Swiss TPH
Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse

Department of Epidemiology and Public Health
Exposure Science Group / EEH Unit

Bridging the Gap:

Bringing measurements closer to health effects

- Ming Tsai

Exposure Science Group head
Research scientist, Swiss TPH, Basel
m.tsai@unibas.ch

17th ETH-Conference on Combustion Generated Nanoparticles,
June 23rd-26th, 2013

Exposure Science as the Bridge

Swiss TPH

"The new field of exposure science provides information and tools to bridge the disciplines of environmental science & environmental health..."

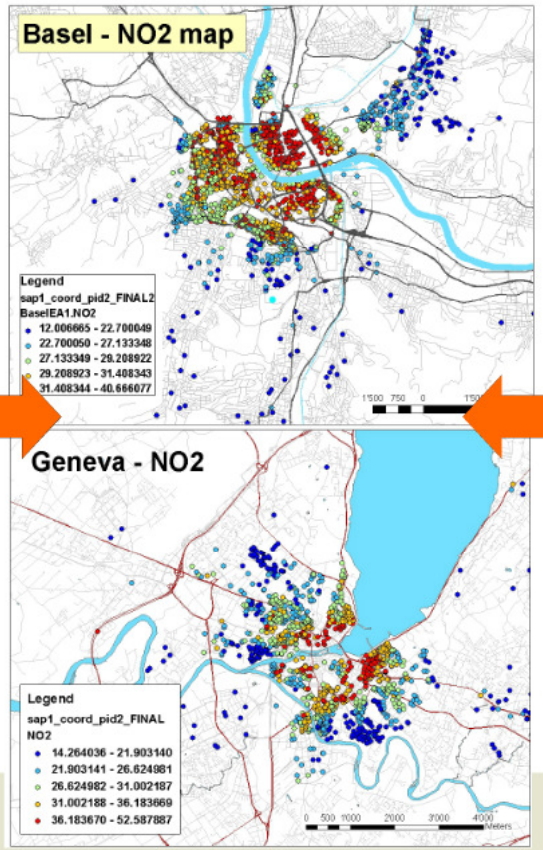
- P. Lioy, EHP 2010.

"Measurement is the foundation of exposure science."

- R. Fenske, JESEE 2010.

Measurements

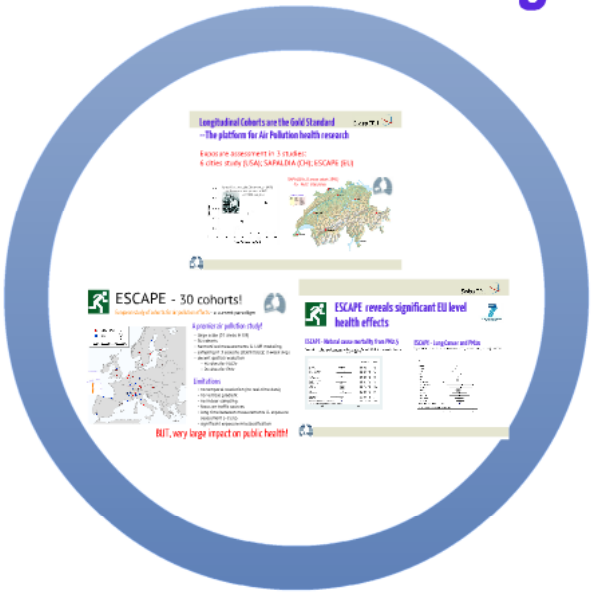
Modeling

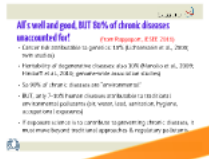


Assessment

The shifting landscape of Exposure Science

The Traditional Paradigm





Current Transformations

Acknowledgments

SwissTPH
SAPALDIA Team
ESCAPE Consortium
EXPOsOMICS Consortium
BAFU – Swiss Federal Office of the Environment
EMPA - Nabel monitoring network
Cantonal air monitoring agencies
University of Basel - MCR
University of Washington, DEOHS, Seattle, WA
FHNW Schweiz – University of Applied Sciences

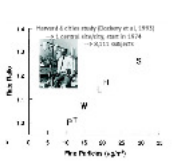
Thank you for your attention!

The Traditional Paradigm

Longitudinal Cohorts are the Gold Standard
Swiss TPH

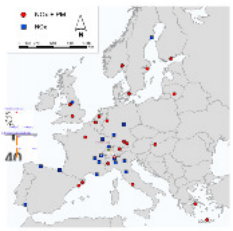
--The platform for Air Pollution health research

Exposure assessment in 3 studies:
6 cities study (USA); SAPALDIA (CH); ESCAPE (EU)



ESCAPE - 30 cohorts!

European study of cohorts for air pollution effects - a current paradigm



A premier air pollution study!

- large scale (37 areas in EU)
- 30 cohorts
- harmonized measurements & LUR modeling
- sampling in 3 seasons (2009/2010); 2-week avgs
- decent spatial resolution
  - 40 sites for NO2x
  - 20 sites for PMx

Limitations

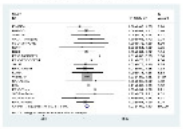
- no temporal resolution (no real-time data)
- no vertical gradient
- no indoor sampling
- focus on traffic sources
- long time between measurements & exposure assessment (~2 yrs)
- significant exposure misclassification

BUT, very large impact on public health!

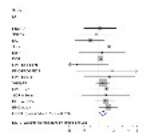
Swiss TPH

ESCAPE reveals significant EU level health effects

ESCAPE - Natural cause mortality from PM2.5



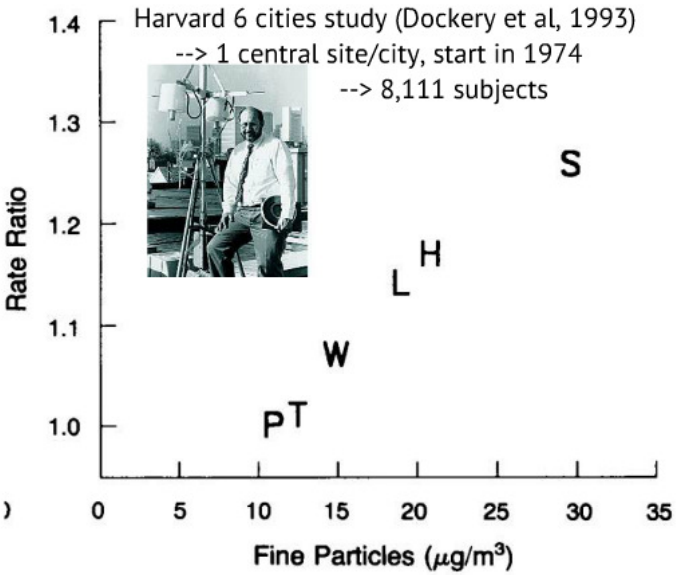
ESCAPE - Lung Cancer and PM10



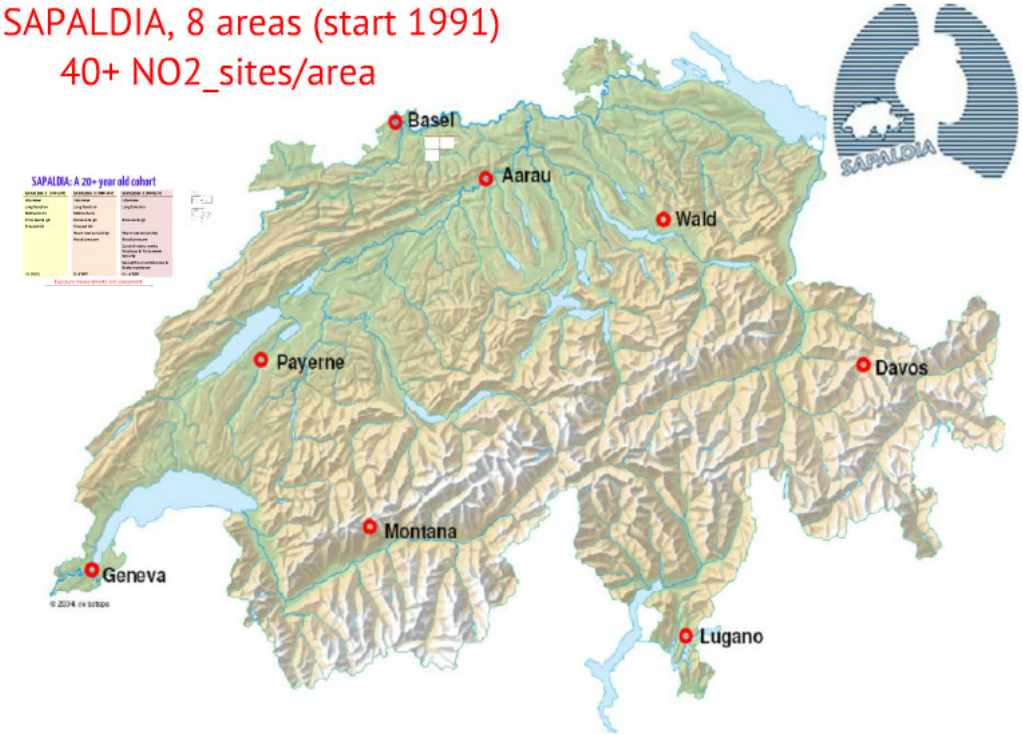
Longitudinal Cohorts are the Gold Standard --The platform for Air Pollution health research

Swiss TPH

Exposure assessment in 3 studies:
6 cities study (USA); SAPALDIA (CH); ESCAPE (EU)



SAPALDIA, 8 areas (start 1991)
40+ NO2_sites/area

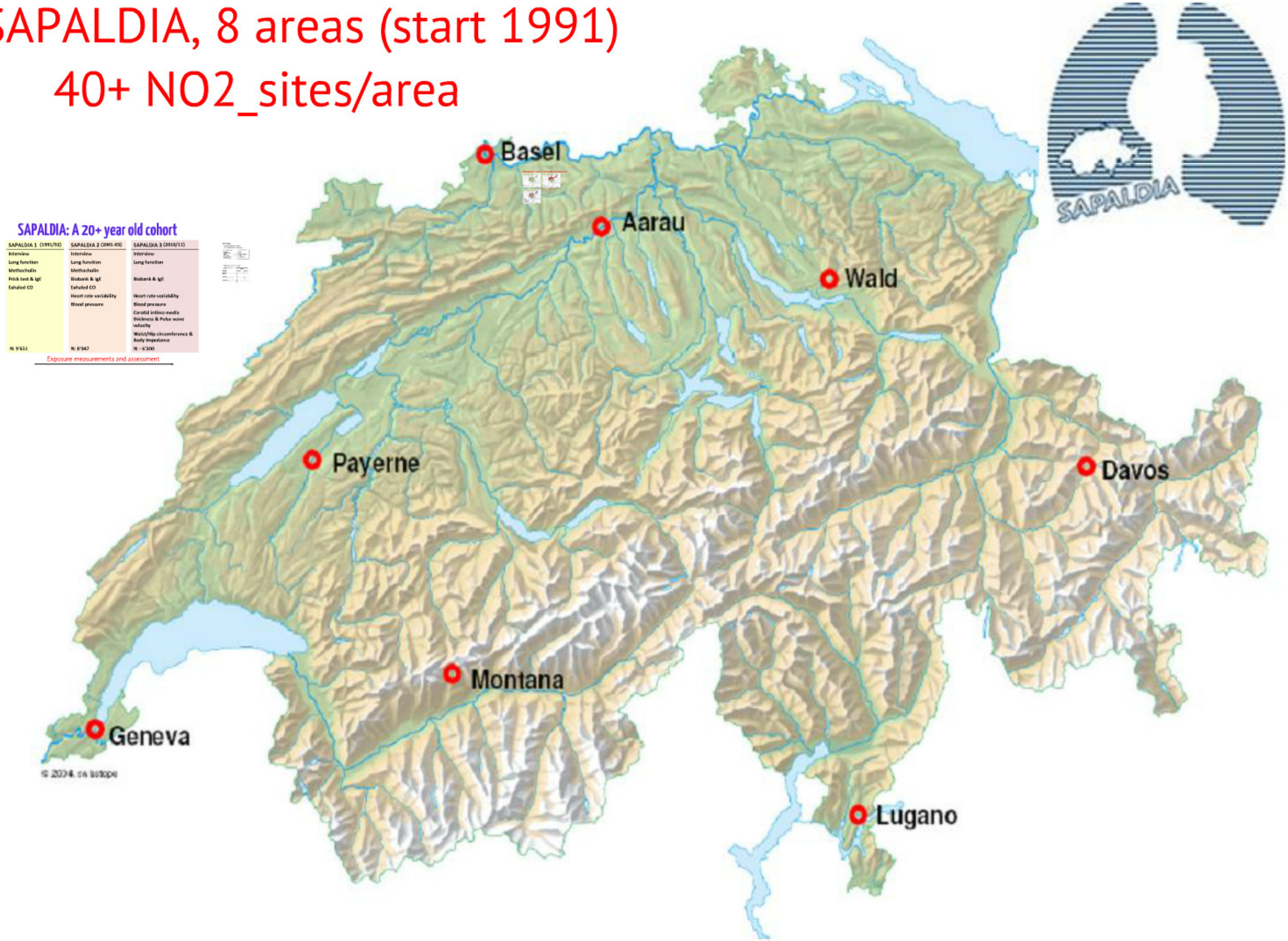


Harvard 6 cities study (Dockery et al, 1993)

--> 1 central site/city, start in 1974

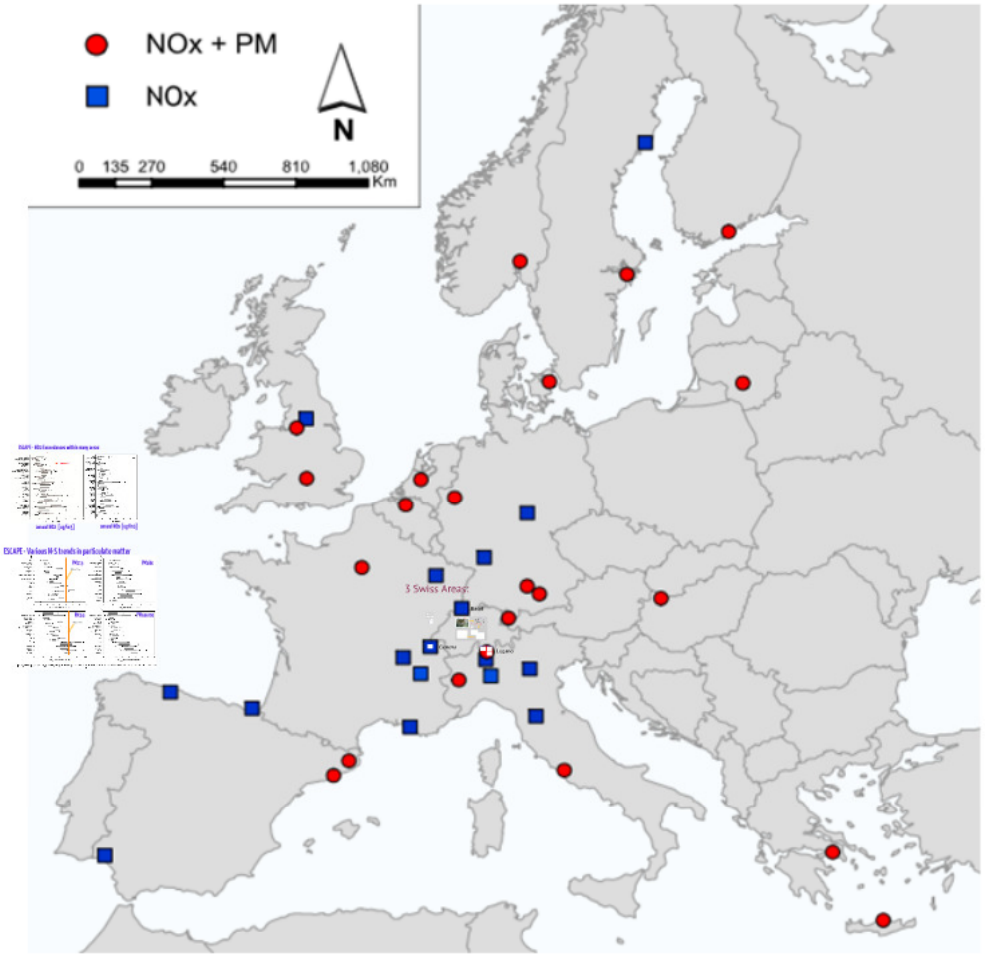
--> 8,111 subjects

SAPALDIA, 8 areas (start 1991)
40+ NO2_sites/area



ESCAPE - 30 cohorts!

European study of cohorts for air pollution effects - a current paradigm



A premier air pollution study!

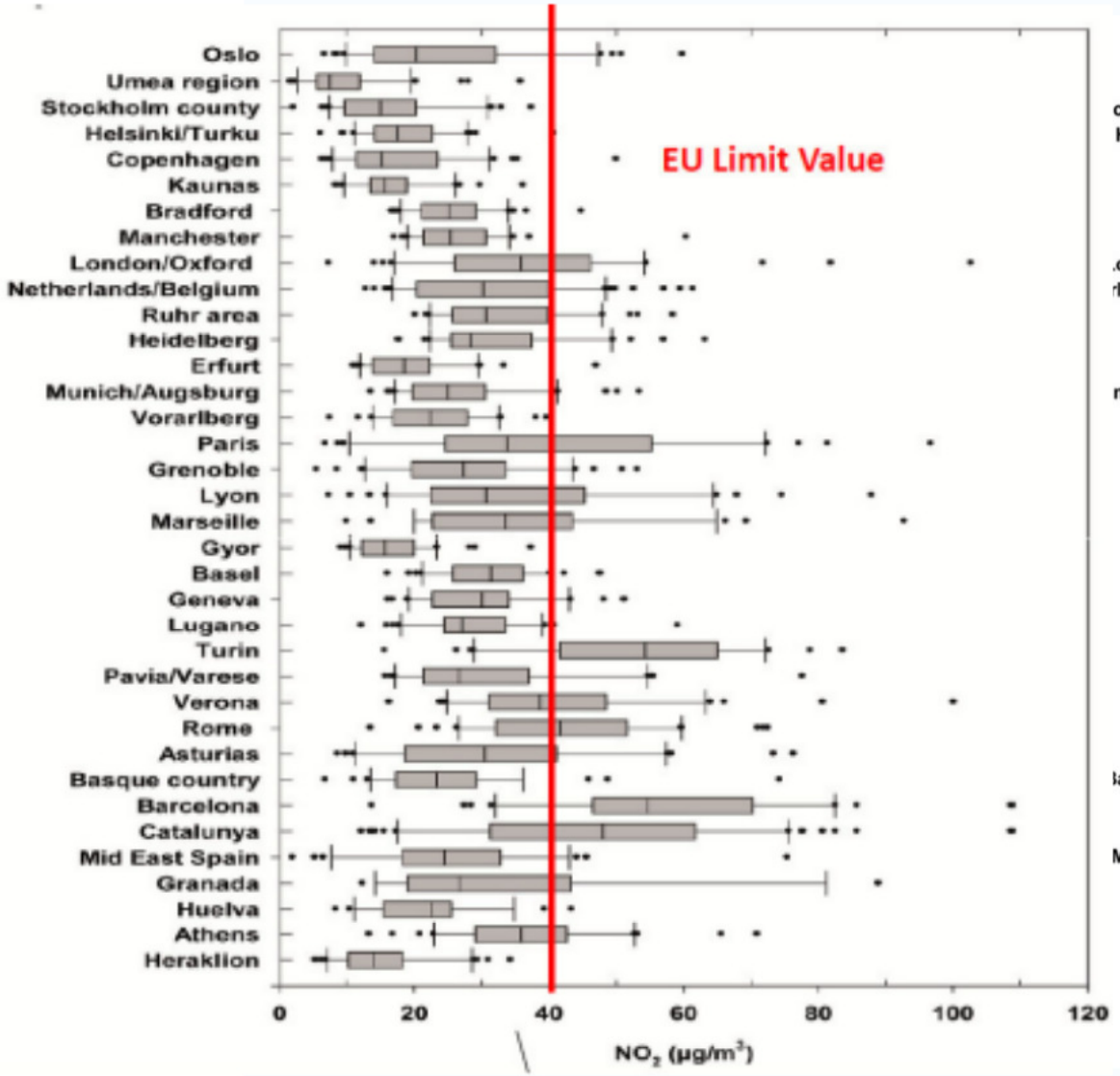
- large scale (37 areas in EU)
- 30 cohorts
- harmonized measurements & LUR modeling
- sampling in 3 seasons (2009/2010); 2-week avgs
- decent spatial resolution
  - 40 sites for NO2x
  - 20 sites for PMx

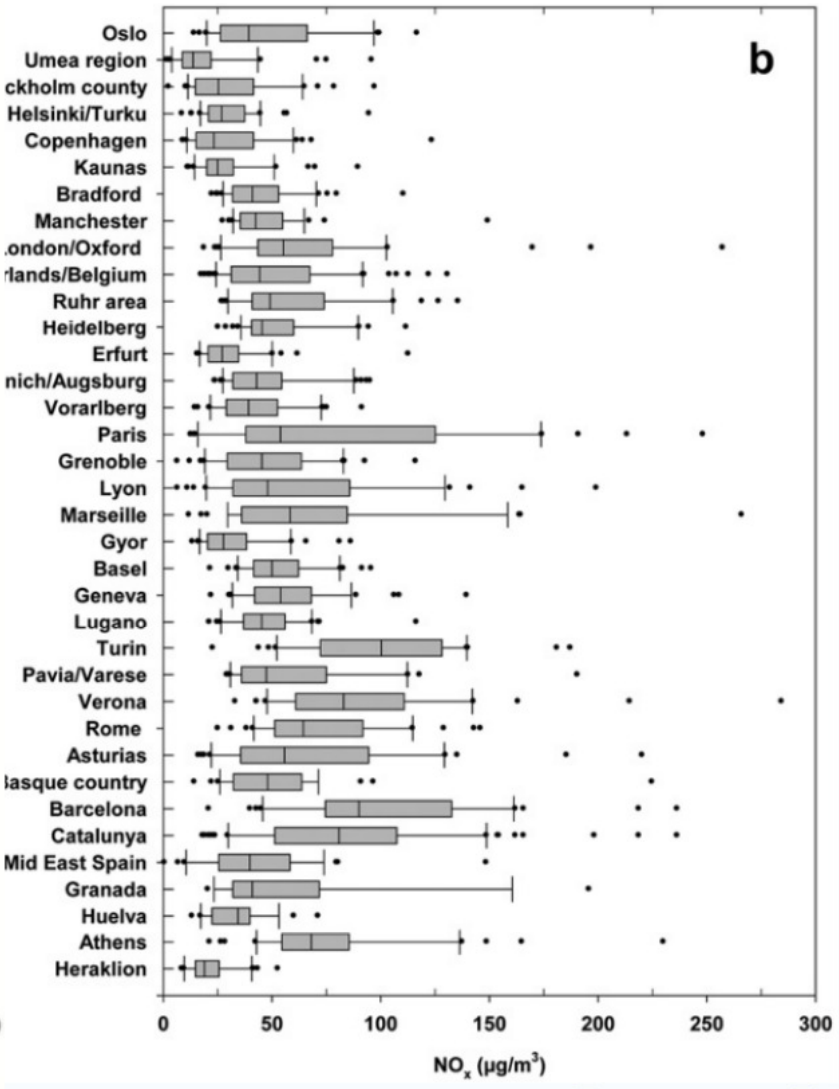
Limitations

- no temporal resolution (no real-time data)
- no vertical gradient
- no indoor sampling
- focus on traffic sources
- long time between measurements & exposure assessment (~2 yrs)
- significant exposure misclassification

BUT, very large impact on public health!

ESCAPE - NO2 Exceedances within many areas



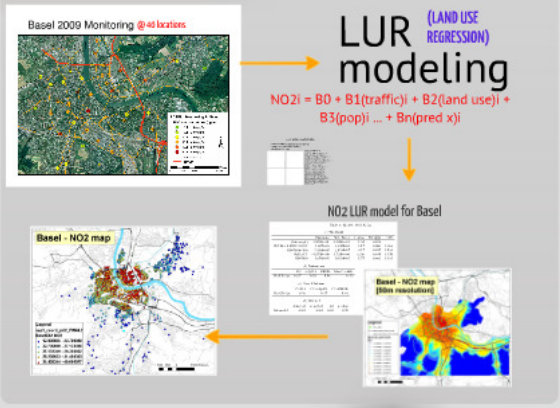


annual NO2 [ug/m3]

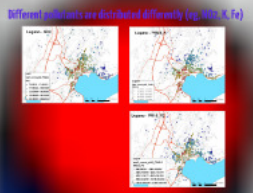
annual NOx [ug/m3]

3 Swiss Areas:

Basel

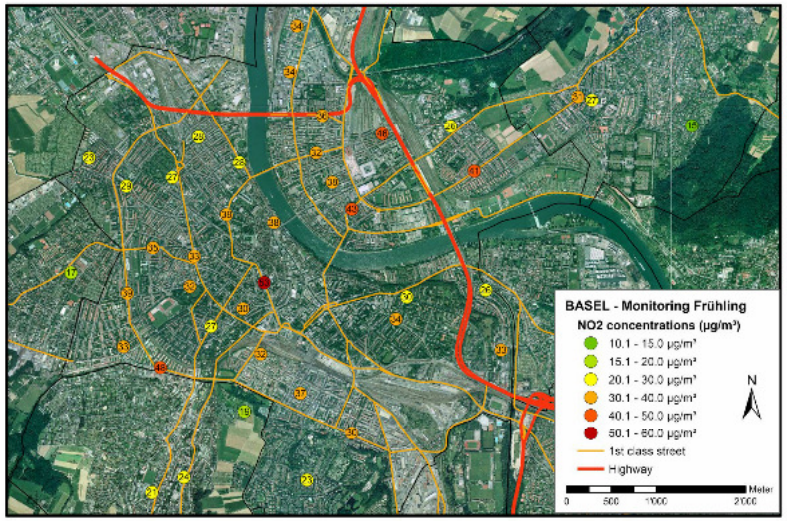


Geneva



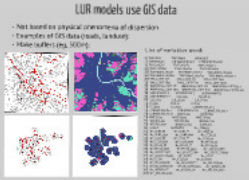
Lugano

Basel 2009 Monitoring @ 40 locations



LUR modeling (LAND USE REGRESSION)

$$NO2i = B0 + B1(traffic)i + B2(land\ use)i + B3(pop)i \ldots + Bn(pred\ x)i$$



NO2 LUR model for Basel

Table 3: Model: BAS.No2a.

(a) The Model

	Estimate	Std. Error	t value	Pr(>|t|)	VIF
(Intercept)	5.435E+01	3.306E+01	1.64	0.109	
INTMAJORINVDIST	1.227E-02	2.244E-03	5.47	0.000	1.082
RES5000_500	5.330E-07	2.452E-07	2.17	0.037	1.482
SQRALT	-3.956E+00	1.523E+00	-2.60	0.014	1.379
RES500	1.878E-05	1.063E-05	1.77	0.086	1.181

(b) Performance

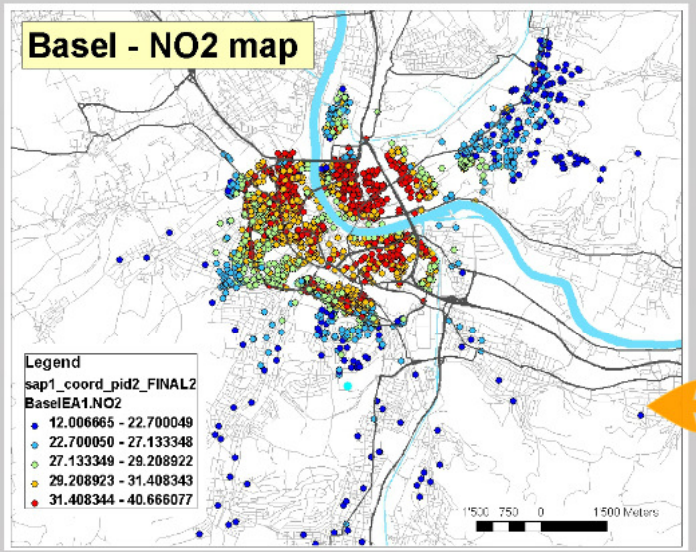
	R2	Adj_R2	RMSE	MaxCooksD
BAS.No2a.	0.67	0.63	4.48	0.16

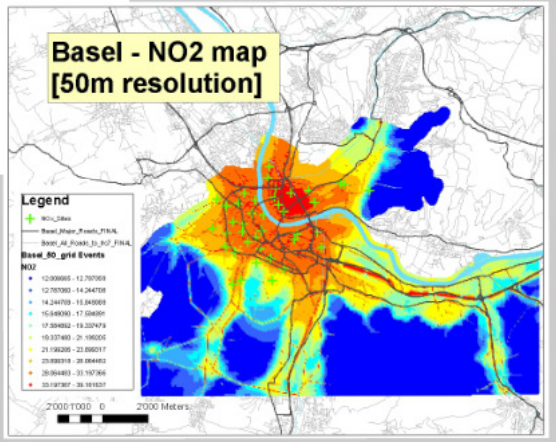
(c) Cross Validation

	CV_R2	CV_Adj_R2	CV_RMSE
BAS.No2a.	0.58	0.57	4.83

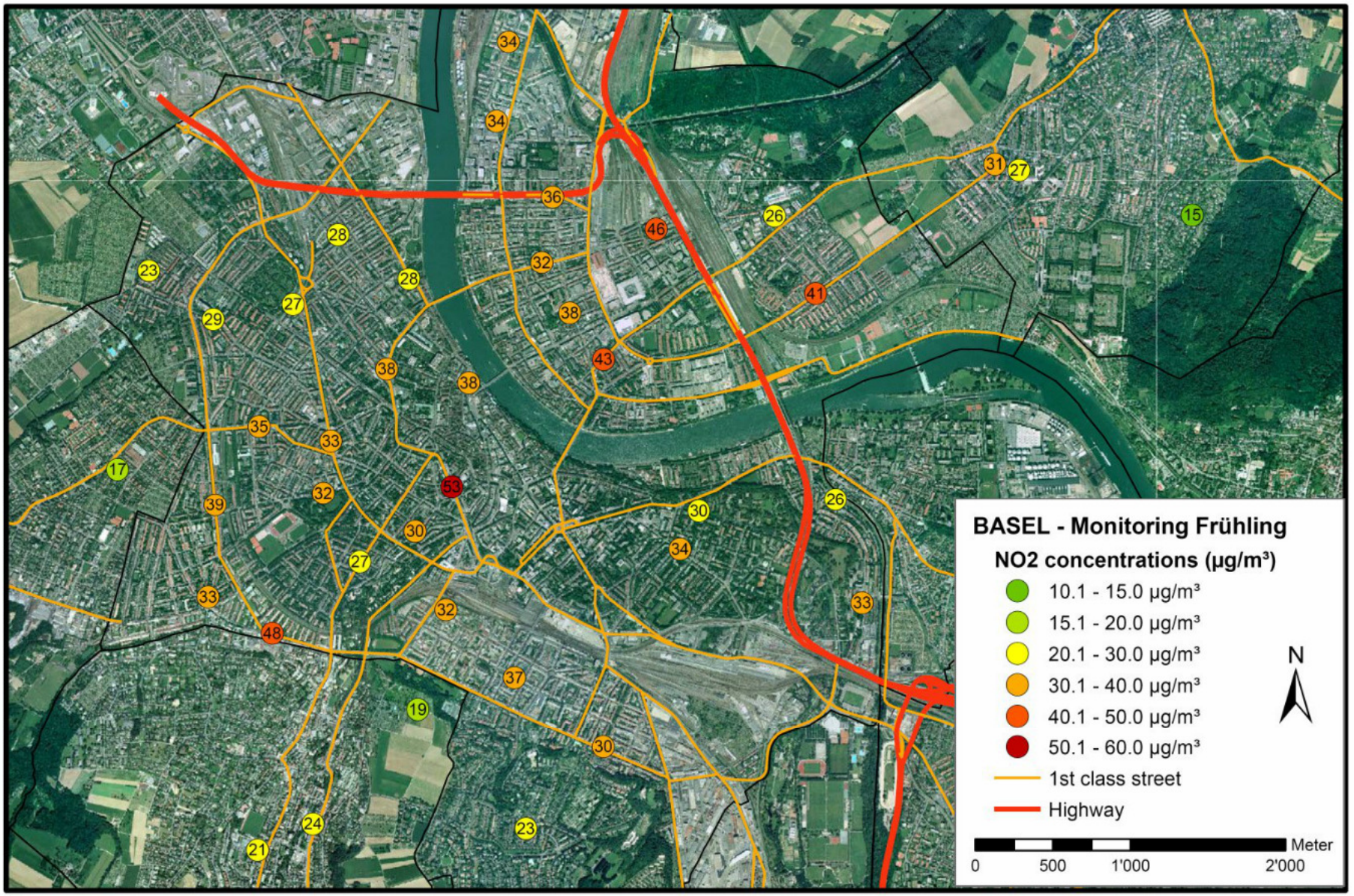
(d) Moran's I

	observed	expected	sd	p.value
Moran's I	-0.05	-0.03	0.03	0.45





Basel 2009 Monitoring @ 40 locations

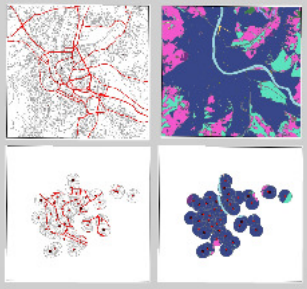


LUR modeling (LAND USE REGRESSION)

$$NO2i = B0 + B1(traffic)i + B2(land\ use)i + B3(pop)i \ldots + Bn(pred\ x)i$$

LUR models use GIS data

- Not based on physical phenomena of dispersion
- Examples of GIS data (roads, landuse):
- Make buffers (eg, 500m):



List of variables used:

NO2 LUR model for Basel

Table 3: Model: BAS.No2a.

(a) The Model

	Estimate	Std. Error	t value	Pr(>|t|)	VIF
(Intercept)	5.435E+01	3.306E+01	1.64	0.109	
INTMAJORINVDIST	1.227E-02	2.244E-03	5.47	0.000	1.082
RES5000_500	5.330E-07	2.452E-07	2.17	0.037	1.482
SQRALT	-3.956E+00	1.523E+00	-2.60	0.014	1.379
RES500	1.878E-05	1.063E-05	1.77	0.086	1.181

(b) Performance

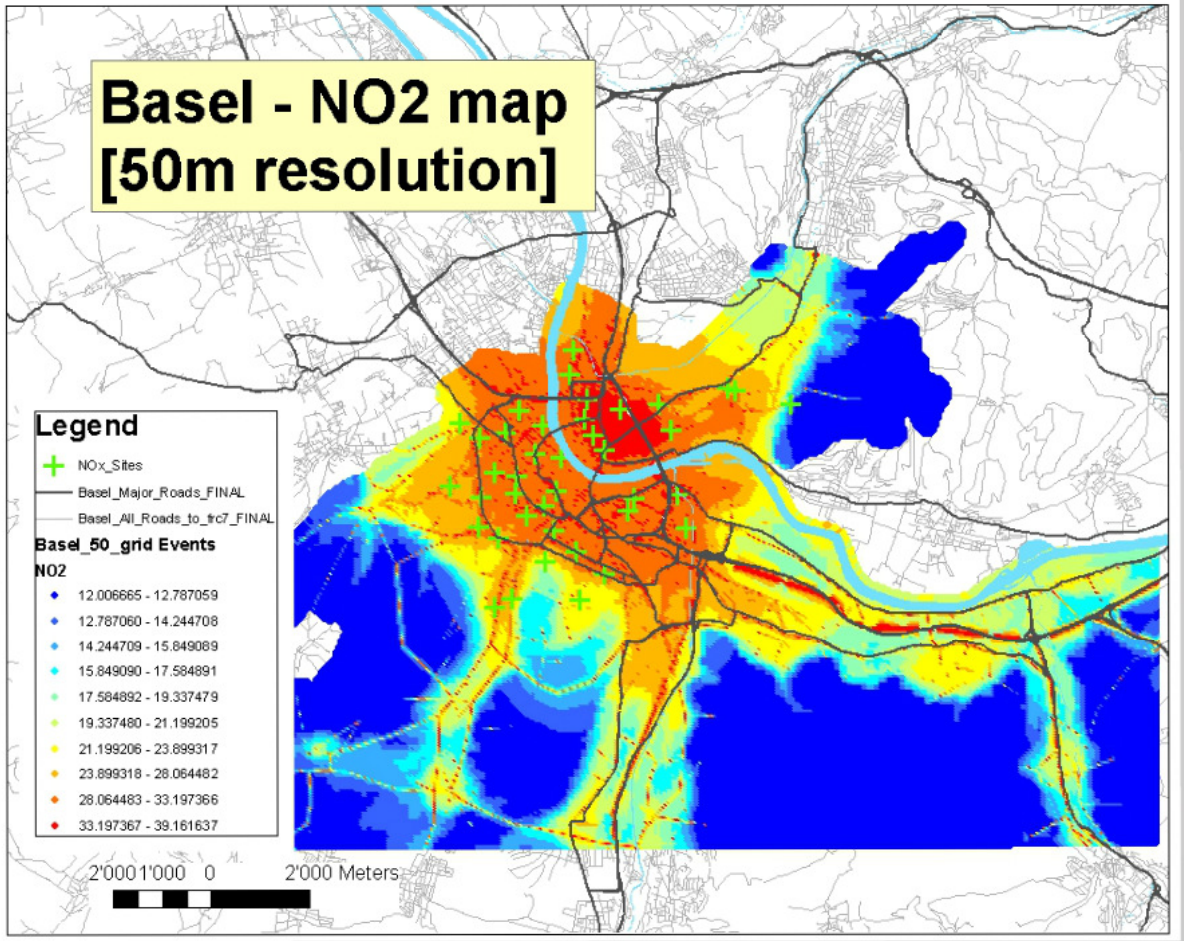
	R2	Adj_R2	RMSE	MaxCooksD
BAS.No2a.	0.67	0.63	4.48	0.16

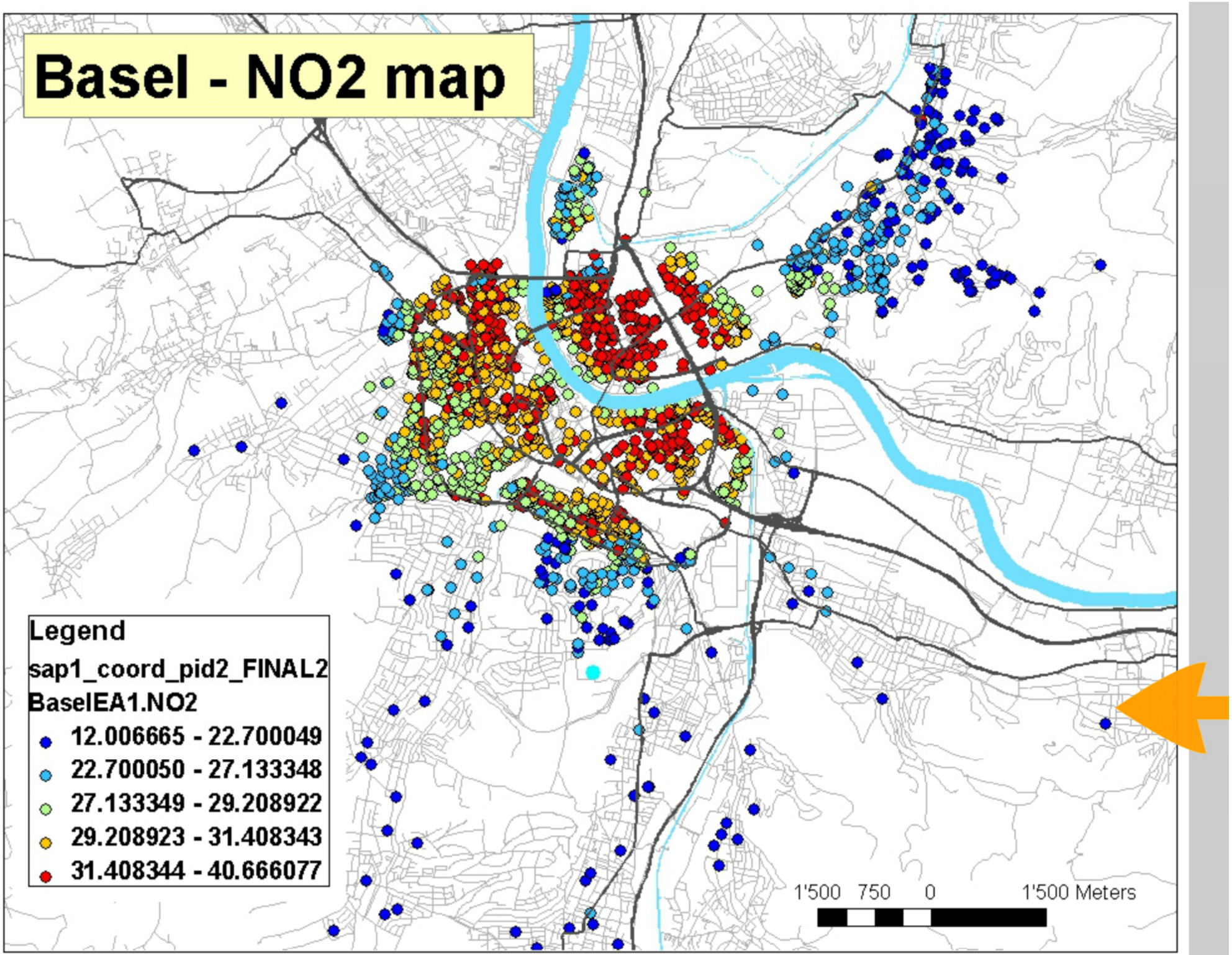
(c) Cross Validation

	CV_R2	CV_Adj_R2	CV_RMSE
BAS.No2a.	0.58	0.57	4.83

(d) Moran's I

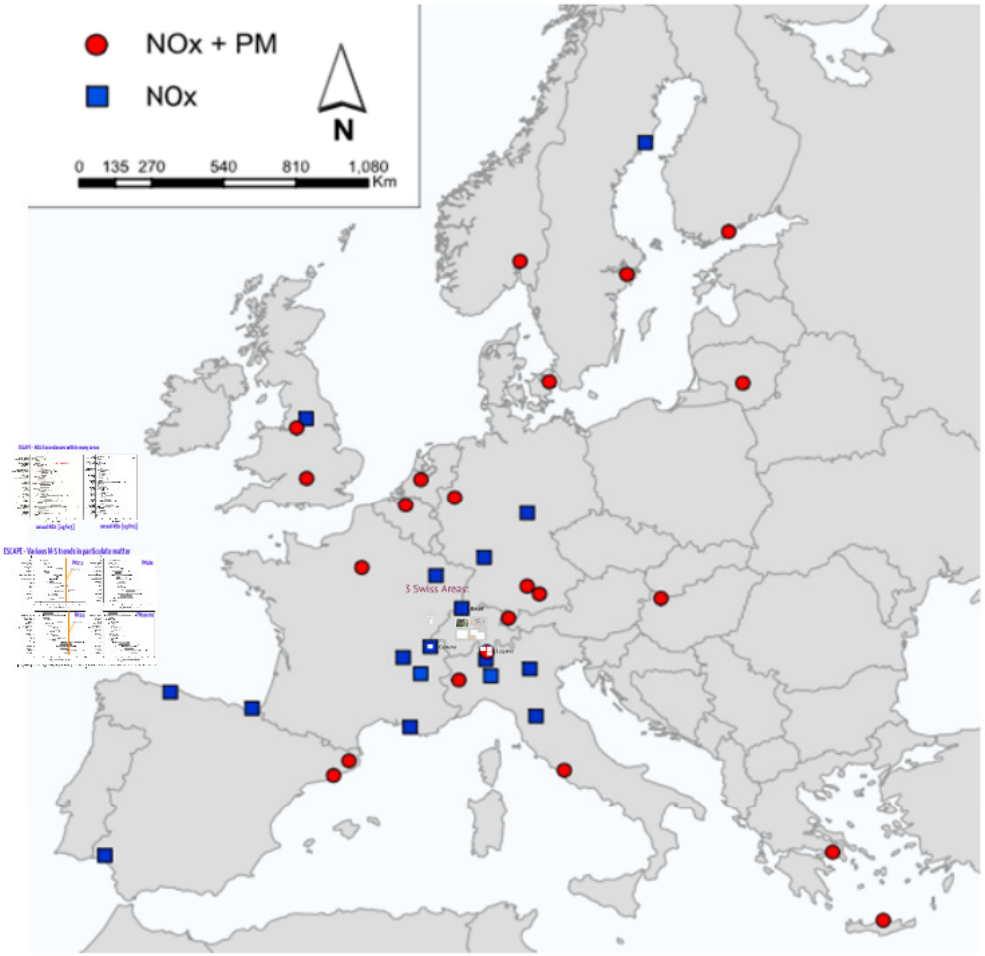
	observed	expected	sd	p.value
Moran's I	-0.05	-0.03	0.03	0.45




Basel - NO2 map
Legend
sap1_coord_pid2_FINAL2
BaselEA1.NO2
12.006665 - 22.700049
22.700050 - 27.133348
27.133349 - 29.208922
29.208923 - 31.408343
31.408344 - 40.666077
1'500 750 0 1'500 Meters

ESCAPE - 30 cohorts!

European study of cohorts for air pollution effects - a current paradigm



A premier air pollution study!

- large scale (37 areas in EU)
- 30 cohorts
- harmonized measurements & LUR modeling
- sampling in 3 seasons (2009/2010); 2-week avgs
- decent spatial resolution
  - 40 sites for NO2x
  - 20 sites for PMx

Limitations

- no temporal resolution (no real-time data)
- no vertical gradient
- no indoor sampling
- focus on traffic sources
- long time between measurements & exposure assessment (~2 yrs)
- significant exposure misclassification

BUT, very large impact on public health!

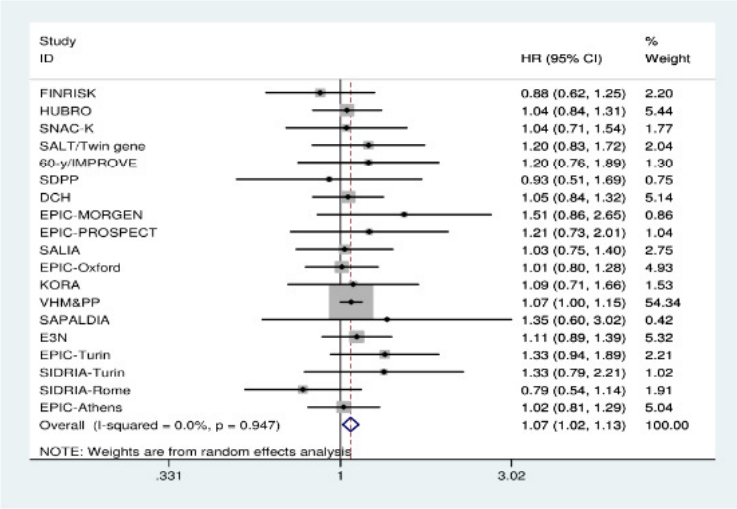
Swiss TPH

ESCAPE reveals significant EU level health effects

SEVENTH FRAMEWORK PROGRAMME

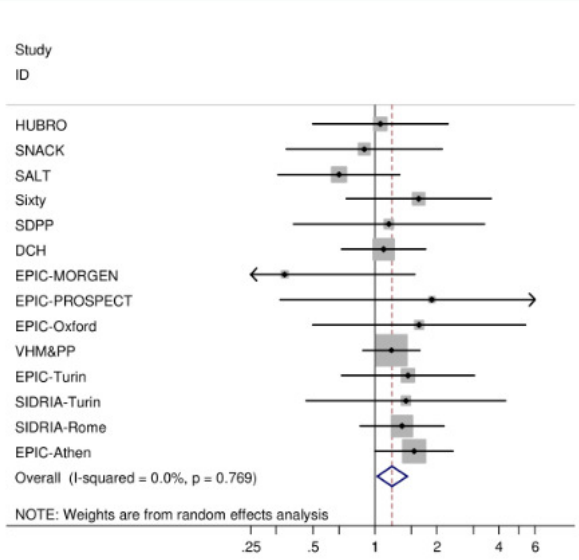
ESCAPE - Natural cause mortality from PM2.5

Figure 6.2 Cohort-specific and meta-analysis results (HRs and 95%-CIs) of association between natural cause mortality and $PM_{2.5}$ (per 5 µg/m^3)



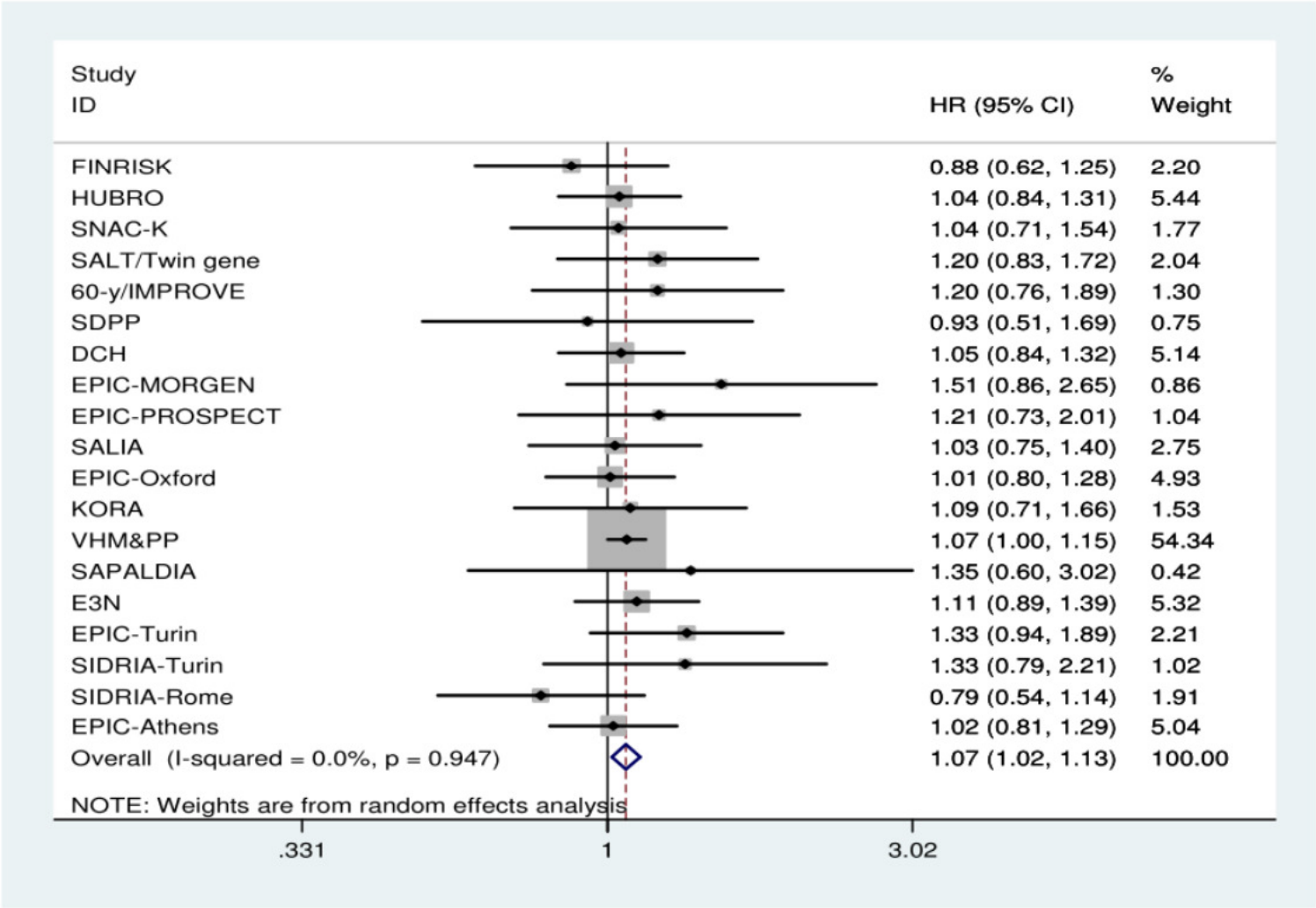
ESCAPE - Lung Cancer and PM10

Figure 6.1 Cohort-specific associations between PM_{10} and risk for lung cancer (Forest Plot)



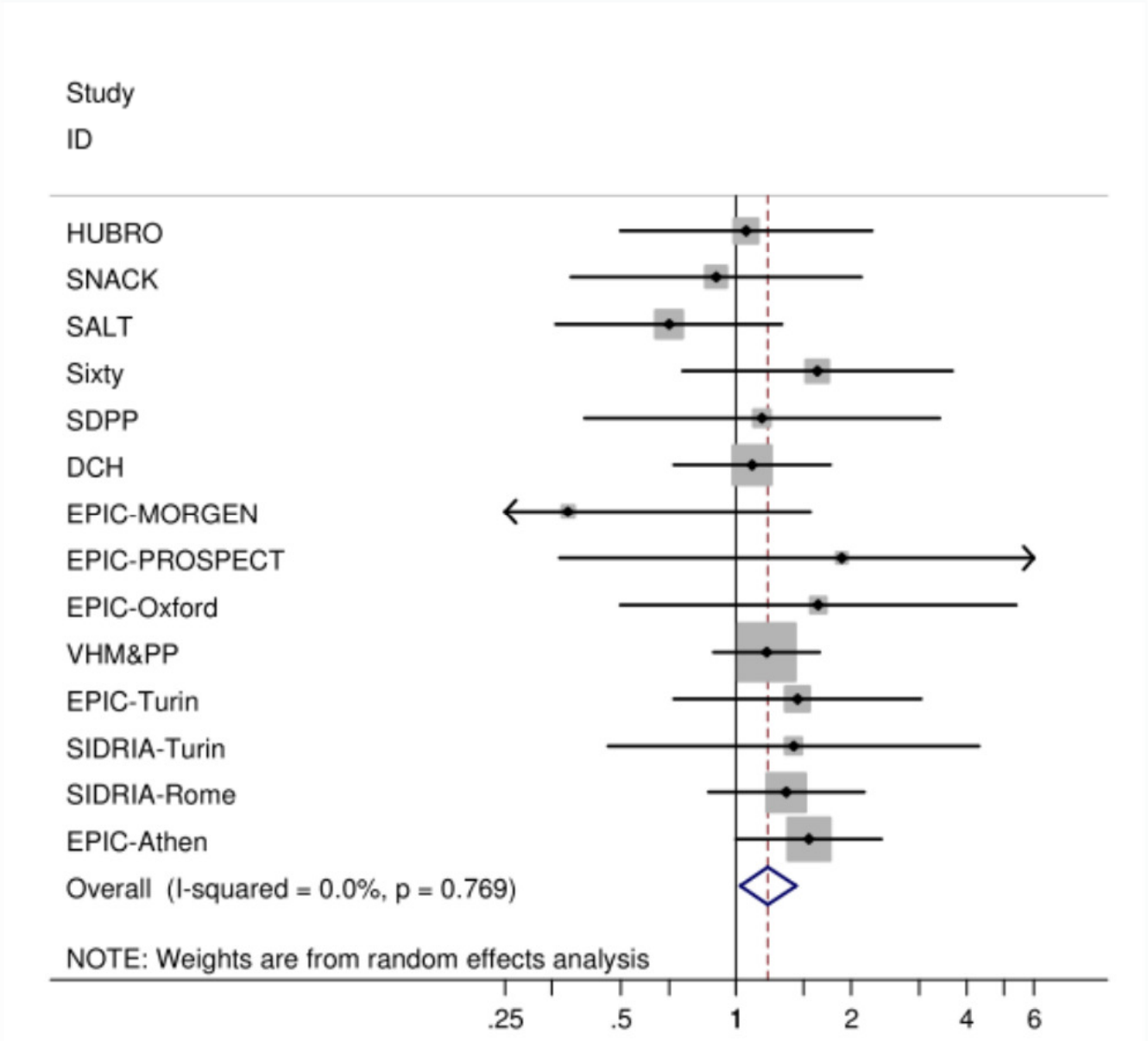
ESCAPE - Natural cause mortality from PM2.5

Figure 6.2 Cohort-specific and meta-analysis results (HRs and 95%-CIs) of association between natural cause mortality and $PM_{2.5}$ (per 5 µg/m^3)



ESCAPE - Lung Cancer and PM10

Figure 6.1 Cohort-specific associations between PM_{10} and risk for lung cancer (Forest Plot)

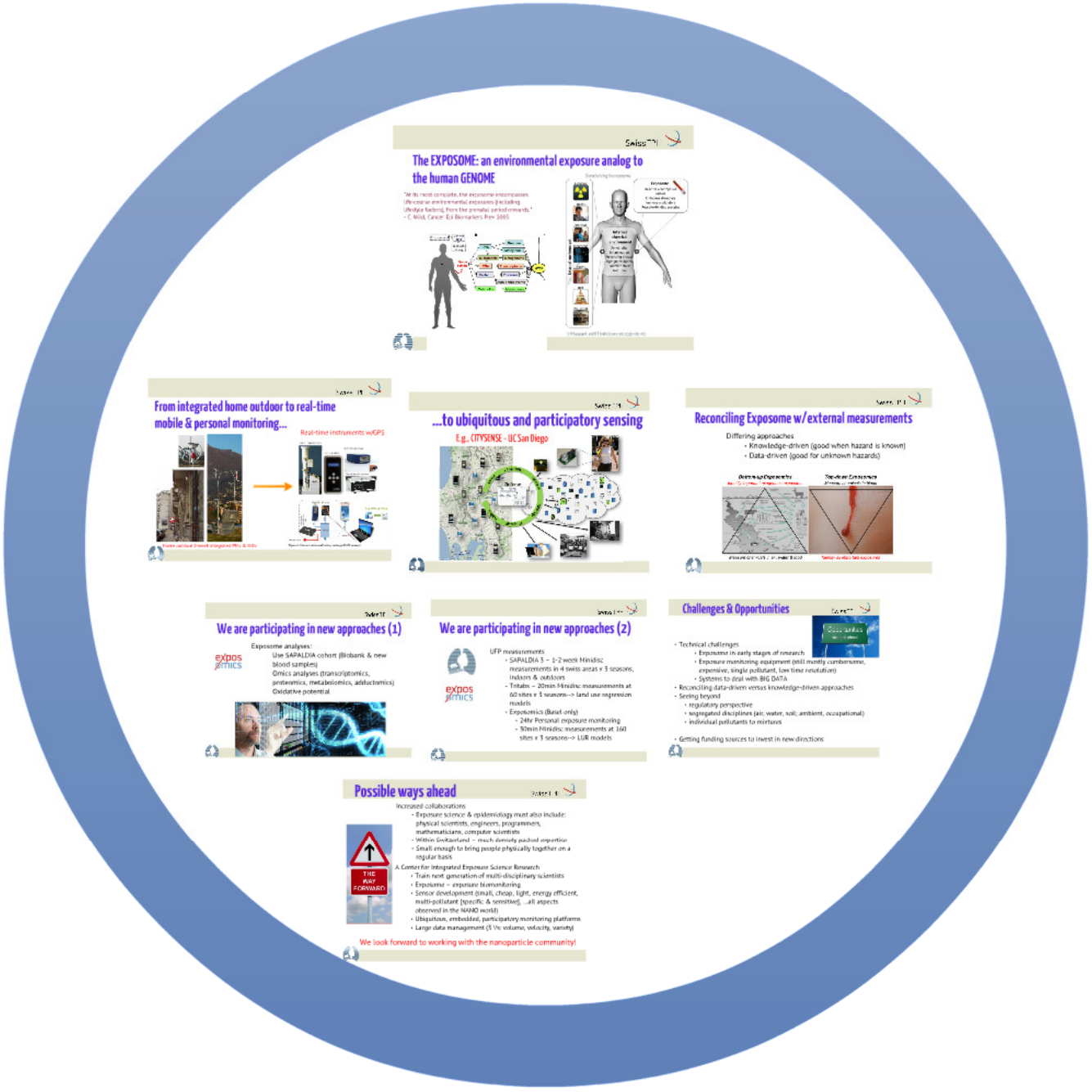


All's well and good, BUT 80% of chronic diseases unaccounted for!

(from Rappaport, JESEE 2011)

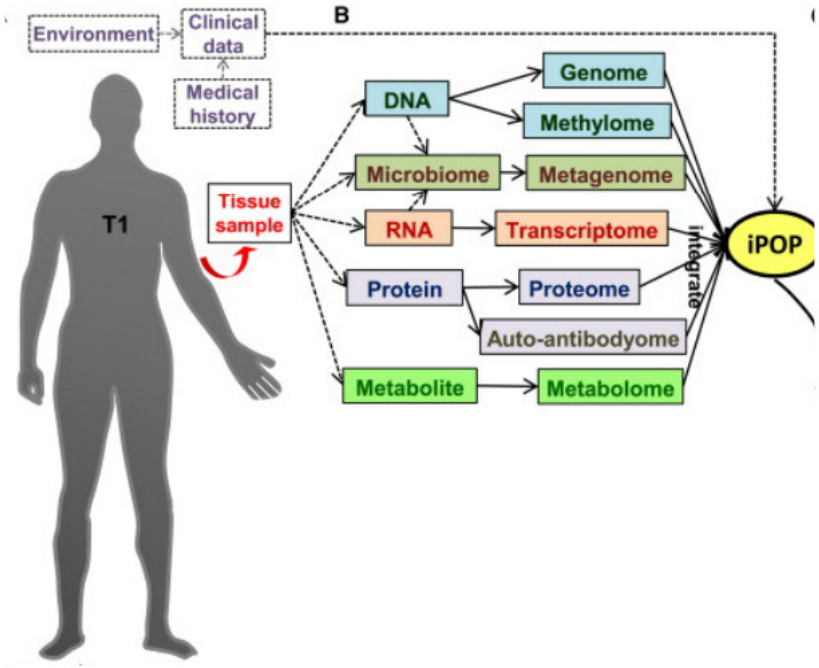
- Cancer risk attributable to genetics: 10% (Lichtenstein et al., 2000; twin studies)
- Heritability of degenerative diseases: also 10% (Manolio et al., 2009; Hindorff et al., 2010; genome-wide association studies)
- So 90% of chronic diseases are “environmental”
- BUT, only 7-10% human diseases attributable to traditional environmental pollutants (air, water, lead, sanitation, hygiene, occupational exposures)
- If exposure science is to contribute to preventing chronic diseases, it must move beyond traditional approaches & regulatory pollutants

Current Transformations

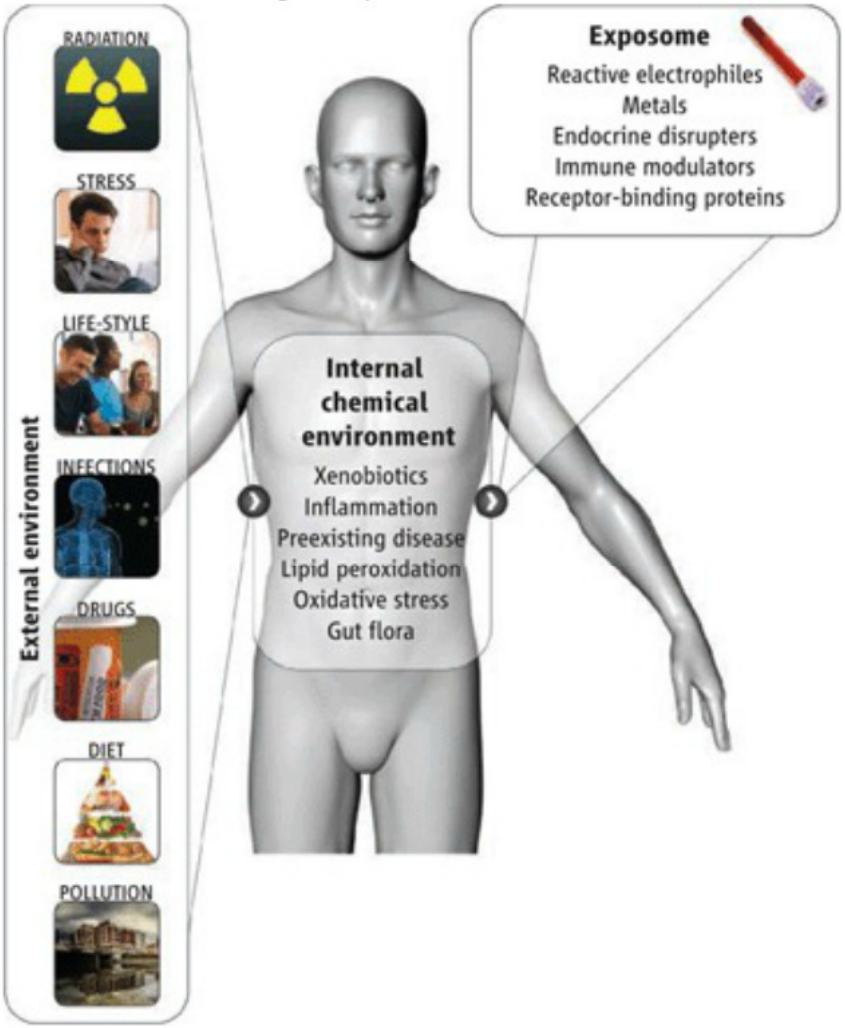


The EXPOSOME: an environmental exposure analog to the human GENOME

"At its most complete, the exposome encompasses life-course environmental exposures (including lifestyle factors), from the prenatal period onwards."
- C. Wild, Cancer Epi Biomarkers Prev 2005

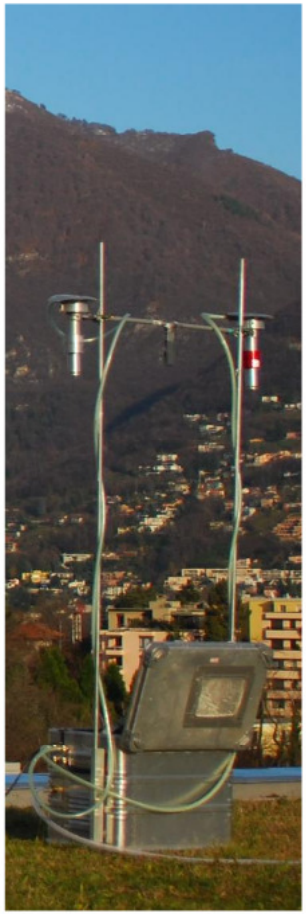


Characterizing the exposome.



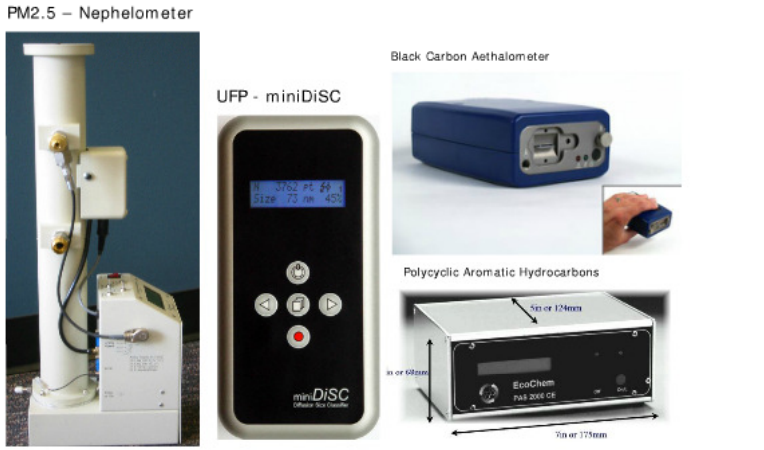
S M Rappaport, and M T Smith Science 2010;330:460-461

From integrated home outdoor to real-time mobile & personal monitoring…



Home outdoor 2-week integrated PMx & NOx

Real-time instruments w/GPS



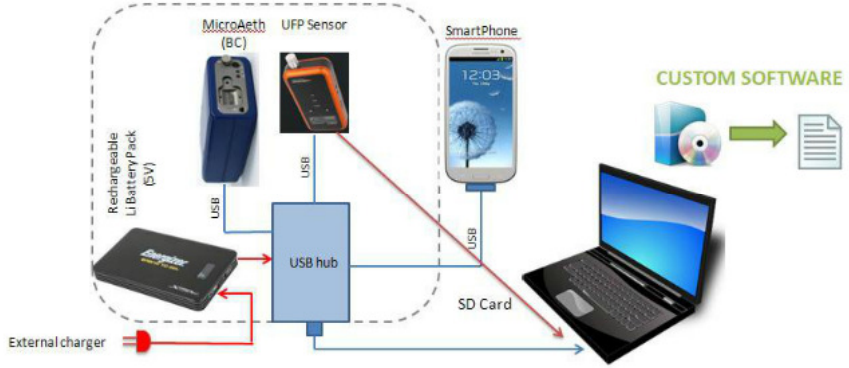
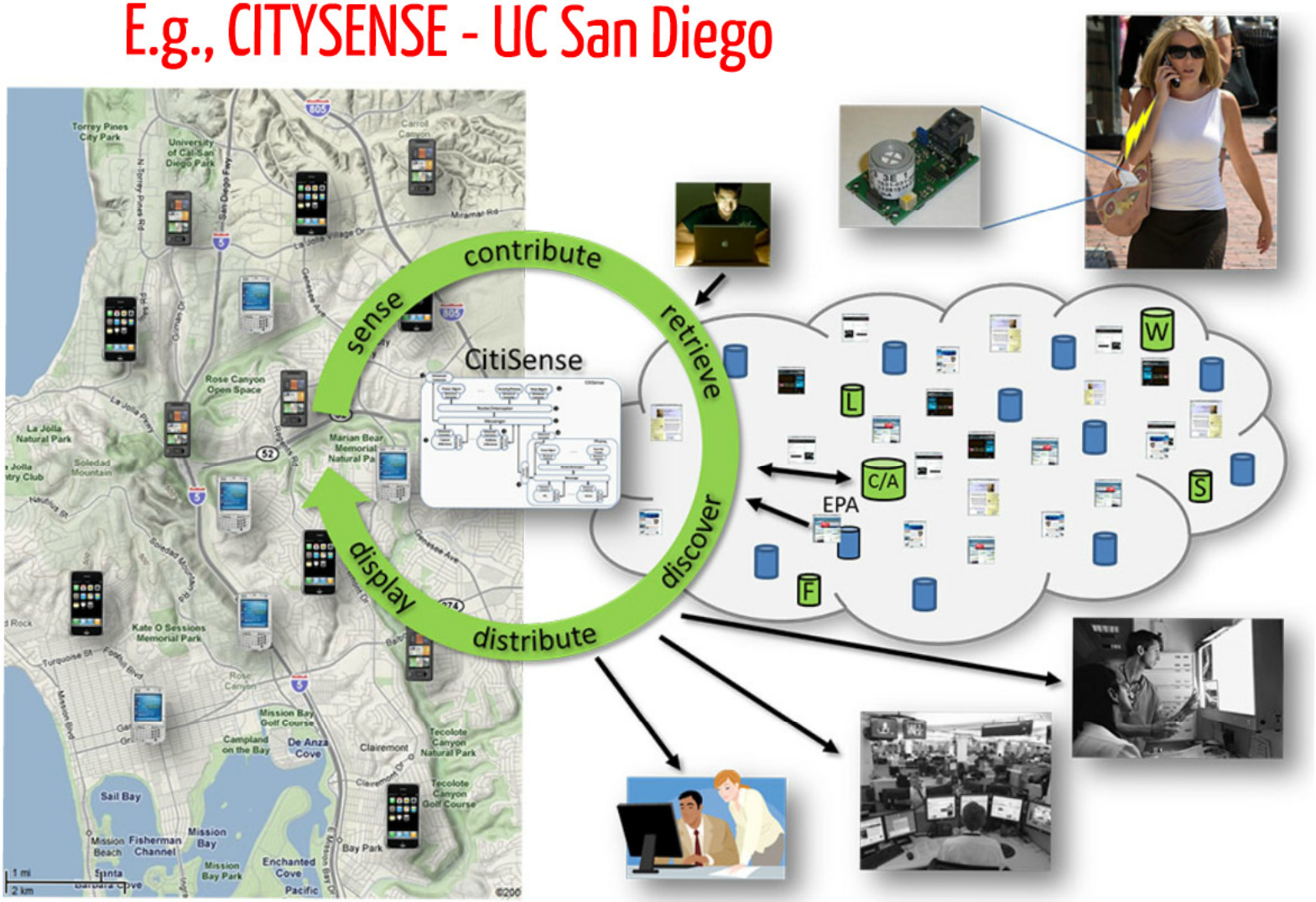


Figure 4 - Data extraction and battery recharge (KOM concept)

Swiss TPH

...to ubiquitous and participatory sensing

E.g., CITYSENSE - UC San Diego



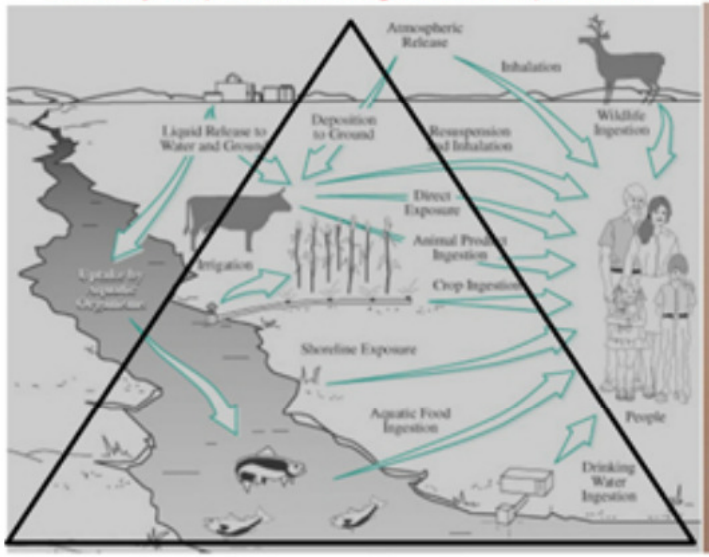
Reconciling Exposome w/external measurements

Differing approaches

- Knowledge-driven (good when hazard is known)
- Data-driven (good for unknown hazards)

Bottom-up Exposomics

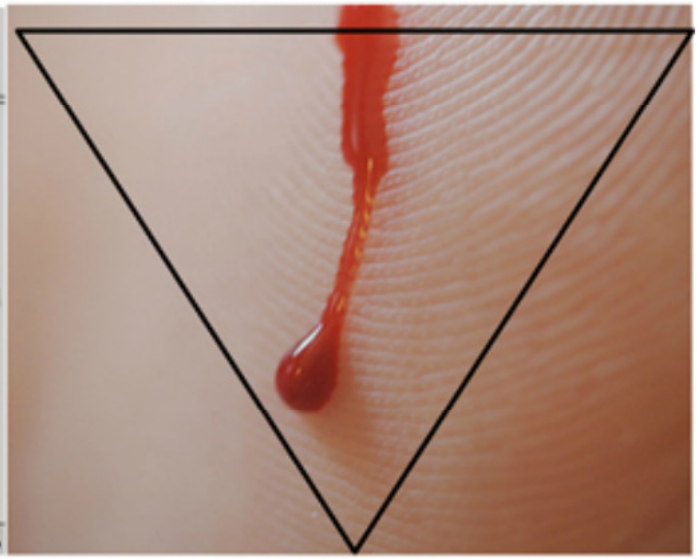
Identify important exogenous exposures



Measure chemicals in air, water & food

Top-down Exposomics

Measure chemicals in blood



Identify all important exposures

We are participating in new approaches (1)

Exposome analyses:

- Use SAPALDIA cohort (Biobank & new blood samples)
- Omics analyses (transcriptomics, proteomics, metabolomics, adductomics)
- Oxidative potential

We are participating in new approaches (2)

UFP measurements

- SAPALDIA 3 – 1-2 week Minidisc measurements in 4 swiss areas x 3 seasons, indoors & outdoors
- Tritabs – 20min Minidisc measurements at 60 sites x 3 seasons--> land use regression models
- Exposomics (Basel only)
  - 24hr Personal exposure monitoring
  - 30min Minidisc measurements at 160 sites x 3 seasons--> LUR models

Challenges & Opportunities

Swiss TPH

- Technical challenges
    - Exposome in early stages of research
    - Exposure monitoring equipment (still mostly cumbersome, expensive, single pollutant, low time resolution)
    - Systems to deal with BIG DATA
- Reconciling data-driven versus knowledge-driven approaches
- Seeing beyond
    - regulatory perspective
    - segregated disciplines (air, water, soil; ambient, occupational)
    - individual pollutants to mixtures

- Getting funding sources to invest in new directions

Possible ways ahead

Swiss TPH

Increased collaborations

- Exposure science & epidemiology must also include: physical scientists, engineers, programmers, mathematicians, computer scientists
- Within Switzerland – much densely packed expertise
- Small enough to bring people physically together on a regular basis

A Center for Integrated Exposure Science Research

- Train next generation of multi-disciplinary scientists
- Exposome – exposure biomonitoring
- Sensor development (small, cheap, light, energy efficient, multi-pollutant [specific & sensitive], …all aspects observed in the NANO world)
- Ubiquitous, embedded, participatory monitoring platforms
- Large data management (3 Vs: volume, velocity, variety)

We look forward to working with the nanoparticle community!

Acknowledgments

SwissTPH — H. Phuleria, A. Ineichen, R. Ducret-Stich, M. Ragettli, M. Eeftens, M. Ritter, N. Kuenzli, ...

SAPALDIA Team — N. Probst-Hensch, T. Rochat, ...

ESCAPE Consortium — B. Brunekreef, G. Hoek, R. Beelen, ...

EXPOsOMICS Consortium — P. Vineis, J. Gulliver, M. Nieuwenhuijsen, ...

BAFU – Swiss Federal Office of the Environment

EMPA - Nabel monitoring network

Cantonal air monitoring agencies

University of Basel - MCR

University of Washington, DEOHS, Seattle, WA

FHNW Schweiz – University of Applied Sciences

Thank you for your attention!