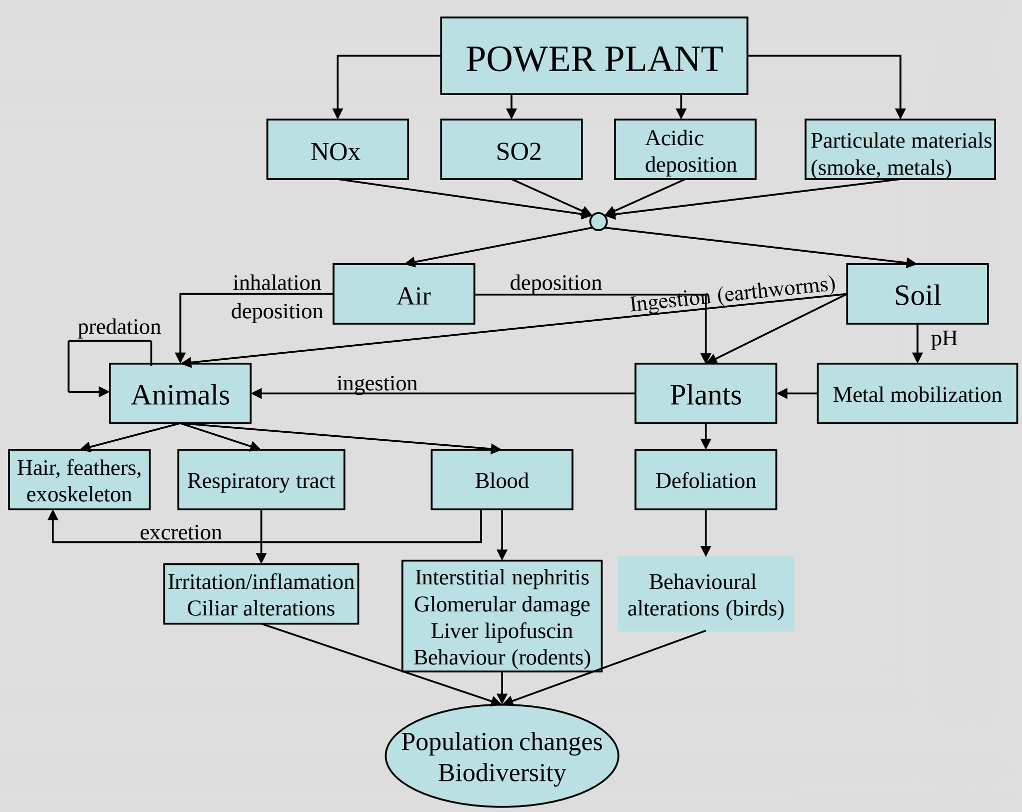
exposure

- bioavailable pollutants
  - edaphic: PCB's in fat, or metals in viscera and fanera, etc.
  - atmospheric: immission gases (gaseous fraction) + "internal" metals (solid fraction)

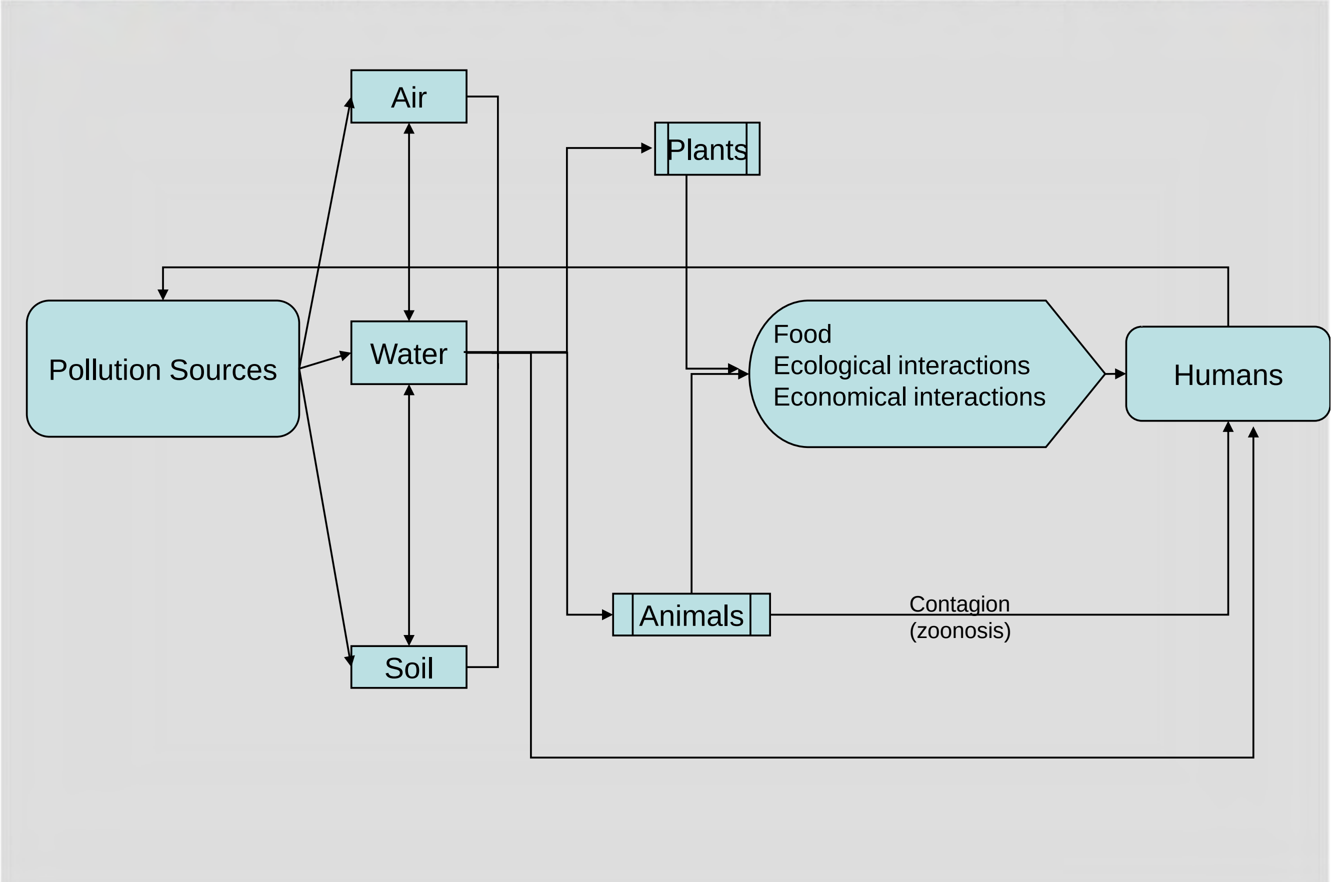
calculations

- regression line "ITH vs exposure"
  - allows to interpolate new exposure data
  - may be assigned to a conventional scale
  - assumes dose-dependence

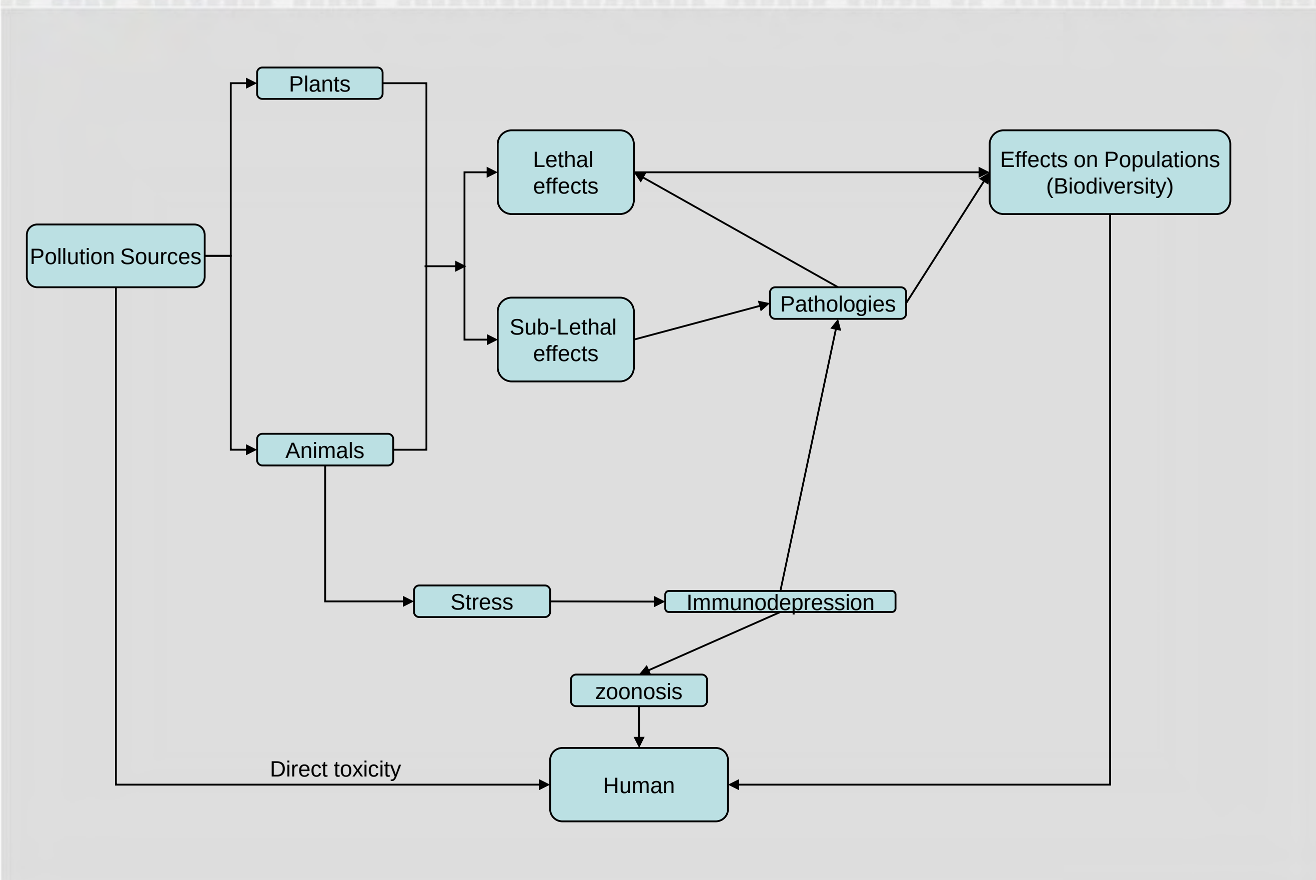
First attempts



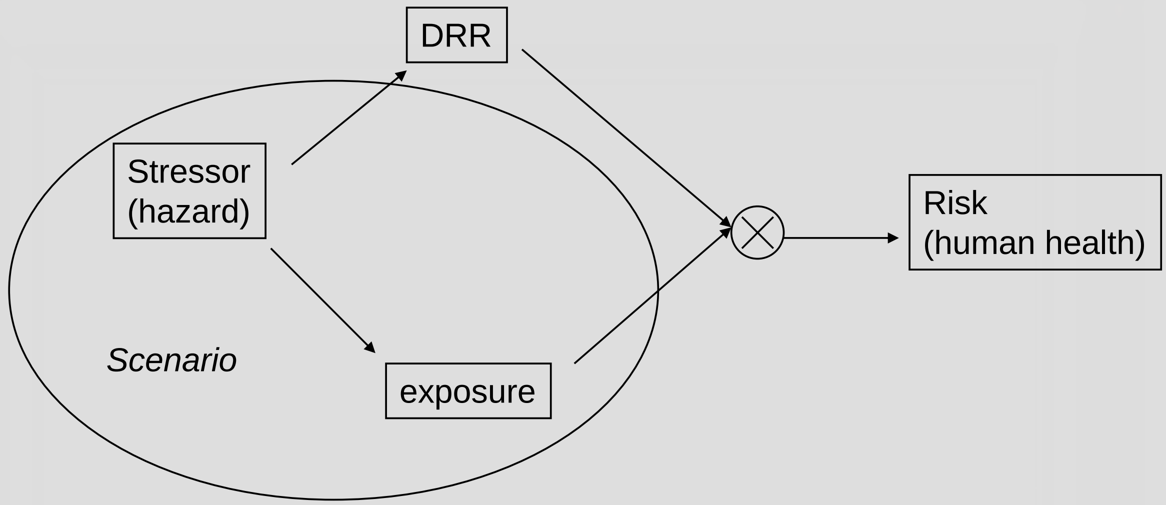
Exposure



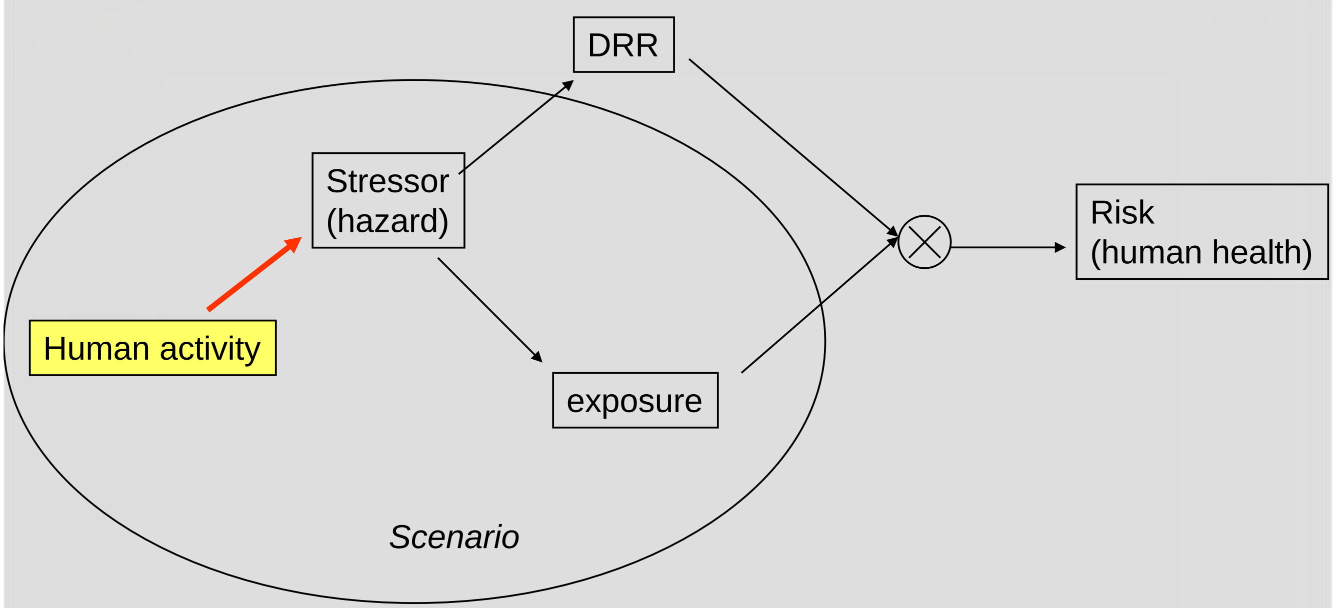
Effects



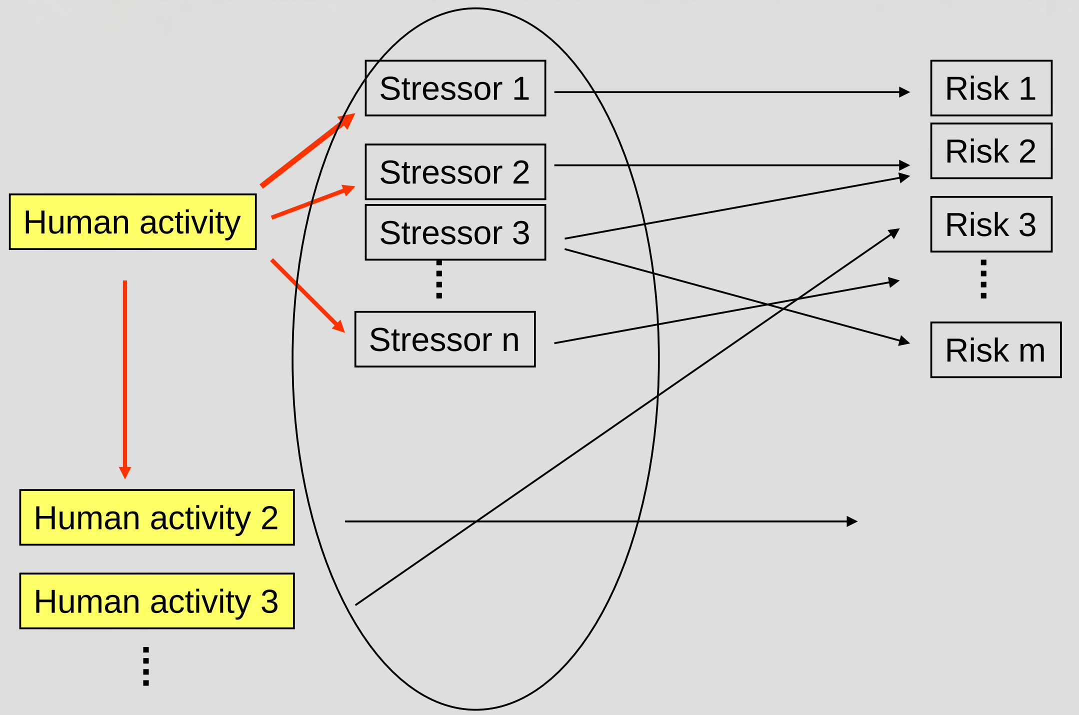
Risk assessment: naïf version



Risk assessment: not so easy I

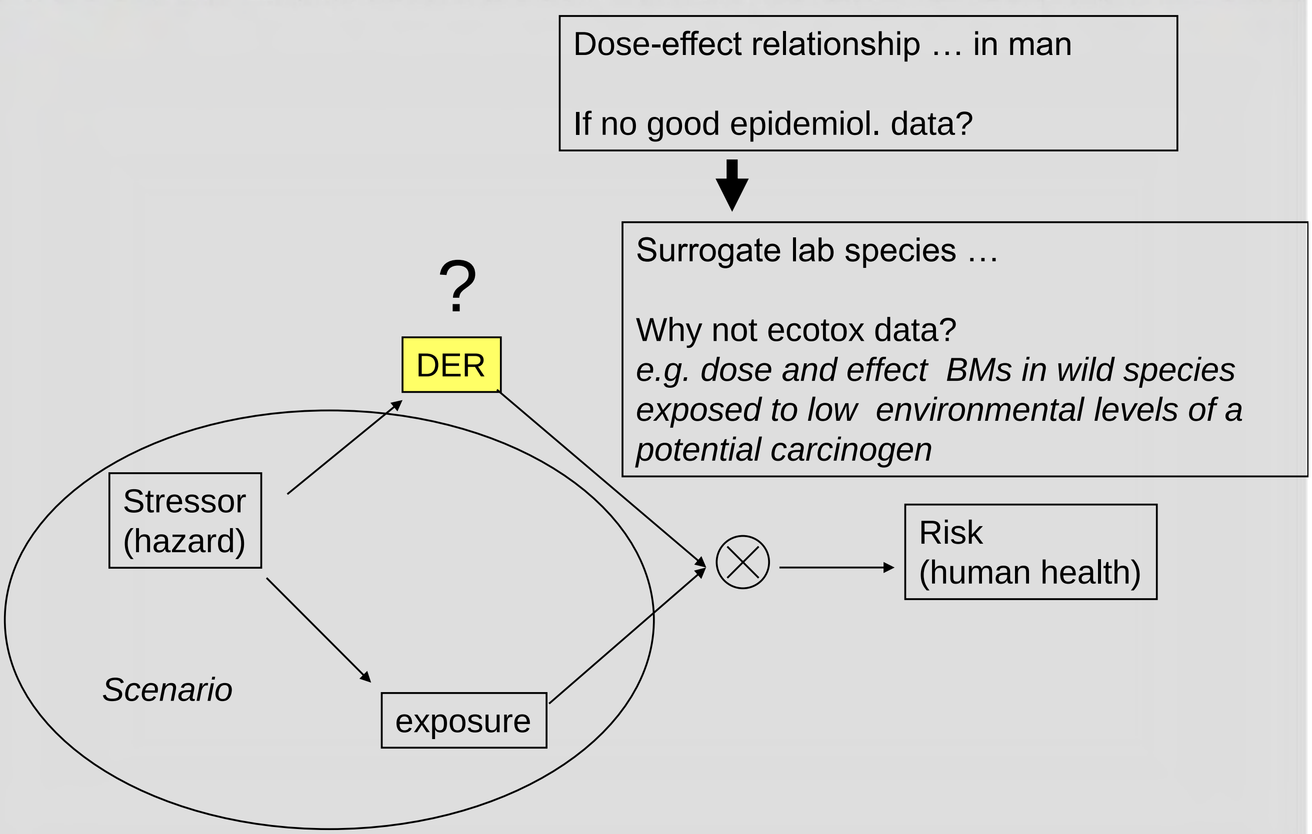


Risk assessment: not so easy I

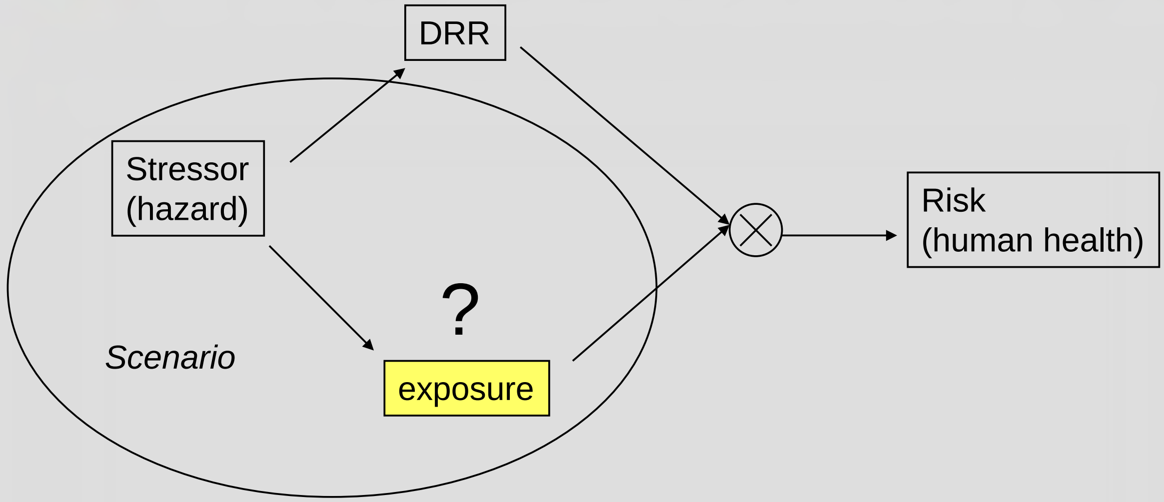


ecotox: integration of stressors? *e.g.: endocrine disruptors*

Risk assessment: not so easy II



Risk assessment: not so easy III



Exposure = Σ [stressor]$_{matrix}$ x intake rate x exposure duration

[stressor]$_{matrix}$ = f(x,y,t) ?

Monitoring: expensive
Modeling: uncertain

Risk assessment: not so easy III

Exposure = Σ [stressor]$_{matrix}$ x intake rate x exposure duration

[stressor]$_{matrix}$ = f(x,y,t) ?

Monitoring: expensive
Modeling: uncertain

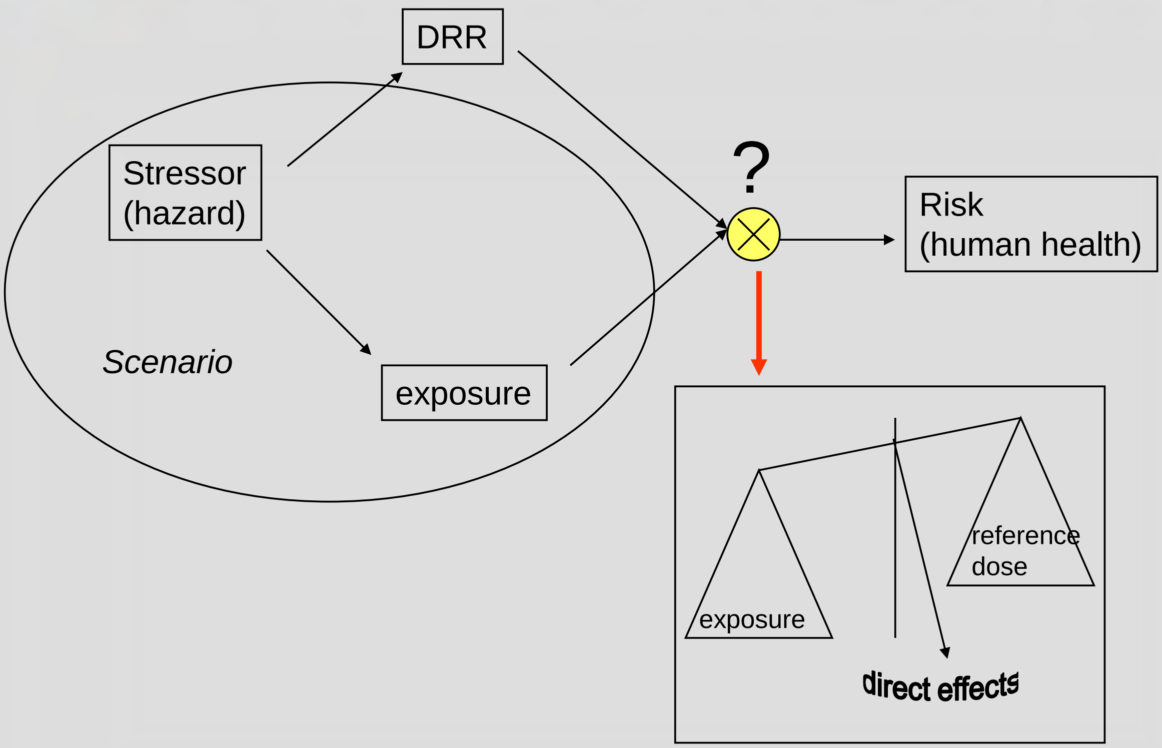
ERA: environmental BMs of exposure
matrix specific sentinels
….

↓

minimize monitoring
improve exposure modeling
integrate long term exposures
…

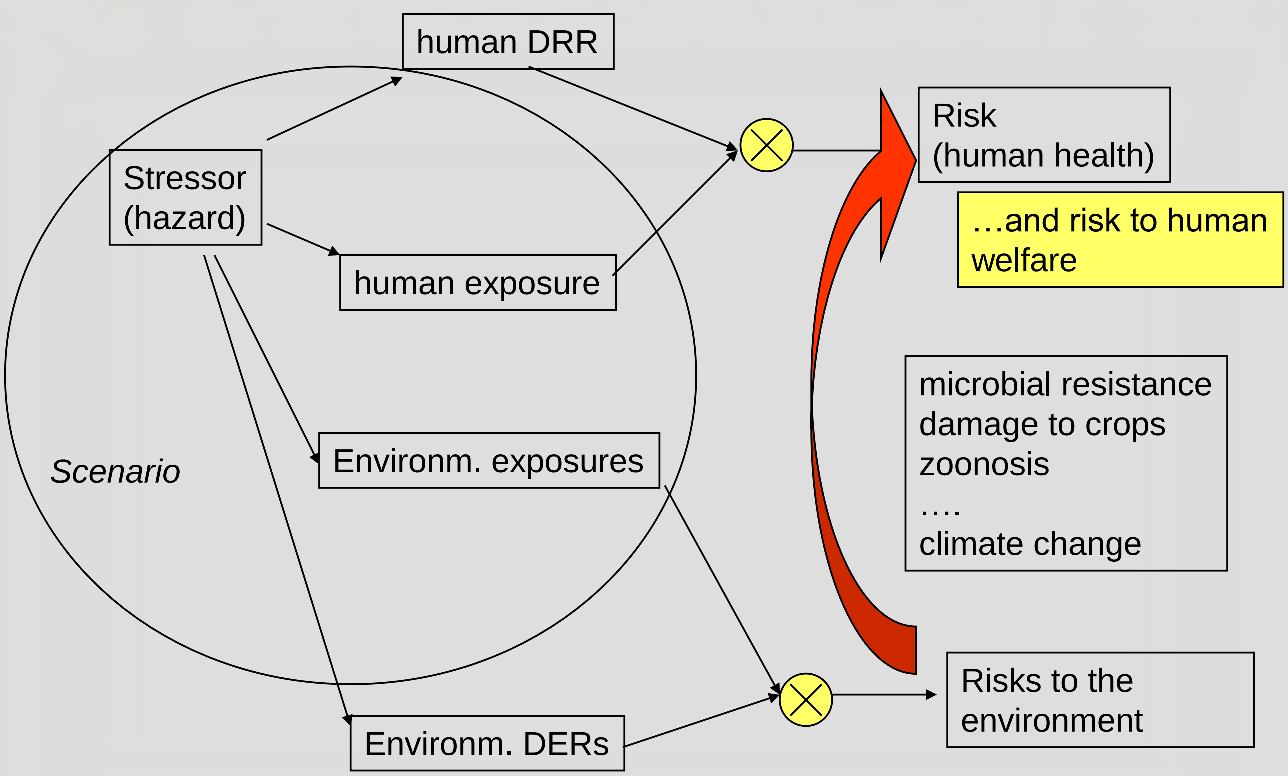
e.g. transfer along food chains

Risk assessment: not so easy IV

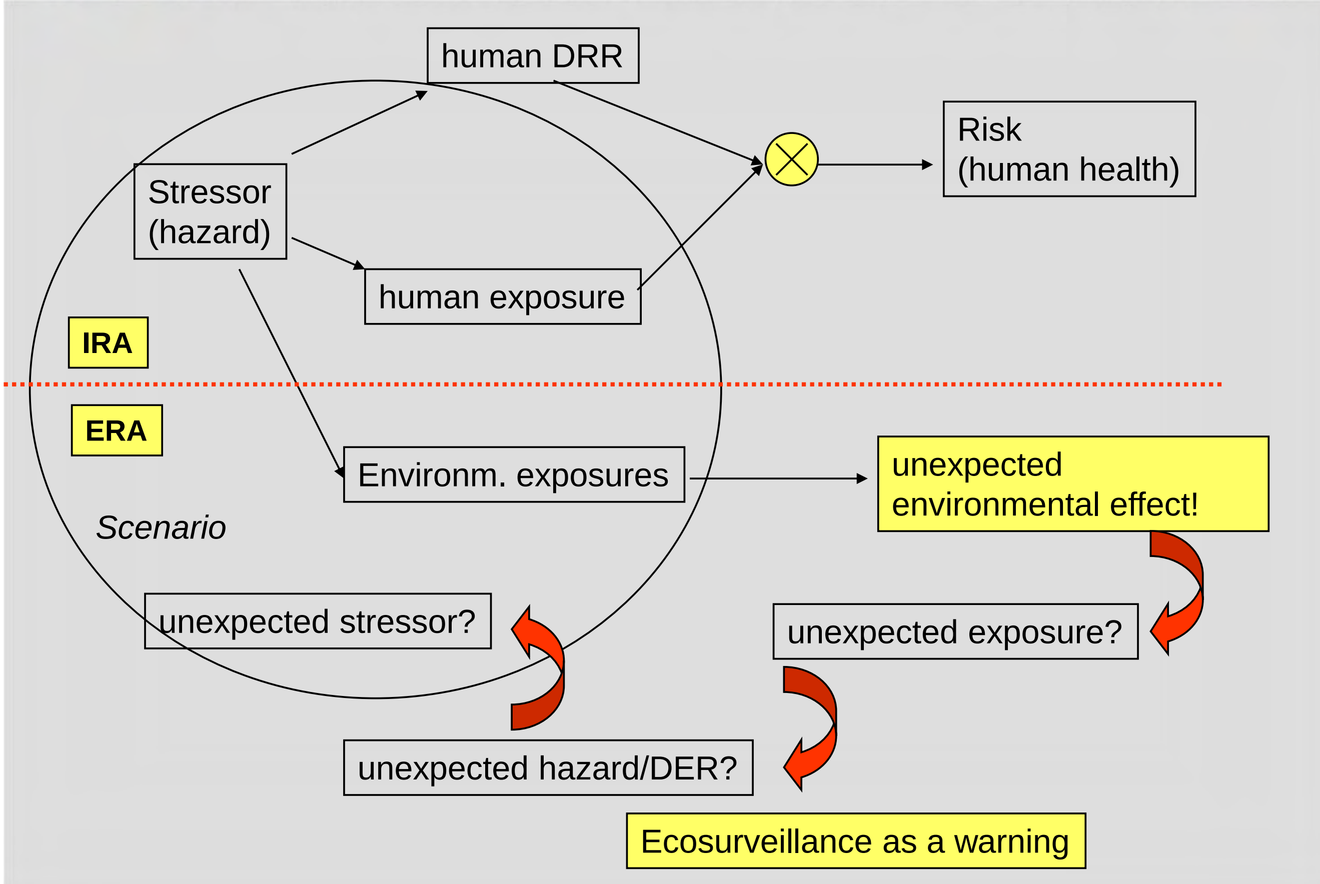


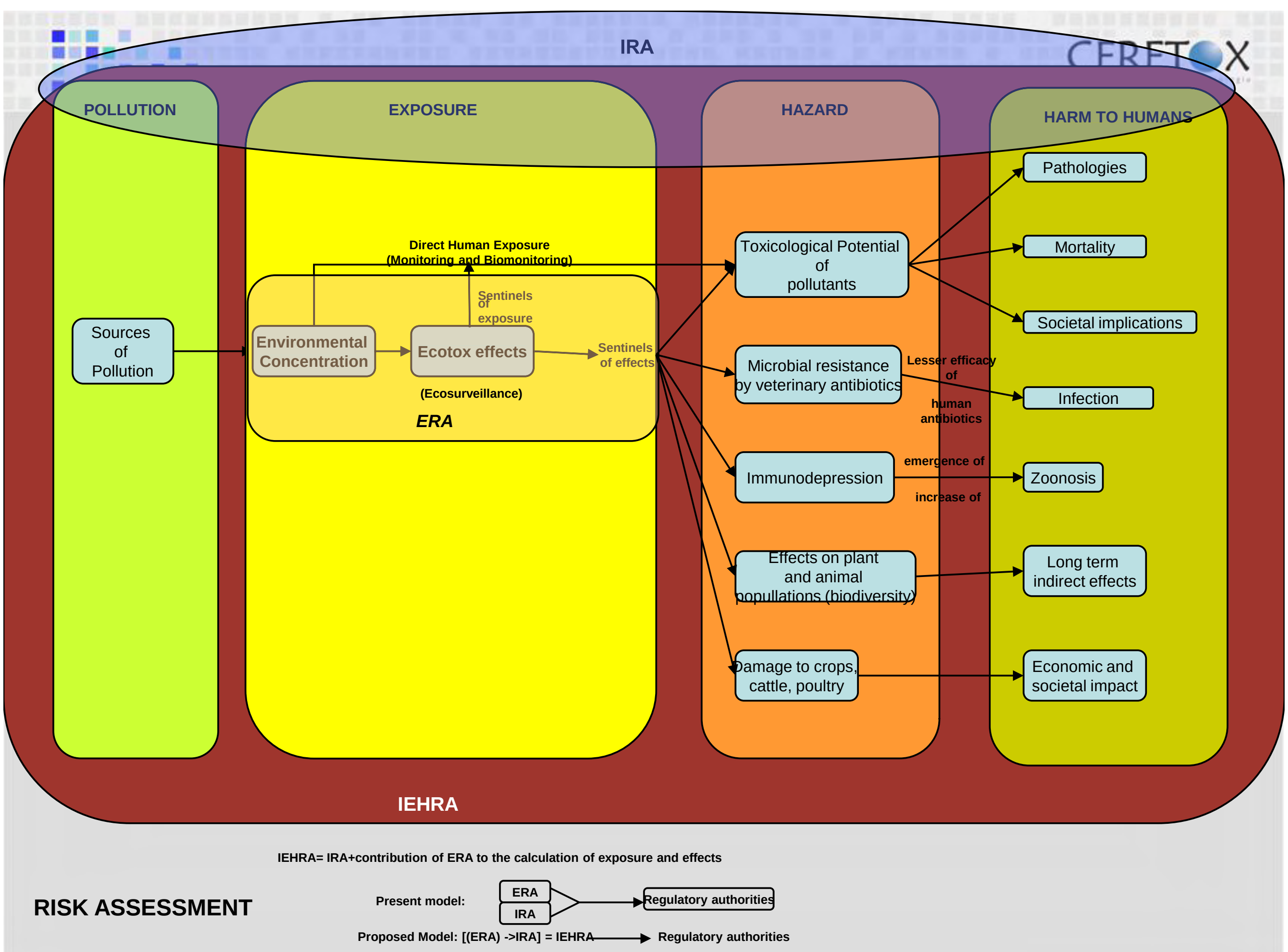
Indirect effects on human health?

Risk assessment: not so easy IV



Risk assessment: not so easy V





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- Use of "general" ecotox data (lab or field) to help in
  - identifyng new hazards
  - refining exposure calculations
  -

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Monitoring of organohalogens body burdens of the Czech population

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[2] Charles Univ., 3rd Fac.Med. Prague
[3] Institute of Public Health, Ostrava
[4] Charles Univ., 1st Fac.Med. Prague

Introduction

The Czech Republic belongs to the countries with a relatively high body burden of PCBs in the past, due to the production of commercial PCB mixtures in the Slovak part of former Czechoslovakia up to 1984 when the production was abolished.

Chlorinated pesticides were used in the agriculture in 60ties – 70ties when they were abolished, but their residua in the food chain and the dietary exposure of the Czech population are still existing.

PCDDs and PCDFs as unwanted by-products of industrial and thermal processes can be detected in the vicinity of chemical industrial plants or hazardous waste incinerators.

Introduction (cont.)

- ✓ Exposure data are essential for health risk assessment and for the efficient regulation of these pollutants.

- ✓ Human biomonitoring is the most appropriate approach to define body burden of lipophilic POPs.

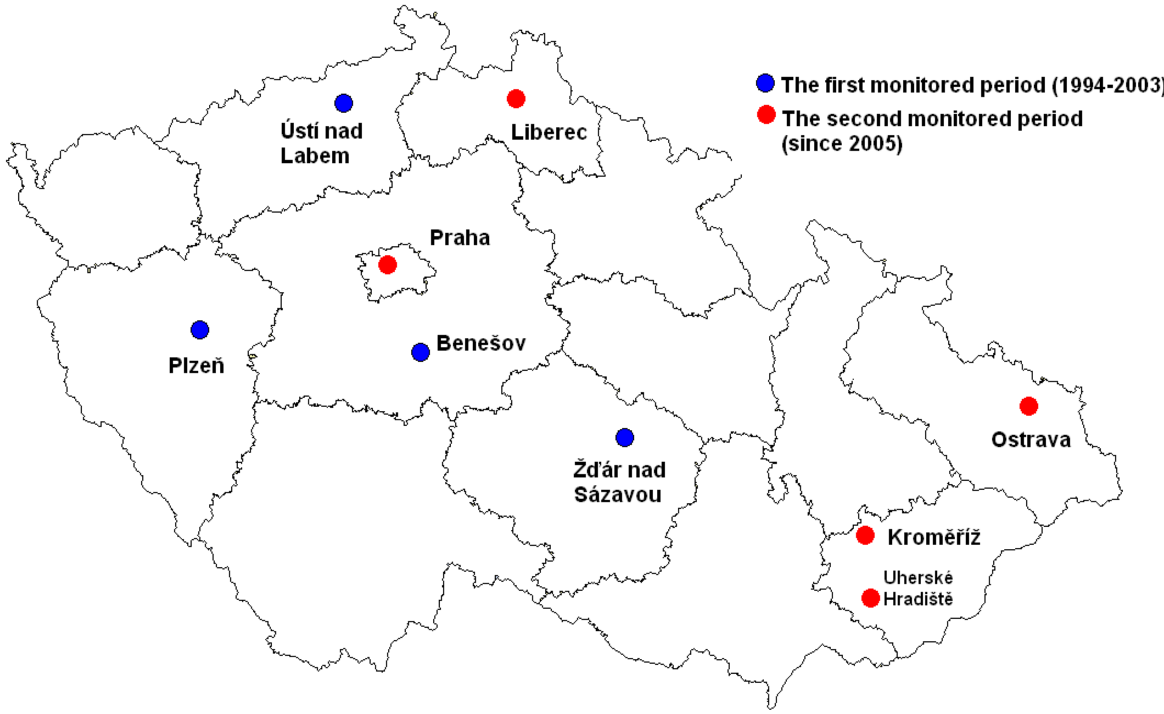
- ✓ Concentrations of POPs are measured in human body fluids and tissues containing lipids; human milk, blood serum or adipose tissue are most often used matrices.

- ✓ Systematic Biological Monitoring Programs have been conducted in several countries to determine the current levels and long-term time trends.

Biomonitoring projects realized in the Czech Republic within the last 15 years

1. CZ-HBM within the nationalwide Environmental Health Monitoring System operated in the Czech Republic since 1994 (human milk, subcutaneous fat, blood serum and others)
2. Participation in the 2nd (1992), 3rd (2000/01) and 4th (2005) round of the international WHO-coordinated Exposure Study of PCBs, PCDDs, and PCDFs concentrations in human milk.
3. Cross-sectional study of the individual levels of PCDDs/PCDFs/PCBs in altogether 81 human milk samples collected in seven regions of the CR (1999-2001).
5. Studies targeted at the residents living in the vicinity of a chemical plant or of a solid waste incinerator.
6. Retrospective study of the levels of PCBs and chlorinated pesticides in the pooled blood serum samples from Serum Biobank (1970-2000) supported by Ministry of Health (IGA NR/9015-3).

CZ-HBM – monitored areas in the 1st and 2nd period

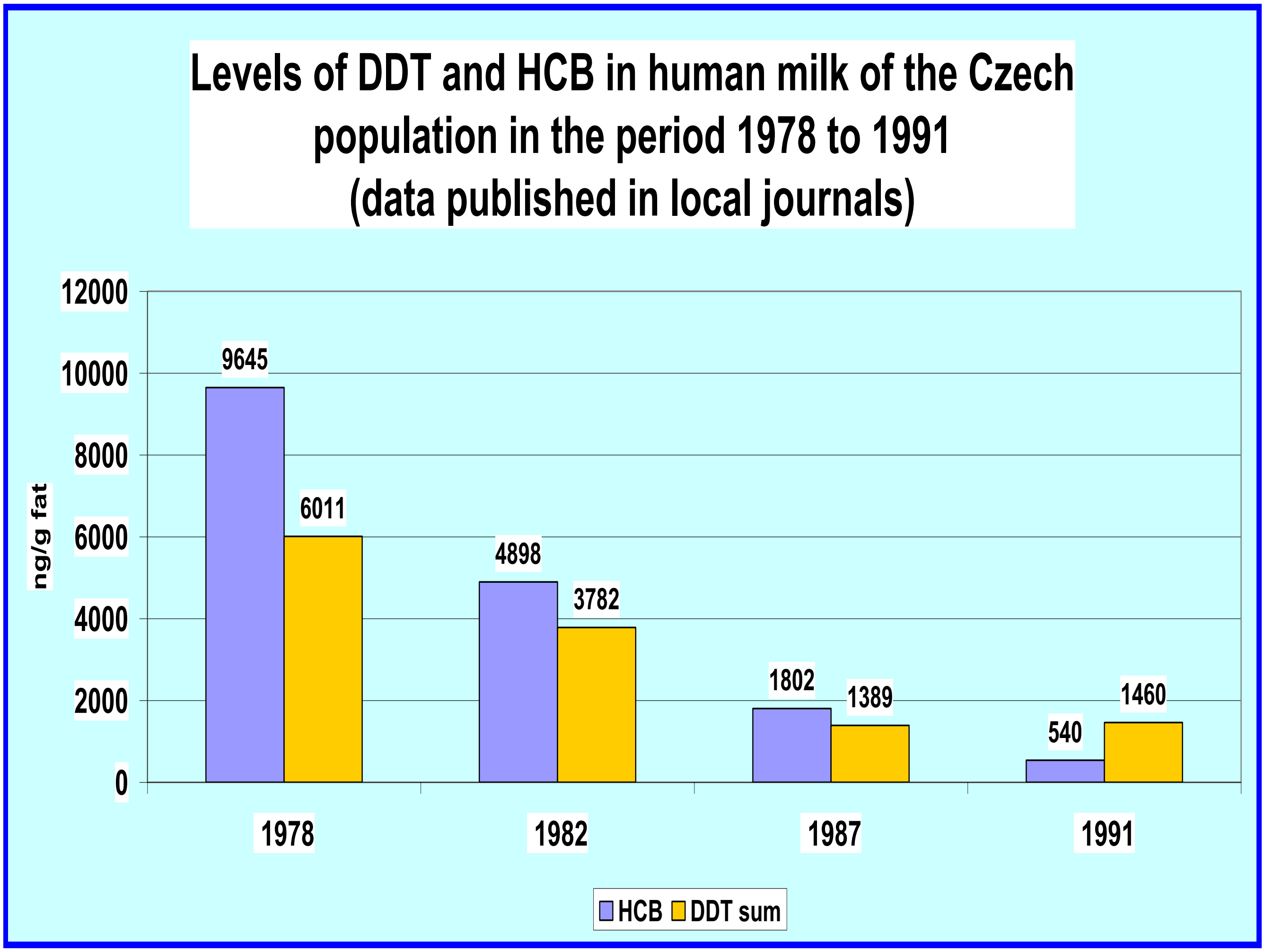


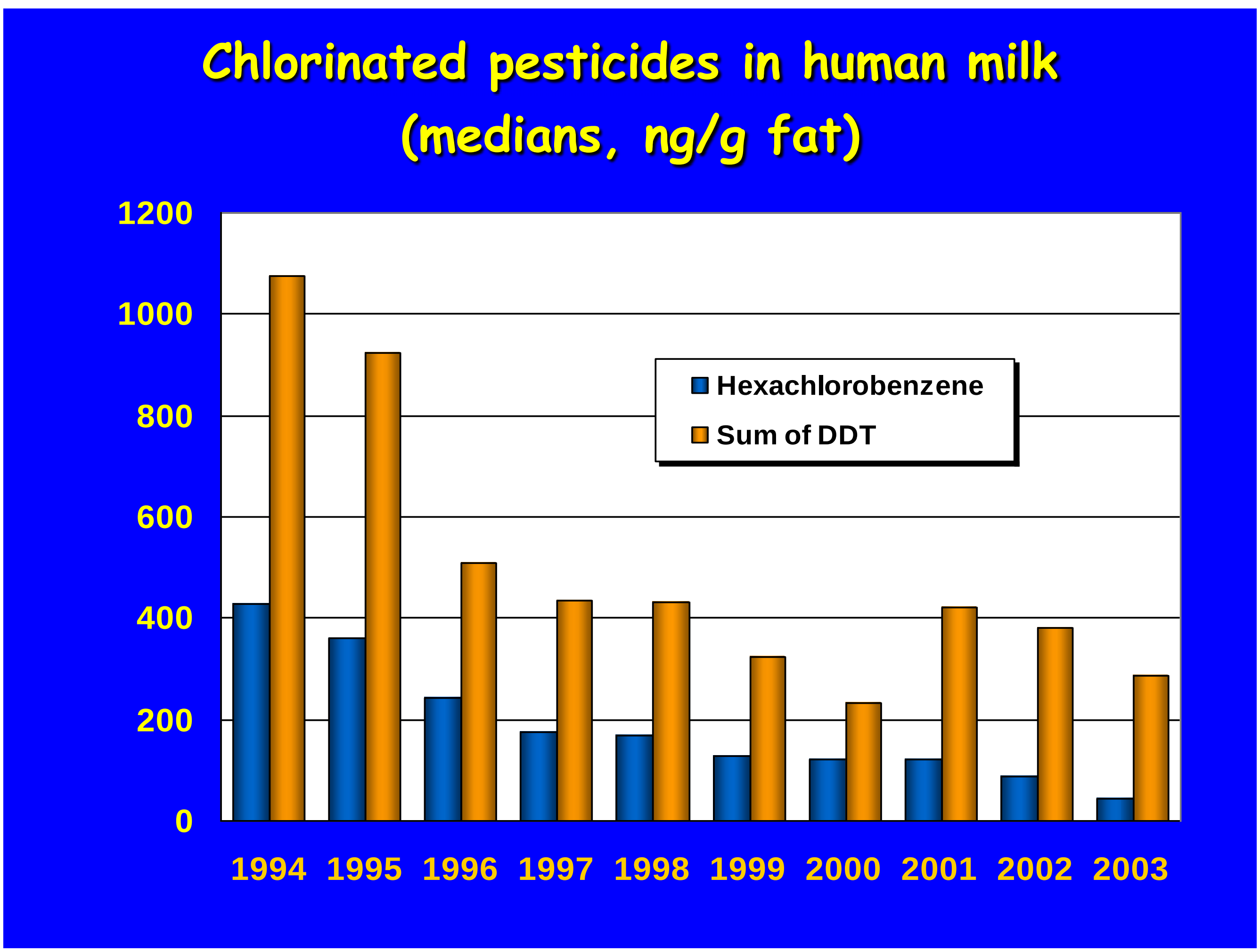
A

Concentrations of selected chlorinated pesticides in human body of the Czech population

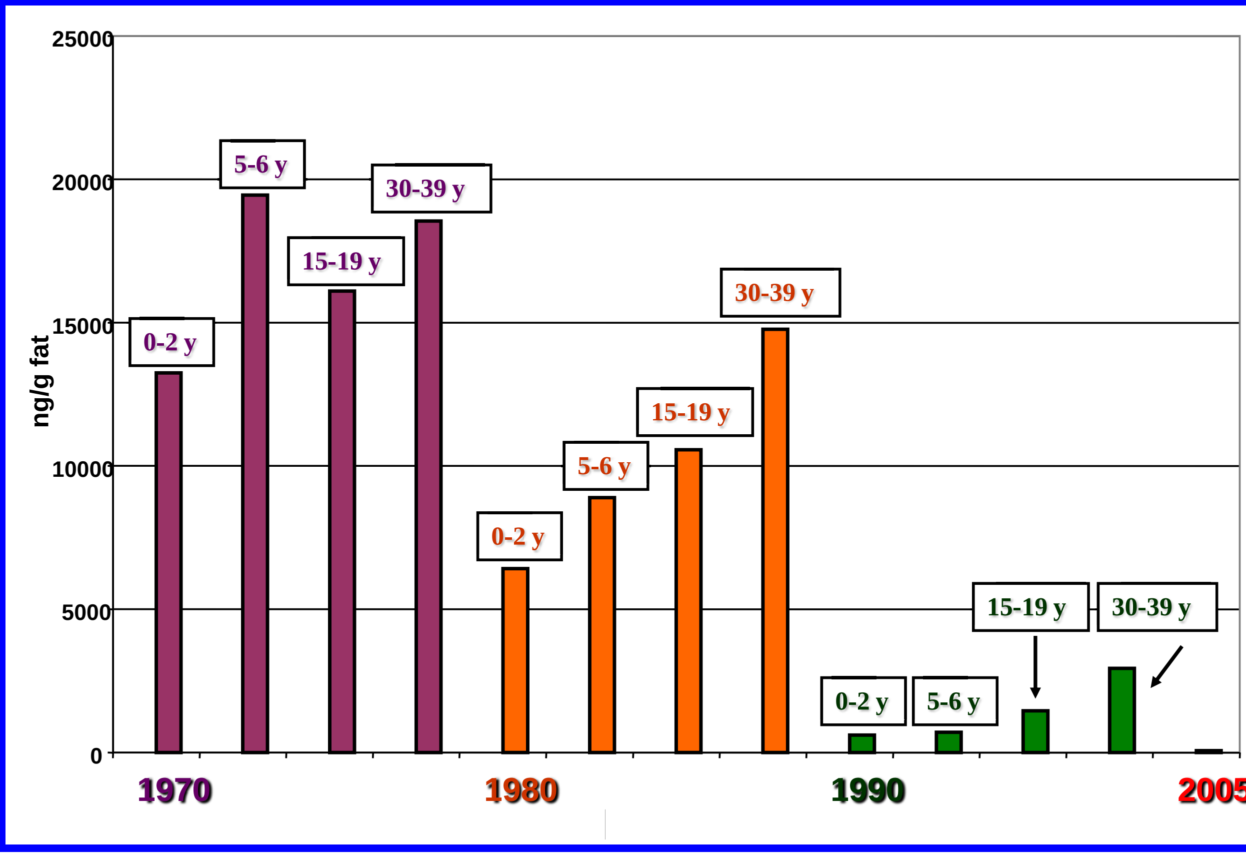
I. Human milk

II. Blood serum

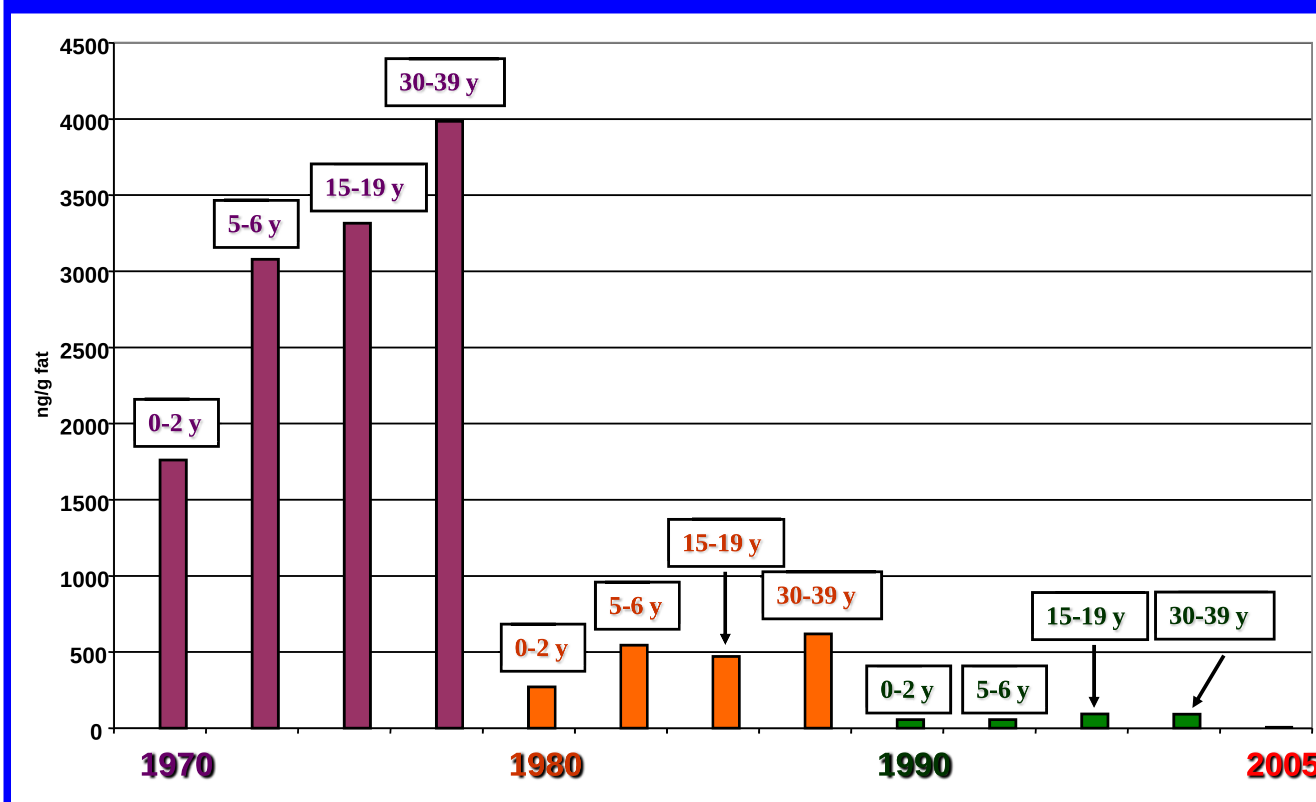

Levels of DDT and HCB in human milk of the Czech population in the period 1978 to 1991
(data published in local journals)
ng/g fat
12000
10000
8000
6000
4000
2000
0
9645
6011
4898
3782
1802
1389
540
1460
1978
1982
1987
1991
HCB
DDT sum


Chlorinated pesticides in human milk
(medians, ng/g fat)
1200
1000
800
600
400
200
0
Hexachlorobenzene
Sum of DDT
1994
1995
1996
1997
1998
1999
2000
2001
2002
2003

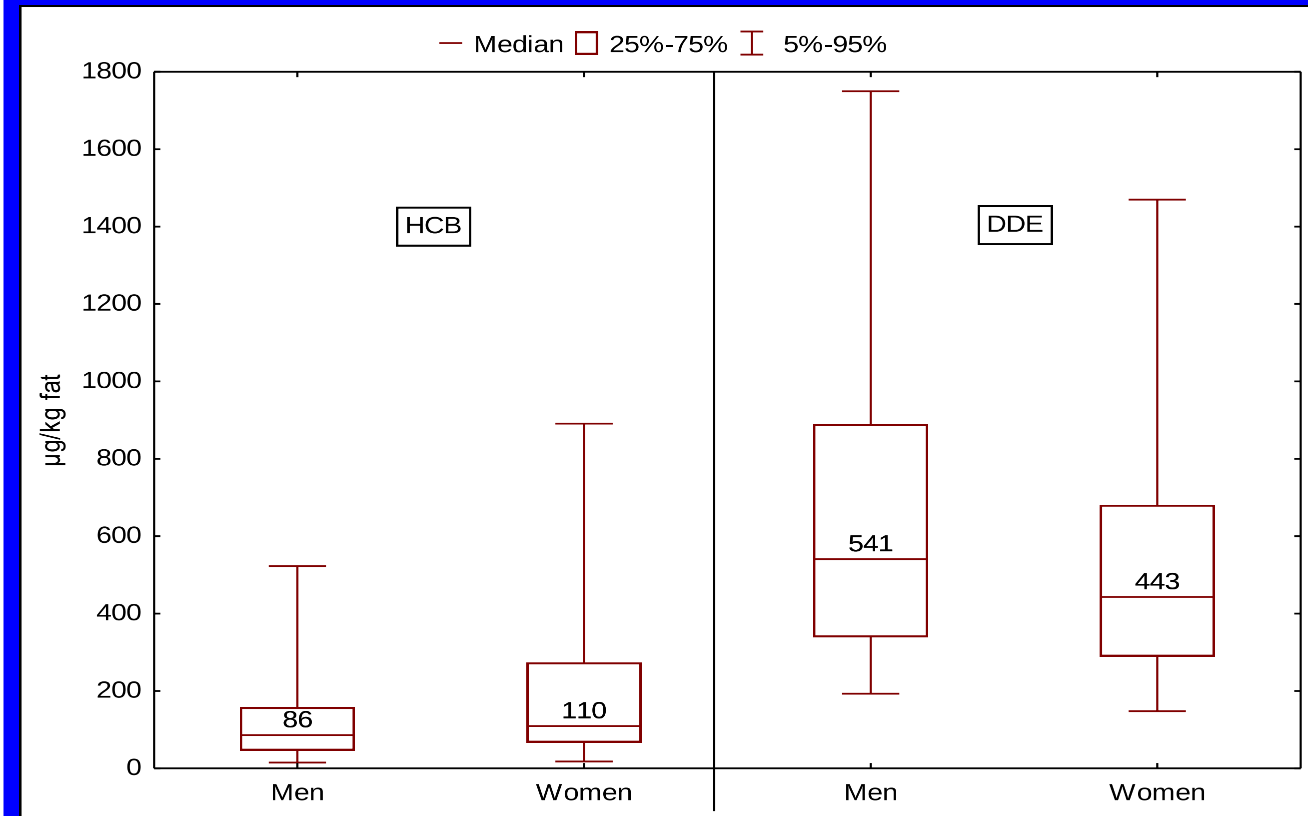
Retrospective study – levels of HCB in the pooled serum samples from Ostrava



Retrospective study – levels of DDT in the pooled serum samples from Ostrava



Levels of HCB and DDE in human blood serum (μg/kg fat) in 2005



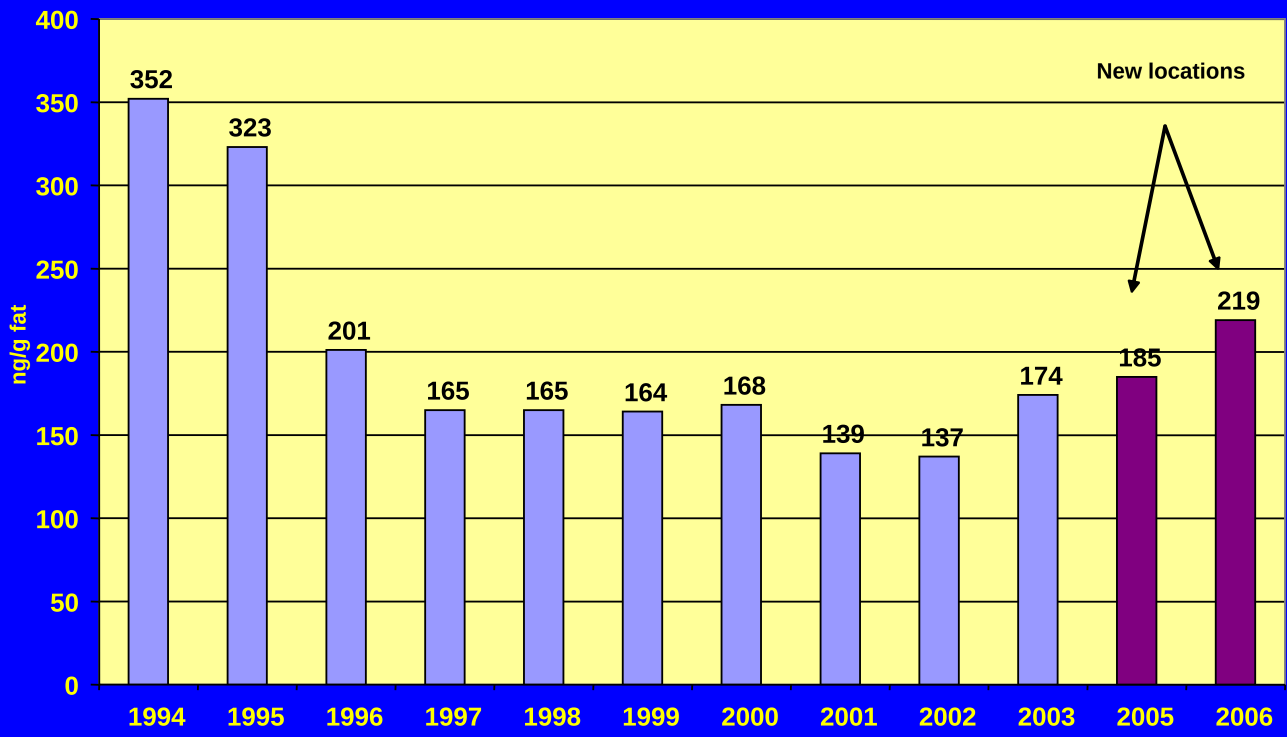
B

Concentrations of polychlorinated biphenyles in human body of the Czech population

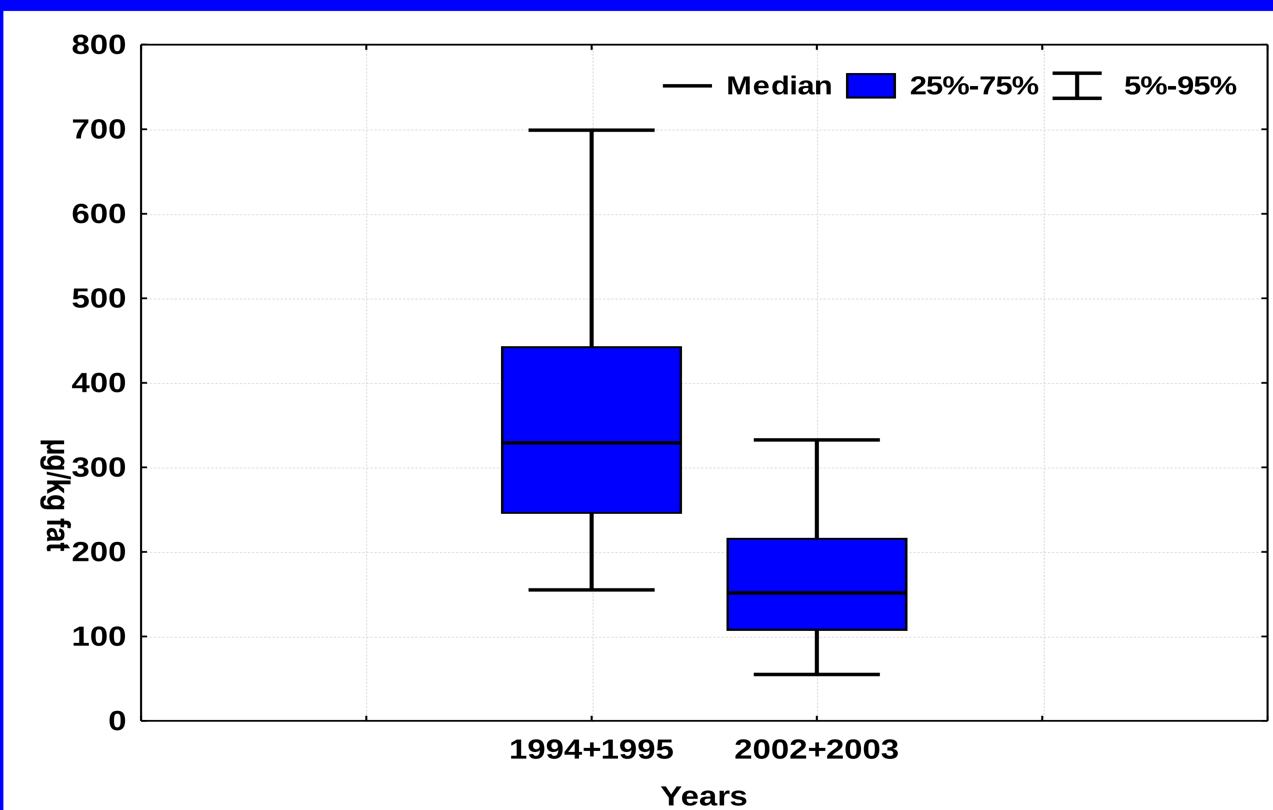
I. Human milk

II. Blood serum

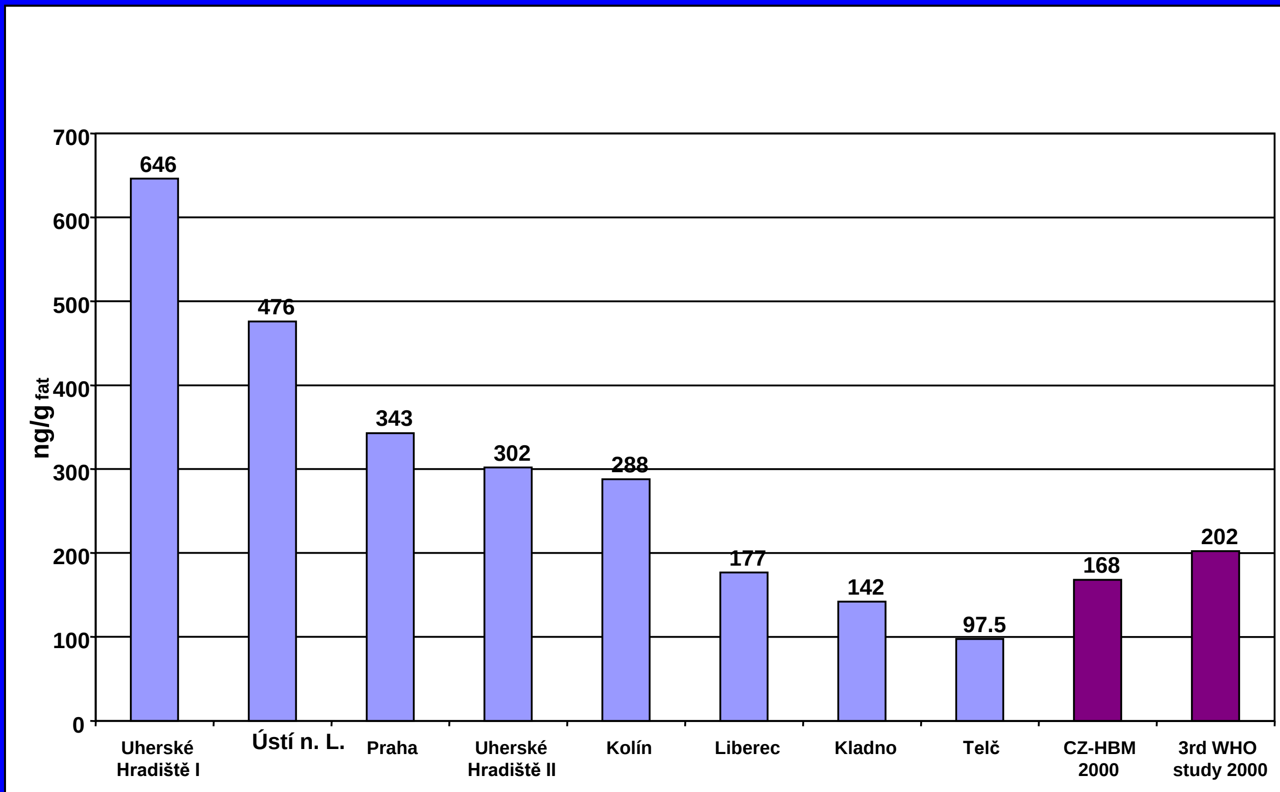
CZ-HBM: time-related median values of PCB congener 153 in human milk



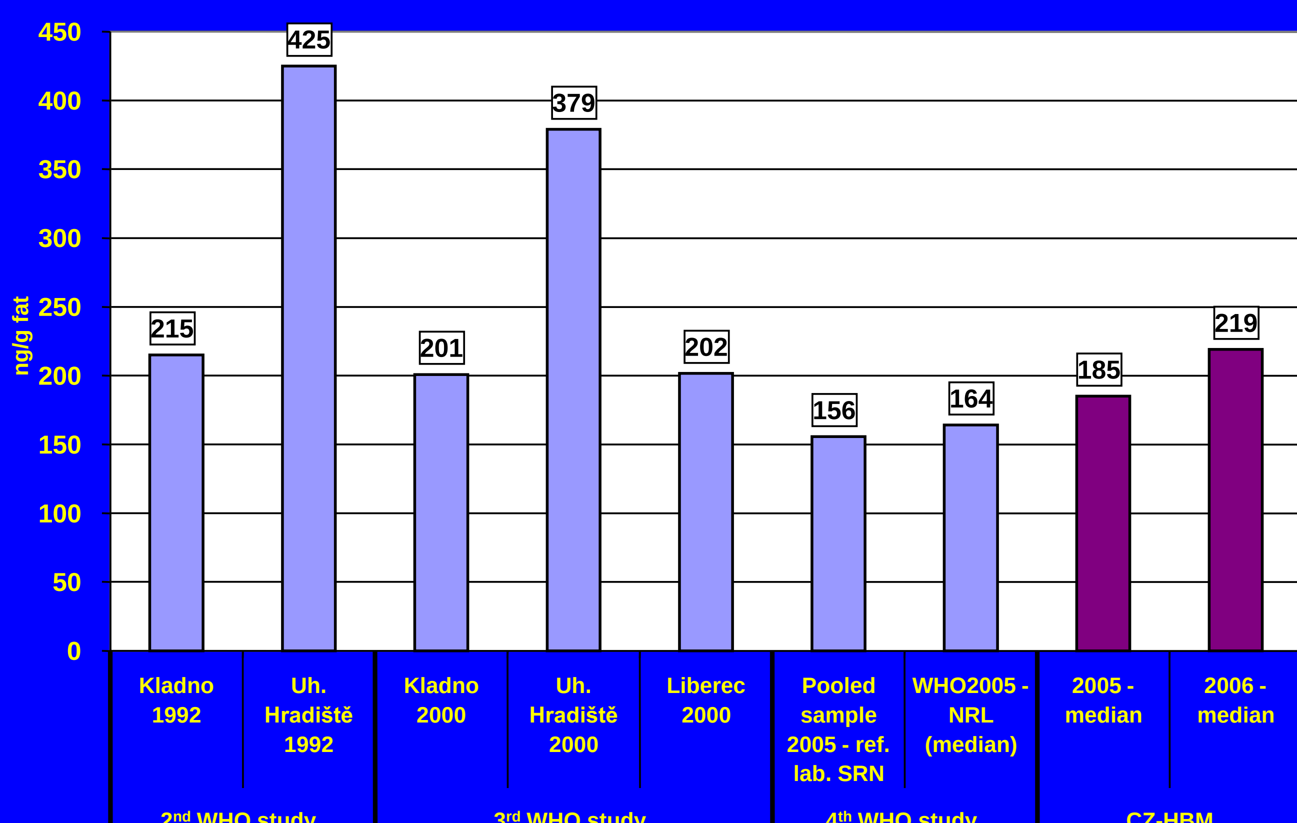
Levels of indicator PCB 153 in human milk fat: differences in reference values throughout the years



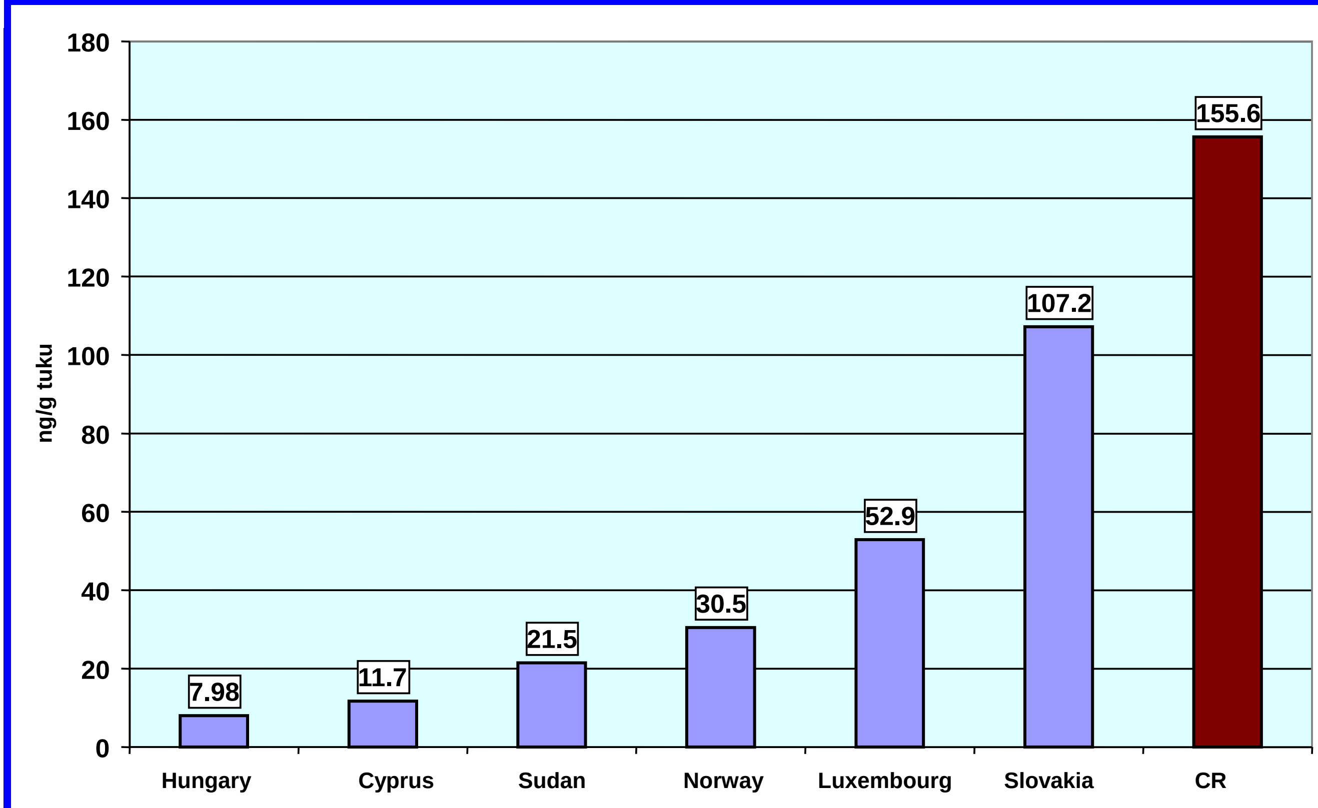
Median levels of PCB 153 in human milk analyzed in cross-sectional study in 2000 - comparison with the CZ-HBM and the 3rd WHO-study data



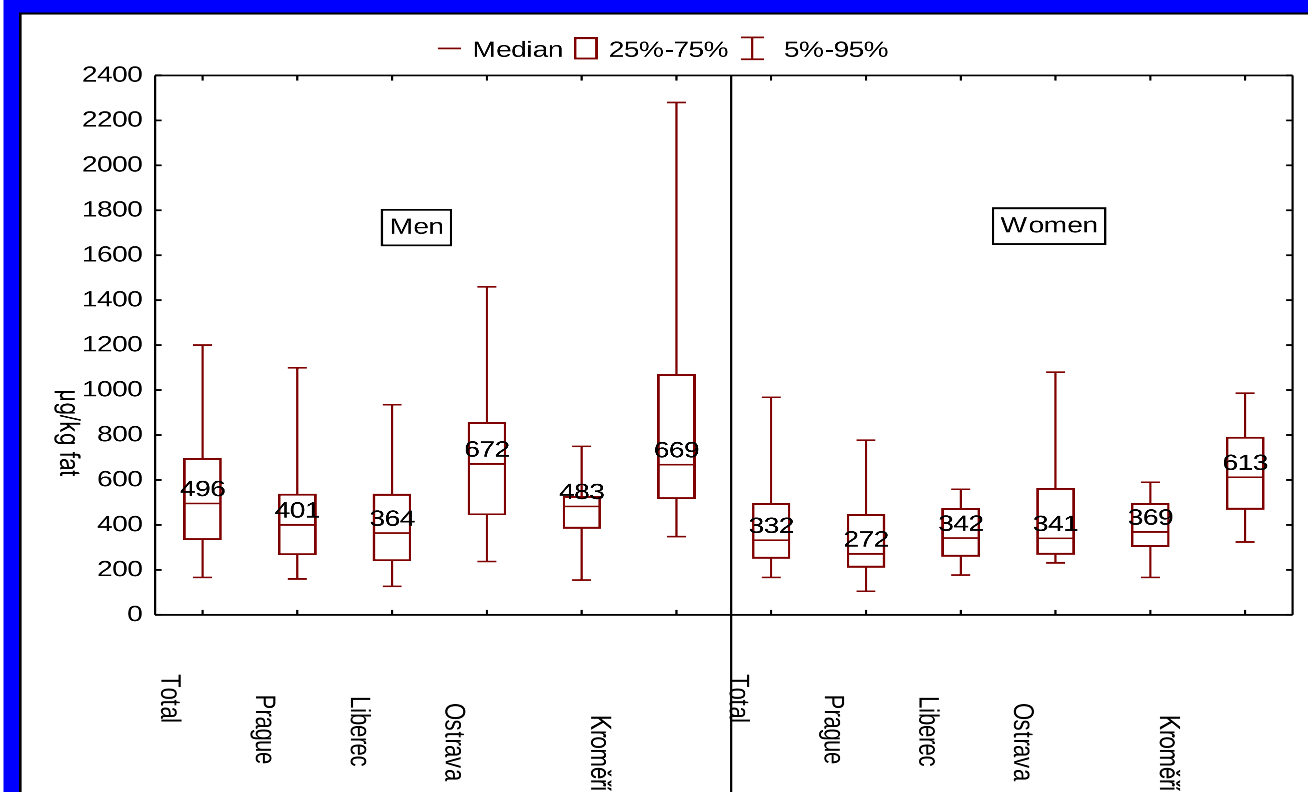
WHO - coordinated studies: levels of PCB 153 in human milk



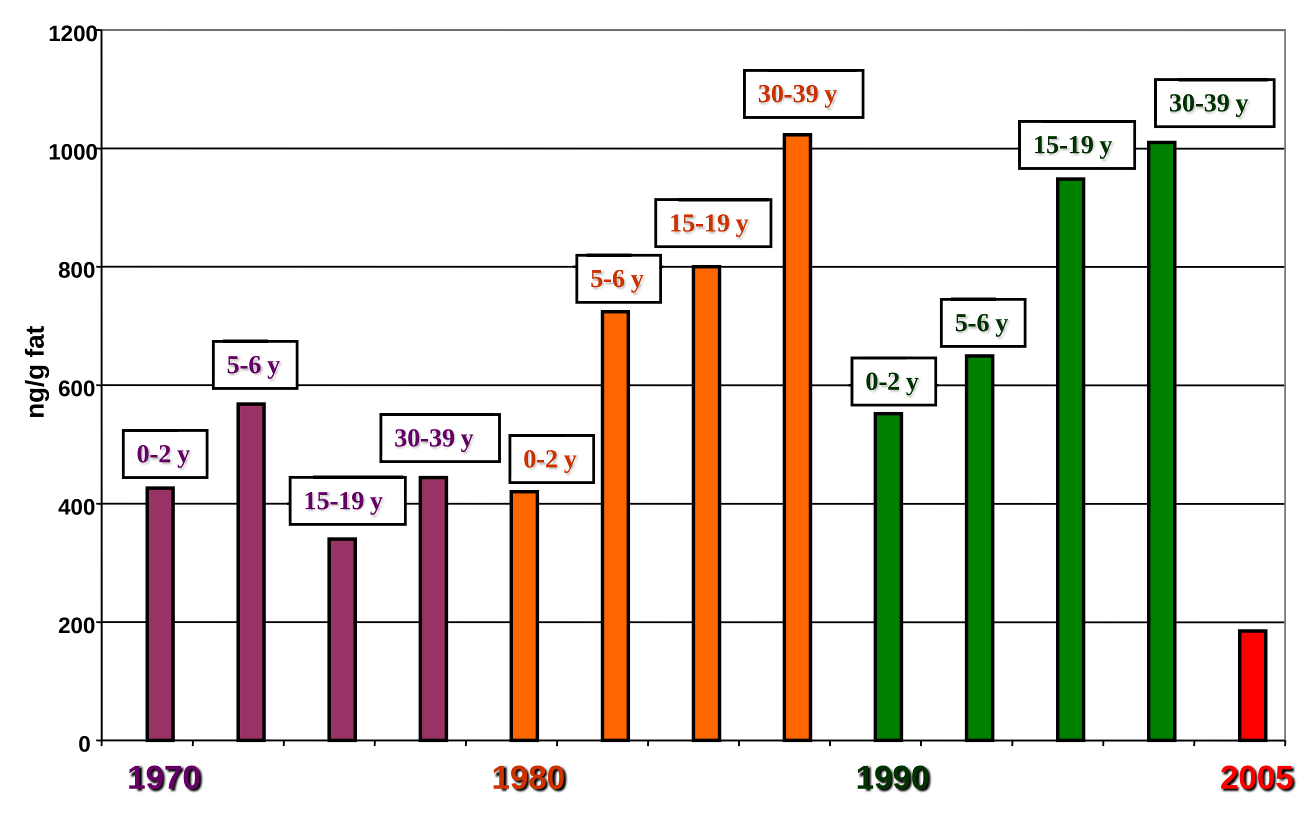
4th international WHO coordinated study: levels of PCB 153 in pooled samples of human milk



Levels of PCB congener 153 in human blood serum (µg/kg fat) in 2005



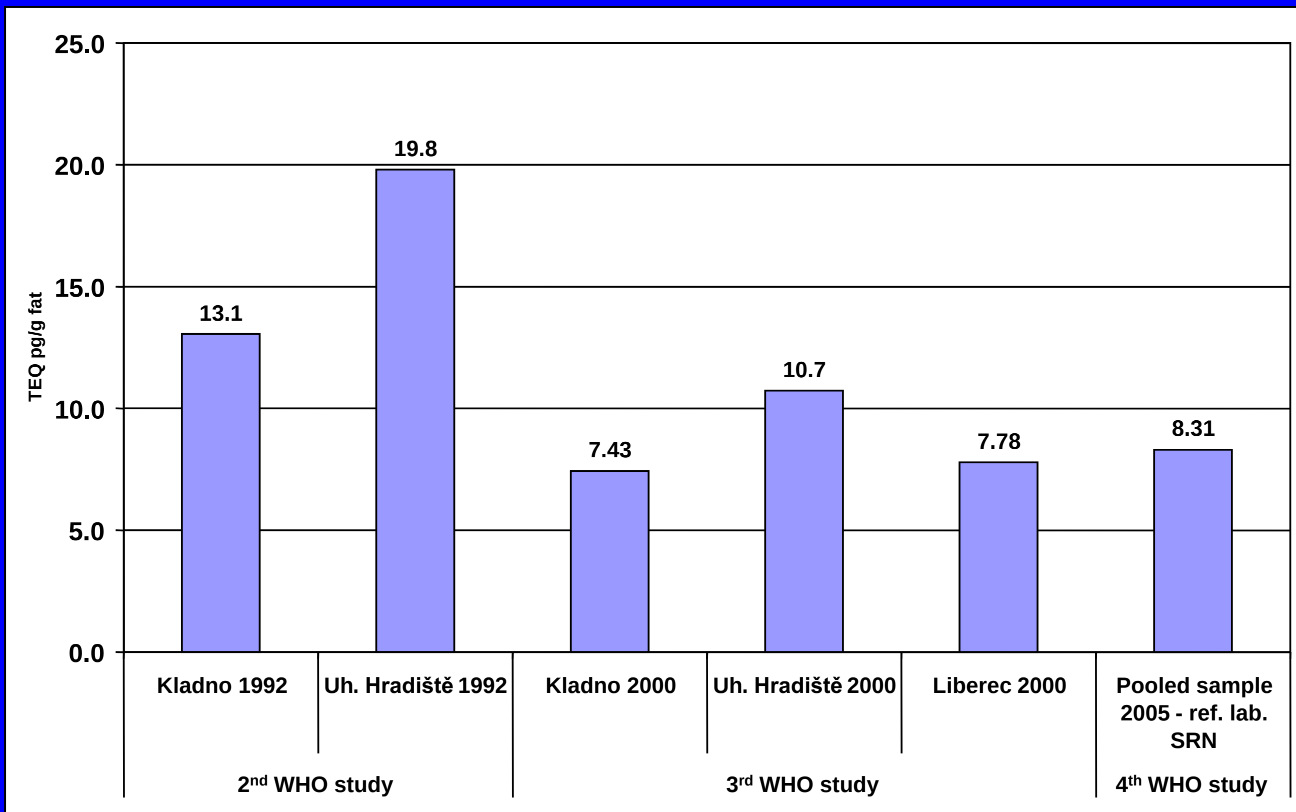
Retrospective study – levels of PCB 153 in the pooled serum samples from Ostrava



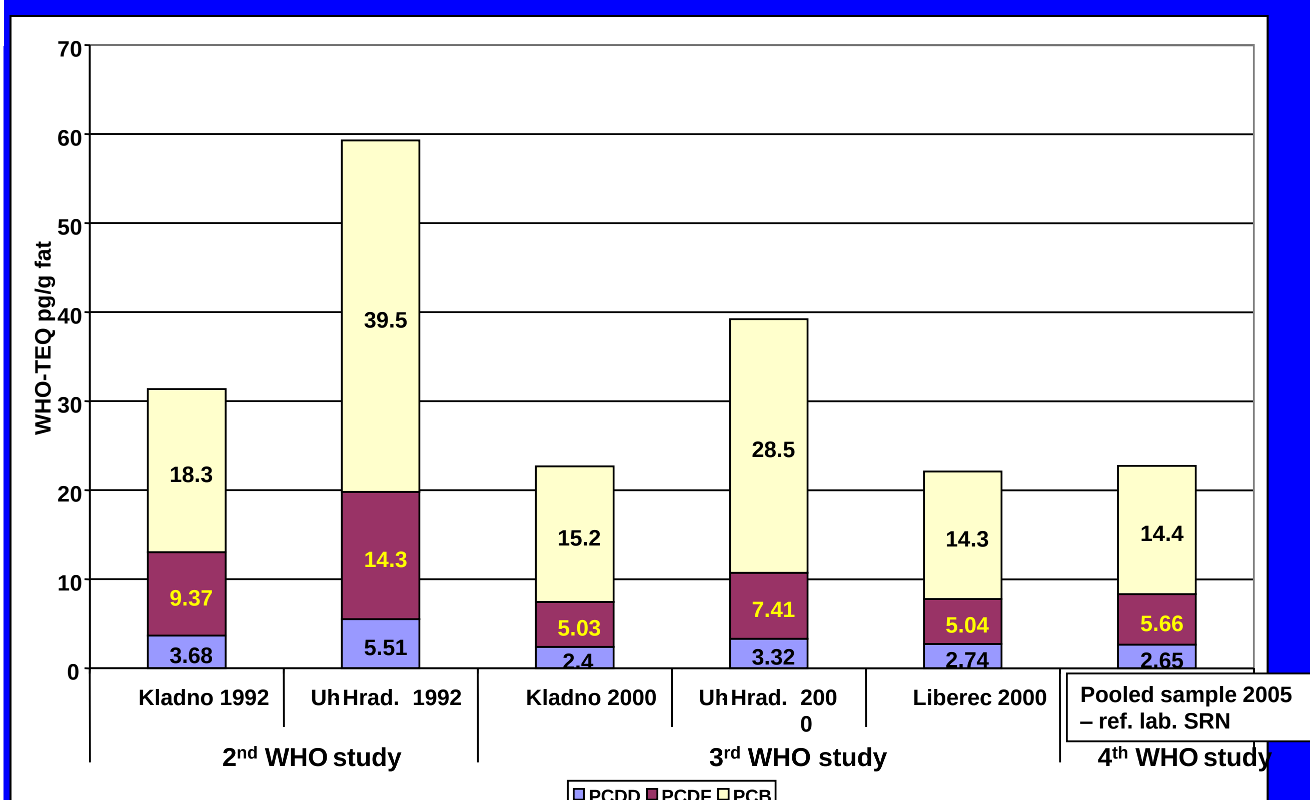
C

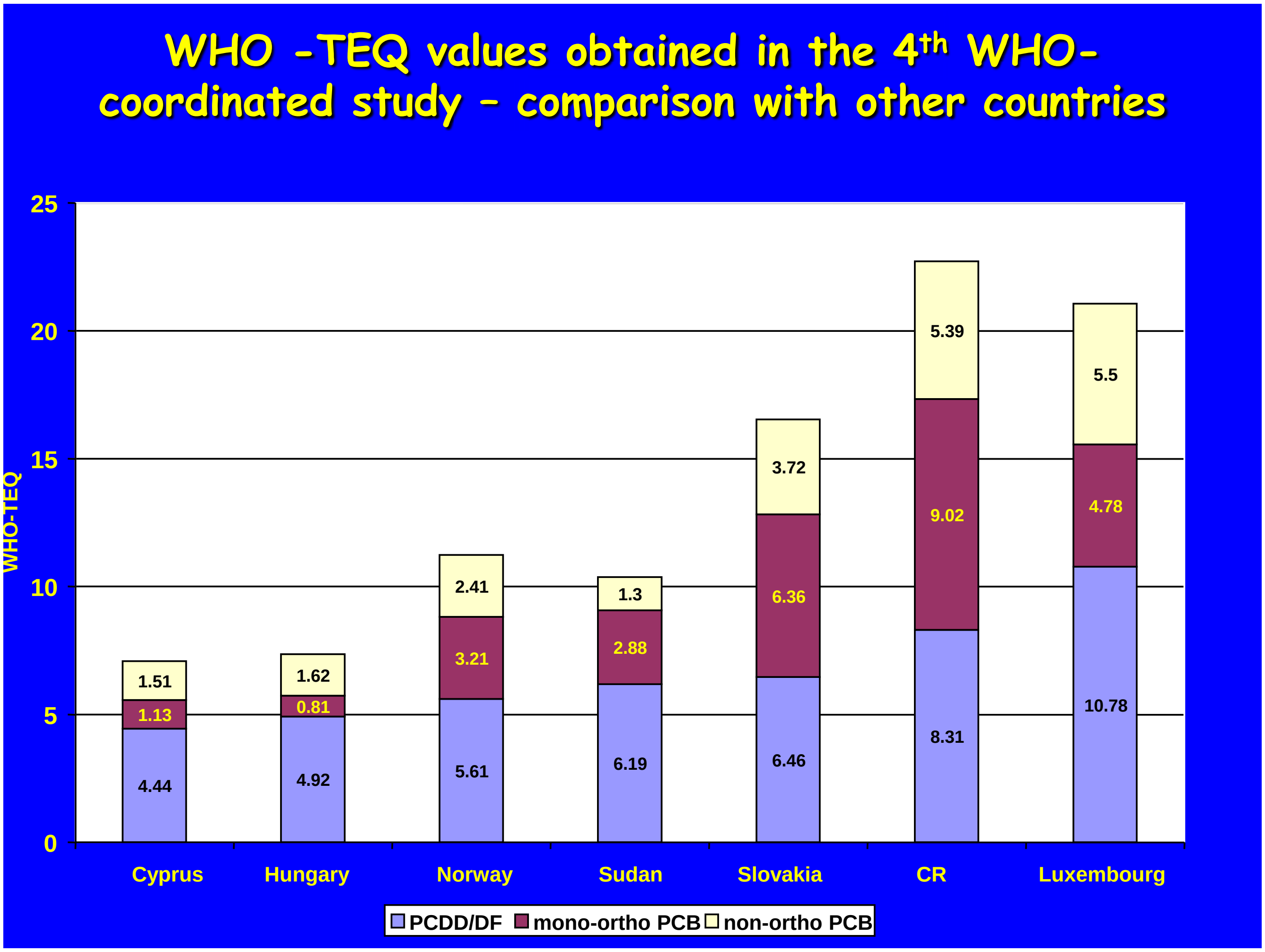
Concentrations of PCDDs, PCDFs, and dioxin-like PCBs in human body of the Czech population

WHO studies - TEQ levels of PCDDs/PCDFs in human milk of the Czech population



WHO -TEQ values obtained in WHO-coordinated studies in the Czech Republic





Conclusions

Sufficient data on the POPs body burden of the Czech population are available.

Significant local differences, individual variability and increased levels of POPs with age are observed.

Despite the significant declining trend (by around 50 %) of PCB in human milk over the 90-ties, Czech population is still at an increased exposure risk.

Long-term declining trends are observed for HCB and DDT sum.

Our results confirmed the existence of hot-spot locations within the country.

The levels of PCDDs/PCDFs in human mílk of the Czech population are comparable with those in EU countries.

Dioxin-like PCBs (mostly 126, 156) contribute more than 60% to WHO-TEQ value.

Future plans

The data presented can be used for estimation of the Czech background exposure (as related to Stockholm convention).

Reference values for POPs components will be assessed with respect to time period, population group and age.

Long-term time trends in body burden will be followed-up.

The health consequences of the temporary elevation of infant body burdens are uncertain.

Further health-related studies in this field are to be recommended.

Thank you for your attention

Acknowledgement:

Partially funded by the Research grant IGA NR/9015-3 of the Czech Ministry of Health

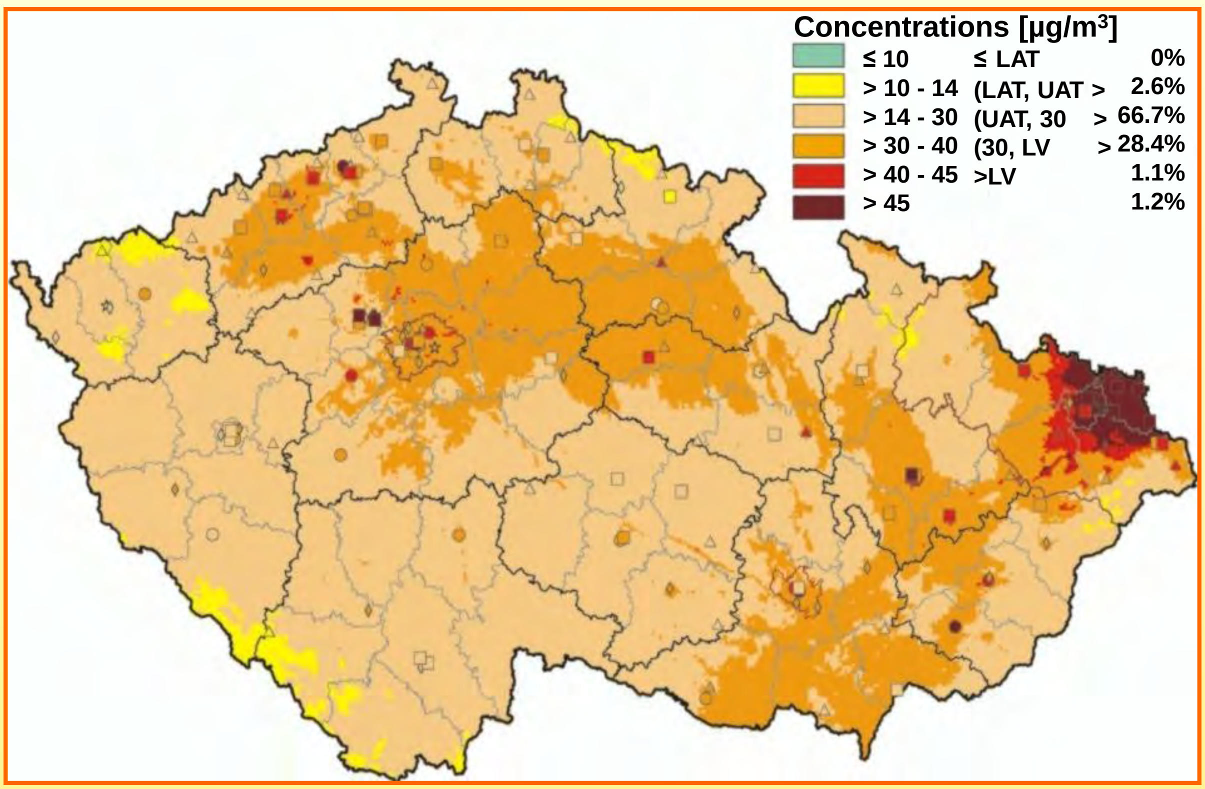
EXPOSURE TO c-PAHS CASE STUDIES

Radim J. Sram

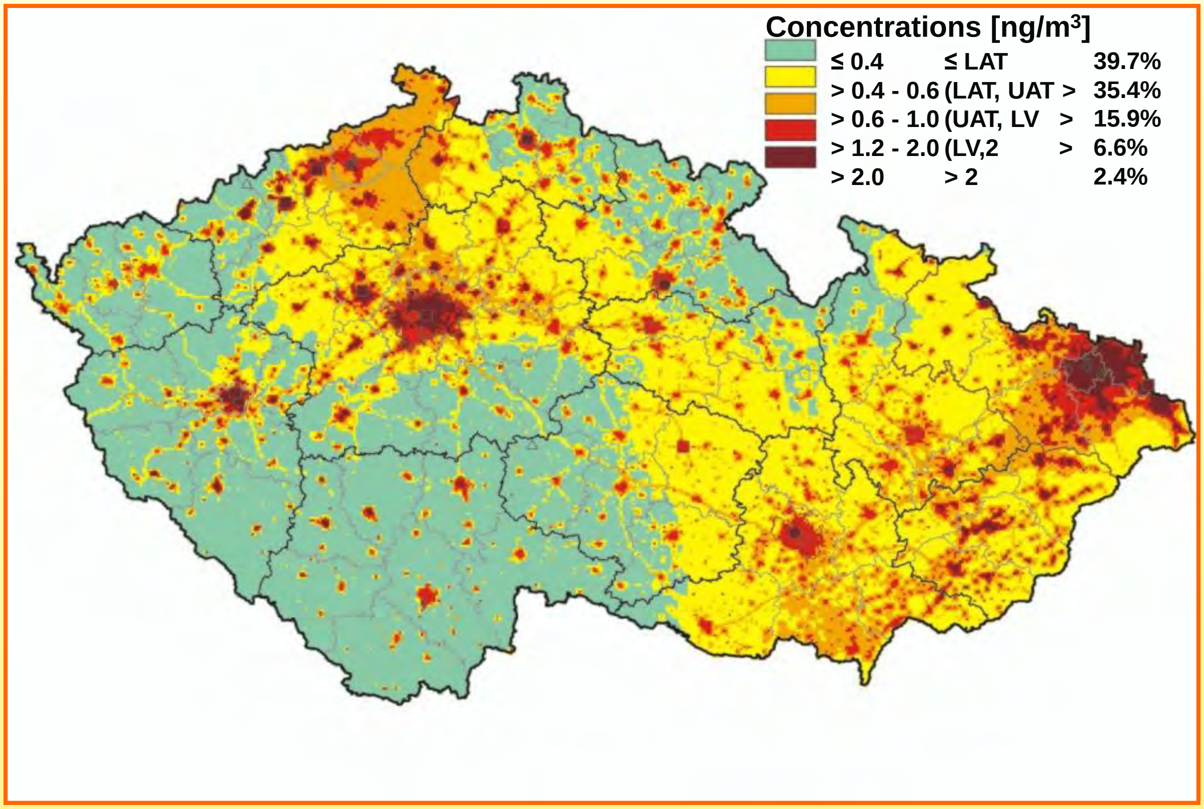
Institute of Experimental Medicine AS CR, v.v.i.,
Prague, Czech Republic

INTARESE, Tromso, Norway, June 2-5, 2008

PM10 - 2006

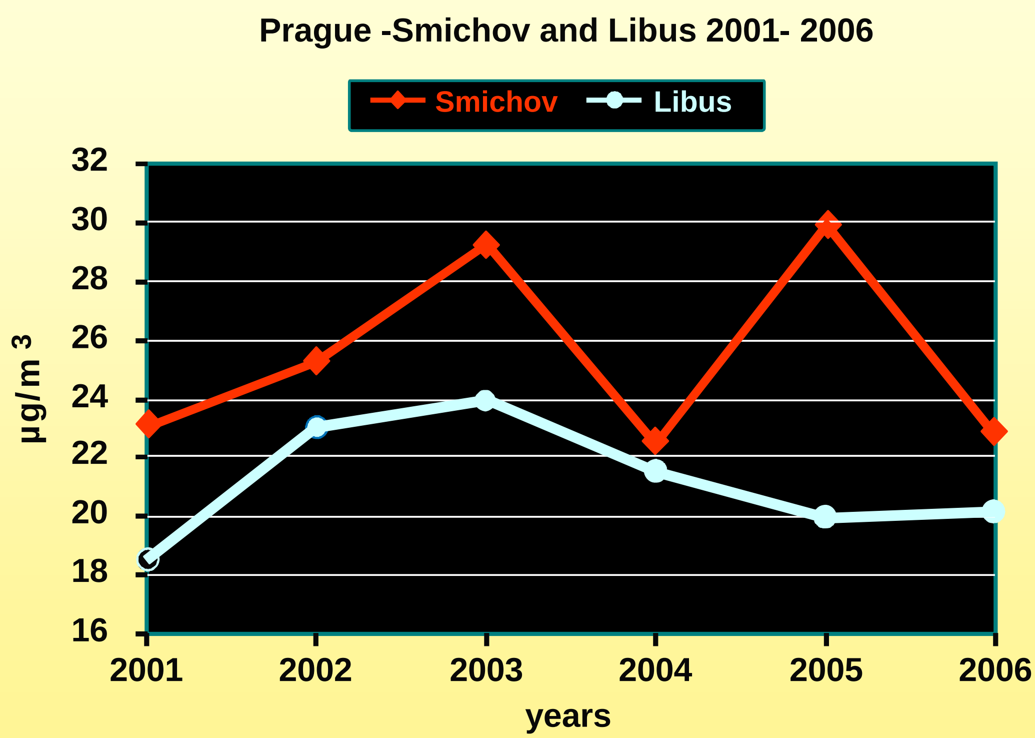


B[a]P - 2006



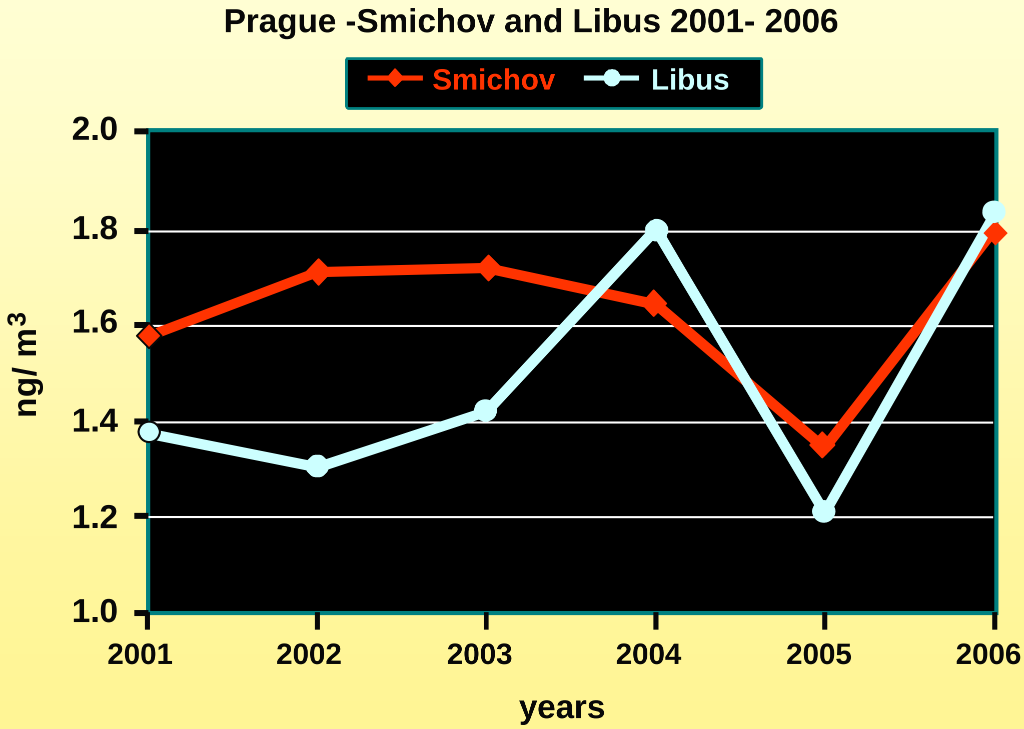
R.J.Sram 2008

Annual average of PM2.5



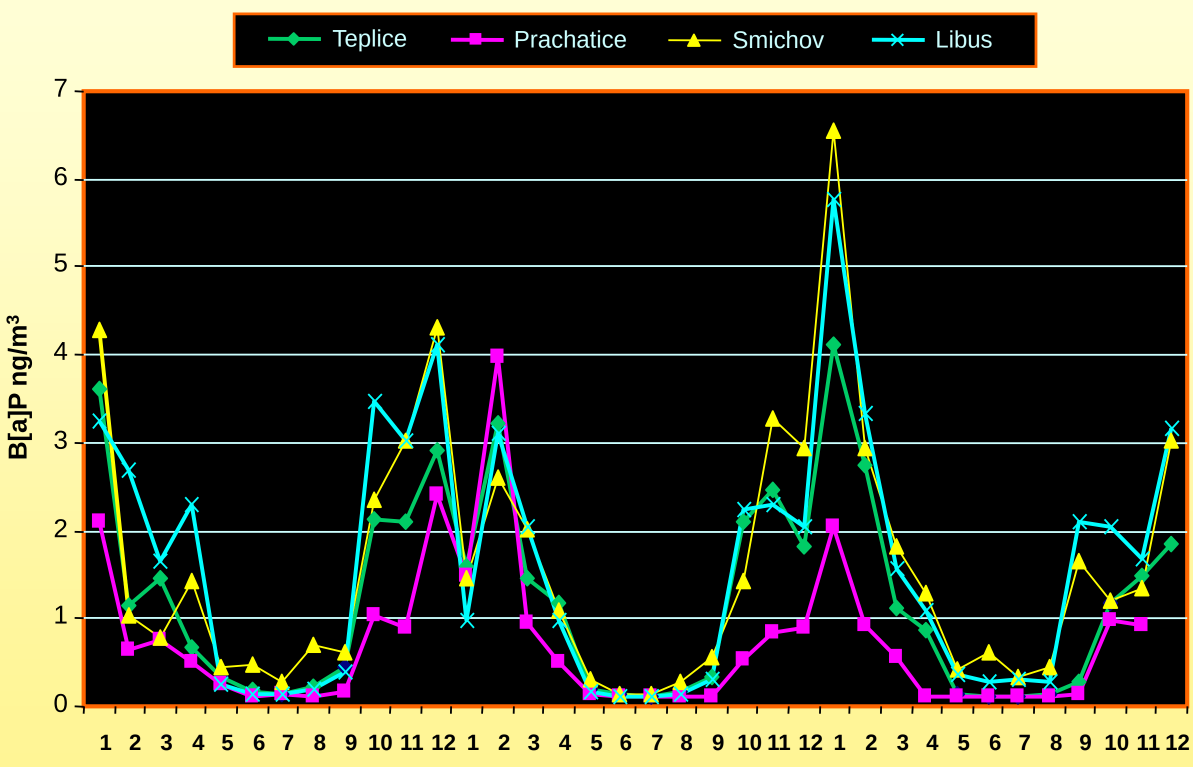
R. J. Sram 2008

Annual average of B[a]P



R. J. Sram 2008

Monthly average concentration of B[a]P



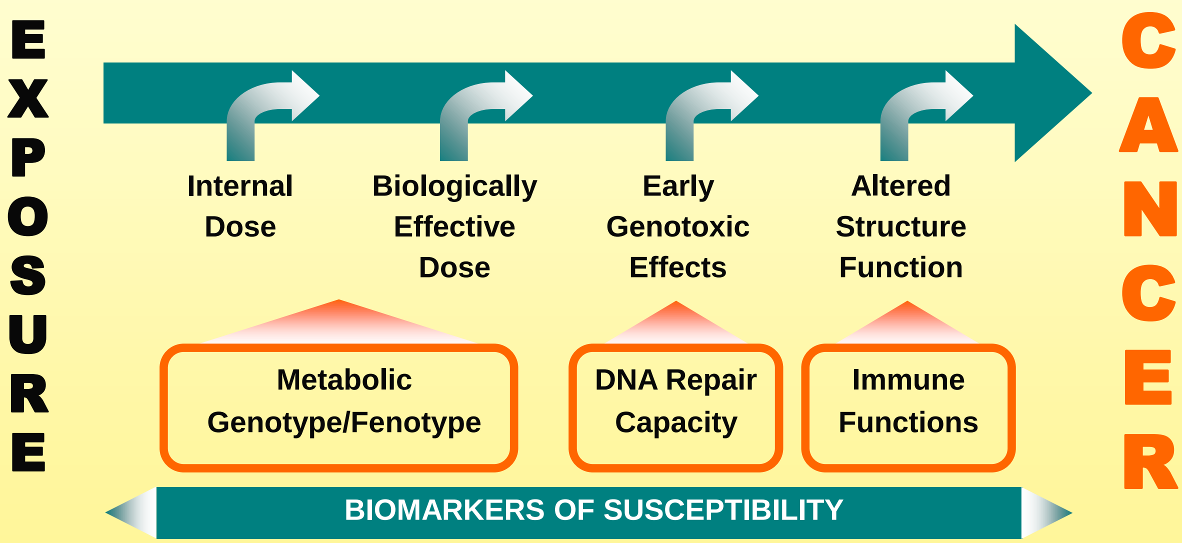
R. J. Sram 2008

BIOMARKERS

R. J. Sram 2008

HUMAN BIOMARKERS

Genetic/Carcinogenic Risks



R. J. Sram 2008

Environ Health Perspect 74: 3-9, 1987

BIOMARKERS OF EXPOSURE

DNA adducts
^{32}P-postlabeling, ELISA

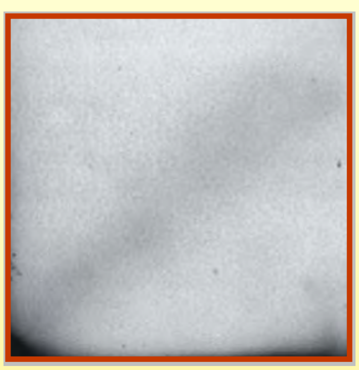
protein adducts
GC-MS

COMET (SCGE)

proteins p53, p21

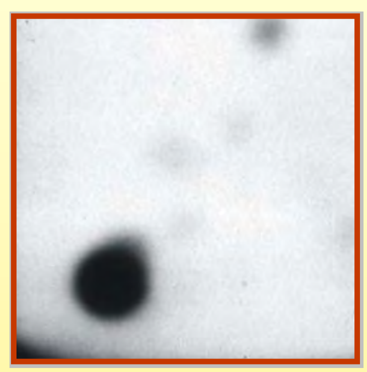
R. J. Sram 2008

Autoradiographs of thin layer chromatograms with DNA adduct pattern of:



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

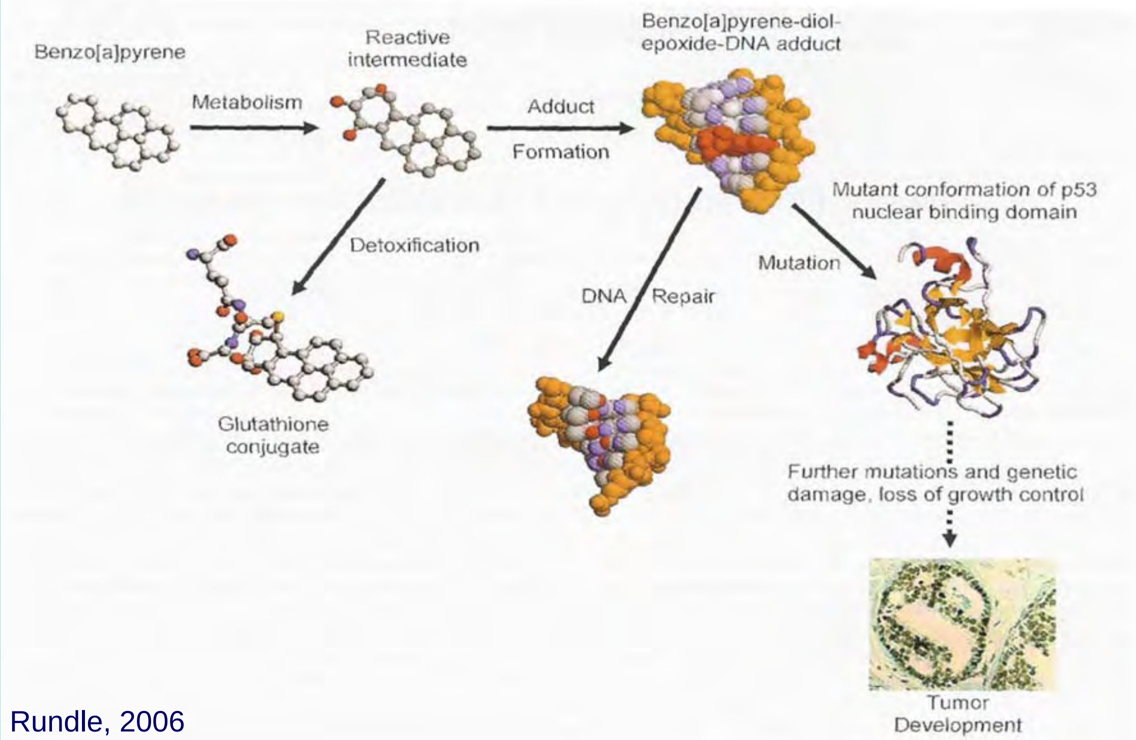
Water blank



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

R. J. Sram 2008

Mechanism of carcinogenic action of PAHs



Rundle, 2006

EXPOSURE VS. BIOMARKERS

STATIONARY MONITORING

PERSONAL MONITORING – 8 h, 24 h, 48 h

BIOMARKERS

hours (SCGE)

weeks (DNA adducts)

months (chromosomal aberrations)

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DNA ADDUCTS -B[a]P concentration

- CRACOW

  B[a]P 12 ng/m³ (Jeddrychowski et al. 2003)

- NEW YORK

  B[a]P 0.5 ng/m³ (Tonne et al. 2004)

- BANGKOK

  B[a]P 1.5 ng/m³ (Tuntawiroon et al. 2007)

- PRAGUE

  B[a]P 1.5 ng/m³ (Binkova et al. 2007)

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Multiple regression analysis

Percentage of aberrant cells (FISH)

Model	Coefficients	Unstandardized Coefficients B	Sig.	95 % Confidence Internal for B		R	Adjusted R square	Sig.
				Lower bound	Upper bound			
6	(Constant)	-0.283	-0.019	-0.518	-0.048	0.58	0.29	0.000
	Age (years)	0.012	0.000	0.007	0.017			
	CYP1A*2C (Ile/Val) (+/+)	0.144	0.024	0.020	0.268			
	B[a]P-like adducts/10+08 ncls	1.399	0.018	0.251	2.548			
	EPHX (high activity)	-0.106	0.036	-0.205	-0.007			
	Folates (nmol/l)	-0.004	0.059	-0.008	0.000			
	p53 mspl (+/+)	-0.324	0.098	-0.709	0.061			

PIN=0.10, POUT=0.15

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AIR POLLUTION

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, folic acid

- DNA adducts by ^{32}P-postlabeling
- Chromosomal aberrations
  Conventional, FISH, micronuclei
- Oxidative damage
  8-oxodG, 15-F2T-isoP, proteins, SCGE
- Genetic polymorphisms
- Gene expression

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STUDIED GROUPS

Policemen represent a model group, which is highly exposed to ambient air pollution as well as they spend the most of their working hours outdoors. Therefore the effect of PAHs adsorbed on air particles < 2.5 mm was studied in two groups:

policemen
from the center of the City
spending daily > 8h outdoors

matched controls working indoors

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STUDIED GROUPS

- POLICEMEN 2001

  EXP N = 53, CON N = 52

- POLICEMEN 2004

  EXP N = 480 (120 x 4)

- BUS DRIVERS 2005 - 2006

  EXP I N = 150, EXP II N= 60, CON N = 150
  (120 x 3)

- POLICEMEN 2007

  EXP N = 120 (60 x 2)

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Multivariate impact of environmental pollution to DNA adducts - nonsmokers

Period 7 days

Variable		Period (days)	c-PAH	B[a]P
Intercept			1.182	1.168
EP	ngm^{-3}		*0.008 (p=0.11)*	0.046 (p=0.0429)
Vitamine A	$\mu moll^{-1}$	1-7	0.132 (p=0.0000)	0.135 (p=0.0000)
GSTM	null/positive		-0.155 (p=0.0260)	-0.157 (p=0.0247)
GSTT	null/positive		-0.153 (p=0.0978)	*-0.153 (p=0.0989)*
Intercept			1.169	1.152
EP	ngm^{-3}		*0.009 (p=0.0570)*	0.057 (p=0.0110)
Vitamine A	$\mu moll^{-1}$	8-14	0.132 (p=0.0000)	0.134 (p=0.0000)
GSTM	null/positive		-0.157 (p=0.0241)	-0.159 (p=0.0224)
GSTT	null/positive		*-0.153 (p=0.0992)*	*-0.153 (p=0.0980)*

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Multivariate impact of environmental pollution to DNA adducts - nonsmokers

Period 14 days

Variable		Period (days)	c-PAH	B[a]P
Intercept			1.141	1.113
EP	ngm^{-3}		0.011 (p=0.0489)	0.072 (p=0.0079)
Vitamine A	$\mu moll^{-1}$	1-15	0.135 (p=0.0000)	0.138 (p=0.0000)
GSTM	null/positive		-0.157 (p=0.0242)	-0.159 (p=0.0224)
GSTT	null/positive		*-0.153 (p=0.0986)*	*-0.152 (p=0.0990)*
Intercept			1.171	1.123
EP	ngm^{-3}		*0.010 (p=0.13)*	0.076 (p=0.0142)
Vitamine A	$\mu moll^{-1}$	16-30	0.131 (p=0.0000)	0.136 (p=0.0000)
GSTM	null/positive		-0.157 (p=0.0249)	-0.159 (p=0.0224)
GSTT	null/positive		*-0.153 (p=0.0992)*	*-0.154 (p=0.0960)*

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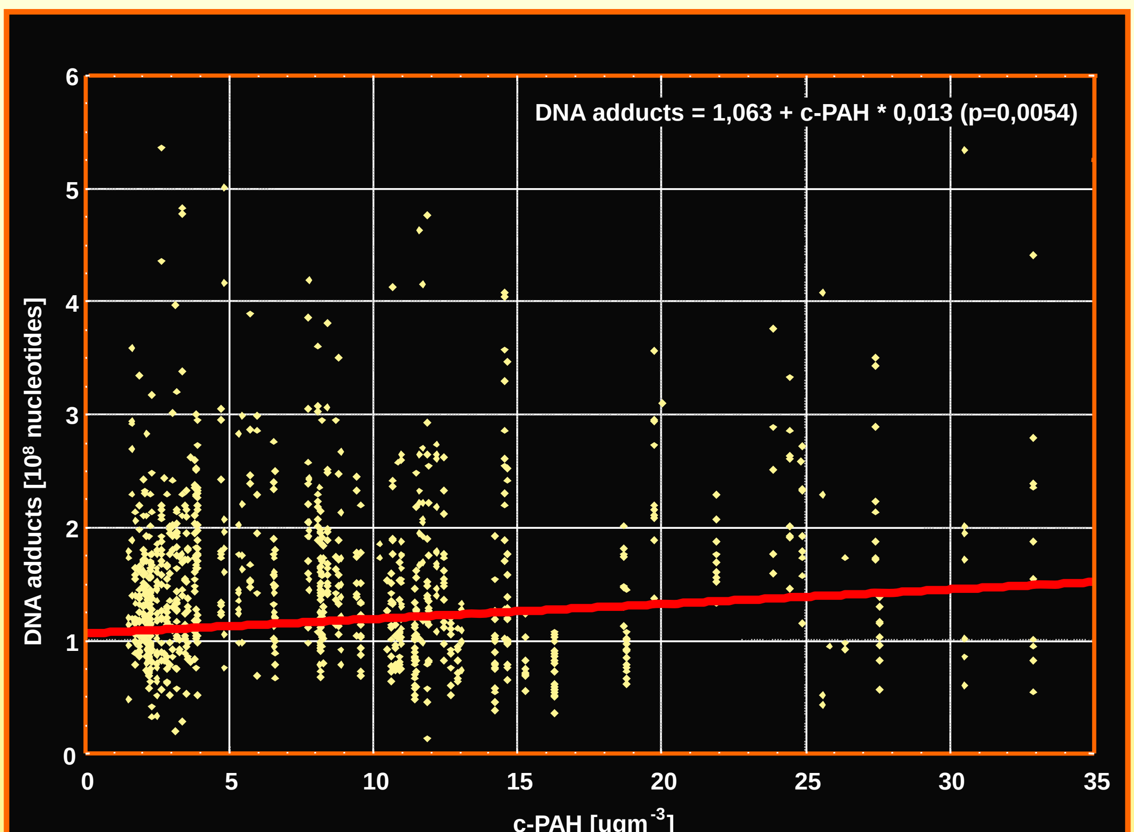
IMPACT OF ENVIRONMENTAL POLUTION TO DNA ADDUCTS



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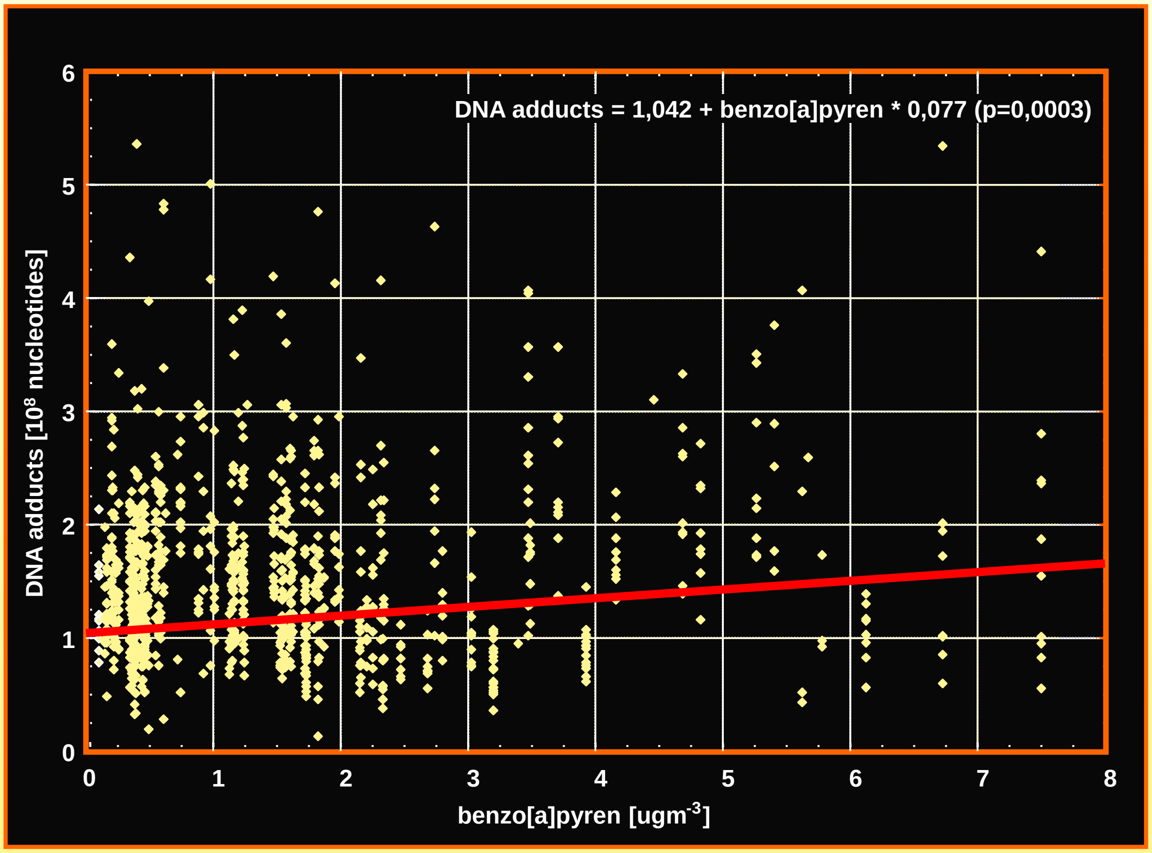
IMPACT OF ENVIRONMENTAL POLUTION TO DNA ADDUCTS



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NEW KNOWLEDGE

- Environmental air pollution by c-PAHs can increase genotoxic risk
- Relationship between c-PAHs exposure, DNA adducts and chromosomal aberrations by FISH
- Decreased DNA repair capacity in environmentally exposed subjects

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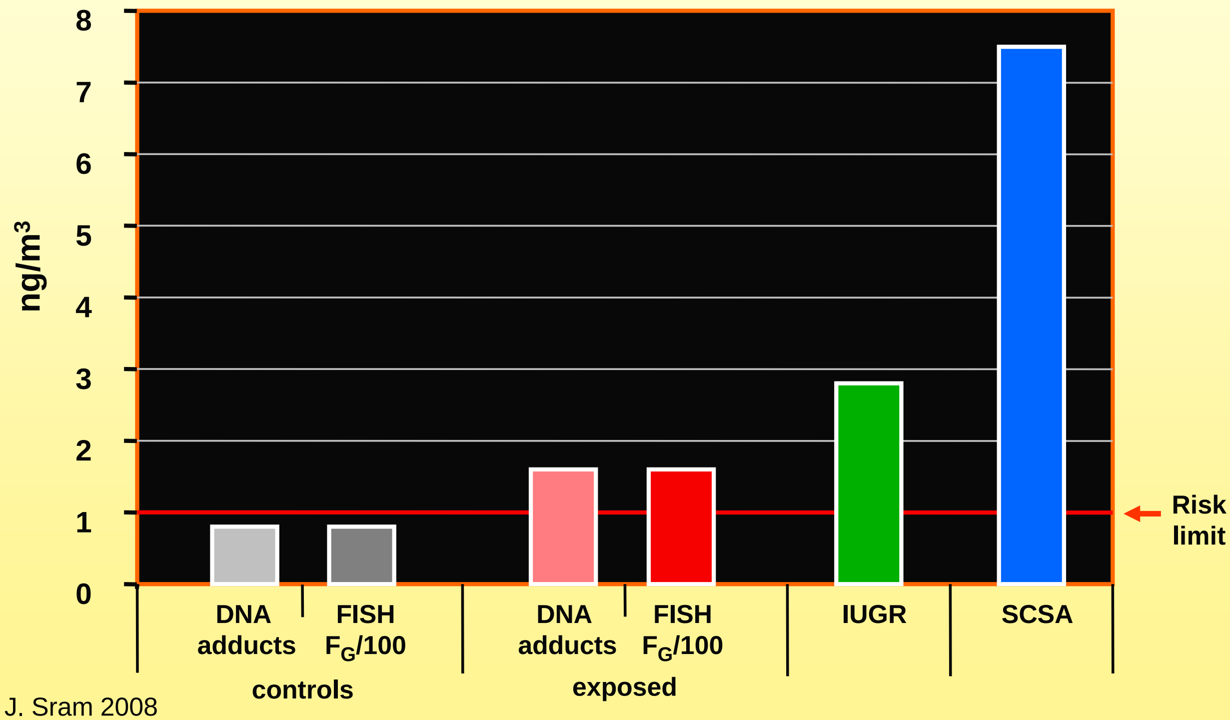
EXPOSURE TO B[a]P IN AIR –RISK ASSESSMENT



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INTERPRETATION OF MOLECULAR EPIDEMIOLOGY STUDIES

NEW KNOWLEDGE
ABOUT c-PAHs AFFECTING HUMAN HEALTH

↕

RISK ASSESSMENT

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ACCORDING TO MOLECULAR EPIDEMIOLOGY STUDIES

concentrations
> 1 ng B[a]P/m^3
in polluted air

RISK FOR HUMAN HEALTH

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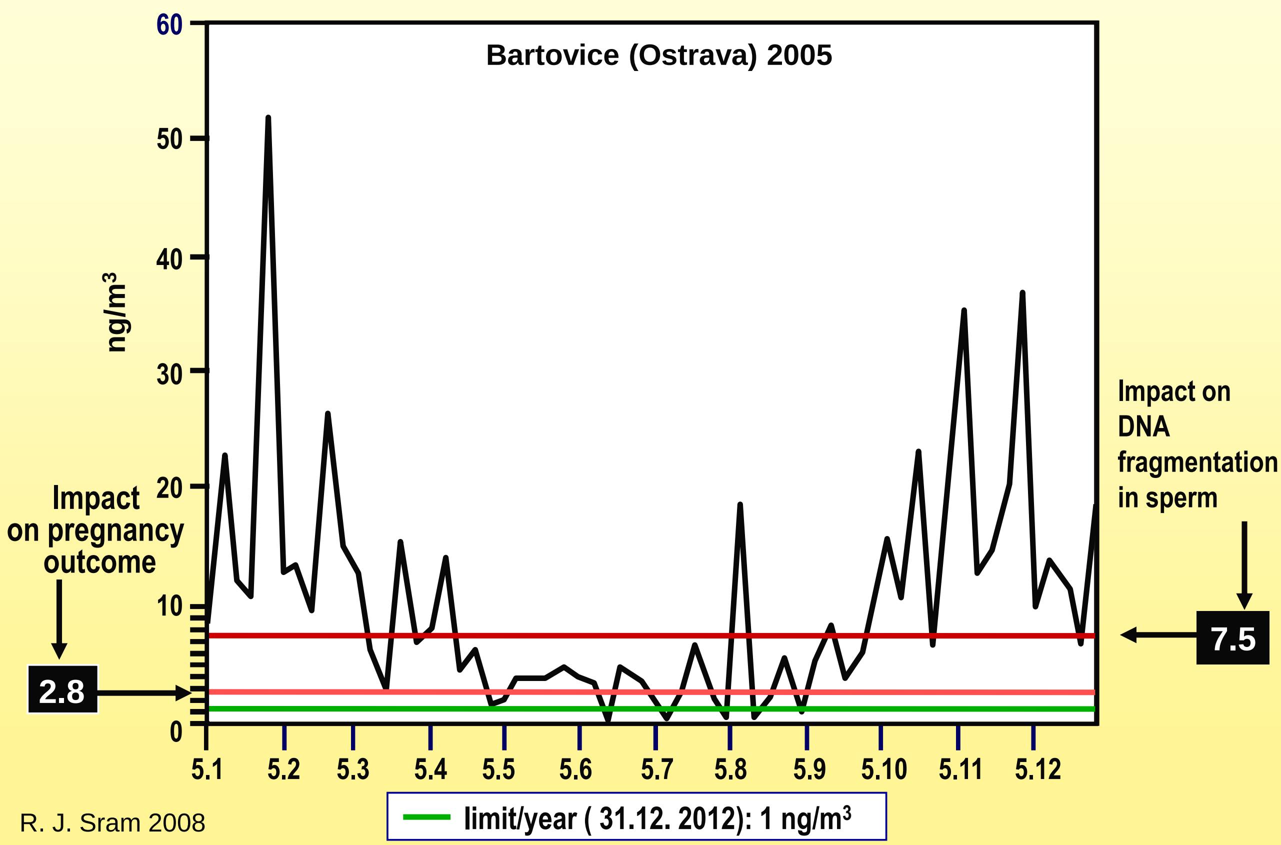
Daily concentrations of benzo[a]pyrene



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IMPACT OF c-PAHs IN POLLUTED AIR

pregnancy outcome
(IUGR, LBW)
act as ED

men
fertility

child morbidity,
mental
development

cardiovascular
diseases,
diabetes,
cancer

RISK FOR HUMAN HEALTH

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Environmental data and Human biomonitoring in France

Tromso, May 2008

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InVS missions

- To implement **ongoing surveillance** of the health status of the population
- To **detect any threat to public health**, to alert, investigate and to provide recommendations for control and prevention
- To participate to France's action in **international public health**

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Environmental data / HBM data Context

- In France, there are different environmental data base which collect contaminants in :

  - Air (collected by ASQAA)
  - Water (Siseaux)
  - Soils (a grid on the territory; BRGM/Inra)
  - Food (campaigns from Ministry of Agriculture and Fishing)

- But not always sufficient to answer to public health questions

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Environmental data / HBM data
Context: different levels of situation

- **Local situations**: usually, the alert → anormal environmental data
  The situation shows a contamination in soils, air and/or water often linked to an industrial area (local studies)
- **Regional or national question** for a kind of environmental exposure: Can a local alert be generalized to a wider territory?
  e.g exposure of the population to a type of industry (MSWI, nuclear site,…), or to a type of contaminant such as mercury (associated with goldmining activities)
- The rising questions:
  - Is the **population really exposed to a contamination** from the environment?
  - Can we identify **risk factors** for the exposure?
  - If the population is really exposed, can we observe an **health impact** in the population?

→ How to use **environmental data** and **HBM data** to answer?

Some case studies

Different kinds of HBM studies

- **Local studies** with pollution from industries, mining activities (e.g. pollution to lead, cadmium, arsenic)

- **Regional studies:** pollution by mercury (15 yrs of HBM) in French Guiana linked to goldmining activities

- **National studies**:
  - exposure to dioxins of the French population (adults) living around municipal solid waste incinerators (MSWI)
  - lead exposure of French children from 6 months to 6 yrs
  - exposure of the French population to river fishes contaminated by PCBs

  - reference values for heavy metals and pesticides from a representative French population (ENNS: National Health Nutrition
  - cohorte Elfe of 20000 children from birth to adolescence to follow the exposure to environmental contaminants during childhood, neurotoxic and reprotoxic effects (also omics), nutritional exposure, socioeconomic sociological

Local studies – A pollution to arsenic Context

- Goldmining activities, pyro and hydrometallurgy in the South of France
  → contamination of **soils** and of the **river** in the valley by different metals, in particular arsenic

- At the beginning: **overview** of available environmental data
  → very scarce environmental data and difficulties to have a clear idea of the activities and releases of these industries in the past :
    - many pollutants (arsenic, cadmium, lead, cyanides)
    - with different possible routes of exposure (soils, air, water, food)
    - by the past (during years) until the time of the study

  → environmental data **completed but still a lot of incertitude** to know the importance of the exposure of the population and to understand the main routes of exposure

  → possible health effects (cancer, renal,…)

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Local studies – A pollution to arsenic Study (1997)

- Launching of a **HBM study**
  - area : 15 km x 15 km
  - 8500 inhabitants : inclusion of people (n ~ 800; random sampling) living in **exposed** and **not exposed areas** (more than 15 km far) defined according to the available environmental data

- Questionnaire (socioeconomic data, habits, environmental and occupational exposure, local food consumption, gardening…)
  + biological samples (urine) to measure heavy metals and Asi+MMA+ DMA, thiocyanates (for cyanides)

- Statistics: multivariate analysis, SAS
  Area : in a **grid** with cells of 1km, mean of urinary concentrations of people adjusted for variation factors were mapped

- (also non specific health symptoms and a study for cancer mortality)

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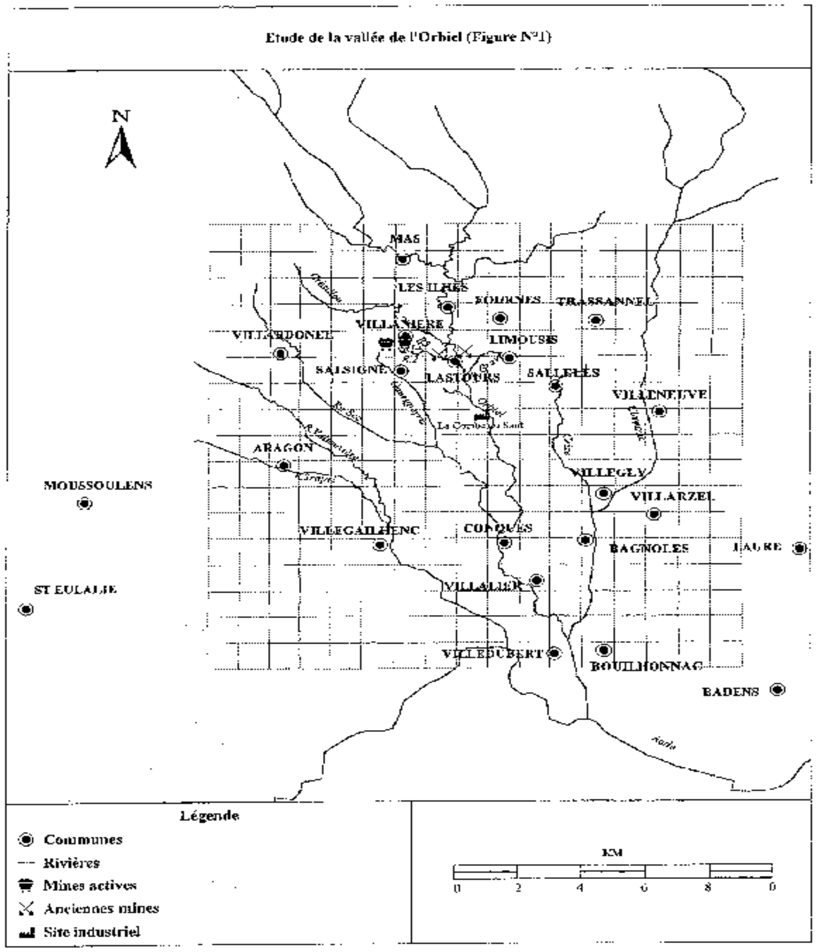

Local study – A pollution to arsenic HBM results

- Importance of the **place of residence** :
  * impact of the mine and industries through water :
    a gradient of concentrations of urinary arsenic in the people living from the top of the river which crosses the mining area to the bottom of the river;

- HBM results permitted us to identify:
  * the importance of the **local food intake from the garden** and of **drinking water from wells** for the contamination of the people by arsenic,
  * people contaminated by the consumption of the vegetables from their **garden close to the river** (even far from the mine site) which were contaminated by the arsenic of the river in case of **flood**
  * **new contaminated areas** (in the North, above the current goldmining area corresponding to an old goldmining area),
  * **contaminated wells**,

- However, few urinary arsenic data above 15 µg/g creatinine

- Many proposals for the risk management

Environmental data → HBM data → Environmental data

Regional studies – Pollution to mercury in French Guiana (Surveillance during 15 years)

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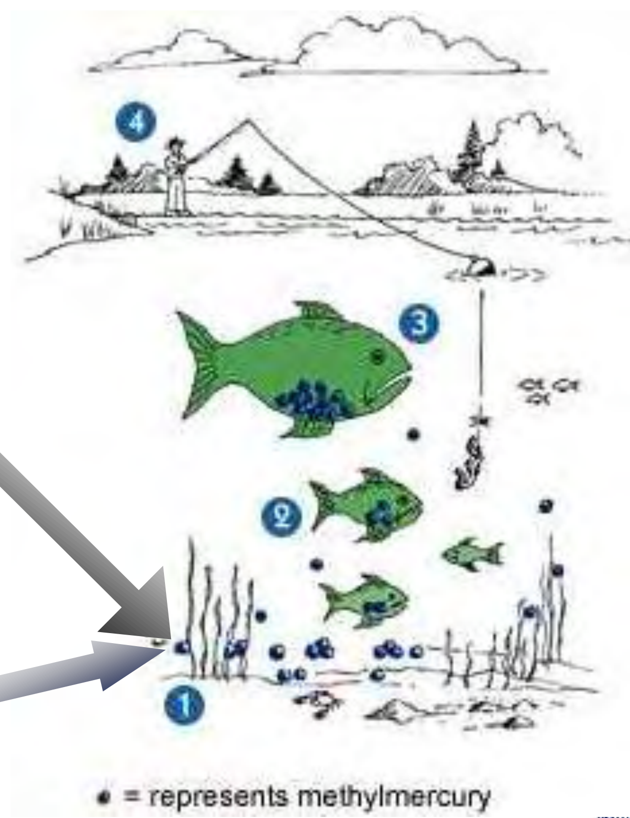
Mercury and routes of exposure



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Regional study – Pollution to mercury
Context

- French Guiana: goldmining activities from the 19th century with important release of mercury in environment (used for the amalgam with gold)
- 1993
  - Environmental impact assessment of the dam of « Petit Saut » (electricity for the spatial center in Kourou)

    → **Hg concentrations in predator fishes** > regulation norms
  - Health impact for the population?

Exposure to Hg →

Alteration of visual and motor fonctions (observed with tests)	Troubles of coordination (observed with tests)	Paresthesia prickle, numbness members and around the mouth	Minamata disease
10 µg/g OMS threshold	**20 µg/g**	**50 µg/g**	**> 100 µg/g**

In hair

Regional study – Pollution to mercury
HBM study in 1994

- 1994: First step : **overview** of the situation in the population (RNSP-Inserm-DGS)
  No available data on contamination to Hg of the river fishes (or very scarce)

→ HBM study using :
* **Hair mercury** as biomarker on 500 people in different:
  - Areas: Maroni (n=140), littoral (276) et Oyapock (84)
  - Populations: *adults (n = 255) et children (n=136) in health care services
    *pregnant women in maternity (n=109)

* Questionnaire on names and frequencies of fishes eaten, teeth amalgam

→ Conclusion:
generally **low exposure** of the population to mercury **except for Amerindians** (particularly Wayana) with concentrations of hair Hg > 10 µg/g

Regional study – Pollution to mercury
3 complementary studies in 1997 (Amerindians)

- 1997: Second step: studies in the Amerindian populations

  – 3 complementary teams :
  - Assessment of environmental contamination:
    Identification of **fishes** in the river and measurement of their **contamination** by Hg (CNRS-Orstom/Ird)

  - Assessment of mercury intake by a **food consumption study** (type and quantity of fish eaten by the population; RNSP) in the Wayana population (villages Cayodé, Twenké, Taluhen, Antécume-Pata) and its impact on hair Hg
    - Hair Hg (total and speciation) in 235 people
    - Food consumption study (2 x 7 days)

  - Assessment of **neurologic and neurodevelopmental disorders** according to Hg exposure (Inserm) :
    - 3 zones : Haut Maroni (Antécume-Pata, Cayodé, Elahé, Taluen, Twenké), Camopi, Awala
    - Neurologic examination and battery tests
    - 9 months to 6 yrs (n = 248), 5 yrs to 12 yrs (n = 206)
    - Hair Hg for couples mother-child

Results * Contamination and food intake

– Majority of the people above the WHO recommandation for Hg food intake

International recommandations Methyl-Hg < 200 µg/week (lower today)
Methyl-Hg = 85 à 97% of total Hg

– Adults		210 to 420 µg/d
– Children	0 – 6 yrs	21 to 105 µg/d
	10 – 15 yrs	210 to 280 µg/d

– Fishes: 4 species contributed to 72% of Hg intake
Huluwi, Aymara, Mita et Piray

– Correlation between **Hair Hg** and **Hg from food intake**

→ Fish: afterwards, **Aymara used as an indicator of the environmental contamination** in the different rivers of French Guiana

*** Neurodevelopment**: **linked to hair Hg exposure** (biomarker)
- Reduction of visuo-spatial coordination, increase of particular reflexe


Wi, Lowi, Huluwi
(Pseudoplatystoma fasciatum)


Aymara, Aimala
(Hoplias aymara)


Meloko fisi, Mita
(Ageneiosus brevifilis)


Piray, Pene
(Serrasalmus rhombeus)

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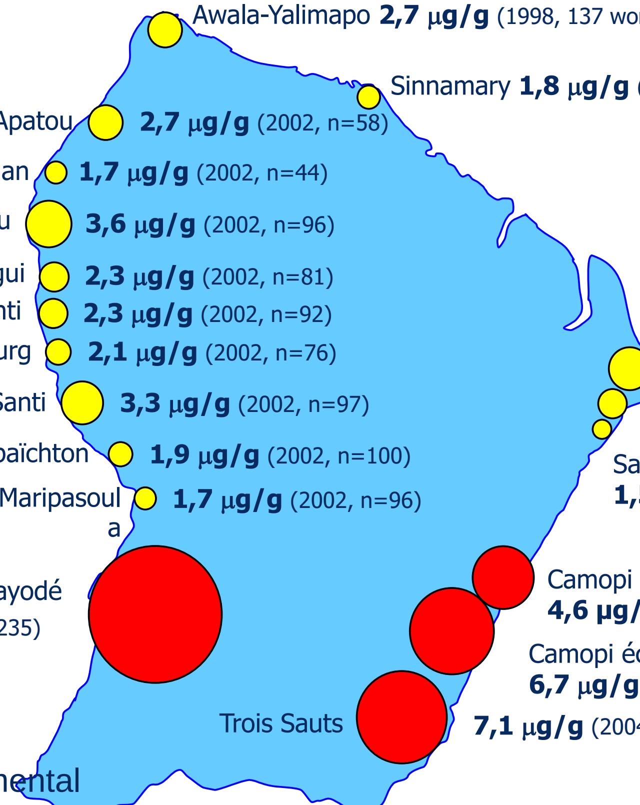
Regional study – Pollution to mercury (N ~ 2500)
HBM studies from 1994 to 2007 (with 2001, 2002, 2004, 2005 HBM)

Map of means* of mercury concentrations in hair (µg/g)



A mapping of environmental and HBM data (GIS)

*** Geometric means**

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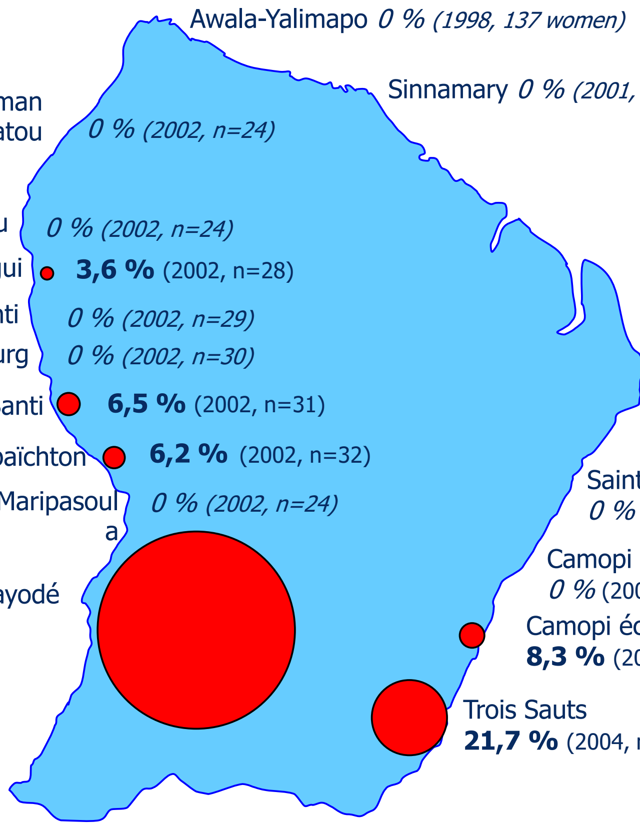
Proportion of women in age to give birth with hair Hg > 10 µg/g



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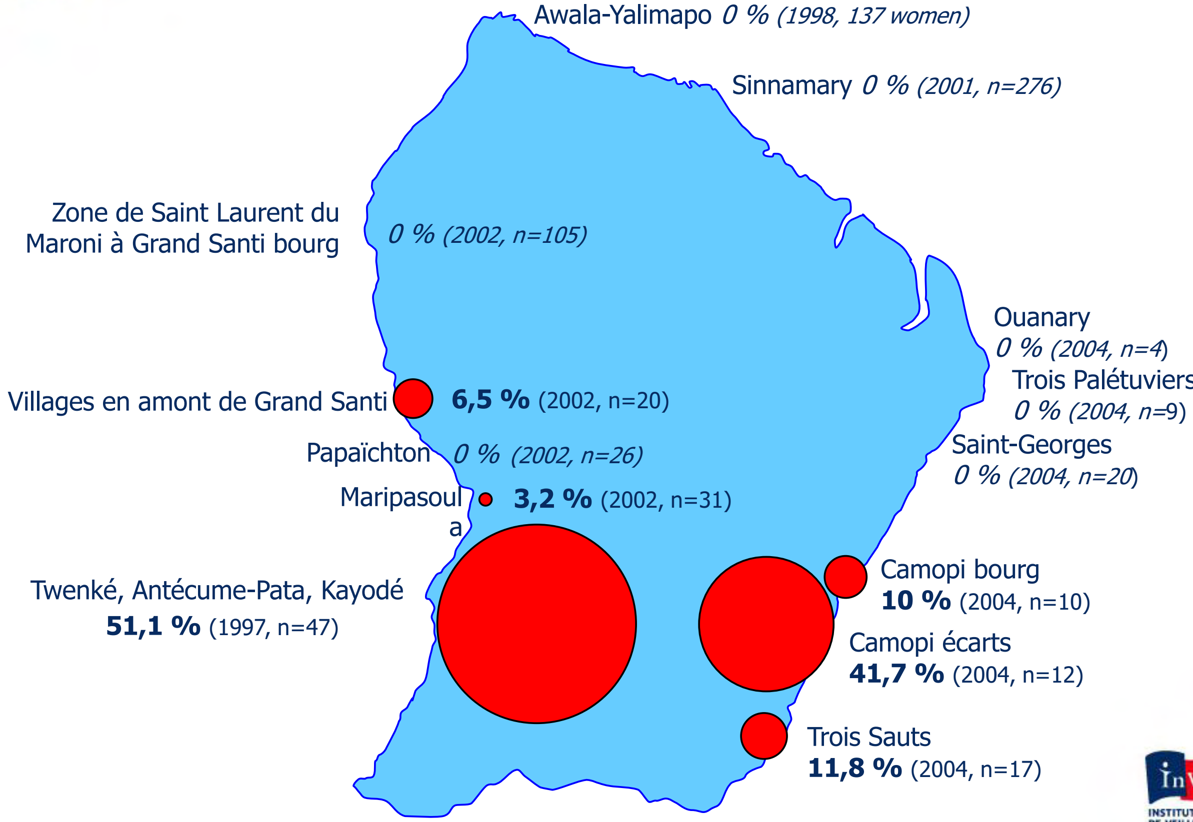
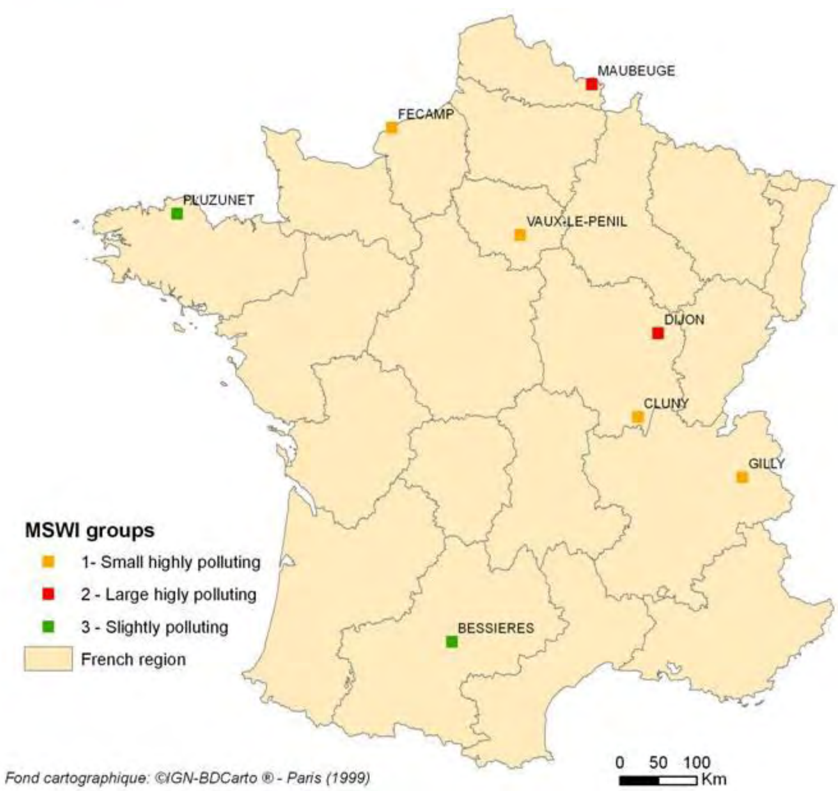
Proportion of children less than 7 yrs with hair Hg > 10 µg/g



National studies – Serum dioxin concentrations in the population exposed to municipal solid waste incinerators (MSWI)



National studies – Serum dioxin study and MSWI Context

- Dioxins : Persistant organic pollutants (POP), which accumulates in lipids
  Generally, food is the main source of exposure (90 %)

- In France, lots of municipal solid waste incinerators (MSWI, which release dioxins):
  - About 120 in 2007
  - About 300 in 1998

- Past crises about dioxins in agricultural areas around MSWI:
  - Contamination of the environment
  - Contamination of food products

- Concern of the French population:
  - Do MSWI influence their serum dioxin level ?

Local question → National question
Environmental data → HBM data

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National studies – Serum dioxin study and MSWI Aims

- To evaluate whether the emissions of the MSWI contribute to the body-burden of dioxins in the surrounding population (studied by serum dioxin levels)

- To study the influence of consumption of locally-produced food products on serum dioxin levels

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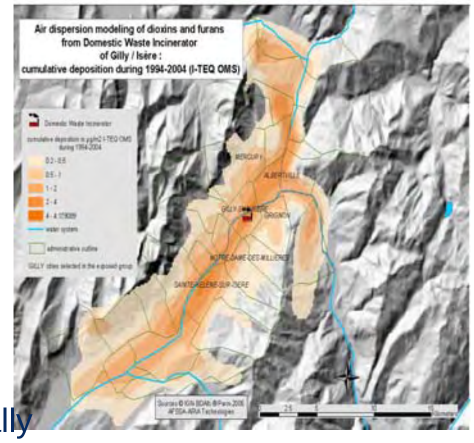
National studies – Serum dioxin study and MSWI Methods

➢ Study population

- **1030** adults randomly selected in 8 areas in France near 3 types of incinerators (cf. map: new, small and large old ones), dispatched between:
  - <u>Exposed group</u> : living under the impact **area of the plume** (n=801) **obtained by modelisation using environmental data** **(capacity, oldness, dioxin emission data, meteo…)**
  - <u>Non-exposed group</u>: living beyond 20 km of the incinerator (n=229)
  - Defined for each area (about n=130)
  - 30-65 years, living at least during the last 10 years at the same place, not occupationally exposed to dioxins, and for women, no or few breastfeeding in the past 15 years



- Eating or not eating locally-produced food products

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➢ Questionnaires:
- socio-demographic
- **food diet** (general, local)
- occupation and environment

➢ 1 030 serum samples (200 mL of blood)
7 PCDDs, 10 PCDFs,
12 DL-PCBs, 3 indicators PCBs

➢ Multivariate statistical analysis ⇨ Stata, SAS, R,
taking into account sampling frame (weights,…) and counfounding factors:
age, sex, BMI, recent change in weight, smoking status, chimney use,
leisure activities linked to dioxins, urbanization, background food intake

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National studies – Serum dioxin study and MSWI Conclusions

- **Serum dioxin levels similar to those observed in other European studies**
- **No influence of inhalation** (which was a question of the population at the beginning of the study) on serum dioxin levels
- **No global difference between exposed and non-exposed people to the plume of a MSWI** for serum dioxin levels
- **Influence of the consumption of animal food products** produced in the impact area of the plume of the incinerators (lipids, dairy products, eggs):
  - particularly for farmers
  - but only around old and polluting incinerators
- **No influence of local vegetables consumption**
- **Influence of fish intake independantly of incinerators**

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National Survey of childhood lead poisoning 2008-2009

Study of sources of exposure to lead in French dwellings

CSTB le futur en construction

InVS INSTITUT DE VEILLE SANITAIRE

ENSP ECOLE NATIONALE DE LA SANTE PUBLIQUE RENNES

Hôpital Lariboisière

- Paris -

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National studies – Survey of childhood lead poisoning Context

- No national data since the Inserm/ InVS study of 1995-1996

(Blood Lead Level (BLL) ≥ 100µg/L estimated prevalence : 2.1 % ± 0.5 %, 85 000 cases)

- Objective of the Law of Public Health, August 2004:

  « to have a 50 % decrease of the BLL *>100µg/L prevalence from 1996 to 2008» among the children aged 1 to 6 years old*

- Probable decrease of the BLL≥100µg/L prevalence
  - Recent local studies : general population lead poisoning decrease
  - Screening activity : in 2004, 5 % of the first BL test ≥100µg/L (25 % in 1995)

- Existence of areas with strong environmental exposure

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National studies – Survey of childhood lead poisoning Context

- Screening:
  - 1.2% children are tested at least once before 7 years old
  - Important geographical heterogeneity

- Questions from the Public Health actors:
  - Should the screening be developed in the areas where it hasn't been yet ?
  - Should the screening be limited to certain populations ? How to locate them ?

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National studies – Survey of childhood lead poisoning Context

- Primary prevention related questions
  - Which actions should be taken in the future in order to prevent from the high level exposures ?
  - How to reduce the basic exposure of the population ?
    - Improvement of old housing ?
    - Removal of lead pipes ?
    - Location and decontamination of the polluted areas ?

- Therefore, the study shall bring answers to the actual known hierarchy of the exposure sources to lead
  - For the elevated exposures
  - For the moderate exposures

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National studies – Survey of childhood lead poisoning Context - French regulatory system

- House or appartment on sales / on renting
  - Diagnostic (Mandatory Statement) of Risk of Exposure to Lead (CREP)
    - Standard NF X 46-030
    - Based on X-Ray fluorescence

- In case of lead poisoned child
  - Environmental investigations by health authorities
  - Injunction to realise building works
  - Control of the conditions of building works

- Official lead analyses
  - Analysis of acido-soluble lead in dusts : NF X 46-032
  - Analysis of acido-soluble lead in paint chips : NF X 46-031

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National studies – Survey of childhood lead poisoning
Context - Current issues

- Unsufficient knowledge about the respective contribution of various sources
- What about moderate lead blood concentration ?
- Could analysis of lead isotopes be of any help to identifying actual sources of poisoning ?
- What is the actual lead exposure situation of the French housing stock ?

National studies – Survey of childhood lead poisoning
Aims

HBM

- To estimate the national prevalence of elevated BLL (≥100 µg/L) among children aged 6 months to 6 years old
- To measure the contribution of the various sources of exposure to BLL
- To determine the distribution of the BLL by area (including French overseas department)
- To validate geographical indicators to target potentially poisoned children

National studies – Survey of childhood lead poisoning Aims

And in particular

- to improve knowledge on **exposure factors** of children's' blood lead levels, including for 'moderate' levels;
- to identify **environmental sources** and **media** responsible for moderate blood lead levels (i.e. from 35 up to 100 µg/l);
- to develop an **empirical model**, predictive of blood lead levels of children, depending on lead concentrations in their environment;
- to provide a **first overview of exposure** to lead in the French national **housing stock**;
- to estimate the **part of children's lead poisoning cases** (blood lead level above 100 µg./l) for which a source could be **identified thanks to isotopic analyses** of lead in the blood and in various environmental compartments.

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National studies – Survey of childhood lead poisoning Methods

- Cross sectional study
- Study population : children from the general population
- Sample size : 3800 hospitalized children in 140 public hospitals
- Children recruitment:
  - In general population : ideal choice (but high risk of refusal, difficult logistic,…)
  - At hospital : reasoned choice (better acceptability, comparable with the 1995-96 study)
- Environmental study on 500 dwellings

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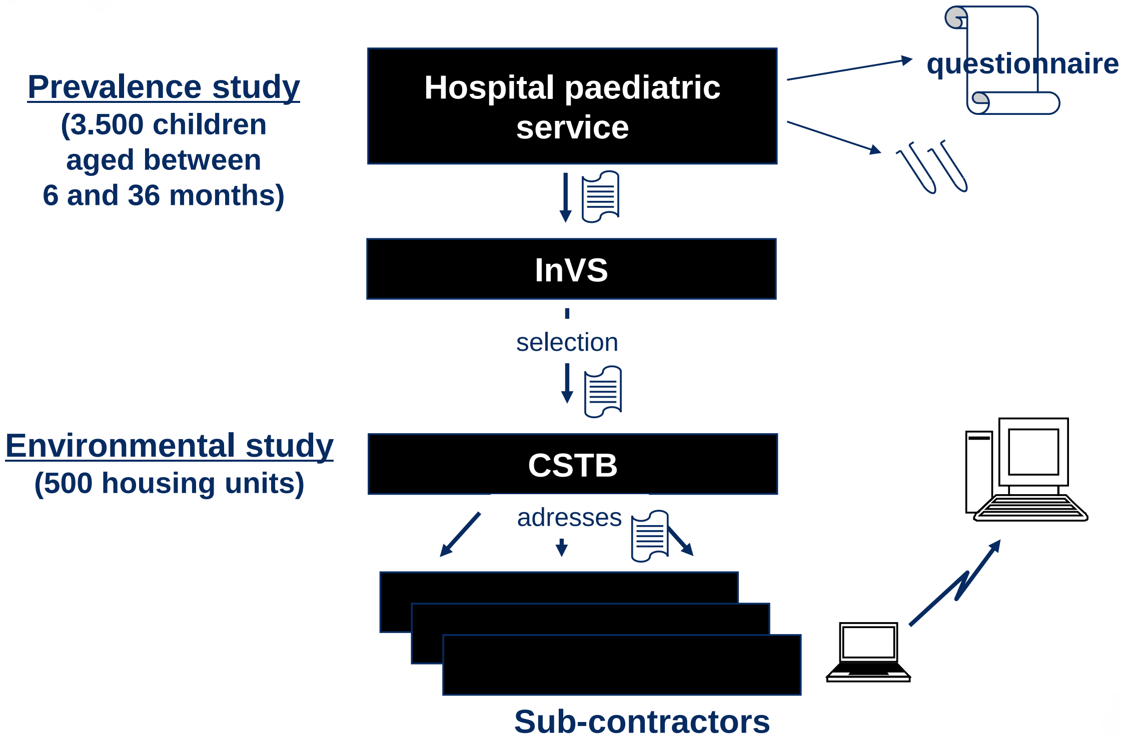
National studies – Survey of childhood lead poisoning Methods – population sampling



National studies – Survey of childhood lead poisoning Methods – Data collection

At the hospital

- Parents' consent
- Questionnaire :
  - **socio-demographic factors** : parents' occupation, parents' study level, child and mothers' birth country, housing status,
  - **housing** : address, date of construction, overcrowding, presence of lead pipes, presence of deteriorated paints, recent renovation works,
  - **child behaviour** : consumption of tap water, tendancy to scrape, suck or nibble the paints, exposure to tobacco smoke
- Lead blood test
- Ecological data
  - Housing and socioeconomic characteristics at cadastral level
  - Lead dissolving capacity of tap water in the local drinking water network

National studies – Survey of childhood lead poisoning
Methods – Data collection at home

- General data :
  - date enquiry (Monday, Tuesday,…), date of entry of the family and the child in the housing,…
- Home :
  - Description inhabitants
  - At risk hobbies
- Space-Time budget of the child:
  - School, day nursey, nany…
  - Identification external playgrounds
  - Occupations during a « typical » week
  - Holiday times
- Child behaviour:
  - Dummy, thumb, nail
  - Scraping, sucking, nibbling,… habits
  - Windows putty
  - Objects containing lead

- Frequentation of the housing's rooms by the child
- Frequentation of the common parts (appartment) by the child
- Description of the housing:
  - Size
  - Housing status
  - Date of construction
  - Moisture and water degradation
- Cleaning habits
- Recent renovation
- Drinking water consumption
- Risks linked to contaminated soil
- Unusual sources of intoxication:
  - Traditional dishes
  - Consmetics
  - Traditional medicines

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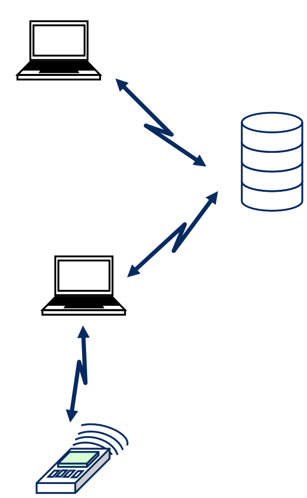
National studies – Survey of childhood lead poisoning
Methods – Data collection at home- For the technician

- General description of the dwelling:
  - Type, environment, size, heating system, comfort, solidity of the structure,ventilation, humidity,…
  - Includes items alowing to calculate « precarity indexes »
- Investigation of:
  - 1. Child's bedroom
  - 2. Common living area
  - 3. Lobby
  - 4. Kitchen
  - 5. Play area or bedroom of the child immediately older or younger
  - In the case of an apartment, stairwell : at the unit's floor, and at the ground floor (building's hall)

If no bedroom is attributed to the child, another room where the child sleeps will be investigated

Investigation includes description of **all surface areas** (size, substratum, covering, moisture,…) and **X-Ray measurements**



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National studies – Survey of childhood lead poisoning Methods – Samples at home

- dust wipes
- water (2L)
- soil
- paint chip
- cosmetics
- traditional dishes

sent to EHESP

National studies – National Health Nutrition Study (NHNS/ ENNS in French)

National studies – National Health Nutrition Study
Context

- **Follow-up of the National Health Nutrition Programme** set up in 2001 and some objectives of this programme are included in the Public Health Law of August 2004

- France: the most important use of pesticides in Europe, but no available HBM data in the population
- Few HBM data available at the national level (except for lead and dioxins)
- Need of **reference values** for exposure to **environmental contaminants** in the French population

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National studies – National Health Nutrition Study
Aims

- **To describe the food consumption, nutritionnal status and physical activity** of French adults and children from a representative sample of the population living in France in 2006

- **Surveillance of chronic diseases**:
diabete, metabolic syndrome, dyslipidemia, arterial hypertension

- **Surveillance of exposure of the French population to environmental contaminants** :
* heavy metals (Lead, cadmium, mercury, arsenic,…) and
* pesticides (organochlorines, organophosphates, pyrethroids)
by using biomarkers of exposure

  - estimation of the exposure
  - study of variation and risk factors
  - to identify and quantify population at risk
  - to establish reference values

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National studies – National Health Nutrition Study Methods

- Transversal study in general population
- Sample included during 1 year
- 3 parts :
  - A food consumption study: three 24H recalls
  - Questionnaires face to face and autoquestionnaires:
    * sociodemographic caracteristics, physical activity,
    * environnemental exposures (oldness of house/appartment, leisures activities, application of pesticides on plants, pets, against insects, frequency of use of pesticides, kitchen garden, orchard,…) and
    * occupational exposures …
  - In health center service or at home :
    * clinical examination (anthropometric mesurements, arterial tension,…)
    * biological samples (blood, urine and hair) to measure nutritionnal and environnemental biomarkers
- Population (available for biomarkers):
  - about 2000 adults 18-74 yrs old
  - About 1700 children 3-14 yrs old

National cohort – ELFE

Cohorte Elfe of 20000 children from birth to adolescence to:

- follow the exposure to environmental contaminants during childhood,

- to study neurotoxic and reprotoxic effects (also omics), respiratory diseases and growth

- to study nutritional exposure, socioeconomic, sociological factors on child developement

→ Lots of teams / difficult to coordinate

National cohort – ELFE
Methods

- A random sampling of birth (4 days x 3) in maternity
- Biological samples on mother (Blood, urine, hair, milk) and children (cord blood, urine)
- Different questionnaires
- Environmental data at home + dust and air sampling
- Follow-up at different ages: Biological samples+examination and tests for development
- Different pollutants/ different biomarkers:
  - POP, metals, organotins, phalates, pesticides, alkylphenols
  - Omics
  - Nutritional biomarkers
- Emergent pollutants → biobank
- Development of mathematic tools

  Toxicocinetic and physiolocal Models (PBPK)
- Expology
  - biomarkers
  - micro-environnemental mesurements (air, dust)
  - questionnaires
- Application to :
  - emergent pollutants / indoor air
  - phtalates/biocides

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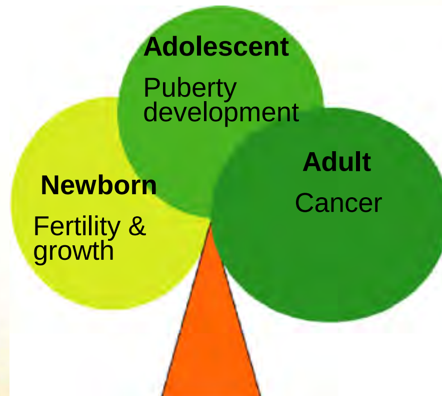
The concept of integrated monitoring in the Flemish Environmental Health Survey (FLESH) 2002 – 2006 - 2011

G. Schoeters , VITO , Belgium

Program supported by the Flemish Ministries of Environment and health

2002-2006:
What is the link between environmental pollution pressure and health in Flanders?

- Concentration of pollutants in humans?
  4400 participants, 8 areas
- Linkage with the **region** where people live? Spatial trends
- Linkage with **health** risks?
  - growth and development
  - fertility
  - astma and allergy
- Early warning system
- Efficacity of environmental measures?
  - **policy** link



Biomonitoring: markers of exposure

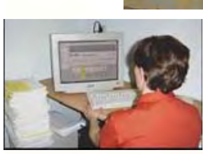
Persistent chlorinated compounds in (cord)serum			
Dioxin-like compounds (pg Calux TEQ/g fat)	newborn		elderly
Marker PCBs 138.153 & 180 (ng/g fat)	newborn	adolesc.	elderly
p,p'-DDE (ng/g fat)	newborn	adolesc.	elderly
Hexachlorobenzene (ng/g fat)	newborn	adolesc.	elderly
Heavy metals (blood & urine)			
Blood lead (µg/L)	newborn	adolesc.	elderly
Blood cadmium (µg/L)	newborn	adolesc.	elderly
Urinary cadmium (µg/g creatinine)			elderly
Metabolites of PAH and benzene (urine)			
1-hydroxy-pyrene (ng/g creatinine)		adolesc.	elderly
t,t'-muconic acid (µg/g creatinine)		adolesc.	elderly

A. Linkage with health

- **Newborns and mothers : n=1200**
  - Recuitment by maternity
  - Cord blood
  - **questionnairs→ time to pregnany, medical assistance to get pregnant, stillbirths, asthma and allergies**
  - **Medical files of maternity→ length, weight, headcircumference,**
- **Adolescents : 14-15 yrs (n=1600)**
  - Recruitment by schools, 42 schools
  - Blood – urine →**hormone levels, comet assay**
  - **questionnairs →asthma, allergy**
  - **Medical files of school doctors→registry of puberty developmental stage**
- **Elderly : 50-65 yrs (n=1600)**
  - Period: Sept. 2004 – June 2005
  - Blood – urine
  - **questionnaires→diabetes , asthma , allergy**

Field work adolescents


toxicological measurements in blood and urine → exposure


- questionnaire data
- existing databases from school health examinations
- hormone levels in serum

→ health effects

Biomarkers of exposure

Persistent Organic Pollutants (POPs)

- *PCBs:* sum of marker PCB138, 153 & 180 (ng/g fat)
- Chlorinated pesticides:
  - Metabolite of DDT: *p,p'-DDE* (ng/g fat)
  - Hexachlorobenzene (*HCB*) (ng/g fat)

Heavy metals

- *Blood lead* (µg/L)
- *Blood cadmium* (µg/L)

Health effects

- Questionnaire data
  - Age at menarche in girls
- School health examination database
  - Tanner stages
    - Girls: breast development & pubic hair growth
    - Boys: genital stage & pubic hair growth
- Serum hormone levels in boys
    - Testosterone, oestradiol, LH, SHBG

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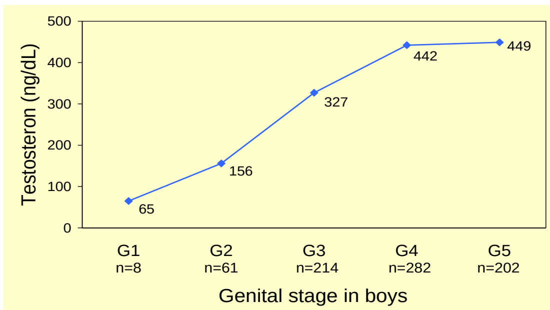
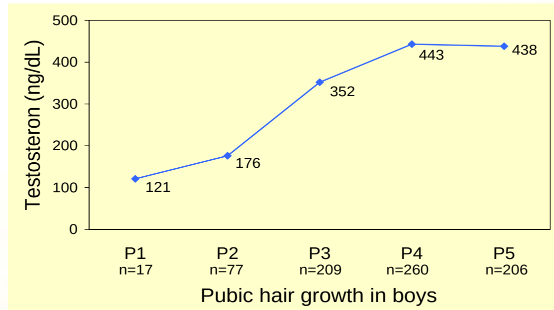
Validation of pubertal stages in boys





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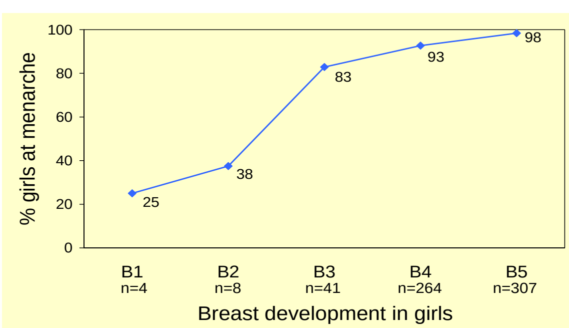
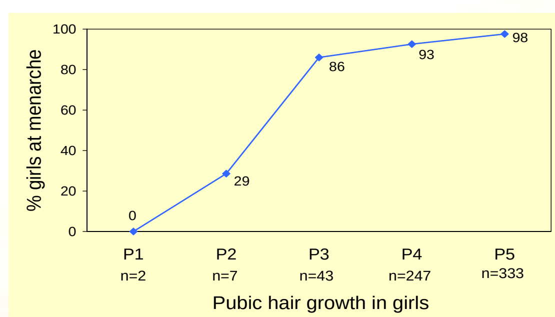
Validation of pubertal stages in girls





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Dose-response relations

Exposure	Effect	Likelihood of adult stage	
GIRLS		Odds (95% CI)	P-value
Blood lead	Pubic hair growth	0.65 (0.45-0.93)	0.02
BOYS		Odds (95% CI)	P-value
PCBs	Genital development	3.12 (1.69-5.75)	<0.001
p,p'-DDE	Genital development	3.03 (1.87-4.89)	<0.001
PCBs	Pubic hair growth	2.58 (1.71-3.91)	<0.001
p,p'-DDE	Pubic hair growth	1.39 (1.13-1.72)	0.002

all relations: adjusted for age and BMI (+ oral contraceptive use in girls)
* for doubling from 50 to 100 ng PCB/g fat

Discussion

- Higher exposure to lead was associated retarded pubic hair growth in girls
  - Findings are in accordance with NHANES data:
    - Wu et al.: negative assocation between lead and pubic hair growth (log scale)
    - Selevan et al.: negative association between blood lead and PH, only significant in blacks (increase 10 to 30 µg/L)
- Higher exposure to POPs in boys was associated with advanced genital stage
  - Findings are in contradiction with estrogenic activities of PCB153 and p,p'-DDE

B. Integration with environmental data

Biomarkers

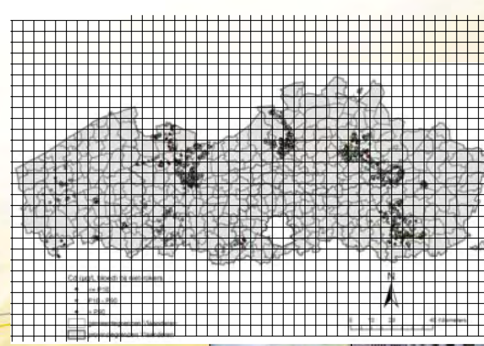
Outdoor air quality

Link individual biomonitoring data with air monitoring data collected from Flemish environmental Agency

- Children followed from birth until age 3→
- Adolescents

Human exposure biomarkers
point data per GPS-code home adress

Air quality data
per grid cell
- Environmental emissions
- Calculated imissions
- Imission measurements



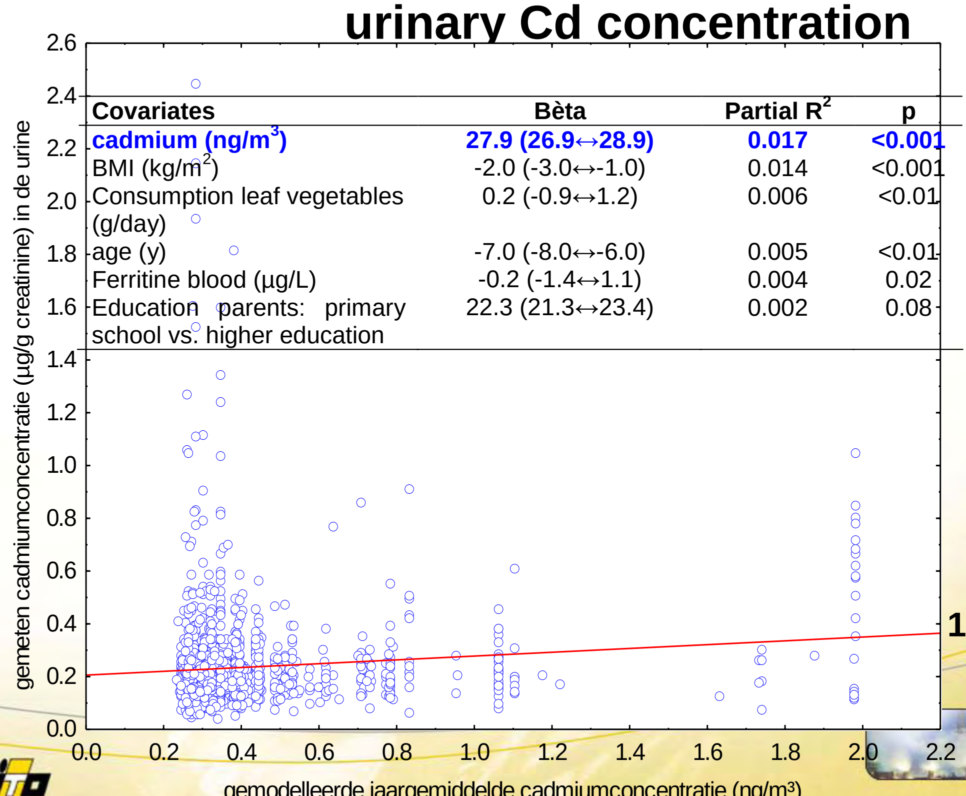
Statistics: regression

x = air quality data, covariates
y = ind. biomarker

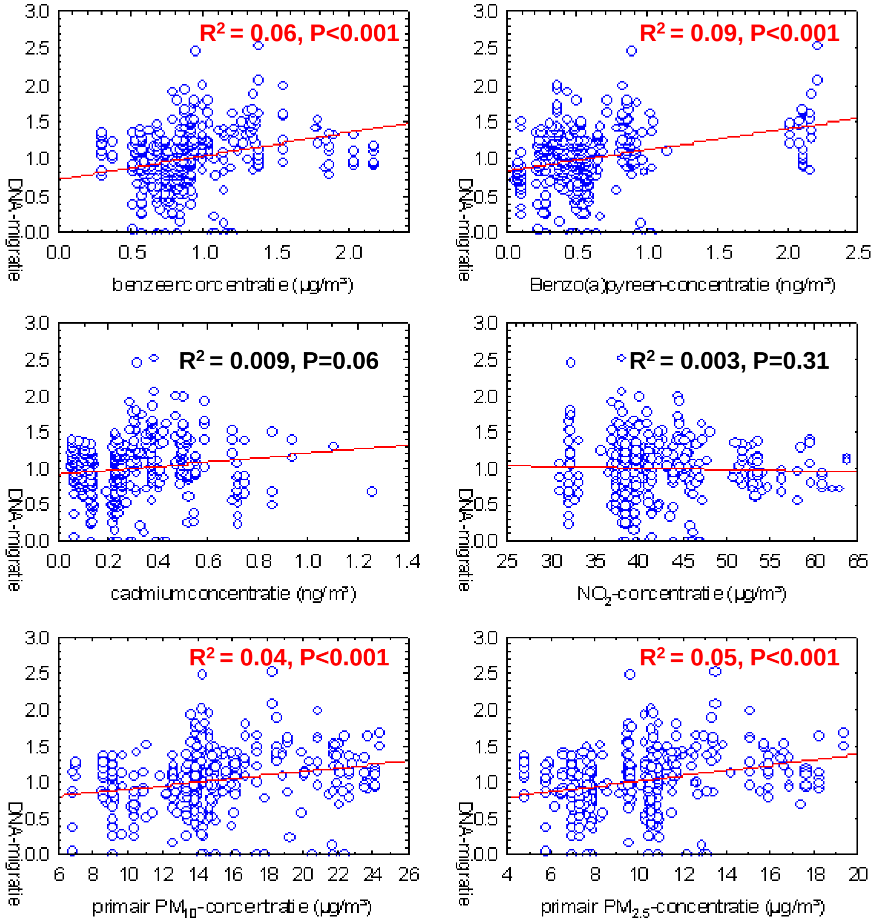
Stepwise multiple regression, including significant covariates of single regression

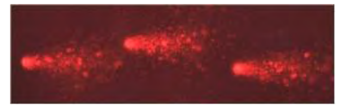
Single pollutant models

Cadmium: yearly average (ng/m³)-urinary Cd concentration



Covariates	Bèta	Partial R^2	p
cadmium (ng/m³)	**27.9 (26.9↔28.9)**	**0.017**	**<0.001**
BMI (kg/m²)	-2.0 (-3.0↔-1.0)	0.014	<0.001
Consumption leaf vegetables (g/day)	0.2 (-0.9↔1.2)	0.006	<0.01
age (y)	-7.0 (-8.0↔-6.0)	0.005	<0.01
Ferritine blood (µg/L)	-0.2 (-1.4↔1.1)	0.004	0.02
Education parents: primary school vs. higher education	22.3 (21.3↔23.4)	0.002	0.08





Air pollutants vs.

comet assay

390 non-smokers

Air pollutents - respiratory complaints

Odds Ratios	***Modelled conc.***		***Emission***	
	Benzene *+ 1µg/m³*	***NO₂*** *+10 µg/m³*	***Benzene*** *g/m²/j*	***NOx*** *g/m²/j*
Doctor diagnosed asthma	3.26 (0.89-11.97)	**1.33 *** (1.04-1.69)	1.58 (0.42-5.89)	1.00 (0.99-1.021)
Ever asthma symptoms	**4.34 **** (1.74-10.80)	**1.39 ***** (1.17-1.64)	**3.2 *** (1.30-7.86)	**1.006 **** (1.002-1.01)

- *Hirsch et al. (1999):* (5421 German children):
Benzene, NO_2, CO vs. coughing/bronchitis **OR= 1.11-1.15**

- *Nocolai et al. (2003):*
Black smoke, benzene vs. current asthma: **OR= 2.05**

Conclusions

Several pollutants present in outdoor air **associated** with human biomarkers measured in youngsters

Lead	**blood lead**
Cadmium	**urinary cadmium**
Benzene, B(a)P, $PM_{2.5\_prim}$, PM_{10_prim}	**comet assay**
Benzene, NO_2	**respiratory**

NB: <u>No</u> association between atmospheric B(a)P and benzene levels and metabolites of pyrene/benzene in urine

Integrated monitoring

- Linkage to environmental monitoring
  - Use of existing monitoring information
  - Points to source and exposure route

  → Importance and efficacy of environmental measures

- Linkage to health
  - Use of questionnaire data
  - Use of existing health registers in hospitals and schools

  → Information on health relevance

- **Thanks to…**
  Flemish Centre of Environment & Health (Steunpunt M&G)

- **G.Koppen, E. Den Hond, V. Nelen, E. Vandemieroop, M. Bilau, K. Desager, N. Vanlarebeke, W. Bayens, K. Keune, I. Loots, L. Bruckers**

- **Financed by…**
  Flemish Administration of Environment, Nature and Energy (LNE) - Department Environment & Health

Air pollutants vs. human blood/urine levels

Air quality	**Averaging time** before blood/urine coll.	**Human biomonitoring** Biomarker	**non-smokers**
Lead	1 month	**Pb blood** 	1368
Cadmium	75 days	**Cd blood**	1368
	1 year	**Cd urine**	1368
B(a)P	1 week	**1-OH pyrene urine**	1386
Benzene	1 week	**Tt'muconic acid urine**	1386
	2 days	**Benzene-dosimetry**	162

Air pollutants vs. 'integrating' human biomarkers

Air quality	Averaging time before blood/urine coll.	Human biomonitoring Biomarker	non-smokers
NO_2, O_3, $PM_{2.5\_prim}$, PM_{10_prim}, Cd, B(a)P, benzene conc. (4x4 km)	2 days	% DNA damage	390
NO_2, O_3, $PM_{2.5\_prim}$, PM_{10_prim}, Cd, Pb, B(a)P, benzene conc. (4x4 km) + CO, NO_x, $PM_{2.5}$, PM_{10}, Cd, B(a)P, benzeen, SO_2, NH_3, VOS_{tot} emissions (0.5x0.5 km)	1 year	Current asthma	1262
		Doctor diagnosed astma	1822
		Ever asthma symptoms	1196
		Airway infections	1304

September 26, 2008

Integrated monitoring – vision or reality?

Milena Černá
Netional Institute of Public Health/
Charles Univ., 3rd Fac. Med., Prague

„Definition“

The integrated monitoring for E & H assesments refers to the simultaneous measurement of physicial, chemical and biological properties of an natural-man made environment, ecosystem and human system over time and across matrices from exposure to effect on human health over both time and spatial scale.

(*Draft review on integrated monitoring (WP 2.4)*

This idea of integrated monitoring was also the starting point for realization of the Environmental Health monitoring system in the Czech Republic, when early in 90-ties the Czech Government decided to finance the project Environmental Health Monitoring system.

The aim of this project was to aggregate the till then existing incomplete data and to produce relevant data for HRA, HIA, EIA, for the decision of the national authorities etc.

Environmental Health Monitoring System (EHMS) in the Czech Republic

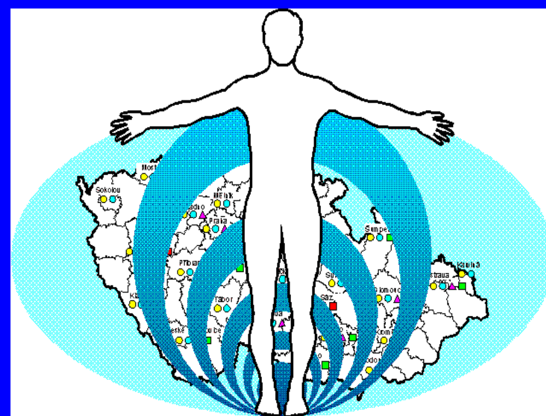
Govt. Decree No. 369/1991

Routinely operated since 1994.

One of the priorities of the National Environmental Health Action Plan (Govt. Decree No. 810/1998).

Relied upon the Act No. 258/2000 on Public Health.

Focused on program HFO 21.



www.szu.cz/chzpa/sumrep.htm

Structure of EHMS

8 subsystems - projects

- Health effects and risks of air pollution
- Health effects and risks of drinking water pollution
- Harmful effects of ambient noise
- Health effects and risks of dietary exposure
- Human biological monitoring
- Health status and health determinants
- Health risks related to urban soil contamination
- Health effects and risks of occupational environment

EHMS outputs

Generally, formation of projects to one integrated system project tries to cover the three important parts of integrated monitoring:

- Presence and levels of indicators in environmental media (air, water, soil, diet, noise), comparison with limit values;
- Exposure, body burden, comparison with the existing biological limit values (biomonitoring)
- Health effects possibly connected with the environmental pollution and lifestyle (respiratory diseases, allergies, water-borne or food-related alimentary infections and intoxication, etc.)

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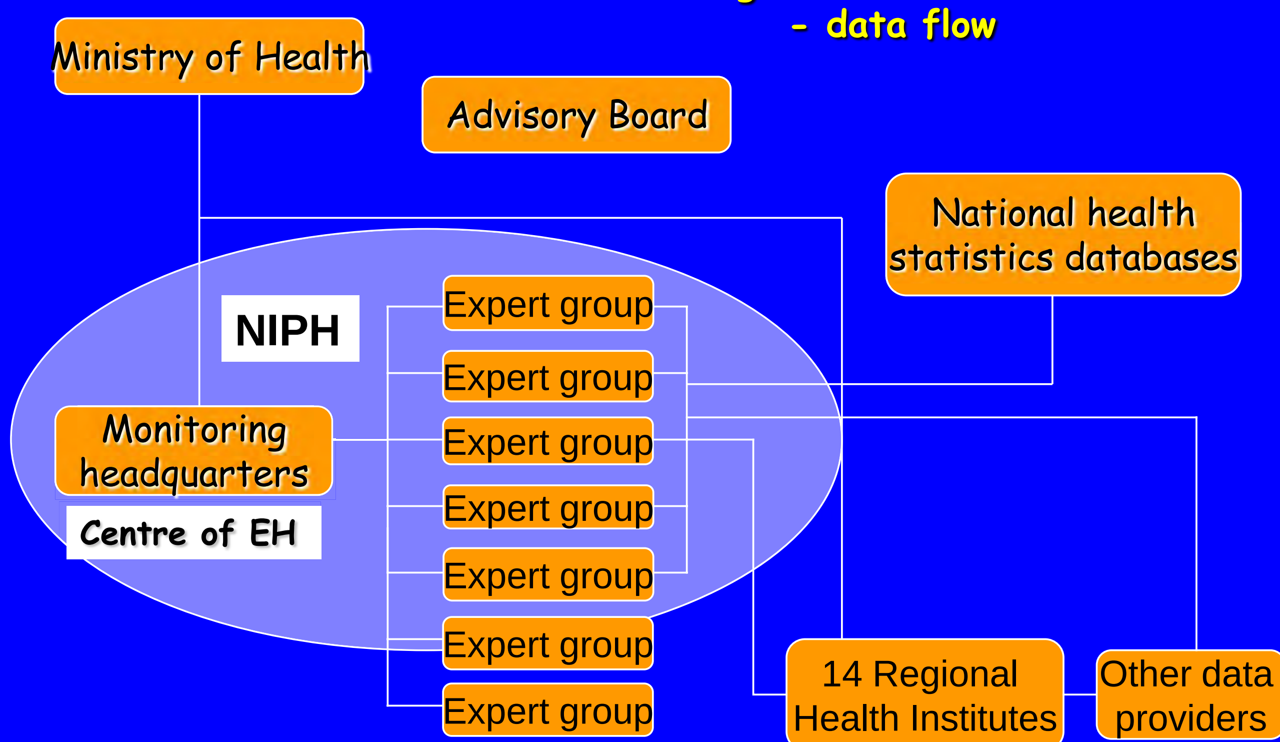
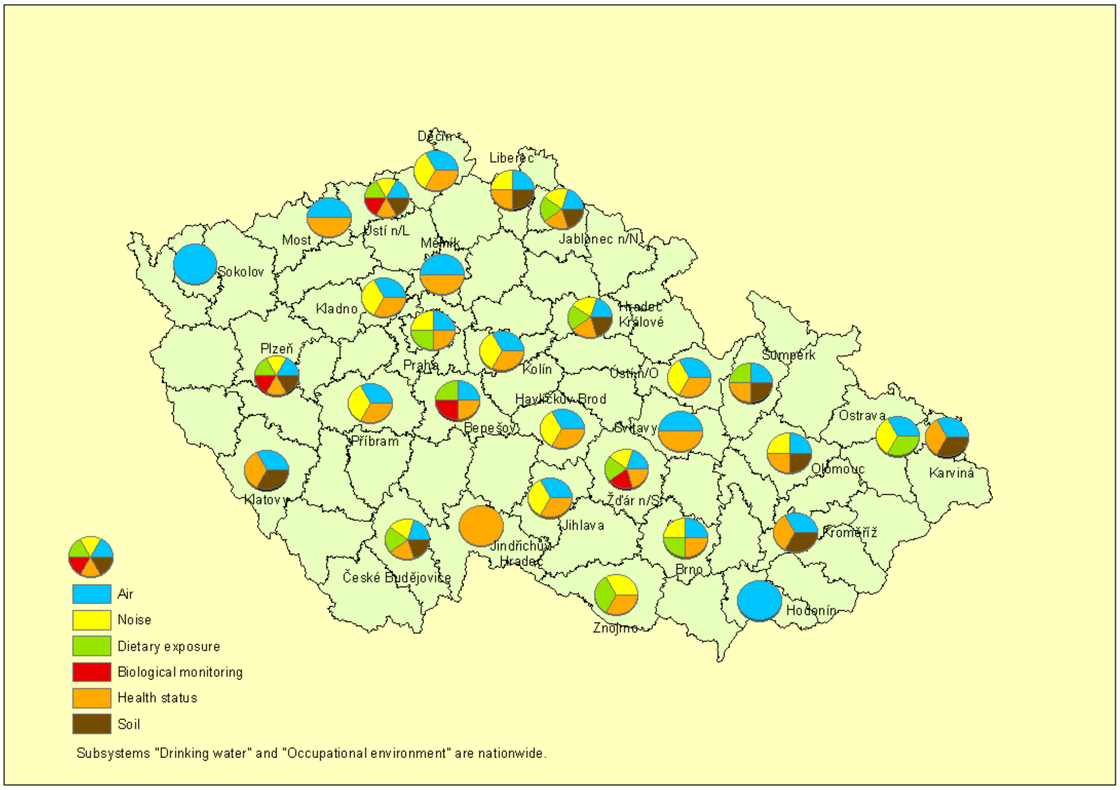
Organization of EHMS - data flow



The cities participating in the EHMS



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Scope of monitoring (Air)

Air quality

(concentrations of classical pollutants, metals, PAHs, VOCs)

Health effects:

Acute respiratory diseases

(records from 120 paediatricians and physicians)

Allergy in children

(records from 54 paediatricians + survey of 7850 children)

Scope of monitoring (water)

Drinking water quality
(within the scope of Directive 98/83/EC)

Health effects:

Water-borne infections and intoxications
(national notification database EPIDAT, reports from Regional Public Health Centres)

Scope of monitoring (noise)

Noise levels in quiet and noisy city streets
(regular daytime and nighttime measurements of acoustic pressure levels)

Health effects:

Health complaints attributable to noise
(survey in population of localities monitored for noise)

Scope of monitoring (dietary exposure)

Contaminants in food consumption basket
(organic (>17 isomers) and inorganic (16) contaminants in 195 different foodstuffs)

Health effects:

Alimentary infections and intoxications
(national notification database EPIDAT)

Scope of monitoring (HBM)

Levels of inorganic and organic contaminants, and beneficial elements in body fluids and tissues of adults and children (**biomarkers of exposure**).

Chromosomal aberrations in peripheral lymphocytes (detected in adults and children - between 300 and 400 subjects per group and year) (**biomarker of both exposure to genotoxic stressors and early adverse effect**) .

Scope of monitoring (health effects)

Questionnaire survey of health status and lifestyle in urban population (study HELEN)

(five-year interval survey with medical checkups, in the last phase responded 14 200 randomly selected subjects aged 45 to 54 years, out of 21 600 subjects: returnability about 70%)

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Scope of monitoring (soil)

Topsoil contamination of children´s playgrounds

(chemical and microbial contamination of kindergarten playgrounds)

Health effects:

Diarrhoeal afflictions and parasitic diseases in children

(health survey of children attending kindergartens)

Scope of monitoring

Occupational environment quality:

Occupational Exposure Registry

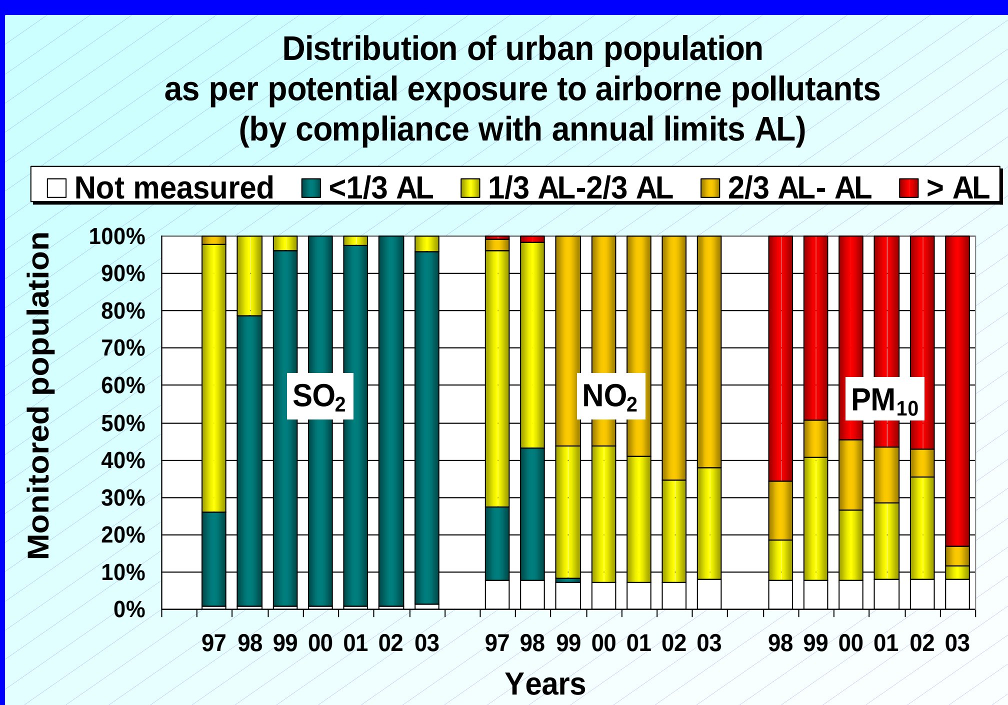
Job categorization

Regex – occupational exposiure to carcinogens

Health effects:

Incidence registry of occupational diseases
(occupational diseases and occupational diseases threats central database)

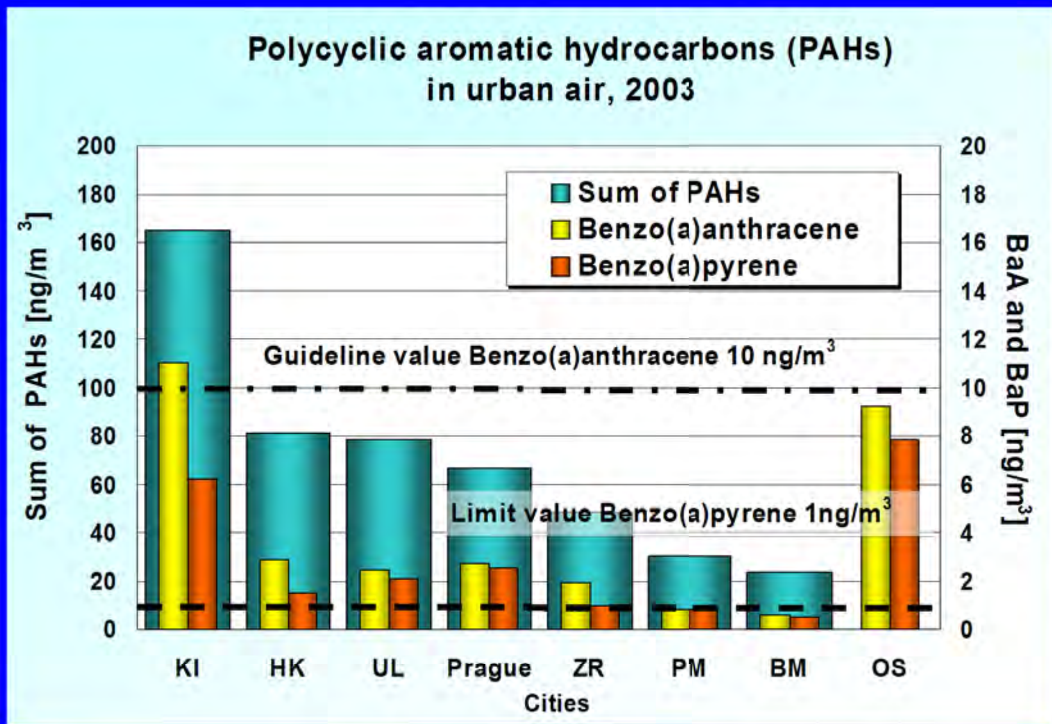
Population exposure estimates



The population exposure to suspended particulate matter becomes more significant

In 2003, the legislative standards for PM were not met in 83% of the population in the monitored cities

CZ – EHMS



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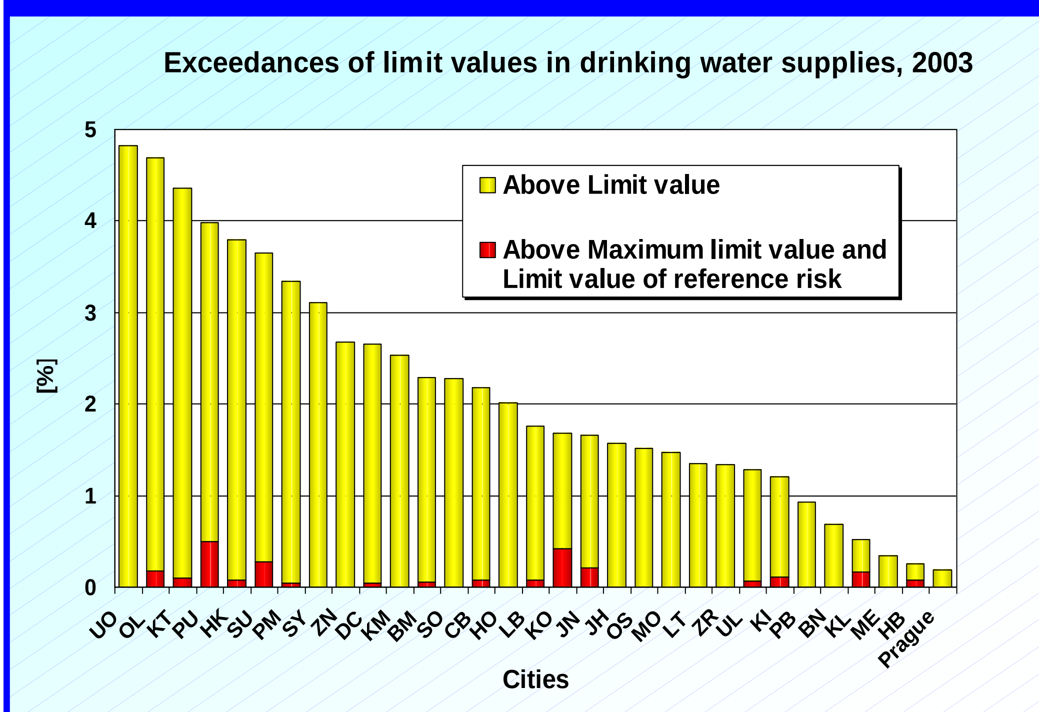
CZ – EHMS
Health effects and risks of water pollution



Drinking water from large public water supplies continues to be of good quality

Hazardous chemical contaminants limits were only exceeded in isolated cases (in red)

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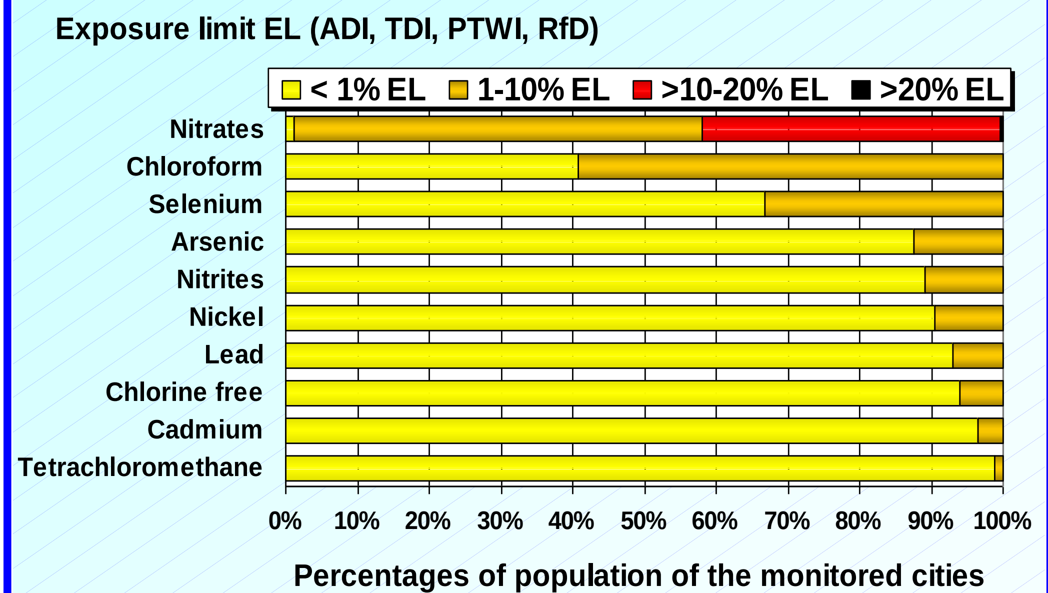
CZ – EHMS
Health effects and risks of water pollution

Distribution of urban population as per their exposure to drinking water contaminants, 2003



From drinking water, nitrate exposure is the highest, reaching up to 10 % of ADI in almost 60 % of population, more than 10 % of ADI in about 40 % of population and more than 20 % of ADI in 0.4 % of population

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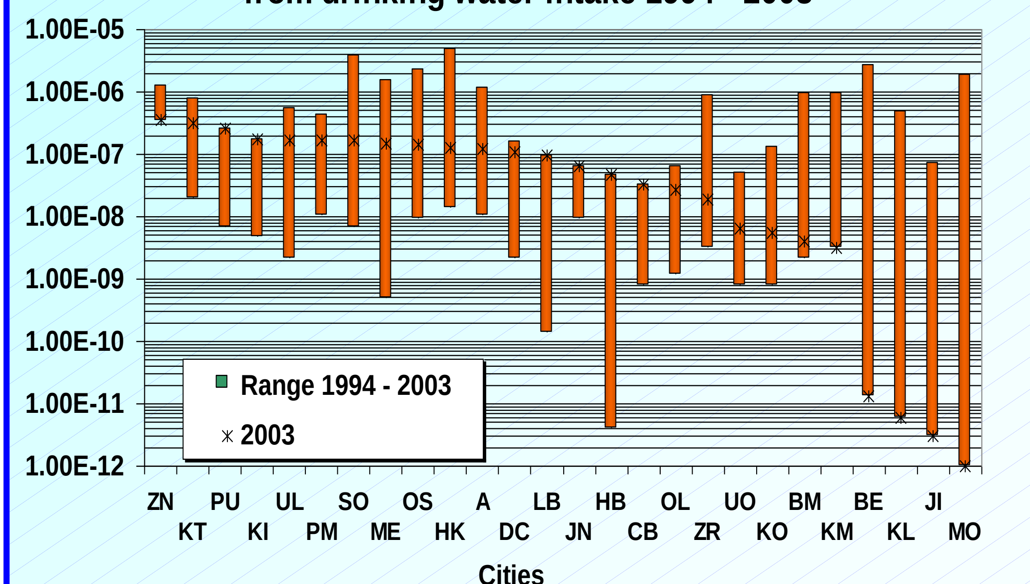
Risk assessment

Estimate of cancer risk increase from drinking water intake 1994 - 2003



Very little cancer risk is associated with consumption of drinking water: the estimated increase in cancer risk is in the range of 1 case per 1 million to 1 billion population annually

Less than 1 additional case of cancer could be expected in all cities monitored (about 3.5 million population)

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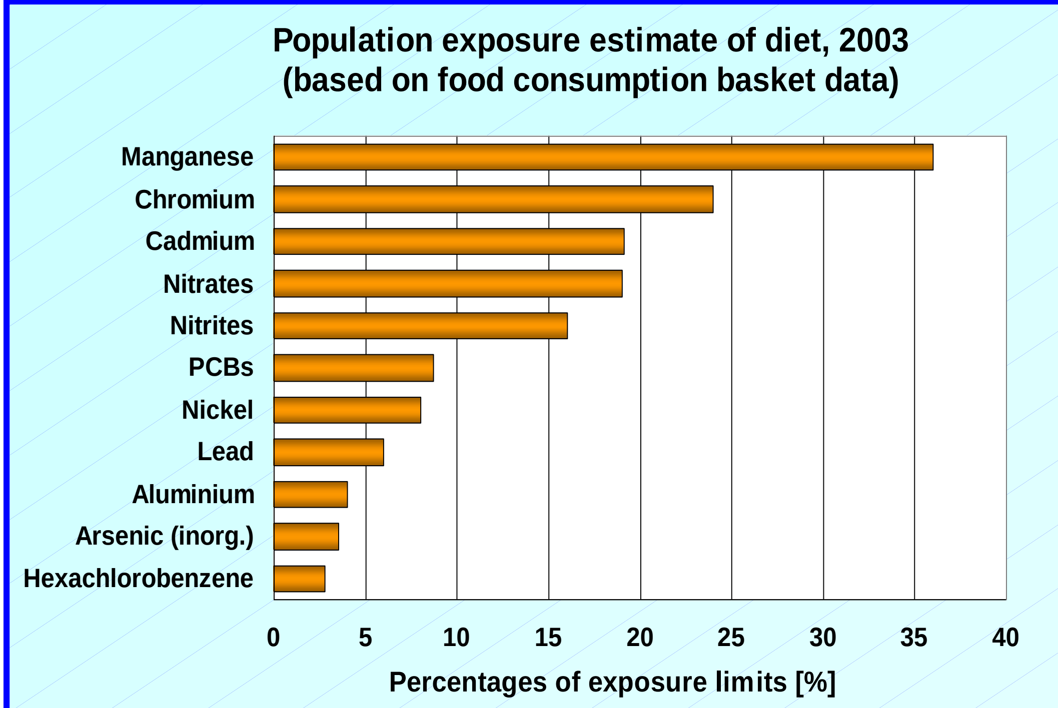
CZ – EHMS

Health effects and risks of dietary exposure



Mean chronic population exposure to organic (>17 isomers) and inorganic (16) substances does not exceed the critical values for inadmissible health risk (for non-carcinogenic effect) and does not exceed exposure limits

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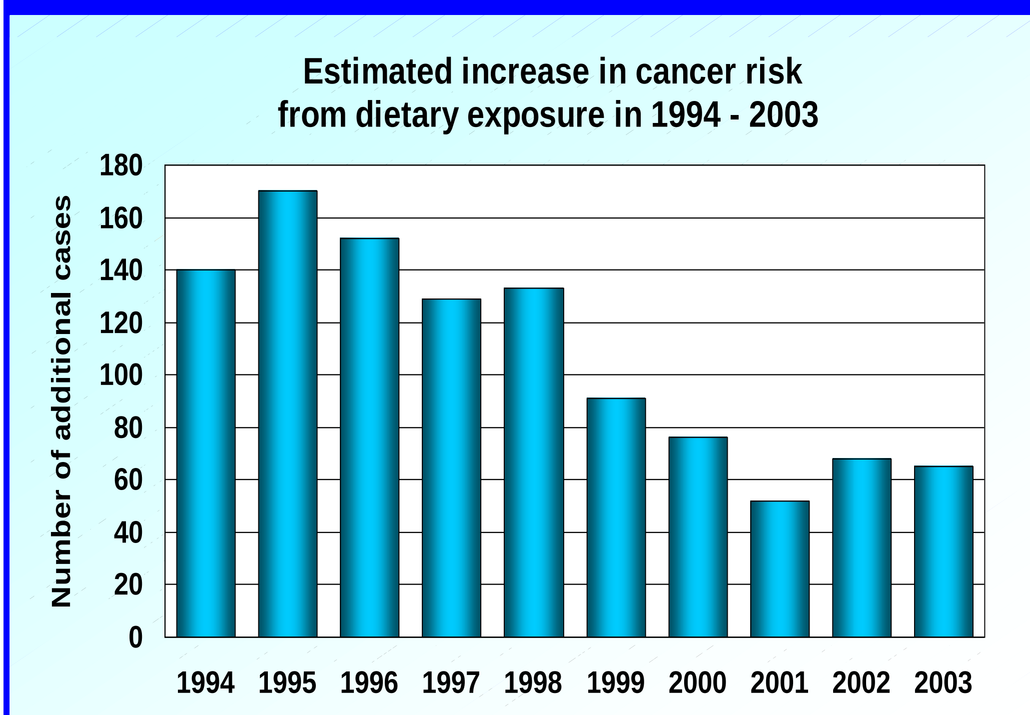
Risk assessment



The theoretical increase in risk of contracting cancer from dietary exposure amounted to about 65 additional cases in CR in 2003

PCBs and arsenic have the greatest share in the estimated increase.

Human Biomonitoring System in the Czech Republic

HBM - objectives

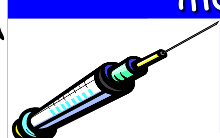
- To assess and evaluate the extent, the distribution and the determinants of exposure of the Czech population to important environmental pollutants.
- To follow up long-term time trends.
- To establish reference values.
- To generate data necessary for preventive measures and control of their effectiveness.
- To use these data for health risk assessment.
- To produce data essential for international comparison.

HBM - scenario

- Where to sample (localities)
- What population
- Ethical questions
- What kind of biomarkers
- What kind of matrices, body fluid/tissues
- Sampling – SOP (timing, sampling devices, storage, transport etc.)
- Selection of analytical methods, laboratories, QAQC
- Questionnaire
- Database
- Data evaluation, presentation, interpretation

HBM – integrated sampling according to SOP

Adults and children – timing March through May

Blood – 5 ml, heparinized Sarstedt monovette declared for metal analysis

2 ml for cytogenetic analysis

2 ml for metal analysis

Blood serum (adults only) – ochratoxin A

Urine – 30 ml, PE container prewashed for metal analysis

(+ creatinine + cotinine)

Hair (child only)

Breast milk – 30 to 50 ml, throughout the year

HBM – integrated analysis according to SOP

Blood – selected toxic and benefit elements
- cytogenetic analysis

Blood serum - ochratoxin A, POPs

Urine – selected toxic and benefit elements
- creatinine
- cotinine
(nitrate, fluoride)

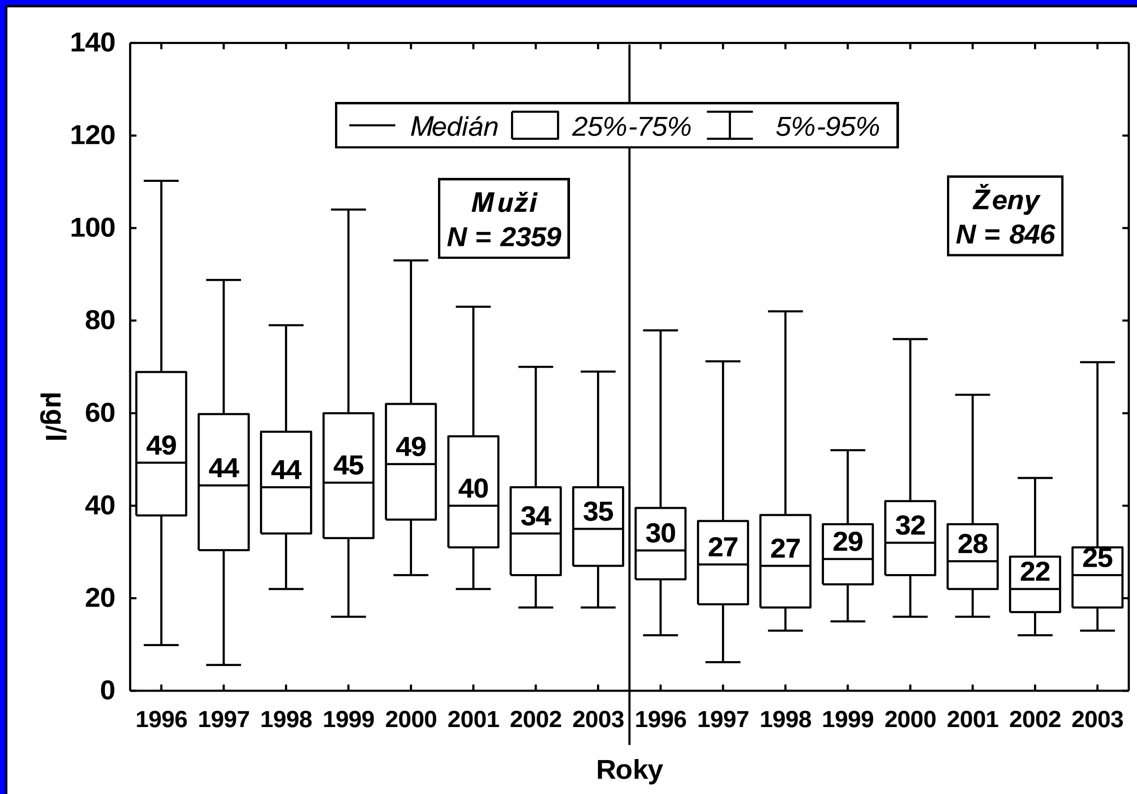
Hair – selected toxic and benefit elements

Breast milk – chlorinated pesticides, indicator congeners of PCBs, (metals, AFM1)

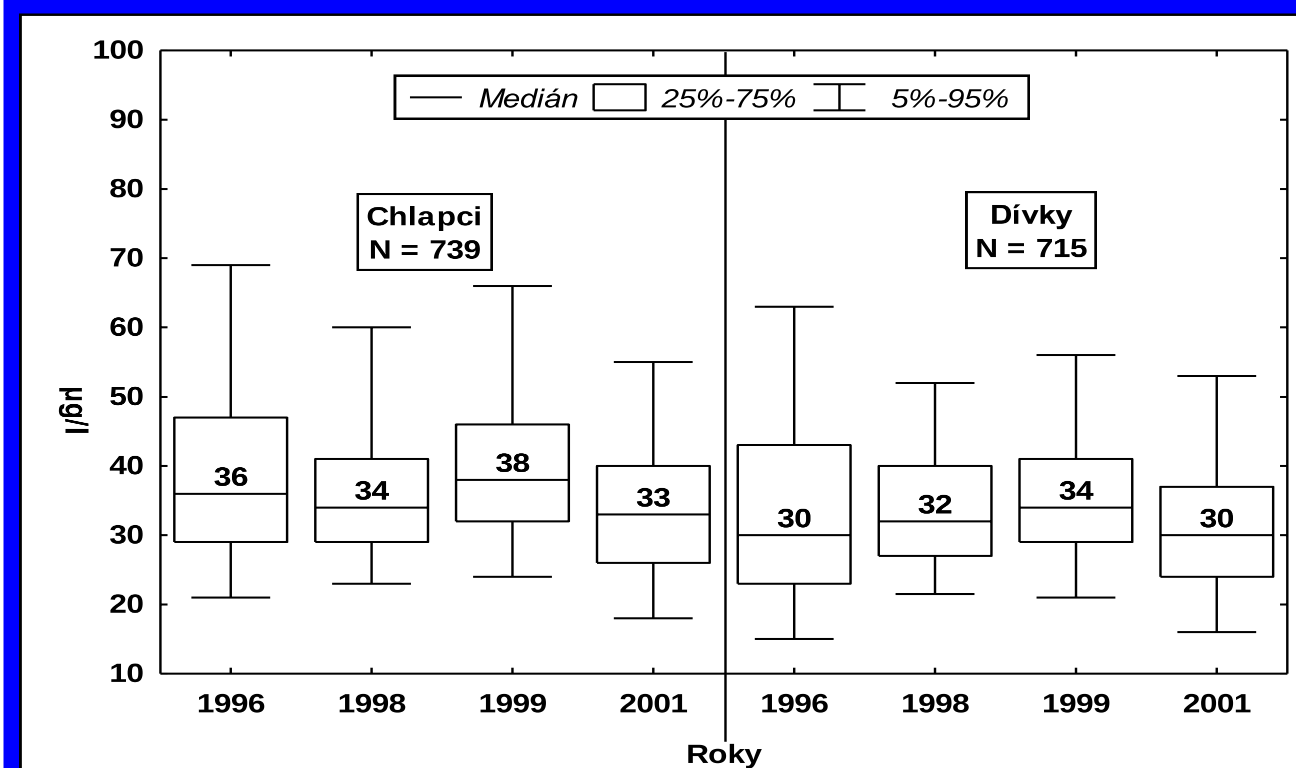
HBM – selected results

Concentrations of selected elements in blood of the Czech population

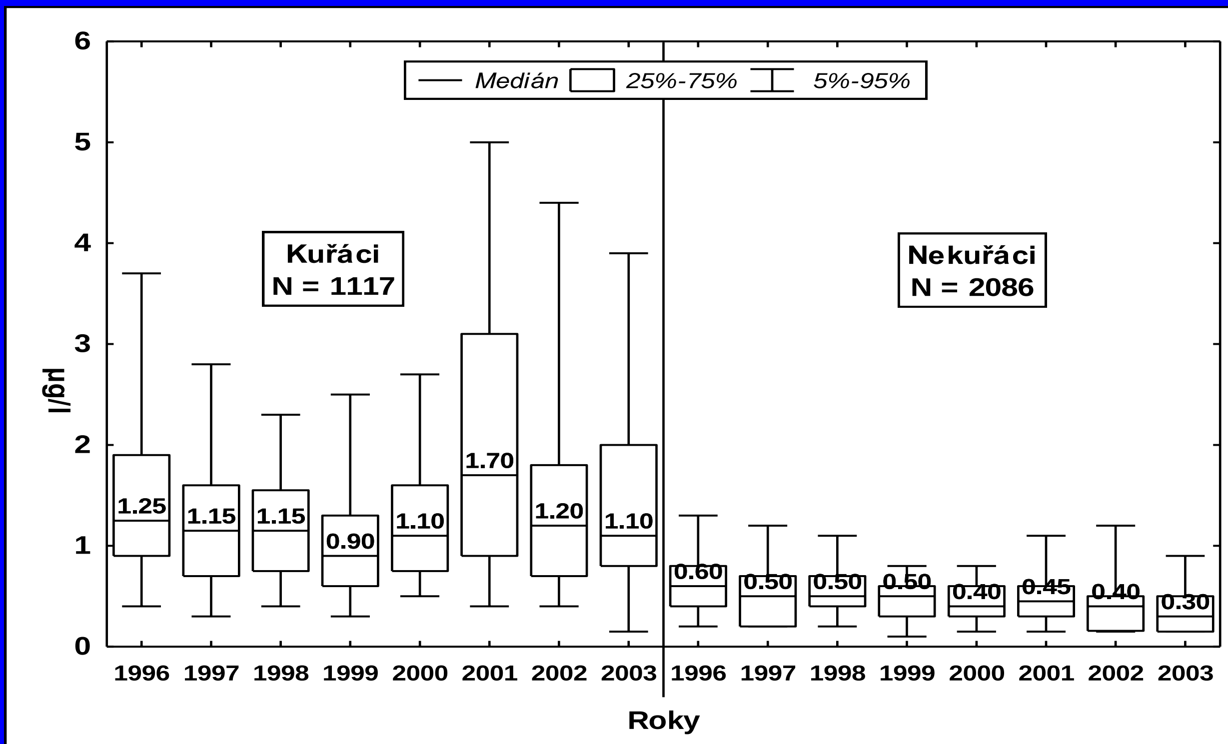
Blood lead levels in adults



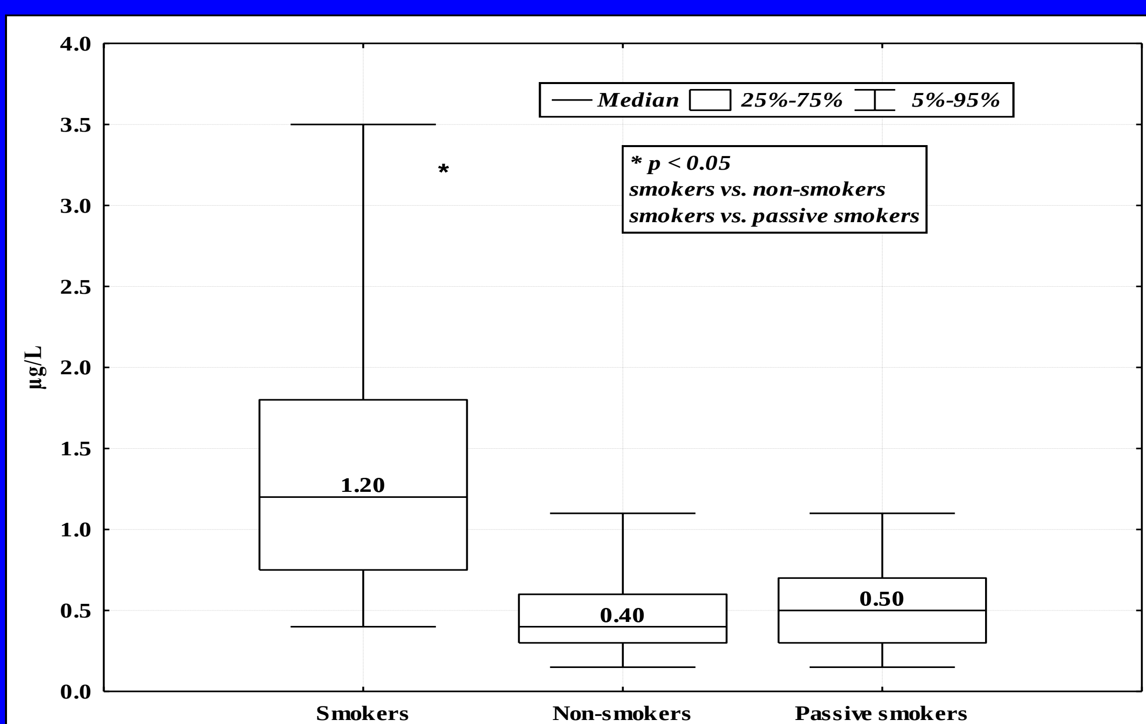
Blood lead levels in children



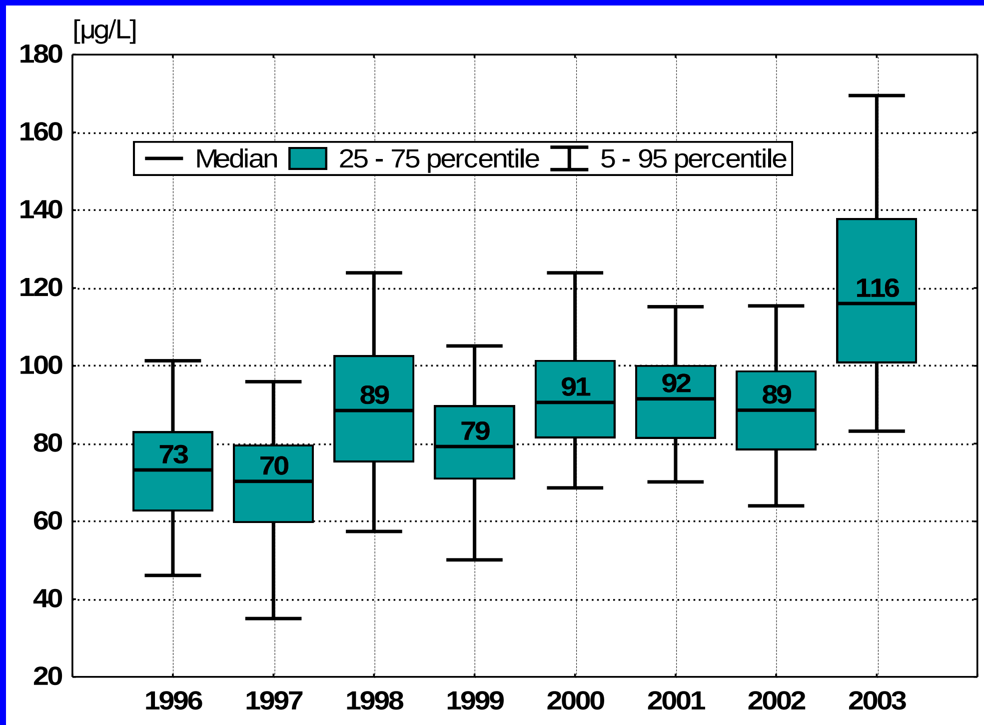
Blood cadmium levels in adults



Blood cadmium levels in adults (1996-2003)

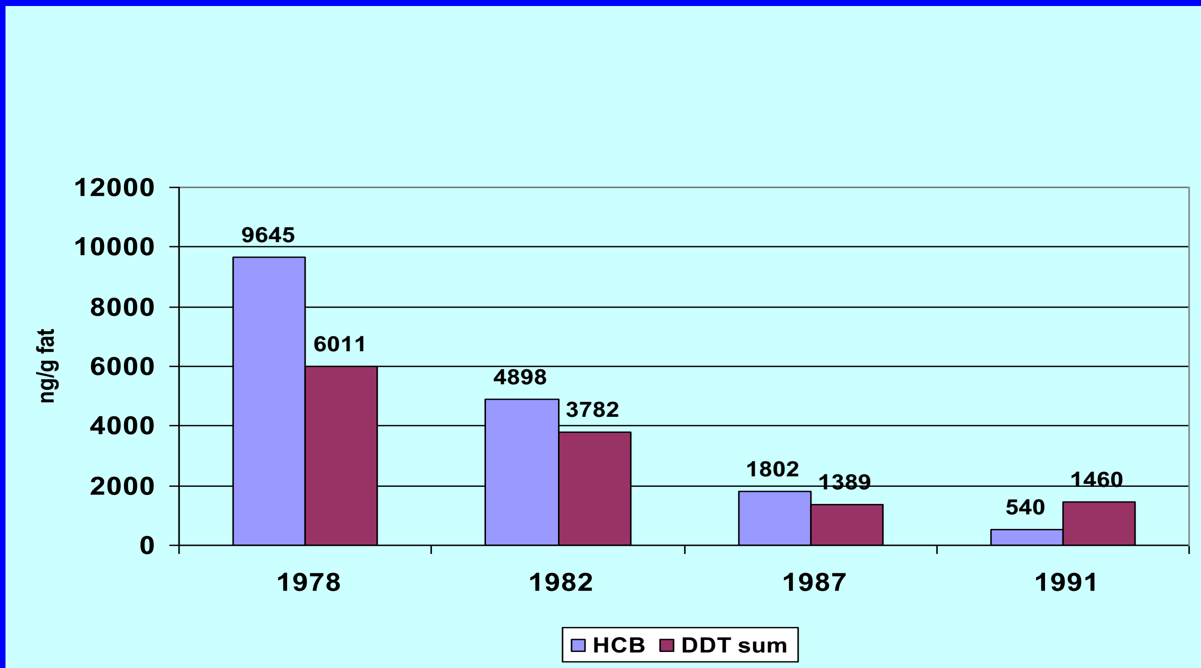


Blood selenium levels in adults

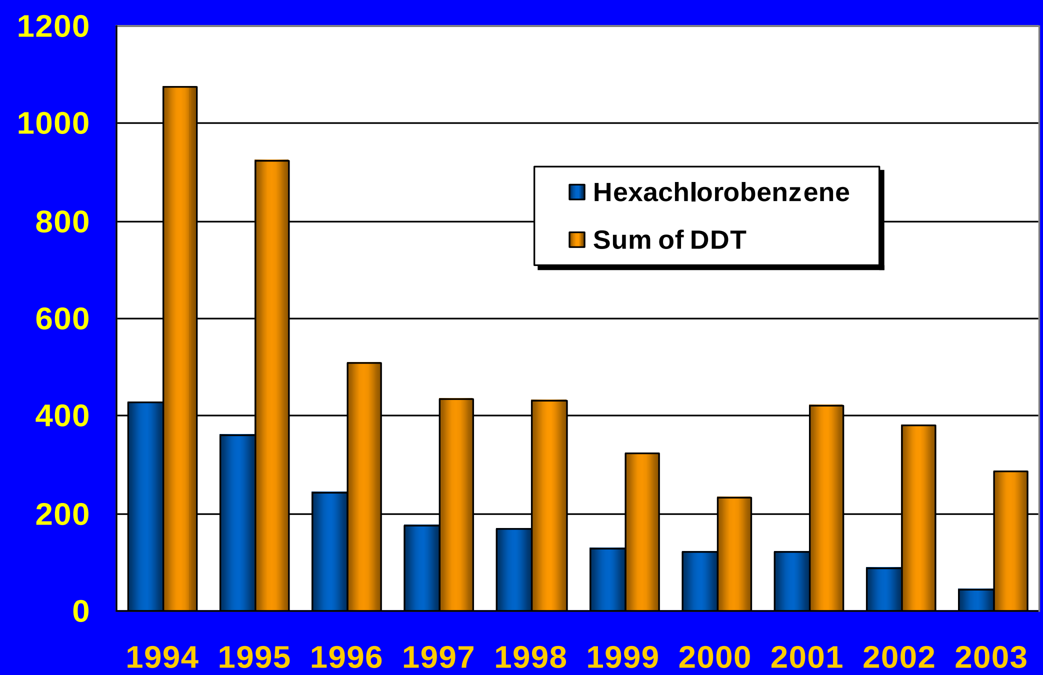


Concentrations of selected persistent chlorinated organic compounds in breast milk of the Czech population

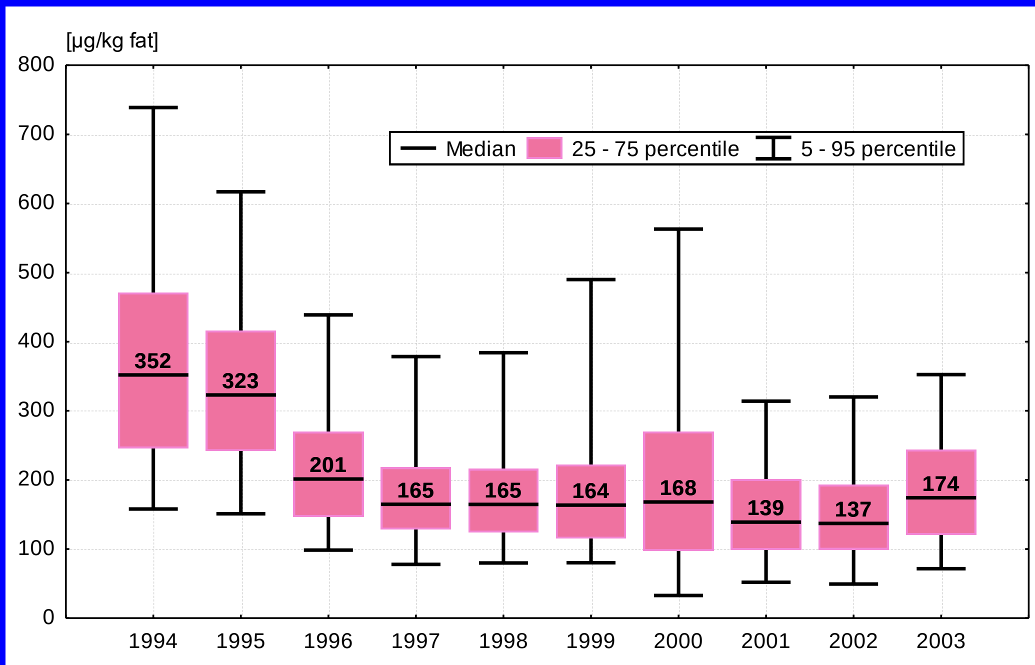
Levels of DDT and HCB in human milk of the Czech population in the period 1978 to 1991 (data published in local journals)



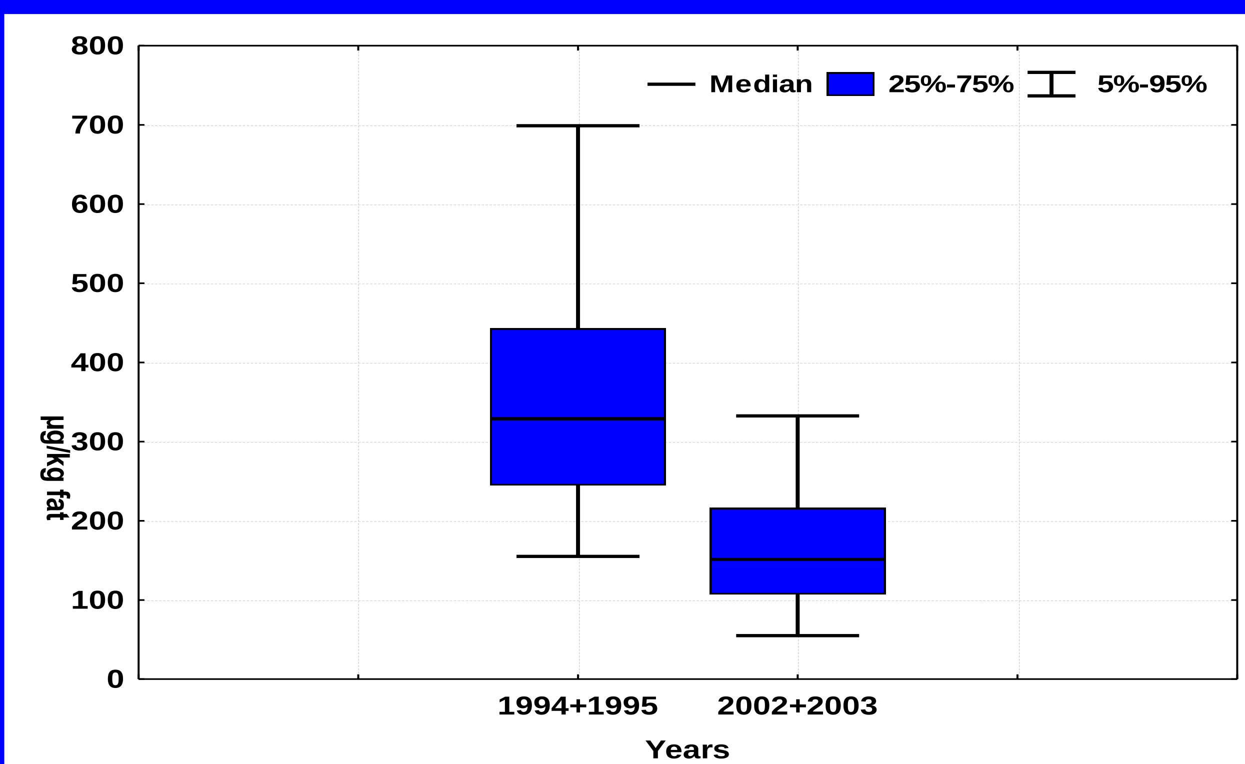
Chlorinated pesticides in human milk (medians, ng/g fat)



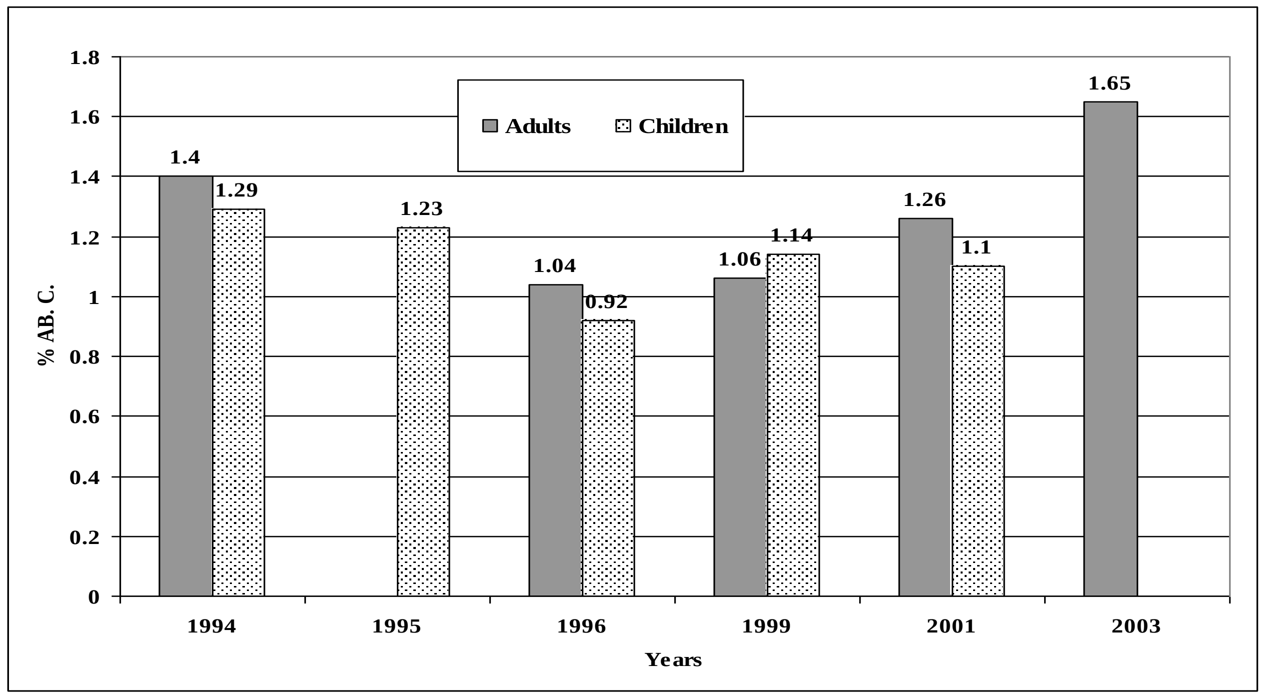
Polychlorinated biphenyls in human milk (indicator congener PCB 153)



Levels of indicator PCB 153 in human milk fat: differences in reference values throughout the years

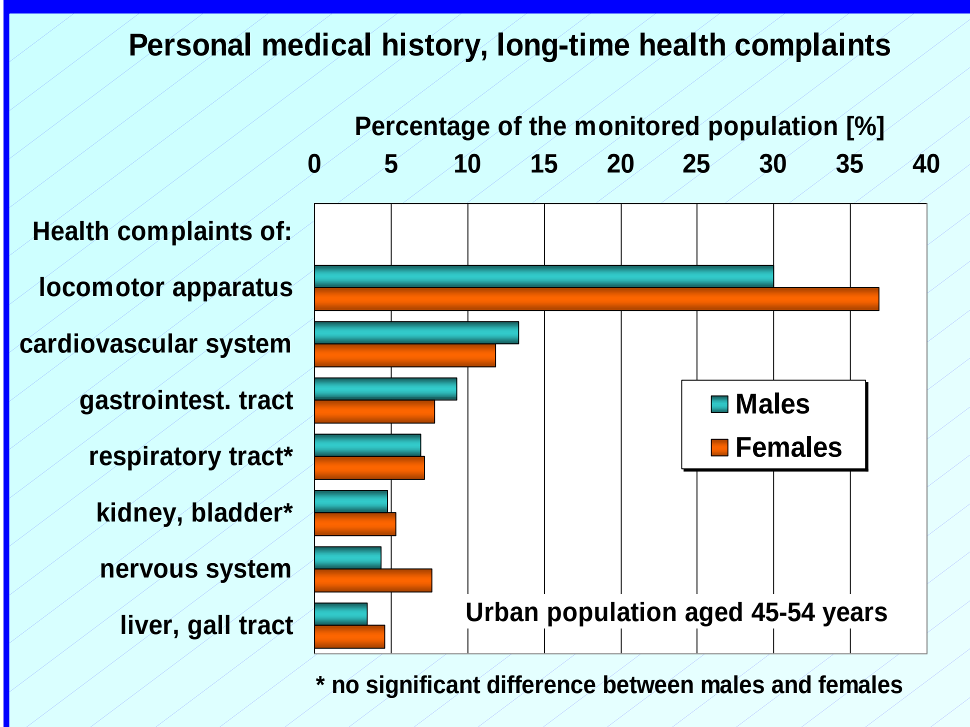


Cytogenetic analysis – frequency of chromosomal aberrations in the peripheral lymphocytes of the Czech population



Centre of Environmental Health, National Institute of Public Health, Prague

Health status

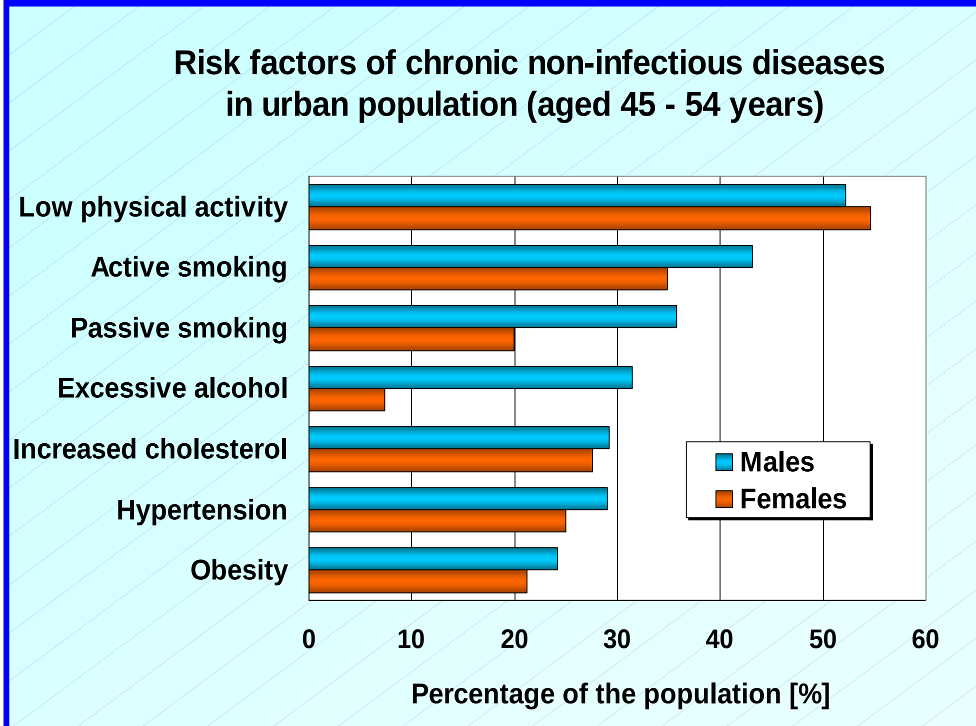


Long-term complaints are most frequently related to the locomotor apparatus (34%) and the cardiovascular system (13%)

Females significantly more frequently suffer from long-term health problems, they visit physicians more often and use the long-term medication more frequently

Centre of Environmental Health, National Institute of Public Health, Prague

Health status II



There were found important differences in risk factor occurence between monitored cities and between males and females

Limitations of the CZ-EHMS

Only selected urban population is covered with the monitoring activities;

The participation of urban areas in the monitoring activities was based at the beginning on voluntary basis;

Not all projects are realized in each urban areas;

Environmental monitoring, biomonitoring, and health status studies are not properly interconnected as to monitored individuals;

Insufficient communication with general public;

Not optimal utilization of monitoring data for risk management.

Some limitations and questions of integrated monitoring in general

How to incorporate the data on **individual susceptibility** (gene – environmental interaction) to the integrated monitoring? (insufficient data, ethical problem, lack of interpretation…)?

How to include **socioeconomical difference** to the evaluation and interpretation of environmental health monitoring data?

How to evaluate differences in dietary habits and nutritional status to the complex approach of integrated monitoring?

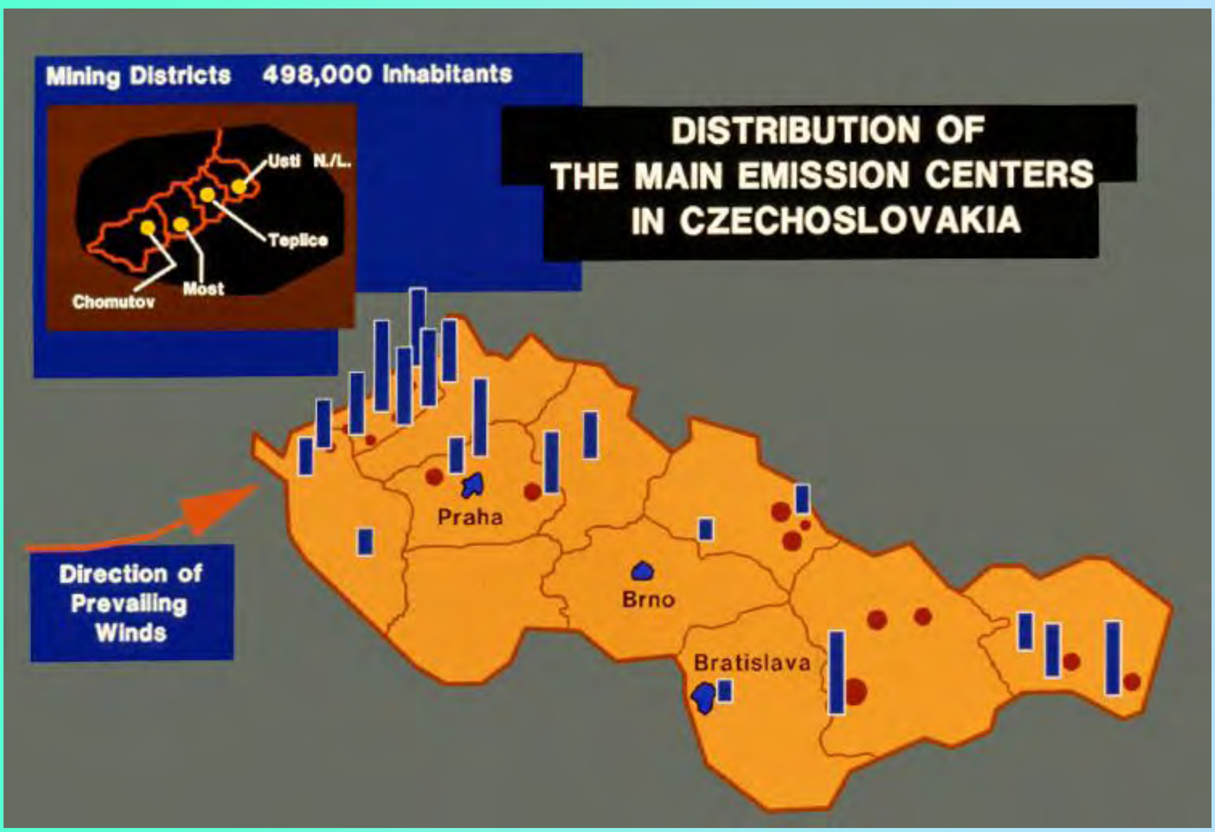
Thank you for your attention

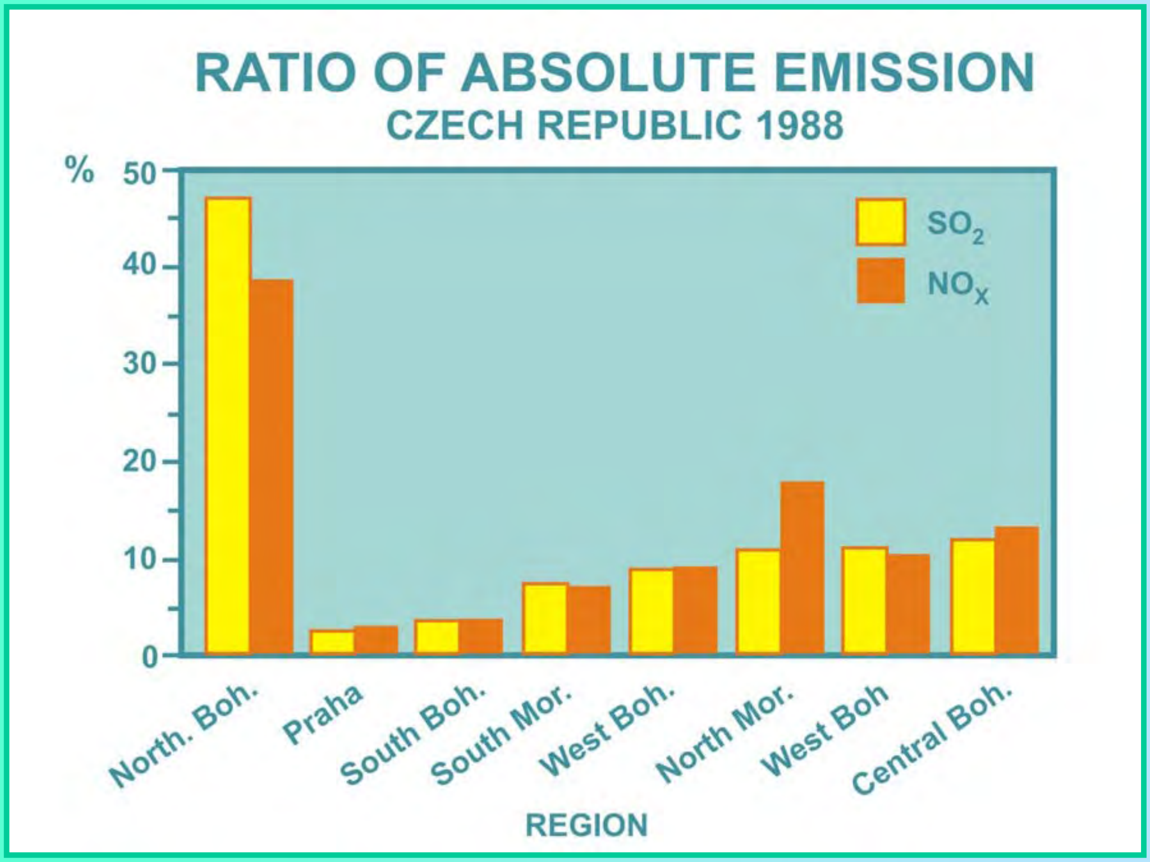
THE IMPACT OF AIR POLLUTION TO HUMAN HEALTH – CZECH EXPERIENCE

Radim J. Sram

Institute of Experimental Medicine AS CR, v.v.i., Prague, Czech Republic

INTARESE, Tromso, Norway, June 2-5, 2008





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LIFE EXPECTANCY
(years)

District of Teplice

YEAR	Czech Republic		Teplice	
	Males	Females	Males	Females
1983	67.0	74.2	65.7	73.1
1984	67.3	74.2	65.1	73.8
1985	67.5	74.7	67.1	73.0
1986	67.5	74.6	65.2	72.4
1987	67.8	75.1	65.3	72.2
1988	68.2	74.4	64.9	73.9

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TEPLICE PROGRAM

IMPACT OF AIR POLLUTION
ON HUMAN HEALTH

Model district	Control district
TEPLICE	**PRACHATICE**
(coal power plant open pit mines industry)	(agricultural area)

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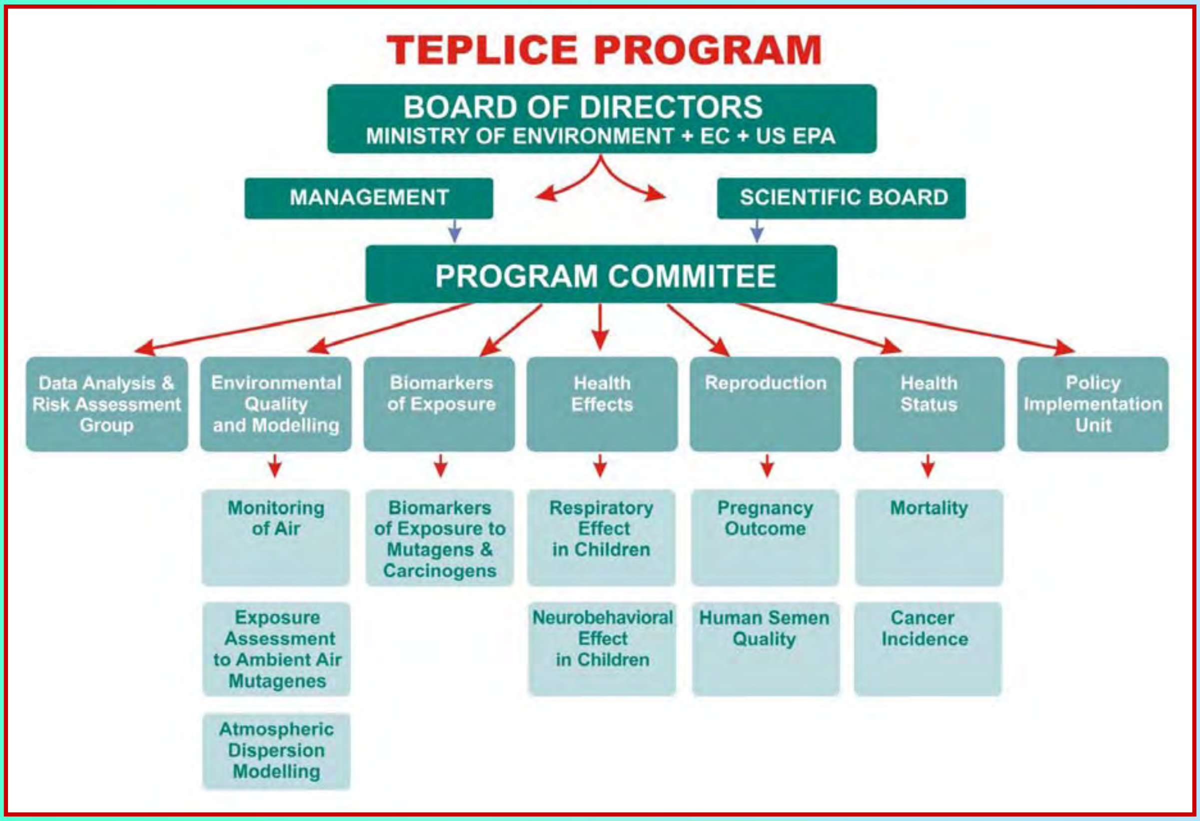
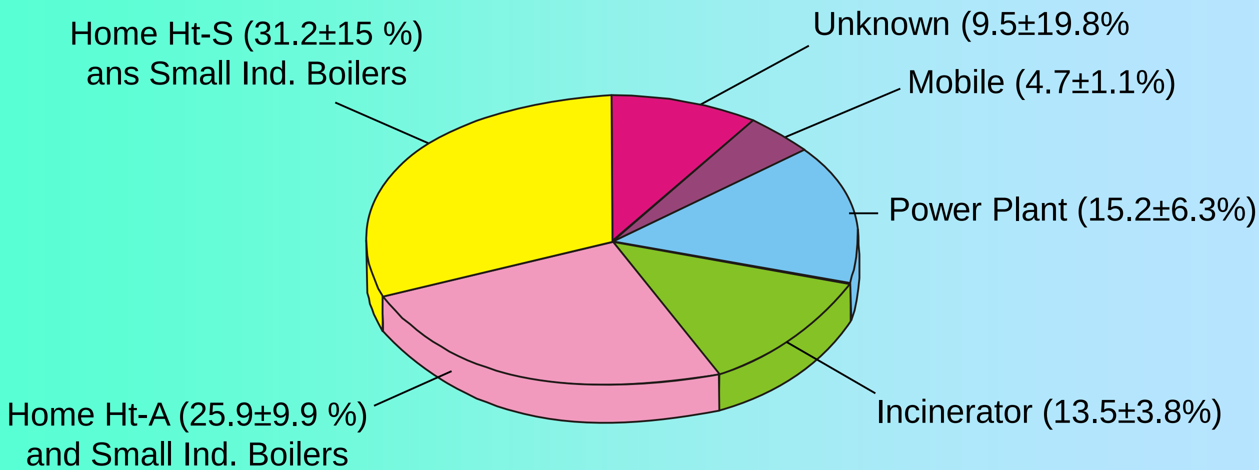


AIR POLLUTION

MONITORING

Apportionment of Teplice Fine Mass

January – February, 1994



Average Fine Mass Concentration=52.6 µg/m³

♍2 =1.3

Mass Accounted for = 90.5%

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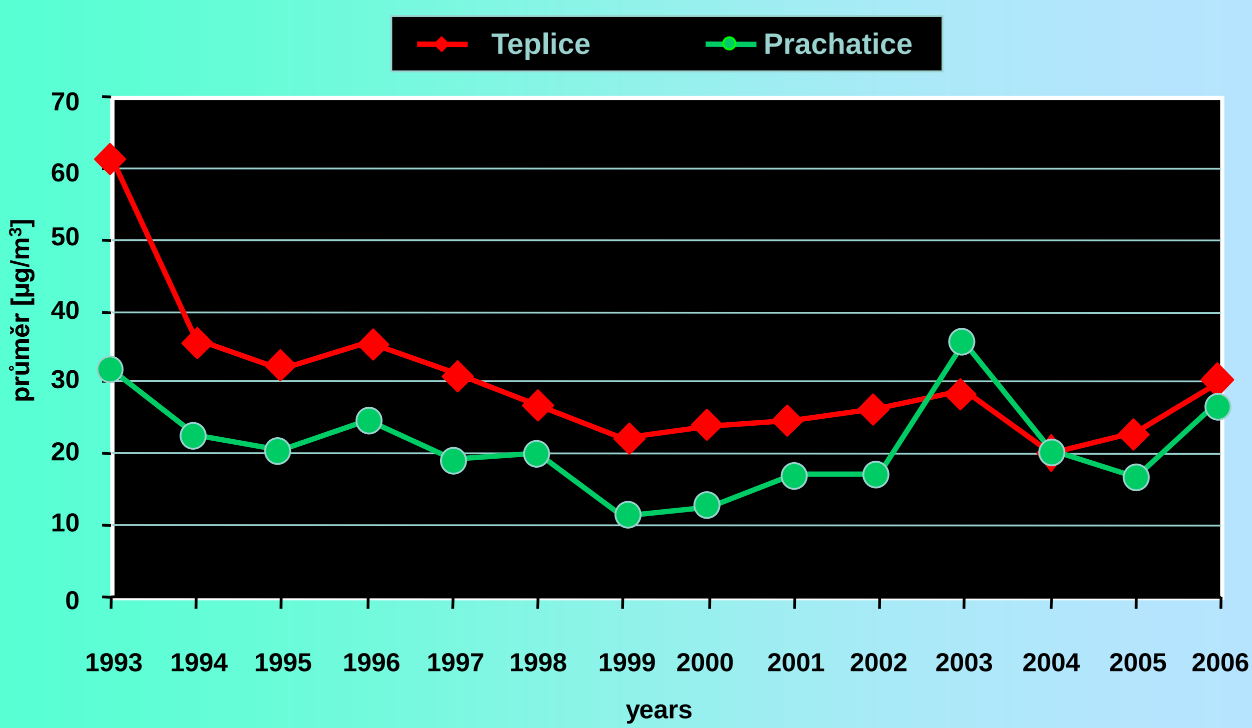
ANNUAL CONCENTRATIONS OF PM2.5



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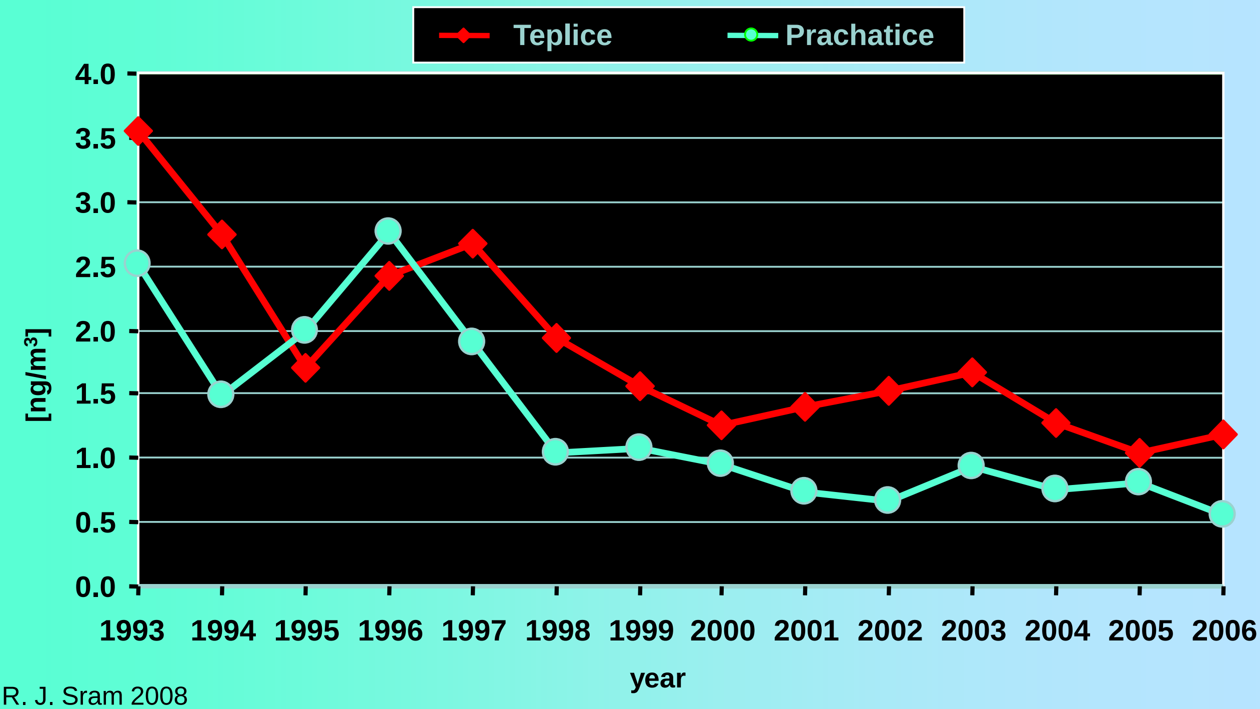
ANNUAL CONCENTRATIONS OF CARCINOGENIC B[a]P



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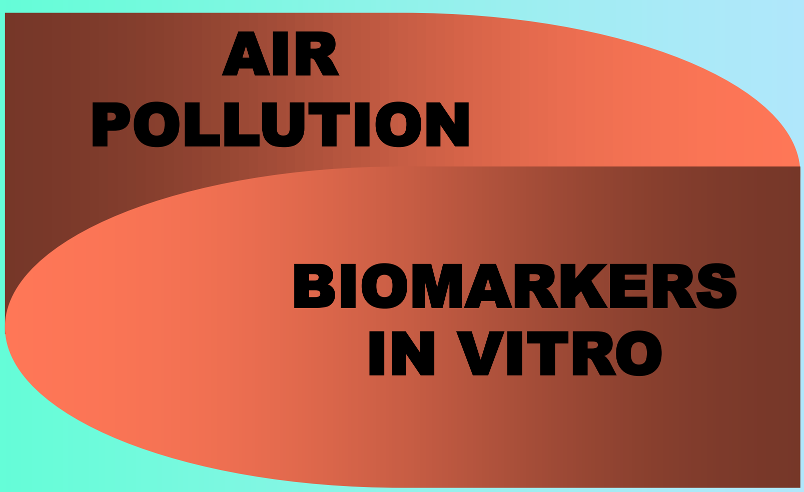

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GENOTOXICITY AND EMBRYOTOXICITY

OF URBAN AIR PARTICULATE MATTER IN VITRO

Characterization

of biologically

active pollutants

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

(Binkova et al. 1999)

PAH-DNA adducts derived from →

9-OH-B[a]P	B[j]F
anti - BPDE	CHRY
B[b]F	B[a]A
B[k]F	I[c,d]P

Total radioactivity from all DNA adducts detected approx. 50 %

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AIR POLLUTION

BIOMARKERS

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c-PAHs CONCENTRATIONS
PERSONAL MONITORING

(median and range)

Group	N	Age (years)	B[a]P ng/m^3	carcPAU ng/m^3
EXPOSED	53	31.6 ± 7.2	1.6 (0.3 - 8.7)	9.7 (3.1 - 58.2)
Smokers	19	32.9 ± 7.0	1.6 (0.3 - 7.5)	10.8 (3.1 - 43.6)
Nonsmokers	34	30.9 ± 7.3	1.5 (0.3 - 8.7)	8.7 (3.1 - 58.2)
CONTROLS	52	29.6 ± 9.1	0.8 (0.3 - 2.8)	5.8 (3.1 - 19.3)
Smokers	7	37.6 ± 14.2	0.3 (0.3 - 1.4)	3.3 (3.1 - 8.2)
Nonsmokers	45	28.3 ± 7.6	0.9 (0.3 - 2.8)	6.1 (3.1 - 19.3)

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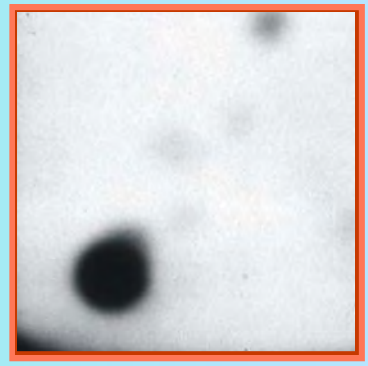
Autoradiographs of thin layer chromatograms with DNA adduct pattern of:

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.)

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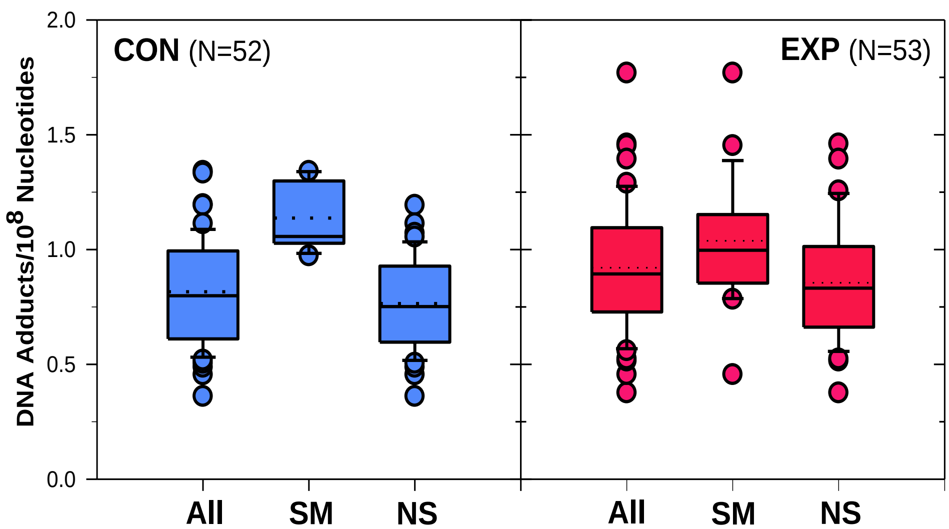
TOTAL DNA ADDUCTS



EXP vs CON: P=0.065

Smokers vs Nonsmokers within groups: P<0.05

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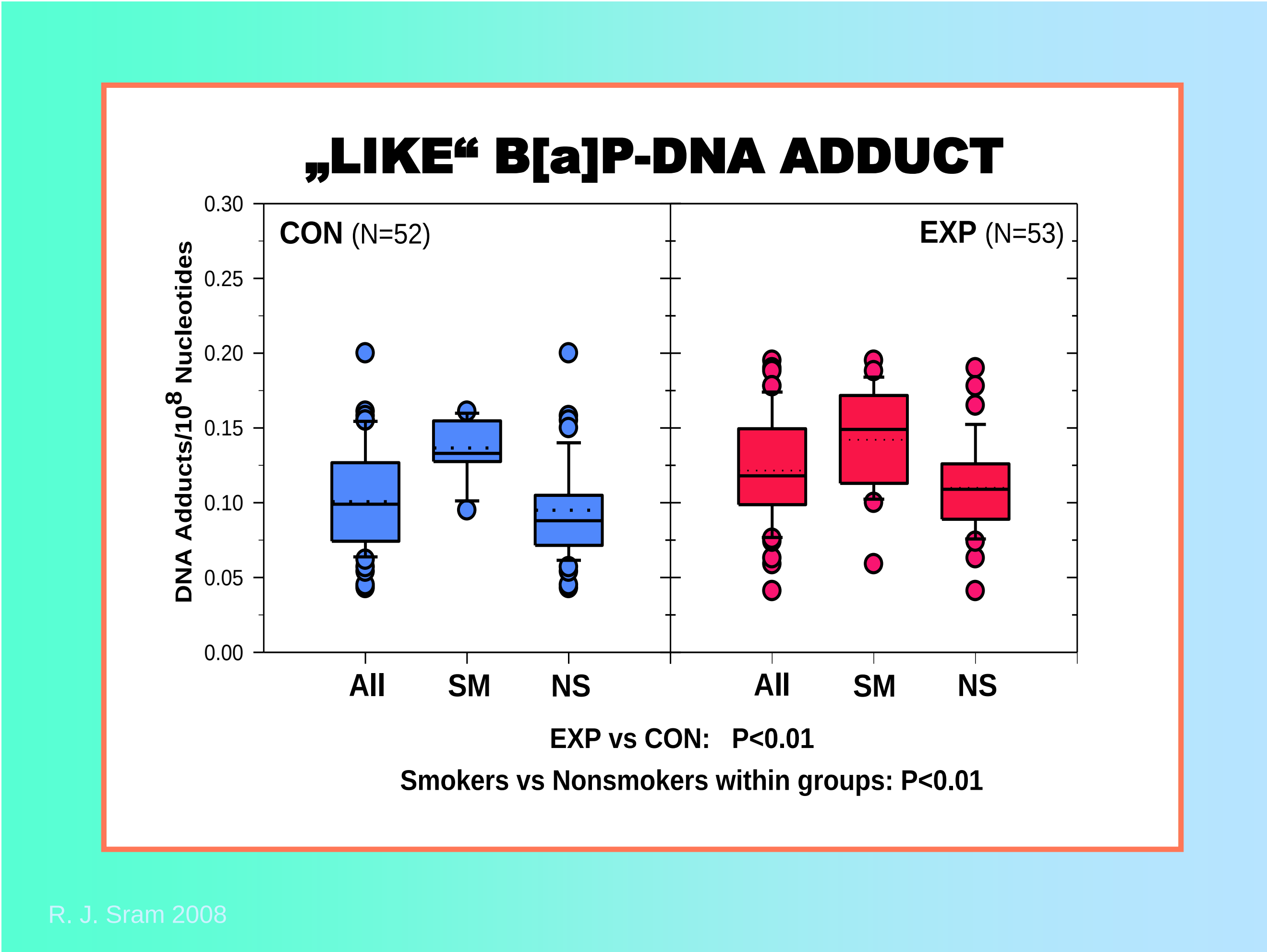
„LIKE“ B[a]P-DNA ADDUCT
DNA Adducts/10^8 Nucleotides
0.30
0.25
0.20
0.15
0.10
0.05
0.00
CON (N=52)
EXP (N=53)
All
SM
NS
All
SM
NS
EXP vs CON: P<0.01
Smokers vs Nonsmokers within groups: P<0.01
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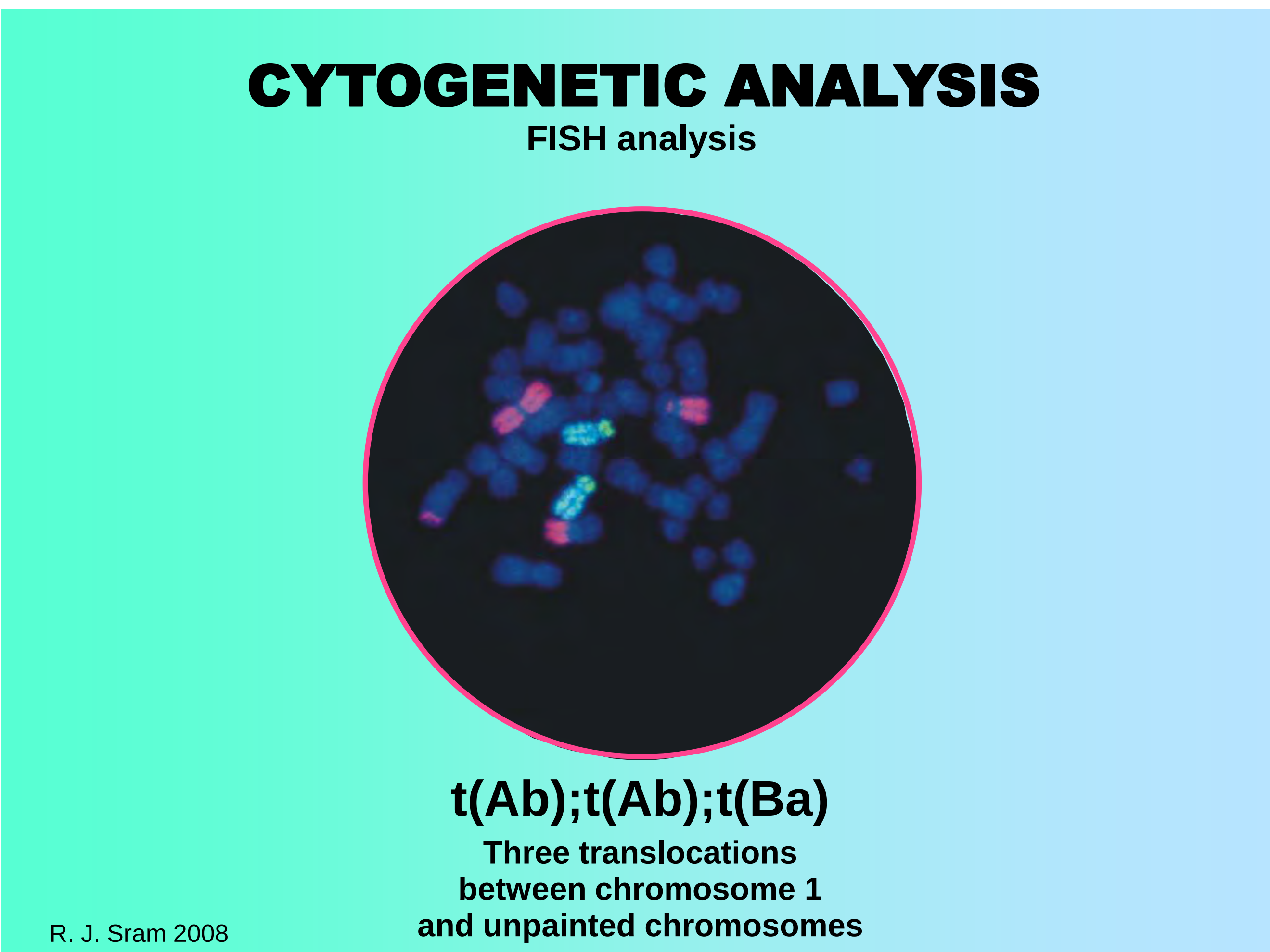
CYTOGENETIC ANALYSIS
FISH analysis
t(Ab);t(Ab);t(Ba)
Three translocations
between chromosome 1
and unpainted chromosomes
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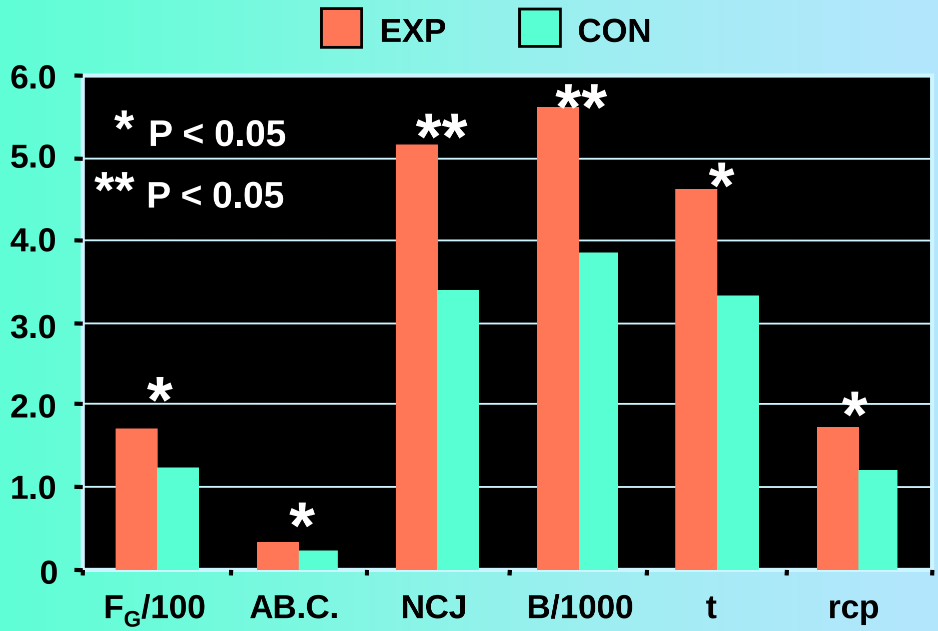
CYTOGENETIC ANALYSIS

FISH analysis



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MULTIPLE REGRESSION ANALYSIS

Percentage of aberrant cells (FISH)

Model	Coefficients	Unstandardized Coefficients B	Sig.	95 % Confidence Internal for B		R	Adjusted R square	Sig.
				Lower bound	Upper bound			
6	(Constant)	-0.283	-0.019	-0.518	-0.048	0.58	0.29	0.000
	Age (years)	0.012	0.000	0.007	0.017			
	CYP1A*2C (Ile/Val) (+/+)	0.144	0.024	0.020	0.268			
	B[a]P-like adducts/10+08 ncls	1.399	0.018	0.251	2.548			
	EPHX (high activity)	-0.106	0.036	-0.205	-0.007			
	Folates (nmol/l)	-0.004	0.059	-0.008	0.000			
	p53 mspl (+/+)	-0.324	0.098	-0.709	0.061			

PIN=0.10, POUT=0.15

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AIR
POLLUTION

PREGNANCY
OUTCOME

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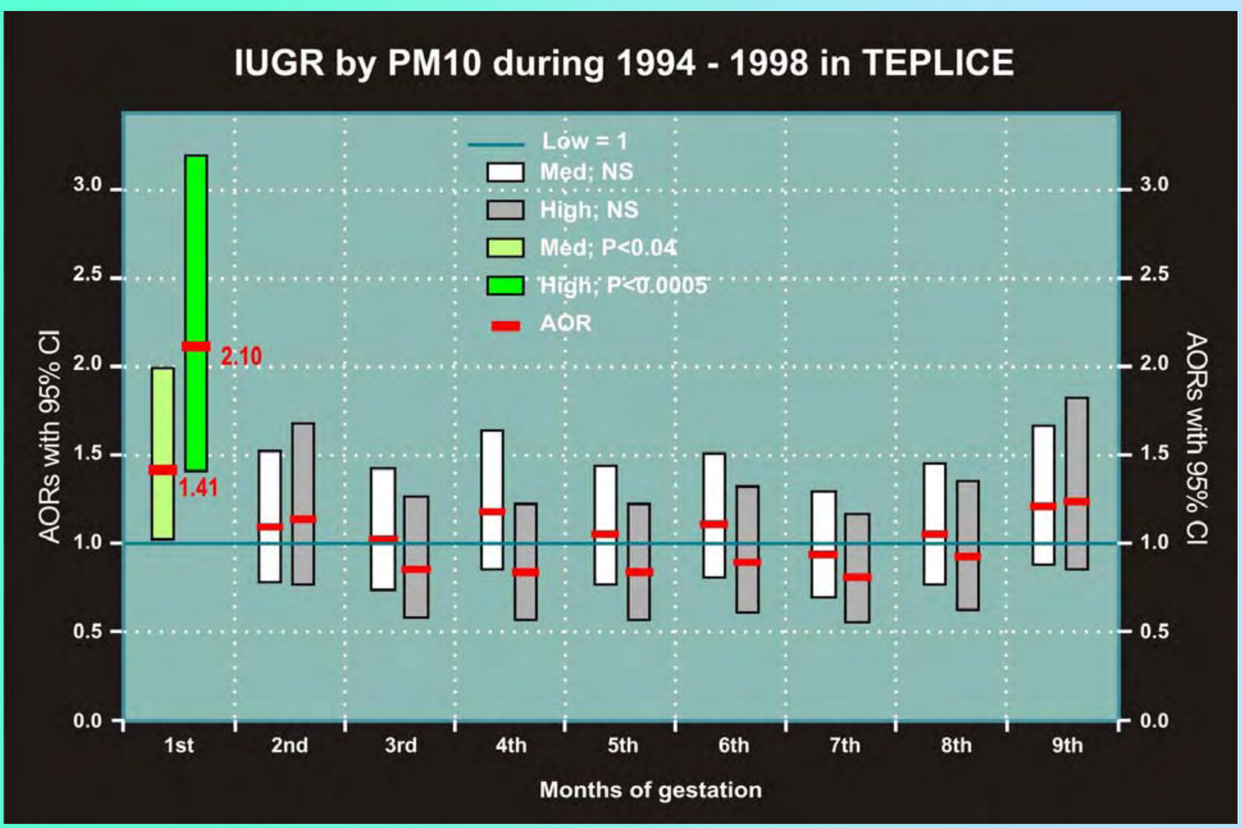

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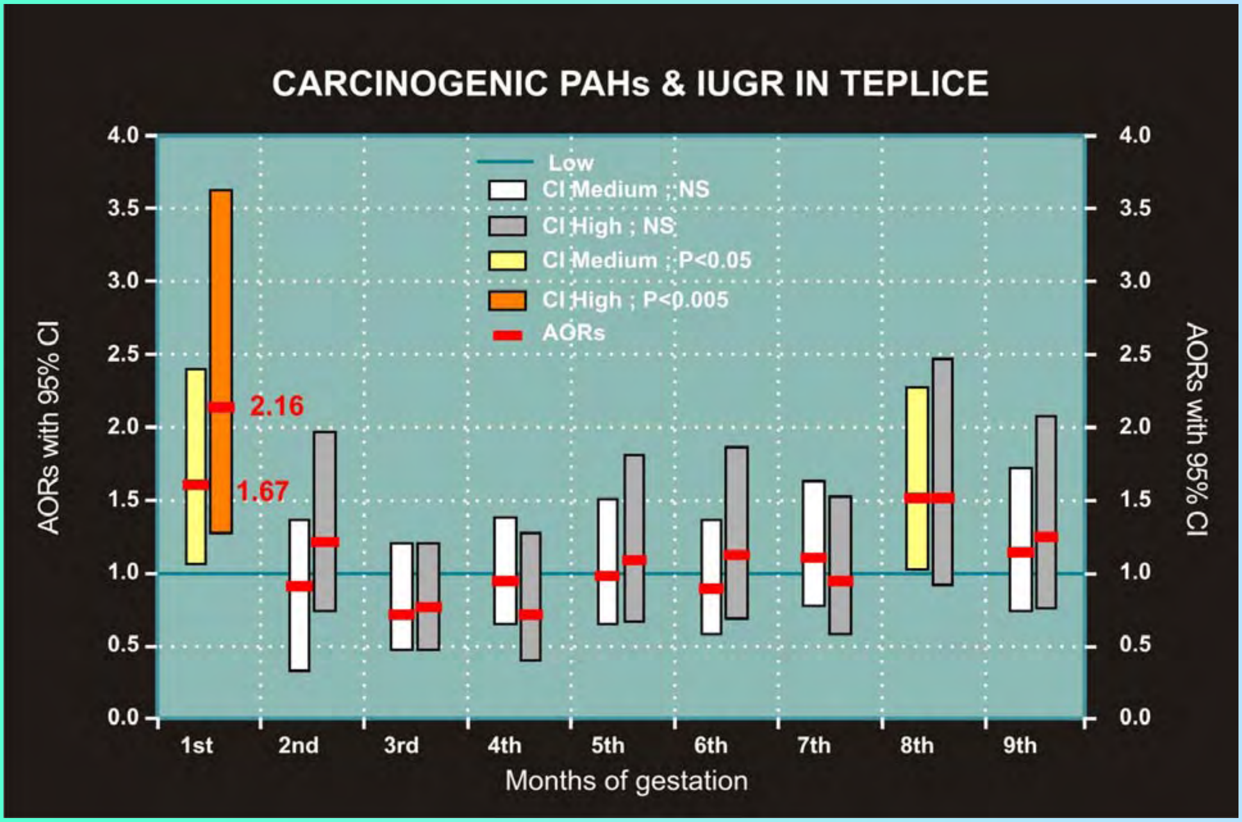

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PREGNANCY OUTCOME - RISK OF c-PAHs

ambient c-PAHs concentrations
higher than 15 ng/m³ (B[a]P 2.8 ng/m3)
should be understood

THE RISK FOR PREGNANCY OUTCOMES

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IMPACT OF IUGR

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

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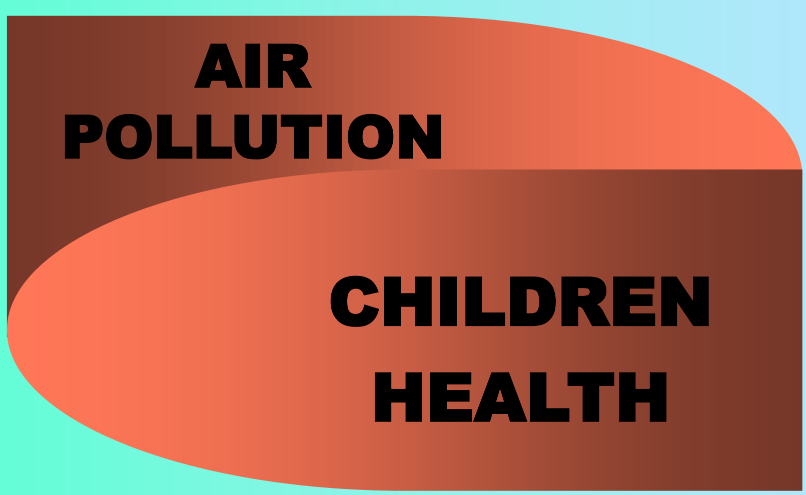

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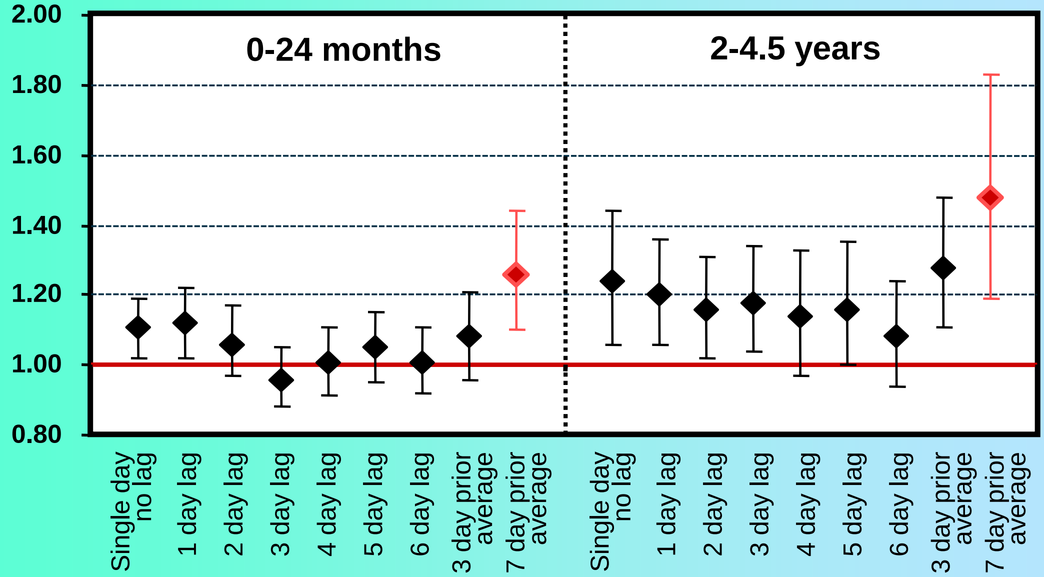
Bronchitis RRs, for acute PAH exposure, 95% CI's, multivariate adjusted



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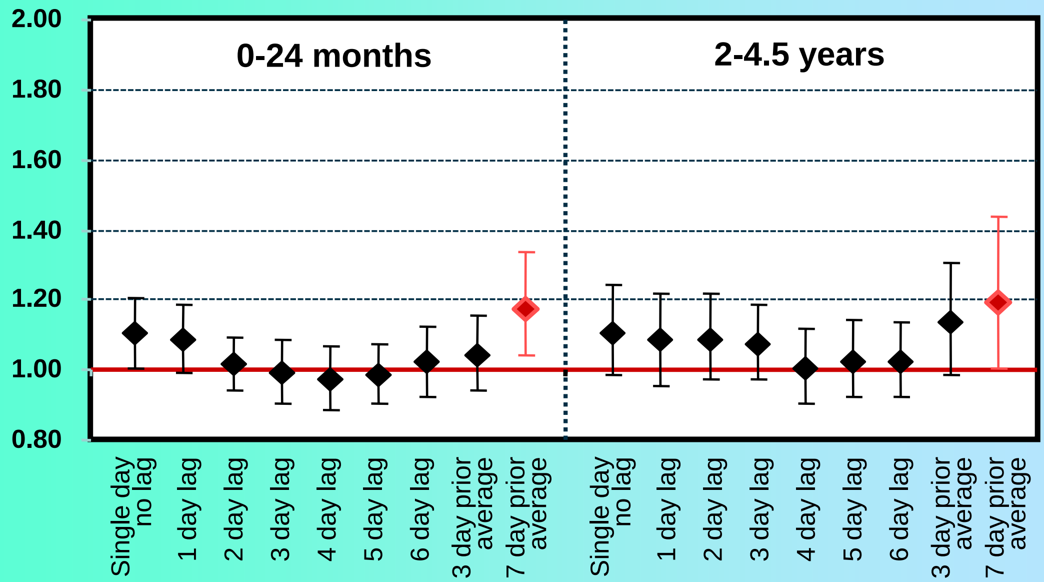
Bronchitis RRs, for acute PM2.5 exposure, 95% CI's, multivariate adjusted



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SIGNIFICANCE

First few years of life

constitute

A CRITICAL PERIOD IN LUNG & IMMUNE DEVELOPMENT

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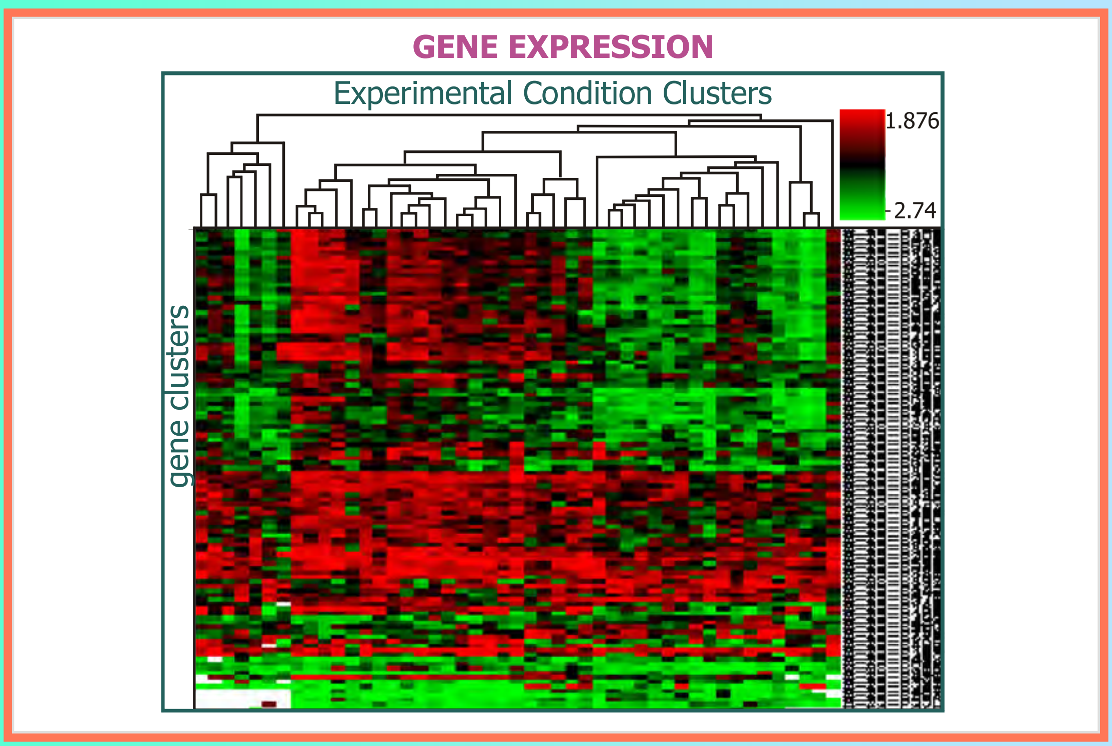
Hierarchical clustering of genes differentially expressed between exposed (black branches) and non-exposed (blue branches) children at p < 0,001



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Overview of the numbers of genes significantly differentially expressed after GEPAS permutation

t-test

p-value 2-tailed significance	# genes differentially expressed in Teplice versus Prachatice children		
	total	upregulated genes	downregulated genes
<0.0001	27	26	1
<0.001	95	81	14
<0.01	487	315	172
<0.05	1727	1001	726

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GENE EXPRESSION

- IMPACT OF AIR POLLUTION (c-PAHs, VOC, metals)
- NEW BIOMARKER OF EXPOSURE TO CARCINOGENS

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AIR POLLUTION

SPERM

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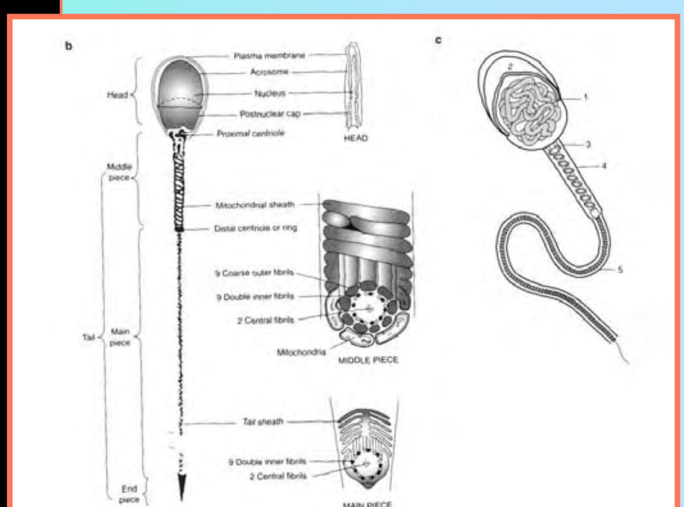
Comprehensive Semen Analysis

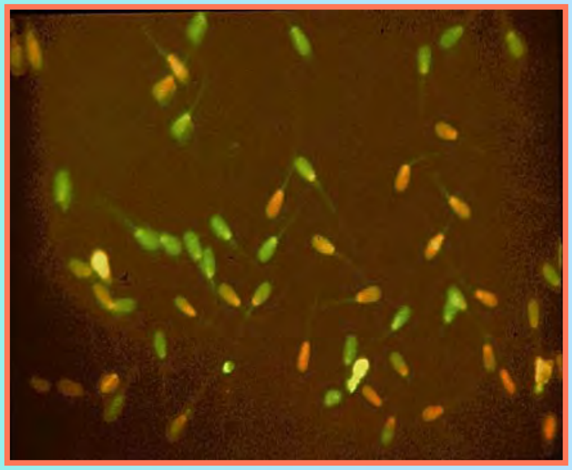
- Volume
- Assessment of concentration using the haemocytometer method
- Assessment of motility – classically and CASA
- Assessment of vitality by dye exclusion: eosin-nigrosin
- Assessment of sperm morphology – strict criteria
- Sperm Chromatin Structure Assay by flow cytometry
- Sperm Aneuploidy by FISH



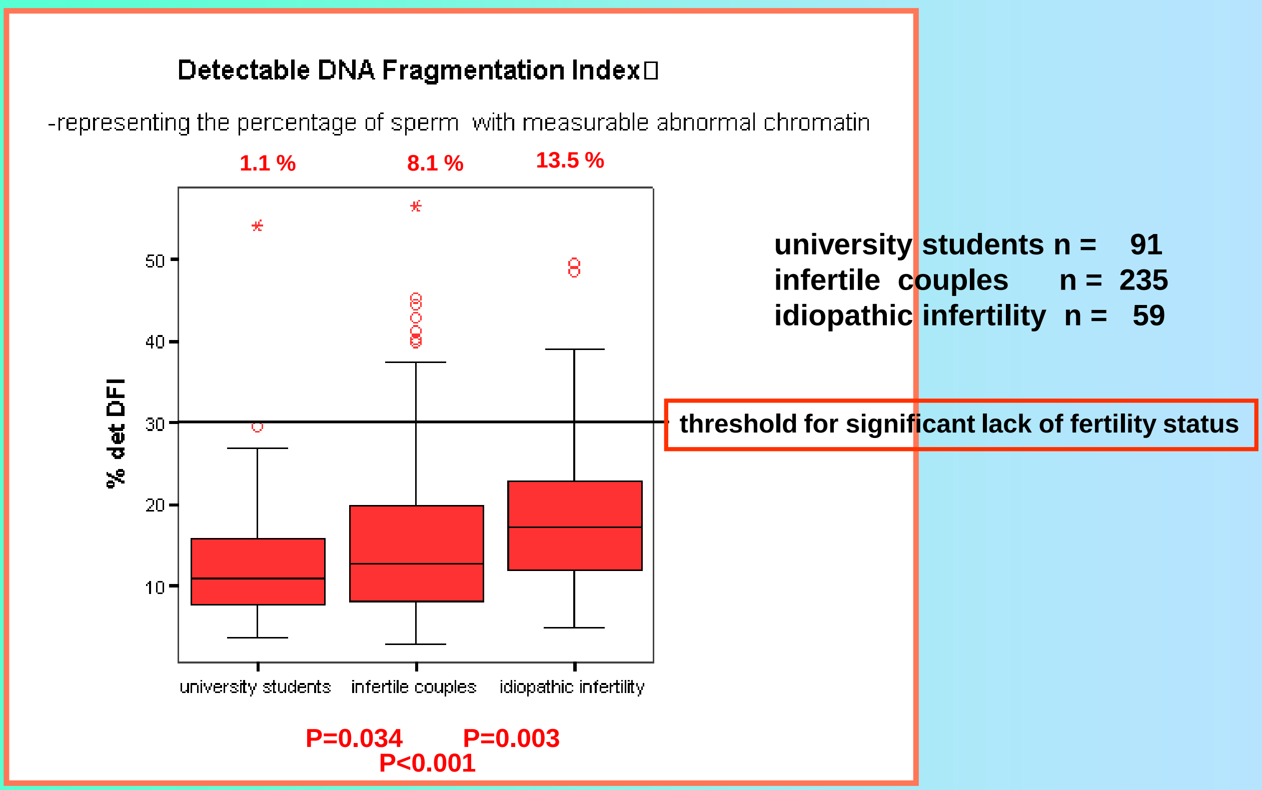
Sperm Chromatin Structure Assay (SCSA)

Don Evenson, SDSU

- Acid denaturation of DNA
- Stain with acridine orange
  - Green = ds DNA
  - Red = ss DNA
- Analyze by flow cytometry
- **Determine % cells outside main sperm population**
- **Moderate and High DFI**
- = DNA Fragmentation Index (DFI)

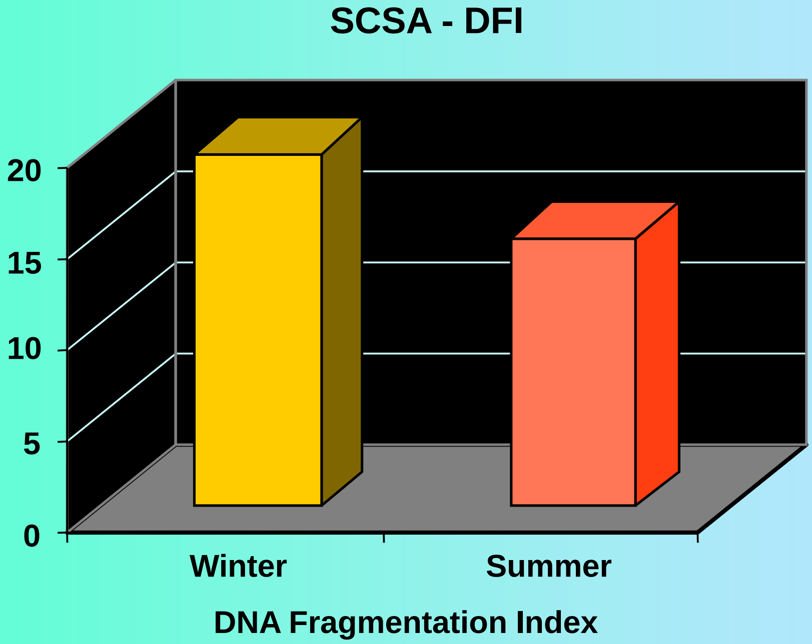


- ***indicates abnormal chromatin packaging and/or DNA damage***
- ***associated with spermatogenic disorders, spontaneous abortion and infertility***



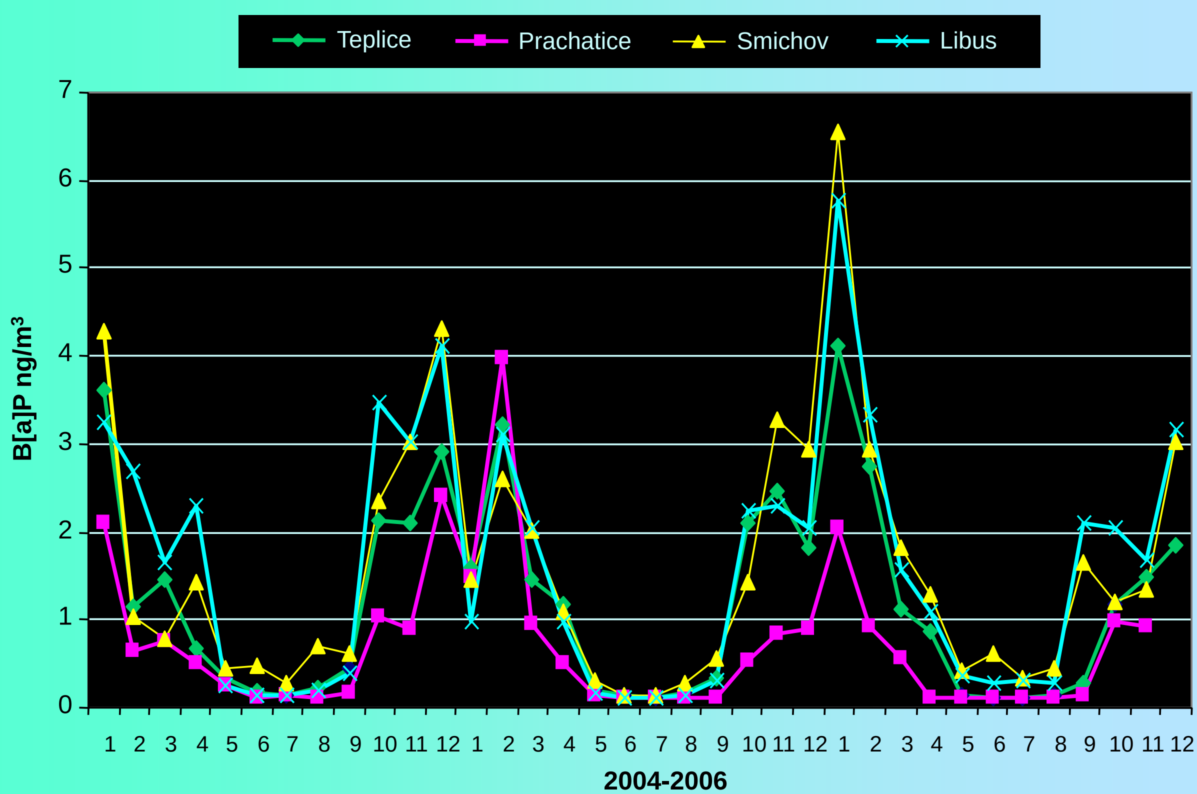
university students n = 91
infertile couples n = 235
idiopathic infertility n = 59

Significant associations with air pollution in longitudinal study



All “high” vs. “low”: 0.19 (0.02, 0.36) - Adjusted Beta (95% CI)

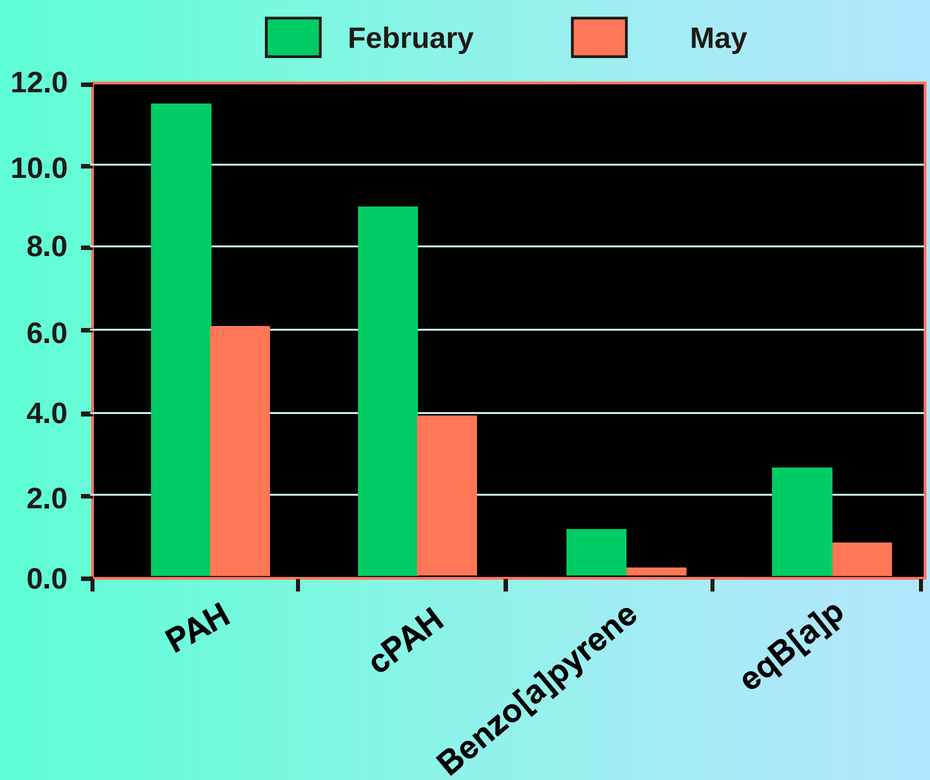
Average monthly concentrations of benzo[a]pyrene



PAHs from personal monitoring

Variable	group	N	2007/2 mean ± SD	P	2007/5 mean ± SD
Benzo[a]pyrene ngm^{-3}	Total	43	1.07 ± 0.78	p=0.0000	0.16 ± 0.06
	non-Smoker	28	1.00 ± 0.68	p=0.0000	0.17 ± 0.07
	Smoker	15	1.22 ± 0.95	p=0.0003	0.15 ± 0.00
PAH ngm^{-3}	Total	43	11.46 ± 6.29	p=0.0000	6.03 ± 1.61
	non-Smoker	28	10.79 ± 5.07	p=0.0000	6.21 ± 1.99
	Smoker	15	12.70 ± 8.17	p=0.0003	5.68 ± 0.09
cPAH ngm^{-3}	Total	43	8.90 ± 5.04	p=0.0000	3.92 ± 1.13
	non-Smoker	28	8.42 ± 4.46	p=0.0000	4.05 ± 1.39
	Smoker	15	9.80 ± 6.04	p=0.0003	3.68 ± 0.09
eqBaP ngm^{-3}	Total	43	2.59 ± 1.69	p=0.0000	0.78 ± 0.14
	non-Smoker	28	2.41 ± 1.49	p=0.0000	0.79 ± 0.17
	Smoker	15	2.92 ± 2.03	p=0.0003	0.75 ± 0.02

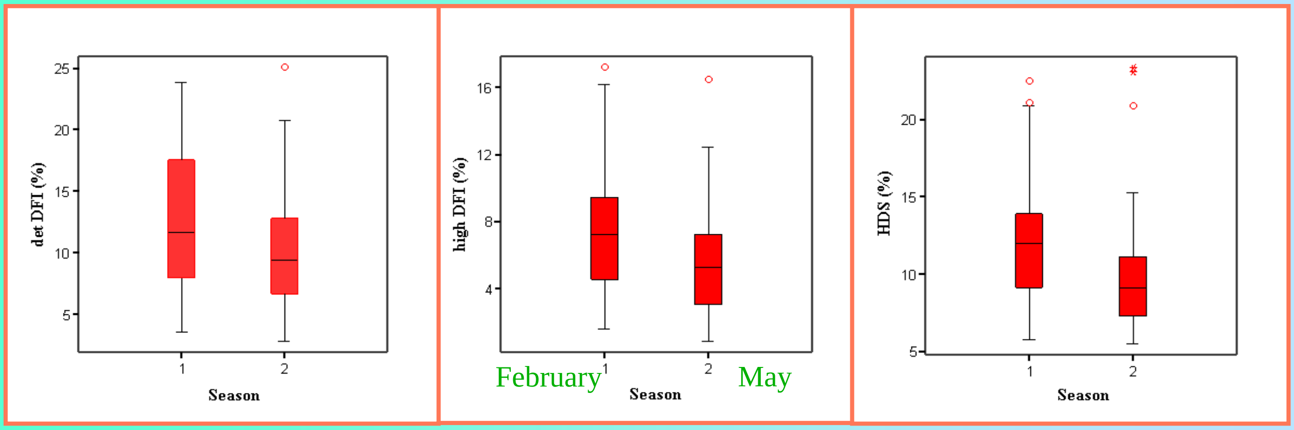
PAHs from personal monitoring



Policemen patrolling the streets in the center of Prague with heavy traffic

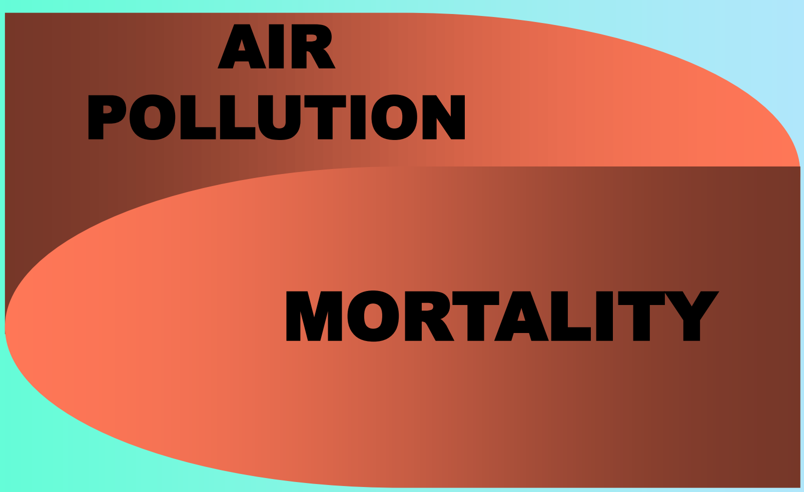
The level of air pollution will be assessed on the basis of information from two source:
-data from stationary measuring stations AIM Prague
-for 48 h using personal sampling devices (URG Corp, USA)

N=46



P≤0.001 P≤0.001 P≤0.001

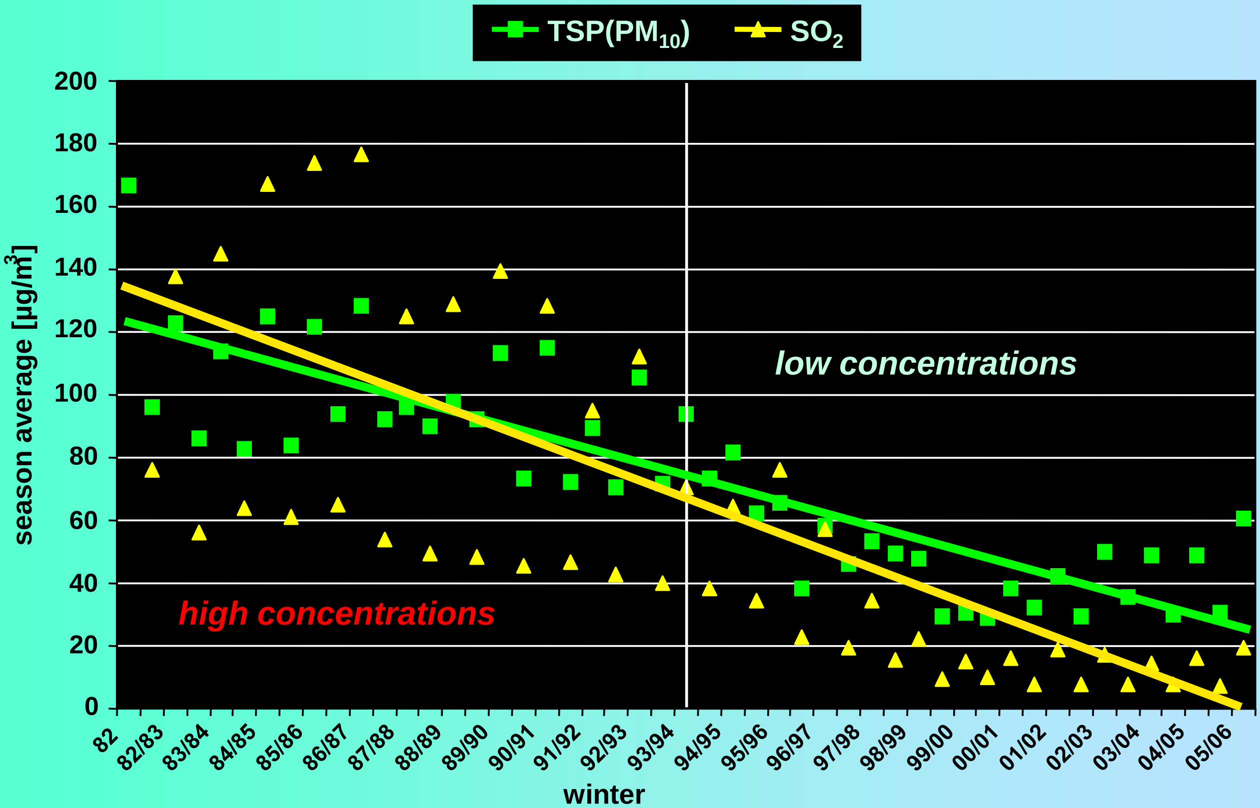
dDFI	< 15%	Feb 30	May 42
dDFI	15 – 30%	Feb 16	May 4
dDFI	>30%	Feb 2	May 2
HDS	>15%	Feb 10	May 4



R. J. Sram 2008

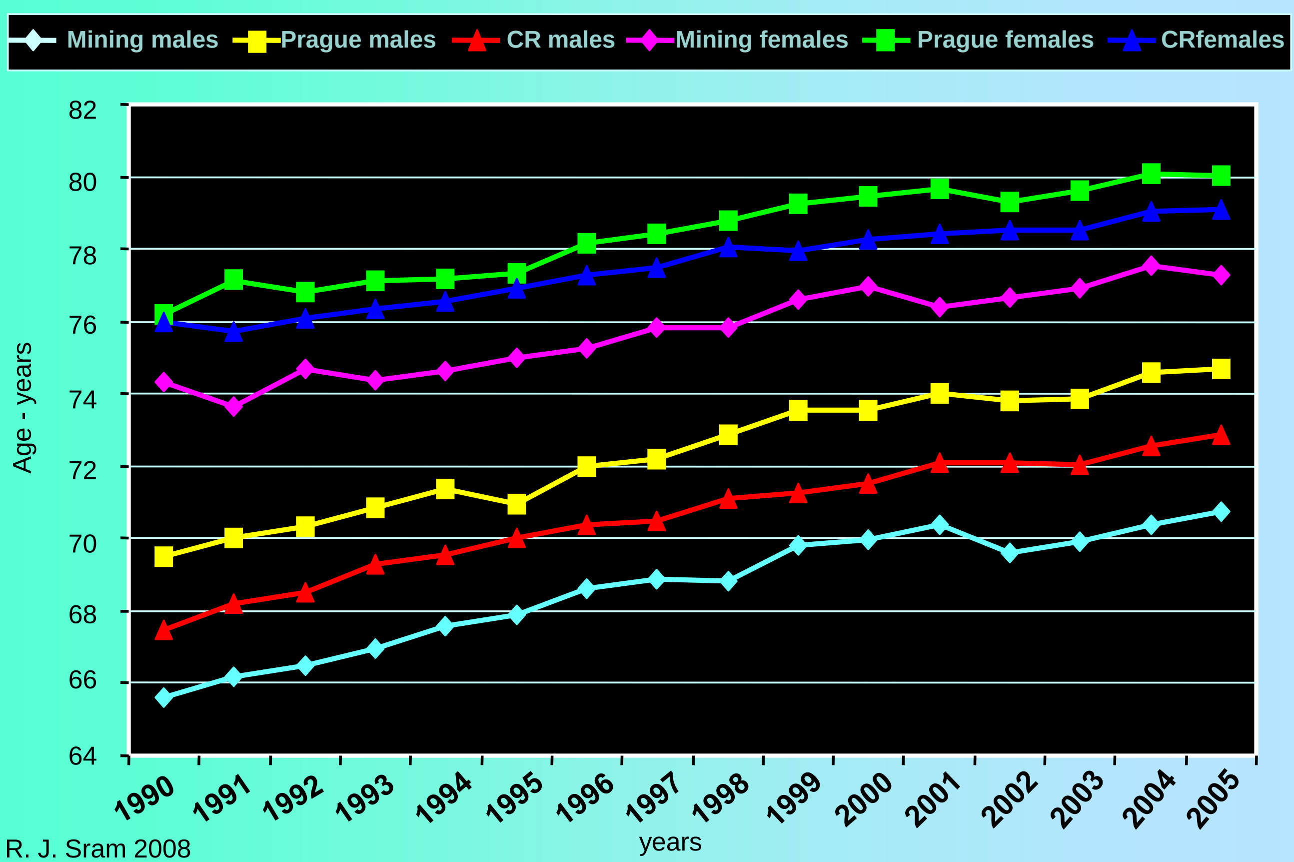
CONCENTRATION OF AIR POLLUTANTS

(Mining districts 1982 – 2006)



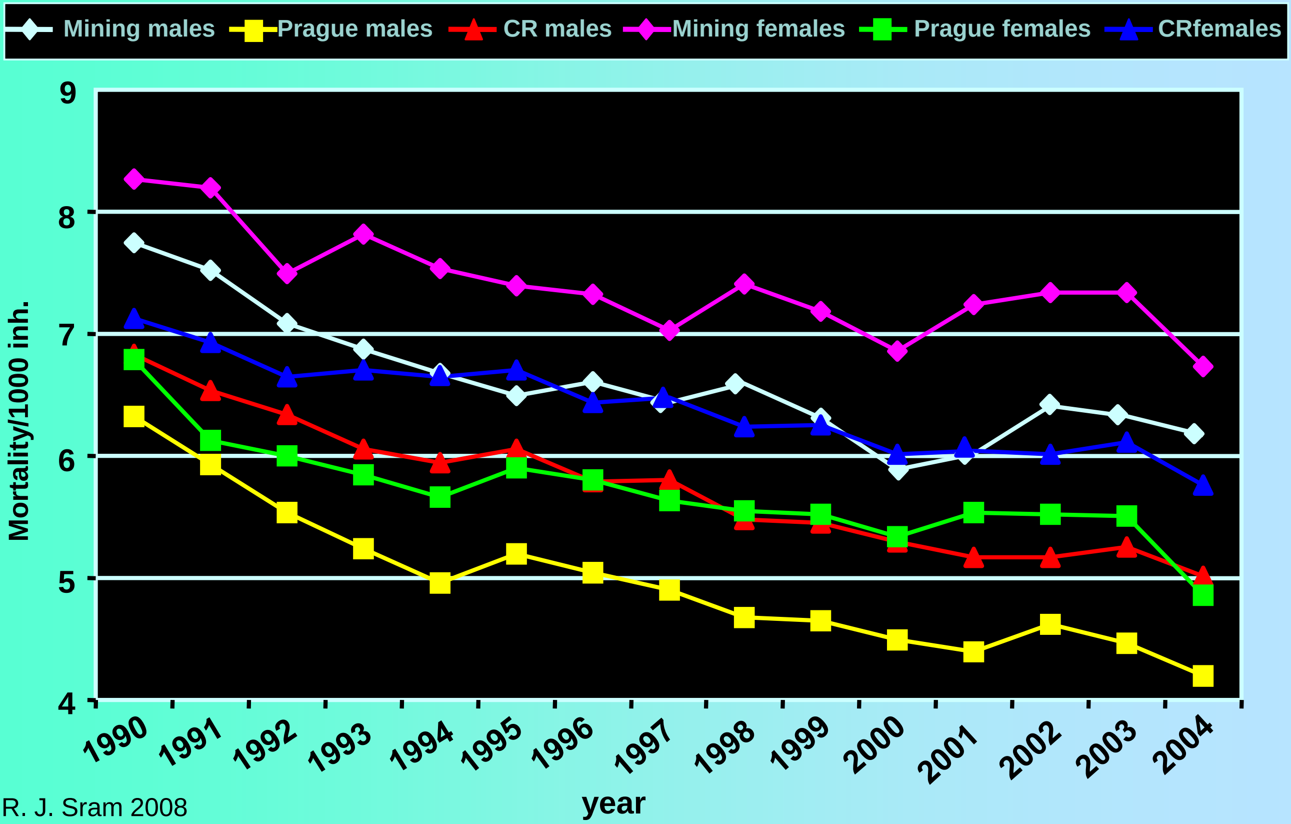
R. J. Sram 2008

LIFE EXPECTANCY



R. J. Sram 2008

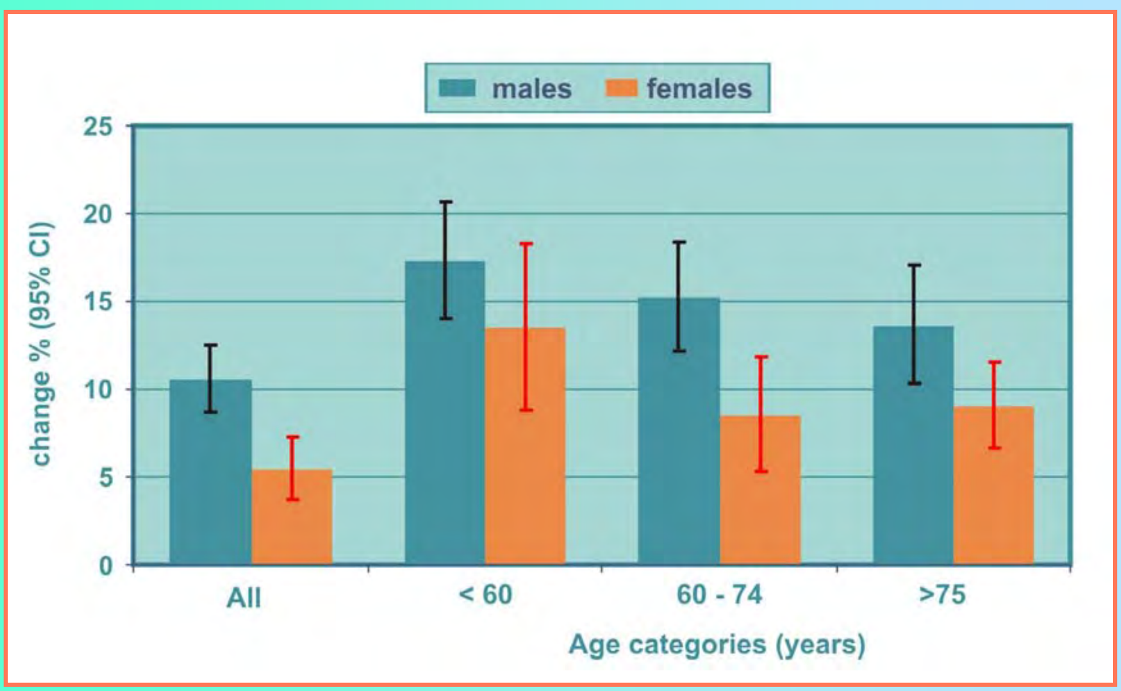
STANDARDIZED CARDIOVASCULAR MORTALITY



R. J. Sram 2008

IMPACT OF AIR POLLUTION TO MORTALITY IN MINING DISTRICTS

periods 1983-1994 vs. 1995-2004



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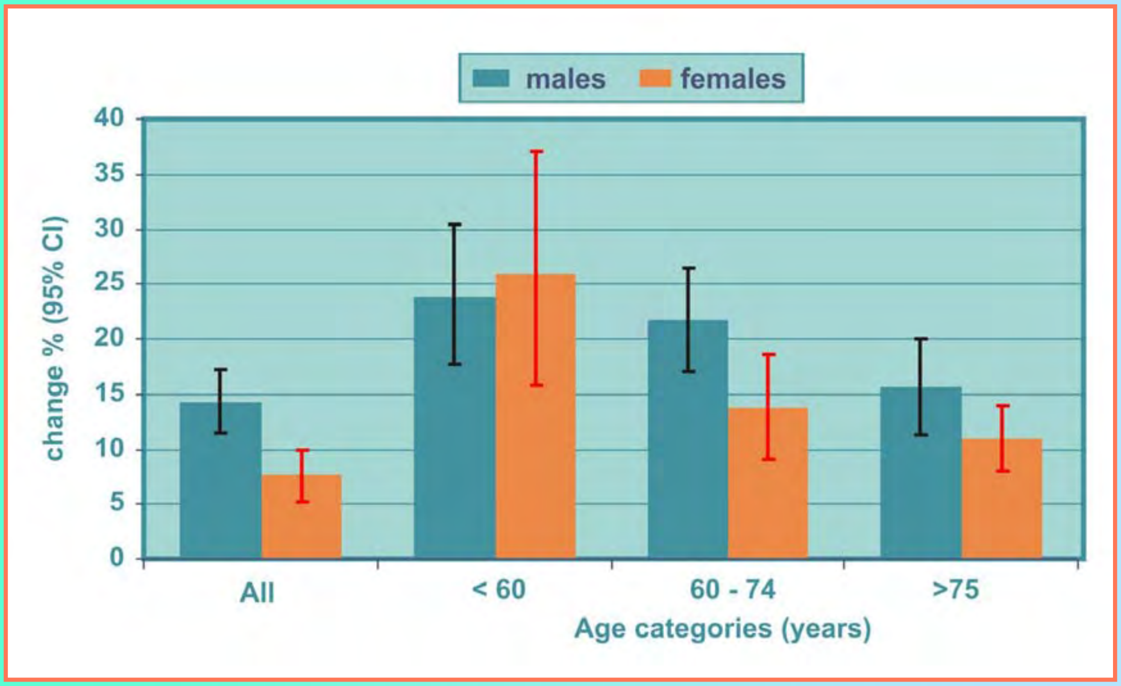
IMPACT OF AIR POLLUTION TO CARDIOVASCULAR MORTALITY IN MINING DISTRICTS

periods 1983-1994 vs. 1995-2004



R. J. Sram 2008

DECREASED AIR POLLUTION

- In the period 1995-2004 the mortality decreased each year by **195 males and 92 females**
- In the period 1995-2004 the mortality decreased in total **by 1950 males a 920 females**

R. J. Sram 2008

AIR POLLUTION

RISK ASSESSMENT

R. J. Sram 2008

IMPACT OF c-PAHs IN POLLUTED AIR

pregnancy outcome (IUGR, LBW) act as ED

men fertility

child morbidity, mental development

cardiovascular diseases, diabetes, cancer

RISK FOR HUMAN HEALTH

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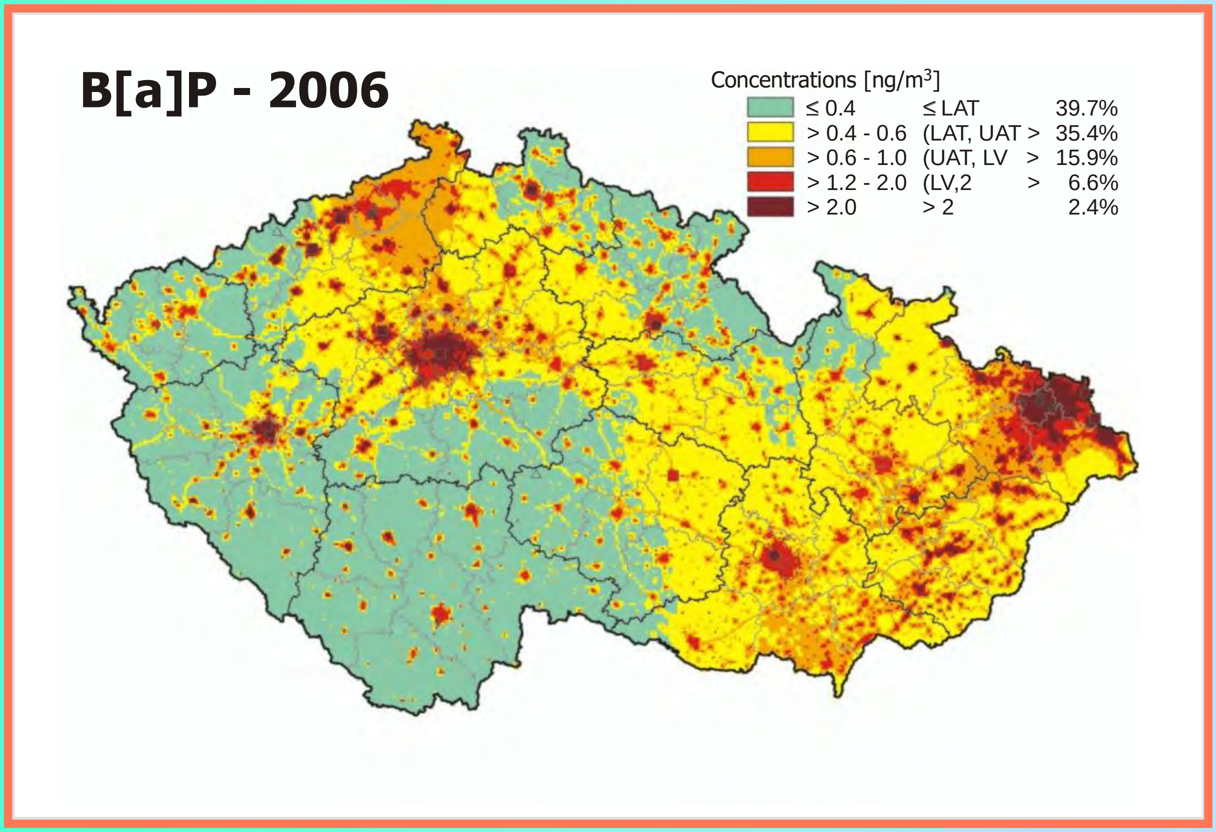
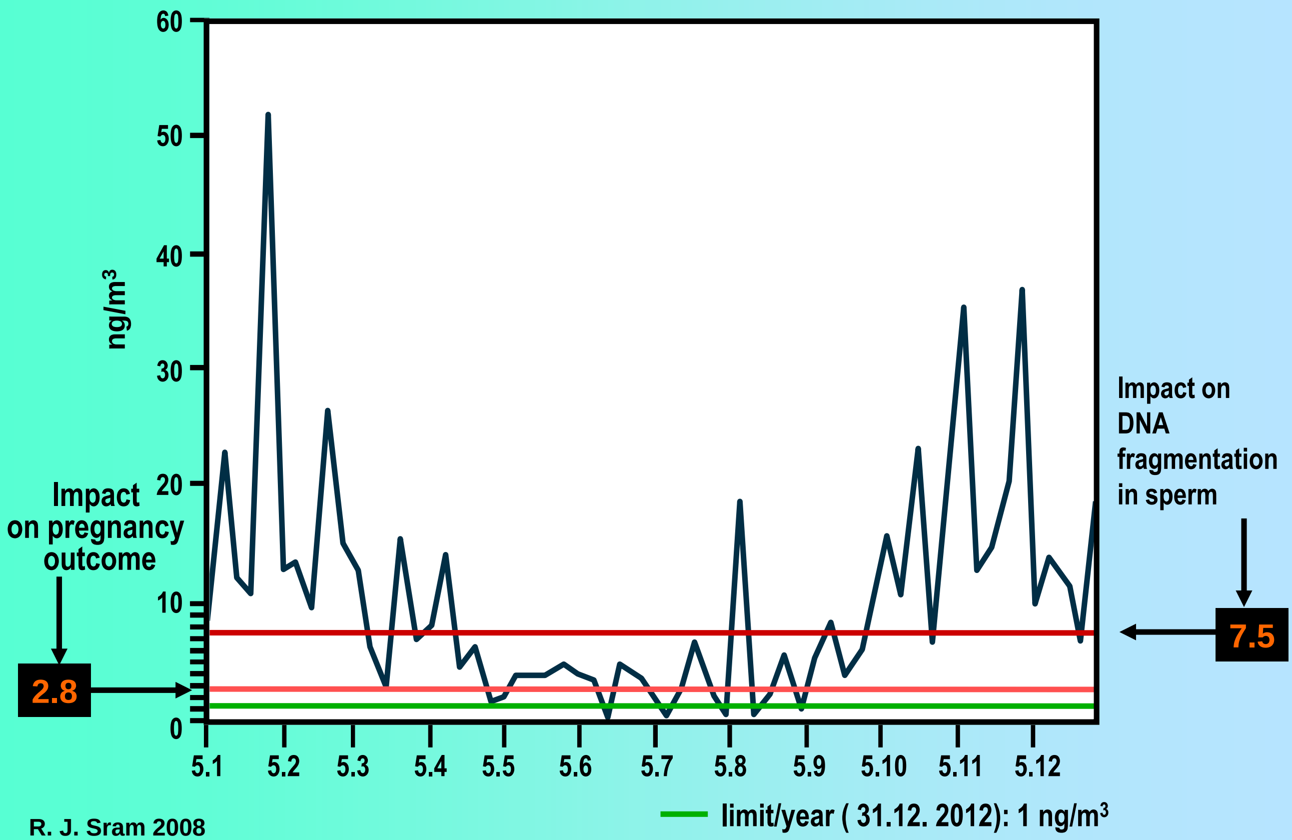


R. J. Sram 2008

Daily concentrations of benzo[a]pyrene

Bartovice (Ostrava) 2005



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Asthma bronchiale in children
Ostrava-Bartovice

year	N	cases
2001	1201	115
2003	1181	139
2005	1133	192
2007	1082	281

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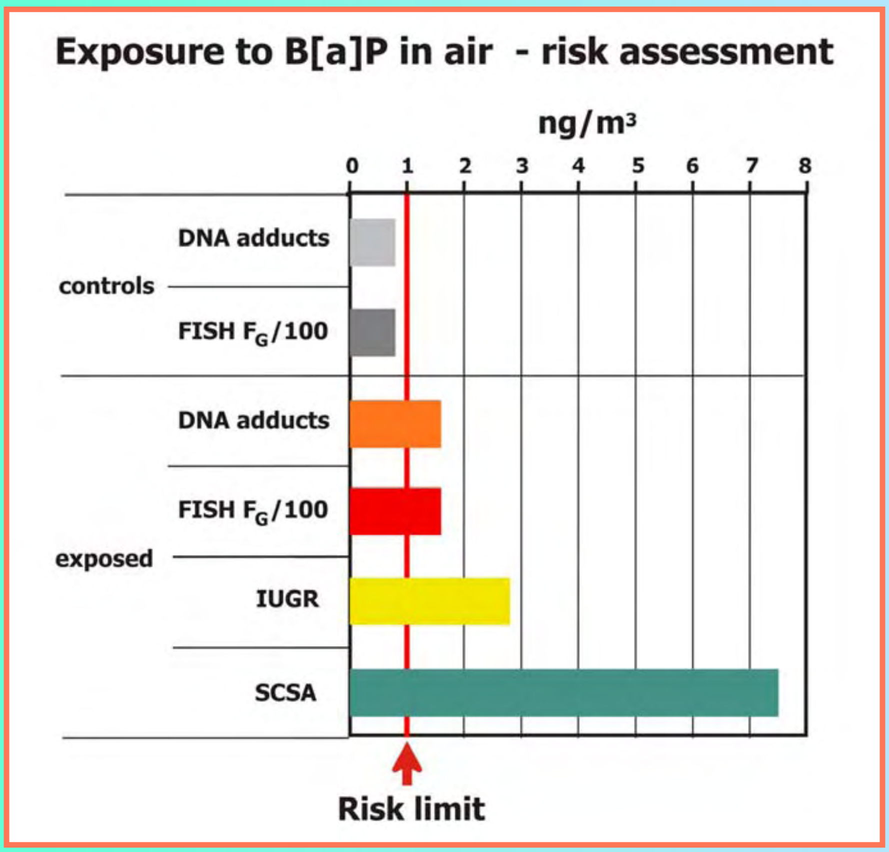

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INTERPRETATION OF MOLECULAR EPIDEMIOLOGY RESULTS

NEW KNOWLEDGE

ABOUT POLLUTANTS AFFECTING HUMAN HEALTH

RISK ASSESSMENT

R. J. Sram 2008

ACCORDING TO MOLECULAR EPIDEMIOLOGY STUDIES

concentrations
> 1 ng B[a]P/m^3
in polluted air

RISK FOR HUMAN HEALTH

R. J. Sram 2008

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R. J. Sram 2008

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US EPA, EC PHARE
EC: INTARESE + ENVIRISK

R. J. Sram 2008

Occupational exposure monitoring; Approach used in FIBRETOX

M Dusinska

Research Base of Slovak Medical University - Institute of Preventive and Clinical Medicine, Bratislava, Slovakia
Norwegian Istitute of Air Research, Norway

Integrated monitoring workshop
Tromso, June 2-5, 2008

There has been no attempt till the time of the project to carry out an integrated investigation into effects of exposure to asbestos fibres involving biomarkers of exposure, effect and susceptibility.

FIBRETOX FP5 EC project (2000 – 2004)

- a molecular epidemiological study in three factories to examine the relationship between various biomarkers and exposure to asbestos and MMMF
- *in vitro* studies on lung cells – primary cultures
- *in vivo* studies on rat and transgenic animals

Molecular epidemiology -Biomontoring

Exposure

Absorption

Metabolism

Excretion
Bioacumulation

Individual susceptibility

DNA polymorphisms

DNA repair

Immunosurveillance

Indvidual differences

Assess risk of exposure

Effects

Mutations

Chromosome aberrations

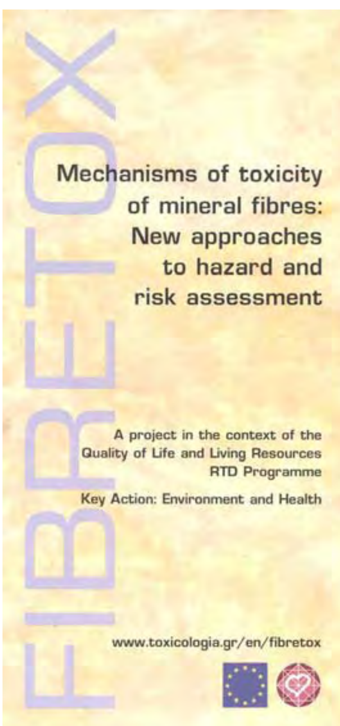
Disease

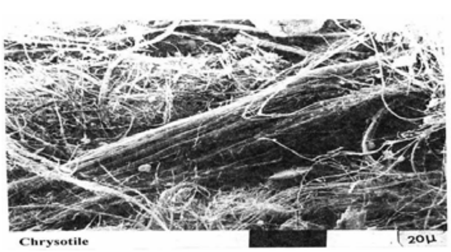
Assess risk of disease

Environmental disease is the result of exposure to environmental agents (including nutrition) – *modulated by individual susceptibility factors*

Molecular epidemiology: applied to studies of environmental or occupational exposure including nutrition – (protective or toxic effects).

Human diseases and aging – cancer, heart disease, obesity, diabetes, allergies, neurodegenerative diseases, reproduction and endocrine disruption diseases





FIBRETOX project was set up to investigate the possible health risks of occupational exposure to mineral fibres used as substitutes for asbestos.

We investigated effects of exposure to asbestos and other mineral fibres (in combination with smoking and PAHs exposure), employing biomarkers of exposure, effect and susceptibility.

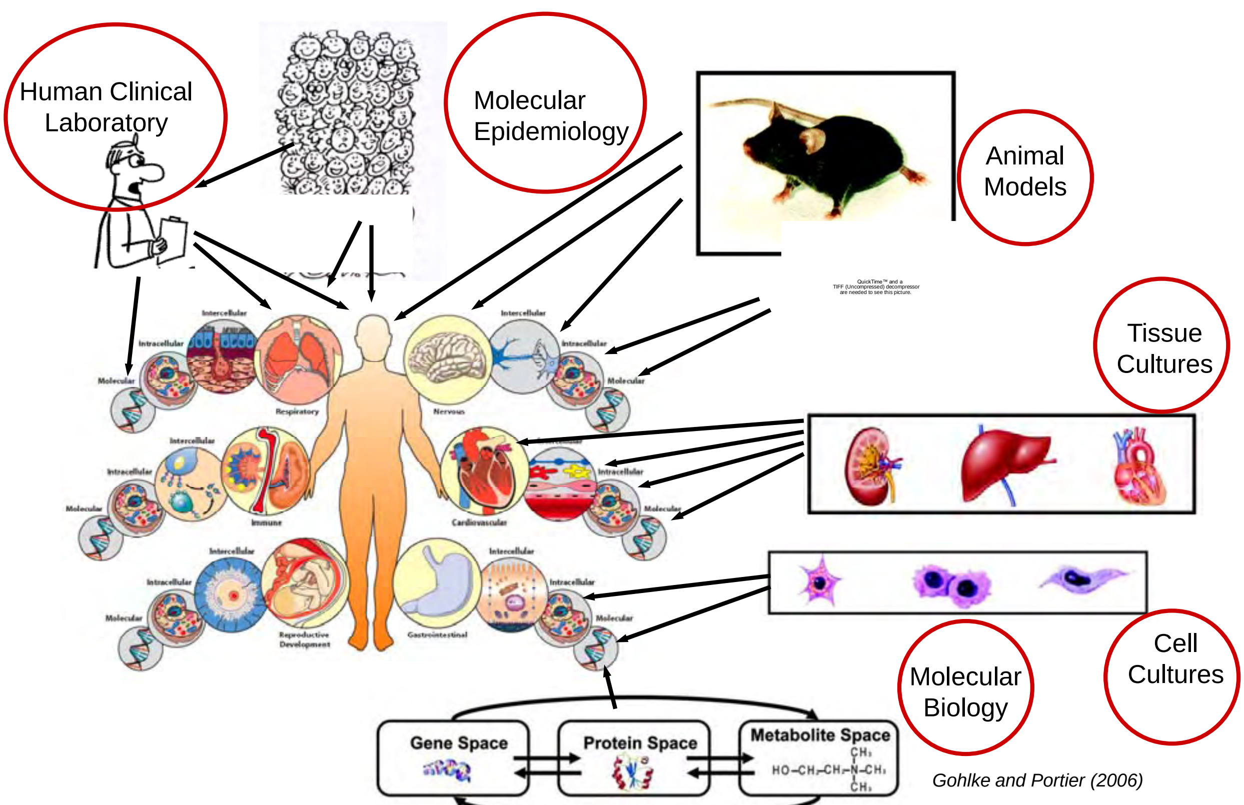
It is well established that asbestos exposure, especially in combination with tobacco smoke, causes lung disease including cancer.

It is generally believed that oxidative stress plays a critical role in the pathogenesis of asbestos-related disease.

Fibres are known to induce inflammation and so can damage DNA via oxidative stress. We were looking at markers of oxidative stress, inflammation / immunotoxicity and genotoxicity.

Integrated monitoring workshop
Tromso, June 2-5, 2008

Across matrices: in vitro, in vivo, human models



Gohlke and Portier (2006)

Boverhof and Zacharewski (Tox. Sci., 2006)

Biomonitoring

Aim: to investigate the possible health risks of occupational exposure to mineral fibres used as substitutes for asbestos. Effect of smoking.

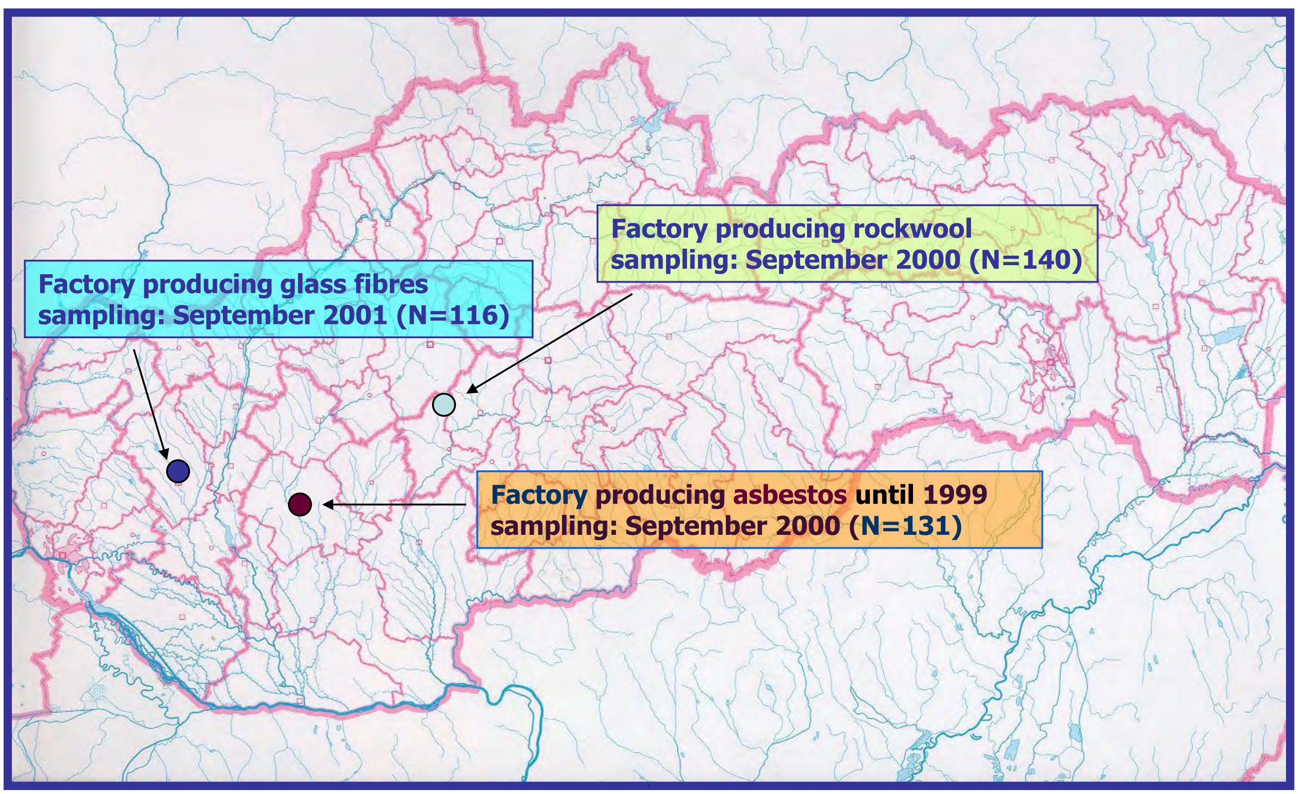
3 factories in Slovakia: asbestos (131 subjects)
rockwool (140 subjects)
glass fibres (116 subjects)

Altogether: 387 subjects; 239 exposed, 148 controls

Selection criteria

Exposed subjects worked minimum 5y in a factory

Controls: matched for sex, age, smoking, alcohol use



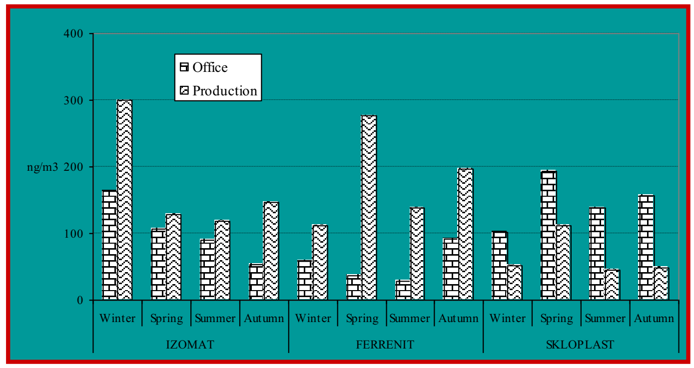
Total number of subjects sampled: 387

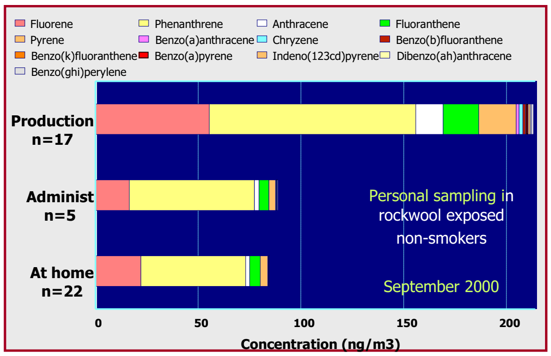
Exposure monitoring

Fibres
PAHs

External exposure

to mineral fibres and PAHs
in workplace in 4 seasons
(including sampling time)





Personal dosimetry

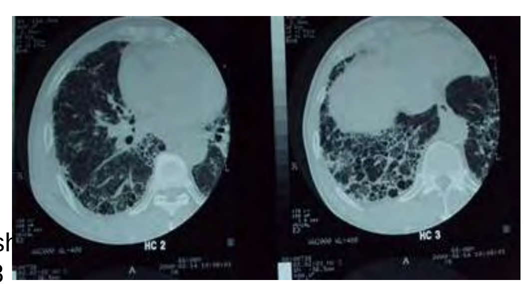
PAHs, mineral fibres, 24h
8h at workplace , 8 h at home

Health effects of asbestos exposure

Diseases/Frequency	Exposed (n=61)	Controls (n=70)
Cardiovascular diseases	27.9 % (17)	14.3 % (10)
Diabetes	13.1 % (8)	4.3 % (3)
Bronchitis	26.2 % (16)	4.3 % (3)
Asbestosis	44.3 % (27)	0.0 % (0)

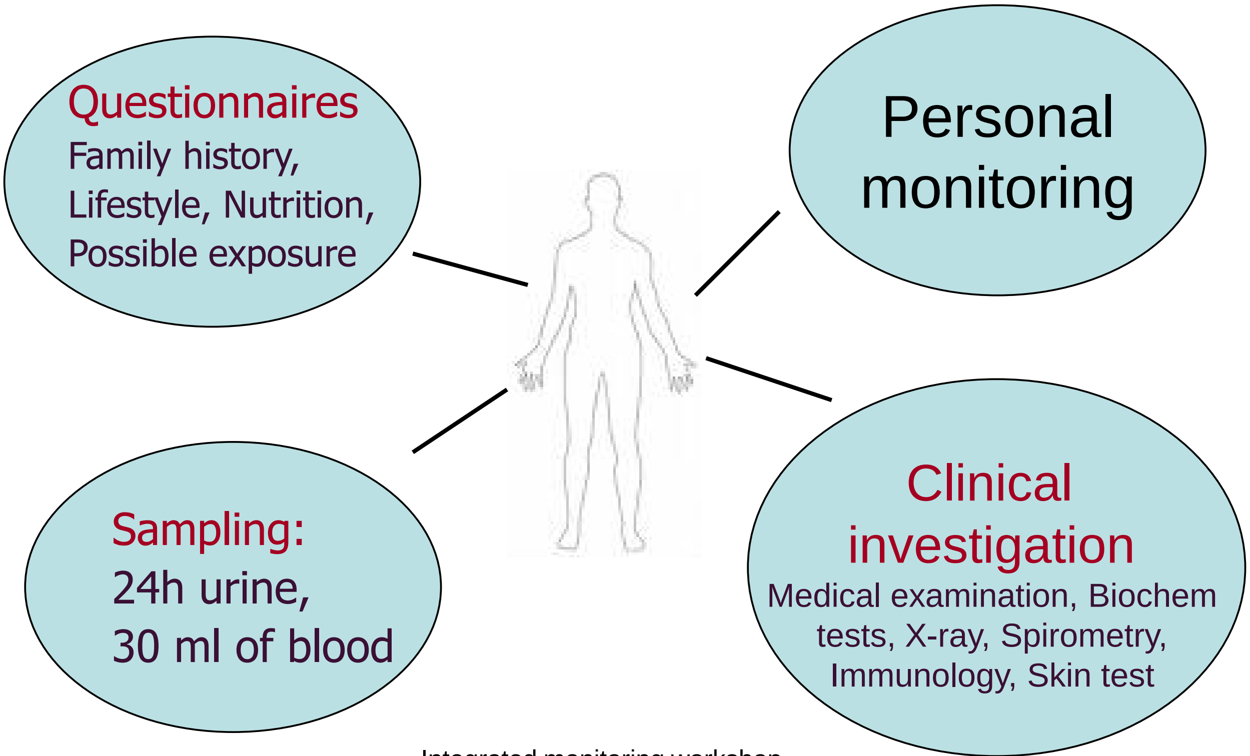
$X^2=18.29$ $p=0.001$

In asbestosis group
- fibrotic plaques: 55.6% subjects
- interstitial fibrosis: 74.1% subjects
- both symptoms: 33.3% subjects



Horská A et al., 2006

FIBRETOX



Biomonitoring data

- Exposure data including personal monitoring data.
- Clinical data and health status and life style questionnaires
- The electronic database for nutritional evaluation of the questionnaires was developed.

Biochemical markers, oxidative damage and cellular defence markers

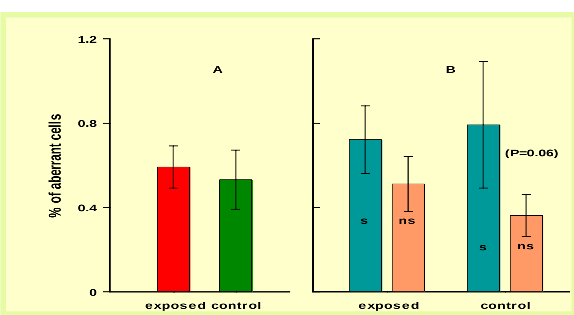
- Triglycerids, cholesterol LDL, HDL, Creatinine, HCY
- FRAP, SOD, GSHPx, GST activities, ceruloplasmin, GSH, MDA, catalase activities
- vitamin C, α and γ tocopherols, folic acids, β-carotene, lycopene, retinol.

- Cotinine was measured in urine.

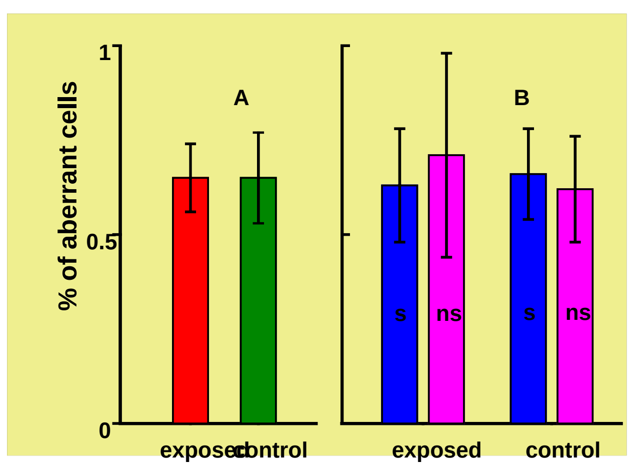
DNA instability

- Chromosomal aberrations

- Micronuclei

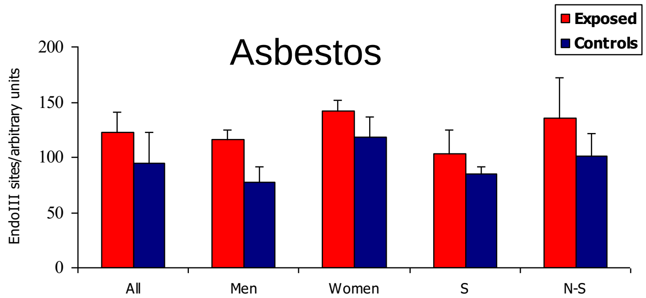


Glass fibre exposure



Rockwool exposure

DNA instability

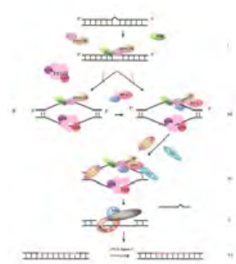


- DNA strand breaks - including AP sites and DNA repair intermediates
- Oxidised bases - (Endo III and FPG-sensitive sites)
- Alkylating damage - 3-Methyladenine DNA glycosylase- (AlkA)-sensitive sites

PAH-DNA adducts, 8-oxodG by HPLC

- DNA repair capacity (incision at 8-oxoGua) was measured in lymphocyte extracts.

Genotyping



Polymorphisms

- in genes for xenobiotic-metabolising enzymes *NQO1, GST-M1, GST-T1, GST-P (105 Ile→Val), NAT1, NAT2, EPHX 3, EPHX4*

- in DNA repair genes *XPA* 5′ region, *XPD exon 10, exon 23, XRCC1* (399 Arg→ Gln), *MGMT* promotor-enhancer (1009)

Immune markers

Non-specific cellular immunity (phagocytic activity of leukocytes in peripheral blood samples), differential white blood cell count.

Specific cellular immunity, using proliferative response of lymphocytes stimulated with mitogens *in vitro*.

Haematological parameters

Immune markers

Immunoglobulins (IgG, IgA, IgM, IgE, component of Complement C3 and C4), phenotyping of lymphocytes (CD3, CD4, CD8, CD16+56, CD3/HLA-DR, CD19).

Expression of adhesion molecules (CD11b, CD18, CD62L, CD54, CD49d), identification of surface molecules associated with activation of eosinophils (CD66, CD81, CD69, CD25).

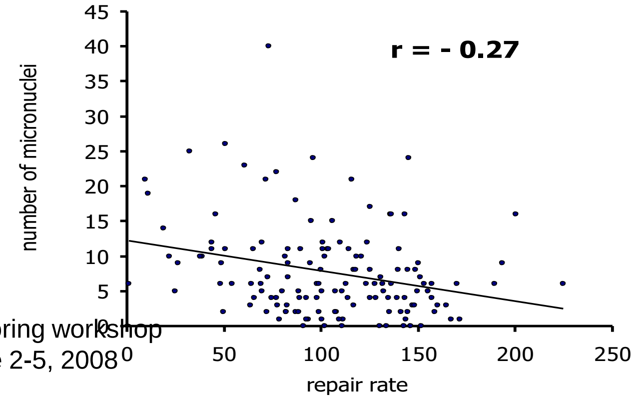
Results

DNA damage (endo III, Alk A) correlated with exposure time.

Micronucleus frequency correlated positively with base DNA damage (EndoIII-sensitive sites, FPG-sites, AlkA-sites) in all 388 subjects and in all subgroups: controls; exposed; men; women

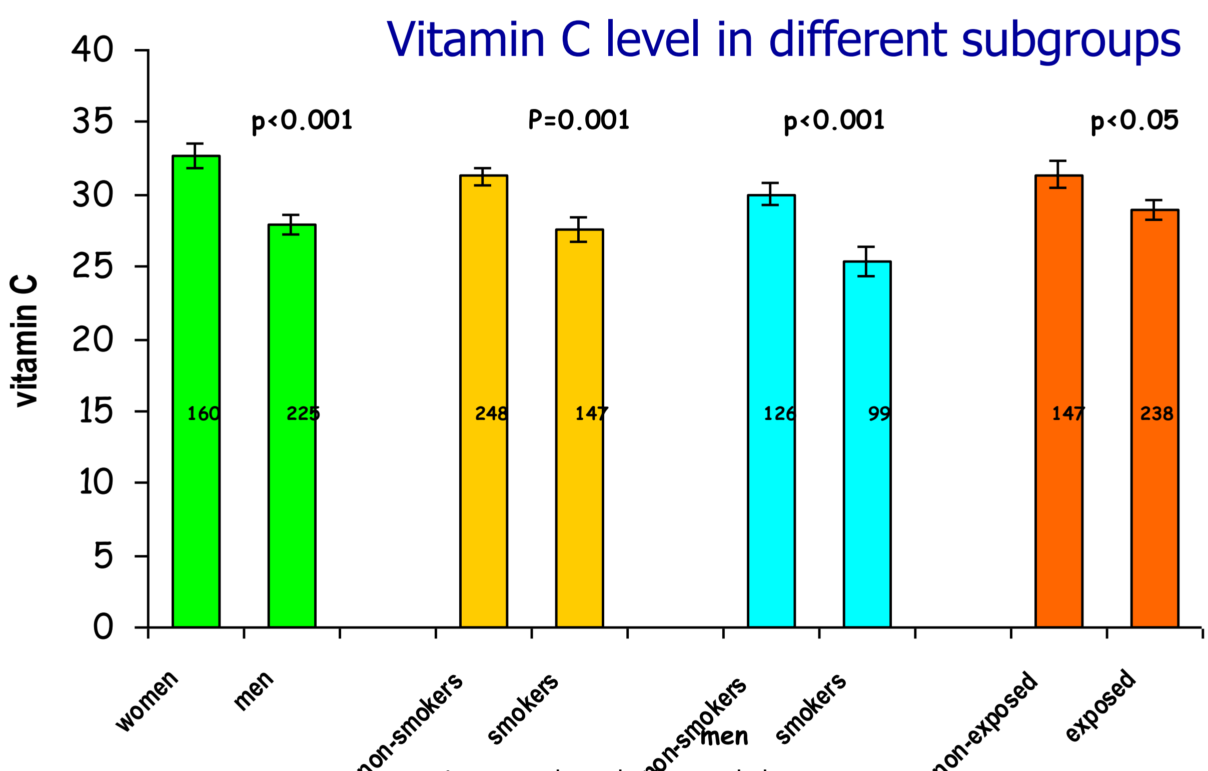
Micronuclei - Inverse correlation with DNA repair (of oxidative damage) implying that oxidative damage, if poorly repaired, can result in micronuclei

– in all exposed,
- rockwool-exposed,
- men and women,
- asbestos-exposed women



Dušinská et al. (2004) Mutat. Res.

Nutrition (questionnaire vs measurements)



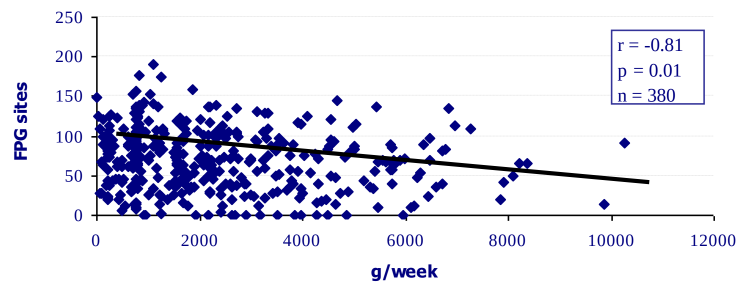
Integrated monitoring workshop
Tromso, June 2-5, 2008

FIBRETOX study

Correlation between oxidative DNA damage and consumption of fruits and vegetables

Intake of fruits (r=-0.117, N=383, p=0.05), vegetables (r=-0.181, N=383, p=0.01), cereals (r=-0.108, N=383, p=0.05) inversely correlated with oxidative DNA damage (net FPG) in **all investigated subjects**.

There was a **negative correlation** between the intake of fruits (r=-0.134, N=239, p=0.05) and vegetables (r=-0.224, N=239, p=0.01) and FPG sites also in all **exposed** subjects.



Staruchová M et al., 2006

We looked for

- exposure and health status
- health status and biomarkers
- differences between various biomarkers
- correlation between various biomarkers and age, exposure, smoking, sex etc.
- association between various biomarkers and genetic polymorphisms (gene-gene and gene-environmental interaction)

We analysed different groups and subgroups to confirm the significance of these findings

In vitro studies

Primary culture cells: Alveolar macrophages
Epithelial type II cells

Treatment with: asbestos, wollastonite, rockwool, glass fibres

Combination with smoking

Markers: oxidative damage and defence, inflammation, genotoxicity

In vivo studies I

- Fisher 344 rats.
- Acute and subchronic exposure
- By intratracheal instillation:
- with amosite asbestos and glass, wollastonite, and rockwool fibres
- Inhalation in chamber: Combination with cigarette smoke
- Endpoints: oxidative damage, inflammation/immunotoxicity, genotoxicity
- Animals sacrificed at 48h, 3 and 6 months

In vivo studies II

λlacI (Big BlueR) transgenic rats treated by intratracheal instillation with different doses of amosite asbestos or ASMF (glass fibre, rock wool) for two different periods.

Each dose of fibres administered alone or in combination with B[a]P

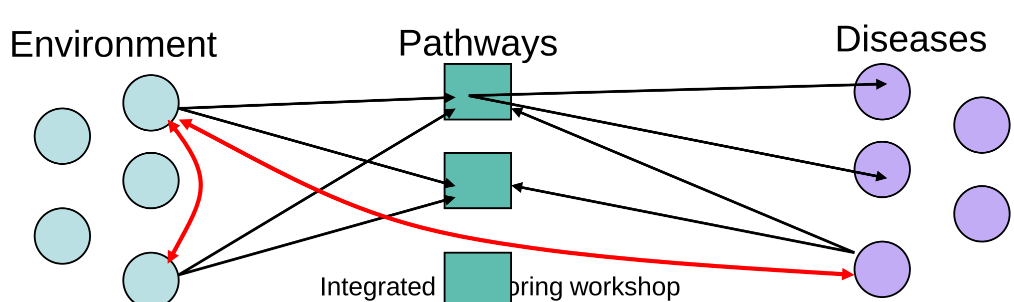
8-Oxoguanine in DNA by HPLC/EC detection and B[a]P-DNA adducts by 32P-postlabelling

Study with transgenic animals were done in Germany

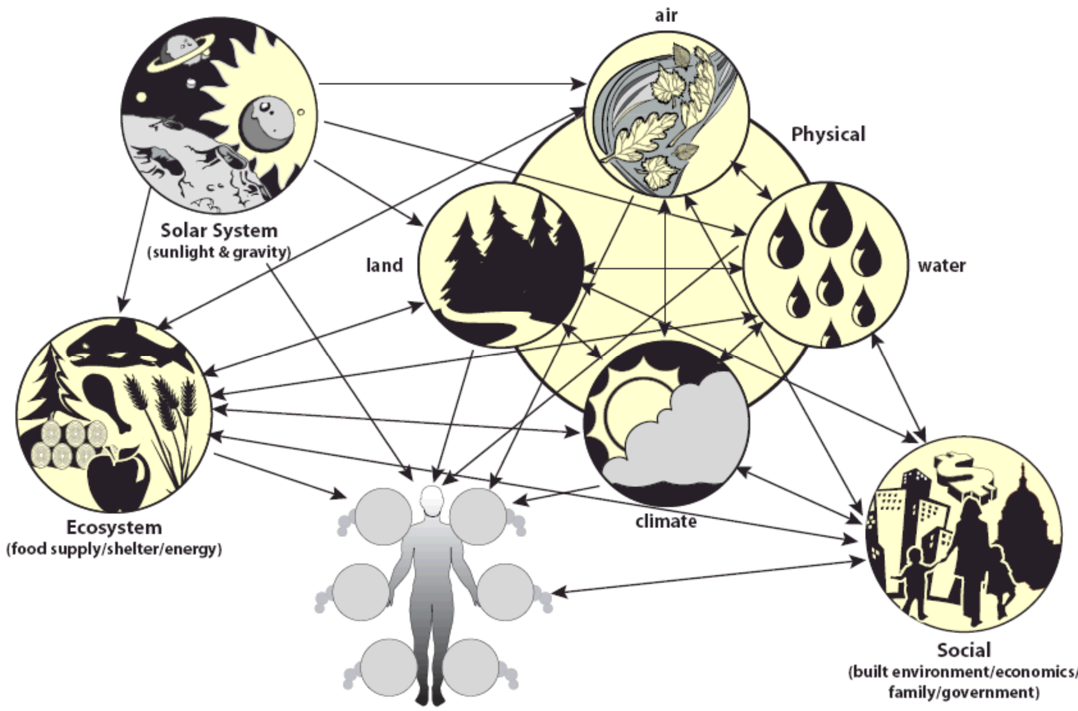
Conclusion

We have confirmed the genotoxic effects of asbestos in humans, consistent with known association of chromosome aberrations with cancer-risk. Although exposure to rockwool and glass fibres in our study was low, we found evidence that oxidative damage is involved also in the mechanism of toxicity of these other mineral fibres.

Determining Relationships
Environmental Factors /genotype/Phenotypes



Interaction Network: Our Environment and Our Health



Gohlke and Portier (2007)

Acknowledgement

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WP4.2 Toolbox / Guidance System

Adapted from Presentation to PSG, London, May 2008

Clive Sabel, Alexandra Kuhn, Rainer Friedrich

SP2 Meeting, June 2008, Tromso, Norway.

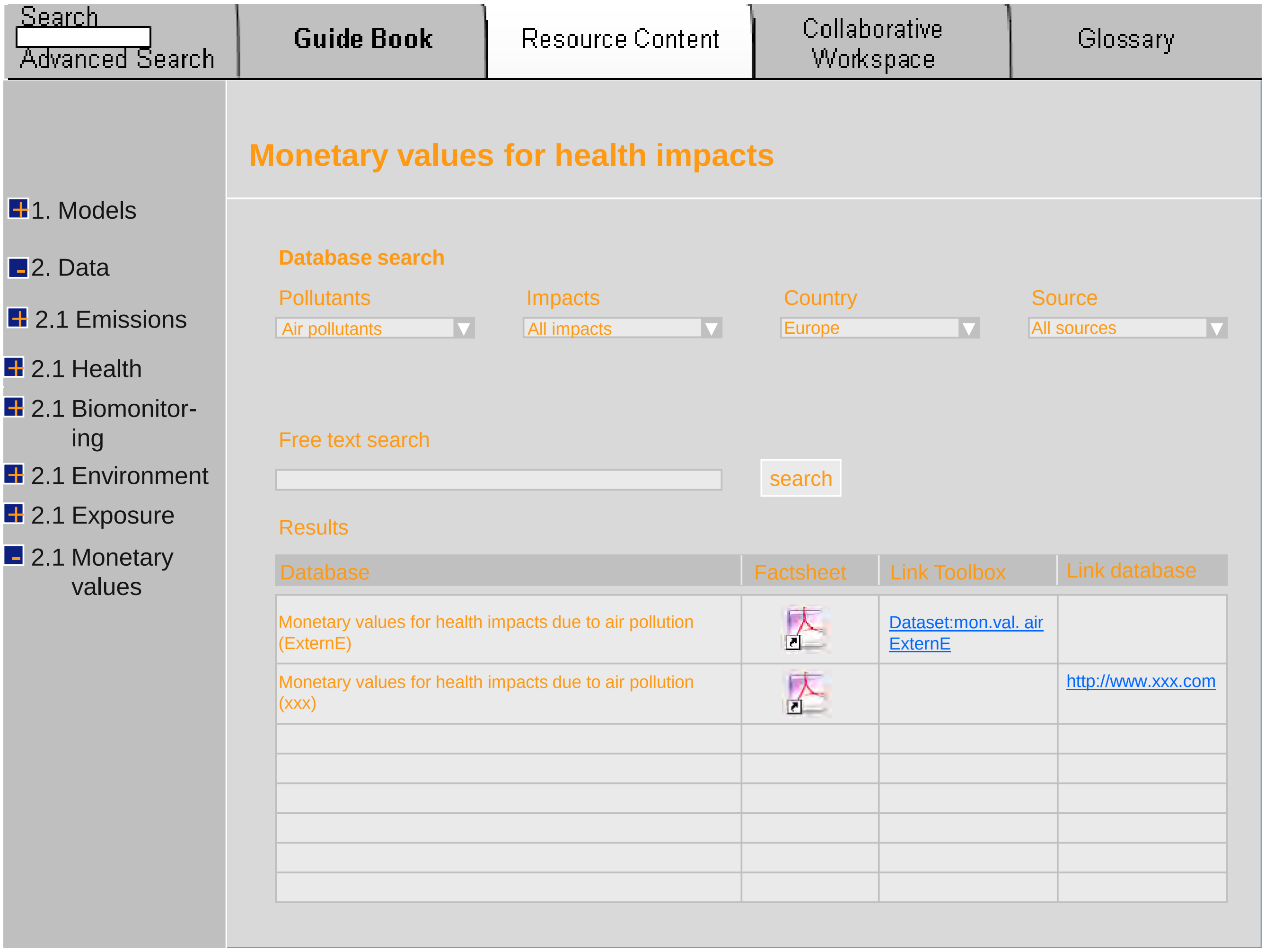
Aims of the system

After canvassing people's expectations and possibilities in the project:

- A system that might not be very ambitious at the beginning
- But that affords opportunities to build on later on

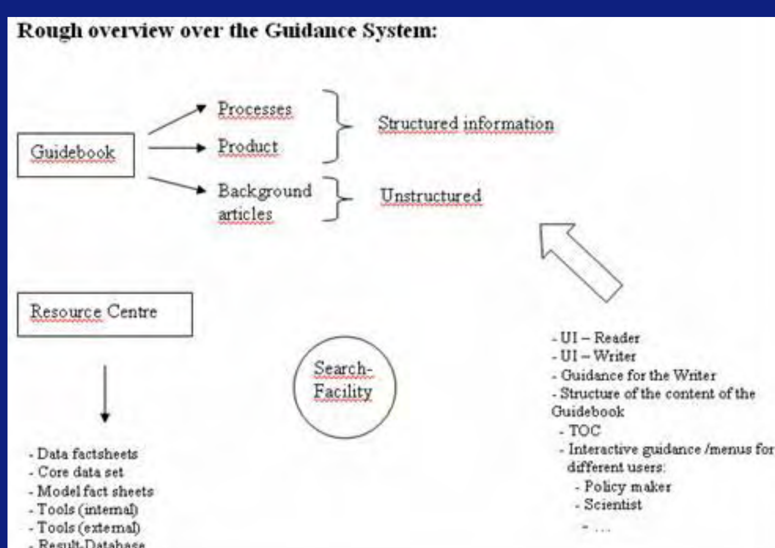
Aims of the system:

- The system should provide information on anything you need to do for an integrated assessment
- Convey the methods used and enhanced to future users for
  - Appliance,
  - Education and
  - Further development



Overview I

- Overall architecture of the Guidance System: *modular*
- Plug in more functionalities later on, e.g. plug-in of Wiki, connection to the Heimtsa-Toolbox



Overview II

- The **Guidebook** should contain all the methods relevant for an assessment. This is the part where SP 1 will locate their work.
- The **Resource Centre** will contain resources, or links to resources, like data fact sheets, model fact sheets, a core dataset and some tools.

User / user Interface / user management / collaborative working I

- Variety of anticipated users: e.g. policy makers, assessors, stakeholders in general, students and maybe even the public
- User interface to be tailored specifically according to expertise
- “Menu” for each user group: guidance to those methods/ pages/ resources it is most interested in
- The users can be “passive” (just reading) or “active” (discussing, using tools, uploading reports)
- User interface: tree structure to organise the main information, highlighting where the user is
- For readability issues: articles will consist of outline and hidden parts (more-parts)

User / user Interface / user management / collaborative working II

- A help system will be implemented
- Access right management according to needs (e.g. log-in)
- Working collaboratively:
  - Uploading of results (e.g. as a report),
  - Shared writing of articles,
  - Shared insight in user profiles and the possibility for contributing to discussions
  - Separately, a collaborative workspace module for directly working on an assessment is developed by KTL, which can later be plugged into the system

Guidebook and articles

- Main part - conveys methodologies to the users
- Helps assessors perform an integrated assessment and is therefore applicable in all phases of an assessment

- Articles: different levels of details
  - Methodology describing articles (structured objects; processes)
  - Product describing articles (structured objects; products) [maybe not needed in the end]
  - “Glue”-articles / introductory articles (unstructured objects)
  - Background articles (unstructured objects)

Resource Centre I

- The Resource Centre will provide information on resources and contains several items:
  - Data fact sheets (descriptions of data or databases)
  - Model fact sheets (descriptions of models)
  - A core data set
  - Internal tools
  - External tools
  - Results database (belonging to the collaborative workspace module, containing all the existent variables)
  - Glossary
  - Worked examples / conducted assessments / results (maybe also called Warehouse; partly overlapping with the collaborative workspace module)

Resource Centre II

- Data and model fact sheets:
  - Purpose: to enable users to find the data and models they need for their assessment
  - Either describe a type of data / model
  - Or describe concrete data(bases) and models
- Core data set
  - Data that might be used for several assessments and is not subject to change very often
  - e.g. population data, meteorology, emission factors, exposure profiles, intake fractions, toxicological constants, dose-response functions; baseline disease or mortality rates, weights for use in DALYs, and discount rates or life-values for cost-benefit analysis

Resource Centre III

- Internal tools:
  - A tool for spatial visualisation, e.g GIS (maybe)
  - Causal diagram tool, software to draw a diagram (nice to have)
  - Health impact calculation tool, including the calculation of DALYs and monetary values
  - Article database (to help to find articles in scientific journals)

Resource Centre IV

- External tools (links to the tools):
  - UU/MNP Uncertainty tool → Jeroen van der Sluijs
  - Aguila (visualisation of probability distribution) → Uni Münster, Edzer Pebesma.
  - R (for statistical analyses and meta-analysis-help)
  - RIVM risk perception web questionnaire
  - Expofacts database → KTL exposure group
  - Exposure assessment platform → KTL exposure group

Search facility

- Advanced search facility
- Over all elements of the system
- Including full text search and search by categories eg:
  - only in the Guidebook
  - only in fact sheets
  - only for a certain part of the fact sheets, e.g.
    - dealing with exposure models/data;
    - only for glossary pages;
    - including or excluding discussion contributions

Life after INTARESE / Heimtsa

- Not only output of Intarese, but a living system that develops in time
- Taking on board other projects' results
- Collaboration with Heimtsa: Heimtsa models could be a further module of the same system/toolbox so that policy makers would only have one address to go to for information on impact assessment and health
- Heimtsa aims to use Graphical information systems (GIS) as the glue to link between models and to join together the different steps of an assessment

SP2 input to the toolbox

- Liaison through Karen Bruusgaard, NILU

- Data and model factsheets for the Resource Centre
- Standardise the factsheets format

- WP2.1 Env. Monitoring ☑
- WP2.2 Biomonitoring ☑
- WP2.3 Health surveillance
- WP2.4 Integrated monitoring

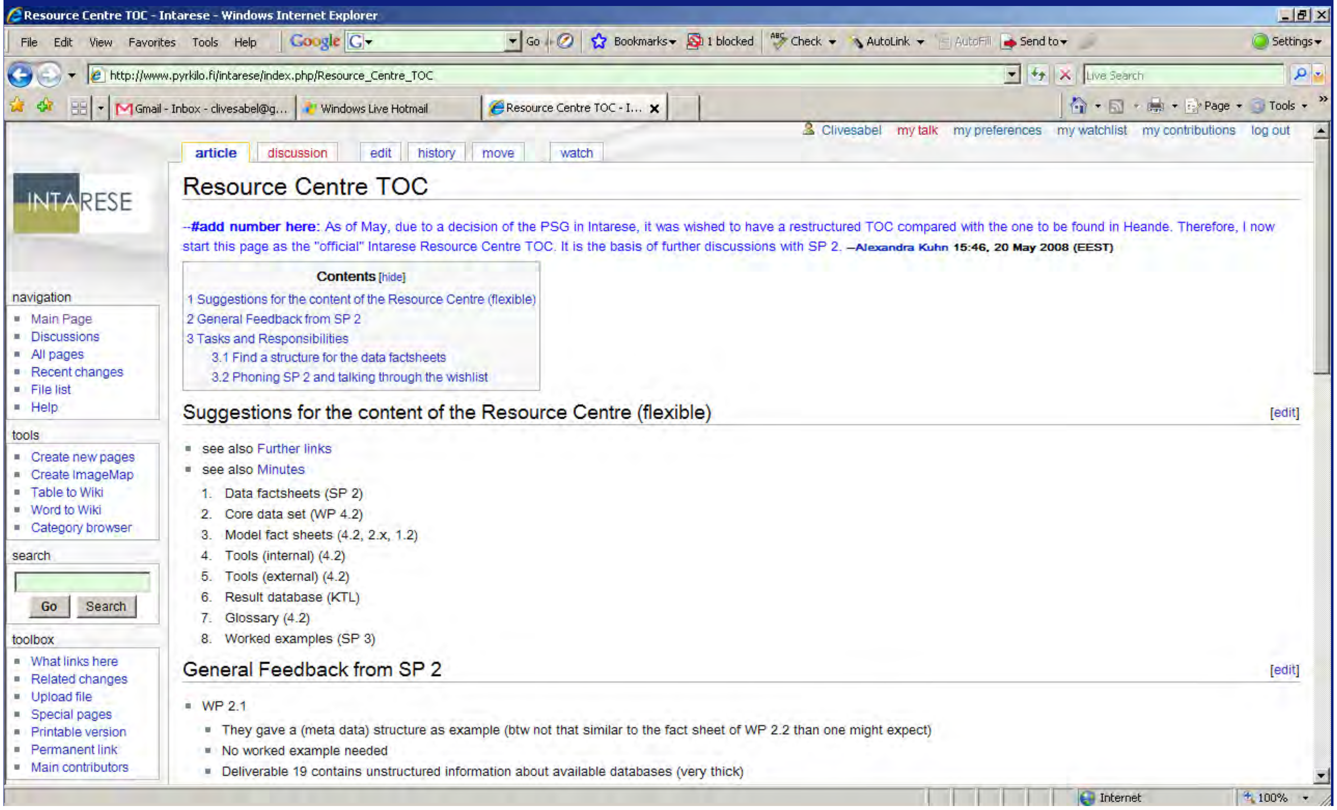
(A lot) More info on the WIKI

- WP 4.2 Toolbox development
- http://www.pyrkilo.fi/intarese/index.php/WP4.2_Toolbox_development

- Guidebook
- http://www.pyrkilo.fi/intarese/index.php/Guidebook_TOC

- Resource Centre
- http://www.pyrkilo.fi/intarese/index.php/Resource_Centre_TOC

INTARESE WIKI



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ABSTRACT
The aim of this report is to address the issues of monitoring for the purposes of integrated environmental health impact assessment, to provide basis for further INTARESE project work towards the objective to give guidance on integrated monitoring. The two specific objectives are: (i) to identify the commonly experienced methodological and practical issues encountered in integrated environmental health impact assessment; and (ii) to specify activities to be performed in SP2 and WP2.4 that would lead to providing the guidance. It includes: (1) integrated monitoring: the way forward; (2) approaches to integrate monitoring for environment and health impact assessment; (3) biomonitoring in the INTARESE concept of interated risk assessment; (4) exposure-Dose-Response integration: looking for a common currency; (5) case study on Pb in blood-Europe; (6) environment and health information system in France; (7) eco-toxicology–use for investigating interaction of stressors for integrated risk assessment –Spain; (8) environmental Exposure and Ecosurveillance; (9) monitoring of organohalogens body burdens of the Czech population; (10) exposure to c-PAHs case studies; (11) environmental data and human biomonitoring in France; (12) the concept of integrated monitoring in the Flemish Environmental Health Survey (FLESH) ; (13) integrated monitoring –vision or reality? (14) the impact of air pollution to human health-Czech Experience; (15) occupational exposure monitoring-approach used in FIBRETOX; and (16) INTARESE toolbox guidance.

** Classification*	*A*	*Unclassified (can be ordered from NILU)*
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