#### SUPPLEMENTARY MATERIAL

## A meta-analysis on ambient ultrafine particles exposure and respiratory morbidity.

Evangelia Samoli<sup>1</sup>, Sophia Rodopoulou<sup>1</sup>, Alexandra Schneider<sup>2</sup>, Lidia Morawska<sup>3</sup>, Massimo Stafoggia<sup>4</sup>, Matteo Renzi<sup>4</sup>, Susanne Breitner<sup>2</sup>, Timo Lanki<sup>5-7</sup>, Regina Pickford<sup>2</sup>, Tamara Schikowski<sup>8</sup>, Okokon Enembe<sup>5</sup>, Qi Zhao<sup>8</sup>, Annette Peters<sup>2,9</sup>.

<sup>1</sup>Dept. of Hygiene, Epidemiology and Medical Statistics, Medical school, National and Kapodistrian University of Athens, 75 MikrasAsias Str, 115 27 Athens, Greece;

<sup>2</sup>Institute of Epidemiology, Helmholtz Zentrum München – German Research Center for Environmental Health, Neuherberg, Germany;

<sup>3</sup> International Laboratory for Air Quality and Health, Queensland University of Technology, Brisbane, Australia;

<sup>4</sup>Department of Epidemiology, Lazio Regional Health Service, Rome, Italy;

<sup>5</sup>Finnish Institute for Health and Welfare, Kuopio, Finland

<sup>6</sup> University of Eastern Finland, Department of Environmental and Biological Sciences, Kuopio, Finland

<sup>7</sup>University of Eastern Finland, School of Medicine, Kuopio, Finland

<sup>8</sup>Leibniz Research Institute for Environmental Medicine, Düsseldorf, Germany.

<sup>9</sup>Ludwig Maximilians Universität München, Germany.

Figure S1. Flowchart of literature search.



**Figure S2.** Meta-analysis results for the effect of an increase of 10,000 particles/cm<sup>3</sup> in PNC on respiratory morbidity endpoints for all ages for individual lags 0-5 (a-f).

#### a) Lag 0



Relative Risk per 10,000 particles/cm<sup>3</sup>

b) Lag 1

Study	Risk Ratio	RR	95%-CI	Weight (fixed)	Weight (random)
Lanzinger et al., 2016, Augsburg	ł	1.12	[1.01; 1.25]	0.3%	3.1%
Lanzinger et al., 2016, Chernivtsi		0.90	[0.70; 1.17]	0.1%	0.6%
Lanzinger et al., 2016, Dresden	· · · · · · · · · · · · · · · · · · ·	- 1.33	[1.15; 1.53]	0.2%	1.9%
Lanzinger et al., 2016, Ljubljana		0.84	[0.65; 1.08]	0.1%	0.6%
Lanzinger et al., 2016, Prague		0.97	[0.77; 1.22]	0.1%	0.7%
Leitte et al., 2011, Beijing (China)		1.01	[0.95; 1.07]	1.2%	8.3%
Samoli et al., 2016, Barcelona	<u> </u>	1.01	[0.99; 1.03]	15.6%	18.8%
Samoli et al., 2016, Copenhagen		1.00	[0.97; 1.04]	2.9%	13.0%
Samoli et al., 2016, Helsinki		0.96	[0.94; 0.99]	6.6%	16.5%
Samoli et al., 2016, Rome		0.99	[0.99; 1.00]	67.0%	20.3%
Samoli et al., 2016, Stockholm		1.00	[0.98; 1.02]	6.0%	16.1%
Fixed effect model		1.00	[0.99; 1.00]	100.0%	
Random effects model	$\rightarrow$	1.00	[0.97; 1.04]		100.0%
Prediction interval			[0.94; 1.07]		
Heterogeneity: $I^2 = 71\%$ , $\tau^2 = 0.0005$ , $p < 0.01$			_		
	0.8 0.9 1 1.1 1.2				
	Relative Risk per 10,000 particles/cm <sup>3</sup>				

## c) Lag 2



#### d) Lag 3

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Study	Risk Ratio	RR	95%-CI	Weight (fixed)	Weight (random)
Lanzinger et al., 2016, Augsburg		1.04	[0.93; 1.15]	0.3%	1.5%
Lanzinger et al., 2016, Chernivtsi		1.05	[0.82; 1.34]	0.1%	0.3%
Lanzinger et al., 2016, Dresden		1.10	[0.97; 1.25]	0.2%	1.0%
Lanzinger et al., 2016, Ljubljana		1.04	[0.81; 1.35]	0.1%	0.3%
Lanzinger et al., 2016, Prague		0.98	[0.79; 1.22]	0.1%	0.4%
Leitte et al., 2011, Beijing (China)		0.97	[0.93; 1.02]	1.5%	6.0%
Samoli et al., 2016, Barcelona		1.02	[1.00; 1.03]	14.9%	21.9%
Samoli et al., 2016, Copenhagen		- 1.02	[0.98; 1.06]	2.9%	9.9%
Samoli et al., 2016, Helsinki		0.98	[0.96; 1.01]	6.2%	15.6%
Samoli et al., 2016, Rome		1.00	[0.99; 1.00]	68.3%	28.5%
Samoli et al., 2016, Stockholm		1.02	[0.99; 1.04]	5.6%	14.7%
Fixed effect model		1.00	[0.99; 1.01]	100.0%	
Random effects model	*	1.00	[0.99; 1.02]		100.0%
Prediction interval			[0.97; 1.03]		
Heterogeneity: $I^2 = 36\%$ , $\tau^2 = 0.0001$ , $p = 0.11$	I I I	1 1			
	0.8 0.9 1	1.1 1.2			
	Relative Risk per 10,000	particles/cm			

## e) Lag 4



Lanzinger et al., 2016, Augsburg Lanzinger et al., 2018, Chernivtsi Lanzinger et al., 2016, Diesden Lanzinger et al., 2016, Diesden Lanzinger et al., 2016, Prague Leitte et al., 2016, Beijing (China) Samoli et al., 2016, Barcelona Samoli et al., 2016, Copenhagen Samoli et al., 2016, Rome Samoli et al., 2016, Rome Samoli et al., 2016, Stockholm

Fixed effect model Random effects model Prediction interval Heterogeneity:  $I^2 = 0\%, \tau^2 < 0.0001, p = 0.57$ 



		Weight	Weight
RR	95%-CI	(fixed)	(random)
1.03	[0.93; 1.15]	0.3%	0.4%
0.89	[0.70; 1.15]	0.1%	0.1%
1.05	[0.93; 1.20]	0.2%	0.3%
0.86	[0.67; 1.11]	0.1%	0.1%
1.03	[0.84; 1.28]	0.1%	0.1%
0.97	[0.93; 1.02]	1.5%	2.2%
1.00	[0.99; 1.02]	14.6%	18.5%
1.02	[0.99; 1.05]	3.0%	4.3%
1.01	[0.99; 1.03]	6.4%	8.9%
1.00	[0.99; 1.00]	68.1%	57.2%
1.01	[0.99; 1.04]	5.7%	8.0%
1.00 1.00	[0.99; 1.01] [0.99; 1.01] [0.99: 1.01]	100.0% 	 100.0%

# f) Lag 5

Study	Risk Ratio	RR	95%-CI	Weight (fixed)	Weight (random)
Lanzinger et al., 2016, Augsburg		1.08	[0.97; 1.20]	0.3%	1.1%
Lanzinger et al., 2016, Chernivtsi -		0.89	[0.69; 1.13]	0.1%	0.2%
Lanzinger et al., 2016, Dresden		1.01	[0.89; 1.15]	0.2%	0.7%
Lanzinger et al., 2016, Ljubliaga		1.07	[0.84; 1.37]	0.1%	0.2%
Lanzinger et al., 2016, Prague	、	1.10	[0.89; 1.36]	0.1%	0.3%
Leitte et al., 2011, Beijing (China)		0.94	[0.89; 0.98]	1.4%	4.6%
Samoli et al., 2016, Barcelona	<u> </u>	1.01	[1.00; 1.03]	14.6%	22.4%
Samoli et al., 2016, Copenhagen		1.00	[0.97; 1.04]	2.9%	8.5%
Samoli et al., 2016, Helsinki		1.00	[0.98; 1.02]	6.6%	14.9%
Samoli et al., 2016, Rome		1.00	[0.99; 1.00]	67.8%	32.9%
Samoli et al., 2016, Stockholm		1.02	[1.00; 1.04]	6.0%	14.2%
Fixed effect model		1.00	[0.99; 1.01]	100.0%	
Random effects model	♦	1.00	[0.99; 1.02]		100.0%
Prediction interval			[0.98; 1.03]		
Heterogeneity: $l^2 = 42\%$ , $\tau^2 < 0.0001$ , $p = 0.07$					
	0.9 0.0 1 11 12				

.8 0.9 1 1.1 1.2 Relative Risk per 10,000 particles/cm<sup>3</sup> 0.8

**Figure S3.** Meta-analysis results for the effect of an increase of 10,000 particles/cm<sup>3</sup> in PNC on respiratory morbidity endpoints for all ages for lag 2 including London, UK.



**Figure S4.** Meta-analysis results for the effect of an increase of 10,000 particles/cm<sup>3</sup> in PNC on respiratory admissions for 0-14 years old for individual lags 0-5 (a-f), without or with results from Evans et al (2014).

a) Lag 0



b) Lag 1





c) Lag 2



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Study	Risk Ratio	RR	95%-CI	(fixed)	(random)
Samoli et al., 2016, Barcelona		- 1.0'	[0.96; 1.06]	4.1%	4.7%
Samoli et al., 2016, Copenhagen		0.98	3 [0.91; 1.04]	2.0%	2.3%
Samoli et al., 2016, Helsinki		1.00	0 [0.95; 1.05]	3.8%	4.3%
Samoli et al., 2016, Rome		1.01	[0.99; 1.02]	54.7%	52.2%
Samoli et al., 2016, Stockholm		— 1.02	2 [0.97; 1.08]	2.9%	3.3%
Atkinson et al., 2010 & Samoli et al., 2016b, London combined		1.02	2 [1.00; 1.04]	32.4%	33.2%
Evans et al., 2014, New York	$\sim \parallel$	→ 1.2 <sup>-</sup>	[0.34; 4.39]	0.0%	0.0%
Fixed effect model		1.01	[1.00; 1.02]	100.0%	
Random effects model	$\diamond$	1.01	[1.00; 1.02]		100.0%
Prediction interval	<u> </u>		[1.00; 1.02]		
Heterogeneity: $I^2 = 0\%$ , $\tau^2 < 0.0001$ , $p = 0.79$					
(	).9 1	1.1			
Relative	Risk per 10,000	particles/cm <sup>3</sup>			









e) Lag 4













**Figure S5.** Meta-analysis results for the effect of an increase of 10,000 particles/cm<sup>3</sup> in PNC on respiratory admissions for individual lags 0-5 (a-f) by for mean city-specific levels below 6,000 particles/cm<sup>3</sup>

a) Lag 0



Between groups difference p= 0.732

#### b) Lag 1

Study	Ri	sk Ratio	RR	95%-CI	Weight (fixed)	Weight (random)
		1			• •	. ,
Mean PNC levels <= 6,000 n/cm3					0.00/	0.40/
Lanzinger et al., 2016, Augsburg			1.12	2 [1.01; 1.25]	0.3%	3.1%
Lanzinger et al., 2016, Chernivtsi —	ŀ		0.90	0 [0.70; 1.17]	0.1%	0.6%
Lanzinger et al., 2016, Dresden			1.33	3 [1.15; 1.53]	0.2%	1.9%
Lanzinger et al., 2016, Ljubljana			0.84	[0.65; 1.08]	0.1%	0.6%
Lanzinger et al., 2016, Prague			0.9	[0.77; 1.22]	0.1%	0.7%
Samoli et al., 2016, Copenhagen	-		1.00	0 [0.97; 1.04]	2.9%	13.0%
Fixed effect model			1.02	2 [0.99; 1.05]	3.6%	
Random effects model			1.04	1 [0.88; 1.23]		20.1%
Heterogeneity: $l^2 = 76\%$ , $\tau^2 = 0.0173$ , $p < 0.01$						
Mean PNC levels > 6 000 n/cm3						
Leitte et al. 2011 Beijing (China)	_		1.0*	I IO 95 1 071	1 2%	8 3%
Samoli et al. 2016 Barcelona			1.0	1 [0.00, 1.07]	15.6%	18.8%
Samoli et al. 2016, Balcelona	-+	_ !	0.06	S [0 04: 0 00]	6.6%	16.5%
Samoli et al. 2016 Rome			0.90	0 [0.94, 0.99]	67.0%	20.3%
Samoli et al. 2016, Stockholm		<u>}</u>	1.00	0 [0.03; 1.00]	6.0%	16.1%
Fixed effect model			1.00	0 [0.30, 1.02]	96.4%	10.170
Random effects model			0.00	0 [0.33, 1.00]	30.470	79.9%
Heterogeneity: $l^2 = 65\% r^2 = 0.0002$ , $p = 0.02$			0.5	[0.57, 1.02]		13.370
Helefogeneity, 7 = 0.5 /0, 1 = 0.0002, p = 0.02						
Fixed effect model			1.00	0 [0.99: 1.00]	100.0%	
Random effects model		<u></u>	1.00	0 0.97: 1.04		100.0%
Prediction interval				[0.94; 1.07]		
Heterogeneity: $l^2 = 71\%$ , $\tau^2 = 0.0005$ , $\rho < 0.01$				. ,		
Residual heterogeneity: I <sup>2</sup> = 72%, p < 0.01	0.75	1	1.5			

Between groups difference p= 0.492

#### c) Lag 2

#### Study

Mean PNC levels <= 6,000 n/cm3 Lanzinger et al., 2016, Augsburg Lanzinger et al., 2016, Chernivtsi Lanzinger et al., 2016, Dresden Lanzinger et al., 2016, Drague Samoli et al., 2016, Prague Samoli et al., 2016, Copenhagen Fixed effect model Random effects model Heterogeneity:  $J^2 = 0\%$ ,  $\tau^2 = <0.001$ , p = 0.50

#### Mean PNC levels > 6,000 n/cm3

Leitte et al., 2011, Beijing (China) Samoli et al., 2016, Barcelona Samoli et al., 2016, Helsinki Samoli et al., 2016, Rome Samoli et al., 2016, Stockholm **Fixed effect model Random effects model** Heterogeneity:  $l^2 = 0\%$ ,  $\tau^2 = 0$ ,  $\rho = 0.75$ 

#### Fixed effect model Random effects model Prediction interval Heterogeneity: $l^2 = 0\%$ , $\tau^2 < 0.0001$ , p = 0.77

Residual heterogeneity:  $l^2 = 0\%$ , p = 0.71

Between groups difference p= 0.619

### d) Lag 3

Study	Risk Ratio		RR	95%-CI	Weight (fixed)	Weight (random)
Mean PNC levels <= 6,000 n/cm3						
Lanzinger et al., 2016, Augsburg			1.04	[0.93; 1.15]	0.3%	1.5%
Lanzinger et al., 2016, Chernivtsi -			1.05	[0.82; 1.34]	0.1%	0.3%
Lanzinger et al., 2016, Dresden		+	1.10	[0.97; 1.25]	0.2%	1.0%
Lanzinger et al., 2016, Ljubljana			1.04	[0.81; 1.35]	0.1%	0.3%
Lanzinger et al., 2016, Prague			0.98	[0.79; 1.22]	0.1%	0.4%
Samoli et al., 2016, Copenhagen			1.02	[0.98; 1.06]	2.9%	9.9%
Fixed effect model			1.03	[0.99; 1.06]	3.6%	
Random effects model			1.03	[1.00; 1.05]		13.3%
Heterogeneity: / <sup>2</sup> = 0%, τ <sup>2</sup> = 0, ρ = 0.92						
Mean PNC levels > 6,000 n/cm3						
Leitte et al., 2011, Beijing (China)			0.97	[0.93; 1.02]	1.5%	6.0%
Samoli et al., 2016, Barcelona			1.02	[1.00; 1.03]	14.9%	21.9%
Samoli et al., 2016, Helsinki			0.98	[0.96; 1.01]	6.2%	15.6%
Samoli et al., 2016, Rome			1.00	[0.99; 1.00]	68.3%	28.5%
Samoli et al., 2016, Stockholm	- <u>+</u>		1.02	[0.99; 1.04]	5.6%	14.7%
Fixed effect model	4		1.00	[0.99; 1.00]	96.4%	
Random effects model	$\rightarrow$		1.00	[0.98; 1.02]		<b>86.7%</b>
Heterogeneity: $l^2 = 66\%$ , $\tau^2 = 0.0002$ , $p = 0.02$						
Fixed effect model	4		1.00	[0.99; 1.01]	100.0%	
Random effects model	÷		1.00	[0.99; 1.02]		100.0%
Prediction interval				[0.97; 1.03]		
Heterogeneity: $l^2 = 36\%$ , $\tau^2 = 0.0001$ , $\rho = 0.11$						
Residual heterogeneity: $l^2 = 31\%$ , $p = 0.16$ 0.8	1	1.25				

Weight Weight **Risk Ratio** RR 95%-CI (fixed) (random) 0.99 [0.89; 1.10] 0.3% 0.3% 1.12 [0.89; 1.42] 1.08 [0.94; 1.23] 0.1% 0.1% 0.2% 0.2% 0.84 [0.64; 1.09] 0.1% 0.1% 1.09 [0.87; 1.37] 0.1% 0.1% 1.00 [0.97; 1.04] 2.8% 3.2% 1.01 [0.97; 1.04] 3.5% 1.01 [0.97; 1.04] 4.0% ---1.01 [0.96; 1.06] 1.6% 1.9% 1.01 [0.99; 1.02] 15.0% 16.5% 0.99 [0.97; 1.01] 6.3% 7.0% 
 1.00
 [0.97; 1.00]
 68.0%

 1.00
 [0.97; 1.02]
 5.6%
64.4% 6.3% 1.00 [0.99; 1.00] 96.5% 96.0% 1.00 [0.99; 1.00] 1.00 [0.99; 1.00] 100.0% 1.00 [0.99; 1.00] --[0.99; 1.01] 100.0% 0.75 1.5 1

Between groups difference p= 0.0349

#### e) Lag 4

#### Weight Weight **Risk Ratio** RR 95%-CI Study (fixed) (random) Mean PNC levels <= 6,000 n/cm3 Lanzinger et al., 2016, Augsburg 1.03 [0.93; 1.15] 0.3% 0.4% Lanzinger et al., 2016, Chernivtsi 0.89 [0.70; 1.15] 0.1% 0.1% Lanzinger et al., 2016, Dresden 1.05 [0.93; 1.20] 0.2% 0.3% Lanzinger et al., 2016, Ljubljana 0.86 [0.67; 1.11] 0.1% 0.1% Lanzinger et al., 2016, Prague 1.03 [0.84; 1.28] 0.1% 0.1% Samoli et al., 2016, Copenhagen 1.02 [0.99; 1.05] 3.0% 4.3% Fixed effect model 1.02 [0.99; 1.05] 3.7% Random effects model 1.02 [0.99; 1.05] ---5.3% Heterogeneity: $l^2 = 0\%$ , $\tau^2 = 0$ , $\rho = 0.69$ Mean PNC levels > 6,000 n/cm3 Leitte et al., 2011, Beijing (China) 0.97 [0.93; 1.02] 1.5% 2.2% 1.00 [0.99; 1.02] Samoli et al., 2016, Barcelona 14.6% 18.5% Samoli et al., 2016, Helsinki 1.01 [0.99; 1.03] 6.4% 8.9% Samoli et al., 2016, Rome 1.00 [0.99; 1.00] 68.1% 57.2% Samoli et al., 2016, Stockholm 1.01 [0.99; 1.04] 5.7% 8.0% 1.00 [0.99; 1.01] 96.3% 1.00 [0.99; 1.01] --Fixed effect model Random effects model 94.7% Heterogeneity: $l^2 = 4\%$ , $\tau^2 = < 0.0001$ , p = 0.391.00 [0.99; 1.01] 100.0% 1.00 [0.99; 1.01] --[0.99; 1.01] Fixed effect model Random effects model 100.0% Prediction interval Heterogeneity: $l^2 = 0\%$ , $\tau^2 < 0.0001$ , p = 0.57Residual heterogeneity: $l^2 = 0\%$ , p = 0.620.8 1 1.25 Between groups difference p= 0.146

f) Lag 5

Study		Risk Ratio		RR	95%-CI	Weight (fixed)	Weight (random)
Mean PNC levels <= 6,000 n/cm3							
Lanzinger et al., 2016, Augsburg				1.08	[0.97; 1.20]	0.3%	1.1%
Lanzinger et al., 2016, Chernivtsi		+		0.89	[0.69; 1.13]	0.1%	0.2%
Lanzinger et al., 2016, Dresden				1.01	[0.89; 1.15]	0.2%	0.7%
Lanzinger et al., 2016, Ljubljana				1.07	[0.84; 1.37]	0.1%	0.2%
Lanzinger et al., 2016, Prague				1.10	[0.89; 1.36]	0.1%	0.3%
Samoli et al., 2016, Copenhagen				1.00	[0.97; 1.04]	2.9%	8.5%
Fixed effect model				1.01	[0.98; 1.04]	3.6%	
Random effects model				1.01	[0.98; 1.05]		11.1%
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , $\rho = 0.62$							
Mean PNC levels > 6,000 n/cm3							
Leitte et al., 2011, Beijing (China)		I		0.94	[0.89; 0.98]	1.4%	4.6%
Samoli et al., 2016, Barcelona				1.01	[1.00; 1.03]	14.6%	22.4%
Samoli et al., 2016, Helsinki				1.00	[0.98; 1.02]	6.6%	14.9%
Samoli et al., 2016, Rome				1.00	[0.99; 1.00]	67.8%	32.9%
Samoli et al., 2016, Stockholm				1.02	[1.00; 1.04]	6.0%	14.2%
Fixed effect model		Ŷ		1.00	[0.99; 1.01]	96.4%	
Random effects model		$\sim$		1.00	[0.97; 1.03]		88.9%
Heterogeneity: $I^2 = 70\%$ , $\tau^2 = 0.0002$ , $\rho = 0.01$							
Fixed effect model		4		1.00	[0.99; 1.01]	100.0%	
Random effects model		<b></b>		1.00	[0.99; 1.02]		100.0%
Prediction interval					[0.98; 1.03]		
Heterogeneity: / <sup>2</sup> = 42%, τ <sup>2</sup> < 0.0001, ρ = 0.07	I	I	I				
Residual heterogeneity: / <sup>2</sup> = 46%, p = 0.05	0.8	1	1.25				

Between groups difference p= 0.508