Short and Long Term Effects of Nitrogen Dioxide on Mortality and Respiratory Health, with Emphasis on Results from the APHEA and the SAPALDIA Study

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Contents

1. Presentation and Discussion of results from the APHEA-2 study on **short term effects** of NO_2 on mortality.

2. Presentation and Discussion of results from the SAPALDIA-study on associations between lung function and average levels of exposure to NO_2 (**long term perspective**).

3. Concluding remarks on existing evidence regarding health effects of NO_2.

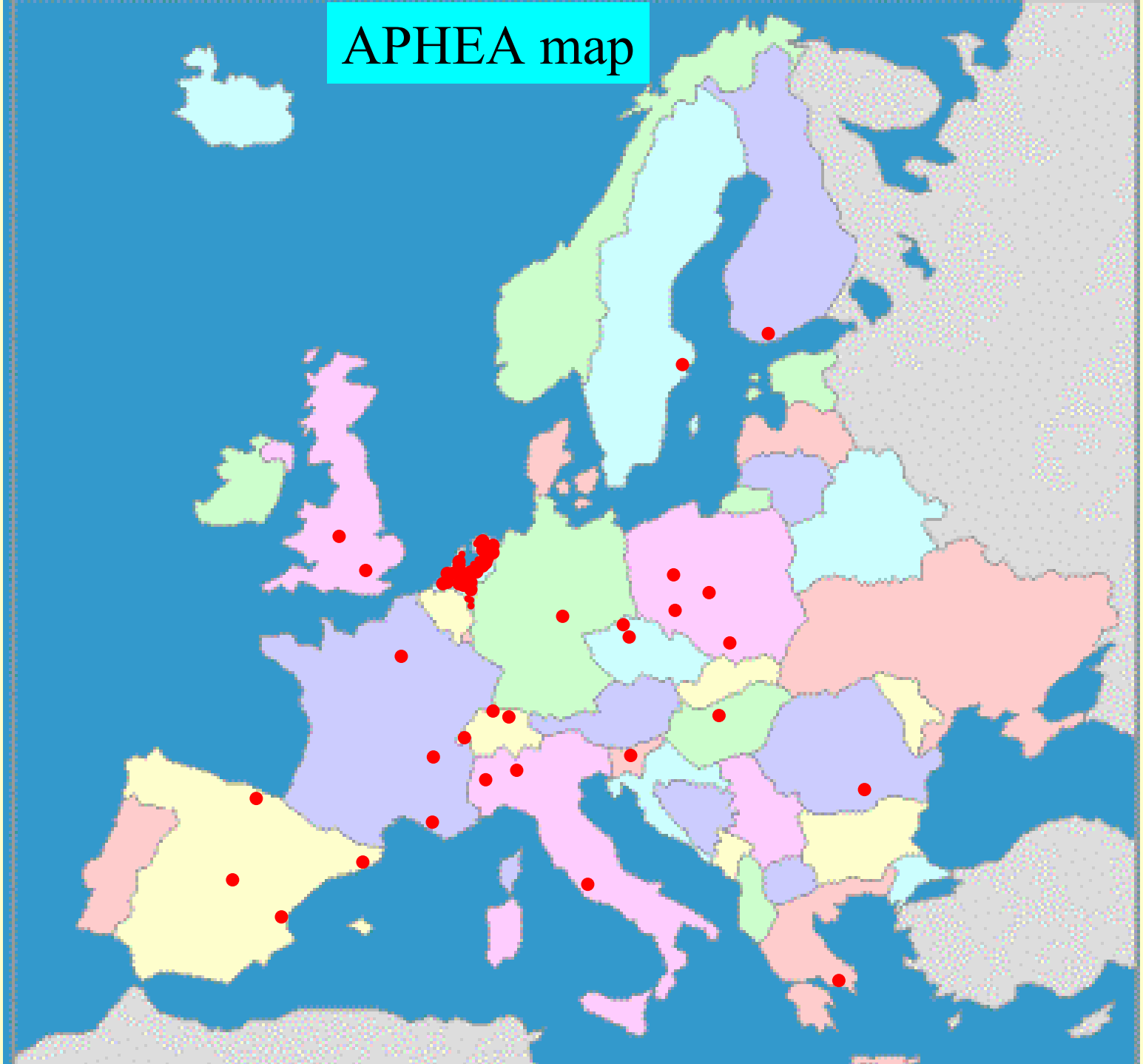
Short-term effects of nitrogen dioxide on mortality:

an analysis within the APHEA project

E. Samoli, E. Aga, G. Touloumi, K. Nisiotis,
B. Forsberg, A. Lefranc, J. Pekkanen, B. Wojtyniak,
C. Schindler, E. Niciu, R. Brunstein,
M. Dodič Fikfak, J. Schwartz, **K. Katsouyanni**

Eur Respir J 2006; 27: 1129-1137

APHEA = Air Pollution and Health: a European Approach


APHEA map

Total population size (across all 30 cities)

60 Mio

Total number of cases of death (1990 - 1997)

2.893 Mio

Average number of deaths per day

1440

Dependent variables

Daily counts of deaths

a) from internal causes

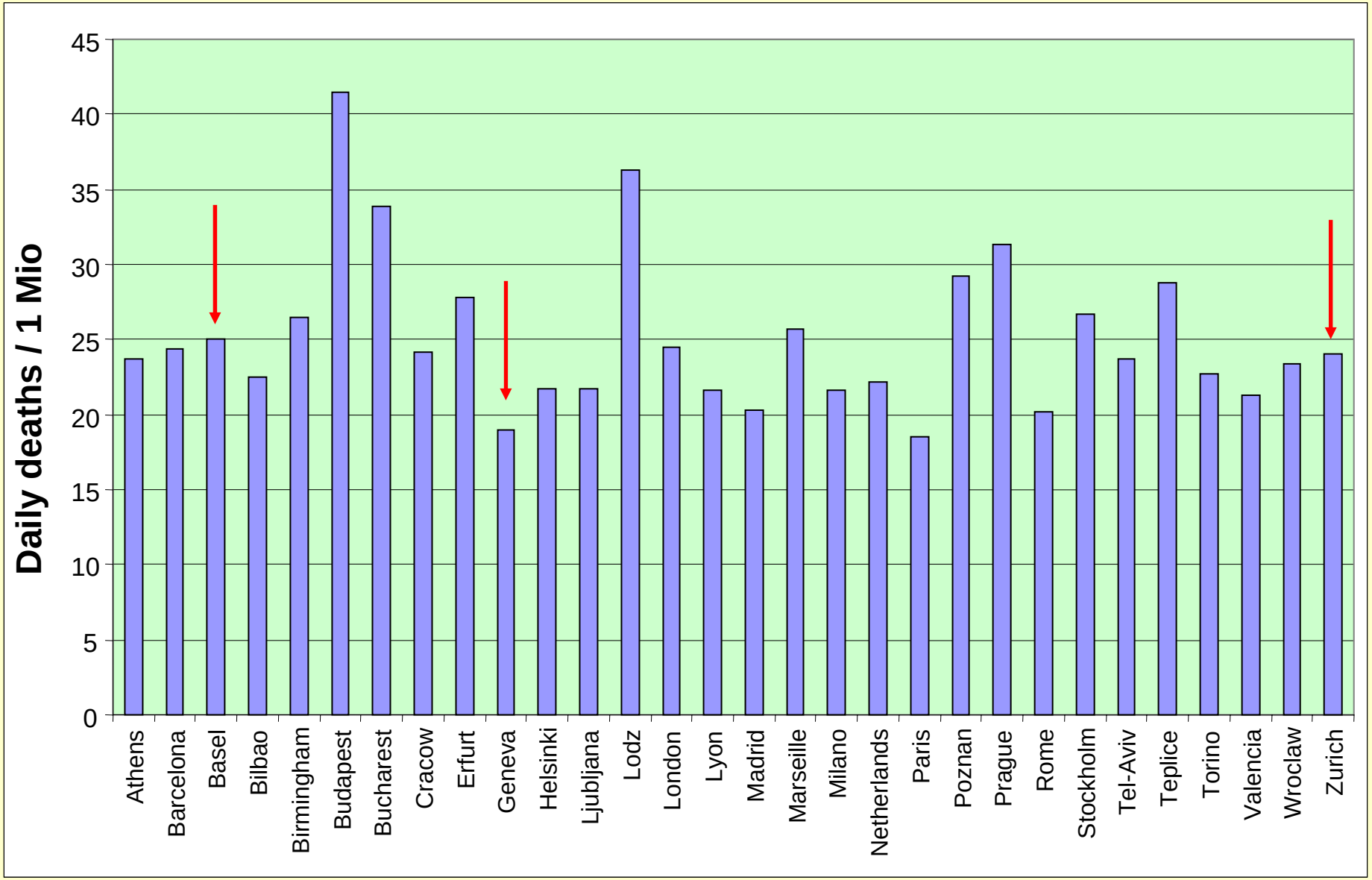
b) from cardiovascular causes

c) from respiratory causes

across cities

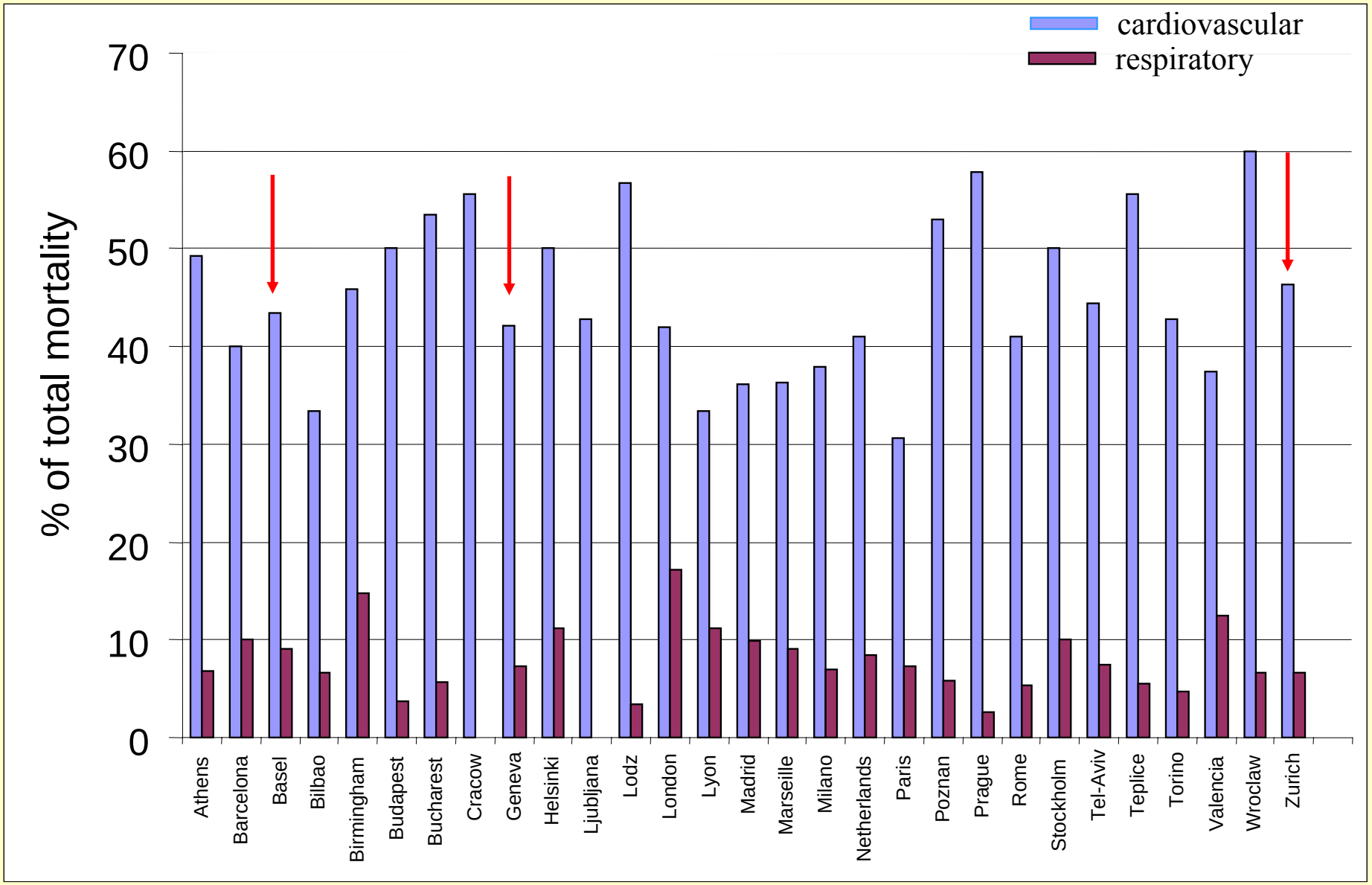
Daily mortality

APHEA



Cardiovascular and respiratory mortality

APHEA



Air pollutant variables

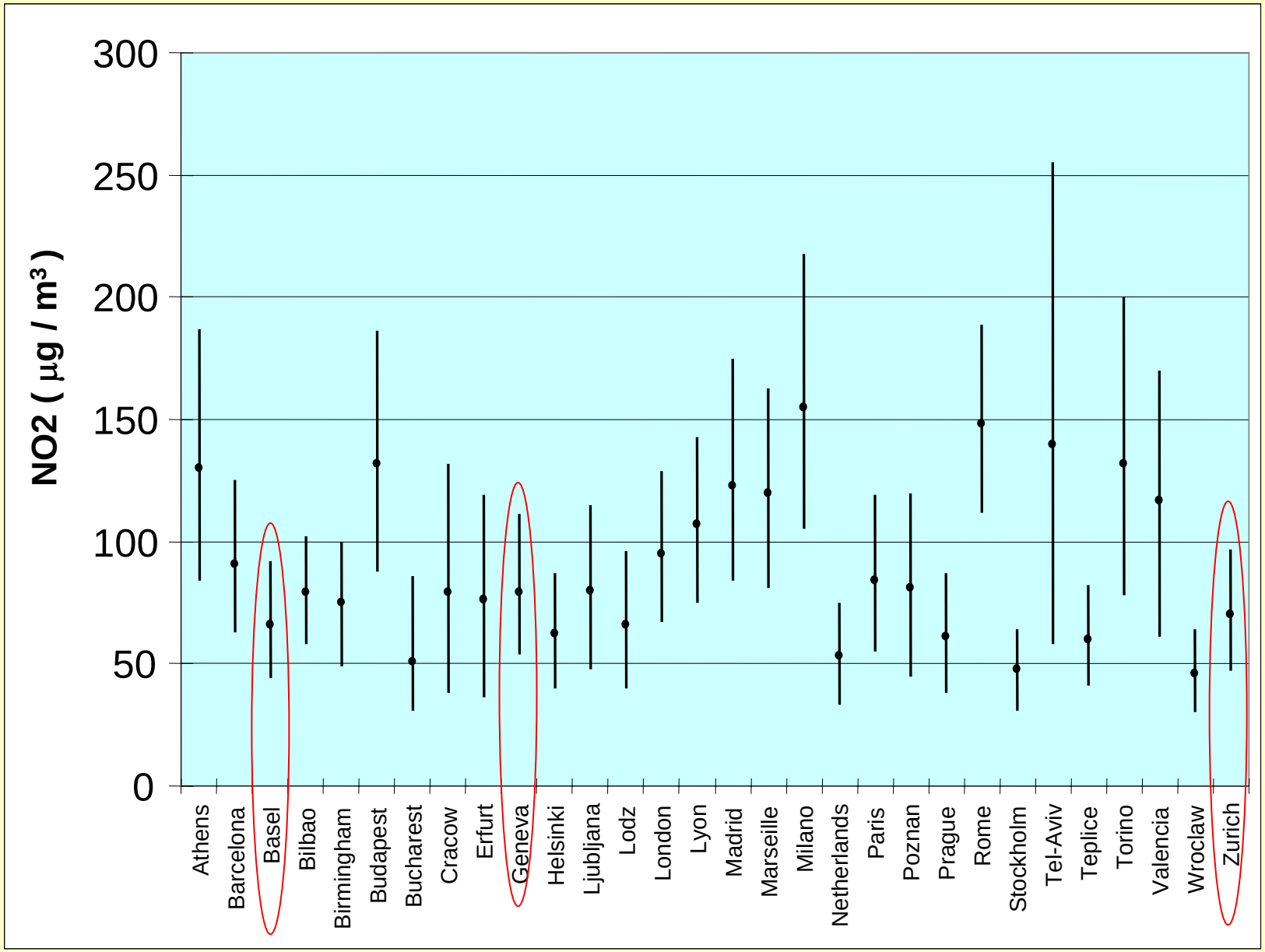
Two-day-means* of

a) 1-hr-maximum of NO_2
b) 24-hr-mean of PM10
c) 24-hr-mean of SO_2
d) 24-hr-mean of black smoke
e) 8-hr-maximum of O_3

* Day of event and preceding day

Mean and range of daily NO_2-values#

APHEA



#mean of 1-hr-maxima of two days

Statistical Analysis

Two stage approach:

1. City specific analyses (Poisson regression models)

2. Meta analysis of city-specific results
   (with and without adjustment for heterogeneity)

City-specific analysis

APHEA

Poisson regression model for daily death counts

including

1. Function of calendar time capturing ***time trends and seasonal variation of mortality.***

2. Indicator variables for the ***days of the week*** capturing weekly cycles of mortality

3. Functions of ***temperature and relative humidity*** of the day and of the two preceding days.

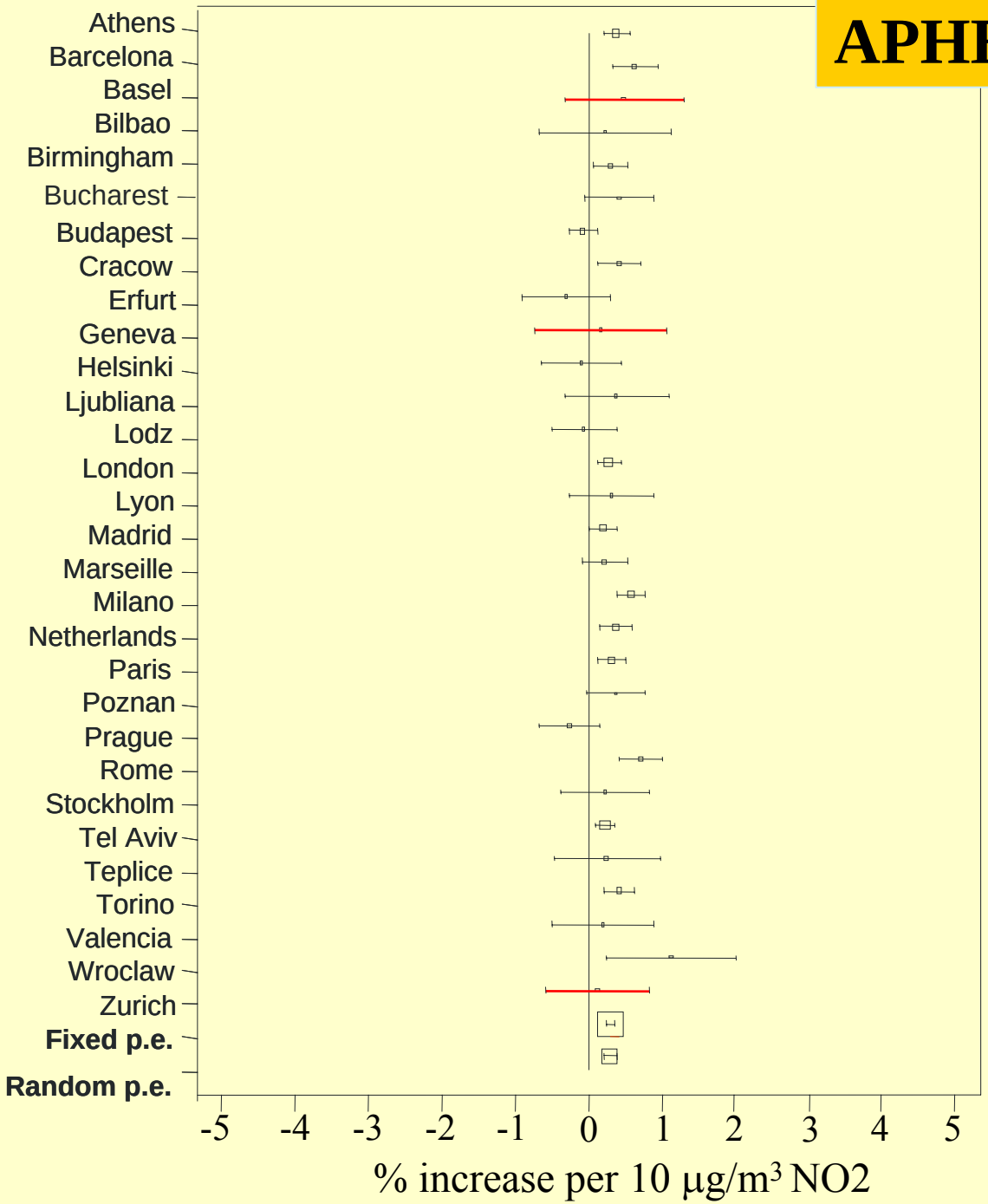
4. Indicator variables for ***periods of influenza epidemics and holidays.***

5. ***Air pollutant level(s)*** (2-day-mean).

6. Autoregressive terms (if necessary)

Total mortality city-specific results

APHEA



Summary estimates of NO_2-effects

Estimated increases (+ 95% confidence intervals) in daily mortality **per 10 μg/m³ increment in NO_2[#].**		
All „natural“ deaths	Cardiovascular deaths	Respiratory deaths
0.30%* (0.22, 0.38)	**0.40%*** (0.29,0.52)	**0.38%*** (0.17, 0.58)

* $p < 0.001$

[#]mean of 1-hr-maxima of two days

Summary estimates of NO_2-effects from two-pollutant models

APHEA

	Estimated increases in daily mortality **per 10 μg/m³ increment in NO_2#.**		
simultaneous control for:	All „natural“ deaths	Cardiovascular deaths	Respiratory deaths
none	**0.30%** (0.22,0.38)	**0.40%** (0.29,0.52)	**0.38%** (0.17,0.58)
Black smoke	**0.33%** (0.23,0.42)	**0.44%** (0.31,0.58)	**0.26%** (-0.12,0.65)
PM10	**0.27%** (0.16,0.38)	**0.35%** (0.21,0.50)	**0.37%** (0.08,0.67)
SO2	**0.26%** (0.18,0.34)	**0.33%** (0.20,0.47)	**0.19%** (-0.07,0.45)
O3 – 8hr max	**0.33%** (0.22,0.43)	**0.42%** (0.27,0.58)	**0.38%** **(0.13,0.63)**

How can systematic differences in results be explained?

Effect estimates for NO_2 were ***higher*** in cities with

lower smoking rates -> Total and CV-mortality

higher proportions of elderly people -> Resp. Mortality

higher average levels of PM10 -> Resp. Mortality

Effect estimates for NO_2 were ***lower*** in cities from

Eastern Europe -> Total and CV-mortality

Summary

In most of the 30 cities, daily mortality was found to be positively associated with concurrent levels of NO_2. The average association was highly significant.

Associations were slightly higher for cause-specific mortality (respiratory and cardiovascular mortality).

Associations between mortality and NO_2 persisted when controlling for PM10 and O_3, but for respiratory mortality they got weaker when effects from black smoke or SO_2 were adjusted for.

Part of the heterogeneity of associations across cities was explained by geographic differences (lower associations in Eastern cities), differences in age structure, smoking prevalences or PM10-levels.

The long term perspective

Associations between Lung Function and Estimated Average Exposure to NO_2 in Eight Areas of Switzerland

C. Schindler, U. Ackermann-Liebrich, Ph. Leuenberger, C. Monn, R. Rapp, G. Bolognini, J-P. Bongard, O. Brändli, G. Domenighetti, W. Karrer, R. Keller, T.G. Medici, A.P. Perruchoud, M.H. Schöni, J-M. Tschopp, B. Villiger, J-P. Zellweger, and the SAPALDIA-Team

Epidemiology 1998; 9:405-411

SAPALDIA = Swiss Study on Air Pollution and Lung Diseases in Adults

SAPALDIA: Areas

SAPALDIA

Study population

7656 subjects between 18 and 60 years having lived in the respective SAPALDIA area for at least 3 years.

Baseline health assessment: 1991

Dependent variables of present analysis

FVC = forced vital capacity of the lung
FEV1 = forced expiratory volume in 1 second

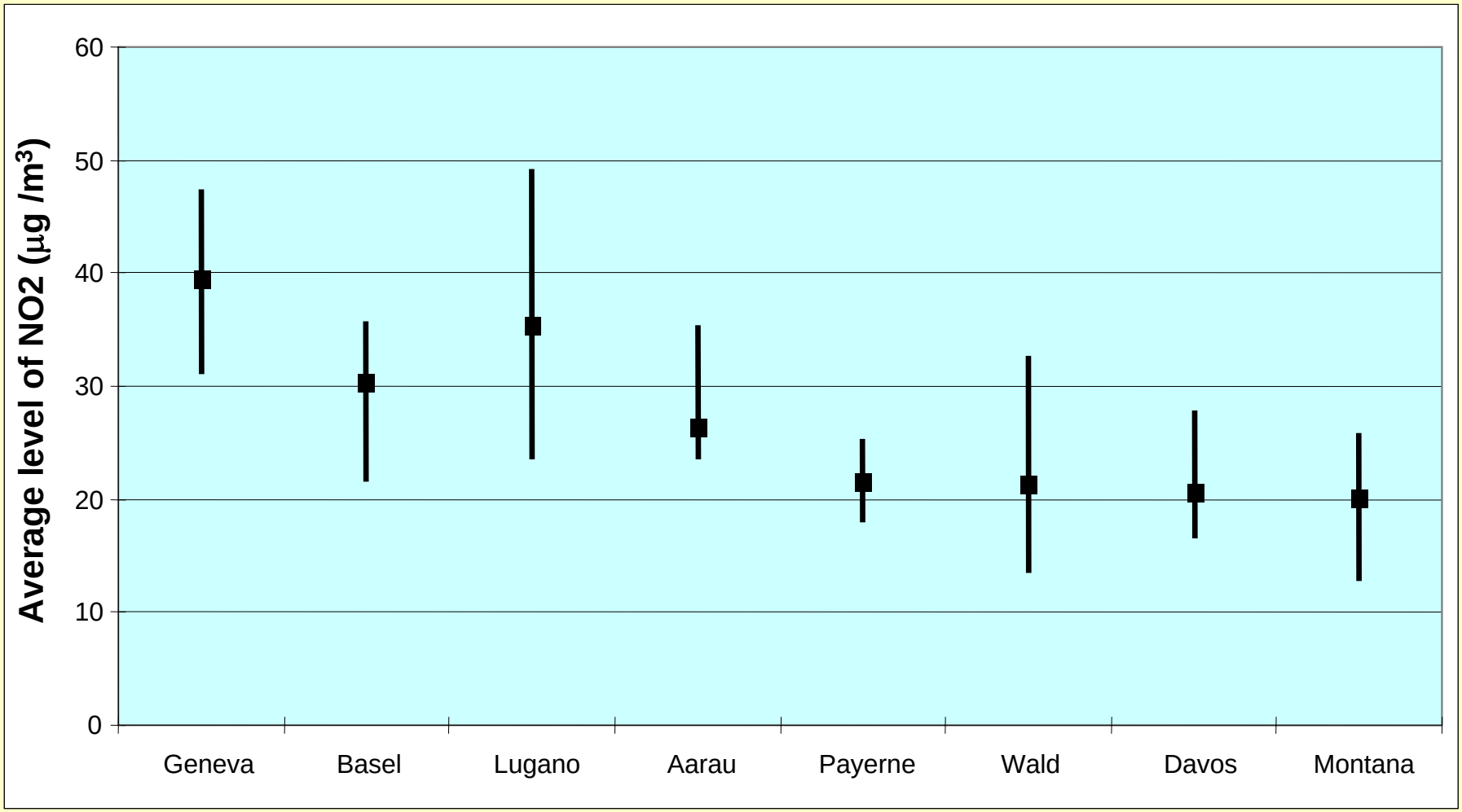
Exposure variables of present analysis

Estimated average level of personal / home outdoor exposure to NO_2 in the subject‘s residential area (based on passive sampler measurements by 560 subjects in 1993 during SAPALDIA diary study).

Covariates: sex, age, height, weight, study area, smoking history (active / passive), family history of asthma and allergy, early respiratory infection, atopy, level of education, nationality, occupational exposure to air-borne irritants, gas cooking.

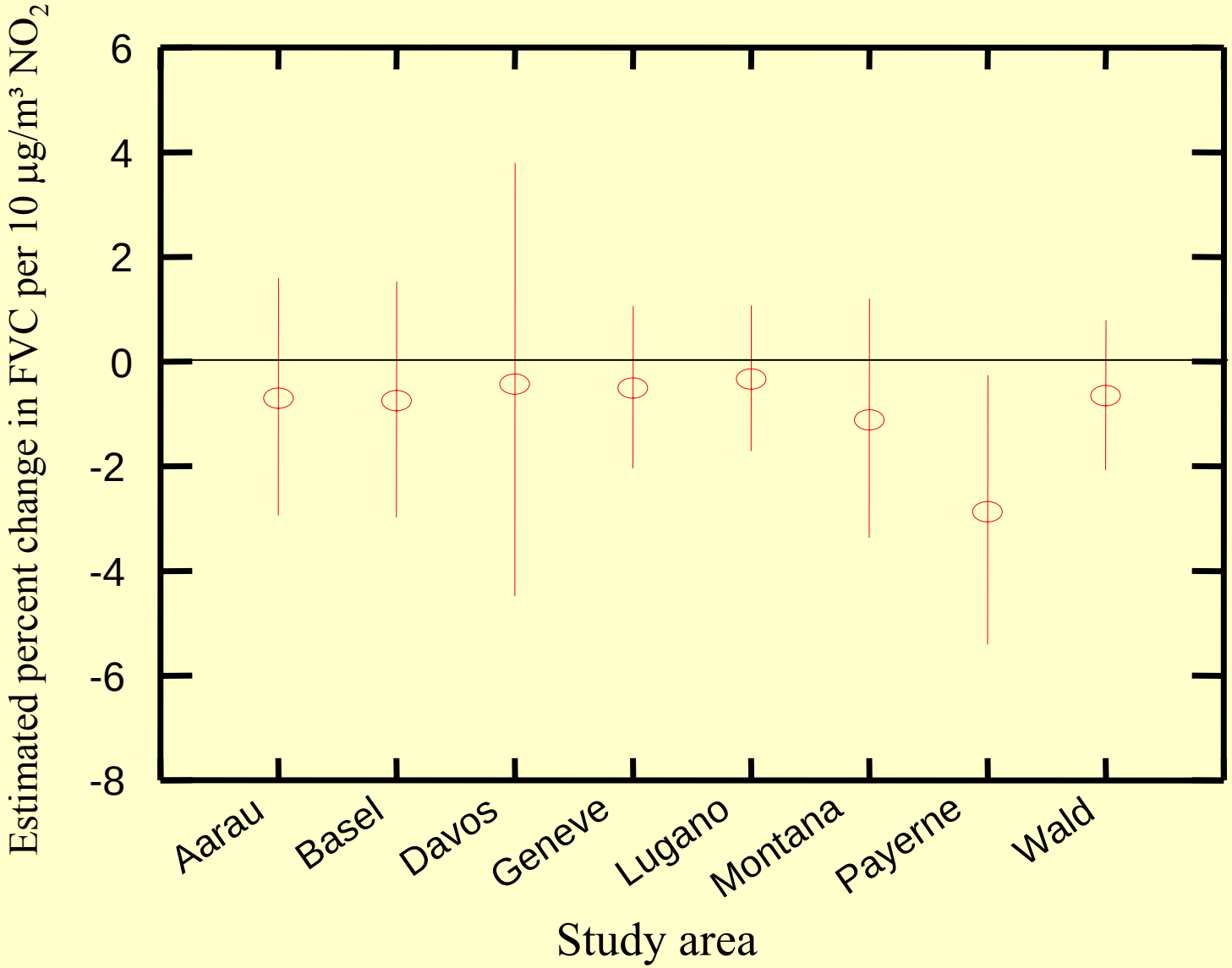
Area-specific ranges and means of average levels of personal exposure to NO_2 in the 82 residential zones considered.

SAPALDIA



Residential zones:	9	13	10	11	6	12	10	11

FVC along gradients of personal exposure to NO_2



SAPALDIA

Association between average forced vital capacity (FVC) of the lung and estimated average personal exposure to NO_2 at the residential zone level within study areas.

	Estimated average level of personal exposure to NO_2 ($\mu g / m^3$)	**Average FVC**
residential zone A	x	4.482 L ↓ **-1.5%**
residential zone B	x + 20	4.416 L

* $p < 0.05$

Summary

In the population-based SAPALDIA-sample of adults from Switzerland:

Forced vital capacity of the lung was negatively associated with the estimated average level of personal eposure to NO_2 in the subject‘s zone of residence in each of the eight study areas.

The respective summary estimate (i.e., of a 1.5%-decrease in FVC for a 20 $\mu g/m^3$-increment average personal NO_2-exposure between residential zones) was statistically significant.

Similar associations were found for estimated average levels of NO_2 outside the subjects‘ homes. But they were slightly less consistent across study areas and reached only marginal statistical significance.

Concluding Remarks

There exists substantial evidence from many experimental and epidemiological studies for short and long term associations between respiratory and cardiovascular health on the one hand and exposure to NO_2 on the other hand.

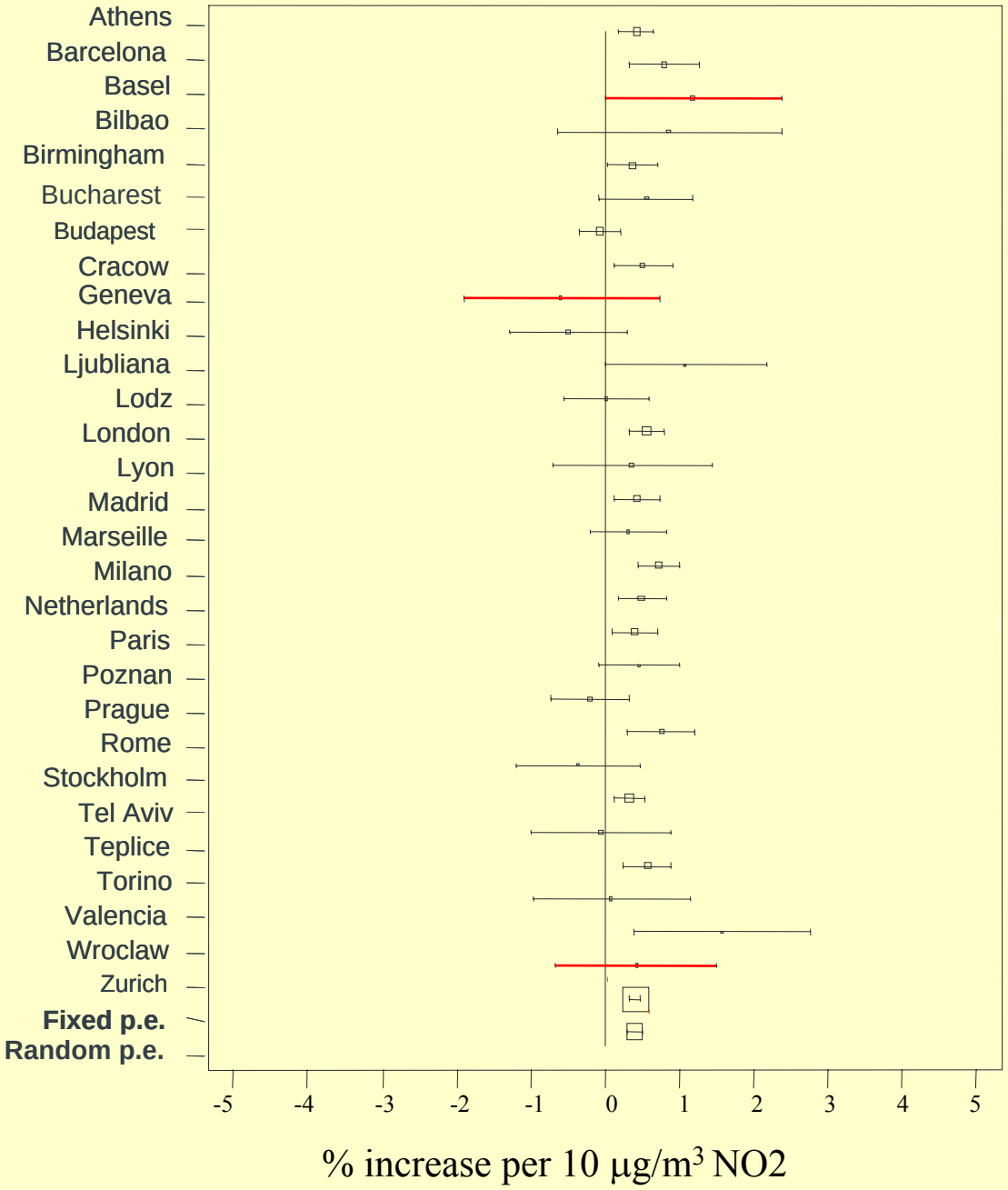
It is unresolved, however, to what extent these associations represent effects of NO_2 itself (either direct or synergistic ones) and to what extent NO_2 acts as a proxy of traffic-related pollutants.

Toxicological evidence for direct effects of NO_2 (oxidative stress, cell membrane peroxidation) exists only for concentrations above current ambient levels.

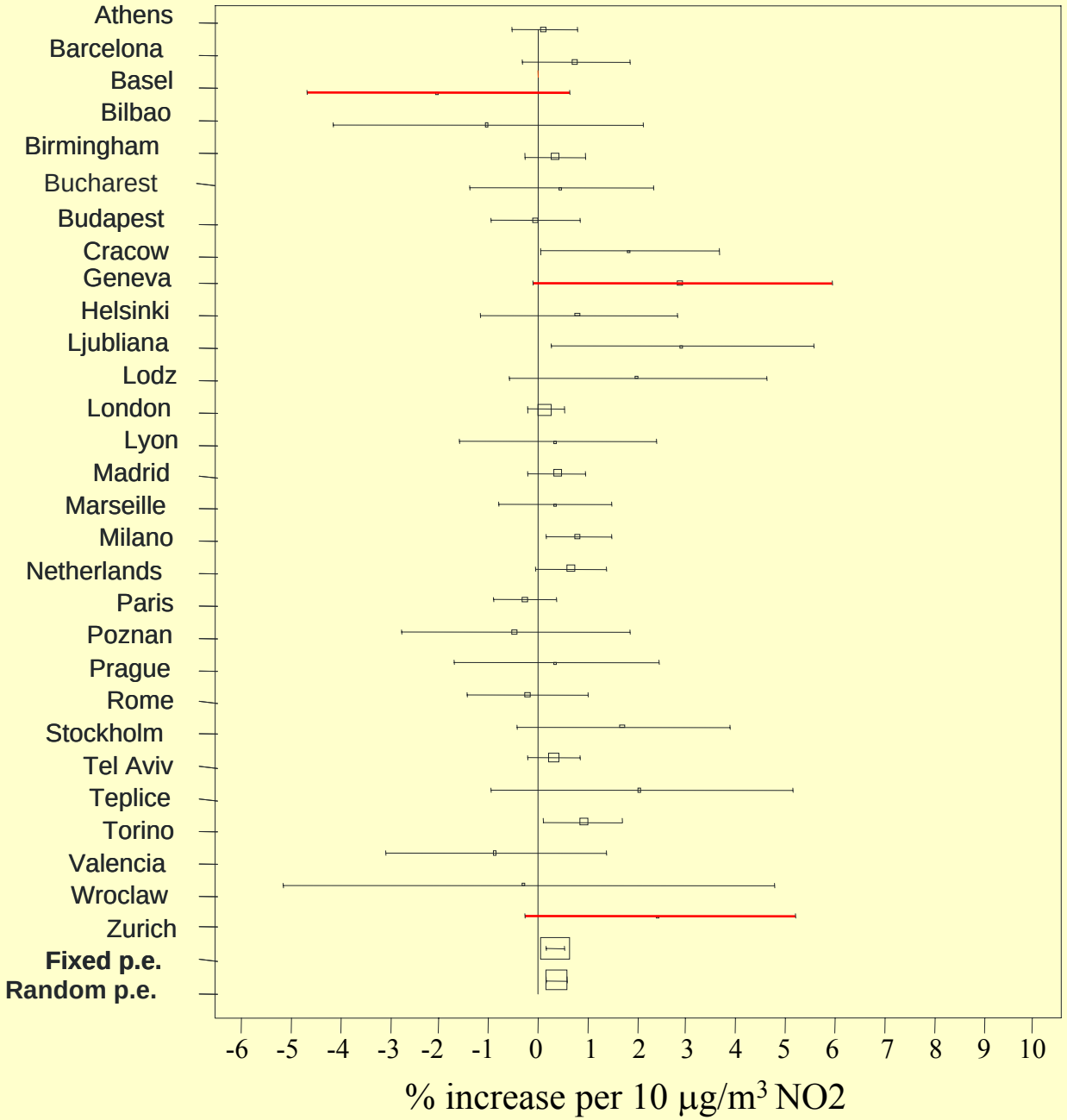
However, several epidemiological studies have demonstrated associations of NO_2 with health outcomes that were independent of other pollutants (e.g., particles).

Thank you for your attention!

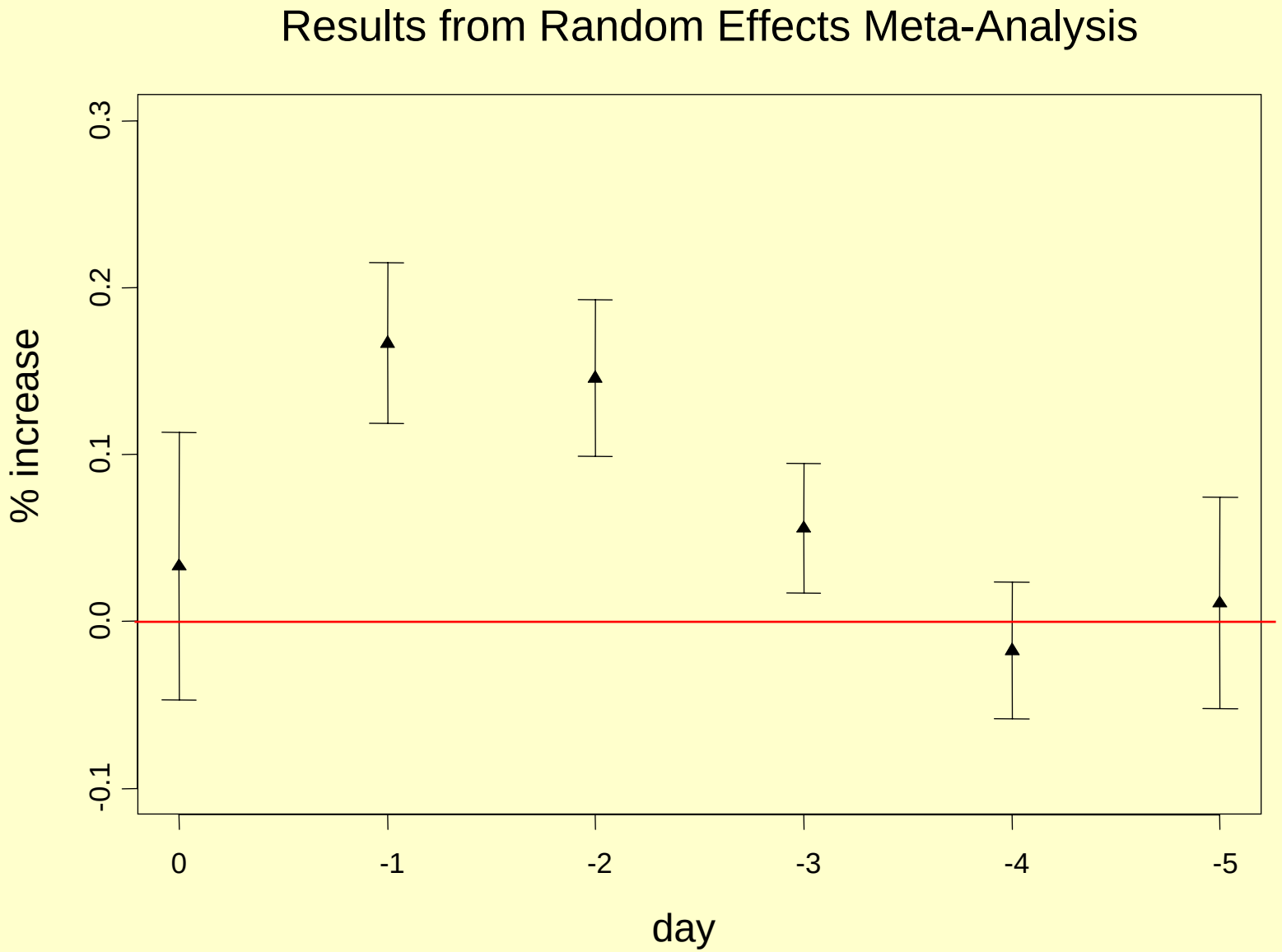
Cardiovascular mortality city-specific results



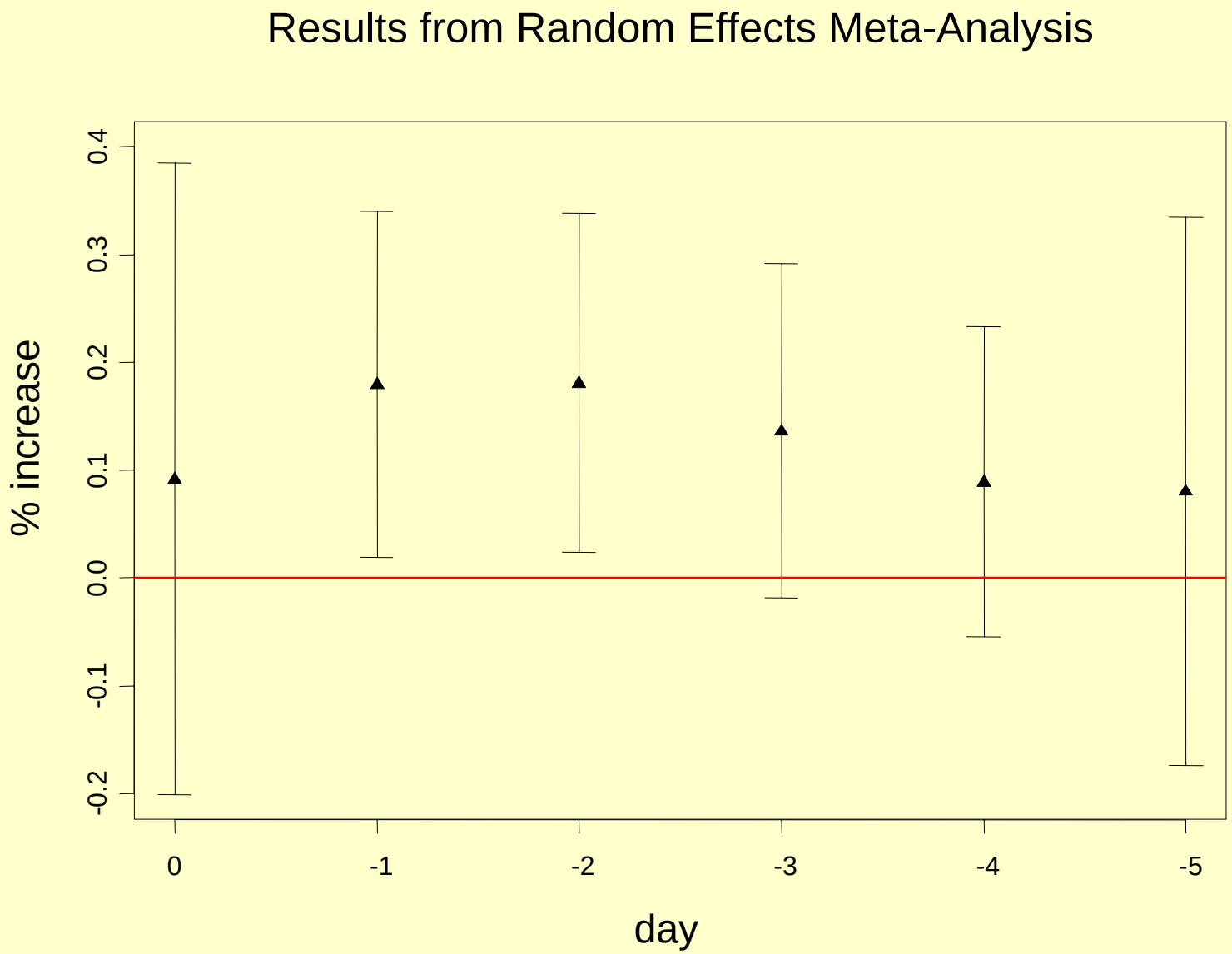
Respiratory mortality city-specific results



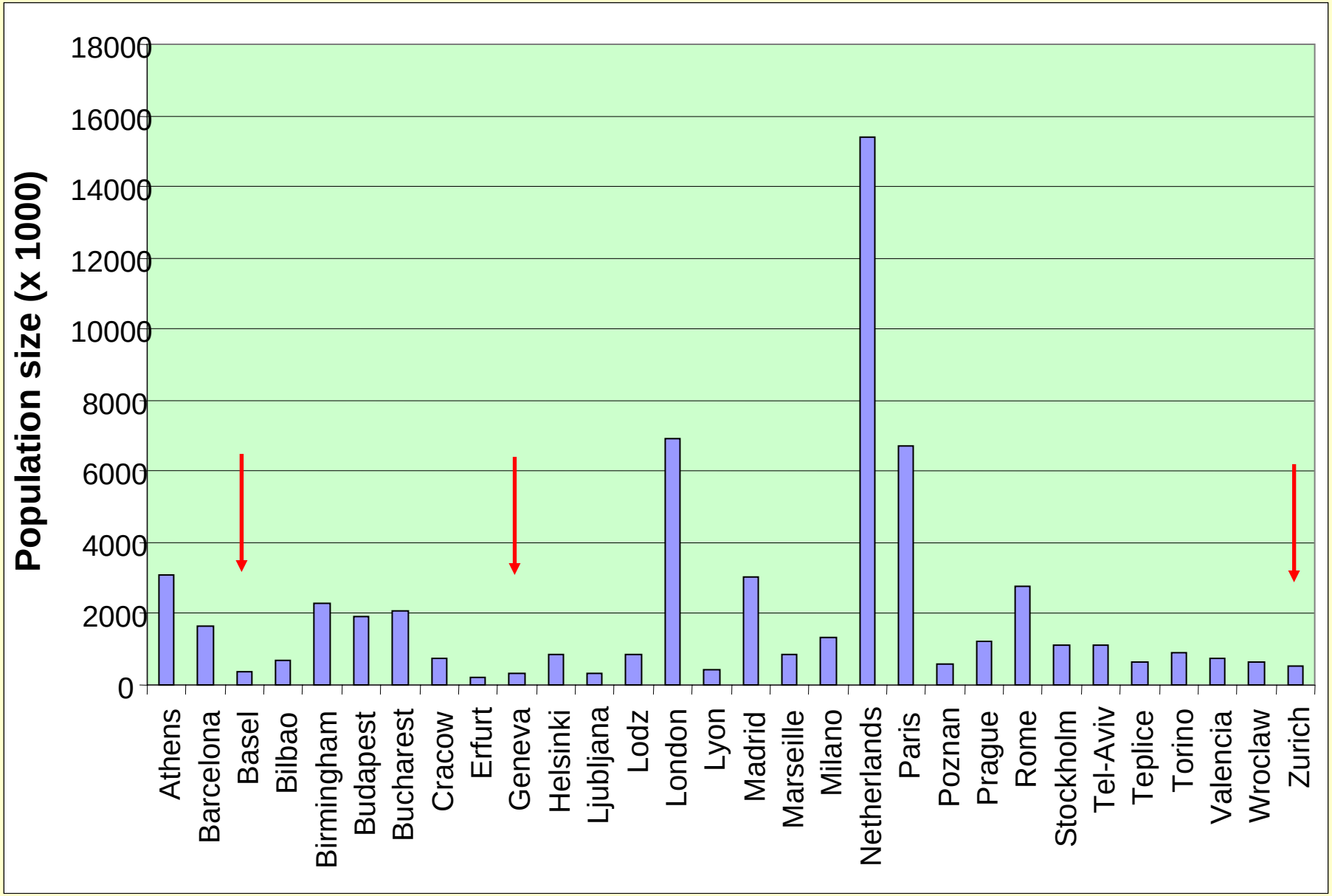
Effect contribution of from different days (total mortality)



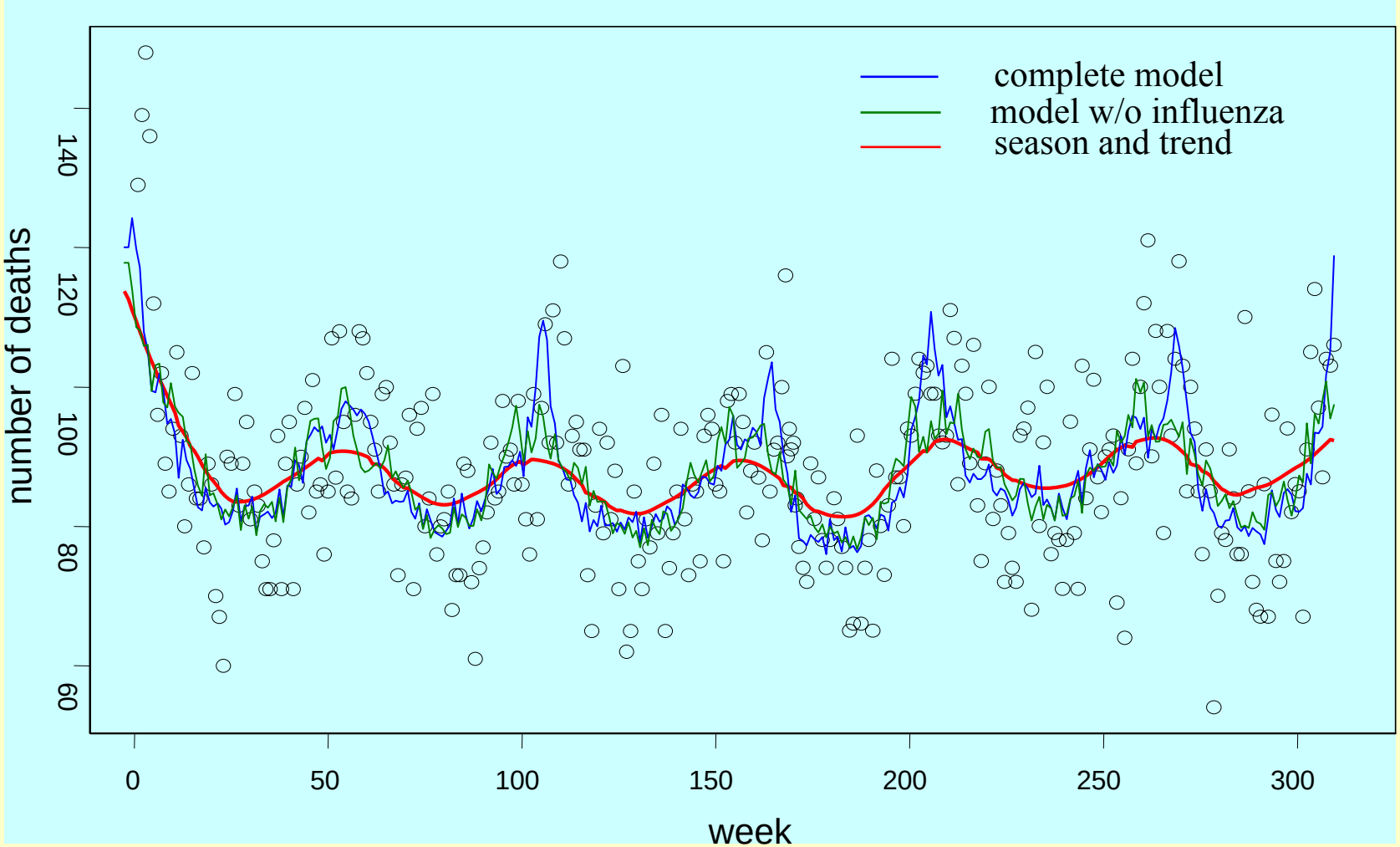
Effect contribution of from different days (respiratory mortality)



Size of local populations



Total mortality in Zurich (1990-1995)



SAPALDIA – study design

Baseline

8 Areas

Interview

Lung function

Methacholine test

Skin prick test

Total IgE

9‘651 Participants

Age 18-60

Longitudinal

Diary

Peakflow

N = 3‘279

+

NO2-passive samplers

N = 560

Address update and mortality follow-up

Follow-up

8 Areas

Interview

Lung function

Methacholine test

Heart rate variability

Blood pressure

Establishment of biobank (blood and DNA)

8‘047 Participants

Age 29-71

NO2 ,SO2
TSP, CO
Ozone
Meteo

PM10

PM2.5

1991 1992/93 1995-2001 2002