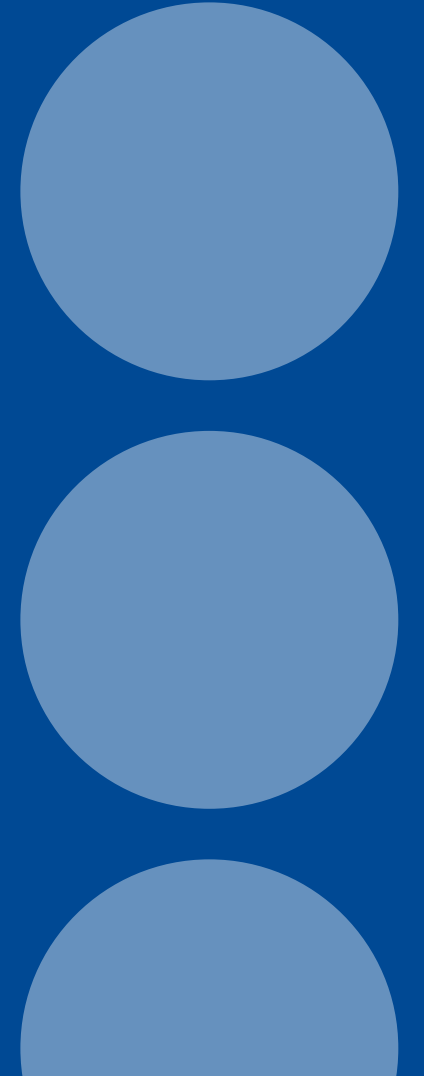


# Carcinogenic Substances at the Workplace - Strengths and Limitations of Biological Monitoring

ISSA Symposium on Carcinogenic Substances:  
Risks and Prevention  
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Dr. Tobias Weiss



# Biological Monitoring – Measuring xenobiotics or their metabolites in body fluids

Biological Monitoring reflects the effective exposure dose and integrates all routes of exposure (inhalative, dermal, oral)

## Requirements

Analytical methods

Calibration standards, internal standards

Values in biological materials for assessment



# Biological Monitoring – Measuring xenobiotics or their metabolites in body fluids

Biological Monitoring reflects the effective exposure dose and integrates all routes of exposure (inhalative, dermal, oral)

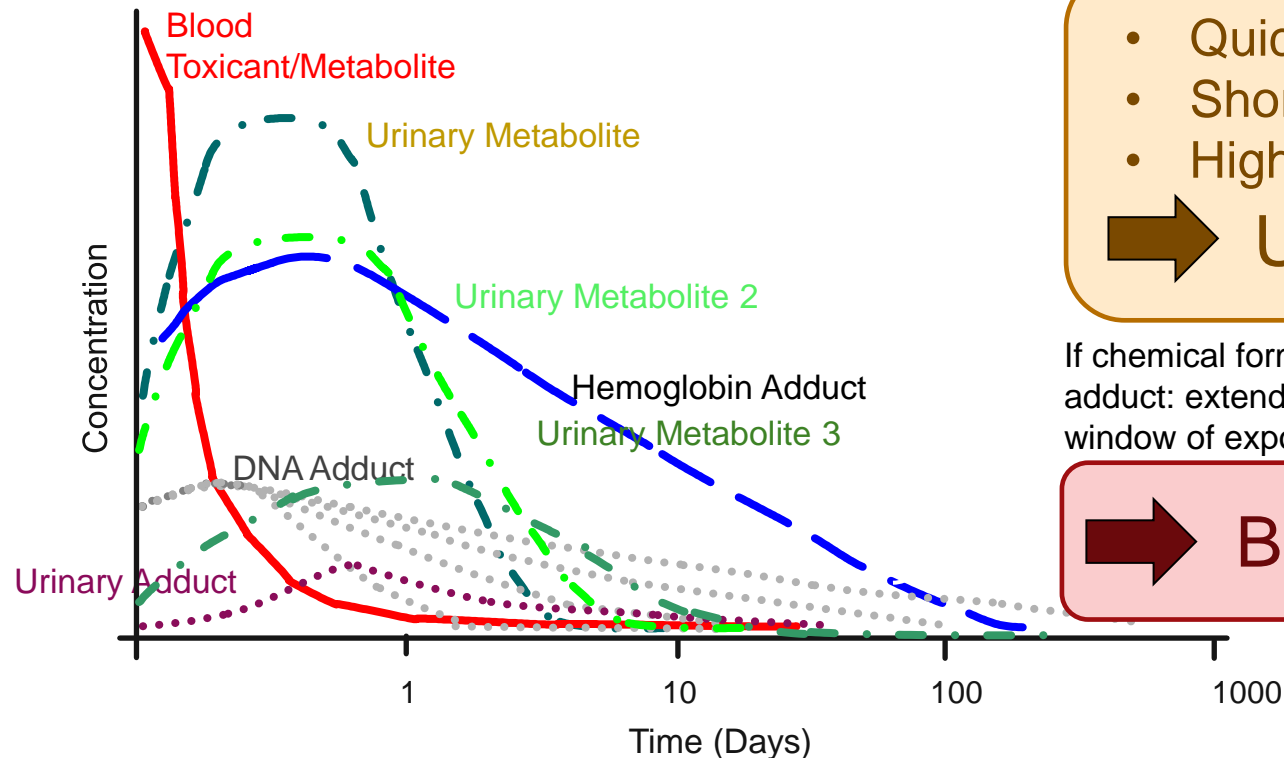


## Legal regulations

- » Part of German GefStoffV / ArbMedVV
  - TRGS 903 (BGW)
  - TRGS 910 (Äquivalenzwerte zum Akzeptanz- und Toleranzrisiko)
  - AMR Biomonitoring



# Toxikokinetics of non-persistent chemicals



- Quick metabolisation
- Short elimination half-times
- Higher urine levels relative to blood

➔ Urine is preferred matrix

If chemical forms an adduct: extends time window of exposure

➔ Blood possible, too

➔ Kinetics determine time of sampling

Needham and Sexton. JEAEE 10 (2000)  
Henderson et al. Crit Rev Toxicol 20 (1989)

# Carcinogenic substances – The situation in Germany in 2021

**Risk-based limit values in air for 23 carcinogens**  
(TRGS 910, 02/2021)

**Risk-based limit values in biological materials for 9 carcinogens**  
(TRGS 910, 02/2021)

**But: About 200 carcinogens (K1 + K2) and 200 suspected carcinogens (K3 – K5)**  
(MAK-List 2020)



Only little surveillance of employees  
exposed to carcinogenic substances



# Reference Values

## Background levels in biological material at a particular time

- » ... in a defined group of the general population (HBM-Kommission, **Reference values**)
- » ... in a reference population of persons of working age who are not occupationally exposed to the substances (MAK Commission, **Biologische Arbeitsstoff-Referenzwerte (BAR)**)
- » 95<sup>th</sup> percentile of the measured concentrations in biological material



... are statistical values  
and *per se* of no health or risk relevance

## Example 1: Biological Monitoring in coke oven workers

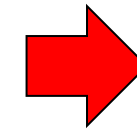
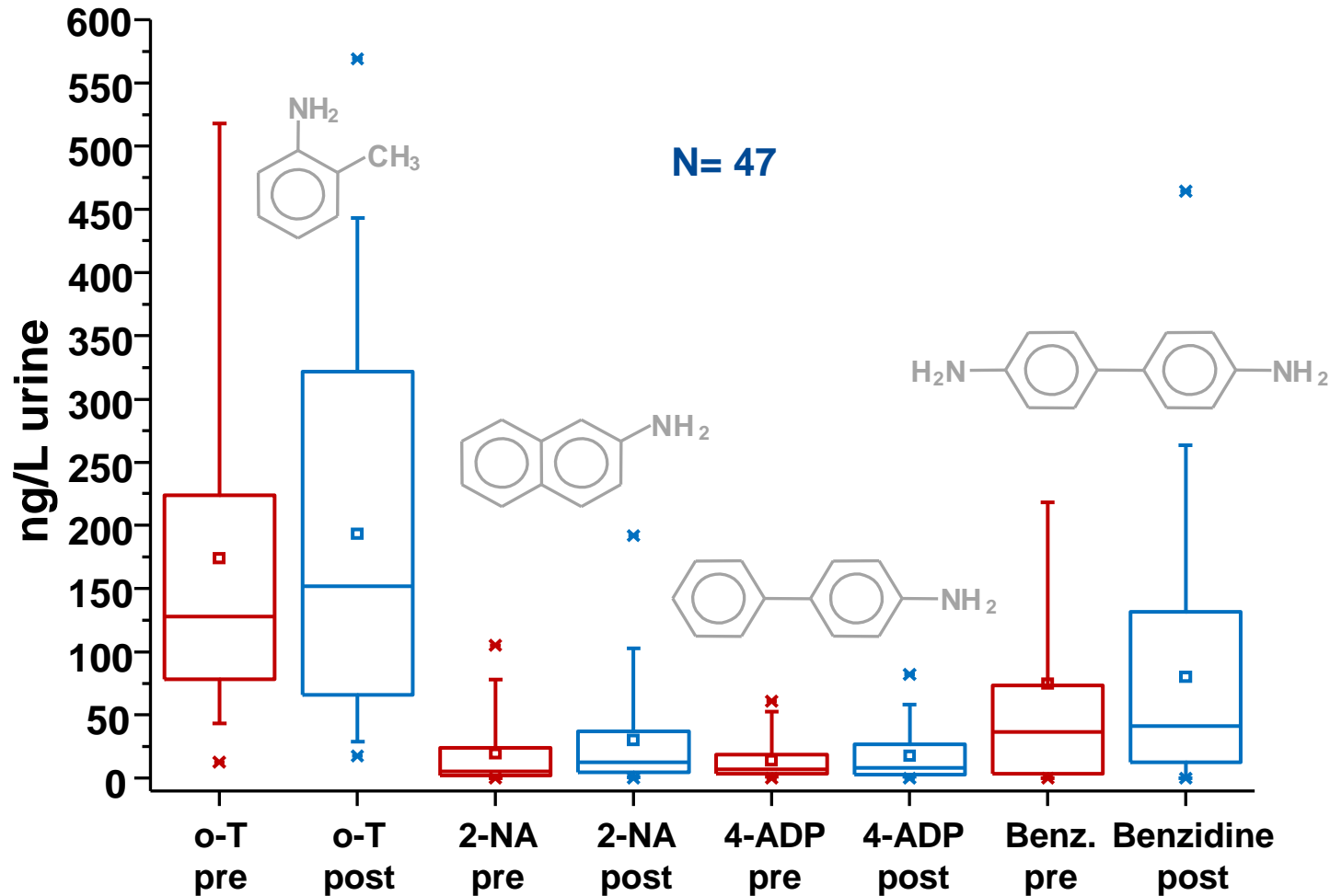
- Modern European coke oven plant (2 million tons of coke per year)
- Recruitment of 47 male workers (62 % of entire personnel)
- Different job tasks, many of them outdoors



Biological Monitoring in pre- and post-shift urine:

- 1) Aromatic Amines (bladder cancer) (Method: Weiss & Angerer 2002)
- 2) PAH (lung and bladder cancer) as 3OH-BaP: LC/LC-UV (Method: Lafontaine et al. 2006)
- 3) Benzene (cancer of the hematopoietic system) as S-PMA (Method: Schettgen et al. 2008)
- 4) Tobacco smoking as 3OH-Cotinine: LC/LC-MS/MS (Method: Koch et al. in prep.)

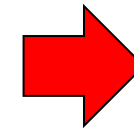
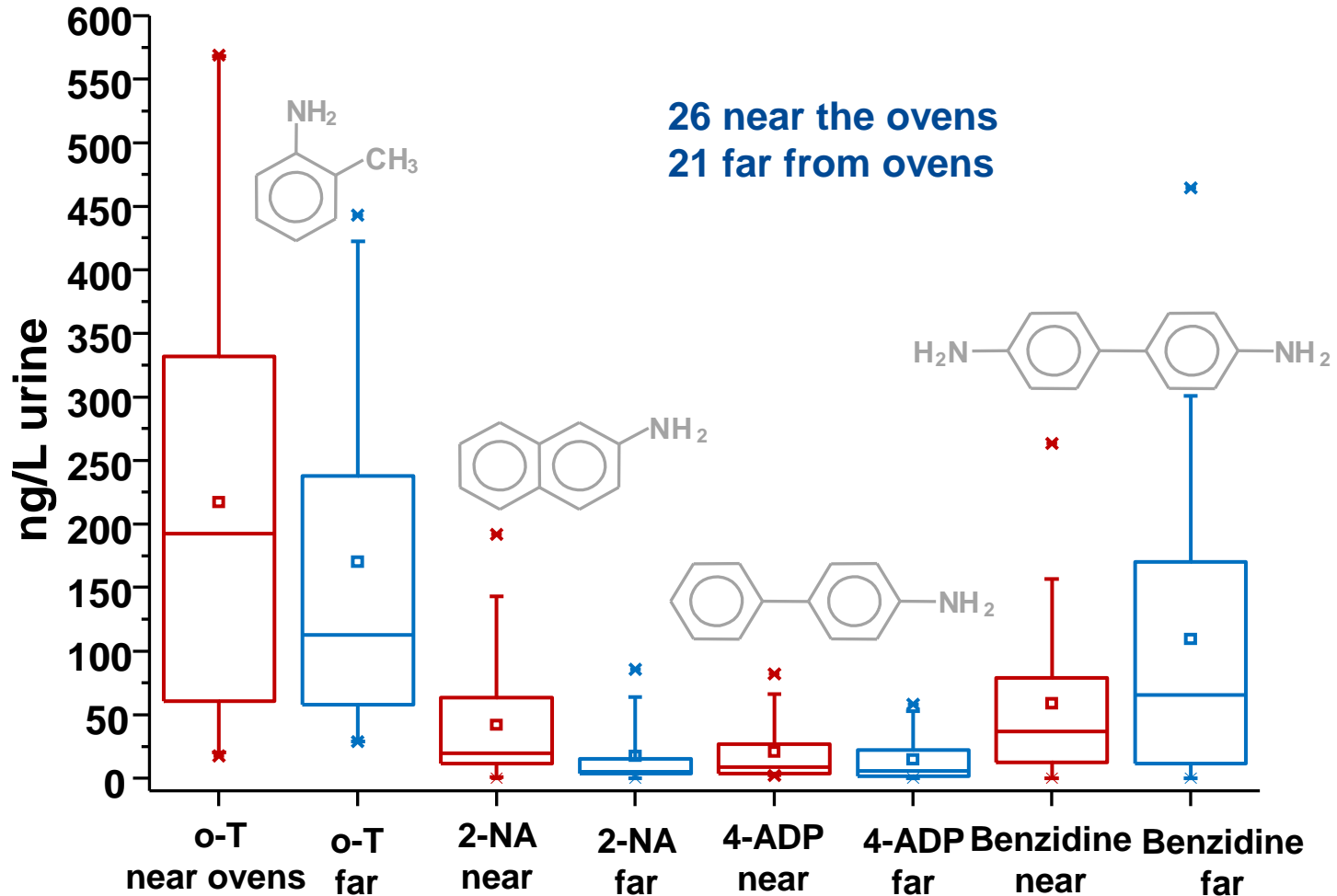
# Aromatic Amines in urine: pre- vs. post-shift



No significant difference

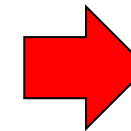
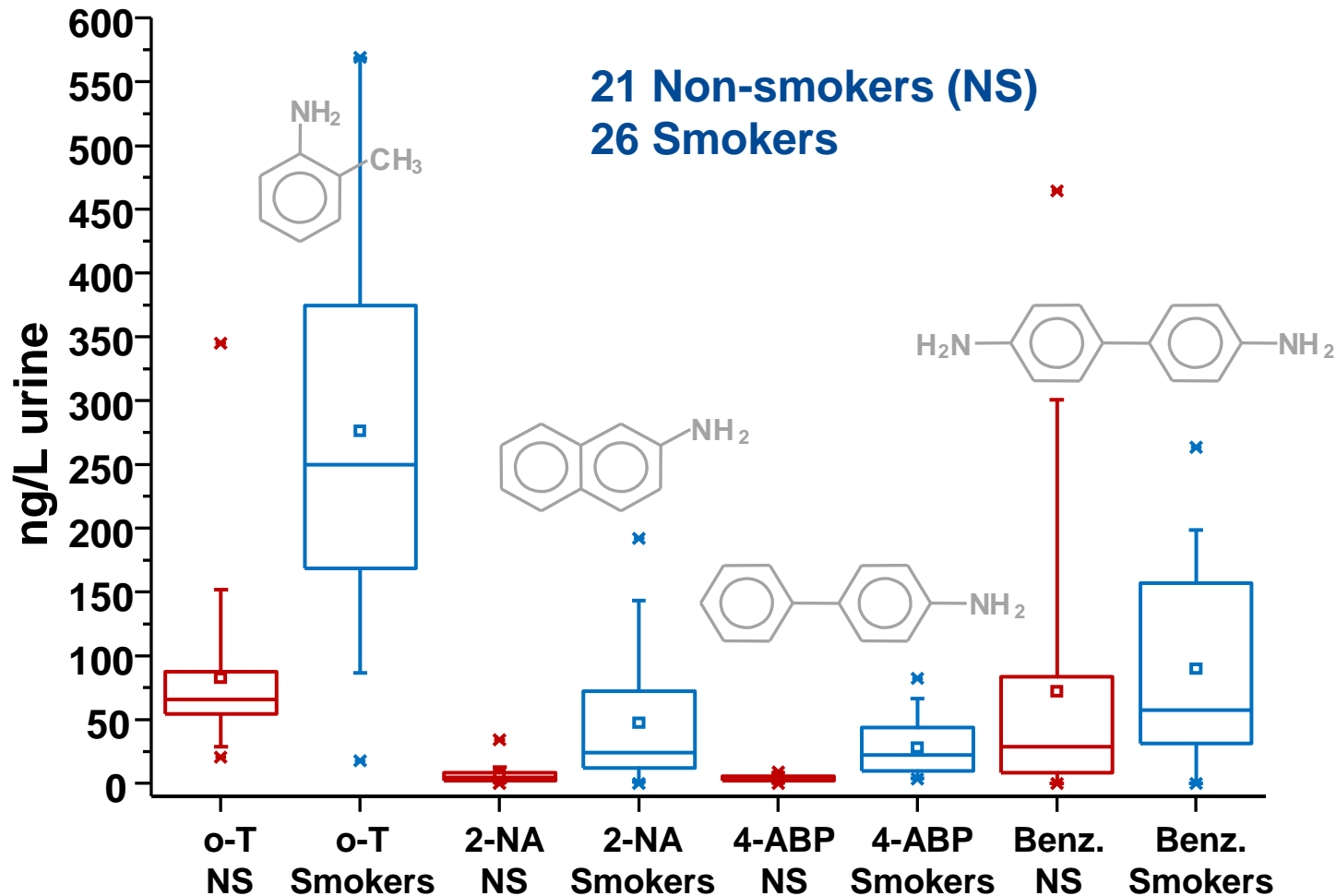


# Aromatic amines: workplaces near vs. far the ovens



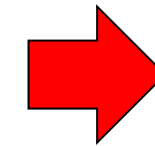
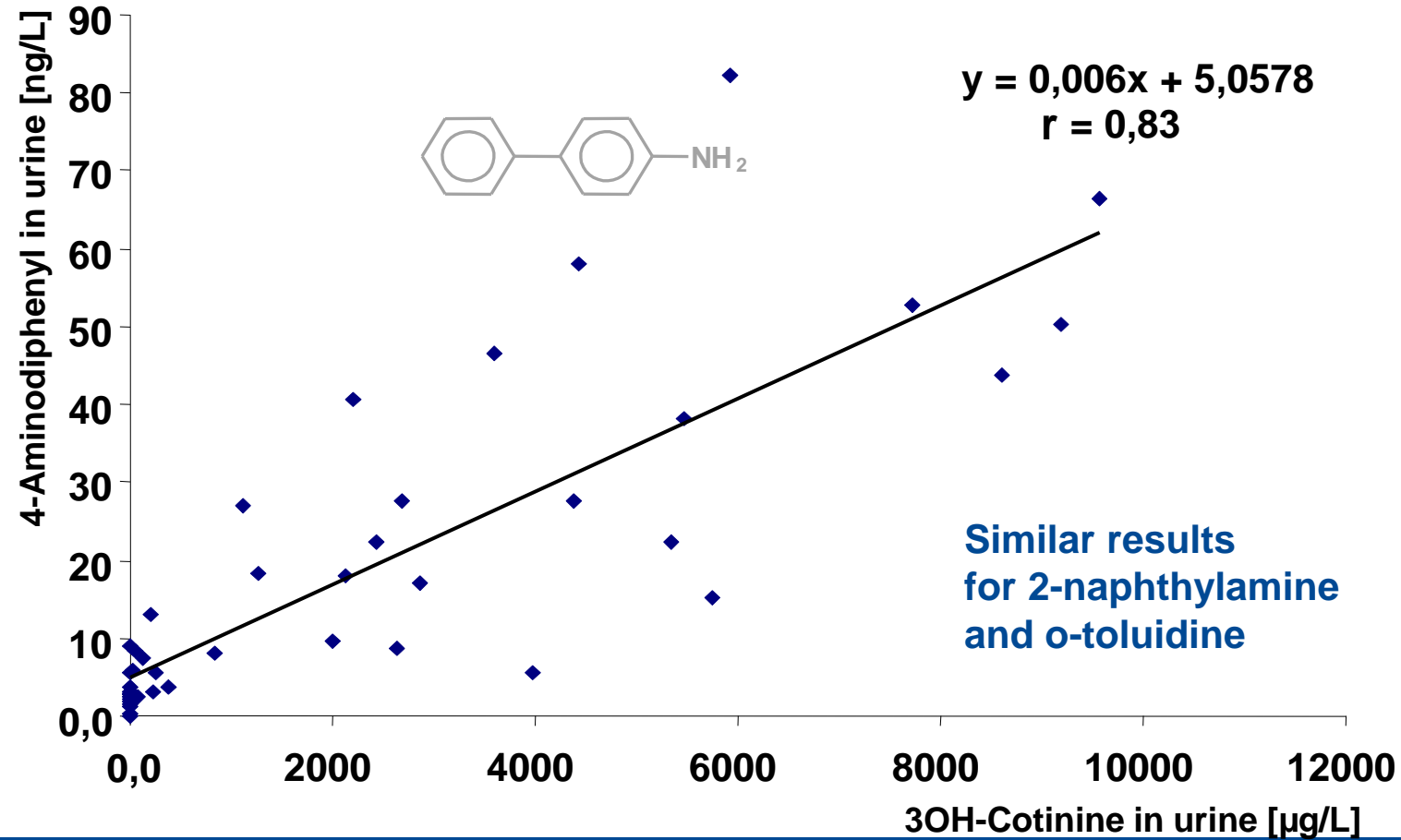
No significant difference

# Aromatic amines: smoking vs. non-smoking



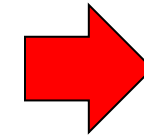
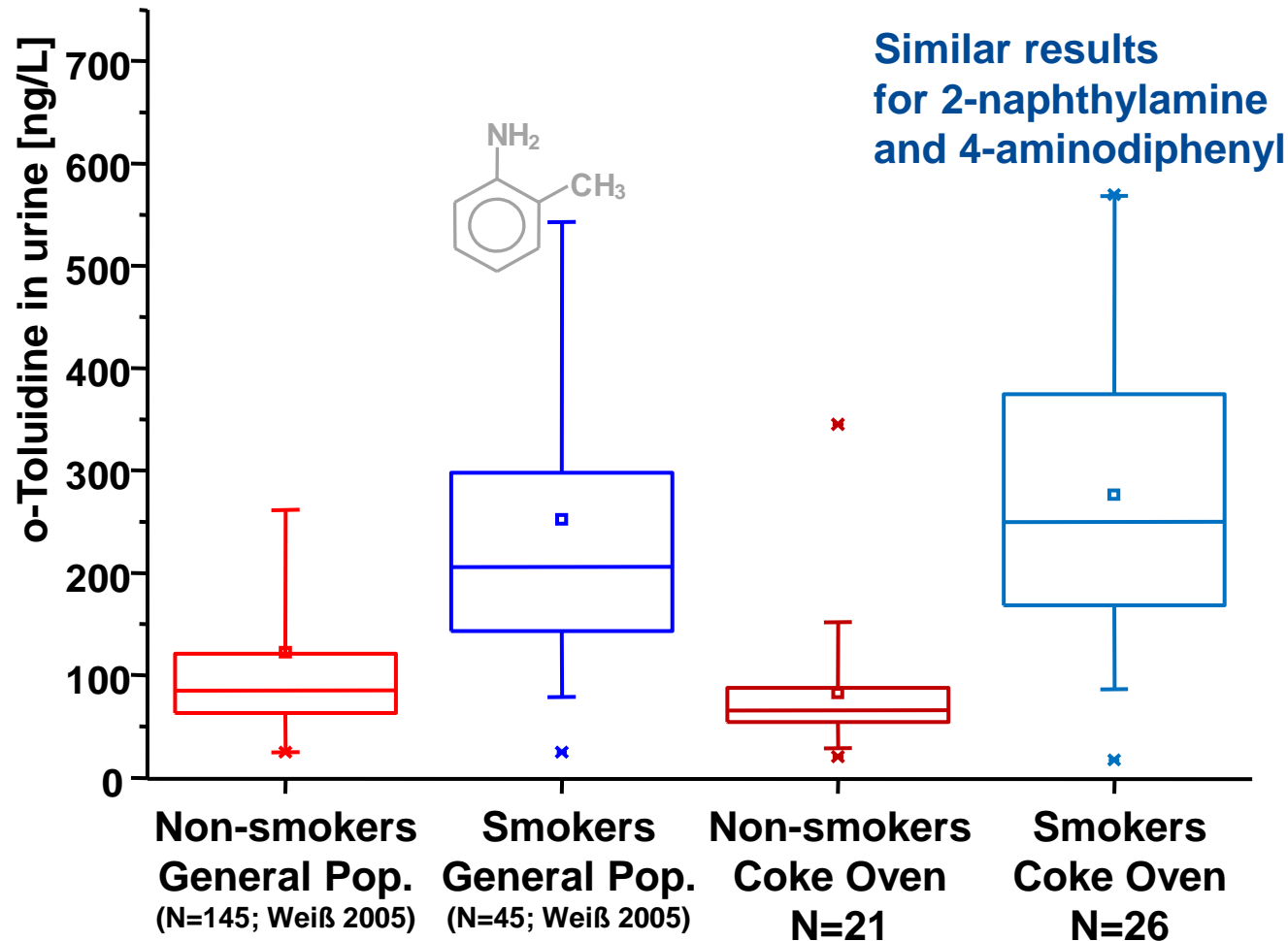
**Significant differences!**  
(except Benzidine (Benz.))

# 4-Aminodiphenyl and Smoking



**Significant association**

## o-Toluidine: Comparison with reference values



**Main Conclusion:  
No relevant occupational  
exposure evident**

## Example 2: Biological Monitoring in the recycling industry (Railway sleepers and contaminated soil)

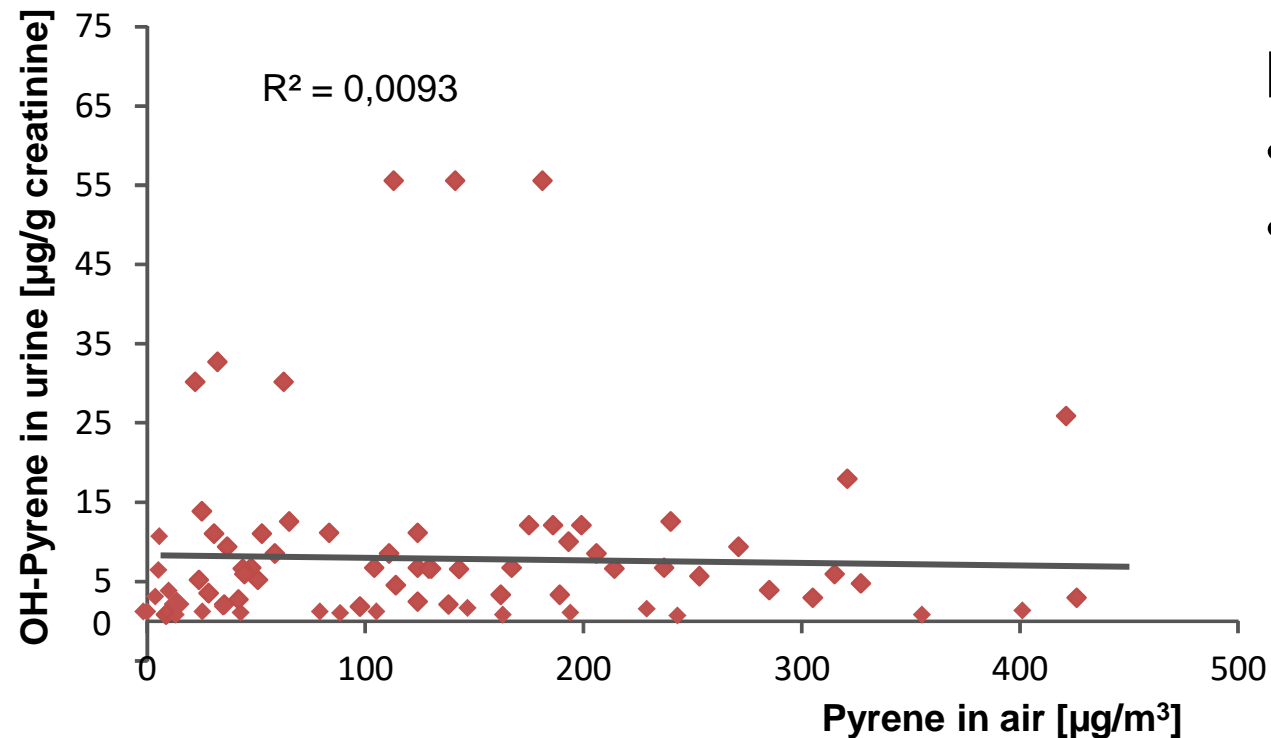
- 3 SME, 2 of them recycled tar oil soaked railway sleepers
- Recruitment of 63 workers
- Different job tasks, many of them outdoors
- BaP in air up to 3x OEL



### Ambient Monitoring and Biological Monitoring

- 16 EPA-PAH in air
- 1-Hydroxypyrene in in pre- and post-shift urine
- Status quo and after 5 turns of establishing safety measures/personal protection equipment

## Association Pyrene in air vs. OH-Pyrene



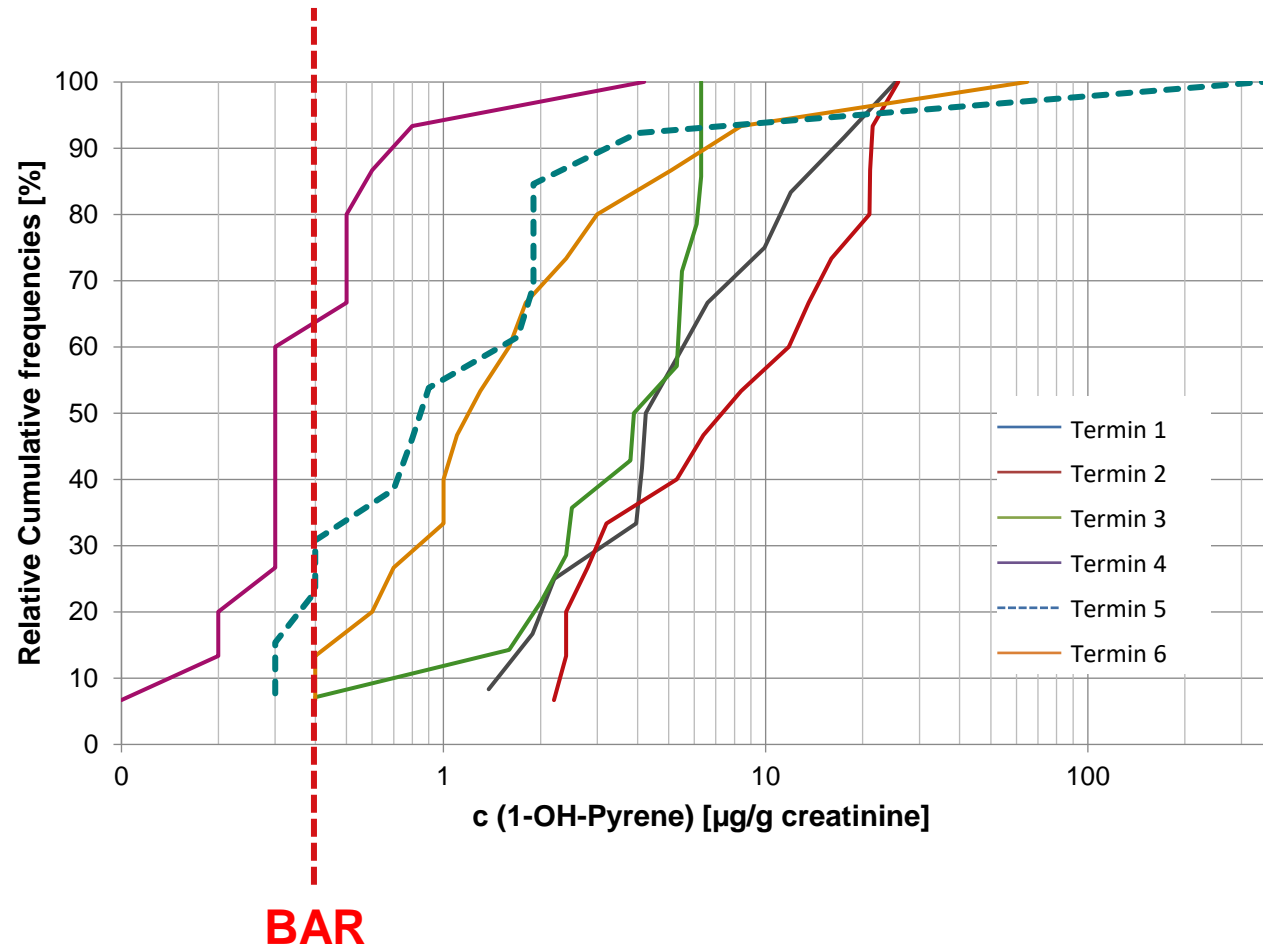
No associations:

- BAP und pyrene in air
- Pyrene in air and OH-pyrene in urine



**Dermal exposure contributes significantly**

# Reduction of exposure by package of measures



Successive reduction of internal exposure to background (General Population; BAR: 0,3  $\mu\text{g/g creatinine}$ )

But: Still very high exposure in single cases

## Summary and Conclusions (Limitations)

Biological Monitoring of carcinogenic substances...

- needs comprehensive knowledge in metabolism und metabolite kinetics to identify suitable markers
  - Extensive investigation of quantitative human metabolism usually not possible
- needs state-of-the-art analytical methods and metabolite standards for method calibration
  - Cost-intensive chemical synthesis of analytical standards and internal standards
- limit values or reference values desired to asses risk but not necessarily essential to improve (individual) prevention

**Biological Monitoring needs quite a lot of work at the beginning, but in the end it's worth**



## Summary and Conclusions (Strengths)

### Biological Monitoring ...

- covers all routes of exposure (inhalative, dermal, oral)
- reflects the effective exposure dose
- uses reference values to differentiate between environmental and occupational exposure
- allows to identify exposure hot spots and to optimize (personal) protection measures
- does not even need limit values to improve primary prevention

**Biological Monitoring is a valuable tool to control occupational exposure to carcinogenic substances in order to minimize risks effectively**